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Investigating severe pediatric traumatic brain injury in South Africa: A demographic profile of admissions, brain oxygenation and neuropsychological outcomes and an attention-training intervention.

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DECLARATION

I hereby declare that this submission is my own work, both in concept and execution, and that to the best of my knowledge and belief it contains no material written by another person nor material that has been accepted for the award of any other degree or diploma of the university or other institute of higher learning, except where due acknowledgment has been made in the text.

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Leigh E. Schrieff (Ms) Date

DEDICATIONS

To my Mother, Ingrid Constance Schrieff (*In memoriam*:13 October 1950 - 23 August 2012).

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ABBREVIATIONS

ABI	Anoxic brain injury; acquired brain injury
ACSENT	Applied Cognitive Science and Experimental Neuropsychology Team
AMAT-C	Amsterdam Memory and Attention Training for Children
APT	Attention process training
ATP	Adenosine tripohosphate
BP	Systemic blood pressure
BRI	Behavioural recognition index
BRIEF	Behaviour Rating Inventory of Executive Function
CBCL	Child Behaviour Checklist
CBF	Cerebral blood flow
CD	Conduct disorder
CDC	Centre for Disease Control
CHD	Congenital heart disease
CHI	Closed head injury
CI	Confidence interval
CNS	Central nervous system
CPP	Cerebral perfusion pressure
CR	Cognitive rehabilitation
CT	Computed tomography
DAI	Diffuse axonal injury
ED	Emergency departments
EEG	Electoencephalogram
EF	Executive functioning
ERP	Electrophysiological
FiO_2	Inspired fraction of oxygen
FSIQ	Full Scale IQ
GCS	Glasgow Coma Scale
GCS	Glasgow Coma Scale
GEC	Global executive composite
GOS	Glasgow Outcome Scale
Hb	Haemoglobin
HI	Head injury
HIC	High-income country
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
ICP	Intracranial pressure
ICU	Intensive Care Unit
LAMIC	Low-and-middle-income country
LOC	Loss of consciousness
MAP	Mean arterial pressure
MFI	Monthly family income

MI	Metacognition Index
MVA	Motor vehicle accident
NAI	Non-accidental injury
NP	Neuropsychological
O_2	Oxygen
ODD	Oppositional defiant disorder
PaO_2	Arterial partial pressure of oxygen
$PaCO_2$	Partial pressure of arterial Carbon dioxide
$PbtO_2$	Brain tissue oxygenation
PCPCS	Pediatric Cerebral Performance Category Scale
PET	Positron Emission Tomography
PIQ	Performance IQ
PTA	Posttraumatic amnesia
pTBI	Pediatric traumatic brain injury
PTSD	Post-traumatic stress disorder
RCTs	Randomized control trials
RTA	Road traffic accident
RXH	The Red Cross War Memorial Children's Hospital
SA	South Africa
SADHD	Secondary attention deficit hyperactivity disorder
SaO_2	Arterial saturation of oxygen
SCED	Single-case experimental design
SDB	Sleep disordered breathing
SES	Socio-economic status
TEA-Ch	Test of Everyday Attention for Children
TBI	Traumatic brain injury
UCT	University of Cape Town
UK	United Kingdom
US	United States of America
VABS	Vinelands Adaptive Behaviour Scale
VIQ	Verbal IQ
WASI	Weschler Abbreviated Scale of Intelligence
WHO	World Health Organization
WM	Working memory

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ABSTRACT

The aim of this dissertation was to investigate severe pediatric traumatic brain injury (pTBI) in South Africa. To that end, I conducted three studies, each examining a different aspect of severe pTBI. Study 1 presents a demographic profile of trends in severe pTBI admissions to the Red Cross War Memorial Children's Hospital (RXH) from June 2006 to April 2011. Study 2 examines the associations between secondary injury, as manifest by low brain oxygenation ($PbtO_2$), and neuropsychological outcomes in severe pTBI. Study 3 evaluates the efficacy of an attention-training intervention for severe pTBI, and discusses the implementation of that intervention in the context of a low- and middle-income country. All three studies were cross-sectional and quantitative. Study 1 ($N = 137$) featured a retrospective and descriptive design. Results showed that trends in admissions for severe pTBI to the RXH were consistent with international trends, and that mortality rates were lower than those reported in previous South African studies. Study 2 was a quasi-experimental case-controlled trial. Using between-groups comparisons, I showed that children who had experienced episodes of low $PbtO_2$ (< 10 mmHg; $n = 5$) post-admission performed more poorly than those who had not ($n = 6$) on measures of general intellectual functioning, attention, verbal memory, executive functions, visuospatial ability, and expressive language. Study 3 ($N = 12$) was also a quasi-experimental case-controlled trial, although in this case I used a pretest-posttest design. The Reliable Change Index (RCI*;* Jacobson & Truax, 1991) and individual case studies were the main analytical tools. Results showed that although the attention-training program showed low efficacy, it was possible to implement it successfully in the South African setting, despite the lack of infrastructure. Taken together, these findings suggest that (a) severe pTBI remains a significant public health problem in South Africa, (b) aggressive management of secondary injury (e.g., episodes of low $PbtO_2$) could contribute to improved neuropsychological outcomes following severe pTBI, and (c) that intervention programs aimed at cognitive rehabilitation following severe pTBI are possible, and necessary, in this country. Despite the limited efficacy shown in this thesis, the continued implementation of such interventions will allow the opportunity to develop and refine such programs for use in South Africa. In general, however, the results suggest that prevention of severe pTBI is paramount.

Traumatic brain injury (TBI) and its associated sequelae have been identified for over a century as a public health problem (see English, 1904). Recent literature reveals that TBI is still a widespread blight on society, leading to death and disability in both high-income and low-and-middle-income countries (LAMICs; Rutland-Brown, Langlois, Thomas, & Xi, 2006).

Unfortunately, however, the serious nature of this public health problem and the far-reaching impact of TBI often go unrecognized, to the extent that TBI is described as a silent epidemic (Goldstein, 1990). There are two reasons for this description. First, relative to the observable physical injuries, the 'invisible' neurocognitive, behavioural, and emotional effects that frequently persist well after physical recovery has occurred are often less apparent. Second, there is limited awareness among the general public of the extent of burden of injury following a TBI. Because TBI can affect an individual across the life spectrum, it creates increased human and economic cost (Eslinger & Oliveri, 2002). Depending on the level of severity, the impact of the injury may extend beyond the individual to social, familial, economic, and in the case of children, academic, spheres of life. An additional concern specific to children is the impact of the brain injury on their ongoing development.

In children, head trauma has long been reported as an area of serious concern (Ryan, Lamarche, Barth, & Boll, 1996). TBI is a leading cause of mortality and morbidity in children and adolescents (Babikian & Asarnow, 2009). Although many children may experience a bump to the head with little or no consequence, there are a considerable number who sustain more serious head trauma that involves brain injuries with significant morbidity. Injuries of this nature are often classified as severe TBI.

The research presented here is focused solely on children who have sustained severe TBIs. One conventional classification of TBI relates to the well-established dose-response relationship between injury severity (as defined by physiological impact) and cognitive, behavioural, and psychosocial outcome (V. Anderson, Northam, Hendy, & Wrennall, 2001). Severe TBIs are therefore associated with the worst outcome and most persistent impairments. There are far fewer severe TBIs than mild TBIs. Therefore, it is often the case that published literature on pediatric TBI (pTBI) includes samples that combine severity groups. Alternatively, if the study focuses solely on severe TBI, then participants from a wide age range are included.

The current research attempts to remedy those methodological limitations by focusing on children with severe TBI from a limited age range.

In addition, this examination of a severe pTBI sample is done against a backdrop of the LAMIC context of South Africa, where limited published research of this nature currently exists. Most TBI research emerges from high-income countries (HICs), even though researchers postulate that the impact of such injuries may be more profound in LAMICs. For this reason, a greater research focus on TBI in LAMICs is necessary.

TBI research, can generally be thought of as encompassing three broad areas: prevention of injury, prediction of outcome following injury, and remediation of injury. When one considers these broad areas of inquiry and the expanse of the literature across them, then the magnitude of the problem of TBI becomes clear. The impact of these injuries is far more profound than the actual primary injury that occurs at the time of the TBI. The effect of TBI occurs over a protracted period and, as mentioned above, can affect the individual across the lifespan. Consideration of the problem of TBI begins before the injury and extends far beyond the primary injury; this is especially true in the case of severe TBI.

One could therefore conceptualize a TBI as occurring along a temporal plane, beginning with the primary injury, the prevention of secondary injuries, attempting to predict the short - and long-term outcome of the TBI, taking into account a myriad of factors affecting such outcome, and then coping with the impact of the injury and the remediation of the outcome. Owing to this potentially profound impact, one may conceive of prevention of TBI as being part of, or even the start of, this process. Indeed, from a public health perspective, prevention is of paramount importance.

This dissertation aims to cover of broad scope of pTBI by providing snapshots of South African research at three different points along the temporal plane of severe TBI. I will highlight the gaps and opportunities for intervention and development. The unique contribution of each study included in this dissertation is as follows:

- Study 1 reports on the trends in admissions for children who had sustained a severe TBI and who were admitted to the Red Cross War Memorial Children's Hospital (RXH) in Cape Town, South Africa. No recent epidemiological data exist for this cohort. Study One ultimately speaks to an opportunity for prevention interventions in this context in the future.

- Study 2 aims to explore the neuropsychological and behavioural outcomes in relation to perfused brain tissue oxygenation ($PbtO_2$) for a group of children who sustained severe TBIs. No previous study has investigated this relationship in children.
- Study 3 reports on the implementation and evaluation of an attention-training program with children who had sustained severe TBIs. Few studies report on the implementation of such an intervention in a severe pTBI sample.

The topics covered by the studies in this thesis are closely aligned with those highlighted in recent literature as requiring attention and funding (e.g., "Traumatic brain injury: time to end the silence," 2010). Leading TBI research groups emphasise, particularly, the need for improved rehabilitation efforts:

> *Little is known about the effects of TBI on the developing brain, the mechanisms and contributions of secondary injury…The need for effective interventions and care is particularly acute in developing countries, where motor car use is increasing: road traffic accidents, which are already a leading cause of TBI in many parts of the world, are expected to become the third largest cause of global disease burden by 2020 (p. 331).*

CHAPTER 1:
TRAUMATIC BRAIN INJURY: AN OVERVIEW

A traumatic brain injury, or TBI, that occurs as a result of a blunt or penetrating insult to the head interferes with brain functioning and affects an individual's state of consciousness. Such an injury is neither degenerative nor congenital, and can lead to physical, cognitive, and psychosocial impairments in varying degrees (V. Anderson, Northam, Hendy, et al., 2001; Tabish, Lone, Afzal, & Salam, 2006).

The phrase 'interferes with brain functioning' clearly differentiates the terms *TBI* and *head injury (HI)*, although these terms were used interchangeably in earlier literature (Bruns & Hauser, 2003; Cooper, 1993). In many cases where the term 'head injury' was used, brain injury was often implied, even though, strictly speaking, the term HI does not necessarily imply that a brain injury has been sustained (Cooper, 1993; Peacock, 1984). This confusion is especially problematic in African literature (Hyder, Wunderlich, Puvanachandra, Gururaj, & Kobusingye, 2007). For this reason, the term HI is slowly becoming antiquated (Bruns & Hauser, 2003).

This dissertation focuses solely on TBI. Studies 1 (Chapter 3), 2 (Chapter 5) and 3 (Chapter 8) examine children who sustained documented severe TBIs. The only instance where the term HI is used is where published articles referred to in the current study make specific use of the term, and where changing the term might therefore change the authors' original meaning.

Types of Injury: Closed Versus Open TBI

Primary and secondary injuries. The mechanics and pathology associated with TBI are generally classified on two levels: primary and secondary. *Primary injuries* occur as a result of the initial trauma and the biomechanical forces acting on the brain either independently of, or concurrently with, the initial trauma (Greve & Zink, 2009). *Secondary injuries* occur because of the presence of the initial (primary) injury (V. Anderson, Northam, Hendy, et al., 2001; Riggio & Wong, 2009). Secondary injuries occur as a result of changes at a cellular or biomolecular level, as well as at more macro-physiological levels, in the brain (Greve & Zink, 2009; Narotam, Burjonrappa, Raynor, Rao, & Taylon, 2006; Zink & McQuillan, 2005).

Primary injuries. In a closed TBI, different types of forces may have been applied to the head, resulting in the primary injury. The brain is vulnerable to these applied forces owing to its viscoelastic nature (Greve & Zink, 2009; Zink, Szmydynger-Chodobska, & Chodobski, 2010).

Biomechanical theories of brain injury differentiate between two kinds of forces: linear (translational) acceleration forces and rotational (acceleration / deceleration) forces (Greve & Zink, 2009). Linear acceleration forces can occur, for example, because of a direct blow to the head. Upon impact of a linear force, the skull may be compressed inwardly or deformed. Contact of brain surfaces with these skull irregularities results in contusion or bruising (V. Anderson, Northam, Hendy, et al., 2001; Sohlberg & Mateer, 1989). Injuries resulting from these linear forces are often superficial because they act on grey matter near the surface of the brain (Greve & Zink, 2009; Sohlberg & Mateer, 1989). Cortical contusions can lead to functional loss, however, if areas subserving specific functions are damaged (Riggio & Wong, 2009), although such contusions are not only limited to the point of direct impact. Other cerebral areas, such as areas opposite to the point of impact, may also be vulnerable to injury. Injuries of this nature are referred to as being contracoup or 'rebound effects' (Sohlberg & Mateer, 1989; Zink & McQuillan, 2005).

In contrast, injuries resulting from rotational, acceleration-deceleration forces, such as those frequently experienced in motor vehicle accidents (MVAs), often have effects on deeper cerebral white matter axons and deep grey matter nuclei (Greve & Zink, 2009). Twisting movements, for example during incidents of high levels of acceleration / deceleration forces, cause the brain to rotate within the skull. These forces can result in shearing, tearing, compression, and stretching of white matter structures (Amacher, 1988; Sohlberg & Mateer, 1989; Zink & McQuillan, 2005). Damage to white matter structures, such as diffuse axonal injuries (DAI) interferes with information transmission between cortical areas (Riggio & Wong, 2009). Thus, DAI can disrupt the speed and efficiency of information processing and has been identified as a major determinant of the profile of cognitive deficits seen post-TBI (Meythaler, Peduzzi, Eleftheriou, & Novack, 2001).

Particular brain regions may be especially vulnerable to these biomechanical forces due to their neuroanatomical position. These regions include the frontal and temporal poles and grey and white matter junctions. Such junctions can be found in areas around the basal ganglia, hypothalamus, cerebellum, brain stem, and corpus callosum (V. Anderson, Northam, Hendy, et al., 2001; Sohlberg & Mateer, 1989; Stuss, 2011; Zink & McQuillan, 2005).

Secondary injuries: physiological and biomolecular changes. For those individuals who survive the biomechanical impact of the primary injury, outcome will be determined by those biomolecular and physiological responses of the brain to this initial injury that "are distinct from but synergistic with, the primary injury" (Greve & Zink, 2009, p. 103). The time it takes for the primary TBI to occur (> 100 milliseconds) is discordant with the gradual

and escalating pathophysiological consequences that may follow. Secondary injuries can be progressive; they can last over hours and even days after the initial injury, and are often the deciding factor in a patient's trajectory of recovery (Bratton et al., 2007; Greve & Zink, 2009).

These secondary responses occur on a cellular level and include a number of processes, including excitotoxicity, disruption of calcium homeostasis, and oxidant damage. Other secondary processes include free-radical generation, blood-brain ischemic injury, edema formation and intracranial hypertension. Physiological changes also include disruption of the blood-brain barrier and cerebral blood flow (CBF) autoregulation (Figaji et al., 2009; Greve & Zink, 2009; Zink & McQuillan, 2005).

Secondary processes have a degenerative effect on neurons, glial cells, and axons. This degenerative effect is evident in DAI. Although DAI may occur as a result of white matter lesions that occur during the primary injury, the subcellular changes also affect optimal functioning of axons and signalling of nerves. The effect of secondary injuries may not only be limited to axons in the immediate lesion environment; even axons remote from the primary injury may be affected. This mechanism is discussed further in Chapter 6; suffice it to say for now that the effects of secondary injuries can be pervasive.

Secondary injury prevention / intervention. Given the pervasive effects of secondary injuries post-TBI, it is not surprising to find researchers suggesting that preventing or limiting such injuries can contribute significantly to improving patient outcomes. Therefore, this stage of injury provides a window of opportunity for intervention in terms of attempting to improve outcome post-TBI (Greve & Zink, 2009; Hession, 2008; Tang & Lobel, 2009).

Clinical management of the primary injury commonly involves early resuscitation, computed tomography (CT) scanning, and surgical evacuations of mass lesions. However, recent literature suggests that it is the interventions aimed at management of secondary injuries that lead to more favourable outcomes and that reduce the risk for mortality. Although direct preventative therapies for secondary injury processes are not yet known, methods to improve outcome are focused on preventing ischemic injury. Research reports that 90% of fatal TBIs have associated cerebral ischemia. For this reason, cerebral ischemia may be considered among the most important post-TBI secondary effects (Greve & Zink, 2009; Tude Melo et al., 2010).

Brain tissue oxygenation ($PbtO_2$). The prevention of ischemia following TBI is traditionally done using methods aimed at improving cerebral perfusion pressure (CPP) and controlling intracranial pressure (ICP). A more recent method of preventing ischemia,

however, is the early detection of diminished cerebral oxygenation. Brain tissue oxygenation ($PbtO_2$) monitoring systems can detect such changes (Figaji et al., 2009b; Maloney-Wilensky et al., 2009). Such monitors have been developed to monitor cerebral oxygenation, brain temperature, and ICP in individuals who have sustained TBI. Research has shown that this early detection of $PbtO_2$ is sensitive to measures of cerebral blood flow (CBF) and oxygenation. Earlier detection of $PbtO_2$ provides an opportunity for early clinical therapies to limit the effects of secondary injuries (Archibald, Fleckenstein, Littlejohns, O'Grady, & Trimble, 2001).

Research suggests that traditional and current methods aimed at preventing ischemia, such as those aimed at improving CPP and controlling ICP alongside $PbtO_2$ monitoring, can, if used concomitantly, result in more favourable outcomes in terms of preventing and treating secondary cerebral ischemia (Hession, 2008).

The way in which the brain responds to the TBI in terms of secondary processes, and the resultant post-TBI cerebral milieu, is fundamentally what will determine an individual's functional outcome. The post-TBI environment may be conducive to recovery of brain cells, or it may be detrimental, leading to ischemia. The task for professionals working in this field is to establish the ideal conditions for an environment favourable to post-TBI recovery of brain cells, and to then decide how to create that environment. In the process of creating this environment, it is important for professionals to have a thorough grasp of the kinds of biomolecular and physiological secondary responses to TBI as previously discussed. Although knowledge is being generated in this area, there is still much to be learned by professionals and practitioners (Greve & Zink, 2009).

Causes of TBI

The leading causes of TBI are falls, motor vehicle accidents (MVAs), sport injuries, assault and being struck by or against an object. MVAs are a primary cause of CHIs because of the high impact acceleration-deceleration and the rotational forces of impact, associated with them (V. Anderson, Northam, Hendy, et al., 2001; Zink & McQuillan, 2005). The causes of TBI vary with demographic (e.g., age and sex) and contextual (e.g., economic) factors (Bruns & Hauser, 2003; Rickels, Von Wild, & Wenzlaff, 2010). I discuss etiological factors associated with TBI in more detail in Chapter 2.

Classification of Severity of TBI

TBIs are generally classified as mild, moderate, or severe. The duration of loss of consciousness (LOC), the duration of posttraumatic amnesia (PTA) and score on the Glasgow

Coma Scale (GCS) have previously been described as "gold standard" indicators of TBI severity (Malec et al., 2007, p. 1422), when assessed concomitantly. Of the three indicators, the GCS score is the most commonly used measure of injury severity (V. Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2009; Ghosh et al., 2009; Semple, Bass, & Peter, 1998).

Glasgow Coma Scale. An individual's state of consciousness post-TBI is an important indicator of injury severity (V. Anderson, Northam, Hendy, et al., 2001). This state is measured by the GCS (Teasdale & Jennett, 1974). Scores of 13-15 on the GCS represent mild injuries, scores of 9-12 moderate injuries, and scores less than 8 severe injuries. These scores are based on eye opening (out of 4), the best motor response (out of 6), and the best verbal response (out of 5) (Zink & McQuillan, 2005). The level of severity of the TBI, as often determined by the GCS score, is associated with a number of outcome measures post-TBI.

Sequelae of TBI

Many bumps to the head do not have any serious consequences. However, in cases where such occurrences do in fact result in concomitant brain injury, these consequences can be far-reaching, especially in the case of severe TBI.

Klonoff and associates (Klonoff, Clark, & Klonoff, 1993; Klonoff, Low, & Clark, 1977; Klonoff & Paris, 1974) were pioneers in investigating the outcome of pediatric TBI. They focused on physical, emotional, familial, adaptive, academic and general intellectual outcomes across these studies (Klonoff et al., 1993).

In these studies, they reported on outcomes at discharge, at 1, 2, and 5 years post-injury, and again at adulthood (23 years post injury). Their sample included patients with mostly (90%) mild HIs. Results showed a consistent pattern of sequelae including concentration, memory and learning problems, difficulties with general intellectual functioning, and emotional problems. Despite recognized methodological limitations (e.g., questionable reliability regarding the measure of severity and a lack of specificity in the outcome measures employed), this study represents a valuable contribution to the literature on the effects of TBI (V. Anderson, Northam, Hendy, et al., 2001).

In the 1980s, Rutter and colleagues also contributed to these pioneering efforts on the outcomes of TBI (Brown, Chadwick, Shaffer, Rutter, & Traub, 1981; Chadwick, Rutter, Brown, Shaffer, & Traub, 1981; Rutter, Chadwick, & Shaffer, 1983; Rutter, Chadwick, Shaffer, & Brown, 1980). These studies included three comparison groups: a severe HI group, a mild HI group, and an orthopaedic control group. The researchers conducted follow-

ups of children immediately post-injury, at 4 months, 1 year, and 2 ¼ years post injury. At each point they measured behavioural, academic, cognitive, and psychiatric domains. Most recovery occurred during the first 12 months post-injury. Results showed a dose-response relationship across domains: Children with severe TBI showed more frequent and persistent sequelae.

Since these pioneering studies, research in the field has burgeoned, especially regarding the effects of TBI on various cognitive domains. These effects commonly include impairments in general intellectual functioning, executive functioning, attention, memory and learning, and language. A brief review of these sequelae follows.

Effects of TBI on cognitive domains.

General intellectual functioning. Impairments in IQ are reported especially following severe pTBI, even 5 and 10 years post-injury (V. Anderson, Catroppa, Haritou, et al., 2001; V. Anderson et al., 2009; V. Anderson, Godfrey, Rosenfeld, & Catroppa, 2012; V. Anderson, Northam, Hendy, et al., 2001; Ewing-Cobbs et al., 1997; Max et al., 1999).

Verbal IQ (VIQ) is less susceptible to the effects of TBI than Performance IQ (PIQ), although both VIQ and PIQ are affected, especially following severe TBI (V. Anderson, Northam, Hendy, et al., 2001; V. Anderson et al., 2009; Ewing-Cobbs et al., 1997). In a recent meta-analytic review of cognitive outcomes post-TBI, Babikian and Asarnow (2009) confirm such impairment in VIQ, PIQ and Full Scale IQ (FSIQ) following severe TBI. Case-control studies included in that review suggest that the dose-response relationship between injury severity and general intellectual functioning may become more apparent over time, although a similar trend was not observed in case-case studies. Longitudinal studies suggest that FSIQ and PIQ may actually recover with time, whereas minimal improvement is reported for VIQ. This suggested improvement in IQ is consistent with previous research showing that, by 6 months post-injury, there is already considerable improvement in IQ (V. Anderson, Northam, Hendy, et al., 2001).

Although some children may still perform in the average range on IQ tasks post-TBI, this intact performance does not preclude them from performing poorly on tests of executive functioning (Gioia, Isquith, Kenworthy, & Barton, 2002).

Executive function. Impairment in executive function is frequently associated with pTBI (Babikian & Asarnow, 2009; H. Levin, 1995; Mangeot, Armstrong, Colvin, Yeates, & Taylor, 2002; Van Heugten et al., 2006). Executive dysfunction post-TBI is not surprising given the vulnerability of the frontal lobes to the biomechanical forces acting on the brain during TBIs (Bamdad, Ryan, & Warden, 2003; Catroppa & Anderson, 2006; Stuss, 2011).

In school-age children, TBI-related deficits have been reported on tasks assessing executive functions such as planning, goal setting, processing speed, problem solving, mental flexibility, generativity, working memory, and inhibition (V. Anderson & Catroppa, 2005; Beauchamp et al., 2011; H. Levin, 1995; H. Levin & Hanten, 2005; H. Levin et al., 2002, 2004, 1994; Slomine et al., 2002). For instance, Beauchamp et al. (2011) reported a dose-response pattern of deficits in goal-setting and processing speed tasks; these deficits persisted even 10 years post-injury. Attentional control and cognitive flexibility tended to show recovery across time, however.

V. Anderson and Catroppa (2005) also reported improvements at 2 years post-injury in attention control with 8-12-year-old children. However, they reported ongoing difficulties in cognitive flexibility and abstract reasoning for the same sample, particularly for children who had sustained severe TBI. These persistent deficits might be a function of age and disparate developmental trajectories for these areas of functioning. The dose-response relationship mentioned above is reported consistently in the literature, even at 10 years post-injury (V. Anderson & Catroppa, 2005; V. Anderson et al., 2012; Mangeot et al., 2002; Nadebaum, Anderson, & Catroppa, 2007).

Optimal executive functioning is important for academic functioning (Farmer, Clippard, Luehr-Wiemann, Wright, & Owings, 1996). A child's ability to function appropriately in a classroom setting, or generally among peers at school, can be hindered by impaired executive functions such as disinhibition or lack of impulse control, or lack of insight into his/her own behaviour. These impairments can translate into untimely and inappropriate behaviours such as grabbing objects instead of politely requesting them, or hurling unwarranted insults, as a function of frustration and agitation (Mayfield & Homack, 2005). These behaviours can result in tension among peers or in the child being ostracized, resulting in further social challenges.

Attention. Closely related to executive dysfunction post-TBI are problems with attention. Impairment in attention may affect the acquisition of knowledge and new learning, necessary for success in the classroom (V. Anderson & Pentland, 1998; Mayfield & Homack, 2005).

Like executive functions, attentional functioning is supported by optimally functional frontal lobes, which, as noted previously, are vulnerable to the impact of TBI. Hence, attentional deficits are a common consequence post-TBI and may be evident for extended periods of time post-injury (Babikian & Asarnow, 2009; Beauchamp et al., 2011; Catroppa, Anderson, Godfrey, & Rosenfeld, 2011; Catroppa, Anderson, Morse, Haritou, & Rosenfeld,

2007; Park, Allen, Barney, Ringdahl, & Mayfield, 2009; Van Heugten et al., 2006; Yeates et al., 2005). Various attentional and attention-related components (e.g., sustained, focused, and divided attention, and response inhibition) appear to be affected differentially post-TBI. Once again this differential effect on the various attention-related functions is likely to be a function of varying developmental trajectories for these components (V. Anderson, Fenwick, Manly, & Robertson, 1998; Catroppa et al., 2011; Fenwick & Anderson, 1999). Post-TBI attentional deficits also occur in a dose-response pattern (Catroppa & Anderson, 2003, 2005; Catroppa et al., 2011; Catroppa, Anderson, & Stargatt, 1999; Fenwick & Anderson, 1999).

Memory. Reports of impairment in various components of memory and learning following TBI are common (V. Anderson, Northam, Hendy, et al., 2001; V. Anderson, Catroppa, Haritou, et al., 2001; Babikian & Asarnow, 2009; Catroppa & Anderson, 2007; Mandalis, Kinsella, Ong, & Anderson, 2007; Slomine et al., 2005). The development of memory in childhood is critical, as the ability to learn, consolidate, retain and retrieve information underlies the acquisition of knowledge and skills crucial to successful academic functioning (Lajiness-O'Neill, Erdodi, & Bigler, 2010). Memory impairments and associated learning difficulties are more persistent following severe TBI than following mild and moderate TBI's. This dose-response relationship is evident in the acute stage and at the long term, up to 2 years post-injury (V. Anderson, Northam, Hendy, et al., 2001; Babikian & Asarnow, 2009; Catroppa & Anderson, 2007; Max et al., 1999; Van Heugten et al., 2006).

Language. Language subserves learning and social interaction, and consequently, academic success, and is therefore essential to and for it (Catroppa & Anderson, 1999; Savage, DePompei, Tyler, & Lash, 2005). Both receptive and expressive language deficits have been reported post-TBI (Farmer et al., 1996; Sullivan & Riccio, 2010). Ewing-Cobbs et al. (1997) found expressive language to be more impaired than receptive language in a sample of children and adolescents. Aphasias do not commonly occur following pTBI, however (V. Anderson, Northam, Hendy, et al., 2001). Also, semantic and pragmatic skills related to language are reportedly more vulnerable to the effects of TBI than skills that become more mechanized over time, such as phonological, morphological, and syntactical elements of language (Farmer et al., 1996). Recently, Sullivan and Riccio (2010) found that various discourse processes and the ability to extract the main point of a story can also be compromised post-TBI.

Reading is also vulnerable to the effects of TBI, especially if the TBI is sustained during the development of this skill. A dose-response relationship between severity and outcome has also been reported for this cognitive domain (V. Anderson et al., 1997; V.

Anderson, Northam, Hendy, et al., 2001; Ewing-Cobbs et al., 1997). In a study with young children, those with mild and moderate TBI performed in the average range, and those with severe TBI showed mild to moderate impairment in language function (V. Anderson, Morse, Catroppa, Haritou, & Rosenfeld, 2004). The groups in this study all showed recovery over time on measures of expressive language, but not of receptive language: There were persistent deficits in this domain for the severe TBI group.

Effect of TBI on psychosocial functioning. The effects of TBI in childhood are not limited to cognitive domains, but extend to behavioural, psychiatric, academic, and familial domains (V. Anderson, Catroppa, Haritou, Morse, & Rosenfeld, 2005; V. Anderson, Northam, Hendy, et al., 2001; Arroyos-Jurado, Paulsen, Ehly, & Max, 2006; Max, Lindgren, Robin, et al., 1997). Intact cognitive functions, such as attention, memory and learning, and executive functions, contribute to optimal functioning in other functional domains. It is already clear from the previous section that these cognitive functions are vulnerable to the effects of TBI. Consequently, impairment in psychosocial functioning is also frequently observed post-TBI.

Behavioural outcomes. Although cognitive impairment may be difficult to contend with, and impacts significantly on academic functions post-TBI, researchers argue that among the range of outcomes, it is behavioural impairment that is most distressing, challenging, and persistent, showing little remittance over time. Behavioural changes are often reported by families / caregivers and health professionals, especially following severe TBI. Children are most often referred to mental health professionals post-TBI as a result of behavioural difficulties. Such difficulties can persist 3 to 5 years post-injury, and even into adulthood (V. Anderson, Northam, Hendy, et al., 2001; Donders & Strom, 2000; Dooley, Anderson, Hemphill, & Ohan, 2008; Fay et al., 2009; Fletcher, Ewing-Cobbs, Miner, Levin, & Eisenberg, 1990; Kinsella, Ong, Murtagh, Prior, & Sawyer, 1999; Taylor et al., 2002).

Behavioural impairment often overlaps with impairments in executive functions, and can be both internalizing and externalizing in nature. *Internalizing impairments* include emotional problems, withdrawal, and apathy, while *externalizing impairments* include problems with aggression (both reactive and proactive), uncontrolled temper, inattention, irritability, impulsivity, and response disinhibition (V. Anderson, Northam, Hendy, et al., 2001; Cole et al., 2008; Donders & Strom, 2000; Dooley et al., 2008; Fletcher et al., 1990; Mayfield & Homack, 2005; Schachar, Levin, Max, & Purvis, 2004; Taylor, 2004). Behavioural problems may be evident despite satisfactory performance on formal cognitive

testing. However, a reliance on self-report measures, which are commonly used to measure behaviour, is a noted limitation (V. Anderson, Northam, Hendy, et al., 2001).

Behavioural difficulties may occur as a direct consequence of the TBI. Damage to the vulnerable frontal lobes during a TBI, and especially during a severe TBI, may result in dysexecutive syndromes that translate into behavioural impairment. However, behavioural impairment post-TBI may also occur as an indirect consequence of the injury. The social and academic knock-on effects of the cognitive problems post-TBI, or the cognitive problems themselves, may lead to a sense of being misunderstood and consequently to a sense of failure and, in turn, to frustration, anger, acting out or withdrawal. Because cognitive and behavioural TBI effects are 'invisible' deficits relative to physical deficits, caregivers or teachers may overlook these effects and place unrealistic demands on the child, leading to further feelings of frustration or inadequacy, which in turn reinforce poor behaviour (Kinsella et al., 1999; Mayfield & Homack, 2005; Savage et al., 2005; Ylvisaker, Feeney, & Szekeres, 1998). These undesirable feelings that translate into behavioural difficulties can be particularly challenging for the affected child and his or her family, and may cause significant disruption to everyday spaces such as the home and the classroom (Hawley, 2004; Savage et al., 2005).

Psychiatric outcomes. Closely associated with negative behavioural outcomes are negative psychiatric outcomes. The latter also contribute to significant distress for both the patient and his or her family post-TBI. However, literature on neuropsychiatric sequelae is not as prolific as that dealing with cognitive and behavioural outcomes (Luis & Mittenberg, 2002; Max, Lindgren, Knutson, et al., 1997; Max, Lindgren, Knutson, et al., 1998; Max, Lindgren, Robin, et al., 1997; Rao & Lyketsos, 2000). Anxiety and mood disorders such as depression, apathy, and post-traumatic stress disorder (PTSD), personality changes, psychosis, oppositional defiant disorder (ODD), conduct disorder (CD), and secondary attention deficit hyperactivity disorder (SADHD) have been reported in reviews and in literature specific to children and adolescents post-TBI. SADHD, in particular, is a common area of inquiry in recent literature (Gerring et al., 2009; Max, Lindgren, Knutson, et al., 1998; Max et al., 2011, 2012, 2005a, 2005b; Rao & Lyketsos, 2000). New psychiatric disorders that were not evident pre-injury have been reported in up to 76% of a sample of 50 pTBI children (Max, Lindgren, Knutson, et al., 1997). This sample was, however, a referred sample, which may explain the elevated rate.

Psychiatric disorders may also occur as a direct or indirect consequence of a TBI. However, researchers have expressed difficulty in teasing apart direct and indirect effects

(Max, Lindgren, Knutson, et al., 1998). Psychiatric sequelae post-TBI are often associated with factors other than or in addition to those that are injury-related. For example, Max et al. (2005a, 2005b) reported that SADHD was predicted by socioeconomic status (SES) and lesion location within the first 6 months post-injury. However, SADHD was not predicted by injury-related factors from 6 to 24 months post-injury but rather by pre-injury adaptive functioning and psychosocial conditions.

Academic outcomes. Academic challenges following pTBI are not surprising, given the range of cognitive and behavioural sequelae post-pTBI. For example, the ability to sustain attention in a classroom, and to learn and remember what is presented by the teacher, are essential to academic success. Behavioural problems such as inattention, impulsivity, and response disinhibition, also interfere with this process. Academic skills include both literacy (reading and spelling) and arithmetic skills; both of these sets of skills are vulnerable to the effects of TBI (Catroppa & Anderson, 1999; Catroppa et al., 2009).

Although academic challenges are present post-TBI regardless of severity, these challenges are particularly common following severe TBI (V. Anderson, Northam, Hendy, et al., 2001; Arroyos-Jurado et al., 2006; Catroppa & Anderson, 1999, 2007; Catroppa et al., 2009; Ewing-Cobbs et al., 2004; Ewing-Cobbs, Fletcher, Levin, Iovino, & Miner, 1998; Fay et al., 2009; Hawley, 2004). For example, V. Anderson, Northam, Hendy, et al. (2001) report that academic difficulties are particularly prominent in the first 2 years following severe TBI. Besides severity, other factors associated with academic outcome include premorbid academic ability, achievement, and verbal memory ability, and acute intellectual function (0-3 months post-injury) (Arroyos-Jurado et al., 2006; Catroppa & Anderson, 2007; Catroppa et al., 2009; Donders, 1994).

A significant number of children with TBI, and especially those with severe TBI, require special education or need to repeat a grade after their return to school (Donders, 1994; Ewing-Cobbs, Fletcher, Levin, et al., 1998; Miller & Donders, 2003). Returning to school following a TBI may be challenging for the child as well as for the educator. Educators have to contend with, and make sense of, the heterogeneity of outcomes associated with TBI in order to plan suitable educational programmes (Stavinoha, 2005). Furthermore, if the child returns to school or to a new class or grade some time after the injury was sustained, the teacher may not always be aware of the fact that the child has sustained a TBI. It may also appear as if the child has recovered completely and the necessary assistance, adjusting of expectations or adapting of teaching plans and methods may not be put in place (Hawley, 2004; Mayfield & Homack, 2005).

Effects on the family. The classroom is not the only environment where challenges for, and unrealistic expectations of, post-TBI children may occur. Family members or caregivers also often mistake physical recovery for full recovery from TBI, ignoring the 'invisible' cognitive and behavioural deficits (Mayfield & Homack, 2005). Given the host of sequelae described above, as well as the financial and emotional effects of TBI, the levels of family stress and burdens frequently reported post-TBI is not surprising. Caring for the child with TBI in the context of the above-mentioned sequelae may be emotionally and financially taxing for the family. These familial effects are not limited to the parents. They also impact on siblings and family activities and are reported to persist at 6 and even 30 months post-injury (V. Anderson, Catroppa, Haritou, et al., 2001; V. Anderson et al., 2005; Hawley, 2003; Sambuco, Brookes, & Lah, 2008). Although TBIs at all levels of severity can result in parental distress, the dose-response nature of TBI also features in this domain, with higher levels of family stress and burden associated with more severe pTBIs. Family stress and burden may persist over time, especially where social resources are scarce (V. Anderson, Catroppa, Haritou, et al., 2001; Prigatano & Gray, 2007; Wade et al., 2006).

Following the hospital admission of a child post-TBI, parents face a number of challenges. Some of these include: concern about whether the child will survive or not, especially following a severe TBI; guilt associated with the fact that the child was injured; adjustment to their daily lives and caring for their child once he/she returns home; an ongoing need for relevant information; challenges in thinking about the future; consideration of the child's return to school and his or her academic performance; concern about the child's peer relations or lack thereof; and the challenge of dealing with the ongoing cognitive and behavioural sequelae of the TBI (Hawley, 2003; Prigatano & Gray, 2007; Savage et al., 2005). The level of parents' coping resources (e.g., support from a partner, friends or work colleagues) also impacts on the child's and family's functioning post-TBI (Kinsella et al., 1999; Wade et al., 2006).

In summary, the literature reviewed in this section describes the outcome of TBI in school-age children in various psychosocial domains. Although general trends in outcomes can be described, each child is affected differently post-TBI. This heterogeneity in effects and outcomes is largely contingent on the myriad of predictors of outcome described in the pTBI literature. The most important of these factors are briefly described below.

Factors Predicting Outcome Following pTBI

Although the general effects of pTBI across various functional domains appear to be fairly well delineated, predicting individual outcomes postinjury is more complicated and not

as clearly understood. There are a number of important predictors, each of which either act independently or interacts with others to determine outcome. These predictors include injury-related, constitutional, and environmental factors (V. Anderson, Catroppa, Haritou, et al., 2001, 2006; V. Anderson, Spencer-Smith, & Wood, 2011).

Injury-related factors.

Age at injury. Researchers have reported frequently that post-TBI outcomes vary as a function of age at injury, with an inverse relationship reported between age and poor outcome (V. Anderson & Catroppa, 2005; V. Anderson, Catroppa, Haritou, et al., 2005; V. Andersson et al., 2009; Catroppa et al., 2011; Fenwick & Anderson, 1999; Javouhey et al., 2006; Mateer, Kerns, & Eso, 1996). The effects of TBI on the immature brain are quite distinct from similar insults to the adult brain. Injury to the immature brain occurs in the context of ongoing developmental processes (V. Anderson, Northam, Hendy, et al., 2001; Giza, Mink, & Madikians, 2007). As Giza, Kolb, Harris, Asarnow, and Prins (2009) describe it, the immature brain has to constantly hit a moving target in the process of recovery. How the immature brain responds to injury relative to the adult brain is related to the longstanding debate about whether the immature brain is more resistant or more prone to the effects of early injury.

Plasticity. The effect of a traumatic insult on the developing brain has long been a controversial issue. There has been a debate between plasticity theorists, on the one hand, and those who support the early vulnerability view, on the other.

Plasticity, an important part of the normal course of development, refers to the structural changes in the brain in response to learning and experience (Kolb & Whishaw, 2003). The developing brain affords greater plasticity than the adult brain (Giza et al., 2007). Hence, an early theory in the field was that, 'younger is better' when it comes to sustaining a TBI (Giza et al., 2007, p. 148). The argument advanced was that capacity for recovery would be greater while the process of CNS development was still underway and neural connections were not yet determined. In other words, there would be greater capacity for recovery when the brain was relatively 'less committed'. This period during which the brain is less 'hardwired' and more redundant would allow greater freedom for reorganising or transferring of function to preserved tissue through either intra- or inter-hemispheric reorganization (V. Anderson, Northam, Hendy, et al., 2001). In summary, plasticity theorists posited that children with cerebral damage had greater potential for recovery than adults with similar damage (Mateer et al., 1996).

Margaret Kennard's work, initially referred to by Teuber (1971, 1974) as the 'Kennard principle', is often quoted erroneously as the basis for this plasticity argument. Although her initial work on the recovery of function following unilateral motor cortex lesions in monkeys showed better outcomes in infants compared to adults, her later work showed similar deficits in infants and adult monkeys with frontal lobe lesions (see V. Anderson et al., 2011).

It has also become clear over time that the strong earlier advocacy for the plasticity theory was based on favourable outcomes of studies that included children with focal lesions during the pre- or perinatal periods. Many of these studies were also conducted before the introduction of neuroimaging data, and many focused mainly on outcomes in the language domain (V. Anderson, Northam, Hendy, et al., 2001; Ewing-Cobbs, Barnes, & Fletcher, 2003). These studies were therefore not representative of the broader scope of, and more typical outcomes associated with, the pTBI population as we understand and characterize it today. For example, acquired brain injuries more commonly lead to diffuse, or a combination of diffuse and focal, damage, rather than purely focal lesions, which may often be the case with deficits in language (Ewing-Cobbs et al., 2003). Studies show that if plasticity occurs in the context of diffuse brain injury, especially after severe TBI, then it may become disrupted or even aberrant (V. Anderson et al., 2005a; Giza & Prins, 2006). Given the right conditions, brain plasticity can be beneficial, for example, with unilateral lesions where interhemispheric transfer might occur. However, this plasticity relies on optimal synergistic molecular, cellular and physiological processes for favourable results; brain injury can disrupt these processes (Giza & Prins, 2006).

The capacity for the transfer of functions from damaged to undamaged tissue following injury may not always be favourable, as 'crowding' may occur. Milner (1974) described this risk of crowding as follows: "... there is always a price to pay for such plasticity ... verbal skills tend to develop at the expense of non-verbal ones in this kind of hemispheric competition, but the fact remains. Both are low" (p. 87). Intrahemispheric transfer of function may also be more problematic where redundant undamaged tissue is scarce (e.g., following diffuse, generalized insults; V. Anderson et al., 2011; see Chapter 6). Therefore, although there are instances where plasticity may account for recovery following early brain injury, there are many instances of poor outcome; plasticity theory cannot account for the latter. These instances, where plasticity cannot account for poor outcome, often occurs with diffuse injury (V. Anderson, Northam, Hendy, et al., 2001).

Early vulnerability. Increasing evidence for the vulnerability of the immature brain has emerged. This evidence is especially strong in cases of severe pTBI (V. Anderson et al., 2005; Giza et al., 2007). A growing body of literature shows that younger age at injury increases a child's vulnerability to poorer outcome, even though greater plasticity may be expected at this earlier stage of development (Ewing-Cobbs et al., 1997; Giza & Prins, 2006; H. Levin, 2003; Taylor & Alden, 1997).

Earlier literature also suggested that skills that were still in the process of development at the time of injury might be disrupted; in other words, that the child might 'grow into the deficit' (V. Anderson, Northam, Hendy, et al., 2001; Mateer et al., 1996). More recent literature appears to challenge this idea, however. In their study with 2-7 year old children, V. Anderson et al. (2009) reported that although the recovery trajectory for children with severe TBIs occurred over a longer period of time, and that they might show greater deterioration in functioning post-injury, such deterioration does not continue indefinitely. These researchers reported that after 30 months this deterioration tended to plateau and it appeared that children began to show some recovery.

As is evident from this brief discussion, the plasticity-early vulnerability debate has evolved over time. In a recent article addressing this topic, V. Anderson et al. (2011) concluded that neither school of thought completely and independently accounts for the range and heterogeneity of TBI sequelae. Rather than a mutually exclusive stance for either theory, these researchers posit a 'recovery continuum', which incorporates both theories at either extreme. A child will veer towards either end of the continuum, greater plasticity or greater vulnerability, depending on the independent and interactive effects of a number of outcome-related factors, many of which are described below.

Time since injury. The amount of time since injury is purported to affect outcome, such that the degree of cognitive impairment appears to lessen with the progress of time after injury (V. Anderson & Catroppa, 2005; Penkman, 2004). Researchers report that a spike in the degree of recovery occurs during the first year post-injury, even though recovery in some domains may continue long after this time (V. Anderson & Catroppa, 2005; Ginstfeldt & Emanuelson, 2010; Yeates et al., 2002). Based on that initial spike in recovery, however, it is common practice for researchers to include in their research samples only children who are at least 1 year post-injury (e.g., Dooley et al., 2008; Van't Hooft et al., 2005). Too short a period of time post-injury may reflect an inflated picture of deficits that are in fact only temporary. Alternatively, it may result in premature detection of other impairments that may only be evident once recovery stabilizes, or one may miss detecting some impairments

completely (e.g., academic, family and social outcome may not be determined until later) (V. Anderson et al., 2010, 2011).

Nature of injury. Where and how the injury occurs, as well as the degree of injury, can also influence outcome. The number and site of the lesions that the brain sustains, or disconnections between brain regions, can also play a role in determining outcome (Slomine et al., 2002). Some researchers argue that the site of injury may be a less powerful predictor of outcome than the amount of brain tissue damaged, however (Power, Catroppa, Coleman, Ditchfield, & Anderson, 2007).

The amount of brain tissue that is damaged, the disconnections that occur, and hence the type of injury, are largely influenced by the mechanism of injury. These factors determine and distinguish between different types of TBI. For example, as discussed earlier in this chapter, TBIs that result from MVAs are associated with acceleration, deceleration, and rotational forces. These forces can often result in DAI and in a host of secondary injury processes. However, TBIs that result from falls are often more focal. Injuries of this nature may lead to neuropathological features different from those resulting from MVAs (Semple et al., 1998).

Severity of injury. A factor related to the nature of injury is the severity of injury. It is already clear from the above section on TBI-related sequelae that severity of injury is a well-established and important factor determining outcome. The dose-response nature of outcomes across various functional domains demonstrates this fact (V. Anderson et al., 2006, 2005, 3009; V. Anderson, Catroppa, Haritou, et al., 2001; Catroppa & Anderson, 2007; Catroppa et al., 2009, 1999; Fenwick & Anderson, 1999; Luis & Mittenberg, 2002; Max et al., 1997, 1999; Max, Lindgren, Knutson, et al., 1998; Nadebaum et al., 2007).

It appears that although injury severity is an independent and particularly powerful predictor of physical and cognitive outcomes, it is less powerful in predicting behavioral, academic, and familial outcomes (V. Anderson, Catroppa, Haritou, et al., 2001; Catroppa et al., 2009; Max et al., 1997). Injury severity is not always related to behavioural outcomes (V. Anderson et al., 2005). Some researchers recognize that, although severity of injury is a good predictor of outcome, it is not sufficient to explain the scope of outcomes observed in children post-TBI. Thus, a combination of outcome factors, such as those outlined here, should be considered; injury severity in isolation is not a powerful enough predictor (V. Anderson et al., 2009).

Management of secondary injuries. Although the management of secondary injuries is a critical factor affecting outcome post-TBI, it is not commonly included in the pTBI

neuropsychological outcomes literature. As Giza et al. (2007) state, "the primary goal of management for any child with severe TBI is the prevention of secondary insults" (p. 145).

How to limit secondary injuries is, however, a key focus of the neurosurgical outcomes literature. As mentioned in the discussion on secondary injuries earlier in this chapter and in Chapter 4, researchers and clinicians place great emphasis on limiting secondary injuries, especially hypoxic-ischemic injury, due to its degenerative and pervasive effects, in order to afford better outcomes (Greve & Zink, 2009; Kumar & Mahapatra, 2009; Tang & Lobel, 2009). The pTBI literature clearly describes the relationship between secondary injuries and unfavourable outcome (Chambers et al., 2006; Downard et al., 2000; Figaji et al., 2009; Jones, Andrews, Easton, & Minns, 2003; Pigula, Wald, Shackford, & Vane, 1993; Rohlwink & Figaji, 2010). However, despite its importance, health professionals do not always prioritize the prevention of secondary injuries. In addition, although protocols for the management of secondary injuries may be clearly delineated, the actual implementation of such protocols may not always be as simple (Alexander et al., 2009).

Constitutional factors.

Premorbid functioning. There is a long-standing idea that children who sustain TBIs are not simply a random sample of the general pediatric population (Rutter et al., 1983). The common finding that pre-injury abilities are linked to TBI outcomes in various domains, including cognitive, familial, academic, adaptive and behavioural outcomes, is consistent with this thinking (V. Anderson & Catroppa, 2005, 2007; V. Anderson, Catroppa, Haritou, et al., 2001; V. Anderson et al., 2006, 2004; Farmer et al., 2002; Fenwick & Anderson, 1999). Researchers in this area have also suggested that certain premorbid behavioral patterns and problems (e.g., externalizing problems (aggression) and thought problems) in children can predispose them to greater risk for certain types of accidents (high or low risk) that can result in TBIs (Olsson, Le Brocque, Kenardy, Anderson, & Spence, 2008).

Developmental stage. Some researchers suggest that the interpretation of outcomes must be done against the backdrop of a child's developmental stage. How cognitive abilities translate in reality, the very ontology thereof, must be understood (Ryan et al., 1996). TBI not only disrupts functions that have already been mastered; it also disrupts those yet to come on board and still in the process of development. TBI can thus disrupt the developmental blueprint of the child. This disruption is problematic, given that earlier developmental stages serve as necessary precursors to later stages. This disruption thus leads to less optimal outcomes (V. Anderson et al., 2011; Brenner et al., 2007; Mateer et al., 1996).

Environmental factors.

Family functioning. There is a bidirectional relationship between family functioning and the family environment, on the one hand, and TBI, on the other. Family functioning, or family environment, are both affected by, and affect the outcome of, TBI (V. Anderson, Catroppa, Haritou, et al., 2001; V. Anderson et al., 2005; Kinsella et al., 1999; Prigatano & Gray, 2007; Taylor et al., 2001).

The family environment, level of family functioning, a history of psychiatric illness in the family and the degree to which families are able to cope with the child's injury, along with other factors, are associated with outcomes for the child. These family-related factors will either buffer the effects of the child's injury or exacerbate them, depending on the nature thereof (V. Anderson et al., 2006; Catroppa et al., 2009; Max et al., 1997; Yeates et al., 1997).

SES and psychosocial adversity. Family SES influences the state of the familial environment to a significant degree. Children from lower SES environments, or from backgrounds associated with greater psychosocial adversity (e.g., family burden and stress), are at greater risk of poorer outcomes across various functional domains (V. Anderson, Catroppa, Haritou, et al., 2001; V. Anderson et al., 2004; Max et al., 1999; Muscara, Catroppa, Eren, & Anderson, 2009; Taylor et al., 1999). As with the family environment, having access to adequate social resources may serve as a buffer against the effects of severe TBI. This buffering effect has been demonstrated in some cognitive domains, including memory and adaptive functioning (Yeates et al., 1997). The level of psychosocial adversity may affect access to necessary resources, for example, rehabilitation services.

Access to rehabilitation. Although the field of cognitive rehabilitation is still, relatively speaking, in its infancy, and some intervention strategies have yielded more promising results than others (see Chapter 7), there is evidence to suggest that a lack of access to rehabilitation services can have a negative effect on outcome. For example, Fay et al. (1994) report poorer outcomes for patients with moderate-to-severe injuries who did not receive rehabilitation. Access to rehabilitation does not, however, preclude patients from having persistent deficits (Kinsella et al., 1997; Taylor et al., 2002). These contradictory findings concerning the value of rehabilitation services might be a function of the challenges related to cognitive rehabilitation (see Chapter 6). These findings are not simply a sign that cognitive rehabilitation makes no difference to outcome or a direct lack of utility for the field. As with other factors affecting outcome, access to rehabilitation may affect outcome in combination with a host of other factors.

Of course, the influence of access to rehabilitation services by families, and by various population income groups, is not only affected by its affordability, but also by the availability of such services. Research shows that such services are lacking generally, but are a particularly scarce resource in LAMICs such as South Africa (e.g., Javouhey et al., 2006; K. Levin, 2004). Given the enormity of the problem of pTBI on a global scale, this lack of rehabilitation services are is surprising.

Summary and Conclusion

Although initially a TBI may, on the face of it, seem like a simple blow to the head, by definition it interferes with brain functioning. The initial blow to the head, and subsequent damage to the brain, is followed by a cascade of potentially detrimental secondary effects. Consequences of TBI are far-reaching and affect various domains: cognitive, behavioural, psychiatric, academic, and familial. These far-reaching consequences are socially, emotionally and economically taxing for both the child and his / her family. A range a factors, including injury-related, constitutional and environmental factors, determines how and to what degree the injury will impact on these domains, depending on who is injured and when and how they are injured.

CHAPTER 2:
EPIDEMIOLOGY OF PEDIATRIC TBI, GLOBALLY AND IN SOUTH AFRICA

TBI is described consistently as a public health problem, both in South Africa (Cywes, 1990) and globally (Abelson-Mitchell, 2008; Baldo et al., 2003; Bener, Omar, Ahmad, Al-Mulla, & Abdul Rahman, 2010; Bruns & Hauser, 2003; Gontkovsky, Sherer, Nick, Nakase-Thompson, & Yablon, 2006; Hyder et al., 2007; Langlois, Rutland-Brown, & Wald, 2006; Rutland-Brown, Langlois, Thomas, & Xi, 2006; Tabish et al., 2006; Tude Melo et al., 2010). It is also described as a 'common problem' (Alexander et al., 2009) and a 'social concern' (Abelson-Mitchell, 2008). These descriptions speak to a prevalence of TBI that one might also associate erroneously with heightened public awareness of TBI. In spite of its significant effects, however, TBI is also described as a silent epidemic (Goldstein, 1990; Langlois, Marr, Mitchko, & Johnson, 2005; Rutland-Brown et al., 2006). This latter description is applied for two reasons. First, because many people remain unaware of the magnitude of the problem, and, second, because the post-injury neuropsychological, behavioural and emotional sequelae are largely 'invisible': these deficits are not as apparent as physical deficits (Langlois et al., 2006; Rutland-Brown et al., 2006). It is these invisible deficits that, to a great degree, contribute to the economic burden of TBI.

The Economic Burden of TBI

TBI is associated with formidable economic sequelae (Flanagan, Kwasnica, Brown, Elovic, & Kothari, 2008; Jaffe, Massagli, et al., 1993; Ragnarsson, 2002). This economic burden results not only from the expenses associated with direct healthcare, but also from the indirect costs linked to a loss of the potential future productivity of that individual. The loss of potential future productivity is especially important in the case of children, clearly because most of their life will be spent in the shadow of the TBI. Also, there are associated costs, such as a loss of productivity for extended periods of time for parents. TBI can therefore be economically challenging and exhausting at the societal, individual and familial levels (Gontkovsky et al., 2006; Jaffe, Massagli, Martin, et al., 1993; Tilford et al., 2005). In the United States, these costs amount to $56.3 billion (Langlois, Rutland-Brown, & Thomas, 2004), with approximately $1 billion of these costs attributed to hospital expenses for pTBI annually (Schneier, Shields, Hostetler, Xiang, & Smith, 2006). Compared to adults, costs related to pTBI, particularly of a severe nature, are especially high as both acute and chronic care such as longer-term rehabilitation may sometimes be required (American Academy of Pediatrics and Pediatric Orthopaedic Society of North America, 2008; Jaffe, Massagli,

Martin, et al., 1993). This need for long-term care has increased as a result of improved management of TBIs in recent times.

The Epidemiology of TBI

The 20th century has witnessed significant advances in the scope of TBI care and management, which has resulted in better outcomes and decreased rates of death (e.g., Coronado et al., 2011). In spite of these advances, TBI is still a leading cause of mortality and morbidity (temporary or permanent) around the world (Bener et al., 2010), and also specifically for children (Babikian & Asarnow, 2009; "Traumatic brain injury: time to end the silence," 2010). The World Health Organization (WHO) projects that this status is likely to strengthen by the year 2020 (Hyder et al., 2007).

Global perspective on the epidemiology of TBI. According to the WHO, the global incidence rate of TBI due to road traffic accidents (RTAs) is estimated to be 106 per 100 000 population. Hence, TBIs are purported to affect at least 10 million people per annum globally. This figure includes individuals who have either been hospitalized or who have died as a result of TBIs (Hyder et al., 2007; Langlois et al., 2006). The global figure for hospital admissions only, as a result of a single or multiple TBIs, was estimated to be 57 million by Murray and Lopez (1996). A more recent global estimate of those living with disability as a result of sustaining a TBI is, however, unknown (Langlois et al., 2006). What is known is that there are disparate effects of TBI in HICs and LAMICs (Hyder et al., 2007).

TBI in high- as compared to low-and-middle-income-countries. Although TBI is a global problem, the effects thereof are reportedly more potent in LAMICs than HICs (Alexander et al., 2009; Bener et al., 2010; Harris et al., 2008; Hyder et al., 2007; Kumar & Mahapatra, 2009). This disproportionate effect on poorer economies is attributed to the quality of the environment and lack of resources. There are a number of factors often associated with LAMICs, such as poverty, lack of access to education, differences in infrastructure, and other social problems like alcoholism, that create greater risk for TBI (Hyder et al., 2007; also see K. Levin, 2004 for the case of SA). For example, a World Health Statistics (2011) report notes the following: the home and work environments in indigent areas are often less secure, and residents and commuters are exposed to more potential hazards. Also, prevention endeavours and access to rehabilitation may be less available in such environments. In addition, the scope of care for individuals who have sustained TBIs is inconsistent in these countries, and many health care facilities are ill-prepared to cope with the scope of injury and degree of care required for this magnitude of a public health problem (Hyder et al., 2007). This degree of care requires systematization, the efficacy of which has

been demonstrated by the relatively recent reduction of mortality rates in sub-Saharan Africa (Van As & Rode, 2006). However, these researchers note that "trauma systems hardly exist" (p. 874) in this context, which does not bode well for curbing the widespread impact of TBI.

Comparing incidence rates between and within HICs and LAMICs can be challenging because the nature of epidemiological studies varies. Whereas some studies include both HI and TBI cases, other studies focus on either HIs or TBIs. Besides definitional inconsistencies, there are also differences in the age and severity of samples included in epidemiological studies, as well as differences in the specific outcomes that are reported (Abelson-Mitchell, 2008; McKinlay et al., 2008). For example, some studies report the total number of admissions over various periods of time, while others report the incidence rate per 100 000 population. Also, in general, literature on the epidemiology of TBI and pTBI around the world is more widely available for HICs than LAMICs. Much of the data for HICs emanates from reports such as those generated by the Centers for Disease Control and Prevention and the National Center for Injury Prevention and Control (Faul, Xu, Wald, & Coronado, 2010) and other US-based literature. A dearth of published research on national trends of TBI in LAMICs is generally described (e.g., Bener et al., 2010; K. Levin, 2004).

Nonetheless, in a review comparing the incidence of TBI in HICs and LAMICs, Hyder et al. (2007) reported higher incidence rates in LAMICs. For HICs, generally, 200 individuals per 100 000 population are purported to be affected by TBI, although this figure usually only accounts for those persons who are hospitalized (Bruns & Hauser, 2003). Incidence rates for some LAMICs appear to be higher than the overall incidence rate for high-income countries. For example, incidence rates for Yemen and Sao Paulo, Brazil have been reported as 219 per 100,000 (Shukri, Bersnev, & Riabukha, 2006) and 360 per 100,000 (De Andrade, Marino, Ciquini, Figueiredo, & Machado, 2001), respectively. In India, TBIs also account for almost 25% of injuries where hospital admissions are required. TBI-related morbidity affects approximately 2 million people and TBI-related mortality, 1million people, annually (Gururaj, 2002).

These disparities between HICs and LAMICs are also evident when considering TBIs that occur as a result of road traffic accidents (RTAs), specifically. The global rate of RTA-related TBIs is 106 per 100,000. In Latin America and sub-Saharan Africa, the incidence rates for RTA-related TBIs range from 150-170 per 100 000 (Alexander et al., 2009; Hyder et al., 2007).

Pediatric TBI. Injury, and TBI in particular, is a serious cause of death and disability in children and adolescents around the world (Kraus, 1995; Kraus, Rock, & Hemyari, 1990;

Pfenninger & Santi, 2002; Segui-Gomez & MacKenzie, 2003). As with the adult population, TBI in childhood and adolescence results in a number of hospitalizations and emergency department admissions (Berry, Jamieson, & Harrison, 2010; Hawley, Ward, Long, Owen, & Magnay, 2003; Kraus et al., 1990; McCarthy, Serpi, Kufera, Demeter, & Paidas, 2002; Tabish et al., 2006). Some comprehensive studies have helped to elucidate the impact of TBI on children (Faul et al., 2010; Langlois, Rutland-Brown, & Thomas, 2004).

As with the adult literature, much of the epidemiological data regarding pTBI stems from the US, where children aged 0-14 years account for almost 500 000 of the new cases of TBI reported at emergency departments (Faul et al., 2010). The incidence rate for pTBI for children aged 1 to 15 years in the US was previously reported to be 200 per 100 000 population per year (Annegers, 1983). For children and young adults, more recently reported annual incidence rates range from approximately 100 to 300 (±30) per 100 000 population (Berry et al., 2010; Bowman, Bird, Aitken, & Tilford, 2008; Hawley et al., 2003; Kraus et al., 1990; Schneier et al., 2006). These findings pertain to high-income countries.

Early studies reported that there are over 500 000 pTBI-related emergency department admissions and 150 000 TBI-related hospitalizations annually in the UK (Sharples, Storey, Aynsley-Green, & Eyre, 1990; G. M. Teasdale, 1995). More recently, Hawley et al. (2003) reported a hospital admission rate of 280 children per 100 000 population at a North Staffordshire hospital. These hospitalization figures refer specifically to the 0-14/15 year age bracket. There seems to be a preponderance of published pTBI epidemiological research that focuses on this age group (e.g., Berry et al., 2010; Engberg & Teasdale, 1998; Parslow et al., 2005), which is not surprising, given that a significant proportion (1/3 x 1 400 000) of the population who sustain TBIs are within this age bracket (Langlois et al., 2004).

Although many children of all ages die as a result of TBI (Tilford et al., 2005), a significant proportion of those deaths occur in the 0-14-year-old age bracket. The reported mortality figures vary across time and for different countries. For example, Tsai et al. (2004) reported that in 1993, this figure was estimated at 50% in China and Parslow et al. reported a figure of 9.2% of deaths for that particular age bracket, among children admitted to 48 adult intensive care units in the UK, in 2005.

Thus, a large number of children incur lifelong disability as a result of TBI and many others do not survive (Langlois et al., 2004). Results of international studies confirm that trauma and injuries, generally, which include TBIs, lead to a significant number of pediatric deaths in high- (e.g. France; USA) and LAMICs (e.g., South Africa) (Haller, 1983; Kibel, Joubert, & Bradshaw, 1990; Tude Melo et al., 2010)

In LAMICs, mortality due to injury, which includes TBI, occurs more often than for any other etiological factor (Van As & Rode, 2006). Also, more pediatric injuries and pTBIs, occur in LAMICs than in HICs. For example, estimated pTBI incidence rates for Yemen and Argentina were 480 and 566 per 100 000, respectively, although the latter study focused only on minor head injuries (Murgio, Fernandez Milà, Manolio, Maurel, & Ubeda, 1999; Shukri et al., 2006). Both of these rates are higher than incidence rates for HICs, as reviewed above.

Published literature on the epidemiology of pTBIs in LAMICs is generally limited, however. Local researchers highlight the dearth of much-needed research of this nature in LAMICs generally and in South Africa in particular (Bruns & Hauser, 2003; Haaring, Mtambeka, Shulman, & Van As, 2011). Although some suggest that the incidence of pTBI in South Africa must be high, exact rates are not available because systematic research on the topic is lacking (K. Levin, 2004; Penn, Watermeyer, & Schie, 2009).

The epidemiology of pediatric TBI in South Africa.

Contextual factors. According to the World Bank (2013), South Africa is classified as a developing country, with an upper-middle income economy, and a population of approximately 45 million (Penn et al., 2009). Youth (0-18 years of age) in South Africa are vulnerable to the risk of non-natural deaths, accounting for at least 10% of all such deaths in the country (Bowman et al., 2002).

Incidence. Previous studies (e.g., De Villiers, Jacobs, Parry, & Botha, 1984; Kibel, Bass, & Cywes, 1990; Lalloo & van As, 2004; Semple et al., 1998) have included analyses of profile admissions for trauma and injuries to the RXH[1] in Cape Town, the third largest city in South Africa (Burrows & Laflamme, 2006). Recent epidemiological data are not available, however.

More than two decades ago, Nell and Brown (1991) reported on a survey conducted in Johannesburg, the largest city in South Africa. They calculated an incidence rate of 316 per 100 000 population for 15- to 24-year-olds, based on pre-hospital admission deaths and cases seen at the trauma hospitals there. More than a decade later, Bruns and Hauser (2003) posited that the incidence of TBI in South Africa could be higher than the incidence rate reported in the US at the time of publishing their paper (i.e., 180-250 per 100 000 population per year in the US). K. Levin (2004) reported that no incidence figures were available for pTBI in South

[1] "The Red Cross War Memorial Children's Hospital was built in 1956 and is the only stand alone, specialist children's hospital dedicated entirely to children in southern Africa" (http://www.childrenshospitaltrust.org.za/page/the-childrens-hospital-trust; Accessed on 9 April 2012).

Africa at the time of her research. This situation has remained largely unchanged over the past decade.

In light of the absence of specific incidence rates for the country, a review of South African studies affords some insight into the magnitude and status of the problem of TBI in SA. These studies suggest that TBI is undoubtedly a serious social concern in this country in terms of both mortality and morbidity (Kibel, Bass, et al., 1990; Knobel, De Villiers, Parry, & Botha, 1984; Nell & Brown, 1991; Peacock, 1984). Although clearly not ubiquitous, there has been some degree of research output in terms of epidemiological data on 'head injury' and/or TBI in South Africa. The trends outlined in this literature are largely consistent with those reported for developed world countries. As mentioned before, these established trends seem to cut across these different societies (Bruns & Hauser, 2003).

Without access to, or knowledge of, the South African pTBI literature, the public in South Africa may not be aware of the scope of TBI as a public health problem, especially with the focus (rightly) on infectious diseases such as HIV/AIDS (Bradshaw et al., 2003; K. Levin, 2004). In fact, in Africa generally, there is a tendency to underestimate the impact of injuries such as TBIs. Researchers suggest that one of the reasons for this behaviour is that there is a tendency to focus on mortality rates only, to the neglect of vital information on morbidity and the SES sequelae (Nwomeh & Ameh, 2004). Both outcome factors, that is, mortality and morbidity, depict the true impact of injuries, generally (Van As & Rode, 2006).

South African studies on head injuries and/or traumatic brain injuries.

Studies relating to morbidity, including prevalence and trends in admission. De Villiers, Jacobs, Parry, and Botha (1984) conducted a retrospective study on trends in head injury admissions for children younger than15 years of age, to two academic hospitals in the Cape Town region, over a 15-year period (July, 1966 – June, 1981). The results were based on 1 820 admissions. The researchers reported that the head injury admissions were higher among mixed race ('Coloured')[2] and Black African children. Admissions were also higher for males among those children not yet of school-going age (< 6 years). MVAs and falls were the leading causes for admissions. These results were organized by age. Falls were a prominent cause of head injury among the very young (< 1 year of age), regardless of race. MVAs, where the child was a pedestrian, prevailed as a leading cause of admissions among the 1-5-year-old and 6-14-year-old age groups, accounting for 63.1% and 46.5% of the admissions for mixed race and Black African participants respectively in the former age

[2] A racial category used in South Africa for persons with mixed ancestry.

group, and 64% of all participants in the latter age group. White children in the 1-5-year-old age group were admitted primarily as a result of falls. Although numbers for different severity groups were not reported, relationships between etiological and severity factors were. The most severe injuries, including those resulting in death, occurred primarily as a result of road traffic-related incidences.

Six years later, Kibel et al. (1990) published a study examining the admissions data of all patients younger than 13 years of age seen at the RXH trauma unit over a 5-year period (24 April 1984 to 31 March 1989). This study therefore did not focus on HIs or TBIs specifically. During that period, 57 468 patients were seen at the trauma unit, with a mean admissions rate of 11 493.6 per annum. Falls accounted for 43% of all injuries and 57% of head injuries. This etiological factor was therefore designated as the most significant cause of injury in this study, regardless of whether patients were hospitalized or not. Given the established association between falls and the very young, this finding is fitting as the mean age of the sample was 4.9 years and almost 50% of the children included in the sample were 0-4 years of age. Most injuries were classified as minor. Head injuries were the major cause of injuries resulting in hospitalization. Other mechanisms of injury were 'bumps and blows' and road traffic-related, accounting for 15.3% and 11.4% of the injuries, respectively. More boys than girls were admitted, with a ratio of 1.5:1, respectively. More injuries occurred in the summer than in the winter months, with the highest incidence of injuries occurring during the month of December. The two peak times of day, around which most injuries occurred, were 13h00 and 17h00.

Semple et al. (1998) conducted a study with a specific focus on children who sustained severe head injuries (GCS < 8). The study was also conducted retrospectively and included children younger than 14 years (N = 102), treated at the trauma and neurosurgery units at RXH over a 4-year period (January 1990 – December 1993). Children aged 0-12 months and 7-13-years were most vulnerable to injury. Boys made up 56% of the sample. A high proportion (83%) of the injuries occurred as a result of MVAs, where the injured child was a pedestrian. More than half (57%) of the children admitted died, including all children (N = 40) with GCS scores of 3 - 4.

Brysiewicz (2001) conducted a pilot study in which she investigated the types of injuries sustained by children (N = 39) involved in RTAs, in Durban, South Africa. The ages of the children ranged from 2-12 years, with 59% aged between 6 and 12 years. Boys made up 56% of the sample. Minor head injuries were the second most frequent type of injury, constituting 35% of the total injuries.

Lalloo and Van As (2004) provided a profile of head injured children (younger than 13 years) treated at RXH for the period January 1991 to December 2001. The mean age of the sample was 4.9 years, and 59% were boys. They reported that approximately 37 610 records out of 94 000 trauma records reviewed were related to head injuries, the majority of which were superficial; therefore, one can assume that many of these cases did not include TBIs. The injuries were mainly as a result of falls and MVAs. With regards to MVAs specifically, the injured child was a pedestrian in 65% of these cases (n = 7167) and 61% of the injuries (N = 37610) occurred in the vicinity of the home.

Of the five studies reviewed above, only one study focused specifically on children who had sustained severe head injuries (Semple et al., 1998). The situation concerning this specific group in the South African context can be , however, by reviewing literature published by neurosurgical groups on neurosurgical topics. For example, in a paper about brain oxygenation in children, Figaji et al. (2009a) reported on all children admitted to the RXH (N = 52; 39 boys) over a 2-year period (June 2006 – May 2008) as a result of severe TBI. All of the children were younger than 15 years of age.

Haaring et al. (2011) conducted a related recent South African study. The purpose of that paper was to report on the incidence and to describe the characteristics of children who sustained injuries in 27 randomly selected suburbs in Cape Town in three non-consecutive years (1996, 2001, and 2007), using patient records at the RXH. The study was therefore not limited specifically to TBIs or head injuries. There were more boys (60%) than girls in the sample. The median ages of the samples were 4 in 1996, and 5 in both 2001 and 2007. Most injuries (95%) were mild to moderate in nature, and occurred more often among boys. Haaring et al. (2011) confirmed the especially high pediatric injury rates that have come to be associated with LAMICs like SA. One of the main findings was that in every 100 children, two are involved in accidents warranting a visit to the emergency department. Overall, the main cause of injury was falls.

Studies relating to mortality. There are fewer published South African studies on TBI-related mortality as compared to morbidity. Knobel et al. (1984) provided a detailed account of pediatric (younger than 15 years) deaths by non-natural causes in the Cape Peninsula over a 15-year period (July 1966 to June 1981). Their results showed a high preponderance for non-natural deaths among Coloured and Black African children, males, and children younger than 6 years of age. Of the 3248 autopsy reports they reviewed, 819 showed that head injuries had resulted in death. Road traffic injuries with or without concomitant head injuries were the

cause of a large number of deaths (54.4%; *n* = 1765). Of the proportion of 819 deaths that were head injury-related, 72% (*n* = 589) of these occurred as a result of MVAs.

Kibel et al. (1990) reported on injury-related mortality among children (younger than 15 years) in South Africa from 1981-1985. Injury accounted for 8% of all deaths in the sample, and for 43% of deaths of children aged 5-14 years of age. These fatal injuries were most often sustained on the road for children aged 1-14 years. There were higher rates of injury-related mortality among boys than among girls almost consistently across age and population groups.

Cywes (1990) also reported an annual mortality rate of approximately 3000 children aged less than 15 years. These deaths occurred as a result of accidents.

Epidemiological trends for pediatric TBI. Although no one is impervious to the effects of trauma generally (Brown, 2010), research repeatedly demonstrates that the effect thereof varies as a function of a range of different variables. Incidence rates, and with that, the associated risk of TBI varies from country to country. However, there are some established trends, or what Hillier, Hiller, and Metzer (1997) refer to as peaks and troughs, that emerge in the occurrence of TBIs and that seems to cut across these different societies (Bruns & Hauser, 2003). These established trends are reported for severity, certain demographic variables such as age and sex, cause of injury and place of residence, to name a few. I review some of the important trends below.

Severity. The trends are quite clear here: Most TBIs are mild and do not lead to chronic disability (Brown, Elovic, Kothari, Flanagan, & Kwasnica, 2008). The typical severity ratios, usually based on the GCS, are approximately 80:10:10 % for mild, moderate, and severe TBI, respectively (Bruns & Hauser, 2003; Hillier et al., 1997; Zulu, Mulaudzi, Madiba, & Muckart, 2007). If the figures for severity vary across studies, it is often as a result of differences in classifying mild cases (differentiating between mild TBIs and HI without TBIs, for example), which then obviously affects the proportions of the moderate and severe injuries relative to the total.

The distribution of TBI severity appears consistent among HICs and LAMICs. For example, in a study in Europe, the severity ratios for 0-15 year olds were estimated as 82.7% mild, 9.1% moderate and 6.1% severe, 0.8% fatal, and 1.3% unknown (Hawley et al., 2003). Those in a South African study were reported as 87.5% mild, 7.9% moderate, and 4.6% severe (Nell & Brown, 1991).

A figure of 5 - 10% for moderate and severe injuries may seem low relative to a figure of 80% for mild injuries. However, bearing in mind the incidence rates reported

before, the raw numbers are quite substantial. This is a significant proportion of children who are highly vulnerable to potential chronic morbidity (Hawley et al., 2003).

Mortality rates associated with severe TBI are also high (Bruns & Hauser, 2003). In children, many who sustain severe TBIs do not survive; some studies report that only 65% do (Berger, Pitts, Lovely, Edwards, & Bartkowski, 1985). For those who do survive severe TBI, the various sequelae (see Chapter 1) often interact with and affect ongoing development (V. Anderson et al., 1997).

Sex. Males are more prone to TBI than females and are therefore classified as a high-risk group for TBIs (Bruns & Hauser, 2003). In fact, pediatric-specific TBI studies show that boys are twice as likely as girls to sustain a TBI. This trend is consistent across HICs and LAMICs (Berry et al., 2010; Engberg & Teasdale, 1998; Hawley et al., 2003; Lalloo & Van As, 2004; Melo, De Santana, Pereira, & Ribeiro, 2006; Schneier et al., 2006; Tsai et al., 2004). In their study, Tsai et al. (2004) ascribe the higher rates of injuries among boys to the stereotypical intrepid and aggressive behaviours often associated with boys. Males, young and old, are also more likely than females to be involved in RTAs (Rickels et al., 2010).

Age. There are also identified age groups at high risk of TBI. Some researchers identify peaks in the very young (0-4 years), adolescent and young adult (15-24 years), and elderly age groups (Brown et al., 2008; Bruns & Hauser, 2003; Langlois et al., 2004). Other researchers emphasize the prevalence of head injuries among those younger than 12 months of age. This group is of particular concern as they are also the group most prone to non-accidental injuries (M. Williamson, Keenan, Kuan, & Mckay, 2010). Injuries sustained during this first year of life are even more threatening than injuries sustained in the second year of life, let alone later on in life (Eisele, Kegler, Trent, & Coronado, 2006). All in all, children are at risk for TBI, with reports of 20% of TBIs occurring among individuals aged 0 to 17 years (Tabish et al., 2006).

Overlapping results are reported in terms of mortality, with studies reporting the highest mortality rates for 15-24-year-olds (Tabish et al., 2006). Tsai et al. (2004) report similar findings and attribute these results to older children embracing their increasing independence during this time, without an adequate sense and means of evaluating their environment.

Age-related trends associated with pTBI are difficult to compare between HICs and LAMICs. Differences in age-related trends often arise as a function of the mechanisms of injury. For example, because older children frequently sustain TBIs as a result of RTAs, and RTAs are often reportedly high in LAMICs, age trends for studies conducted in LAMICs

might be skewed towards older children (Bahloul et al., 2009; K. Levin, 2004; Penn et al., 2009).

Mechanisms of injury. The leading mechanism of injury for TBI among children seems to vary primarily between RTAs (Conner et al., 2010; Emanuelson & Wendt, 1997; Parslow et al., 2005) and falls (Falk, 2010; Melo et al., 2006), depending on the sample. One study (Tsai et al., 2004) reported both falls and RTAs as leading mechanisms. These etiological factors are reported to vary with age, primarily (e.g., Hawley et al., 2003; Tabish et al., 2006), as well as with other demographic (e.g., sex) or contextual (e.g., economic) factors (Bruns & Hauser, 2003; Rickels et al., 2010). A review on the global impact of TBI, however, reports that most TBIs (approximately 60%) occur as a result of RTAs, followed by falls (20-30%), violence (10%) and sport- and/or work-related injuries (10%) (Gururaj, 1995 as cited Hyder et al., 2007). RTAs, especially, appear to vary between HICs and LAMICS (Alexander et al., 2009; Hyder et al., 2007), with higher rates reported in some LAMICs (Latin America and sub-Saharan Africa) than the global rate. In general, TBIs are a major cause of RTA-related deaths across the economic strata, however (Toroyan & Peden, 2007). I review this and other mechanisms of injury, below, with an extended focus on RTAs.

Road traffic- related accidents. RTAs are one of the 15 leading causes of injury-related death generally (Hyder et al., 2007). More specifically, MVAs are a primary cause of death among youth and young adults aged 5-24 years of age in the US (Centers for Disease Control and Prevention, and National Center for Injury Prevention and Control, 2010a). This finding is not surprising, given that MVAs are closely and negatively associated with the high prevalence of TBI, including pTBI.

In terms of stratification by age group, studies report that a number of young children (0-4 years) are hospitalized for TBI occurring as a result of MVAs (Langlois et al., 2004). RTAs affect older age groups more often, however (Bener et al., 2010; Hawley et al., 2003; Tabish et al., 2006). Tsai et al. (2004) propose that older children are more at risk for RTA-related TBIs as a result of more exposure to road traffic threats: Their extramural time is often spent outdoors, or they are more likely to be travelling to school independently. Increased risk of, and vulnerability to, injury occurs because many children engage in outdoor activities without adequate adult supervision (Jamison & Kaye, 1974). Hence, many RTAs occur where children are injured as pedestrians (Jamison & Kaye, 1974; Parslow et al., 2005; Peacock, 1984; Tabish et al., 2006; Venter, 2000). These children often sustain polytrauma, which results in significant hospital and related costs annually in the US (Brysiewicz, 2001; Conner et al., 2010). This burden is even greater in Africa, where children

younger than16 years make up 50% of the population, and where the problem of RTA, pedestrian-related, TBIs are rife (Toroyan & Peden, 2007).

Road traffic accidents in Africa and South Africa. In 2000, RTAs contributed to 18 000 of the total number of deaths (approximately 500 000) in South Africa (Walker, Walker, & Wadee, 2005). Consistent with global etiological trends, RTAs have long been a major cause of severe head injuries and/or TBIs in the South African context (K. Levin, 2004; Peacock, 1984; Penn et al., 2009). RTAs involving pedestrians claim more casualties than passenger-related RTA-injuries and lead to serious head injuries and TBIs in South Africa (Brysiewicz, 2001; Lalloo & Van As, 2004; Semple et al., 1998), and 34% of cases in Africa, generally (Toroyan & Peden, 2007).

The ramifications associated with motor vehicle usage in Africa and other LAMICs, are even more potent than in HICs (Toroyan & Peden, 2007). In fact, researchers report that there are 200 times more MVAs and related morbidities and mortalities in Africa than in HICs (Van As & Rode, 2006). In a Nigerian study, RTAs accounted for 26.5% of the pediatric trauma-related mortality (Adesunkanmi, Oginni, Oyelami, & Badru, 1998). In South Africa, specifically, infants and children often die as a result of injuries sustained in pedestrian-related RTAs (Bowman et al., 2002).

In 1996, the mortality and morbidity figures for pedestrian-related RTIs in South Africa for 1-18-year-olds were 605 and 5509 cases, respectively. For 0-6-year-olds specifically, the proportions of deaths and injuries were 46% and 35% of those figures, respectively (Venter, 2000). In 1998, in South Africa, the rates for pedestrian- and passenger-related MVAs were 49% and 37%, respectively (Brysiewicz, 2001; K. Levin, 2004). These figures are consistent with findings that, in most cases, children are involved in MVAs as pedestrians (Peacock, 1984; Toroyan & Peden, 2007).

Semple et al. (1998) concluded that "pedestrian motor vehicle accidents are the most common cause of serious pediatric head injury in the Cape Town area" (p. 440). In their sample, 83% (n = 83) of the severe head injuries could be attributed to MVAs. Brysiewics (2001) also reported that pedestrian-related injuries contributed significantly to admissions to emergency departments in South Africa. Previous incidence figures for pedestrian-related injury in South Africa include that pedestrians account for 45% of the mortality-associated road traffic accidents. In 1999, an estimate of the number of pedestrian-related deaths was 4500 and the estimate of those injured in similar accidents, 26 000 (see Health Systems Trust, 1999 as cited in Brysiewicz, 2001). A number of researchers have posited various possible reasons for the burden of pTBI as a result of RTAs.

Reasons for high rates of RTA-related pTBIs in South Africa. South African law requires that seatbelts are used and that young children and infants travel in car seats while being transported (Cywes, 1990). However, non-compliance is rife. K. Levin (2004) highlights some of the reasons for this non-compliance. These relate primarily to the use of public transport for lower-SES families who do not own a car. Many of these families make use of minibus taxis, which are a common mode of transport in South Africa. This mode of transport is problematic for a number of reasons. First, many of these minibus taxis are in bad form. Second, the drivers and their assistants frequently overload their less-than-roadworthy vehicles. Third, adults travelling in taxis with young children are permitted to travel with a child on their lap until approximately 4 years of age (in such cases, that adult is only charged for one seat in the taxi instead of two). There are neither car seats for young children nor seatbelts for passengers in these taxis (K. Levin, 2004). These situations create risks for injuries, especially where the child can be injured as a passenger.

In South Africa, a large proportion (65%) of pedestrian injuries are reported to occur in the process of crossing, or being in the vicinity of, the road. The infrastructural shortfalls that seem to contribute to the high incidence of these injuries are mainly centred on a lack of dedicated pedestrian space whether it is for recreation, crossing a road, or walking alongside it (Ribbens, 2000).

With regards to older children and road traffic accidents, Selecki et al. (1968) explained that with increased age comes an associated reduction of parental/adult supervision. However, despite the assumed independence, the older child still carries a degree of naivety and perhaps a lack of awareness. The natural adoption of autonomy with age does not necessarily translate into a complete and mature understanding and awareness of the environment and the potential for road traffic accidents (Selecki et al., 1968; Semple et al., 1998) .

In many cases, the adult supervision role is delegated to the older child in the family. There is also often a lack of suitable recreational facilities, leading to a lack of dedicated pedestrian space, especially among lower-income families. This lack of dedicated space results in children playing in and/or alongside busy roads, which often lack proper pavements and are not well lit. These poor conditions increases the risk for potential injuries, especially among younger children. Children from lower SES areas often need to travel to schools on foot, and to walk to recreational facilities. There appears to be an increase in traffic volume and density, but without notable increases in methods to regulate traffic and pedestrian safety

(e.g, scholar patrols). There is also a lack of formal road safety education (Peacock, 1984; Ribbens, 2000; Selecki et al., 1968; Semple et al., 1998).

Falls. Falls are the a leading cause of nonfatal injuries (Centers for Disease Control and Prevention, and National Center for Injury Prevention and Control, 2010b), accounting for 20-30 % of TBIs (Gururaj, 1995, as cited in Hyder et al., 2007). Falls often result in hospitalizations, with figures of up to 40.7% (n = 6000) reported. Most falls related to pTBIs are typically reported for very young children. One of the highest incidence rates for falls, 594.2 / 100 000 population, are reported for children younger than 4 years of age in the United States (Langlois et al., 2004). With the 0-4 year age bracket, children under 1 year of age are particularly vulnerable to TBI-related falls (Eisele et al., 2006). Just as older children are more vulnerable to RTAs as a direct consequence of the amount of time spent playing outdoors, younger children are more vulnerable to falls because of the amount of time spent indoors, playing within the confines of that space (Tsai et al., 2004).

Assaults and non-accidental injuries. A high incidence of assaults (125.9 per 100 000) occurs among individuals of 15-19 years of age. However, young children are also at risk. Assault accounts for 6.8% (n = 1000) of hospital admissions and 31.7% (n = 348) of deaths, in the 0-4 year old age bracket (Langlois et al., 2004). Researchers also report that children younger than 1 year of age are also particularly at risk (Eisele et al., 2006).

Researchers in the field report consistently that there are a preponderance of non-accidental TBIs among the very young, especially during the first year of life (Duhaime et al., 1992; Eisele et al., 2006; Keenan et al., 2003; Wetherington & Hooper, 2006). Child abuse falls within the scope of non-accidental injuries. Hence, assaults and non-accidental injuries, especially in the very young, are often regarded with extreme caution, as child abuse is often questioned (Duhaime et al., 1992). A significant number of young children who suffer abuse also have concomitant head injuries. Child abuse is therefore also listed among the mechanisms of pTBIs, especially in the 0-2 year old age bracket (Billmire & Myers, 1985; Keenan et al., 2003; Lundar & Nestvold, 1985).

Temporal-related factors: time of day and/or year. A few studies highlight specific times during the day or year when TBI is more prominent. For example, Elgmark Andersson, Lund, and Månsson (2010) found that most injuries occurred in the afternoon and in the month of March in Sweden. However, Engberg and Teasdale (1998) previously reported that June and July were the peak months in Denmark.

When doing global comparisons of these specific trends, specific times of day that children may be more prone to injury appears to be consistent across studies. However,

comparing the prevalent months of the year may be trickier, as there will be seasonal hemispheric differences as well as varying school vacation periods. Therefore, this latter trend will likely be differentiated by country of residence or climate.

SES and minority groups. SES is another factor associated with TBI that tends to vary by country. SES is directly linked to the HIC-LAMIC comparison, such that the incidence of TBI varies as a function of SES in these contexts. There is generally an inverse relationship between low SES and higher rates of TBI. Hence, individuals from poorer socioeconomic backgrounds are at high risk for TBI. This trend extends to children too, with those residing in poorer areas at greater risk for severe TBI (Abelson-Mitchell, 2008; Bruns & Hauser, 2003; Hyder et al., 2007; K. Levin, 2004; Parslow et al., 2005).

Poverty is related to factors that place children (in particular) at risk for TBI, especially RTA-related TBI. These factors may include, for example, a lack of (a) education about road safety behaviours, (b) supervision, and (c) adequate play areas or facilities (Peacock, 1984; Ribbens, 2000; Selecki et al., 1968; Semple et al., 1998).

Bruns and Hauser (2003) also note that there may be a higher prevalence of TBIs in minority groups. South Africa is a prime example of this association (K. Levin, 2004) . In South Africa, in light of the prevalence of head injuries among low-SES groups, Coloured and Black African children, who often make up large proportions of these low-SES groups, may be disproportionately affected (De Villiers et al., 1984; Knobel et al., 1984).

Summary and Conclusion

In summary, TBI remains a leading cause of mortality and morbidity among children, globally. It is a serious public health problem that affects both HICs and LAMICs. There are, however, more risk factors for TBI in LAMICs; this increase is associated primarily with the lower SES of the latter. Epidemiological studies have identified trends related to severity, sex, age and mechanisms of injury and temporal factors.

There is huge economic burden associated with TBI-related mortality and morbidity. In spite of the impact of TBI and pTBI, specifically, it remains a silent epidemic. More research that consistently creates and maintains public awareness of the problem is needed both globally and in South Africa, where only a few studies have focused on the South African population.

CHAPTER 3:
STUDY 1: A DEMOGRAPHIC PROFILE OF CHILDREN ADMITTED TO THE RXH FOR SEVERE TBI

In this chapter, I present recent information trends in admissions for children who were admitted to the Red Cross Children's Hospital (RXH) for severe TBI over a 5-year period (June, 2006 to April, 2011).

Chapter 2 provided a review of the epidemiological trends associated with TBI, and of pTBI in particular, both globally and in South Africa. It is clear that TBI in both adults and children is a public health problem around the world. It is also clear that there are differences in the ways that TBI impacts, is experienced, and is managed across HIC and LAMICs. The literature shows that there are established epidemiological trends in terms of which segments of the population are more vulnerable to TBI, and also in terms of etiological factors. Certain trends (e.g., mechanisms of injury) vary in accordance with particular demographic variables (e.g., age). A prime example of such a trend is the evidence that falls are the major cause of injury among the very young.

Records of recent incidence rates for TBI, and pTBI in particular, are lacking in South Africa. For this reason in Chapter 2 I relied on previously published South African literature in this area of research to provide some insight into the magnitude of the problem of pTBI in this country. Researchers often allude to the fact that incidence rates for pTBIs, especially RTA-related pTBIs, are higher in sub-Saharan Africa and other LAMICs, including South Africa, than in high-income world countries (Hyder et al., 2007). One of the major factors to support such a trend is that South Africa has one of the highest motor vehicle accident (MVA) rates in the world (K. Levin, 2004) and that MVAs and RTAs in general are a leading cause of TBI in both young and older populations around the world. These findings suggest potentially high rates of injury and hospital admissions in South Africa.

The South African pTBI literature reviewed in Chapter 2 includes studies describing various profiles of pTBI admissions to the RXH in Cape Town. Close inspection of these studies suggests a pattern of continuity between some of these studies (De Villiers et al., 1984; Kibel et al., 1990; Lalloo & Van As, 2004; Semple et al., 1998). These specific publications have emerged every 6-8 years from 1984, with the last one covering a period of 10 years, up to and including 2001 (Lalloo & Van As, 2004). In this context, the current study is timely, given existing publishing trends in the area of pTBI. Regular studies and profiling of this nature are required in order for both researchers and practitioners in the field

to remain well informed and up to speed with the problem of TBIs in South Africa, particularly in the absence of formal incidence rates.

Of the four South African studies referred to above, only one (Semple et al., 1998) focused specifically on children who had sustained severe head injuries. Prevention and treatment of TBIs is reliant on such current information as there is about admissions, etiological trends and outcomes (Peacock, 1984). In this context, studies such as the current study are urgently required for both researchers and practitioners.

Aims and Expected Trends

The aim of this study is to provide a profile of the demographic characteristics of children admitted to the RXH for severe TBI over the period June 2006 to April 2011. The variables of interest included: outcome (survivors vs. non-survivors), trends by year of admission, and trends in age, sex, language, mechanism of injury, time of day, and monthly family income (MFI).

Based on the literature reviewed in Chapter 2, certain trends were expected: most TBIs would be classified as closed rather than open, there would be more boys than girls in the sample, and most children in the sample would emerge from low-SES backgrounds. This last expectation is based on the fact that "most of the patients [at RXH] are from disadvantaged communities throughout South Africa and Africa" (Dodd, 2006, p. 109). Further, I expected that MVAs would constitute the primary mechanism of injury in the sample, especially where the child was injured as a pedestrian. Finally, I expected that the frequencies in etiological factors would vary as a function of age: falls would be the more prominent cause of injury among the very young, while MVAs would be the more prominent cause of injury among the older children.

Methods

Study Setting and Design

This is a demographic profile study of children admitted to the RXH in Cape Town, SA. It adopted a retrospective, descriptive, quantitative design. Retrospective designs permit data to be collected expeditiously and over a longer period of time than may be afforded by prospective studies.

Sample

The study sample included all children admitted to, and treated at, the RXH neurosurgical ward for severe TBI from June 2006 to April 2011.

At the RXH, the triage system includes initial admission to a general trauma ward before referral to specialist units. A trauma register of all patients is maintained at this general trauma ward. The register includes relevant sociodemographic and clinical details for each patient, including name, age, sex, folder number, and the nature of the accident and injury. The Division of Pediatric Neurosurgery has direct access to these data, which have, over recent years, been captured and converted from handwritten, paper forms to electronic files.

I included in the sample all children whose names appeared in the Division of Pediatric Neurosurgery database, and who were admitted to the RXH from July 2006 to April 2011 for a severe TBI. All of these patients had an initial GCS score of ≤ 8, as reported in patient records. Outside of these eligibility criteria, no patients were purposefully excluded.

Procedure and Data Collection

Initially, I approached the Head of the Division of Pediatric Neurosurgery about conducting the study. Once permission was granted, I could access the patient records. I obtained the information for this study from two sources: the Division's database, which includes information about children admitted and treated for severe TBI at that unit, and the actual patient case folders at the RXH.

Information from the Division of Pediatric Neurosurgery Database. The database for pTBI includes demographic data about patients, similar to those details captured in the trauma register. In addition to those demographic data, the database includes other neurosurgically relevant data (e.g., GCS scores and other neuromonitoring data). Hence, the classification of severe pTBI for all children included in the study was professionally determined in Division. I obtained information for the following variables through this initial step: age, sex, mechanism of injury, GCS score on admission, time and date of injury, nature of injury (open vs. closed), and outcome. Following this step, I searched for each of the case folders.

Case folders. Following typical hospital admission protocol, a case folder containing the patient's records is created for every patient admitted to the RXH. This folder is stored at the Records Department at RXH. In addition to the medical history of the patient and other important documents, the case folders include a trauma unit record form (detailing the accident and injury) and an information sheet (including personal details, details of the parents/guardians and their contact information and sometimes, the monthly family income (MFI)). These forms are not always complete, with various pieces of information being omitted. These omissions may occur if, for example, a person other than the parent admits the child and that person does not have the necessary information about the parents at hand.

Despite these omissions, with the assistance of a postgraduate student in Psychology, I obtained all of the available information for the following variables: language, MFI, names and contact information for parents and/or guardians, and outcome. Eventually, the search for information about language and MFI was only collected for survivors, because the case folders for non-survivors were stored separately from those for survivors and were not accessible at the time of data collection.

Statistical Analysis

I conducted statistical analyses of the data to assess the demographic trends in pTBI admissions. These trend analyses are descriptive and were computed for the following variables: rate of survival, nature of injury, yearly admissions, age, sex, and language, mechanism of injury, time of day, and MFI. I computed these analyses using SPSS version 20.0.

Ethical Considerations

The University of Cape Town Faculty of Health Sciences Ethics Review Committee approved this study (Reference Number: 166/2009; see Appendix A). This study forms part of a larger ongoing study, the aim of which is to create a registry for neurotrauma. This study did not involve contact with patients. The Head of the Division of Pediatric Neurosurgery provided me with access to the initial data set and I collected subsequent data through manual perusal of patient files.

Because RXH is an academic hospital affiliated to UCT, permission for the use of children's medical data for research purposes is sought from parents and guardians upon hospital admission of their children. Permission to access the folders at RXH had previously been granted (see Appendix B).

The research team maintained confidentiality when dealing with patient records and information. I do not include patients' names or any other potential individual identifiers in this report.

Results

The sample included 137 children. There was a 14.6% (20/137) mortality rate. Of the 117 survivors, 110 (94.02%) of the TBIs were classified as closed and 6 (5.13%) as open, with data missing for one participant.

Trends

Annual admissions. Figure 1 presents the admissions for each of the years included in the study period. Note that admission data for the years 2006 and 2011 do not cover the

entire year. Therefore, for fair comparisons of annual admissions, the years 2007 to 2010 present the most complete data sets, and are therefore a fairer reflection of annual trends (see Figure 2 for annual admissions of survivors only). Figure 2 shows that the number of admissions did not vary substantially, year-on-year from 2007 through 2010.

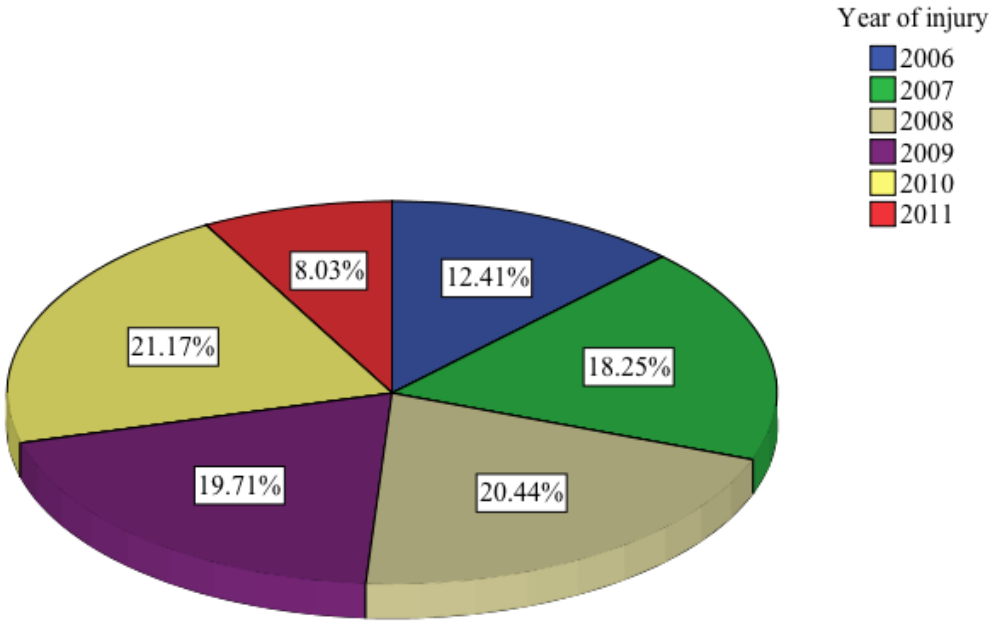

Figure 1. Number of admissions per year. *N* = 137; Months covered in 2006 are April to December, and for 2011, January to June.

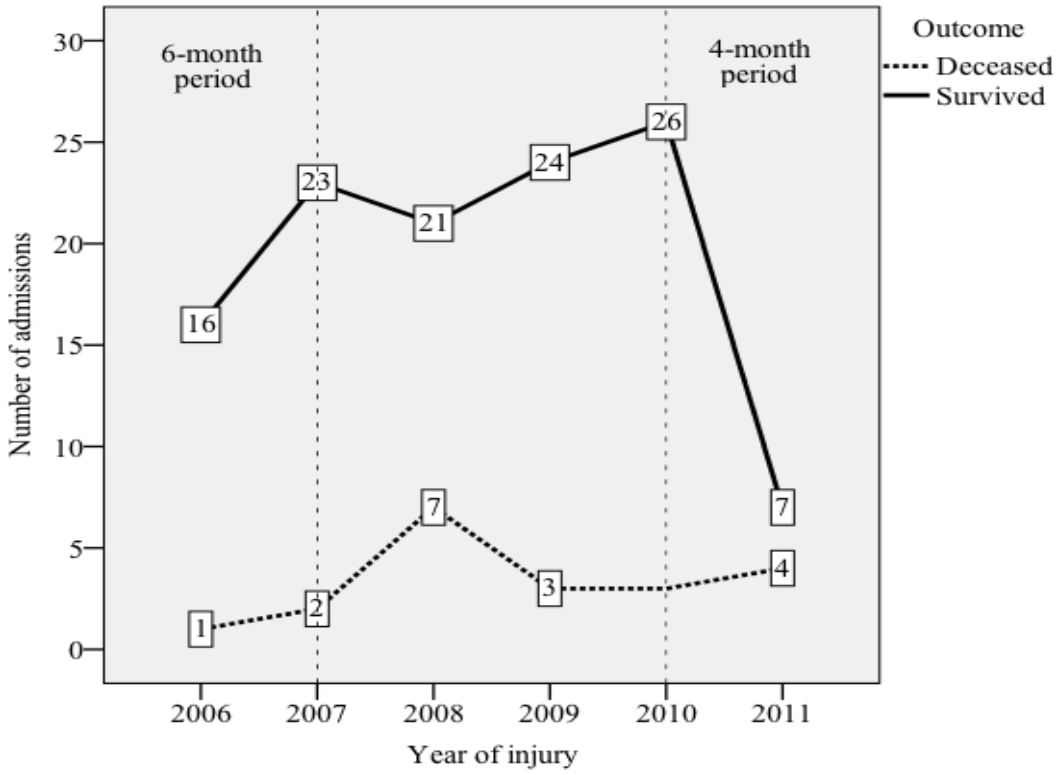

Figure 2. Number of admissions per year for survivors and non-survivors.

Age. The mean age of the total sample (*N* = 137) was 6.14 years (*SD* = 3.71, range: 0-14.75 years). In Table 1 the sample is divided into four groups based on age. The highest number of injuries occurred in the 0-4-year-old age group, followed by the 5-8 and 9-12-year-old age groups. The smallest number of participants was in the 13-15-year age group. There were 117 (85.4%) survivors.

Table 1

Age of Participants by Group vs. Outcome: Crosstabulation (N = 137)

Age by group	Outcome		Total	Percent (Total)
	Deceased	Survived		
0-4 years	9	40	49	35.77
5-8 years	6	40	46	33.58
9-12 years	5	35	40	29.2
13-15 years	0	2	2	1.46
Total	20	117	137	100

Figure 3 displays the number of children admitted at each age, from 0 to 15 years. As can be seen, the peaks in admissions by age occurred at 4, 6, 7, and 10 years.

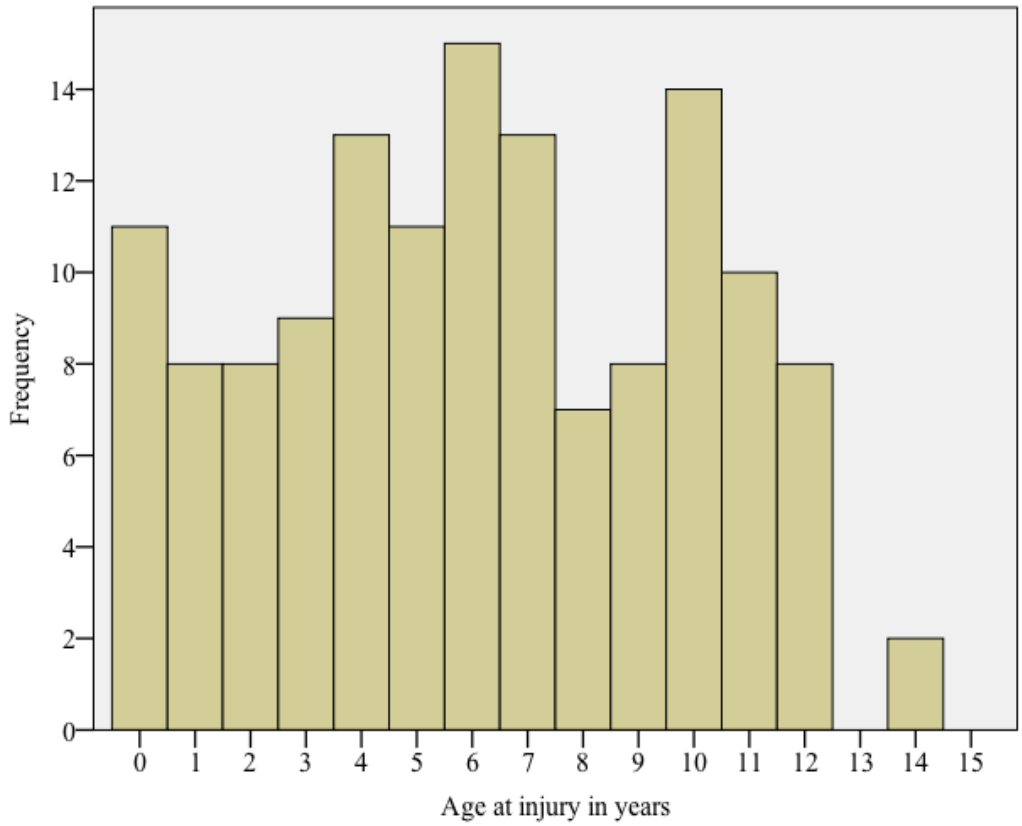

Figure 3. Number of admissions for each year of age (0-15 years). $N = 137$; $M = 6.14$; $SD = 3.71$.

Sex. There were more males (n = 89) than females (n = 48) in the sample. Hence, males made up 64.96% of the sample. This ratio held constant across all five years of admission, with the exception of 2009, where an equal number of boys and girls were admitted. This ratio also held constant for all ages, except for 3- and 10-year-olds, as depicted in Figure 4.

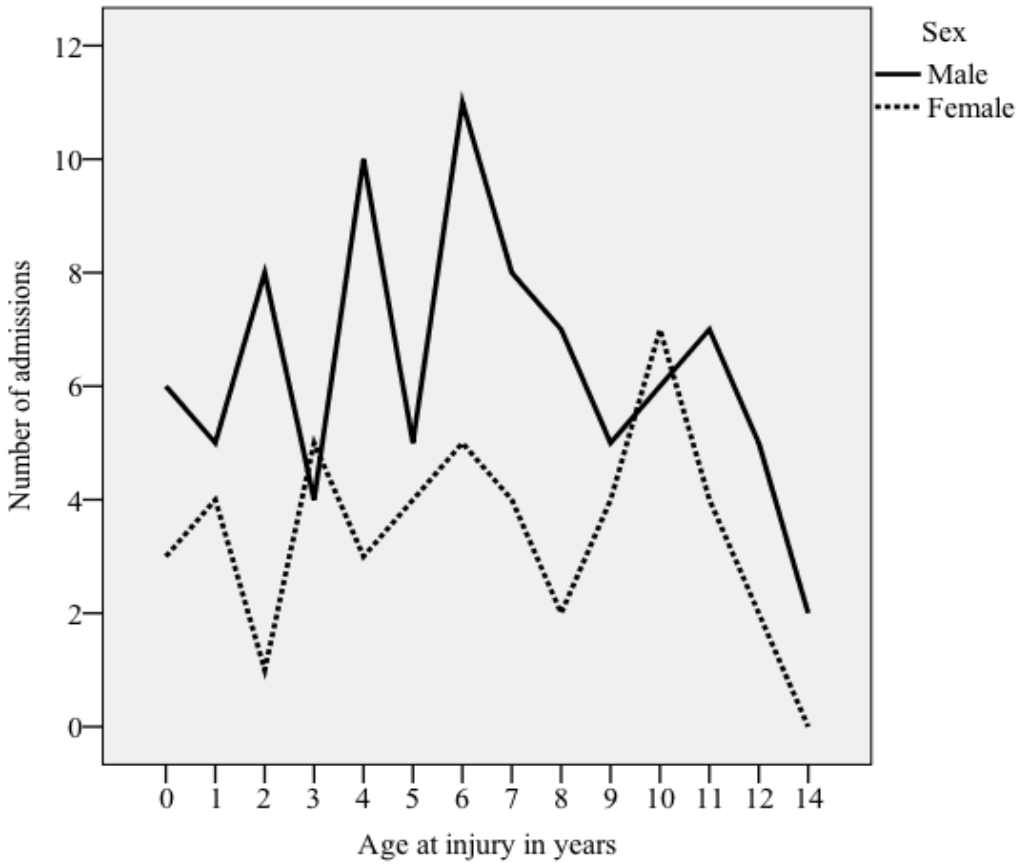

Figure 4. Age at admission, for boys and girls separately.

Table 2 presents a crosstabulation of the number of male and female admissions for the four age group categories. Most male and female patients were 0-4 years of age, followed closely by those aged 5-8 years.

Table 2

Age by Group vs. Sex: Crosstabulation

	Gender			
Age by group	Male	Female	Total	Percent
0-4 years	33	16	49	35.77
5-8 years	31	15	46	33.58
9-12 years	23	17	40	29.19
13-15 years	2	0	2	1.46
Total	89	48	137	100

Language. There were three languages spoken by the children and their families in the sample: English, Afrikaans, and isiXhosa (see Table 3), with the highest frequency being for Afrikaans. Frequencies for the three languages did not differ substantially. These results only reflect the languages spoken by the survivors in the sample, as the information for non-survivors could not be accessed at the time of the study.

Table 3

Home Languages of Survivors (N = 117)

	Frequency	Percent
English	37	31.6
Afrikaans	41	35.04
isiXhosa	34	29.06
Other	1	0.85
Missing	4	3.42
Total	117	100

Mechanisms of injury. Table 4 lists the mechanisms of injury for the sample. As can be seen, most injuries occurred as a result of pedestrian-related MVAs, followed by passenger-related MVAs. This trend was consistent for both survivors and non-survivors. Among the non-survivors, 11/20 (55%) deaths were road traffic-related and 7/20 (35%) were specifically MVA-pedestrian related. Falls and non-accidental injuries (NAIs) each accounted for 10% (2/20) of the total mortalities in the sample.

Table 4

Mechanisms of Injury for Survivors and Non-Survivors (N = 137)

	Survivors	Non-survivors	Total
MVA pedestrian	68	7	75 (54.7%)
MVA passenger	25	4	29 (21.2%)
MVA other	5	0	5 (3.6%)
Fall	5	2	7 (5.1%)
Assault	1	0	1 (0.7%)
Struck by/against an object	2	0	2 (1.5%)
Non-accidental injury	2	2	4 (2.9%)
Crush injury	2	1	3 (2.2%)
Gunshot wound	4	0	4 (2.9%)
Stab wound	2	0	2 (1.5%)
Missing data	1	4	5 (3.6%)
Total	117	20	137

Peaks and troughs in the mechanisms of injury can vary as a function of age and/or sex. These results are presented below.

Cause of injury vs. age at injury. Table 5 depicts the trends in cause of injury across different age categories. There was a significant association between these variables, $p = .03$. MVAs involving the child as a pedestrian accounted for large proportions of injuries in the 0-

4-, 5-8-, and 9-12-year-old age categories. Larger proportions of children in the older age groups sustained MVA-related injuries. Few falls were reported relative to MVA-related injuries. Falls were highest in the 0-4 year age group followed by the 5-8 year age group.

Table 5

Crosstabulation of Cause of Injury by Age Group (N = 137)

Cause of injury	Age group				Total
	0-4 years	5-8 years	9-12 years	13-15 years	
MVA pedestrian	22 (44.90%)	26 (56.52%)	26 (65.00%)	1 (50.00%)	75 (54.74%)
MVA passenger	11 (22.45%)	11 (23.91%)	7 (17.50%)	0 (0.00%)	29 (21.17%)
MVA other	0 (0.00%)	1 (2.17%)	4 (10.00%)	0 (0.00%)	5 (3.65%)
Fall	5 (10.20%)	2 (4.35%)	0 (0.00%)	0 (0.00%)	7 (5.11%)
Struck by/against an object	0 (0.00%)	1 (2.17%)	0 (0.00%)	1 (50.00%)	2 (1.46%)
Crush injury	2 (4.08%)	1 (2.17%)	0 (0.00%)	0 (0.00%)	3 (2.19%)
Non-accidental injury	4 (8.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (2.92%)
Gunshot wound	3 (6.12%)	0 (0.00%)	1 (2.50%)	0 (0.00%)	4 (2.92%)
Stab wound	1 (2.04%)	0 (0.00%)	1 (2.50%)	0 (0.00%)	2 (1.46%)
Assault	0 (0.00%)	1 (2.17%)	0 (0.00%)	0 (0.00%)	1 (0.73%)
Missing data	1 (2.04%)	3 (6.52%)	1 (2.50%)	0 (0.00%)	5 (3.65%)
Total	49	46	40	2	137

Cause of injury vs. sex. Figure 5 depicts the trends in cause of injury for boys vs. girls in the sample. Boys and girls show similar trends across the various mechanisms of injuries. The association between cause of injury and sex was not significant, $p = .78$. However, the proportion of boys injured as pedestrians in MVAs was almost double the proportion of girls injured in this way.

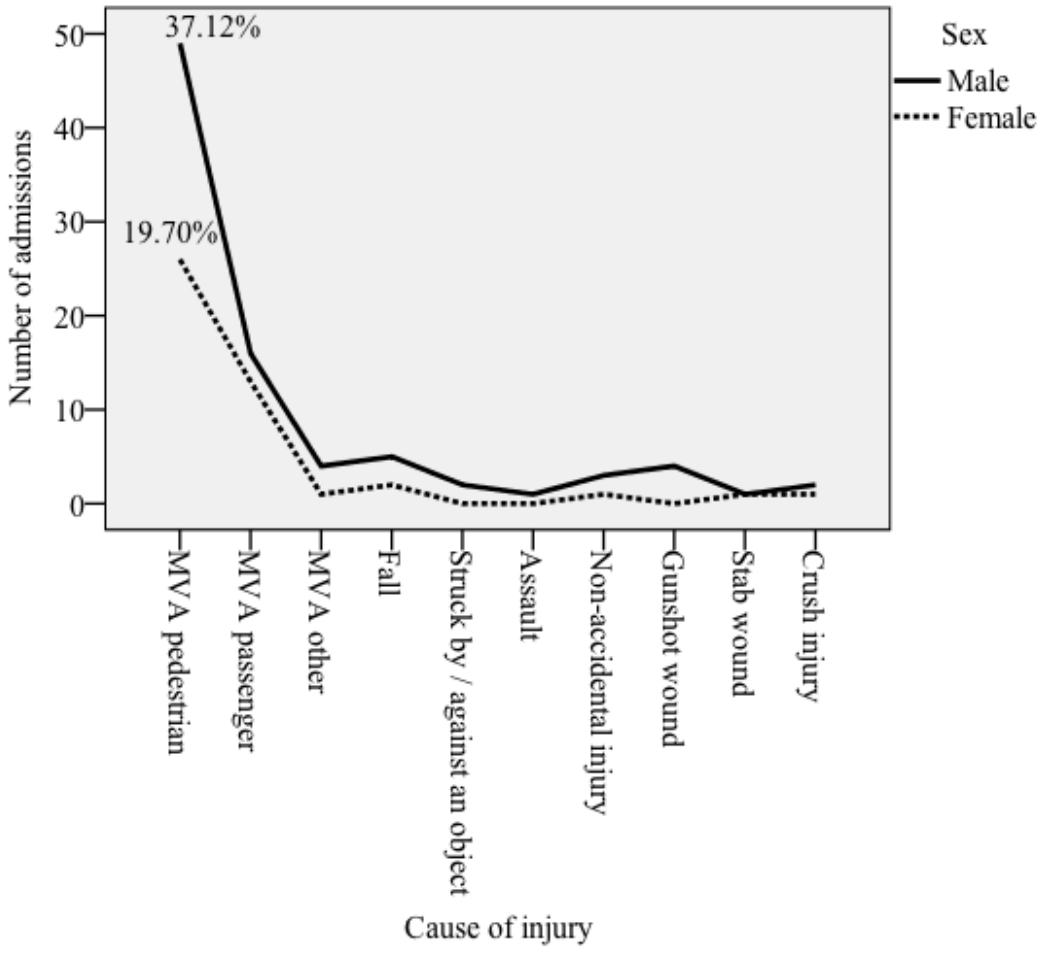

Figure 5. Trends in cause of injury for male vs. female participants

Time of day. Figure 6 displays a crosstabulation of the time of injury by the day of the week when the injuries were most frequent. Most injuries occurred during the afternoon (from noon to before 5pm), followed by injuries in the early evening (5pm to before 8pm). Most injuries also occurred on weekends.

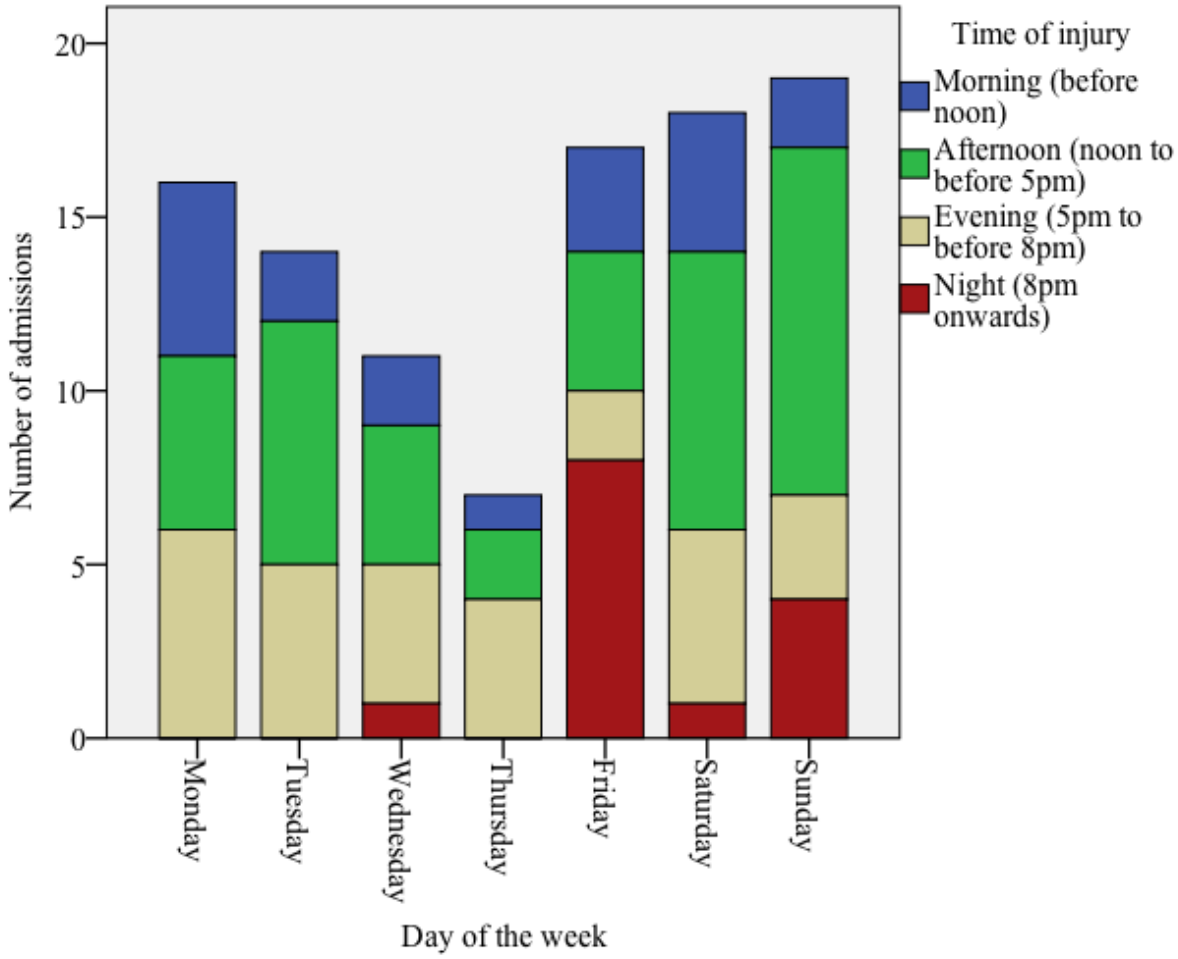

Figure 6. Day of the week vs. time of day when most injuries occurred.

Monthly family income (MFI). Table 6 lists categories for monthly family income as they appear in the patients' case folders. This information is often omitted, hence the proportion of missing data (39.4%; $n = 54$). Most parents/caregivers (> 50%) of patients for whom this information was available were either unemployed (26.3%; $n = 36$) or did not earn more than ZAR5000 per month (29.2%; $n = 40$).

Table 6

Monthly Family Income for All Participants (N = 137)

	Frequency	Percent
ZAR0/unemployed/housewife	36	26.3
ZAR1-R5000	40	29.2
ZAR5001-R25000	5	3.6
>ZAR25000	2	1.5
Unknown/Missing	54	39.4
Total	137	100

Discussion

The purpose of the study was to provide an updated profile of children admitted for severe TBI to the RXH in Cape Town, South Africa. A similar study on the profile of children admitted for severe TBI to the same health care facility was conducted more than a decade ago (Semple et al., 1998). The importance of generating this updated profile is two-fold. First, this profile is important in terms of staying abreast of current trends in this major public health problem. This updating process is especially important when local published research on this subject in South Africa is, in general, limited. Generating current knowledge of the profile of pTBI is crucial for prevention of, and intervention efforts in, pTBI. Second, data described and analysed in this study provide a contextual backdrop to those described in the other two studies included in this dissertation.

In the remainder of this discussion, I elaborate on the findings of this study and compare them to previously reported results in the literature. I also discuss the use and value of these findings for pTBI prevention campaigns. Finally, I note the limitations of this research and put forward recommendations for future research.

Trends

Age. Although the age range of the sample extended from 0 to 14.75 years of age, there were only two children in the 13-15-year-old age bracket. This piece of data is not surprising, as the RXH mostly admits children up to 12 years of age. The fact that most

children in the sample fall within the 0- to 12-year old age range is fitting, given that there appear to be a significant proportion of children who sustain TBIs within this age bracket, generally. This is evident from the volume of published literature focused on this age group (Berry et al., 2010; Elgmark Andersson et al., 2010; Engberg & Teasdale, 1998; Langlois, Rutland-Brown, & Thomas, 2005; Parslow et al., 2005; Tsai et al., 2004).

Sex. The results for this study were consistent with the long-established trend (e.g., Abelson-Mitchell, 2008; V. Anderson, Northam, Hendy, et al., 2001; Bruns & Hauser, 2003; Faul et al., 2010) that TBIs occur more frequently among males than females. In this sample, boys were 1.86 times more likely than girls to sustain a severe pTBI. Berry et al. (2010) and Parslow et al. (2005) report similar rates of 1.9 (high-threat-to-life TBIs) and 2.02 for similar age groups, respectively.

Mortality. In Chapter 2, I reviewed literature indicating that many children of different ages die as a result of TBI (e.g., Tilford et al., 2005; Tude Melo et al., 2010). Based on this evidence and the preponderance of TBI in the 0-14 year old age group as reported before, it is not surprising that mortality is often described as a consequence of TBI in this age bracket (Bahloul et al., 2009; L. Williamson, Morrison, & Stone, 2002). It has also previously been reported that 65% of children who sustain severe TBIs survive (Berger et al., 1985).

There are varying rates of mortality from pTBI reported in published SA-based research. For example, in their 15-year study of trends in mortality, Knobel et al. (1984) reported that in 3248 autopsy reports reviewed for children, 819 (25.2%) deaths occurred as a result of severe head injuries. Semple et al. (1998) reported a mortality rate of 57% (58/102) over a 4-year period (January 1990 – December 1993). In a later study, Figaji et al. (2009a) reported a mortality rate of 9.62% (5/52) over a 2-year period (June 2006 – May 2008).

Varying, and mostly lower, mortality rates are also reported in studies from HICs. For example, Parslow et al. (2005) reported a mortality rate of 9.2% among 0-14 year olds, over a 2.5-year period (February 2001 – August 2003) in the United Kingdom. A number of studies do not specifically focus on severe pTBI and therefore include samples that include participants from all severity groups. For example, Tsai et al. (2004) reported a 2.4% mortality rate for their total sample, where mild TBI participants made up 83% of their sample. They reported that there were more fatalities among those admitted for severe pTBI, but did not include the actual figure.

Although the proportion of fatalities in our sample (14.6%) is higher than the proportion of deaths reported in some other studies mentioned above (Figaji et al., 2009;

Parslow et al., 2005), it is still lower than the findings reported by Knobel et al. (1984). It is also substantially lower than the proportion of deaths reported by Semple et al. (1998), whose study is the similar in most respects to the current study in terms of context, design, and sample size. In the current study, 85.4% of the sample in this study survived, a proportion which is also higher that a survival rate of 65%, previously reported (Berger et al., 1985).

Although severe pTBIs are still associated with a significant number of deaths, the results reported here are promising and, most importantly, show a downward trend in terms of mortality rates over the past decade for children admitted to the RXH for severe TBI. These findings shed a positive light on the management and care of children admitted for pTBI in South Africa, and, specifically, at the RXH. A further positive step towards reducing pTBIs and pTBI mortality rates would be for the country to devise a strategy to curb the incidence of accidents resulting in pTBI, especially given that MVAs remain the leading cause of such injuries globally and in South Africa.

Main mechanism of mortality and morbidity: motor vehicle accidents (MVAs). Globally, a significant proportion of TBI-related injuries and deaths are associated with MVAs (Abelson-Mitchell, 2008; Baldo et al., 2003; Hillier et al. 1997; Hyder et al., 2007). These findings apply specifically to children and adolescents too, with MVAs cited as a primary cause of death among youth (ages 1-19) in the US (Borse et al., 2008).

In many MVAs, children are injured as pedestrians (Brysiewicz, 2001) or as "soft" road users. This latter term is derived from the fact that pedestrians have limited protection against injury and that they travel more slowly than motorcars (Engberg, 1995 as cited in Emanuelson & Wendt, 1997). Researchers also report pedestrian-related MVAs to be a major cause of injury and death in South African studies, which is not surprising given that this country has one of the highest MVA rates in the world (K. Levin, 2004).

In the current study, road traffic-related incidences, generally speaking, accounted for 109/137 (79.56%) of the injuries and 11/17 (64.71%) deaths. However, these figures include MVAs involving pedestrians and passengers, as well as 'other' MVA incidences (e.g., bicycle, motorcycle, or unspecified MVAs). MVAs, where the child was injured as a pedestrian, specifically accounted for 75/137 (54.74%) of the total admissions and 7/17 (41.18%) mortalities. The finding that RTAs, especially those involving pedestrians, constituted the leading cause of injury and death in this sample of children with severe TBI, is consistent with previous South African and international literature (De Villiers et al., 1984; Knobel et al., 1984; Lalloo & Van As, 2004; Parslow et al., 2005; Semple et al., 1998; Tsai et al., 2004). Although the results reported in this study are less favourable than those reported

in some international studies (e.g., Parslow et al., 2005; Tsai et al., 2004), they appear to be show an improvement in terms of the number of MVA-related injuries as compared to those reported in a previous comparative SA study (Semple et al., 1998), where pedestrian-related MVAs accounted for 83% (83/100) of injuries. More effective injury prevention efforts could be responsible for this improvement.

However, although the number of injuries as a result of pedestrian-related MVAs appears to have diminished, the overall morbidity and mortality rate related to MVAs generally remains of concern (MVA-related morbidity: 79.56% (109/137); MVA-related mortality: 64.71% (11/17)). Thus attention to, and intervention in this preventable public health problem, would seem to be of some urgency.

Age effects related to MVAs. Even though the frequencies of both MVAs generally, and pedestrian-related MVAs specifically, may be similar across the three main age groups (0-4, 5-8, and 9-12 years)[1], the proportion of injuries relative to the total number of children in each of those age groups tells a different story: Older children are more prone to injuries as a result of MVAs, and as a result of pedestrian-related MVAs in particular. These results are consistent with findings reported both locally and internationally (Brysiewicz, 2001; Tsai et al., 2004).

Researchers suggest various reasons for this trend. These include that children in this age group spend a large amount of their extramural time outdoors, in the absence of suitable recreational areas, and the likelihood of their travelling to school independently, i.e., without adequate adult supervision (Jamison & Kaye, 1974; Peacock, 1984).

Among the younger age groups, especially the 0-4-year-old group, the finding that pedestrian-related MVAs accounted for 44% of injuries is of serious concern. Researchers have suggested that this vulnerability of young children to MVAs may be a developmental issue; their sensory perception, reflexes, and their ability to judge the speed and distance of oncoming traffic may not be fully developed (Venter, 2000). Another possibility is that these young children are injured while playing unsupervised on the sidewalks in the vicinity of their homes, or that they are involved in pedestrian-related MVAs while being carried by an adult.

Sex-related trends associated with MVAs. The well-established trend that males are more likely to sustain TBIs than females holds true for MVA-related injuries as well (Brysiewicz, 2001; Rickels et al., 2010). For instance, Rickels et al. (2010) found that males

[1] Recall that there were only 2 participants in the 13-15 year age group.

were 1.4 times more likely than females to be involved in accidents. In the current study, the number of MVA etiologies was generally higher for males (63.3%; 69/109) as compared to females (36.7%; 40/109), but this difference was mainly because of the high number of pedestrian-related MVAs for males (65.34%; 49/75) as compared to females (34.67%; 26/75). Researchers attribute this trend to the relatively rash behavioural tendencies of boys (Tsai et al., 2004; Venter, 2000).

Other mechanisms of injury. There were no other substantial differences in terms of the mechanisms of injury for males as compared to females. As mentioned above, MVA-related incidences accounted for the major proportion of the injuries for both sexes, even though males were more prone to these injuries. Nonetheless, although the important causal role of MVA-related events is clear in the current sample, 20.44% of the TBIs were attributable to other causes.

In some studies, both falls and RTAs are described as leading causes of TBI (e.g., Tabish et al., 2006). In others, the leading mechanism of injury for pTBI varies between RTAs (Conner et al., 2010; Emanuelson & Wendt, 1997; Parslow et al., 2005) and falls (Falk, 2010; Melo et al., 2006), depending on the sample. In the current study, falls were not the leading cause of TBI, nor were they the leading cause within the 0-4-year-old age group, where, according to literature, this latter outcome may have been expected (Eisele et al., 2006; Langlois et al., 2004). Indeed, falls accounted for only 5.11% of TBIs in this sample. This result is consistent with, and even lower than, previously published studies that included children of the same age range. For example, Tsai et al. (2004) reported a rate of 5.1 % (105/2078) in Taiwan and Parslow et al. (2005) reported a rate of 15% (18/118) in the UK among children with severe TBI. The current results are similar or lower but offset by the relatively high rates of MVAs.

Two South African studies described falls as the leading cause of injuries. Kibel, Bass, and Cywes (1990) found that falls accounted for 40.78% (10181/24964) of injuries generally, and 39.61% (4033/10181)of head injuries; they constituted the most significant cause of injury in that study. Similarly, in a recent report, Haaring et al. (2011) found falls to be the main cause of trauma in their study sample. However, most injuries in the reports referred to above (Haaring et al., 2011; Kibel, Bass, & Cywes, 1990) were minor or mild to moderate, respectively.

Thus, it appears that falls generally predominate where mild injuries are most prevalent. The current results fit this trend: The sample for this study included only children who had sustained severe TBIs, and there were few TBIs caused by falls. Hence, outcomes

for pTBIs associated with falls may be relatively better than outcomes associated with MVAs. TBIs that occur because of MVAs often lead to DAI and severe or even fatal outcomes. Falls more commonly lead to focal insults because of translational forces (Wetherington & Hooper, 2006). We would therefore not expect falls to be a etiological factor in a high number of TBIs in this sample.

Although MVAs accounted for more than 85% (76/88) of TBIs in the 5-8-, 9-12-, and 13-15-year-old groups taken together, leaving minimal room for other causes of injury, more than 30% (15/49) of injuries were caused by non-MVA-related mechanisms in the 0-4 year-old age group. Falls accounted for 10.20% (5/49) of that 30.61% (15/49), leaving 20.41% (10/49) of injuries in the 0-4-year-old age bracket occurring because of non-MVA-related and non-fall-related causes.

The remaining causes of injury in the 0-4-year-old age group (n = 10) in the current study included: three incidents of gun-shot wounds, 1 incident of a stab wound, two incidents of crush injuries, and four occurrences of non-accidental injuries. Non-accidental injuries are most often reported for this age group. Hence, these findings are consistent with reported trends in the literature (Ewing-Cobbs, Prasad, Kramer, & Landry, 1999).

Language and monthly family income. I included these variables because of their importance in assessment and intervention, the core neuropsychological elements in Studies 2 and 3. MFI can also serve as a proxy for SES.

Language. Knowing the mother tongue languages of participants is key for neuropsychological assessment and intervention, which are important in the overall care of these children. Hence, the current results can be used to inform future studies that include assessment and intervention. Many neuropsychological test batteries, including those designed for children, originate from HICs, where English is the dominant language. In the current study, three dominant languages emerged, reflecting the three dominant languages spoken in the Western Cape: English, Afrikaans, and isiXhosa. Studies on this population will be limited in the scope of assessment and sample size (see Study 2) if efforts are not made to translate and validate measures for assessment into the mother tongue of participants.

Monthly family income. Although almost 40% of the data regarding MFI were missing, the remaining data show most children in this sample as coming from low SES backgrounds. There were substantial proportions of the sample that reported monthly income rates of ZAR5000 or less. The percentage of those family members that reported being unemployed or being a housewife was 26.28 % (36/137).

These findings have implications for the affordability of specialized health care e.g., rehabilitation. Although conventional rehabilitation, comprising speech therapy, occupational therapy, and physiotherapy, is available for children who have suffered TBIs, neuropsychological rehabilitation is not readily available to the general public in South Africa. The low SES of the majority of the population and the large number of families living in poverty dictate the way in which pTBI is experienced in the South African context (K. Levin, 2004).

Time of day and day of the week. The discussion on pTBI up to this point has outlined the profile of the children with pTBI who are injured, and how they are injured. This section focuses on when they are most likely to be injured.

The data showed that most injuries occurred during the afternoon (noon to 5pm), followed by the evening (until 8pm). This finding is consistent with previous studies (Kibel, Bass, & Cywes, 1990; Parslow et al., 2005). Children are generally returning home and engaging in extramural play at these times of day.

With regard to the day of the week, the current data showed that Saturdays and Sundays were the peak days on which TBIs occurred. Knobel et al. (1984) also reported that most deaths in their study occurred following injury on Saturdays and Sundays. Weekend days are non-school going days in South Africa, which allow for more activity and more exposure of children to the environment. These and the other trend-related results discussed above have the potential to provide important information for pTBI prevention campaigns.

Prevention

The results presented and discussed above highlight subgroups within the pTBI population admitted for severe TBI to the RXH who are potentially more vulnerable to injuries of this nature. The high-risk profile presented includes those who are most vulnerable, based on these results, and how their injuries occur, as well as when these injuries are most likely to occur. Based on this profile, prevention efforts should focus broadly on children from low SES backgrounds within the 0-12-year-old age range, with special attention given to the 0-4-year-olds.

Boys appear to be more at risk, regardless of age. Therefore, some prevention efforts should be directly focused on this group. Prevention strategies also need to target pedestrian-related MVAs, in particular. In doing so, such strategies should take into account the finding that most TBIs occur on the weekends, during the evening and afternoon.

The reasons presented by researchers to account for trends such as these, such as poor supervision of young children, speak to a need for such campaigns. These campaigns could

focus on road safety awareness, and should highlight pediatric groups that appear to be especially vulnerable to MVA-related incidents. The dissemination of road safety information and active awareness-building campaigns appear to be key in these prevention efforts.

Significance of the Study

Any TBI prevention strategy is reliant on current information about admissions, etiological trends, and outcomes (Jamison & Kaye, 1974; Peacock, 1984). Injury surveillance is also necessary and important (Tabish et al., 2006). The current study provides recent information on admissions and trends in admissions for a group of South African children who were admitted to the RXH for severe TBI. Few studies of this nature focus specifically on severe TBI within a restricted age range. Regular, up-to-date profiles, such as those presented in this current study, are needed to inform prevention strategies. Such profiles might also be viewed as contributing to surveillance efforts.

The mortality rate in the current study was 14.6% (20/137). The apparent decrease in mortality rates over the past decade may suggest the positive impact of current prevention efforts. In this context, the current study may contribute to existing prevention and awareness building efforts (e.g. Arrive Alive campaigns; Arrive Alive South Africa, 2013) by specifying the demographic target groups in most need of intervention following severe TBI.

Limitations and Future Directions

One limitation of the study may be that information on multiple TBIs within individuals was not included in the analyses. Previous research shows that sustaining a TBI increases one's vulnerability to future TBIs, with a cumulative effect in terms of risk (McKinlay et al., 2008). Recurring incidences of TBIs among participants in a study would be an aspect to consider in a future update of this or other similar profiles.

This limitation could be addressed by using a prospective instead of a retrospective design, as was employed in this study. A prospective design could afford the collection of a wider scope of information about each child included in the sample, including the history of each child's admissions and the circumstances surrounding these admissions. Further, this design would also allow for the collection of data on all pTBI severities so that an estimate of the overall prevalence of pTBI for 0-12-year-olds at RXH can be computed (McKinlay et al., 2008). Prospective designs are commonly used in TBI epidemiology studies (Parslow et al., 2005; Rickels et al., 2010). Time and resource constraints did not allow for the option of a prospective design for this study, however.

In addition to the retrospective nature of the study, its cross-sectional design may also be considered a limitation, as outcome or long-term follow-up data are not included.

However, the specific purpose of this study was to generate a profile of children admitted for severe TBI to the RXH, and based on the results, one can consider this aim met.

Finally, the fact that the case folders for non-survivors were not accessible at the time of this study might also be considered a limitation. This non-accessibility meant that data on two variables, language and MFI, could not be collected for 14.6% (20/137) of the sample, however.

In spite of these limitations, this study provides a valuable contribution to the South African pTBI literature. Bearing in mind both the magnitude of the problem of pTBI in LAMICs like South Africa, and the poor outcomes associated with it, especially with regards to severe TBI, it is essential that epidemiological, follow-up and outcomes studies, be conducted in these countries. A follow-up study on the educational and behavioural outcomes of the children included in this study who were of school-going age at the time of sustaining their TBI, is currently underway.

The results of this study have implications for a range of different related processes and research activities. Prevention strategies developed and found to be effective in South Africa could be adopted in other LAMICs. In addition, this study contributes to the global epidemiological literature on severe pTBI in general, and the 0-14-year-old age category, specifically.

Conclusion

This purpose of this study was to present a snapshot of the profile of children admitted to RXH for severe TBI from June, 2006 to April, 2011. More than 100 children are included in the sample to generate this profile. Of course, the data presented in this study show only a fraction of the whole problem. Greater efforts at prevention and surveillance, as well as at generating awareness among the public, are required to address this public health problem, particularly in South Africa and other LAMICs. Without an increase in efforts of this nature, TBI, and in particular pTBI, will remain "a neglected disease of modern society" (Cywes, 1990, p. 381).

This 'disease' is not, however, foreign or unknown. We know the trends, we have an idea of the short- and long-term impact of it on our children and on our society, and we have some idea of the projected impact. The WHO projects that by 2020 the number of deaths and disabilities attributed to TBI will have increased (Hyder et al., 2007). On a positive note, however, with the technological advancements currently underway, this forecast for the next decade could be matched, or even neutralized, by the advancement of modern medicine. There is hope that these advances will outstrip the rise in numbers of TBIs in years to come.

However, such advances in medical science may not be accessible to all who need the benefit of them, especially in light of the high prevalence of TBI in lower SES contexts.

Therefore, the standard and most accessible or implementable approach to this global public health epidemic remains prevention. Failing this, particularly in the case of severe TBI, we will continue to be faced with increasing rates of TBI-associated pediatric morbidity and mortality. Better care leads to lower mortality, but lower mortality can translate into greater morbidity, suggesting greater needs for long-term care and rehabilitation. Therefore, prevention is paramount. For those children who survive a severe TBI, a crucial step in the process of management and care is to find a way to limit the short- and long-term effects of the injuries that were not prevented in the first place. The greatest challenge in the scope of care is perhaps that of limiting the effects of potential secondary injuries.

CHAPTER 4:
BRAIN OXYGENATION AND NEUROPSYCHOLOGICAL AND BEHAVIOURAL OUTCOMES FOLLOWING SEVERE PEDIATRIC TBI.

A significant number of deaths and disabilities in children are associated with traumatic or other acute brain injuries (Coronado et al., 2011; Faul et al., 2010; Figaji, 2010a; Narotam et al., 2006). As noted earlier, the injuries from TBI are not only limited to those sustained on impact (i.e., to the primary injury/ies). There are also secondary injuries that can occur as a consequence of the primary injury. Primary injuries are aptly described as better prevented than cured, because specific treatments for such injuries per se are limited (Figaji et al., 2009b; Peacock, 1984). The degree of seriousness of the primary injury may escalate rapidly and be aggravated at a secondary injury level (Narotam et al., 2006). Hence, TBI should not be seen as one single treatable injury: it is a dynamic, progressive process (Figaji, 2010b; Rohlwink & Figaji, 2010).

Secondary Injuries

The association between secondary neuronal injuries, including hypoxia (systemic or injury-related), hypotension and intracranial hypertension, and unfavourable outcome is well documented in both the adult and pTBI literature (Chambers et al., 2006; Chesnut et al., 1993; Downard et al., 2000; Figaji et al., 2009a, 2009b; Jones et al., 2003; Pigula et al., 1993; Rohlwink & Figaji, 2010). In spite of this well-known association, the role of secondary injuries in outcome is often underestimated (Figaji, 2010a). This underestimation is surprising given that secondary injuries may account for up to 42% of TBI-associated mortality in children (Sharples et al., 1990). Consequently, the degree of secondary injury is an important prognosticator (Figaji, 2010a). From a medical standpoint, because secondary injuries contribute significantly to outcome, but are often preventable, such injuries have been described as presenting a window of opportunity for intervention (Greve & Zink, 2009; Sharples et al., 1990).

Acute care management is therefore currently focused on controlling the primary injury and on avoiding potential secondary injuries (Chesnut et al., 1993; Figaji et al., 2009; Rohlwink & Figaji, 2010). This management is largely achieved by a process of controlling appropriate physiological parameters: reducing intracranial pressure (ICP), maintaining adequate cerebral perfusion pressure (CPP) and systemic blood pressure (BP), and ensuring satisfactory oxygen delivery (Adelson et al., 2003b, 2003c, 2003d; Chambers et al., 2006; Figaji et al., 2009a; Morris, Forsyth, Parslow, Tasker, & Hawley, 2006; Narotam et al., 2006; Pigula et al., 1993; Prabhakaran et al., 2004; Tang & Lobel, 2009). Failure to maintain

recommended thresholds for each of these parameters may be detrimental to patient outcomes.

Of particular importance in controlling these physiological parameters is the prevention of the deprivation of oxygen to an injured brain. Such deprivation may lead to secondary hypoxia-ischemia (V. Anderson, Northam, Hendy, et al., 2001; Arciniegas, 2010). This outcome is often concomitant with severe TBI (Graham et al., 1989; Van den Brink et al., 2000).

Cerebral Hypoxia-Ischemia in TBI

The terms *hypoxia* and *anoxia* refer to partial and complete oxygen deprivation, respectively (Ochoa, Erhan, & Feinberg, 2003). Hypoxia is frequently, but not necessarily, concomitant with ischemia. *Cerebral ischemia* refers to the reduction of oxygen- and glucose-enriched blood; such reduction can result in damage to brain tissue (Lezak, Howieson, Loring, Hannay, & Fischer, 2004). When this is the case, the clinical picture is often referred to as anoxic- or hypoxic-ischemia (Spreen, Risser, & Edgell, 1995).

One of the primary reasons for the aggressive management of TBI is to prevent cerebral ischemia (Figaji, 2010a). Following the primary injury, an ischemic cascade can be initiated at the secondary level, which can play a critical role in the pathophysiology of TBI and which is detected in up to 90% of fatal TBIs (Enriquez & Bullock, 2004; Graham et al., 1989; Greve & Zink, 2009; Manley et al., 2001; Marshall, 2000). For this reason, cerebral ischemia may be considered the most important secondary event to affect outcome following a TBI (Greve & Zink, 2009).

The probability of tissue damage as a result of ischemia is dependent on the degree and duration of hypoxia (Siesjo, 1992; Zauner, Daugherty, Bullock, & Warner, 2002). Various studies document the relationship between cerebral hypoxia and/or hypotension and unfavourable outcome in both adults and children (Chesnut et al., 1993; Manley et al., 2001; Michaud, Rivara, Grady, & Reay, 1992; Pigula et al., 1993). Others note that preventing and monitoring cerebral hypoxia and ischemia may improve patient prognoses (Bardt et al., 1998; Valadka, Gopinath, Contant, Uzura, & Robertson, 1998; Van den Brink et al., 2000).

Pathophysiology of ischemia. The brain consumes a large amount of systemic oxygen (approximately 15%) (see Caine & Watson, 2000, for a review). Optimal cell function relies on the production of energy or adenosine triphosphate (ATP), and mitochondria use more than 90% of the oxygen supply to produce it (Astrup, Sørensen, & Sørensen, 1981). Brain cells therefore require a constant supply of oxygen and glucose to enable cerebral metabolism. However, in spite of the constant need for it, the brain does not

store oxygen (Kuroiwa & Okeda, 1994). The continuous supply of oxygen and glucose is sustained through normal cerebral blood flow (CBF), normal mitochondrial function, and normal cerebral oxygen tension and delivery (Maloney-Wilensky & Le Roux, 2010).

Among a host of other damaging effects, TBI can lead to reduced CBF in an injured brain that has more metabolic demands. CBF values normally range between 45 and 60 ml/100g/min for both grey and white matter for adults. In children, the level is approximately 75 to 110 ml/100g/min. Ischemia is estimated to occur at 18 ml/100g/min (Astrup et al., 1981; Hession, 2008; Marshall, 2004; Siesjo, 1992). Membrane failure occurs with a further reduction in CBF, with levels less than 10ml /100g /min precipitating infarction (Marshall, 2004).

There is often a reduction in CBF in the early stages following a TBI. This reduction is associated with the cerebral metabolic rate of oxygen. In light of the aforementioned need for oxygen and glucose through continuous CBF, the decrease in CBF is therefore associated with poor outcome in children following severe TBI (Adelson et al., 1997; Kelly et al., 1997; Sharples, Stuart, Matthews, Aynsley-Green, & Eyre, 1995). Both human and animal studies have repeatedly demonstrated that the level of supply of oxygen and glucose determines the survival of neurons post-TBI (Maloney-Wilensky et al., 2009).

When tissues are starved of oxygen through reduced CBF, anaerobic metabolism and energy failure occurs (Rohlwink & Figaji, 2010). However, this relationship between CBF and metabolism is much more intricate (Cunningham et al., 2005; Figaji, 2010b). For example, there may be times when lower CBF may actually be appropriate, such as when injured tissue has reduced metabolic demands, or when a disjunction between CBF and metabolic demands occurs and normal levels of CBF may prove insufficient (Figaji, 2010b; Rohlwink & Figaji, 2010). These conflicting physiological events contribute to cerebral ischemia and to raised intracranial pressure (ICP; Hession, 2008). Therefore, understanding CBF requires consideration of metabolic demands and their connection with CBF, mitochondrial dysfunction, and level of oxygen extraction (Rohlwink & Figaji, 2010).

In the wake of a hypoxic episode, a number of homeostatic and adaptive responses are effected. The initiation of these responses is also referred to autoregulation. These responses are aimed at preserving oxygen delivery through maintaining a normal CBF even while blood pressure changes (Caine & Watson, 2000; Spreen et al., 1995; Udomphorn, Armstead, & Vavilala, 2008). Thus, when a hypoxic episode occurs, the negative effects of the episode must persist beyond these autoregulatory responses to impact on the brain (Caine & Watson, 2000). This is one opportunity for intervention in limiting the effects of a TBI.

For this reason, even though the incidence of TBI and pTBI remains a public health concern, advances in acute care management and related increased knowledge of opportunities for intervention, like preventing secondary injuries, have improved the prognosis for survivors of traumatic brain injuries (Hartl & Ghajar, 2004). However, managing or preventing secondary injuries, considering the complexity of the pathophysiology surrounding these injuries, is not a simple and straightforward task.

Challenges in Managing Secondary Injuries

Managing secondary injuries is difficult and complex due to the myriad of possible physiological and biochemical disturbances that can occur post-TBI (Figaji, 2010b; Rohlwink & Figaji, 2010). ICP and mean arterial pressure (MAP) monitoring and resulting cerebral perfusion pressure (CPP) monitoring are recommended as part of the standard management protocol following severe TBI (Lannoo et al., 1998). Data from ICP monitoring is used to estimate CPP. CPP, calculated as the mean arterial blood pressure minus ICP (CPP = MAP-ICP), and defined as the pressure gradient driving cerebral blood flow and metabolite delivery, has a strong link with cerebral ischemia (Hartl & Ghajar, 2004). Both high ICP and low CPP are associated with poor outcome in adults (Changaris et al., 1987; Cortbus, Jones, Miller, Piper, & Tocher, 1994; Farahvar et al., 2011; Marmarou, Saad, Aygok, & Rigsbee, 2005; Saul & Ducker, 1982; Vik et al., 2008) and children (Barzilay et al., 1988; Downard et al., 2000; Jones et al., 2003; Kasoff, Lansen, Holder, & Filippo, 1988).

The utility of these monitors is therefore well-recognized. In fact, ICP monitoring has been described as a "cornerstone of" and as the "gold standard monitor in" TBI care (Figaji, 2010a, p. 199; Figaji et al., 2009b, p. 1340, respectively). Both ICP and CPP management are included in the guidelines for the care of severe pTBI (Adelson et al., 2003b, 2003c, 2003d). These methods are used primarily to prevent secondary injury through maintaining CPP at the recommended threshold (Stiefel et al., 2006).

It is now also well-recognized, however, that adhering to the recommended thresholds for ICP (≤ 20 mmHg) and CPP (> 50/60 mm Hg) does not preclude the occurrence of brain hypoxia ischemia or neuronal injury in all patients (Figaji, Fieggen, Argent, Le Roux, & Peter, 2008; Figaji et al., 2009a; Narotam et al., 2006; Stiefel et al., 2005, 2006; Van den Brink et al., 2000). In other words, hypo-oxygenation can occur, in both adults and children, even when ICP and CPP treatment targets are met (Figaji, Fieggen, Argent, et al., 2008; Narotam et al., 2006; Stiefel et al., 2006; Van den Brink et al., 2000). Hence, the need for an additional treatment target is clear.

Brain Oxygenation Monitoring ($PbtO_2$)

The introduction of $PbtO_2$ monitors. Direct brain tissue oxygen tension ($PbtO_2$) monitoring, and the idea that it may influence treatment, was introduced by Meixensberger, Dings, Kuhnigk, and Roosen (1993) almost two decades ago. The United States Food and Drug Administration approved the clinical use of the $PbtO_2$ monitor in October 2001 (Maloney-Wilensky et al., 2009; Maloney-Wilensky & Le Roux, 2010). However, $PbtO_2$ monitoring has only really become feasible and part of standard monitoring recently (Figaji et al., 2009b; Maloney-Wilensky et al., 2009). $PbtO_2$ monitoring was introduced at the RXH in Cape Town in June 2006 (Figaji, Fieggen, Argent, et al., 2008).

Along with this development, literature on $PbtO_2$ monitors has burgeoned in the last decade. The recent inclusion (in 2007) of brain oxygen monitors in treatment guidelines for severe TBI (Bratton et al., 2007) is in keeping with these developments. These monitors have demonstrated their utility of in a range of disease processes (Figaji, Fieggen, Argent, et al.; Figaji, Sandler, Fieggen, 2008; Lang, Mulvey, Mudaliar, & Dorsch, 2007; Mazzeo & Bullock, 2007). However, TBI represents the largest field of clinical application for $PbtO_2$ monitoring, which has been described as safe, sensitive and reliable (Dings, Meixensberger, Jäger, & Roosen, 1998; Lang et al., 2007).

Although $PbtO_2$ measurements are focal, which means that capturing and understanding the data is subject to the position of the probe, these measurements are considered reliable estimates of global measurements of ischemic episodes (Dings et al., 1998; Kiening, Unterberg, Bardt, Schneider, & Lanksch, 1996; Rossi et al., 2001; Stiefel et al., 2006). Despite the technical expertise required, its ease of use in the critical care of TBI patients is notable. Researchers therefore recognize it as complementary to conventional monitoring (Maloney-Wilensky et al., 2009; Maloney-Wilensky & Le Roux, 2010; Rohlwink & Figaji, 2010; Stiefel et al., 2006; Valadka et al., 1998; Van den Brink et al., 2000).

Definition of $PbtO_2$: What does this technology measure? $PbtO_2$ monitoring technology allows clinicians, most of whom work in neurosurgical or neurological ICUs, to observe, track, and respond to changes in brain oxygen that could potentially lead to cerebral ischemia. Such changes might otherwise go undetected (Figaji et al., 2009a; Lang et al., 2007; Maloney-Wilensky & Le Roux, 2010). Owing to the adverse effects of hypoxia-ischemia, the opportunity afforded by $PbtO_2$ technology to monitor tissue oxygen changes and to detect hypoxia is integral to critical care management (Maloney-Wilensky et al., 2009).

Although a $PbtO_2$ monitor is "not simply an ischemic monitor" (Rohlwink & Figaji,

2010, p. 458), exactly what $PbtO_2$ reflects and the determinants thereof are unclear. An ongoing debate revolves around whether $PbtO_2$ measures CBF or oxygen extraction (Scheufler, Röhrborn, & Zentner, 2002). However, it has been proposed that $PbtO_2$ is "likely... a marker of the balance between regional oxygen supply and cellular oxygen consumption" (Maloney-Wilensky et al., 2009, p. 2061).

$PbtO_2$ thresholds. Normal $PbtO_2$ values range between 20 and 35 mmHg (Meixensberger et al., 2003; Pennings, Schuurman, Van den Munckhof, & Bouma, 2008; Spiotta et al., 2010) and that intervention be introduced when the 20 mm Hg level is compromised (Chang et al., 2009). For example, Narotam et al. (2006) have demonstrated the positive effects of raising $PbtO_2$ levels above 20 mm Hg on clinical outcomes. There is reportedly a dose-response relationship as $PbtO_2$ values drop below 20mmHg, with lower $PbtO_2$ values corresponding to greater likelihood of unfavourable outcomes (Valadka et al., 1998).

The critical threshold, that is, the ischemic threshold, is reported to be 10 mm Hg / 1.33 kPa (Figaji, Fieggen, Argent, et al., 2008; Maloney-Wilensky et al., 2009; Meixensberger et al., 2003; Valadka et al., 1998; Van Santbrink et al., 2003). Neurological outcome seems to be strongly tied to this threshold (Bratton et al., 2007; Figaji et al., 2009b; Lang et al., 2007). Other authors report a more stringent critical threshold of $PbtO_2$<15 mmHg to be associated with possible ischemia (Maloney-Wilensky & Le Roux, 2010). $PbtO^2$ values below the upper threshold often occur, even in up to 70% of patients when conventional treatment targets are met (Stiefel et al., 2006, Valadka et al., 1998; Van Santbrink et al., 1996, Gracias et al., 2004).

In addition to the effect of reaching critical thresholds, outcome is also influenced by how often, for how long and how intense these episodes of compromised $PbtO_2$ are (Figaji, 2010b; Maloney-Wilensky et al., 2009; Maloney-Wilensky & Le Roux, 2010). With these established thresholds, normal oxygenation, imminent, and acute ischemia can be distinguished (Maloney-Wilensky & Le Roux, 2010). However, in spite of this recognised value, the use of $PbtO_2$ monitors is not yet standard practice in all critical care units.

Utility, validation, and randomised controlled trials (RCTs). Because this is a relatively new method of monitoring, $PbtO_2$ technology has not yet been subjected to RCTs and therefore it is not yet widely used (Figaji, 2010a). Therefore, the role of these monitors in patient management and outcome has not yet been determined definitively. However, this does not negate its utility, which is duly recognized: "Although a randomized outcome study is not available its [$PbtO_2$] clinical utility has repeatedly been clearly confirmed because it

adds a monitoring parameter, independent from established cerebral monitoring devices" (Lang et al., 2007, p. 99).

No RCTs have been conducted for more long-standing ICP monitoring either. In the hypoxia-ischemia literature, conducting of RCTs is ethically problematic, as it would require deliberate exposure of children to oxygen deprivation in light of the known potential adverse effects (Bass et al., 2004). Although evaluating $PbtO_2$ monitoring through RCTs would establish its effectiveness, and would be beneficial to clinical practice, not intervening for low oxygenation would also pose an ethical dilemma. Treatment effects of $PbtO_2$ -directed therapies require validation. A phase II trial comparing $PbtO_2$ and ICP-directed therapies is reportedly underway (P. D. LeRoux, personal communication as cited in Rohlwink & Figaji, 2010).

As noted by Figaji (2010a), however, the utility (efficacy) of the monitors is not determined by the presence of the monitors per se, but rather by how the clinician interprets and responds to the data. Notwithstanding the need for RCT validation, some evidence does demonstrate a favourable association between the use of individual monitors and improved mortality rates (Bulger et al., 2002; Stiefel et al., 2005). Studies report such favourable associations particularly when such monitoring follows recognized protocol and guideline-based care in a specialized neurocritical care unit. Therefore, the benefit of using such monitors may be institution-dependent (Figaji, 2010a).

Relationships between $PbtO_2$ and other variables / parameters. Achieving and maintaining acceptable levels of brain oxygenation is influenced by several factors. These factors include systemic oxygenation, blood oxygen content and oxygen delivery, and other physiological parameters, such as the inspired fraction of oxygen (FiO_2), arterial partial pressure of oxygen (PaO_2), arterial saturation of oxygen (SaO_2), the level of hemoglobin (Hb), MAP, CPP, and CBF (Figaji et al., 2009b; Rohlwink, 2009; Rohlwink & Figaji, 2010). The influence of these factors on brain oxygenation is described in adult studies, with limited published literature of relationships between $PbtO_2$ and other physiological parameters, typically used in the ICU, in pTBI (Figaji et al., 2009b).

In a pTBI study that examined the relationships between low $PbtO_2$ and various permutations for ICP, CPP, systemic oxygenation and Hb, Figaji et al. (2009a) found only limited specific relationships. For example, even though several ICP parameters were investigated in relation to various $PbtO_2$ variables, only one weak relationship emerged, between the average number of episodes of ICP > 20 mmHg and the average $PbtO_2$ value, within 1 day post-injury. These results, specifically related to ICP, are supported by findings

of a complex and weak relationship between $PbtO_2$ and ICP, also in relation to pTBI (Rohlwink, 2009).

Other limited individual relationships emerged between measures of CPP and systemic oxygenation in the same study by Figaji and colleagues (2009a). These specific relationships included associations between (a) low $PbtO_2$ and the lowest CPP value, and (b) the number of times that CPP was < 40mmHg, PaO_2 was <60 mmHg, and SaO^2 was <90; the latter two variables are both measures of systemic oxygenation (Figaji et al., 2009b). Low $PbtO_2$ was also predicted by the initial GCS score. In general, however, taking into account the various relationships considered by Figaji et al. (2009a), there was an overall poor association between commonly measured ICU parameters and low $PbtO_2$, even though these parameters (e.g., initial GCS score, raised ICP, and reduced CPP) and PbtO2 separately (Figaji, Fieggen, Argent, et al., 2008; Figaji et al., 2009a), "are all common covariates associated with outcome in many clinical TBI studies" (Figaji et al., 2009a, p. 1331).

The link between low $PbtO_2$ and outcome: adults. The use of $PbtO_2$ monitors is implicitly related to the fact that maintaining optimal $PbtO_2$ is associated with favourable outcomes. These outcomes often refer to a reduced risk of mortality or morbidity as measured by the Glasgow Outcome Scale (GOS) (e.g., see Bardt et al., 1998; Changaris et al., 1987; Kiening et al., 1997; Van den Brink et al., 2000) or positive effects on treatment such as a reduction in the number of cerebral hypoxic episodes (e.g., Meixensberger et al., 2003). In extant studies, outcome measures do not typically include neuropsychological or cognitive variables.

This link between $PbtO_2$ and favourable outcomes is based on positive findings for those therapies based on, or guided by, $PbtO_2$ monitoring (Meixensberger et al., 2003; Narotam, Morrison, & Nathoo, 2009; Stiefel et al., 2005). Conversely, the relationship between low levels of $PbtO_2$ and unfavourable outcome is also well documented in the adult TBI literature (Lang et al., 2007; Mazzeo & Bullock, 2007; Meixensberger et al., 2003; Narotam et al., 2009; Stiefel et al., 2005, 2006; Valadka et al., 1998; Van den Brink et al., 2000; Van Santbrink et al., 2003).

However, one recent study failed to demonstrate this relationship, and even suggested a negative relationship between $PbtO_2$ and outcome. In that study, Martini et al. (2009) compared two groups of patients: One group underwent ICP monitoring only, and another, both ICP and $PbtO_2$ monitoring. The latter group did not show better outcomes in terms of mortality rates, functional independence at discharge, and utilization of hospital resources. Rohlwink and Figaji (2010) point out a limitation of this study, however, stating that the

decision for patients to undergo $PbtO_2$ monitoring was not taken systematically. Moreover, the groups were unequal terms of age and injury severity: the ICP monitoring group were older and had less severe injuries than the $PbtO_2$ /ICP group.

Other studies have noted limitations with regards to $PbtO_2$ monitoring, for example, when it fails to detect delayed cerebral ischemia (Kett-White et al., 2002). However, most published studies of adult TBI still seem to report that that $PbtO_2$ monitoring is beneficial. It is purported that outcome may be influenced by treatment, which is influenced in turn by monitoring, thereby creating this relationship between monitoring and favourable outcome, but it is not yet certain (Maloney-Wilensky et al., 2009; Rohlwink & Figaji, 2010; Stiefel et al., 2005).

The utility of $PbtO_2$ monitors is also related to the fact that compromised levels of $PbtO_2$, and concomitant hypoxia, lead to unfavourable neurological outcomes. In a recent systematic review of available English medical literature, Maloney-Wilensky et al. (2009) confirmed this association between brain hypoxia (as defined by $PbtO_2 < 10$mmHg) and increased mortality and morbidity.

Low $PbtO_2$ and outcome: children. Few studies have investigated the relationship between low $PbtO_2$ and unfavourable outcome following TBIs in children (Figaji, Fieggen, Argent, et al., 2008; Figaji et al., 2009a; Narotam et al., 2006). In these few studies, outcome was defined by the GCS, clinical evaluations of the Glasgow Outcome Scale (*GOS*; Jennet & Bond, 1975) and the Pediatric Cerebral Performance Category Scale (*PCPCS*; Fiser, 1992), mortality, and radiologic, treatment and physiological outcome variables, all of which are relatively blunt as measures of functional outcome (Figaji, Fieggen, Argent, et al., 2008; Figaji et al., 2009a, 2009b).

Most of these studies featured a small sample. In two of these studies, the participants included $N = 6$ children with severe pTBI (Stiefel et al., 2006) and $N = 16$ children, 15 of whom had sustained severe TBI (Narotam et al., 2006). The two studies conducted by Figaji and colleagues included sample sizes of $N = 26$ (Figaji, Fieggen, Argent, et al., 2008) and $N = 52$ (Figaji et al., 2009a).

Figaji, Fieggen, Argent, et al. (2008), using a sample of 26 children who had experienced a severe TBI, reported significant relationships between the 6-hour period that $PbtO_2$ was lowest and the amount of time that $PbtO_2$ was below the 15 and 10mmHg thresholds, and poor outcome (GOS and PCPCS). They also found that at least one episode of $PbtO_2 < 20$ occurred in 80% of the patients and that episodes of $PbtO_2 < 10$mmHg (previously described as the ischemic threshold) occurred in 1/3 of their patients, despite

meeting recommended thresholds for ICP, CPP and systemic oxygenation. Both studies by Figaji and colleagues (i.e., Figaji, Fieggen, Argent, et al., 2008 and Figaji et al., 2009a) provided evidence for low $PbtO_2$ as associated with poor outcome and mortality following severe pTBI. This association between $PbtO_2$ and poor outcome was independent of reaching traditional treatment targets for ICP, CPP, systemic oxygenation and Hb.

Much like the adult literature, these, and the other two pediatric studies outlined above, did not include neuropsychological or cognitive outcome variables.

$PbtO_2$ and neuropsychological (NP) outcomes. As reviewed above, it seems clear that low $PbtO_2$ episodes are associated with poor morbidity and mortality outcomes. More specific neuropsychological outcomes have rarely been investigated. Only one study, by Meixensberger et al. (2004), examined neuropsychological outcomes in relation to $PbtO_2$ levels. Those authors investigated levels of cerebral oxygenation and neuropsychological outcomes in the acute stage following severe TBI in adults (N = 20, mean age of 31.9 years, SD = 13.57, range = 17-68), 2-3 years post-injury. The patients were divided into two groups, based on the percentage of hypoxic episodes recorded during the monitoring period (< 20% of recorded values lower than 15 mm Hg (group A) or > 20% of recorded values lower than15mmHg (group B)). There were no between-group differences in terms of GOS. Of group A, 65% managed to attain a GOS score of 5 as compared to 50% of group B. Group A generally performed better as compared to group B in terms of test performance. The researchers observed better performances for group A on measures of long- and short-term memory and IQ. Participants in Group B reported poorer outcomes in terms of their performance in their professions. Despite these results suggesting that association between brain oxygenation and neuropsychological test performance, no follow-up studies of this nature have been conducted in either adults or children.

CPP, ICP, and neuropsychological outcomes. Studies on neuropsychological outcomes in relation to other measures of cerebral monitoring, such as CPP and ICP, are limited in number in both the adult and pediatric literatures. Uzzell, Obrist, Dolinskas, and Langfitt (1986) reported an association between intracranial hypertension (ICP ≥ 20 mmHg) and persistent memory difficulties within the first year following injury for patients (20 – 30 years) following closed severe TBI. H. Levin et al. (1991), however, found that increased ICP was only associated with minor changes in visual and verbal memory tasks at 6 months post injury, and that these difficulties seemed to resolve by 1 year post injury in a young adult sample. This relationship was not confirmed for impairments in other cognitive domains and increased ICP in a previous study however (H. Levin et al., 1990). Finally, Lannoo et al.

(1998) examined a number of neuropsychological outcome measures in a sample of moderate-to-severe participants (n = 43; GCS scores of 3-12) and trauma controls (n = 22) with an age range of 15-65 years (M = 33 and 39; SD = 15 and 13, for the two groups, respectively) at 6 months post injury. They failed to find a definite association between CPP and ICP on the one hand, and measures of attention, information processing, motor functioning, memory and learning, visuoconstructional ability and executive functions, on the other.

In one of the few pediatric studies in this area of research, Slawik et al. (2009) reported long-term persistent deficits on attention and executive function tasks in their ICP group. Their sample included 33 participants (13 in the ICP group), who were 8.4 to 13 years of age at injury (M = 11.5) and followed up an average of 3.9 years later (range 3.2 to 4.6 years).

In summary, the brief review above demonstrates a dearth of research in the area of $PbtO_2$ (and other physiological parameters) and outcome, and especially neuropsychological outcome. As episodes of low $PbtO_2$, especially those where $PbtO_2$ values fall below the ischemic threshold (10 mmHg), essentially translate into episodes of hypoxia, I briefly review the neuropsychological sequelae associated with hypoxia-ischemia below.

Neuropsychological sequelae of hypoxia-ischemia. Secondary hypoxia is a risk when optimal levels of O_2 are compromised. Hypoxic/anoxic-ischemic neuropathology involves watershed areas[1] of the cerebral cortex, the basal ganglia, the hippocampus, thalamus, and cerebellum (Caine & Watson, 2000). Even though outcome studies following anoxic episodes most often report damage to the hippocampus, thereby leading to the assumption that this is the quintessential outcome of cerebral anoxia, Caine and Watson (2000) found that, across the 58 studies they reviewed, watershed areas of the cerebral cortex and the basal ganglia were more often affected than the hippocampus.

Severe episodes of hypoxia-ischemia, in general, are associated with poor cognitive outcome (Caine & Watson, 2000; Lezak et al., 2004; Menkes, Hurvitz, McDiarmid, & Williams, 1995). In addition to contributing to the neuropsychological sequelae (including deficits in attention, memory, and executive functions) of pTBI, secondary brain hypoxia-ischemia may exacerbate an already injured or vulnerable brain.

Although neuropsychological studies of TBI-related secondary hypoxia-ischemia are

[1] Watershed areas are those areas that lie distally to, or are perfused by, the remote branches of the major cerebral arteries and therefore receive the lowest perfusion of direct blood supply (Spreen et al., 1995). These areas are therefore vulnerable to ischemic injury.

limited in number, it is possible to extrapolate from other studies that report on hypoxic-ischemic injuries (e.g., following cardiac arrest or respiratory failure). Those studies have reported a range of neuropsychological sequelae of hypoxia-ischemia. These sequelae commonly include some degree of generalized cognitive impairment, as well as specific impairment in the domains of learning and memory, executive functions (e.g. poor planning, impulsivity and disinhibition), visuospatial and visual abilities, language, motor and sensory functioning (V. Anderson, Northam, Hendy, et al., 2001; Bigler, 1989; Caine & Watson, 2000; Lezak et al., 2004).

In a recent review, specifically focused on the effect of chronic or intermittent hypoxia on cognition in children, Bass et al. (2004) found that more than 78% (43/55) of the articles that they reviewed reported unfavourable cognitive outcomes. The studies included were focused on congenital heart disease (CHD), sleep-disordered breathing (SDB), asthma, chronic ventilatory impairment, and respiratory instability in infants. According to the review, a number of well-designed studies conducted on children with CHD and SDB convincingly demonstrate that hypoxia, either chronic or episodic, impacts negatively on children's development, behaviour, and academic ability. Unfavourable outcomes occurred regardless of age (except for newborns born prematurely) and regardless of levels of O_2 desaturation that children were exposed to.

Following the publication of the Bass et al., (2004) review, Hopkins, Tate, and Bigler (2005) investigated and compared neuropsychological outcomes in two clinical groups: one including participants who had sustained moderate-severe TBIs, and the other including participants who had sustained anoxic brain injury. There were no between-group differences on measures of memory, attention, EF, and speed of information processing, although both groups showed impaired performances on these tasks, as compared to normative data.

In summary, hypoxia-ischemia can contribute to or exacerbate an already injured brain. Both TBI and hypoxia-ischemia are associated with poor cognitive outcomes, although neuropsychological studies of TBI-related secondary hypoxia-ischemia specifically, remain few in number. As a potential secondary injury, the role of hypoxia-ischemia in outcome underscores why such injuries require aggressive and priority management.

Conclusion

The purpose of this chapter was to explore the relationship between brain tissue oxygenation and neuropsychological and behavioural outcomes in children following severe TBI. The belief that prevention of secondary injuries can improve outcome is commonplace. In order to identify such injuries, reliable neuromonitoring is requisite (Figaji et al., 2009b).

In light of the limitations of standard/conventional monitoring in detecting brain hypoxia, clinicians support the introduction of brain tissue oxygen monitors as a useful addition to the monitoring regime. Such monitors are already established as a predictor of mortality and morbidity (e.g., as measured by GOS and the PCPCS). However, existing outcome studies have rarely included neuropsychological or behavioural measures. In fact, such outcomes have not been assessed in pTBI in relation to cerebral oxygenation. Some evidence exists for this relationship between ICP and outcome, however.

CHAPTER 5:
STUDY 2: INVESTIGATING BRAIN OXYGENATION AND NEUROPSYCHOLOGICAL OUTCOMES FOLLOWING SEVERE PEDIATRIC TBI

The relationship between secondary brain injury and poor outcome in adults and children post-TBI is well known (Chambers et al., 2006; Chesnut et al., 1993; Downard et al., 2000; Figaji et al., 2009b). Therefore, crucial among the efforts aimed at improving outcome following a TBI are those directed at preventing, limiting, or managing secondary injuries (Figaji, Zwane, Fieggen, Peter, & Le Roux, 2008; Tang & Lobel, 2009). Although direct preventative therapies for secondary injury processes (e.g., edema formation, intracranial hypertension, disruption of CBF autoregulation) are not yet known, methods to improve outcome are largely focused on preventing ischemic injury (Greve & Zink, 2009). Ischemia or hypoxia following TBI is associated with unfavourable outcome and is regarded as a key determinant of secondary injury (Bass et al., 2004; Hopkins & Haaland, 2004; Narotam et al., 2006; Rohlwink & Figaji, 2010). Early identification and intervention is critical to the prevention of this secondary injury (Figaji et al., 2008; Rohlwink & Figaji, 2010).

Prevention of ischemia following TBI is traditionally performed through methods aimed at improving cerebral perfusion pressure (CPP) and controlling intracranial pressure (ICP). Although standard interventions for TBI are guided and regulated according to ICP and CPP thresholds, these values are not strong indicators of acceptable levels of brain oxygenation (Figaji et al., 2008, 2009a; Narotam et al., 2006; Stiefel et al., 2005, 2006; Van den Brink et al., 2000).

In children, determining what represents adequate ICP and CPP control is even more complex than in adults, given that children of different ages have different and less well established normative thresholds for intracranial pressure and blood pressure (Figaji et al., 2008). To date, no age-based recommendations for these thresholds can be made due to lack of evidence, and so data are extrapolated from adult studies (Adelson et al., 2003a). This strategy is inappropriate given that children are physiologically different from adults. Therefore, a measure of the adequacy of brain oxygenation, regardless of ICP or blood pressure – an 'end-target' variable – is necessary (Figaji et al., 2008).

$PbtO_2$ monitors have therefore been proposed as a complementary tool to ICP monitoring in order to detect the adequacy of brain perfusion and oxygenation. These monitoring systems have only become available in recent years.[1] $PbtO_2$ monitoring is used in

[1] $PbtO_2$ monitoring was introduced in the Division of Pediatric Neurosurgery at RXH in June

both adults and children where patients are at risk for cerebral ischemia, for example, after TBI (Figaji et al., 2008; Maloney-Wilensky et al., 2009; Nortje & Gupta, 2006; Spiotta et al., 2010). Hence, $PbtO_2$ technology in particular is being utilized increasingly in the management of patients with severe TBI (Rohlwink & Figaji, 2010).

The aim of $PbtO_2$ monitoring systems is to maintain normal $PbtO_2$ values, ideally greater than 20-25 mmHg. $PbtO_2$ values less than 20 mmHg suggests progressively increased tissue hypoxia or ischemia. $PbtO_2$ values less than 10mmHg are deemed critical, as this represents the ischemic threshold (Maloney-Wilensky et al., 2009). Continuous monitoring of $PbtO_2$ therefore provides feedback about cerebral oxygen levels and may represent an early warning system for imminent cerebral ischemia or hypoxia (Albano, Comandante, & Nolan, 2005). Earlier detection of low $PbtO_2$ may therefore facilitate opportunities for intervention to limit the effects of secondary injury.

The relationship between low $PbtO_2$ and poor outcome has been established clearly in adults (Rohlwink & Figaji, 2010). The utility of this parameter has been recognized to the extent that oxygenation monitoring has been proposed as a recommendation to prevent brain hypoxia in adults, although more evidence supporting its clinical effectiveness is needed (Tang & Lobel, 2009). In particular, $PbtO_2$-directed treatment appears to be associated with reduced mortality after severe TBI in adults (Narotam et al., 2009; Spiotta et al., 2010).

Fewer studies of this kind have been conducted with children (Figaji et al., 2008, 2009b; Narotam et al., 2006; Stiefel et al., 2006). The findings of these few studies are consistent with studies in adults showing that low $PbtO_2$ post-TBI is common and is associated with increased mortality and morbidity (Maloney-Wilensky et al., 2009; Rohlwink & Figaji, 2010).

In the most recent pediatric study investigating the relationship between low $PbtO_2$ and outcome following TBI, and one that included the largest pTBI sample to date, low $PbtO_2$ was independently associated with poor outcome (as defined by trauma scores on the GOS and PCPCS) and was a stronger predictor than other factors traditionally associated with outcome (Figaji et al., 2009a). Further, in that study, low $PbtO_2$ was not predicted by measures of initial injury severity, suggesting that the contribution of low $PbtO_2$ to poor outcome represents secondary brain injury that is, at least in theory, amenable to treatment.

Up to one-third of children with severe TBI may experience episodes of $PbtO_2 <$ 10mmHg, even when recommended treatment targets for ICP, CPP, and systemic

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2006 and is now standard practice for children following severe TBI there.

oxygenation are reached (Figaji et al., 2008). The relationship between $PbtO_2$ and other traditional parameters is complex. In particular, the relationship between $PbtO_2$ and ICP is complicated (Rohlwink et al., 2012).

To date, published studies have rarely investigated the relationship between specific neuropsychological outcomes in children and $PbtO_2$-based monitoring (Figaji et al., 2009b). Limited evidence does suggest a relationship between $PbtO_2$ and performance on neuropsychological tests in adults, however. Specifically, low $PbtO_2$ is reportedly associated with poor performance in the domains of general intellectual functioning and memory (Meixensberger et al., 2004).

In summary, although there is growing evidence describing the association between $PbtO_2$ and clinical outcome factors, there is a dearth of research on the relationship between $PbtO_2$ monitoring and neuropsychological and behavioural outcomes, especially in children (Figaji & Kent, 2010). This is an important consideration given that TBI is a leading cause of neurological disability in children (Babikian & Asarnow, 2009; Brysiewicz, 2001; Kraus, 1995; Kraus et al., 1990; K. Levin, 2004; Pfenninger & Santi, 2002; Semple et al., 1998). TBI-related neuropsychological outcome studies rarely consider, as part of the myriad of factors that affect outcome, neurosurgical monitoring variables such as $PbtO_2$ levels. Conversely, TBI-related neurosurgical outcome studies rarely include neuropsychological outcome variables. In this study, I aimed to investigate whether reaching an ischemic threshold for $PbtO_2$ affects children's neuropsychological and behavioural outcomes. Hence, the results of this study can contribute to both the TBI-related neuropsychological and neurosurgical literatures.

Specific Aims and Hypotheses

I investigated the relationship between levels of $PbtO_2$ and outcomes on a comprehensive battery of neuropsychological and behavioural tests in a sample of children who had experienced severe TBI. The broad aim was to investigate the potential prognostic value of PbtO2 for neuropsychological and behavioural functioning following severe pTBI. Specifically, I investigated whether maintaining $PbtO_2$ levels above the ischemic threshold results in more favourable outcomes for children who have sustained severe TBIs.

This is the first pediatric $PbtO_2$ study in which neuropsychological and behavioural outcomes are investigated; it complements previous findings by Figaji and colleagues, which did not include neuropsychological and behavioural outcomes (e.g., Figaji et al., 2009a). The study tested the following specific hypotheses:

1. Participants who have sustained severe TBI will perform more poorly than matched healthy controls on neuropsychological and behavioural measures.
2. Among the participants who have sustained TBIs, those who have experienced at least one episode of $PbtO_2 \leq 10$ mmHg will perform more poorly on neuropsychological and behavioural measures than those for whom $PbtO_2$ levels remained at > 10 mmHg for the entire monitoring period. Even though 20mmHg is the optimal threshold for $PbtO_2$, 10mmHg is the critical one, representing episodes of brain hypoxia (Figaji et al., 2008). In other words, those participants who sustained TBIs, and who experienced at least one episode of brain hypoxia, will perform more poorly on the administered tests than those who sustained TBIs and who did not experience an episode of brain hypoxia.

Methods

Research Design

This was a case-control study. The study design was quantitative, retrospective, and cross-sectional. It included two between-group comparisons. The first between-group comparison featured two independent groups: a group of children who had sustained severe TBIs and who underwent $PbtO_2$ monitoring, and a healthy matched control group. The pTBI and control groups were matched as closely as possible on age, sex, language, SES, and race.

The second between-group comparison involved dividing the pTBI group into two subgroups: one group who had experienced at least one episode of $PbtO_2$ lower than 10mmHg (i.e., they reached the ischemic threshold) during the period of monitoring (hypoxia group), and another group for whom $PbtO_2$ had remained above 10mmHg throughout the monitoring period (No Hypoxia group). For both between-group comparisons, the outcome variables were a range of neuropsychological and behavioural measures.

Sample

The patient sample included 11 children who had been admitted to RXH following severe TBI, and who had undergone $PbtO_2$ monitoring. Owing to a dearth of local norms for the assessment tools employed, a healthy matched control group (n = 11) was included against which to compare the performance of the TBI participants.

TBI participants. I collected data from a group of 11 patients who the Head of the Division of Pediatric Neurosurgery at RXH identified as suitable for the study. The RXH team considered children with TBI for $PbtO_2$ monitoring if their post-resuscitation GCS score was 8 or less, or deteriorated to this level after admission. This protocol was followed, unless

extubation was recommended within 12 hours for a rapidly waking patient or if brain death was imminent. Only children in whom monitoring was started within the first 24 hours were considered for inclusion in the study.

Of those for whom complete monitoring data were available, only those who were English and/or Afrikaans-speaking, who were admitted for closed[2] severe TBI, who were at least 1 year post-injury[3], who were aged 6-16 years at the time of assessment, and for whom informed consent and assent were granted, were eligible for the study.

Reasons for exclusion of participants. The Head of the Division of Pediatric Neurosurgery referred 16 children who met the eligibility criteria as potential participants for this study. Of these 16, 11 were included in the final analyses. The other five were excluded for these reasons: One participant was lost to follow-up – we were unable to establish communication through telephone or other means; two had Xhosa as their home language[4]; and two were assessed, but their data not included in the final analyses. The complete set of monitoring data was not available for one of the latter two. For the second of those two, it was established only after completing the assessment that he may have had exposure to alcohol on the day of the assessment.

Healthy control participants. Once the TBI participants were tested, I generated a list detailing the demographics for a desired group of matched control participants. I used two strategies to identify and recruit these participants. The first strategy involved identifying potential participants from some of the schools that the TBI participants attended. The second strategy involved consulting and liaising with other local researchers who were conducting pediatric neuropsychological studies and who had included healthy participants in their studies. In their consent forms for those previous studies, these participants had indicated a willingness to be contacted for future studies.

Healthy control participants (n = 11), recruited in those ways, were matched as closely as possible to the participants in the TBI sample on a range of demographic variables, including age, sex, language, SES, and race. In brief, inclusion criteria for these control

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[2] The majority of TBIs in childhood are closed injuries (as opposed to penetrating TBIs), and the pathophysiology for closed TBIs differs from that of open TBIs (V. Anderson, Catroppa, Haritou, et al., 2001; Greve & Zink, 2009). For these reasons I included only patients who sustained closed TBIs in order to promote homogeneity in the sample.

[3] Although the recovery period for children following TBI continues well beyond 6 months post-injury, 1 year represents a reasonable plateau phase of recovery for assessment (Ginstfeldt & Emanuelson, 2010; Yeates et al., 2002).

[4] The instructions for the tests used in the study were only translated into English and Afrikaans at this stage. In addition, the researcher and other trained assistants who completed the testing were fluent in only one of these languages.

participants were that they were English and/or Afrikaans speaking, that they were between 6 and 16 years of age, that they matched the TBI participants on other demographic factors such as sex, SES and race, and that there was informed consent and assent for their participation. Exclusion criteria included any previous head injuries that resulted in hospitalisation or loss of consciousness, and any formally diagnosed learning, psychiatric, neurological, or developmental disorders. I obtained these data from parents.

Measures

The assessment battery included a comprehensive set of neuropsychological and behavioural measures (see Appendix C). The neuropsychological assessment tools covered a range of cognitive domains, including general intellectual functioning, verbal and visual memory, attention, executive functions, and visuospatial functioning. In addition, the behavioural assessment tools provided information on both internalizing and externalizing behaviours. These tests were all originally published in English. The test instructions were therefore translated into Afrikaans. The University of Stellenbosch Language Laboratory (Cape Town, South Africa) carried out this process through forward and back translations and an authentication process.

Procedure

TBI participants: physiological monitoring. The neurosurgical team at RXH practices standard monitoring and management of children with severe TBI according to the local protocol. Conventional acute patient care is unaffected by this process.

For the current sample, intracranial catheters for ICP (Codman, Raynham, MA, USA) and $PbtO_2$ (Licox; Integra Neurosciences, Plainsboro, NJ) were inserted into the right frontal lobe or on the side of the greatest cerebral swelling or most significant lesion as shown by the admission head CT scan. $PbtO_2$ catheters are typically inserted 2.5 to 3 cm below the surface in uninjured frontal white matter. CT scans are used to confirm the accurate positioning of the monitor. Treatment was initiated at a $PbtO_2$ threshold of 20 mmHg, as per local protocol. A number of physiological variables were recorded, including: ICP, CPP, $PbtO_2$, temperature, heart rate, invasive blood pressure (BP), pulse oximetry, arterial partial pressure of oxygen (PaO_2), partial pressure of arterial carbon dioxide ($PaCO_2$), fraction of inspired oxygen (FIO_2), Hb, and serum sodium. Physiological data were recorded hourly in the nursing records and via an electronic system (ICMPlus®, Cambridge University, UK), which is set up to sample data at 50 Hz and averages data points every 10 seconds (Figaji et al., 2009a, 2009b).

TBI and healthy control participants: Neuropsychological and behavioural testing. Parents/caregivers were contacted via telephone and invited to participate in the study, the details of which were explained to them. If the parent/caregiver agreed to the assessment, I scheduled an appointment. The assessments took place mainly at the RXH Developmental Clinic or in the Department of Psychology at the University of Cape Town. I tested one of the participants who had sustained a TBI at the children's home where she resided, in a quiet room especially arranged for the assessment.

Upon arrival at the test venues, informed consent and assent was sought from the parent/caregiver and child, respectively. The duration of testing was approximately 3 hours, and the children were allowed to take breaks whenever necessary or requested. Parents completed the demographic questionnaire and the BRIEF and CBCL forms during that time. Trained postgraduate neuropsychology students and interns assisted me in carrying out the assessments.

Scoring Procedures and Statistical Analyses

Identifying and measuring episodes of low $PbtO_2$. The Head of the Division of Pediatric Neurosurgery and his team analyzed the patient physiological data and identified episodes of low $PbtO_2$. They identified and recorded (a) the lowest $PbtO_2$ reading that persisted for at least 30 minutes during the entire monitoring period, and (b) the cumulative time that $PbtO_2$ was less than thresholds of 20, 10, and 5 mmHg. Due to the fact that PbtO2 readings may take up to 1 to 2 hours to stabilize, data from the first 2 hours of $PbtO_2$ monitoring were excluded from analyses.

Scoring procedures for neuropsychological and behavioural data. I followed the scoring procedures as described in each of the test administration manuals for each subtest in the test battery. All raw scores obtained were converted to age-adjusted scaled scores, following conventional procedures outlined in the various test manuals.

Statistical procedures. I used SPSS version 20.0 to carry out the statistical analyses, and for each analysis calculated the appropriate effect size estimate.

Preliminary analyses.

Demographic data. The first step here was to compare the demographic data for the pTBI and healthy control groups. I used Levene's test of homogeneity and the Shapiro-Wilk test for normality to assess whether the assumptions for parametric testing were upheld. Depending on the outcome of these tests, I employed one-way ANOVAs or Mann-Whitney *U*-tests to assess between-group differences on continuous variables, and Chi-square or Fisher's exact test to assess between-group differences on categorical variables. I used the

latter statistical procedure in instances where the sample was small and where the cells of the variables in the analyses had expected counts of less than 5.

Deriving and comparing composite scores. A sizeable number of tests and subtests comprised the test battery. Hence, there were a large number of dependent variables (32) in proportion to the sample size ($N = 22$) for the comparison between TBI and control participants. Therefore, I used a standardized set of procedures to reduce the number of dependent variables to 10. These 10 variables included three IQ measures: WASI Verbal IQ, Performance IQ, and Full Scale IQ (see Appendix C for a full description of these measures), and seven composite measures covering the following domains: basic and higher-order attention, verbal and visual memory, executive function, visuospatial ability, and expressive language. I created these composites using a hybrid method (see Ferrett, Carey, Thomas, Tapert, & Fein, 2010; Medina et al., 2007).

This hybrid method included the following steps: First, all the individual measures included in the test battery were sorted into domains. These domains were determined in two ways: (1) based on established categorizations and theoretical assumptions (Lezak et al., 2004), and (2) through reliability analyses using Cronbach's α coefficients. Second, all of the dependent variables (individual neuropsychological measures) were converted into *z*-scores. This computation was based on data from the complete sample of children. Third, I derived a composite *z*-score for each domain by averaging the *z*-scores for the individual measures in that domain.

Neuropsychological tests. I compared the neuropsychological test scores for the TBI and healthy control groups using the composites and IQ scores (using one-way ANOVAs and Mann Whitney *U*-tests, depending on whether assumptions for parametric statistical tests were upheld).

Behavioural data. I compared the scores from the behavioural measures for the TBI and healthy control groups (using one-way ANOVAs and Mann Whitney *U*-tests, depending on whether assumptions for parametric statistical tests were upheld). I also compared the results from the CBCL for the TBI and healthy control groups using the qualitative clinical descriptions provided in the test manual.

Despite the multiple comparisons carried out, a Bonferroni correction was not applied to the results of these analyses. Although one might typically control for the risk of Type I error using a conservative measure such as this, in other public health research contexts (e.g., pediatric exposure to neurotoxins), researchers raise more concern about missing important effects (Type II errors) than about the strict control of alpha values (Jacobson & Jacobson,

2005). This concern might also be extrapolated to TBI research. Hence, employing a Bonferroni adjustment may result in an underestimation of the effects of TBI on neuropsychological and behavioural outcomes.

Major analysis. I compared outcome on the (a) demographic and injury variables, (b) SES data, (c) neurosurgical variables, and (d) neuropsychological and behavioural variables for the Hypoxia and the No Hypoxia groups. I repeated the steps outlined above for TBI vs. healthy control group comparisons in terms of checking assumptions, deriving composites, between-group comparisons of demographic, neuropsychological, and behavioural data, and non-use of Bonferroni adjustment.

In addition, I correlated the $PbtO_2$ variables with other monitoring variables and compared the neurosurgical monitoring data for the Hypoxia and the No Hypoxia groups using *t*-tests and Mann Whitney *U*-tests, depending on whether assumptions for parametric statistical tests were upheld. I conducted ANCOVAs for all dependent variables with significant differences in neuropsychological and behavioural results, using injury and monitoring variables that were significantly different between groups as covariates. I conducted the ANCOVAs to control for the effects of these injury and monitoring variables on between-group differences, and to assess the performance of the two groups when these variables were controlled for. Where assumptions were not upheld, I implemented a non-parametric ANCOVA equivalent (viz., Quade's (1967) method; see Olejnik & Algina, 1984).

Quade's (1967) test. I ranked the dependent variables and the covariate on SPSS with the smallest value ranked as 1, using the SPSS rank function. I then ran linear regression analyses of the ranks of each of the dependent variables on the ranks of the covariate. I saved the residuals in the datasheet. Finally, I ran one-way ANOVAs using the residuals from the regressions as the dependent variable and the grouping variable (hypoxia or no-hypoxia) as the factor. Quade's method uses the resulting *F*-statistics from these ANOVAs.

Effect size. I used the *r*-statistic as a measure of effect size. This statistic is a commonly used measure of effect size. Values of .10, .30, and .50, represent small, medium and large effect sizes, respectively (Field, 2009). The use of this statistic also allowed for the calculation of effect sizes for nonparametric statistical analyses. In practice, the *r*-statistic and Cohen's *d* can be used interchangeably; both can be employed when using a dichotomous and a continuous variable in analyses. Under certain circumstances, however, *r* and *d* are not equivalent; outcomes for these effect size estimates can vary depending on whether sample sizes are equal and on the variance of the dichotomous variable (McGrath & Meyer, 2006).

Considering the results after the removal of outliers for purely statistical reasons. Because the findings of this study may have important implications for the role of $PbtO_2$ in neuropsychological and behavioural outcomes post-pTBI, the results needed to be scrutinized carefully for the presence of outliers. There were a number of outliers for many of the outcome variables. Because outliers can affect the outcome of analyses, for purely statistical reasons, I decided to recompute the main analyses without the outliers as identified through box plots.

However, after manually reviewing those outliers, the scores used in the actual analyses were deemed as valid and as reflecting true performances of participants. That is to say, if all identified outliers were removed for purely statistical reasons, the general trends suggested by the results remained largely consistent. I have, however, highlighted below the instances where the removal of outliers resulted in potential changes to the trends.

Ethical Considerations

This study is part of a larger research programme being run out of the RXH Division of Pediatric Neurosurgery. The aim of this research programme is to compile a registry of pediatric neurotrauma. The registry includes collection of brain oxygen monitoring data as well as all forms of follow-up, including occupational and speech therapy and neuropsychological data. Ethical approval for this study was obtained from the University of Cape Town's Faculty of Health Sciences Ethics Committee (see Appendix A). Permission to include the school learners and to use the school facilities for testing was obtained from the Western Cape Education Department (Appendix D).

Informed consent and assent. Verbal and written assent were obtained from the participants. Informed consent was obtained from the participants' parents (see Appendices E and F, respectively).

Confidentiality, voluntary participation and deception. The principal researcher or research assistant conducting the testing reminded the participant that all information obtained throughout the study was confidential and would be used for research purposes only. At the same time, it was also emphasized to participants that participation was voluntary and that they could withdraw from the study at any point should they desire to do so. The researcher noted that they would not incur a penalty from the hospital or school as a result. This study did not use any deception.

Risk and benefits. There were no risks to participants in the study. However, participants may have experienced fatigue throughout testing sessions or during the

implementation of the intervention or the assessment sessions. Participants were given refreshments and regular breaks to avoid such fatigue.

Participants did not benefit directly from this study. However, parents may have benefitted indirectly by gaining insight into their child's functioning. Parents/caregivers were also compensated ZAR100 (approximately US$11, at the time of the study) for their participation and to cover their and their children's transport costs to and from the assessment venue. In the case of the assessment that took place at the children's home, this amount was donated to the home.

Debriefing and feedback. The researcher conducting the assessment fully debriefed parents and children after testing. They were allowed to ask questions and they were given the contact details of the principal researcher. The results were made available to participants' parents upon request.

Results

Results of the preliminary analyses (i.e., pTBI vs. Controls) are presented first, followed by the results for the major analyses (i.e., Hypoxia vs. No-Hypoxia group).

Preliminary Analyses

There were 16 boys and 6 girls in the sample, with a mean age at assessment of 129.45 months (10.87 years; *SD* = 31.49). Regarding race, most (*n* = 20) were mixed race, with the rest (*n* = 2) being White. Regarding home language, most (*n* = 16) reported they spoke English and Afrikaans equally well; the rest (*n* = 6) reported they spoke Afrikaans only. There were no significant between-group differences in terms of age at assessment, or in terms of the distribution of sex, race, and language (see Table 7).

Table 7
Demographic Characteristics of the Sample (N = 22): TBI vs. Controls

Variable	Group		
	TBI (*n* = 11)	Controls (*n* = 11)	*p*
Sex			
Male: female	8: 3	8: 3	1.000
Age at assessment	129.36 (31.34)	129.55 (33.17)	.936
Race			1.000
Mixed race	10	10	
White	1	1	
Home language			.857
English and Afrikaans	8	8	
Afrikaans	3	3	

Note. For *Age at assessment*, data are presented in months, as means with standard deviations in parentheses.

There were also no significant between-group differences for any of the SES measures (see Table 8).

Table 8

Socioeconomic Status and Asset Index Data (N = 22): TBI vs. Controls

	Group		
Variable	TBI (*n* = 11)	Controls (*n* = 11)	*p*
Household income per year[a]			.500
0	1	0	
1 - 5 000	4	2	
5 001 - 25 000	2	5	
25 001 - 100 000	3	4	
100 001 +	1	0	
Parental education (father: mother)			.137; .565
1-6 years	1: 0	0: 0	
7 years	3: 0	0: 0	
8-11 years	2: 6	3: 6	
12 years	3: 4	7: 3	
13 years +	0: 0	1: 2	
Unknown	2: 1	0: 0	
Parental employment (father: mother)			.842; .725
Higher executives, major professionals	1: 0	0: 0	
Business managers of medium businesses, less professions	0: 1	0: 0	
Administrative personnel, managers, minor professionals	0: 1	1: 2	
Clerical and sales, technicians, small businesses	0: 2	2: 4	
Skilled manual (with training)	3: 1	4: 1	
Semi-skilled	1: 1	2: 1	
Unskilled, unemployed	1: 1	0: 0	
Homemaker	0: 1	1: 3	
Student, no occupation	1: 2	1: 0	
Unknown/incomplete	4: 1	0: 0	
Material and financial resources (Asset Index)			.387
0-5 assets (low)	0	0	
6-12 assets (medium)	3	6	
13-17 assets (high)	8	5	

Note. [a]Presented in South African Rands (ZAR). At the time of the study, the US$: ZAR exchange rate was 1 : 9.01.

Table 9 presents the results of the between-group comparisons on measures of IQ and neuropsychological test performance. Assumptions of normality and/or homogeneity were violated for the following outcome variables: PIQ, FSIQ, and Verbal Memory Composite. I therefore used Mann-Whitney *U* tests for these analyses.

As the table shows, there were significant between-group differences on the following: PIQ, FSIQ, Basic Attention Composite, Higher-Order Attention Composite, Visual Memory Composite, Executive Functions Composite, Visuospatial Skills Composite, and Expressive Language Composite. In all cases, the Control group performed better than the pTBI group. There were moderate to large effect sizes associated with each of these comparisons. These results remained consistent even with the removal of outliers identified through box plots, except in the case of the Visuospatial Skills Composite, which was no longer significant (see Appendix G).

For between-group differences for the subtests making up these composites, see Appendix H.

Table 9

IQ Variables and Neuropsychological Composites: Between-group Comparisons for TBI vs. Controls (*N* = 22)

	TBI			Controls			Test statistics		
	n	Range	*M* (*SD*)	*n*	Range	*M* (*SD*)	*F/U*	*p*	*r*
General Intellectual Functioning									
VIQ	11	55-106	77.82 (12.68)	11	66-119	86.45 (15.28)	2.08	.083	.31
PIQ	11	56-86	77.27 (8.91)	11	79-107	88.55 (8.69)	15.00[a]	.001**	-.64
FSIQ	11	52-94	75.27 (10.53)	11	74-111	85.73 (10.89)	28.00[a]	.016*	-.46
Basic Attention Composite (α = .753)	10	-1.35-0.72	-0.36 (0.67)	11	-0.27-1.18	0.35 (0.48)	7.79	.006**	.54
Higher-Order Attention Composite (α =.828)	8	-1.34-0.40	-0.46 (0.61)	11	-0.50-1.43	0.45 (0.64)	9.75	.003**	.60
Verbal Memory Composite (α = .929)	11	-2.20-1.37	-0.40 (1.15)	11	-0.73-1.50	0.40 (0.54)	36.50[a]	.060	-.34
Visual Memory Composite (α = .771)	10	-1.20-0.42	-0.43 (0.59)	11	-0.56-1.11	0.48 (0.50)	14.50	< .001***	.66
Executive Functions Composite (α =.774)	10	-1.83-0.65	-0.42 (0.69)	11	-0.36-1.24	0.44 (0.47)	11.28	.002**	.61
Visuospatial Skills Composite (α = .626)	11	-2.00-0.71	-0.33 (0.76)	10	-0.54-1.39	0.23 (0.54)	3.61	.037*	.40
Expressive Language Composite (α = .683)	11	-1.32-0.53	-0.46 (0.68)	11	-0.79-1.09	0.46 (0.60)	11.04	.002**	.60

Note. For qualitative descriptions for VIQ, PIQ and FSIQ, see Appendix I. [a]Mann-Whitney *U*; for PIQ, mean rank of the TBI group = 7.36 and of the Control group = 15.64; for FSIQ, mean rank of the TBI group = 8.55 and of the Control group = 14.45; for Verbal Memory Composite, mean rank of the TBI group = 9.32 and of the Control group = 13.68. The *r* value presented here is an estimate of effect size.

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

Tables 10 and 11 present results from the between-group comparisons of behavioural data. Table 10 shows that the groups differed significantly on all of the BRIEF indices, with the Controls reportedly scoring better than the pTBI participants. There were large effect sizes associated with these comparisons. These results remained consistent even with the removal of outliers identified through box plots (see Appendix J).

Table 10
BRIEF Indices: Between-group Comparisons for TBI vs. Controls (*N* = 22)

	Group						
	TBI (*n* = 11)		Controls (*n* = 11)				
Indices	Range	*M* (*SD*)	Range	*M* (*SD*)	*F*/*U*	*p*	*r*
Inhibit	41-103	71.64 (18.38)	42-65	54.18 (7.4)	8.54	.004**	.55
Shift	53-80	67.64 (7.83)	41-74	51.45 (9.42)	19.21	< .001***	.70
Emotional Control	56-82	69.73 (16.50)	36-60	49.55 (6.5)	5.50[a]	< .001***	-.77
BRI	53-92	72.36 (11.83)	39-62	52.09 (7.62)	22.82	< .001***	.73
Initiate	53-80	64.45 (9.52)	38-75	53.27 (10.19)	7.07	.008**	.51
Working memory	65-93	74.00 (8.47)	40-78	54.64 (10.55)	22.53	< .001***	.73
Plan/organization	50-84	69.27 (8.42)	37-69	51.18 (10.69)	19.46	< .001***	.70
Org. of materials	39-72	57.00 (9.84)	34-55	45.00 (6.66)	11.22	.002**	.60
Monitor	47-84	65.27 (11.15)	31-72	52.27 (10.49)	7.94	.006**	.53
MI	55-80	69.55 (7.84)	41-72	53.82 (8.67)	19.91	< .001***	.71
GEC	55-85	72.09 (8.69)	36-67	51.91 (8.93)	28.87	< .001***	.77

Note. For each comparison presented here, degrees of freedom = (1, 20). BRI = Behaviour Regulation Index; Org. of materials = Organization of materials; MI = Metacognition Index; GEC Global Executive Composite. [a]Mann-Whitney *U*; for Emotional Control, mean rank of the TBI group = 8.19 and of the Control group = 9.29. The *r* value presented here is an estimate of effect size.
*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

Table 11 shows that the groups also differed significantly on the Anxious/ Depressed, Withdrawn Depressed, Rule-breaking, and Aggression syndrome scales, and on the Externalizing Behaviour syndrome grouping, with the Controls reportedly scoring better than the pTBI participants. There were moderate to large effect sizes associated with these

comparisons. These results remained consistent even with the removal of outliers identified through box plots (see Appendix K).

Table 11

CBCL Syndrome Profiles: Between-group Comparisons for TBI vs. Controls (*N* = 22)

	Group						
	TBI group (*n*=11)		Healthy control group (*n*=11)				
CBCL syndrome profiles	Range	*M* (*SD*)	Range	*M* (*SD*)	*F/U*	*p*	*r*
Anxious/Depressed	51-86	62.82 (9.22)	50-80	57.91 (8.86)	34.00[a]	.041*	-.37
Withdrawn/Depressed	56-82	65.73 (8.81)	50-73	58.45 (8.63)	3.83	.033*	.40
Somatic Complaints	50-74	60.73 (8.39)	50-74	64.00 (6.74)	1.02	.163	.22
Internalizing Problems	54-80	65.00 (6.97)	33-77	59.64 (11.66)	1.72	.103	.28
Rule-Breaking Behaviour	50-80	63.36 (11.59)	50-63	53.73 (4.08)	32.00[a]	.031*	-.40
Aggressive Behaviour	57-87	69.36 (8.33)	50-61	53.36 (2.87)	2.00[a]	<.001**	-.82
Externalizing Problems	54-79	67.55 (8.31)	46-60	52.18 (4.00)	4.00[a]	<.001**	-.79

Note. For each comparison presented here, degrees of freedom = (1, 20). [a]Mann-Whitney *U*; for Anxious/Depressed, mean rank of the TBI group = 13.91 and of the Control group = 9.09; for Rule-breaking Behaviour, mean rank of the TBI group = 14.09 and of the Control group = 8.91; for Aggressive Behaviour, mean rank of the TBI group = 16.82 and of the Control group = 6.18; for Externalizing Problems, mean rank of the TBI group = 16.64 and of the Control group = 6.36. The *r* value presented here is an estimate of effect size.
*$p < 0.05$. **$p < 0.01$.

Consistent with the previous results, the data presented in Table 12 show that parents of the pTBI participants described their children's behaviour less favourably than parents of the Control participants on the Externalizing Behaviour syndrome grouping and in both the Rule-Breaking and Aggressive Behaviour syndrome scales. Overall, Fisher's Exact Test showed that there were more participants in the pTBI group than in the Control group whose behaviours could be classified, using the test manual's norms, as 'borderline' or 'clinical' and fewer participants in the pTBI group than the control group whose behaviours were classified as 'normal'.

Table 12

CBCL Categorizations: Between-group Comparisons for TBI vs. Controls (*N* = 22)

CBCL syndrome profiles		Group: TBI (*n*=11)	Group: Controls (*n*=11)	*p*
Anxious/depressed	Normal	7	9	.781
	Borderline	3	1	
	Clinical	1	1	
Withdrawn/depressed	Normal	5	8	.513
	Borderline	3	1	
	Clinical	3	2	
Somatic complaints	Normal	5	8	.513
	Borderline	3	1	
	Clinical	3	2	
Internalizing problems	Normal	2	4	.738
	Borderline	3	2	
	Clinical	6	5	
Rule-breaking behaviour	Normal	6	11	.035*
	Borderline	1	0	
	Clinical	4	0	
Aggressive behaviour	Normal	2	11	< .001***
	Borderline	4	0	
	Clinical	5	0	
Externalizing problems	Normal	2	10	.001**
	Borderline	2	1	
	Clinical	7	0	

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

Major Analyses

Table 13 shows that there were no significant differences between the Hypoxia and the No Hypoxia groups in terms of age at assessment, and in terms of sex, race, and language distribution.

There were no significant between-group differences for the injury-related variables with the exception of *Time Since Injury*: participants in the Hypoxia group had experienced a significantly longer time since injury than participants in the No Hypoxia group. There was a

large effect size associated with this finding (r = .68). The result remained consistent even after the removal of outliers (see Appendix L).

Table 13

Demographic Characteristics and Injury Variables (N = 11): Hypoxia vs. No Hypoxia

Variables	Group: Hypoxia (n = 5)	Group: No Hypoxia (n = 6)	t / U	p
Sex				1.000
Male: Female	4:1	4:2		
Age at injury (months)			-1.23[a]	.248
M (*SD*)	91.60 (36.02)	117.34 (33.09)		
Range	56-152	75-150		
Age at assessment (months)			14.00	.931
M (*SD*)	122.00 (31.50)	135.50 (32.72)		
Mean rank	5.80	6.17		
Range	105-178	91-169		
Time since injury (months)			1.50	.011*
M (*SD*)	30 (10.65)	17.50 (5.36)		
Mean rank	8.70	3.75		
Range	24-49	12-25		
Race				1.000
Mixed race	5	5		
White	0	1		
Home language				.545
English / English and Afrikaans	3	5		
Afrikaans	2	1		
GCS			9.00	.284
M (*SD*)	5.60 (2.07)	7.00 (1.10)		
Mean rank	4.80	7.00		
Range	3-8	6-8		
Motor GCS			7.50	.152
M (*SD*)	3.40 (1.82)	4.83 (0.41)		
Mean rank	4.50	7.25		
Range	1-5	4-5		
Cause of injury				.221
Passenger in MVA	0	3		
Pedestrian in MVA	3	3		
Assault	1	0		
Other	1[b]	0		

Note. [a] t-statistic, [b] The participant sustained a crush injury as a result of a quad bike accident. GCS = Glasgow Coma Scale; MVA = Motor vehicle accident.

*$p < 0.05$

There were no significant between-group differences on any of the SES measures (see Table 14).

Table 14

Socioeconomic Status and Asset Index Data (N = 11): Hypoxia vs. No Hypoxia

Variable	Group		*p*
	Hypoxia (*n* = 5)	No Hypoxia (*n* = 6)	
Household income per year			.558
0	1	0	
1 - 5 000	2	2	
5 001 - 25 000	0	2	
25 001 - 100 000	1	2	
100 001 +	1	0	
Parental education (father: mother)			.190; .571
0 years	0: 0	0: 0	
1-6 years	0: 0	1: 0	
7 years	3: 0	0:0	
8-11 years	0: 3	2: 3	
12 years	1: 1	2: 3	
13 years +	0: 0	0: 0	
Unknown/incomplete	1: 1	1: 0	
Parental employment (father: mother)			.286; 1.000
Higher executives, major professionals	1: 0	0: 0	
Business managers of medium businesses,	0: 0	0: 1	
Administrative personnel, managers, minor	0: 0	0: 1	
Clerical and sales, technicians, small	0: 1	0: 1	
Skilled manual (with training)	0: 1	3: 0	
Semi-skilled	0: 0	1: 1	
Unskilled, unemployed	1: 0	0: 1	
Homemaker	0: 1	0: 0	
Student, no occupation	0: 1	1: 1	
Unknown/incomplete	3: 1	1: 0	
Material and financial resources (Asset Index)			.545
0-5 assets (low)	0	0	
6-12 assets (medium)	2	1	
13-17 assets (high)	3	5	

Note. [a]Presented in South African Rands (ZAR). At the time of the study, the US$: ZAR exchange rate was 1 : 9.01.

Table 15 presents the results of between-group comparisons for the categorical neurosurgical monitoring variables. There were no significant between-group differences.

Table 15
Descriptive Statistics for Categorical Neurosurgical Variables (N = 11): Hypoxia vs. No Hypoxia

	Group		
Variable	Hypoxia (n = 5)	No Hypoxia (n = 6)	p
Pupils on admission	0 : 3: 1: 1	3: 2: 0: 1	.286
Initial systemic hypoxia	5 : 0	5 : 1	1.000
Initial SBP < 90	3 : 2	4 : 2	1.000
Polytrauma	3 : 2	3 : 3	1.000
ICU risk of mortality score[a]	4 : 1	3 : 2[a]	1.000

Note. Pupils on admission: 0 = unilaterally reactive, 1 = bilaterally reactive, 2 = unilaterally non-reactive, 3 = bilaterally non-reactive. Initial systemic hypoxia: 0 = no, 1 = at least one episode. Initial SBP (systemic blood pressure): 0 = no, 1 = yes. Polytrauma: 0 = isolated TBI, 1 = polytrauma. ICU risk of mortality score: 1 ≥ 0.50, 0 < 0.50. [a]Data missing for one participant.

Table 16 presents the results of between-group comparisons for the continuous neurosurgical monitoring variables. I used two-tailed tests of significance (Mann-Whitney U and one-way ANOVA tests), as no a priori predictions were made. Apart from the significant differences between the groups for the $PbtO_2$ < 10mmHg and lowest PbtO2 variables, the basis on which the two groups were formed, the groups also differed significantly on the following variables: Mean ICP > 20, Highest ICP, Lowest CPP, and Lowest PaO_2 (although the latter variable was not significant after the outliers were removed, U = 4.00; p = .11 (see Appendix M). The effect size estimates suggest that $PbtO_2$ accounted for greater variance between the groups than the ICP, CPP, and PaO_2 variables, however.

Table 16

Descriptive Statistics for Continuous Neurosurgical Variables (N = 11): Hypoxia vs. No Hypoxia

	Group								
	Hypoxia (n = 5)			No Hypoxia (n = 6)					
Variable	*M* (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*F*/*U*	*p*	*r*
Mean ICP value > 20	30.32 (7.18)	23-42	8.60	11.72 (12.88)	0-25	3.83	2.00	.017*	-.72
Mean ICP value: first 24 hours	22.01 (11.42)	14-42	7.90	12.74 (4.97)	8-19	4.42	5.50	.091	-.52
Highest ICP value	50.80 (19.08)	34-77	8.40	25.17 (10.36)	16-44	4.00	3.00	.030*	-.66
Duration of monitoring (hours)	174.00 (71.43)	91-268	7.80	111.50 (93.37)	33-296	4.50	6.00	.126	-.50
Number of episodes: ICP > 20	24.60 (12.76)	10-45	7.80	13.33 (24.65)	0-62	4.50	6.00	.104	-.50
Number of episodes: CPP < 40	3.00 (4.24)	0-9	6.90	0.17 (0.41)	0-1	5.25	10.50	.303	-.32
Number of episodes: CPP < 50	8.40 (0.55)	8-9	8.00	3.50 (5.43)	0-14	4.33	5.00	.071	-.56
Number of episodes: PaO_2 < 8	0.40 (0.89)	0-2	6.20	0.17 (0.41)	0-1	5.83	14.00	.727	-.08
Number of episodes: $PbtO_2$ < 5	0.80 (1.79)	0-4	6.60	0.00 (0.00)	0-0	5.50	12.00	.455	-.33
Number of episodes: $PbtO_2$ < 10	5.60 (6.62)	1-17	9.00	0.00 (0.00)	0-0	3.50	0.00	.002**	-.90
Number of episodes: $PbtO_2$ < 20	24.40 (21.41)	3-51	7.80	8.83 (12.21)	0-31	4.50	6.00	.115	-.50
Initial MAP	65.53 (12.73)	47-79		76.00 (16.82)	57-101		1.30[a]	.283	.36
Mean ICP value	15.72 (3.12)	13-21		12.96 (3.76)	10-19		-1.71[a]	.224	.40
Lowest PaO_2 value	9.00 (1.47)	6.5-10.2		13.16 (3.37)	8-16.7		6.50[a]	.031*	.65
Mean PaO_2 value	23.42 (9.36)	14.7-37.0		21.14 (5.12)	15.5-29.3		-0.27[a]	.619	.17
Lowest Hb	8.28 (1.17)	7-10		9.05 (0.82)	8.2-10.5		1.65[a]	.231	.39
Mean Hb	10.30 (0.64)	9.5-11		10.07 (0.94)	8.9-11.3		-0.22[a]	.651	
Lowest $PbtO_2$	5.80 (2.52)	2-8		16.97 (5.40)	12-27		17.87[a]	.002**	
Mean $PbtO_2$: first 24 hours	30.64 (11.07)	13-40		28.00 (5.32)	21.6-36.8		0.27[a]	.615	
Lowest CPP	28.60 (15.16)	10-44		51.33 (10.63)	39-64		8.55[a]	.017*	

Note. Means and ranges are presented with standard deviations in parentheses. For between-group comparisons using *F*-tests, degrees of freedom were (1, 9) in each case. [a] *F*-statistic. The *r* value presented here is an estimate of effect size.

*$p < 0.05$. **$p < 0.01$.

Table 17 presents the significant correlations between neurosurgical monitoring variables. Several of these significant correlations are for variables for which there were significant differences between the Hypoxia and No Hypoxia groups. These correlations were computed in service of the ANCOVA analyses, which follow.

Not surprisingly, there were strong significant correlations among related parameters. For example, there were strong negative correlations between the lowest $PbtO_2$ value and both the number of episodes that $PbtO_2 < 10$ and < 20. Similarly, there was a strong positive correlation between the mean ICP value > 20 and the highest ICP value during the monitoring period. Both of these ICP variables are have strong positive correlations with the mean ICP score within the first 24 hours of monitoring, the mean ICP score during the monitoring period, and the number of episodes of ICP > 20. The lowest CPP value also correlates negatively with the number of times that CPP < 50.

There were also strong correlations between the PbtO2-related variables that differed significantly between the Hypoxia and the No Hypoxia groups and other neuromonitoring parameters. For example, both the lowest $PbtO_2$ value and the number of episodes that $PbtO_2 < 10$ correlated significantly with the mean ICP > 20, the highest ICP values, and the lowest $PbtO_2$ values for the duration of monitoring. The lowest $PbtO_2$ value also correlated significantly with the number of episodes of ICP > 20 and the mean ICP value in the first 24 hours of monitoring. All of these relationships were in the expected directions.

The lowest CPP value for the duration of monitoring correlated negatively and significantly with the mean ICP value > 20, the highest ICP value for the duration of monitoring, the number of episodes that ICP > 20 and the mean ICP value within the first 24 hours. Further, the number of episodes of CPP < 40 and CPP < 50 were correlated with the highest ICP value for the duration of monitoring and the lowest $PbtO_2$ values, respectively. These relationships were also in the expected directions.

For all other non-significant correlations, see Appendix N.

Table 17

Spearman's Rho Correlations for Neurosurgical Variables (Significant Correlations Only; N = 11)

Variable 1	Variable 2	ρ	*p*
ICP > 20	Mean ICP > 20	.71*	.014
	Mean ICP first 24	.75**	.008
	Mean ICP	.81**	.003
	Highest ICP	.88***	< .001
	Lowest CPP	-.62*	.042
	CPP < 40	0.71*	.014
	Lowest $PbtO_2$	-0.72*	.012
	$PbtO_2$ < 20	0.71*	.014
Mean ICP > 20	Mean ICP first 24	.92***	< .001
	Mean ICP	.82**	.002
	Highest ICP	.90***	< .001
	Lowest CPP	-.81**	.003
	Lowest $PbtO_2$	-0.75**	.008
	PbtO2 < 10	0.64*	.033
Mean ICP first 24	Mean ICP	.85**	.001
	Highest ICP	.93***	< .001
	Lowest CPP	-.82**	.002
	CPP < 40	0.66*	.027
	Lowest $PbtO_2$	-0.69*	.019
Mean ICP	Highest ICP	.81**	.002
	CPP < 40	0.66*	.027
Highest ICP	Lowest CPP	-.82**	.002
	CPP < 40	0.79**	.004
	Lowest $PbtO_2$	-0.85**	.001
	$PbtO_2$ < 10	0.62*	.043
Lowest CPP	CPP < 50	-0.74**	.009
CPP < 40	$PbtO_2$ < 5	0.64*	.035
CPP < 50	PaO_2 < 8	0.63*	.036
	Lowest PaO2	-0.89***	< .001
PaO_2 < 8	Lowest PaO2	-0.67*	.023
Lowest PaO_2	Lowest PbtO2	0.65*	.032
	$PbtO_2$ < 10	-0.61*	.048
Lowest Hb	Mean $PbtO_2$ 24hrs	-0.64*	.035
Mean Hb	$PbtO_2$ < 20	0.86**	.001

Variable 1	Variable 2	ρ	*p*
Lowest $PbtO_2$	$PbtO_2 < 10$	-0.89***	< .001
	$PbtO_2 < 20$	-0.75**	.008
Initial MAP	Initial SBP<90	-0.84**	.001
	Mean Hb	-.87**	.001
	$PbtO_2 < 20$	-.81**	.003
Initial SBP < 90	Mean Hb	.66*	.028

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

Table 18 presents the results for the between-group on measures of IQ and neuropsychological test performance. Assumptions of normality and/or homogeneity were violated for the following outcome variables: PIQ, FSIQ, and Higher-Order Attention Composite.

As Table 18 shows, there were significant between-group differences on the following: VIQ, FSIQ, Basic Attention Composite, Higher-Order Attention Composite, Verbal Memory Composite, Visual Memory Composite, Executive Functions Composite, Visuospatial Skills Composite, and Expressive Language Composite. In all cases, the No Hypoxia group performed better than the Hypoxia group. There were large effect sizes associated with each of these comparisons. These results remained consistent even with the removal of outliers identified through box plots (see Appendix O).

Table 18

Between-group Comparisons for General Intellectual Functioning and Neuropsychological Composites: Hypoxia vs. No Hypoxia Groups (N = 11)

	No Hypoxia			Hypoxia			Test statistics		
	n	Range	*Mean* (*SD*)	*n*	Range	*Mean* (*SD*)	*F/U*	*p*	*r*
General intellectual functioning									
VIQ	6	76-106	84.67 (11.59)	5	55-77	69.40 (8.50)	5.96	.019*	.63
PIQ	6	77-85	81.50 (3.08)	5	56-86	72.20 (11.3)	6.50[a]	.069	-.47
FSIQ	6	76-94	81.33 (6.77)	5	52-77	68.00 (9.93)	1.00[a]	.004**	-.78
Basic attention composite (α = 0.726)	5	0.17-1.04	0.52 (0.36)	5	-0.95 – 0.05	-0.53 (0.38)	19.86	.001**	.84
Higher order attention composite (α = 0.831)	5	-0.28-1.22	0.55 (0.62)	3	-1.08-(-0.41)	-0.67 (0.36)	0.00[a]	.018*	-.67
Verbal memory composite (α = 0.957)	6	0.15-1.53	0.72 (0.52)	5	-1.54-0.05	-0.86 (0.59)	22.18	<.001***	.84
Visual memory composite (α = 0.686)	6	-0.84-1.00	0.38 (0.65)	4	-0.62-0.04	-0.39 (0.29)	4.82	.03*	.61
Executive functions composite (α = 0.840)	6	0.16-1.23	0.54 (0.39)	4	-1.56-(-0.20)	-0.70 (0.61)	16.02	.002**	.82
Visuospatial skills composite (α = 0.572)	6	0.13-0.73	0.37 (0.25)	5	-0.98-0.12	-0.45 (0.40)	17.53	.001**	.81
Expressive language composite (α = 0.622)	6	0.20-1.06	0.62 (0.31)	5	-0.97-(-0.48)	-0.74 (0.19)	73.49	< .001***	.94

Note. For qualitative descriptions for VIQ, PIQ and FSIQ, see Appendix I. [a]Mann-Whitney *U;* for PIQ, mean rank of the No Hypoxia group = 7.42 and of the Hypoxia group = 4.30; for FSIQ, mean rank of the No Hypoxia group = 8.33 and of the Hypoxia group = 3.20; For Higher Order Attention Composite, mean rank of the No Hypoxia group = 6.00 and of the Hypoxia group = 2.00. The *r* value presented here is an estimate of effect size.
*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

For between-group differences for the subtests making up these composites, see Appendix P.

Tables 19 and 20 show that the Hypoxia and the No Hypoxia groups did not differ significantly on any of the BRIEF indices, on any of the CBCL syndrome scales, or on the Internalizing and Externalizing syndrome groupings. This pattern of data remained largely consistent even after outliers were removed (see Appendices Q and R). The only change to the pattern was that scores on the CBCL Rule-Breaking syndrome scale was significantly different between groups after the removal of outliers, F (1,7) = 38.260; $p < .001$. Despite this pattern of data, there were moderate effect sizes associated with the Plan/Organization and MI indices of the BRIEF, and the Withdrawn Depressed, Rule-Breaking and Aggressive Behavior syndrome scales, and Externalizing Behavior syndrome grouping of the CBCL, suggesting that with a larger sample size, these comparisons could reach significance.

Table 19

BRIEF Indices: Between-group Comparisons for Hypoxia vs. No Hypoxia (*N* = 11)

	Group						
	No Hypoxia (*n* = 6)		Hypoxia (*n* = 5)				
Indices	Range	*M* (*SD*)	Range	*M* (*SD*)	*F*/*U*	*p*	*r*
Inhibit	41-103	70.50 (25.23)	66-84	73.00 (6.67)	0.05	.418	.07
Shift	53-80	66.33 (10.17)	63-74	69.20 (4.27)	0.34	.287	.19
Emotional control	56-82	70.83 (9.30)	58-78	68.40 (7.44)	0.22	.325	.16
BRI	53-92	71.83 (16.07)	65-78	73.00 (5.15)	0.02	.441	.05
Initiate	53-73	62.67 (7.74)	53-80	66.60 (11.89)	0.44	.262	.22
Working memory	65-93	73.17 (10.44)	67-84	75.00 (6.40)	0.12	.371	.11
Plan/organization	50-74	66.00 (8.97)	67-84	73.20 (6.42)	2.25	.084	.45
Org. of materials	39-72	56.00 (13.37)	56-84	58.20 (3.90)	14.50 [a]	.483	-.03
Monitor	47-76	62.50 (11.22)	31-72	68.60 (11.31)	0.80	.197	.29
MI	55-80	66.67 (8.52)	68-80	73.00 (5.96)	8.00[a]	.113	-.39
GEC	55-85	70.00 (11.14)	69-79	74.60 (4.39)	0.75	.205	.28

Note. For between-group comparisons using *F*-tests, degrees of freedom were (1, 9) in each case. BRI = Behaviour Regulation Index; Org. of materials = Organization of materials; MI = Metacognition Index; GEC Global Executive Composite. [a]Mann-Whitney *U*; for Org. of Materials, mean rank of the Hypoxia group = 5.92 and of the No Hypoxia group = 6.10; for MI, mean rank of the Hypoxia group = 4.83 and of the No Hypoxia group = 7.40. The *r* value presented here is an estimate of effect size.

Table 20

CBCL Syndrome Profiles: Between-group Comparisons for Hypoxia vs. No Hypoxia ($N = 11$)

	Group						
	No Hypoxia		Hypoxia				
Syndrome Profile	Range	*M* (*SD*)	Range	*M* (*SD*)	*F/U*	*p*	*r*
Anxious/Depressed	51-69	60.83 (6.05)	55-86	65.20 (12.40)	0.59	.232	.25
Withdrawn Depressed	56-68	62.67 (5.32)	58-82	69.40 (11.31)	1.71	.112	.40
Somatic Complaints	50-70	58.83 (7.50)	50-74	63.00 (9.70)	0.65	.221	.26
Internalizing Problems	58-68	63.33 (3.33)	54-80	67.00 (9.93)	11.00[a]	.268	-.22
Rule-breaking Behaviour	50-80	58.50 (11.31)	53-78	69.20 (9.88)	7.50[a]	.104	-.42
Aggressive Behaviour	57-75	66.17 (7.17)	65-87	73.20 (8.70)	2.17	.088	.44
Externalizing Problems	54-78	64.00 (8.41)	62-79	71.80 (6.54)	2.85	.063	.49

Note. For between-group comparisons using *F*-tests, degrees of freedom were (1, 9) in each case. [a]Mann-Whitney *U*; for Internalizing Problems, mean rank of the No Hypoxia group = 5.33 and of the Hypoxia group = 6.80; for Rule-breaking Behaviour, mean rank of the No Hypoxia group = 4.75 and of the Hypoxia group = 7.50; The *r* value presented here is an estimate of effect size.

The results of the non-parametric ANCOVA analyses are presented in Appendix S. Recall that I used Quade's Test to calculate the test statistics here; this procedure was designed specifically to allow ANCOVA under conditions where assumptions of the parametric test are violated. The results show that the Highest ICP variable played a role in significantly predicting the Expressive Language Composite. However, Highest ICP was significantly correlated with both the number of episodes that $PbtO_2 < 10$ and the Lowest $PbtO_2$ value during the monitoring period (see Table 17 for correlations).

The results of the ANCOVA analyses also showed that Lowest PaO_2 played a role in significantly predicting the Basic Attention Composite, the Verbal Memory Composite, the Visuospatial Skills Composite, and the Expressive Language Composite. However, PaO_2 was significantly correlated with both the Lowest $PbtO_2$ and the $PbtO_2 < 10$ variables.

Finally, Lowest CPP played a role in significantly predicting the Basic Attention Composite, the Verbal Memory Composite, the Executive Functions Composite, the Visuospatial Composite and the Expressive Language Composite. Lowest CPP was not, however, correlated with either Lowest $PbtO_2$ or $PbtO_2 <10$.

All other analyses did not produce statistically significant results, $p > .05$ in each case.

Discussion

Summary of Results and Hypothesis Testing

Preliminary analyses and hypothesis 1: pTBI participants vs. healthy controls. Hypothesis 1 stated that participants who had sustained TBIs would perform more poorly than matched healthy controls on neuropsychological and behavioural measures. This hypothesis was confirmed.

There were no significant between-group differences on any of the demographic variables, including measures of SES. These factors, and SES in particular, can impact on neuropsychological test performance (e.g., see V. Anderson, Catroppa, Haritou, et al., 2001; V. Anderson, Morse, Catroppa, Haritou, & Rosenfeld, 2004; Max et al., 1999). Hence, it is important that the groups were matched as closely as possible on these factors.

The groups did, however, differ significantly on measures of PIQ, FSIQ, and on composite indices of basic and higher-order attention, visual memory, executive functioning, visuospatial skills, and expressive language; in each case, the TBI participants performed more poorly than their matched controls. These outcomes are consistent with the literature describing expected neuropsychological sequelae following pTBI (V. Anderson, Northam, Hendy, et al., 2001; Babikian & Asarnow, 2009; Beauchamp et al., 2011; Catroppa et al., 2011, 2007; Catroppa & Anderson, 2007; Ewing-Cobbs et al., 1997; H. Levin, 1995; Mandalis et al., 2007; Mangeot et al., 2002; Park et al., 2009; Slomine et al., 2002, 2005; Sullivan & Riccio, 2010; Van Heugten et al., 2006; Yeates et al., 2005).

There were no significant differences, however, on VIQ and on the Verbal Memory Composite. Examining the means, however, the data were in the expected direction, with the TBI participants performing more poorly than the healthy control participants, with medium effect sizes. Hence, these comparisons could potentially reach statistical significance with a larger sample size.

The groups also differed significantly on all of the BRIEF indices, which measure parent reports on various everyday executive functions, with the Controls reportedly scoring better than the pTBI participants. These results are consistent with those from the neuropsychological tests. Executive functions are primarily subserved by the frontal lobes, and in particular, the prefrontal cortex. The frontal lobes are especially vulnerable to the effects of TBI owing to their neuroanatomical positioning and the kinds of biomechanical forces acting on the skull in many TBIs (Bamdad et al., 2003; Catroppa & Anderson, 2006;

Stuss, 2011). In view of this vulnerability, the BRIEF data are consistent with expected outcomes.

Regarding the CBCL, the groups differed on the Externalizing Behaviour syndrome grouping and both of the syndrome profiles (Rule-Breaking and Aggressive Behaviour) included in this grouping, with the pTBI group reportedly showing more problems in these domains than the Controls. The groups also differed significantly on the Anxious/Depressed and Withdrawn/Depressed profiles of the Internalizing Behaviour syndrome grouping, with the Controls reportedly scoring better than the pTBI participants. They did not differ on the Somatic Complaints syndrome profile, or on the Internalizing Behaviour syndrome grouping as a whole.

Behavioural and emotional problems (particularly internalizing and externalizing problems) are reported to be the main reason that children who have sustained TBIs are referred to mental health and rehabilitation professionals (Dooley et al., 2008). If one examines the results for the Internalizing Behaviour syndrome grouping, it is evident that although this between-group comparison is not significant, the mean score for the TBI participants falls within the clinical range, whereas the mean score for the healthy controls falls within the normal range. There is a small effect size associated with this comparison, however. Hence, these results show a trend in the expected direction. Only the Somatic Complaints syndrome profile does not fit this trend, with parents reporting similar behaviour for both groups. Although it forms part of the internalizing syndrome grouping, somatic complaints are not necessarily suggestive of emotionally based problems. Therefore, a non-significant finding here does not conflict with reports of emotional and behavioural problems commonly associated with TBI.

The syndrome profiles on which significant between-group differences were detected are commonly reported behavioural sequelae following pTBI. Rule-breaking is often a manifestation of executive dysfunction owing to a lack of inhibition and insight (Cook, Chapman, & Levin, 2008; Schachar et al., 2004; Taylor, 2004). Post-TBI aggression is often described and may be attributed to emotional lability and to a lack of frustration tolerance, especially when coping with new impairments or disabilities (Cole et al., 2008; Dooley et al., 2008). Finally, children who have sustained TBI are often anxious and/or depressed (e.g., Max et al., 2012), which is not surprising, given the traumatic ordeal and often adverse consequences associated with severe TBI.

In summary, the current data confirmed Hypothesis 1, and thereby confirmed that the patterns of group performance observed here are consistent with those observed in previously published studies.

Major analyses and hypothesis 2: Hypoxia vs. No Hypoxia groups. The 10mmHg $PbtO_2$ threshold, used as the basis upon which to form the Hypoxia and No Hypoxia groups, is widely accepted as a critical threshold for ischemia/hypoxia (Figaji, Fieggen, Argent, et al., 2008; Maloney-Wilensky et al., 2009; Valadka et al., 1998; Van Santbrink et al., 2003). Knowing the detrimental effects of hypoxia, either chronic or episodic, on neuropsychological outcomes, one might anticipate that those participants for whom this threshold was crossed would experience more unfavourable outcomes generally. Hence, Hypothesis 2 stated that participants who had sustained TBIs and who had experienced at least one hypoxic episode ($PbtO_2 \leq 10$ mmHg) would perform more poorly on neuropsychological and behavioural outcome measures than participants who had sustained a TBI and for whom $PbtO_2$ values remained above 10 mmHg during the monitoring period.

There were no significant between-group differences on any of the socio-demographic variables, including the SES measures. There were also no significant between-group differences on the injury variables, except in terms of time since injury. Participants in the Hypoxia group had experienced a significantly longer period of time since sustaining injury. However, the significant difference in time since injury is not expected to have an effect on the outcome. Even if the overall time since injury differed significantly between the two groups, all of the participants in both groups were at least 1 year post-injury. It has long been reported that improvement in outcome post-TBI is more limited and plateaus after 1-year post injury, particularly in children who have sustained severe TBIs (Chadwick et al., 1981; Ginstfeldt & Emanuelson, 2010; Yeates et al., 2002).

Between-group differences in neuropsychological outcomes. The Hypoxia and No Hypoxia groups differed significantly on measures of VIQ and FSIQ, as well as on the composite measures of basic and higher-order attention, verbal and visual memory, executive functioning, visuospatial ability, and expressive language. On all of these measures, participants in the Hypoxia group performed more poorly than those in the No Hypoxia group. These findings suggest that secondary injury effects, such as exposure to episodes of hypoxia, create further unfavourable outcomes in children who have sustained severe TBI. Overall, these data are consistent with literature on neuropsychological sequelae following hypoxia-ischemia (V. Anderson, Catroppa, Haritou, et al., 2001; Bigler, 1989; Caine & Watson, 2000; Lezak et al., 2004).

Between-group differences in behavioural outcomes. The results show that the experience of one or more hypoxic episodes does not, however, seem to be directly related to outcome on any of the behavioural measures. The Hypoxia and No Hypoxia groups did not differ significantly on any of the BRIEF indices or any of the CBCL syndrome scales or Internalizing and Externalizing syndrome groupings, as reported by participants' parents. There were, however, moderate effect sizes associated with some of these comparisons, suggesting that results could potentially reach significance with a larger sample size.

The literature on investigations into the predictors of cognitive and behavioural outcomes post-TBI suggests a divide in terms of predicting these two areas of outcome. Although cognitive outcomes are strongly determined by injury-related variables, a combination of injury-related factors (e.g., severity) and environmental factors (e.g. family functioning and psychosocial adversity), rather than injury-related factors on their own, is strongly predictive of behavioural outcome (V. Anderson, Catroppa, Haritou, et al., 2001; V. Anderson et al., 2005, 2004; Jaffe et al., 1993; Johnson et al., 2011; Knights et al., 1991; Yeates et al., 2004).

Hence, predictors of behavioural outcomes are viewed more broadly than those for cognitive outcomes. Researchers view behavioural outcomes following TBI as complex and as a product of a range of interacting factors that are not only limited to injury severity, but extend to the family environment and to resources both prior to and after the injury (Fletcher et al.; Kinsella et al., 1999; Rutter, 1982). There is a dose-response relationship between the predictors of behavior and associated outcome, such that more marked and persistent behavioural difficulties are associated with more severe TBI and poorer family environments (Taylor et al., 2002).

Brain hypoxia-ischemia is a secondary injury-related factor and not an environmental factor. In line with the argument above, it is not surprising that $PbtO_2$ on its own would not predict behavioural functioning, at least not directly or not as strongly as the cognitive outcomes. This being the case, in light of the aforementioned literature on predictors of cognitive and behavioural outcomes, the fact that episodes of $PbtO_2 < 10$mm Hg may be associated more strongly with cognitive rather than behavioural outcomes is consistent with the literature.

An alternative explanation might consider how behaviour is typically measured (i.e., via self- or other-report) in this field. In contrast, there are objective measures for cognition. Hence, reports on behaviour might be less accurate than data collected for more objective cognitive measures.

Significant differences on other physiological parameters. Besides significant differences between the groups on the $PbtO_2$ variables (number of episodes when $PbtO_2 < 10$ mmHg and lowest $PbtO_2$ value), the basis on which the groups were formed, the Hypoxia and No Hypoxia groups also differed significantly on variables relating to raised ICP, low CPP, and lowest $PbtO_2$. The Hypoxia group experienced higher ICP values, a higher mean of ICP values greater than 20, and lower CPP and PaO_2 values.[1] There were large effect sizes associated with these comparisons.

Hence, there were possible covariate effects that needed to be elucidated. The ANCOVA results suggested that neuromonitoring variables other than $PbtO_2$ might also contribute to the significant differences found between Hypoxia and No Hypoxia groups on measures of neuropsychological test performance. Highest ICP contributed significantly to between-group differences on the Expressive Language composite. Lowest $PbtO_2$ contributed significantly to between-group differences on composite measures of basic attention, verbal memory, visuospatial ability, and expressive language. Lowest CPP contributed significantly to between-group differences on composite measures of basic attention, verbal memory and executive function.

There was a large effect size associated with the between-group comparison on Lowest CPP. This piece of data suggests that this physiological parameter accounts for a substantial proportion of the total variance in neuropsychological test performance between the two groups. The Lowest CPP value and the $PbtO_2$ variables were not significantly correlated, however, suggesting an additional role for CPP in predicting neuropsychological performance. Very limited literature exists exploring the relationship between CPP and cognitive outcomes specifically. Lannoo et al. (1998) failed to find a definite association between CPP and ICP on the one hand, and measures of attention, memory and learning, executive functions, and other cognitive domains (information processing, motor reaction time, and visuoconstructional ability) on the other. Those results are not consistent with the current data. However, Lannoo et al. included both CPP and ICP measures in combination, and focused on an older sample (15-65 years). Hence, follow-up studies are required to investigate the specific relationship between CPP and the cognitive domains identified in this study. CPP and ICP parameters are strongly associated (CPP = MAP-ICP), however, and the latter parameter is, in turn, closely related to $PbtO_2$. Hence, the CPP results may also be an

[1] The ICP threshold is 20 mmHg, with higher values being increasingly detrimental. Lower CPP and PaO_2 values are more detrimental.

indirect product of the interactions between the CPP and ICP, and between the ICP and $PbtO_2$, monitoring parameters.

Because $PbtO_2$ was significantly correlated with the lowest $PbtO_2$ and various ICP-related variables, it is more difficult to tease apart the effects here. Both the lowest $PbtO_2$ value and the number of episodes of $PbtO_2 < 10$ correlate strongly with the mean ICP > 20, the highest ICP values, and the lowest P_aO_2 values for the duration of monitoring. P_aO_2 variables represent systemic oxygenation; hence, this parameter is directly associated with episodes of low brain oxygenation. The overlap between these variables and outcome is expected.

Inconsistent with our findings and with the fact that there is a strong negative relationship between very high levels of ICP and low $PbtO_2$, Rohlwink et al. (2012) describe a complex and weak relationship between $PbtO_2$ and ICP, also in relation to pTBI. Those authors reported that low $PbtO_2$ is independently associated with poor outcomes. However, they also reported that controlling or treating high ICP may influence the effect of $PbtO_2$ on outcome. Conversely, low $PbtO_2$ may contribute to the poor outcome associated with high ICP.

In spite of these covariates influencing outcome, I have, however, made a concerted effort to take into account and to control for a number of potential confounders. It seems clear that, even when the covariates are controlled for, $PbtO_2$ still plays a key and independent role in influencing cognitive outcome.

In summary, the data reported here suggest that reaching a critical $PbtO_2$ threshold of ≤ 10 mmHg may be detrimental to cognitive outcomes following pTBI. Therefore, over and above the effects of the TBI, which leads to poor neuropsychological and behavioural outcomes (Hypothesis 1), there may also be additional post-TBI hypoxic effects that contribute to even worse cognitive outcomes (Hypothesis 2).

Limitations and Directions for Future Research

Perhaps the most obvious limitation in this study is the small sample size, which limits the strength of the conclusions that can be drawn and the generalisability of the results. In mitigation, however, effect sizes are large and suggestive of real between-group differences. I will aim to increase the sample size in follow-up studies.

A second limitation relates to the study design. I recognize that implementing a three-group comparison (i.e., a pTBI/Hypoxia group, a pTBI/No Hypoxia group, and a healthy control group) might have been most ideal for the analysis in this study. The ultimate aim in implementing this design would be to attempt to tease apart TBI and hypoxic effects, both

independently and combined. One way to do this legitimately, however, would be in a regression model where one could partial out the two effects and look at an interaction effect. This design was not implemented, however, because there were only a limited number of participants who had sustained TBI, for whom monitoring data was available, and who met the inclusion criteria. The Hypoxia and No Hypoxia groups included five and six participants, respectively. Therefore, I separated the analyses into two parts: a preliminary analysis where I compared all of the pTBI participants to matched healthy controls, with 11 participants in each group, and a major analysis where I compared those participants who had sustained TBI and at least one episode of hypoxia to those participants who had sustained TBIs and for whom $PbtO_2$ levels remained above 10mmHg. The preliminary analysis established that the pTBI sample performed worse than the controls. In doing so, this analysis grounds the data in previous literature and provides some validation for the use of the chosen measures in this context.

The broad age range among the participants might be interpreted as a third limitation, due to the fact that a great degree of neurodevelopment can occur during these years. In this study, there was, however, a closely matched control group. An increased *N* would not only give the study better power, but would also allow one to include more participants within each age band (7-8; 9-10; 11-12; etc.), which would then allow detection of developmental trends. Further, although the age range is wide it is an improvement on previous similar studies (e.g., Figaji et al., 2009b), where the age range extended from 9 months to 14 years of age.

A fourth possible limitation is that the measures of behavioural outcomes included in this study were all self-report measures and hence depend solely on reliable reporting by parents. There are obvious limitations to using this method that affect the validity thereof. These include: (a) social desirability biases, and with that, (b) under- or over-reporting of behaviours, (c) problems related to accessing data on moods and behaviours retrospectively, which can lead to inaccurate reporting, or (d) potential lack of information from respondents on the wide range of behaviours surveyed in the questionnaires, rendering the data incomplete (Holden & Troister, 2009; Hunsley, 2009; A. Williamson, 2007). Administering teacher versions of each of the behavioural measures would have strengthened the power of these results. Multiple converging sources of data serve to confirm the reliability of behavioural observations (e.g., Coie & Dodge, 1988). However, I used the measures as is for two reasons: resource limitations and reported strong psychometric properties.

In spite of these limitations, the findings presented here and their potential implications warrant attention and further inquiry. This study is an important first step in comprehending and discerning the prognostic value of $PbtO_2$ in determining neuropsychological and behavioural outcomes post-pTBI. However, although the conclusions that may be drawn from these results are noteworthy and could have important implications, they are tentative at this stage, requiring repeated studies and further investigations into the effects and trends suggested by the results, as well as further validation in larger studies.

Summary and Conclusion

The contribution of TBI to mortality and morbidity in children is concerning. Prevention is therefore paramount. Besides the primary injury that occurs on impact, a range of secondary injuries (e.g., decreased brain oxygenation) that occur as a consequence of the primary injury contribute markedly to negative outcomes. A growing body of research demonstrates the association between decreased brain oxygenation and increased mortality and morbidity in both adults and children, although relative to adult studies, research of this nature remains limited in children. In the few pediatric studies that have been conducted, these have not included neuropsychological outcome measures, which Figaji and colleagues (2009a) list as a methodological limitation. The inclusion of both neuropsychological and behavioural outcome measures is therefore a major strength of this study. This research serves to highlight the importance of including neuropsychological and behavioural outcomes, and the contribution of these specific variables to understanding outcome, in studies of this nature.

Understanding the relationship between $PbtO_2$ and neuropsychological and behavioural outcome, through conducting studies such as the current one, is of benefit to both health professionals and patients in several ways. First, it helps clarify the role of $PbtO_2$ monitoring in pediatric TBI, an important topic of urgent and immediate global interest. Second, it contributes to an important foundation for further studies of outcome after $PbtO_2$ monitoring, and in particular a multicenter-trial of $PbtO_2$ monitoring in children, preferably of a population randomized to conventional treatment and $PbtO_2$-based treatment in children. With the expertise available at the Division of Pediatric Neurosurgery at the RXH, it is possible that such a trial could be performed with that department as the co-ordinating centre. Given that few therapies have been of benefit in pediatric TBI, this kind of trial would represent a major advance. Third, if $PbtO_2$ has an association with neuropsychological and behavioural outcome, as suggested by the preliminary results presented here, then knowledge of the $PbtO_2$ course during the patient's acute illness would help in prognostication,

counseling of the parents, and directives for further rehabilitation strategies for physiotherapy, occupational therapy, and neuropsychological rehabilitation.

CHAPTER 6:
COGNITIVE REHABILITATION

In Chapters 4 and 5, I focused on the association between secondary injury (specifically, from low brain oxygenation) and neuropsychological outcomes. As emphasized in those chapters, preventing secondary injury is an important step in reducing levels of morbidity and mortality following TBI. The prevention of secondary injuries therefore represents one of the major intervention efforts in the management of TBI.

Cognitive rehabilitation represents another such intervention effort. Once children are discharged from the ICU, a range of cognitive and behavioural problems may persist, especially following severe TBI. Some of these deficits are evident soon after the injury, whereas others may only become apparent later on, as the child fails to acquire certain age-appropriate skills. Cognitive rehabilitation is thus an important component of the management of long-term cognitive and behavioural outcomes.

Background

Definition of Cognitive Rehabilitation

Cognitive rehabilitation is a long-standing form of intervention within a diverse range of rehabilitation therapies (Kreutzer, Gordon, & Wehman, 1989). This form of rehabilitation therapy refers to a range of systematic interventions using retraining or compensatory methods, aimed at improving cognitive performance (Tsaousides & Gordon, 2009). The fundamental goal of cognitive rehabilitation is to assist an individual to function at his/her highest potential (Constantinidou, Thomas, & Best, 2004).

Neurobiological Basis of Cognitive Rehabilitation

The rationale for these systematic interventions is often attributed to neurobiological mechanisms of recovery (Ben-Yishay et al., 1985). These mechanisms are classified into two groups: restitution and substitution (Rothi & Horner, 1983).

Restitution of function. Restitution refers to direct restorative processes in the course of which previous functions and neural pathways are reinstated at the original sites of injury. The idea of restitution is based on the proposition that, following brain injury, there is a period of spontaneous physiological recovery. As the site of injury heals, there is a positive knock-on effect resulting in connected neural pathways being reactivated and a subsequent restoration of those functions that were interrupted by neural systemic injuries (V. Anderson et al., 2011; Rothi & Horner, 1983).

Various physiological processes are thought to subserve the mechanism of restitution. The first and most widely recognized of these processes is *diaschises* (Stein & Hoffman,

2003; Von Monakow, 1914), or what Luria (1963) referred to as de-inhibition. Following diaschises, other recovery processes including regeneration, collateral sprouting, and denervation supersensitivity may take over (V. Anderson, Northam, Hendy, et al., 2001; V. Anderson et al., 2011; Rothi & Horner, 1983).

Diaschises. Diaschises refers to temporary cessation of functions of structures that are remote from, but neuronally connected to, injury sites (Duffau, 2006; Thomas, 2003). Researchers theorize that due to the pervasive effects of brain injury on physiological functions (e.g., degree of blood flow, level of ICP, and release of neurotransmitters), the brain may go into a temporary state of general inertia or shock that temporarily inhibits cerebral and synaptic activity. This process occurs in the acute stage at injury sites where tissue is severed, but not destroyed. These injury sites can be located both centrally and peripherally; location can be peripheral if neuronally connected to the central area (V. Anderson et al., 2001a, 2011).

As these temporary effects subside, the cessation of this inhibition results in corresponding improvement in behavioural function (Rothi & Horner, 1983). Following diaschises, other restorative processes may take over.

Regeneration. *Regeneration* refers to "the process by which damaged neurons, axons, and terminals regrow and establish" (V. Anderson, Northam, Hendy, et al., 2001, p. 110-111). There are, however, limitations to this process. First, this process is generally local and requires clear pathways. Scar tissue and blood clots can obstruct paths for reconnection. Second, the potential for recovery is dependent on where the neuron is damaged, as only certain cell components (e.g., axons but not cell bodies) have potential for regeneration (V. Anderson, Northam, Hendy, et al., 2001; V. Anderson et al., 2011; Rothi & Horner, 1983).

Sprouting. Although necrosis is a common consequence of brain trauma, there may be a number of cells that are spared (either partially or completely), from which new branches may develop or sprout. These branches connect to and reinnervate sites that are deprived of input as a result of damaged cells. Axons may facilitate this process by sprouting and attaching to new post-synaptic cells, and reinervating these cells, thereby re-establishing functional networks. This process of restitution is referred to as collateral or axonal sprouting (V. Anderson, Northam, Hendy, et al., 2001; Dancause et al., 2005; Erb & Povlishock, 1991; Kozlowski & Schallert, 1998; Rothi & Horner, 1983).

Not all axons will resprout and attach to the intended targets successfully, however, which can lead to less than optimal, or even dysfunctional, outcomes (V. Anderson et al., 2011). For example, in a study with chronic sublethal hypoxic mice, hyperactivity and

anxiety were associated with such misconnections (Hu & Strittmatter, 2004). Also, 'bad plasticity' can occur when excitatory connections are reinforced in an uncontrolled manner, leading to seizures (Giza & Prins, 2006, p. 375).

Denervation supersensitivity. Finally, restitution of function may also occur as a result of denervation supersensitivity. As mentioned above, all neurons within and surrounding the area of infarction are not necessarily ablated. Researchers postulate that the sensitivity of the surviving post-synaptic cells to neurotransmitter input is enhanced as a result of prolonged deprivation of this chemical stimulation, resulting in increased receptivity to neurotransmitter release. This process is referred to as denervation supersensitivity (V. Anderson, Northam, Hendy, et al., 2001; Salpeter, Cooper, & Levitt-Gilmour, 1986; Thesleff & Sellin, 1980; Ungerstedt, 1971).

Substitution of function. *Substitution* refers to the taking over of the functions of damaged tissue by healthy tissue at different sites, either through the transferring or through the reorganisation of functions. The two aspects underlying this mechanism of substitution of function include the capacity of the brain to recover, either through anatomical reorganization, or through functional adaptation/behavioural compensation (V. Anderson, Northam, Hendy, et al., 2001; V. Anderson et al., 2011).

Anatomical reorganization. Substitution mechanisms relating to anatomical reorganization date back to the work of Munk (1881), Lashley (1929), and Luria (1963). The general idea proposed by these pioneers in the field was that of a take-over of impaired function or of damaged tissue, either by homologous healthy tissue or by unaffected cortical areas, even if the healthy / unaffected tissue is not connected directly to the site of injury (V. Anderson, Northam, Hendy, et al., 2001; Rothi & Horner, 1983). The type of anatomical reorganization that ultimately occurs is determined by the site, size and type of injury, the kind of neural network that is disrupted (focal vs. distributed) and the age at injury (V. Anderson et al., 2011).

This reorganization can occur in a number of ways, including inter- and intrahemispheric reorganization and intrahemispheric maintenance. *Interhemispheric reorganization* refers to a transfer of functions to the same neuroanatomical site in the opposite hemisphere. This kind of reorganization occurs most often in the case of unilateral lesions (e.g., in the case of hemispherectomies). *Intrahemispheric reorganization* refers to a transfer of functions to other undamaged sites within the same hemisphere. This kind of reorganization occurs in the case of focal, unilateral lesions. Finally, *intrahemispheric maintenance* involves no transfer of function, but rather maintenance of functions within the

same damaged tissue. This maintenance occurs in the context of bilateral or diffuse brain damage (e.g., as occurs frequently in TBI), where there is limited available healthy tissue to compensate for the injury (V. Anderson et al., 2011).

Behavioural compensation. An alternative mechanism proposed for substitution of function is behavioural compensation, or functional adaptation (V. Anderson, Northam, Hendy, et al., 2001; Rothi & Horner, 1983). According to this model, alternative strategies are developed to compensate for functions previously maintained by damaged tissue, rather than effecting a recovery of function per se. These strategies occur in a variety of compensatory forms, which can be applied internally or externally. For example, a patient may learn to use the opposite uninjured limb spontaneously, or to verbally mediate a non-verbal activity that he/she has difficulty implementing.

Additional approaches to behavioural compensation include direct retraining activities through drill and practice tasks, or modification of the environment to accommodate the patient in some way. An example of the latter approach is the use of a notebook to compensate for memory difficulties (Cicerone et al., 2000; Kerns & Thomson, 1998; Sohlberg & Mateer, 1989). These compensatory strategies mirror some of the common approaches to cognitive rehabilitation described below. Therefore, although the basis for cognitive rehabilitation is often attributed to neurobiological mechanisms of recovery in general, behavioural compensation appears to represent the true basis for it (V. Anderson et al., 2011).

Restitution and substitution mechanisms in the immature brain. Contrary to typical assumptions about increased plasticity in the immature brain, there appears to be no unequivocal evidence for either restitution or substitution mechanisms in children being more effective over those in adults (V. Anderson & Catroppa, 2006; V. Anderson, Northam, Hendy, et al., 2001; V. Anderson et al., 2011).

Generally, evidence for the existence and operation of restitution mechanisms (e.g., diaschises, regeneration, and denervation supersensitivity) stems largely from animal studies (Dallison & Kolb, 2003; Felderhoff-Mueser & Ikonomidou, 2000; Ward, 2005). Findings for some restitution mechanisms (e.g., regeneration) in the human brain are limited, and there is an even greater dearth of evidence for restitution mechanisms in the immature human brain (V. Anderson et al., 2011).

Such evidence as exists for restitution mechanisms in the immature brain shows that outcomes for these mechanisms may be unfavourable. For example, Felderhoff-Mueser and Ikonomidou (2000) reported that the cascade of events occurring in the inhibition phase of

diaschises may be more damaging to the immature than the mature brain. Similarly, because pediatric brain injury unfolds in the context of ongoing brain development brain and has the potential to disrupt this development, a process like regeneration may interfere with the normal processes. Without a clear understanding of the interaction between these restitution mechanisms and developmental processes, the potential for regeneration processes to translate into functional recovery remains equivocal (V. Anderson et al., 2011).

Thus, in summary, although animal and human studies provide evidence for the pathophysiological cascade of events and biological mechanisms of recovery following brain injury for both children and adults, this information remains limited and tentative, especially with regards to the developing brain (V. Anderson et al., 2011).

There are also few studies relating to substitution of function in children. With regards to anatomical reorganization, both interhemispheric and intrahemipheric transfer of functions is reported in infancy and in the prenatal to preschool stages, respectively. Intrahemispheric maintenance can occur throughout childhood (V. Anderson et al., 2011; DeVos, Wyllie, Geckler, Kotagal, & Comair, 1995; Kadis et al., 2007; Northam et al., 2012; Beharelle et al., 2010).

As mentioned above, intrahemispheric maintenance is the mechanism of anatomical reorganization purported to occur most often following TBI. It is especially most likely to occur after severe TBI, as severe injuries of this nature are often associated with generalized and diffuse lesions. Owing to the nature of this mechanism, that is, ongoing maintenance of functions by damaged tissue, intrahemispheric maintenance post-TBI may be associated with poor outcome (V. Anderson et al., 2011; Thomas, 2003).

Thus, although some researchers may be inclined to argue that neurobiological mechanisms could provide support for plasticity in the immature brain (based on favourable outcomes for young children with focal lesions; Aram & Ekelman, 1986; Dennis, 1980), V. Anderson et al. (2011) argue that there is no evidence of greater benefit in recovery for children than for adults. Although children often show promising potential for neurologically-based recovery following, for example, unilateral lesions (Aram & Eisele, 1994; Feldman, Holland, Kemp, & Janosky, 1992; Vargha-Khadem, Isaacs, Papaleloudi, Polkey, & Wilson, 1991; Vargha-Khadem, Isaacs, Van der Werf, Robb, & Wilson, 1992), with generalized cerebral insults that often occur with severe TBI, recovery may be slower and the outcome may be poorer for children compared to the outcome for adults who have insults of a similar nature (V. Anderson & Moore, 1995; Gronwall, Wrightson, & McGinn, 1997; Taylor & Alden, 1997). Although some children may initially appear functionally

intact after TBI, the effects of the insult may only emerge as these children develop and fail to reach age-appropriate goals (Giza & Prins, 2006). Hence, researchers in the field often argue that children grow into their deficits (V. Anderson & Moore, 1995; Eslinger, Biddle, Pennington, & Page, 1999; Taylor & Alden, 1997; Wrightson, McGinn, & Gronwall, 1995). Therefore, according to this argument, substitution mechanisms of recovery, and intrahemispheric maintenance in particular, do not advantage the immature brain following TBI.

This conclusion extends to behavioural compensation, even though it is not based on the supposition of underlying neural changes, but rather on functional adaptation. There are few research studies investigating the brain's response to the kinds of compensatory or direct retraining interventions described above, for example, in motor and language areas of the brain (Duffau, 2006; B. Hoare, Imms, Carey, & Wasiak, 2007; Kuhnke et al., 2008; Sakzewski, Ziviani, & Boyd, 2009). Once again, available evidence does not support increased receptivity or any other advantage for the immature brain over the adult brain in terms of these interventions (V. Anderson & Catroppa, 2006; V. Anderson et al., 2011).

These findings have implications for cognitive rehabilitation. I stated earlier that the rationale for cognitive rehabilitation is often based on neurobiological mechanisms of recovery (Ben-Yishay et al., 1985). The general idea, which is pervasive in the cognitive rehabilitation literature, is that the different approaches to cognitive rehabilitation are associated with either restitution or substitution mechanisms.

Approaches to Pediatric Cognitive Rehabilitation

Although researchers and clinicians employ various approaches to pediatric cognitive rehabilitation, they agree that there are three general principles guiding this process: restoration of function, functional adaptation, and environmental modification (V. Anderson, Northam, Hendy, et al., 2001). These principles are consistent with restitution and substitution theories, and inform the major approaches to the management of cognitive impairments. Each of these approaches can generally be categorized as one of three types.

One approach involves externally focused interventions. These interventions do not rely on creating changes in the individual's cognitive capacity, but focus on adapting external aspects to accommodate the individual. These intervention strategies are often context-specific and therefore generalization to other contexts is not expected. Examples of this approach to cognitive rehabilitation include modifying the environment to suit the individual's needs, adjusting expectations for the individual's functioning, or employing adapted teaching strategies (e.g. using simpler tasks, limiting unnecessary distraction, or

increasing time for task completion (Catroppa & Anderson, 2006; Mateer et al., 1996; Van't Hooft et al., 2005).

The other two approaches involve internally focused interventions. One of these approaches includes strategies aimed at actual restoration of cognitive functions. These approaches are often labelled as being process-specific, and they usually target a specific cognitive deficit. As will be evident later in this review, this approach has yielded some positive results, particularly in the domain of attention, for both adults and children. Findings for studies on memory restoration have not been as promising (Mateer et al., 1996; NIH Consensus Developmental Panel on Rehabilitation of Persons with Traumatic Brain Injury, 1999).

The other internally focused approach involves training in compensatory techniques that may help the individual adapt to and cope with the cognitive impairments. These techniques can range from simple techniques, such as using checklists, to more sophisticated methods like using electronic memory or organizational devices. This approach rests on the idea that the supportive device will help improve rather than change an individual's functioning (Mateer et al., 1996). Restorative and compensatory approaches are not mutually exclusive and can be implemented individually or in combination (Carney et al., 1999; Constantinidou et al., 2004).

Thus, although some rehabilitation programs do adopt a single strategy targeting a single cognitive domain (e.g., restorative training for attention and/or memory deficits), others use a more comprehensive, holistic, multidisciplinary approach in which multiple or even combined approaches are implemented targeting various cognitive domains simultaneously. Although there is evidence to support both single and multidisciplinary approaches, researchers in the field more often advocate comprehensive holistic approaches to cognitive rehabilitation. Even though in general, and in TBI rehabilitation specifically, a holistic approach may be the preferred modus operandi, this method relies on available human and financial resources and on a supportive infrastructure. Such programs are also, for obvious reasons, more difficult to evaluate. On the other hand, some restorative approaches are criticized for their lack of generalizability (Cernich, Kurtz, Mordecai, & Ryan, 2010; Cope, 1995; Gordon et al., 2006; NIH Consensus Developmental Panel on Rehabilitation of Persons with Traumatic Brain Injury, 1999; Slomine & Locascio, 2009).

Contrary to expectations regarding comprehensive, holistic approaches however, in a recent meta-analysis evaluating the effectiveness of cognitive rehabilitation following acquired brain injury (ABI), comprehensive treatments did not produce an overall significant

effect in terms of demonstrating improvement, whereas specific training strategies, e.g. for attention, did (Rohling, Faust, Beverly, & Demakis, 2009). According to the review, the effects of comprehensive programs also failed to generalize outside of the treatment environment.

According to earlier studies on mechanisms of recovery after TBI, particularly those done on children, the direct restorative and the compensatory approaches (i.e., internally focused interventions) are the approaches commonly associated with the neurobiological mechanisms of recovery. Previous research suggested that direct restorative approaches are subserved by restitution mechanisms, and that compensatory approaches are subserved by reorganization mechanisms (Ben-Yishay & Diller, 1993). However, a more recent review and discussion of these mechanisms (V. Anderson et al., 2011) suggests that it is the substitution mechanism, namely behavioural compensation, that underlies the efficacy of cognitive rehabilitation for children. According to V. Anderson et al. (2011), evidence for restitution processes has been used primarily to inform pharmacological interventions.

The pressing issue arising from the conclusions drawn in that review concerns the availability of evidence and the efficacy of restitution and substitution processes in the immature brain. The review states: "there appears little reason to expect that the immature brain will be advantaged by these processes, and may in fact be at greater risk" (V. Anderson et al., 2011, p. 2204). So, on the one hand these theories of recovery have provided (a) a platform for cognitive rehabilitation efforts, and, consequently, (b) the development of various forms of interventions. On the other hand, however, there is little conclusive evidence that these recovery processes actually benefit the developing brain. Hence, it stands to reason that there would be a similar lack of evidence for the efficacy of rehabilitation programmes based on these processes. The status of cognitive rehabilitation in TBI, especially for children, is similarly and fittingly inconclusive. However, this inconclusiveness is generally attributed to a lack of evidence and methodological limitations, rather than to a weakness in the theoretical framework underlying it. This direct association between mechanisms of recovery and approaches to cognitive rehabilitation has not yet been discussed in the literature.

The Status of Cognitive Rehabilitation

Besides the limitations and lack of conclusive evidence for the restitution and substitution processes thought to underpin cognitive rehabilitation in children, there is also a host of other limitations that affect the status of the discipline. The two most important of these shortcomings are the limited evidence base for cognitive rehabilitation and the

methodological shortfalls that affect much of the evidence that is available. These limitations are more prominent in the pediatric than in the adult literature. Below, I review the pediatric literature briefly, and highlight the associated limitations.

Pediatric literature. In contrast to the burgeoning body of evidence for the efficacy of cognitive rehabilitation in adults (see, e.g., Cappa et al., 2005; Cernich et al., 2010; Cicerone et al., 2000, 2005; Cope, 1995; Gordon et al., 2006; Rohling et al., 2009; Tsaousides & Gordon, 2009), the evidence for children remains limited. It is, however, expanding slowly. There have been three general reviews to date. These reviews are based on a limited number of studies, each featuring, for the most part, only a few patients. Patient etiologies in these reviews are not TBI-specific, but relate to ABIs in general. The studies reviewed also cover a wide range of interventions for different cognitive domains, including attention, memory, and executive functioning (Laatsch et al., 2007; Limond & Leeke, 2005; Slomine & Locascio, 2009).

The results of, and conclusions drawn from, these reviews, show a positive progression for the efficacy of cognitive rehabilitation. The first review, conducted by Limond and Leeke, (2005) reported on published interventions (1967-2002) on attention, memory, and executive functions for children and adolescents with ABI. The review was based on 11 studies. In that review, the authors concluded that there (was) no conclusive evidence for cognitive rehabilitation" (Limond & Leeke, 2005, p. 339). This conclusion was based on the methodological problems often highlighted in the published pediatric literature. Limond and Leeke (2005) argued that these methodological deficiencies result in limited reliable evidence for cognitive rehabilitation from which to draw any sound conclusions for efficacy.

Laatsch et al. (2007) demonstrated this positive progression by gathering sufficient evidence to put forward two practice guidelines and one practice option for pediatric cognitive rehabilitation. These researchers conducted a systematic review on cognitive and behavioural interventions, published from 1980-2006, for children and adolescents following ABI. The review was based on 28 studies. Systematic reviews generate recommendations on three levels: practice standards, practice guidelines, and practice options. These three levels of recommendation are determined by the amount of available evidence: substantive, probable and possible evidence (Slomine & Locascio, 2009). One of the practice guidelines put forward in the Laatsch et al. (2007) review was attention-training interventions for children and adolescents.

In addition to these general reviews, there have been others that review interventions for specific cognitive domains, with studies and reviews on attention-training strategies being

among the most popular. Therefore, attention training is one of the domains for which the most extensive evidence exists for the efficacy of cognitive rehabilitation for children.

Hence, there appears to be a move away from the initial firm conclusions put forward by Limond and Leeke (2005), with sufficient evidence for the recommendations proposed by Laatsch et al. (2007). In spite of this apparent progression, however, in the most recent of the pediatric reviews, the need for methodologically sound research studies to investigate the efficacy of cognitive rehabilitation interventions persists (Slomine & Locascio, 2009). Slomine and Locascio (2009) conducted their review on interventions, for children and adolescents with ABI, in the following domains: attention, memory, unilateral neglect, speech and language, executive functioning, and family involvement/education. The review was based on 21 studies published after the Laatsch et al. (2007) review.

Methodological limitations in pediatric cognitive rehabilitation studies. The methodological limitations often highlighted in the pediatric cognitive rehabilitation literature and the criticisms drawn from these (see Limond & Leeke, 2005), contribute substantially to the pervasive scepticism that surrounds the discipline; a scepticism which has given rise to such questions as to whether "rehabilitation [is], in fact, only a benevolent charlatanry?" (Cope, 1995, p. 649). Whether their effects are exaggerated or not, methodological limitations do exist in research into pediatric cognitive rehabilitation. These limitations are described below.

Limitations related to randomized controlled trials (RCTs). The implementation of randomized controlled trials (RCTs) is a major issue in the debate on cognitive rehabilitation. RCTs, prospective, double-blind RCTs in particular, are regarded as constituting the highest standard of evidence for, and most sound means of, evaluating treatment efficacy (Cope, 1995). Unfortunately, creating the necessary research conditions for RCTs is extremely challenging and often impossible (Carney et al., 1999; Cicerone et al., 2000) .

One of the drawbacks associated with conducting RCTs include sample availability and having sufficient numbers of similar participants for randomization. The latter is a difficult proposition in pTBI research given the heterogeneity associated with such injuries. Another drawback may arise when long-term interventions and outcomes are of interest and the pragmatics in maintaining prospective RCTs over extended periods can become challenging. Hence, RCTs may provide information only on the *efficacy* rather than the *effectiveness* of treatment, which limits the generalizability of findings (Sanson-Fisher, Bonevski, Green, & D'Este, 2007). Treatment efficacy studies are mainly used in research settings for evaluating interventions of a limited duration and scope with specific, homogenous samples. Clinical

effectiveness studies, in contrast, are conducted in clinical settings for evaluating treatment protocols that involve and can be modified based on continued clinical evaluation and judgment (Cicerone et al., 2000).

In addition to the challenge of creating the research conditions for RCTs, there are also ethical and financial issues that affect the implementation of these trials and that account for their dearth in the cognitive rehabilitation literature (Cope, 1995). RCTs, and large RCTs in particular, can be costly to implement. Also, researchers conducting RCTs often need to defend against the fact that a potentially beneficial intervention is being withheld from one group of participants, while being administered to another (Sanson-Fisher et al., 2007). These economic and ethical challenges lead to a paradoxical situation where the best method of evaluation may also be the most challenging to implement.

This situation also leads to a dilemma in terms of the efficacy of cognitive rehabilitation. RCTs are lacking for good reason. Therefore, previous reviews could only base conclusions on rehabilitation studies that do not include evidence from RCTs. The lack of RCTs therefore contribute indirectly to conclusions that cognitive rehabilitation is neither efficacious nor useful (Carney et al., 1999; Cope, 1995; Limond & Leeke, 2005).

Thus, against this backdrop, the need for RCTs has been highlighted in the pediatric literature within the last decade (Limond & Leeke, 2005), and studies employing this design are slowly emerging (e.g., see Van't Hooft et al., 2005). However, due to the inherent difficulties with the RCT approach as outlined above (in studies included in the existing reviews, and in the cognitive rehabilitation literature in general), most researchers in the field employ other, non-RCT research designs (e.g., case studies or controlled trials; Butler, 1998; Butler & Copeland, 2002; Kerns & Thomson, 1998; Van't Hooft, Andersson, Sejersen, Bartfai, & Von Wendt, 2003).

Limitations related to studies with non-RCT designs in the pediatric cognitive rehabilitation literature. These studies show promise in identifying effective rehabilitation strategies but require duplication and further evaluation (Laatsch et al., 2007). However, as with RCTs, the significance of the findings from these studies is limited by methodological constraints. Reviews of these studies highlight a host of methodological limitations that affect studies of various designs, including RCTs, in the cognitive rehabilitation literature.

Other methodological limitations. These limitations range from (a) *participant-related variables*, such as the heterogeneity of participants, lack of representativeness of participants, small sample sizes and lack of control groups, to (b) *treatment-related variables* such as heterogeneity in methodology (frequency and duration) of interventions, standardization and

target of treatment, and (c) *outcome-related variables* such as variability in outcome measures and a lack of blind outcome evaluations (Cappa et al., 2003, 2005; Gordon et al., 2006; Laatsch et al., 2007; Limond & Leeke, 2005; Rohling et al., 2009). In children, there are also the added complications with regard to developmental factors, such as variability in age at injury and age at intervention among participants (Slomine & Locascio, 2009). Further, there are also limitations in design pertaining to carry-over or retest effects and confounding variables.

Rohling et al. (2009) outline the problem of test-retest effects. Such effects are often seen in control participants who demonstrate improvement from pre- to post-test evaluation without exposure to the intervention. An increase in motivation from one testing session to the other, the individualized attention received during testing or control placebo activities, practice effects and spontaneous recovery (in clinical control samples) are offered as possible explanations for these test-retest effects.

Confounding variables also contribute to difficulties in evaluating outcomes (Laatsch et al., 2007). An important confounding variable relates to the SES of participants. The effect of SES is especially applicable to, and an important consideration for, research in LAMICs, because of the wide disparity in SES in countries like South Africa.

There is a well-established association between SES and cognitive ability and achievement in childhood. It is consistently documented that lower SES environments and deprivation are associated with poorer cognitive achievement (Hackman, Farah, & Meaney, 2010; Noble, McCandliss, & Farah, 2007; Noble, Norman, & Farah, 2005). This association was initially demonstrated in IQ and achievement tests (Brooks-Gunn, Klebanov, & Duncan, 1996; McLoyd, 1998; Smith, Brooks-Gunn, & Klebanov, 1997). However, these tests are generally broad (non-specific) measures of cognition. More recent research has explored and demonstrated this association between low SES and other specific neurocognitive functions that could underlie or contribute to the broad-based relationship.

Specifically, recent research shows that low SES is associated with various neurocognitive systems differentially (see Hackman and Farah, 2009, for a review), with language and executive/attentional function systems being the most vulnerable to such effects. Within the executive/attentional function systems, selective attention, inhibitory control, cognitive flexibility and working memory are some of the specific functions that are often implicated (Farah et al., 2006; Lipina, Martelli, Vuelta, & Colombo, 2005; Sarsour et al., 2011; Stevens, Lauinger, & Neville, 2009). These findings for negative association of low SES with executive/attentional systems in children and adolescents have come from a

number of behavioural studies (Farah et al., 2006; Lipina et al., 2005; Lupien, King, Meaney, & McEwen, 2001; Mezzacappa, 2004; Noble et al., 2005, 2007; Sarsour et al., 2011) and have been demonstrated recently in electrophysiological (ERP) studies (Kishiyama, Boyce, Jimenez, Perry, & Knight, 2008; Stevens et al., 2009). These ERP studies show consistent findings with poorer outcomes on prefrontal electrophysiological measures of attention in low SES children.

A myriad of factors are purported to mediate the relationship between low SES and impaired cognition. These factors include, but are not limited to, pregnancy- (pre- and perinatal complications), parenting (inconsistent, harsh or distant parenting styles where children may receive less attention than those in other families), family/home environment (nuclear family structure more often consists of a single parent, less cognitive stimulation or access to it, more exposure to stress, less companionship), and school-related issues (low level of school preparedness and expectations from teachers) (Bradley & Corwyn, 2002; Kishiyama et al., 2008; McLoyd, 1998; Sarsour et al., 2011).

Children in LAMICs like South Africa, where poverty and unemployment are rife in large parts of the country, and are particularly vulnerable to the effects of low SES (Barbarin & Richter, 1999; K. Levin, 2004). Therefore, in addition to other methodological limitations, potentially confounding variables such as the SES status of participants need to be considered in cognitive rehabilitation studies.

A young field of research. In spite of the problems identified above, much of the literature still seems to provide positive support for TBI rehabilitation (Cope, 1995), motivating new and revised research efforts. In spite of the identified need for well-designed methodologically sound studies, it is important to weigh up the research expectations of the field against the age of the field (Gordon et al., 2006). Early interest in TBI can be traced back to only 1979. Hence, one can assume that TBI as a focus of cognitive rehabilitation would only emerge even later on. Although the interest in cognitive rehabilitation following TBI may have proliferated since then, this field of research is still fairly young. It is clear that, although the whole field of cognitive rehabilitation research is a fairly recent development, pediatric research is a younger field than that of adult research, and therefore expectations of this field need to be adjusted even further.

Thus, some of the problems and limitations reported in terms of research and cognitive rehabilitation strategies may be attributed to the age of the discipline. This conclusion is demonstrated in the accumulating evidence for adult cognitive rehabilitation, being both efficacious and beneficial, having progressed from an ‘absence of strong evidence’ (Carney

et al., 1999) to the point of 'substantial evidence' (Cicerone et al., 2005). Foundational evidence is required before more sophisticated designs can be employed (Gordon et al., 2006). However, even if approaches do improve, there is still the issue of access to, and availability of, cognitive rehabilitation.

Access to, and availability of, cognitive rehabilitation. Reports of limited access to cognitive rehabilitation on the part of post-ABI patients are particularly prevalent in the pediatric literature (Laatsch et al., 2007; Limond & Leeke, 2005; NIH Consensus Developmental Panel on Rehabilitation of Persons with Traumatic Brain Injury, 1999; Slomine & Locascio, 2009). It is clear that not all children have equal access to cognitive rehabilitation post-ABI. This lack of access is not only due to a lack of evidence to support the implementation, and hence availability of, interventions, as outlined above, but also due to a lack of financial and human resources for the recommended approaches. Even in cases where cognitive rehabilitation is offered, many families may have limited access to health care.

Closely related to these issues of access are issues of awareness. Children are dependent on their parents for their health care advocacy, and may therefore not always be able to express their needs; hence, the health care advocate (the parent) remains unaware of the injured child's needs. Similarly, irrespective of the SES of a family or of the community, cognitive impairment in the post-acute stage following brain injury is often 'invisible' and can go unrecognized by parents, teachers, and other professionals caring for the child (Laatsch et al., 2007; Limond & Leeke, 2005; Slomine & Locascio, 2009).

Access to, and availability of, cognitive rehabilitation in high-income countries. The scope of, and access to, cognitive rehabilitation varies globally. However, literature documenting international perspectives on TBI rehabilitation seems to show greater promise for future access to cognitive rehabilitation in HICs than LAMICs. Disparities in terms of access to cognitive rehabilitation apply not only when comparing HICs and LAMICs, but also when comparing different HICs to one another, and even among sectors of the populations of HICs. Contrary to what one might expect, cognitive rehabilitation is not available routinely in all HICs. For instance, access might vary across provinces within some countries (e.g., Canada; Cullen, 2007).

In a special journal issue on international perspectives on TBI, researchers describe rehabilitation initiatives and strategies for individuals with TBI for several countries: Canada, Denmark, Sweden, the Netherlands and the United Kingdom. The reviews highlighted the fact that each country has its unique strengths and weaknesses, and that the uneven growth

and ongoing development of health care initiatives in various countries reflects the current evolving state of TBI rehabilitation globally (Cullen, 2007; Engberg, 2007; Lexell, 2007; Nyein, Thu, & Turner-Stokes, 2007; Ribbers, 2007).

This unevenness in the development of public health care systems in terms of making TBI rehabilitation universally accessible is illustrated if one draws comparisons between the above-mentioned countries in the special issue. For example, in Canada, the ultimate aim is to make TBI rehabilitation accessible to all citizens. Such efforts are hampered, however, by the lack of a centralized public health care delivery system. The Danish national strategy, implemented in 1997 and based on a centralized system and equal accessibility to all citizens, has led to improved outcomes over the past 10 or more years. For example, patients admitted post-centralization appear to show better outcomes, as measured by the Glasgow Outcome Scale, than patients admitted prior to this period.

In Sweden, healthcare is relatively free of charge and this is promising for access to cognitive rehabilitation. A major development in the effort to improve health services in Sweden is the recommendation that all rehabilitation departments in that country undergo an accreditation process. The Netherlands has seen a growth in awareness of the impact of TBI in the last 15 years, paralleled by an increase in clinical knowledge and in more sophisticated treatment and rehabilitation programs, including successful cognitive rehabilitation initiatives. Other strengths of TBI rehabilitation in the Netherlands include surveillance of rehabilitation centres by the Netherlands Association for Medical Rehabilitation, and the provision of funds for rehabilitation and chronic care through mandatory healthcare insurance, primarily for individuals with moderate-to-severe TBI. Finally, in the UK, although TBI rehabilitation has evolved and improved in the past 20 years, consistency in the provision of rehabilitation services is affected by the non-availability or lack of funding (Cullen, 2007; Engberg, 2007; Lexell, 2007; Nyein et al., 2007; Ribbers, 2007).

Access to, and availability of, cognitive rehabilitation in LAMICs. Even though the incidence of TBI and the associated human and economic cost is greatest in LAMICs (De Silva et al., 2009), most of the cognitive rehabilitation literature (and therefore the cognitive rehabilitation programs being evaluated) emanates from high-income countries. Cognitive rehabilitation programs for individuals who have sustained TBIs are scarce in LAMICs (e.g., Brazil; De Pereira, 2011). Specifically, there are no professional pediatric cognitive rehabilitation programmes offered as a standard practice post-TBI in LAMICs (e.g., South Africa and Malaysia; Abdullah, Kumaraswamy, Awang, Ghazali, & Abdullah, 2005; K. Levin, 2004).

Cognitive rehabilitation in South Africa. Part of the burden of care facing relatives or caregivers of persons with TBI is identifying and accessing the necessary health care services. This burden of care may be exacerbated, however, when appropriate services are lacking.

K. Levin (2004) confirmed that in South Africa, "there are very few places of care following acute stages of recovery, and there are no dedicated pediatric rehabilitation units for children with TBI" (p. 309). She reported that, even though South Africa is one of the wealthiest and most resourceful countries in Africa, the low SES of the majority of the population of the country (which stems from its apartheid history), dictates the level of healthcare offered (K. Levin, 2004, 2006).

There is also a clear economic disparity amongst South Africans. Whereas many citizens are illiterate and unemployed, there are others who are particularly affluent. Health professionals and researchers working in the area of rehabilitation and related disciplines need to pay more attention to issues such as: (a) the clear socio-economic divide in the areas of health care and education provision, (b) the vast majority of people in South Africa, especially Black African and mixed-raced people, living in impoverished environments, and (c) the fact that unemployment plagues at least 50% of the adult population. All of these factors exert significant pressure on the development of rehabilitation programs, and influence their accessibility and affordability by the majority of the population (Statistics South Africa, 2012; Chibba & Luiz, 2011; K. Levin, 2004, 2006)

K. Levin argues that the SES-, sociocultural- and educational-related disparities that are specific to LAMICs, and to South Africa in particular, make the experience of TBI in the country more challenging than in HICs. Therefore, the management of TBI in countries such as South Africa also requires a specialized approach. Relatively few people have access to medical subsidies, either through legislative or insurance schemes there. Access to rehabilitation services is no more than 'inadequate' (p. 306) for most South African children, although independent efforts by various groups of primary health care professionals are recognized (K. Levin, 2004).

Even though the health care system in South Africa is slowly transforming, the demand for professional public health care services continues to outweigh the provision of such services (Haig, Im, Adewole, Nelson, & Krabak, 2009; K. Levin, 2006; Petersen & Lund, 2011; Phaswana-Mafuya et al., 2008; Smit, Church, Milford, Harrison, & Beksinska, 2012).

Summary

Neurobiological mechanisms of recovery are often presented as the basis for cognitive rehabilitation for adults and children. However, recent reviews suggest there is limited evidence to support the fact that these mechanisms, and especially restitution mechanisms, provide a greater advantage in the immature as compared to the adult brain.

Issues regarding the efficacy and effectiveness of cognitive rehabilitation also affect the status of the discipline. Perceptions of the efficacy and benefits of cognitive rehabilitation have been undermined by methodological challenges. Researchers acknowledge, however, that cognitive rehabilitation, and TBI cognitive rehabilitation in particular, is still a fairly young field and that therefore current expectations for the field should be realistic.

On a global scale, the levels of access to, and availability of, cognitive rehabilitation vary significantly, but they are particularly low in LAMICs countries such as South Africa, where the socio-economic context plays a major role in the lack of facilities in the country.

However, despite these issues, there is increasing support and emerging evidence for some forms of cognitive rehabilitation for children. Attention remediation is among those consistently reported as potentially efficacious. Attention, and attention remediation, as a form of cognitive rehabilitation post TBI, will be described in detail and discussed in the next chapter.

CHAPTER 7:
ATTENTION

Despite the methodological and consequent efficacy-related limitations associated with the field, there is increasing support and emerging evidence for some forms of cognitive rehabilitation for both adults and children. Attention remediation is among those consistently reported as potentially efficacious.

Cooley and Morris (1990) underscore the importance of specifying the theoretical model upon which studies of attention in children are based. They emphasize that the links between tasks, measures, and theory should be specified and clear to the reader. Hence, the purpose of this chapter is to set the stage for Chapter 8 (Study 3) by outlining the theoretical basis for the chosen target construct and intervention strategy. In this chapter, I review the definition, models, developmental trajectory, post-TBI effects, and cognitive rehabilitation interventions associated with the construct of attention.

Definition of Attention

Although most laypeople understand what is meant by the word attention, a formal, consensual, operational definition of the construct remains elusive. This protean quality of attention stems in part from its multidimensional nature. Attention is not a unitary concept (Fletcher, 1998; Sinclair & Taylor, 2008); the term refers to a wide variety of states, processes, and abilities that include the "regulating of various brain networks by attentional networks involved in maintaining the alert state, orienting, or regulation of conflict" (Posner & Rothbart, 2007, p. 2). The ability to attend is achieved though bottom-up and top-down processing of environmental information, garnered through the directing of consciousness in both voluntary and involuntary ways (Harris, 1998).

Attentional abilities are integral to optimal everyday functioning (Wassenberg et al., 2008). Amongst other important capacities, our capacity to attend to our environment is crucial to our ability to learn and to acquire new concepts and strategies in the face of current, anticipated, and new events. It is also important in the developmental process, as memory and learning are dependent on its integrity (Cohen, 1997; Lyon, 1996). In essence, attentional processes have a bidirectional relationship with other and higher cognitive activity; they affect, and are affected by, other cognitive processes (Sinclair & Taylor, 2008). Attention is, therefore, often regarded as serving a gateway function to information processing (Zillmer, Spiers, & Culbertson, 2008).

Attentional processes also often overlap with other multidimensional constructs like executive functions (Fletcher, 1998; Morris, 1996). Active awareness or online control is

necessary in order to navigate through novel situations or to solve problems. Therefore, contemporary models of executive functions frequently include attentional control as a core component (e.g., P. Anderson, 2002).

Models of Attention

The clinical and neuroanatomical models of attention outlined below demonstrate clearly that attention is not a single entity. Posner and Peterson's (1990) neuroanatomical model demonstrates that different neuroanatomical networks underlie attention and its various components. This model is important for studies on clinical populations, such as TBI populations, where generalized injuries are common and attention deficits may, consequently, result from damage to various regions or networks within the brain. Posner's model demonstrates the overlap between attention and executive function networks. Sohlberg and Mateer's (1987, 1989) clinical model also demonstrates this overlap in their nested model of lower and higher-order attentional components. Their model includes five different forms of attention. To elaborate on this association between attention and executive functioning, I also briefly outline P. Anderson's (2002) developmental model of executive functions, which includes attentional control as the integral component. This design provides evidence for the proposition that attention is integral to the functioning of other cognitive modalities.

Posner's neuroanatomical model of attention. Posner and colleagues (Posner & Petersen, 1990; Posner & Rothbart, 2007) propose that three interrelated neuroanatomical networks enable attention. These networks involve alerting, orienting, and executive attention; and each network is anatomically and functionally unique (Constantinidou et al., 2004). Evidence from neuroimaging studies supports the existence of these networks (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Sinclair & Taylor, 2008). This organization of attention networks exemplifies the neuroscientific principle of modularity, i.e. the idea that separate or isolated cognitive subsystems can function independently or as discrete modules (Fodor, 1983; Shallice, 1988). Similarly, attention networks "can operate independently and be selectively influenced (e.g., impaired) but are usually coordinated in complex cognitive tasks" (Constantinidou et al., 2004, p. 344).

The *alerting network* is also referred to as the sustained attention or vigilance system. This network plays an important role in arousal, in alerting, and in maintenance of attention. It is the oldest attentional system, phylogenically (Constantinidou et al., 2004; Zhan et al., 2011). In this system, alerting refers to being highly responsive to information received (Posner & Rothbart, 2007). The brain structures and systems purported to be involved in maintaining this alert state are the reticular formation, the amygdala, the thalamus, locus

coeruleus, and parts of the right frontal and parietal cortices. The associated neurotransmitter is norepinephrine (Constantinidou et al., 2004; Posner & Rothbart, 2007; Sinclair & Taylor, 2008; Spevak, 2007).

The *orienting network* is also referred to as the selective attention network or the posterior attention system. Orienting is the process of directing attention to sensory information. The orienting network interacts with sensory functions to facilitate this process (Posner & Rothbart, 2007). The main purpose of this system is to direct the sensory organs to particular locations in the environment (sensory orienting component) so that there is heightened information processing for and filtering of stimuli in those locations (selective component). For example, in vision, this process would be closely related to directing the gaze of the eyes to that part of the visual field containing stimuli that one must attend to. The effect of the different senses is weighted with respect to activating properties, and it is proposed that the system acts as a filter allowing the brain to concentrate only on those stimuli that are pertinent to the organism's activity at that particular time (Constantinidou et al., 2004; Sinclair & Taylor, 2008).

The brain structures associated with this network include the posterior and superior parietal lobes and the temporoparietal junction, the lateral pulvinar nucleus of the midbrain, the lateral posterior nucleus of the thalamus, the superior colliculus, and the frontal eye fields. The relevant neurotransmitter is acetylcholine (Constantinidou et al., 2004; Posner & Rothbart, 2007).

Finally, the *executive attention network* or anterior attention system receives information from, and activates selective attention functions of, the posterior attention system (Stuss et al., 2002). This system is recruited when typical frontal tasks are carried out, including those that draw on divided attention. These latter tasks require attentional control and includes a decision-making component (in terms of what to focus on when various aspects of a stimulus are presented; e.g., Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991). These tasks may also include an inhibitory control component. This control component is evident in tasks that require the suppression of prepotent responses and attention to salient stimuli in order to attend to and express novel responses (Casey, 2001; Casey, Giedd, & Thomas, 2000; Rothbart & Posner, 2001). This network therefore also oversees the functions of conflict monitoring and resolution in thinking, feeling and responding (Posner & Rothbart, 2007; Sinclair & Taylor, 2008). The neuroanatomical structures involved in this network include the anterior cingulate, the dorsolateral and

ventromedial prefrontal cortex, and the basal ganglia. The associated neurotransmitter is dopamine (Posner & Rothbart, 2007; Stuss et al., 2002).

The multifaceted nature of attention, as described by Posner's model, is also exemplified in a clinical model of attention proposed by Sohlberg and Mateer (1989).

Sohlberg and Mateer's clinical model of attention. Sohlberg and Mateer (1989) proposed a model of attention based on their (a) clinical experience with, and observation of, patients with brain injuries and (b) attention-focused research. Their taxonomy includes five separate categories of attention (three basic components and two higher-order components).

The three basic components are *focused*, *sustained,* and *selective attention*. *Focused attention* refers to the ability to direct attention to, and to respond to, specific stimuli in various sensory modalities. *Sustained attention* refers, at a basic level, to the ability to maintain vigilance or to respond consistently to continuous or repetitive stimuli over prolonged periods of time. At higher levels, it can incorporate working memory or cognitive control functions. *Selective attention* refers to the ability to free oneself from distractibility; that is, being able to maintain a response set while ignoring distracting, competing information.

The two higher-order components of attention are *alternating* and *divided attention*. *Alternating attention* refers to the ability to shift attentional focus between disparate cognitive tasks. *Divided attention* refers to the ability to respond to and to monitor two or more tasks simultaneously.

This model proposes that attentional components are hierarchical, with each component in the hierarchy necessary for the functioning of the next, and with the lower levels of attention required for the optimal functioning of the higher-order components. The hierarchy proceeds as follows: *focused*, *sustained*, *selective*, *alternating,* and *divided attention.*

Higher-order components of attention are subsystems of, and are therefore influenced by, executive functions such as inhibition, cognitive flexibility, and the ability to shift response sets. For example, divided attention is a subcomponent of the cognitive flexibility domain in the P. Anderson's (2002) model, and cognitive flexibility is influenced by attentional control, of which inhibition as a subcomponent. Again, this nested model demonstrates the overlap between attentional and executive functioning (Mateer, 2000; Sohlberg & Mateer, 1987, 1989; Thomson, Kerns, Seidenstrang, Sohlberg, & Mateer, 2005).

P. Anderson's model of executive function. P. Anderson (2002) conceptualized executive function as having four discrete systems that function in an integrated manner to

achieve overall control. The systems are attentional control, cognitive flexibility, goal setting and information processing. As depicted in Figure 7, attentional control lies at the core of this model, and influences the functioning of the other domains.

The subcomponents of each system are listed in Figure 7. The bi-directional arrows between the domains of information processing, cognitive flexibility, and goal setting demonstrate the interdependence of those systems. Speed of processing, included in the information processing system, is deemed essential for the efficient operation of the entire system (Catroppa & Anderson, 2005). V. Anderson, Anderson, Northam, Jacobs, and Catroppa (2001) elaborated on that model by including sustained attention and attentional shift as subcomponents of the attentional control and cognitive flexibility domains, respectively.

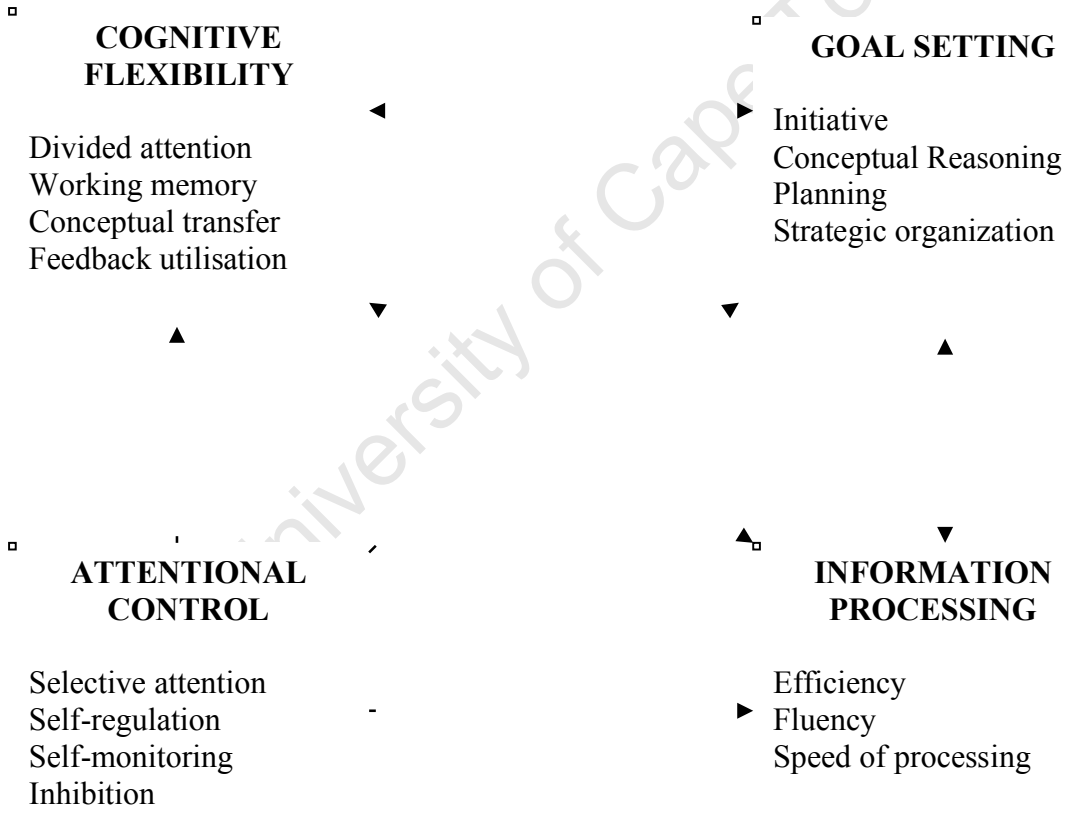

Figure 7. P. Anderson's (2002) executive function model.

Parallel development of attention and executive functions

The separate, but interrelated, components and related subcomponents in P. Anderson's (2002) model follow independent developmental trajectories, which complicates the understanding of such processes even further. This pattern of independent developmental

trajectories also applies to the development of attention and its subcomponents. The idea of parallel development of attention and executive functions is well documented and supported (Klimkeit, Mattingley, Sheppard, Farrow, & Bradshaw, 2004). For example, in their study, Klimkeit et al. (2004) showed similar growth trajectories and plateauing effects for attention and executive functions (EF) in children aged 8-10 and 10-12 years of age, respectively.

Development of Attention in Children

Since the ability to attend is a foundational skill in the elementary school years (6-12 years), the subject of the development of attention is fundamental to cognitive developmental psychology and to the developmental neuropsychology literature (Erikson, 1964, as cited in Brenner et al., 2007; Vakil, Blachstein, Sheinman & Greenstein, 2009). Specifically, the 7- and 8-to-10-year-old and 10-to-12-year-old stages are of particular significance, with most development occurring during the former stage (Klimkeit et al., 2004; Rebok et al., 1997; Vakil et al., 2009; Wassenberg et al., 2008).

A number of different studies show that performance on tests of various basic attentional and executive functions and subcomponents improves rapidly up to 10 years of age. This stage is followed by a period of more gradual change or plateauing until 12-13 years of age. The period of rapid development appears to begin around 7-8 years for most attentional components including focused, shifting, sustained, and selective attention (e.g., Betts, McKay, Maruff, & Anderson, 2006; Greenberg & Waldman, 1993; Klenberg, Korkman, & Lahti-Nuuttila, 2001; Klimkeit et al., 2004; Rebok et al., 1997; Wassenberg et al., 2008). Other attentional markers of dysfunction such as inattention, impulsivity and response inhibition appear to come online and stabilize in early childhood (5-7 years) (Bartgis, Thomas, Lefler, & Hartung, 2008; Kanaka et al., 2008; Klenberg et al., 2001; Wassenberg et al., 2008). Hence the various attentional components outlined above appear to follow general patterns of development. However, some studies report exceptions and contradictions to these general trends (e.g., Manly, Anderson, Nimmo-Smith, et al., 2001; McKay, Halperin, Schwartz, & Sharma, 1994).

Other abilities, primarily those associated with higher-order attentional / executive function abilities appear to mature later in adolescence. For instance, Zhan et al. (2011) report that response times in visual search tasks and target detection in vigilance tasks mature between 12 and 14 years of age. Although some of the basic attentional functions are in place in early childhood, the control of some of these abilities only develops later on. The development of these higher-order attentional processes is underpinned by the varying developmental trajectories of its subcomponents. For example, *attentional control* consists of

a number of subcomponents (selective attention; self-regulation; self-monitoring; inhibition), each with its own developmental trajectory. As noted earlier, development of selective attention begins around 7-8 years, whereas inhibition appears to stabilize around 5-7 years of age. In terms of self-regulation and -monitoring abilities, children are proposed to manage such skills by age 9. The ability to curb impulsivity, however, increases briefly around 11 years of age (P. Anderson, Anderson, & Lajoie, 1996; P. Anderson, Anderson, Northam, & Taylor, 2000; Klenberg et al., 2001; Wassenberg et al., 2008).

Although the information-processing component of P. Anderson's (2002) executive function model is considered relatively mature by 12 years of age, development continues along a more gradual slope until adolescence (P. Anderson, 2002; V. Anderson et al., 2001c; Wassenberg et al., 2008). There are gains in speed of processing through middle childhood (P. Anderson et al., 2000; Hale, 1990; Welsh, Pennington, & Groisser, 1991), with the most rapid development occurring until about 11 years of age and a second, more gradual spurt occurring from 12-13 years of age (Kanaka et al., 2008; Rebok et al., 1997; Wassenberg et al., 2008). Efficiency in information processing also improves into the adolescent stage, although this development is purported to plateau after 15 years of age (V. Anderson et al., 2001; Hale, 1990; Kail, 1986) .

Cognitive flexibility appears to mature earlier than other attention-related components of Anderson's model, with the ability to switch between activities with multiple stimuli showing significant improvement between 7 and 9 years of age. Monitoring of cognitive-flexibility appears to mature by late childhood, while the fluency in the ability to switch attention continues to improve into adolescence (P. Anderson, 2002; P. Anderson et al., 2000; Chelune & Baer, 1986; H. Levin et al., 1991).

In summary, the most significant improvements in attention and executive functions occur from 7 and 8 to 10 and 11 years of age, and a number of functions plateau thereafter. However, some functions only mature fully at puberty (Zhan et al., 2011). Therefore, differences across domains of attentional ability are more discernable among younger than older groups (Vakil et al., 2009). Establishing this trajectory is far from simple, with rates and peaks of maturity not only differing for different attentional domains, but also for the subcomponents of those domains. These differences in the rates of development of various attentional components and subcomponents are an important consideration in the assessment of attentional functions in children. Zhan et al. (2011) emphasize the importance of considering the various underlying subcomponents when interpreting outcome on attentional measures. For example, if one considers a selective attention measure, one may base

interpretation of a child's performance on the idea that selective attention appears fully developed by about 10 years of age (Wassenberg et al., 2008). However, a number of selective attention tasks may include underlying subcomponents such as processing speed (number of items processed), inattention (errors of omission), and impulsivity (commission errors), which, as outlined above, mature at different rates; and any or all of these abilities may affect performance in the assessment of attention (Manly, Knudson, Morabito, et al., 2001). It is therefore important to consider the developmental trajectories of the overall and the subcomponents of attentional or executive-related attentional domains, which are purported to develop in a stepwise or multistage manner (Klenberg et al., 2001; Klimkeit et al., 2004; Wassenberg et al., 2008).

A number of researchers remark on the approximate parity in timing of these cognitive developmental spurts with cerebral developmental spurts, particularly in the prefrontal cortex (see Klimkeit et al., 2004; Epstein, 1986; Hudspeth & Pribram, 1990; Thatcher, 1991). Epstein (1986) reviewed data on head circumference, cortical thickness, neuronal arborisation, and electroencephalogram (EEG) energy in alpha frequencies. These data consistently indicated peaks in brain growth rates at ages 7, 11–12, and 15 years of age. In addition, an EEG relative power study indicated a number of changes in frontal brain regions through childhood, the first between birth and 2 years, another between 7 and 9 years, with a final developmental change between 16 and 19 years (Thatcher, 1991). These ages are similar to those reported by Hudspeth and Pribram (1990), in their study of quantification of changes in the EEG frequency spectrum in frontal brain regions.

Attention post-pTBI. A number of studies report on attentional deficits in children who have sustained TBIs. These deficits are especially common following severe TBI. In some studies, this finding is consistent even when controlling for possible confounders like SES and premorbid attention problems (Babikian & Asarnow, 2009; Yeates et al., 2005). Attentional impairment following pTBI is neither surprising nor uncommon given (a) the extensive neuroanatomical networks associated with attentional function, and (b) the fact that the anterior attentional network is subserved by the prefrontal cortex, an area most vulnerable to the impact of TBI (Babikian & Asarnow, 2009).

DAI is often the hallmark of severe TBI, especially following MVAs (Meythaler et al., 2001). There is an established association between DAI and attentional and executive-related impairments (Wozniak et al., 2007). Furthermore, studies show that children with processing speed deficits also tend to have severe, diffuse injuries (Donders & Warschausky, 1997; Felmingham, Baguley, & Green, 2004). Deficits in this domain are likely to interfere

with the efficiency of attention and executive function systems (P. Anderson, 2002; V. Anderson & Pentland, 1998; Willmott, Ponsford, Hocking, & Schönberger, 2009).

Attentional and related executive skills are not affected uniformly post-TBI. Outcome depends on a number of factors, which commonly include age and severity (V. Anderson, Fenwick, Manly, & Robertson, 1998; V. Anderson & Pentland, 1998; Babikian & Asarnow, 2009; Catroppa & Anderson, 2005; Ewing-Cobbs et al., 1998b; Ginstfeldt & Emanuelson, 2010; NIH Consensus Developmental Panel on Rehabilitation of Persons with Traumatic Brain Injury, 1999). Deficits in attentional and executive functioning may be apparent in both the acute and chronic stages of injury, with impairment of some components of attention persisting up to 5 and 10 years post-injury (Beauchamp et al., 2011; Catroppa et al., 2007, 2011; Park et al., 2009; Yeates et al., 2005).

A recent overview of studies on attention post-TBI (Ginstfeldt & Emanuelson, 2010) and meta-analysis on the neurocognitive outcomes following pTBI (Babikian & Asarnow, 2009) confirms the presence of attentional impairment and the consistently reported idea that attention can be affected in various ways in children, post-TBI. This latter idea makes sense given the fact that the various components and subcomponents of attention develop at different rates and may therefore be disrupted in disparate ways. The effects of TBI on the various attentional and executive-related components are outlined below.

Sustained attention/vigilance. Research shows that sustained attention is impaired among children and early adolescents especially following moderate-to-severe TBI (V. Anderson et al., 1998; Catroppa & Anderson, 1999a, 2003, 2005; Fenwick & Anderson, 1999; Park et al., 2009). These studies often compare children with moderate and/or severe injuries to mild TBI or healthy control groups.

However, not all studies investigating this attentional domain have shown impairment post-TBI (V. Anderson et al., 2005a; V. Anderson & Pentland, 1998; Catroppa et al., 2007; Ewing-Cobbs et al., 1998b; Kramer et al., 2008; Wassenberg, Max, Lindgren, & Schatz, 2004). Studies reporting these discrepant results often include different target samples (e.g., young children or only older adolescents), small sample sizes, different severity comparison groups (e.g. comparing children with mild-to-moderate and severe TBI). Despite these discrepancies, in their overview of attention deficits post-TBI, Ginsfeldt and Emanuelson (2010) report sustained attention to be one of the most vulnerable attentional domains following TBI.

Selective / focused attention A number of studies report significant deficits in selective / focused attention post-TBI, especially following severe TBI, with impairment

reportedly persisting up to 4 years post injury (V. Anderson et al., 2005a; Catroppa & Anderson, 2005; Fenwick & Anderson, 1999; Yeates et al., 2005). However, the results of some studies do not support this trend (V. Anderson et al., 1998; V. Anderson & Pentland, 1998). Also, the dose-response relationship is not always evident (Park et al., 2009).

Shifting attention. Studies report impairment in this component of attention across various age groups in children and adolescents, with some studies demonstrating a dose-reponse relationship between severity and outcome (V. Anderson & Pentland, 1998; Catroppa, Anderson, & Stargatt, 1999; Catroppa & Anderson, 2005; Ewing-Cobbs et al., 1998b; Park et al., 2009). Impairments in this domain can persist up to 4 years post-injury (Yeates et al., 2005).

Divided attention. The capacity to divide attention is also related to cognitive flexibility (see Nadebaum et al. , 2007). Few studies specifically investigate divided attention or cognitive flexibility post-TBI in children and adolescents, however.

Existing studies do, however, report impairment in divided attention and cognitive flexibility across various age groups in children and adolescents, with some studies demonstrating a dose-response relationship between severity and outcome (V. Anderson et al., 1998; V. Anderson & Pentland, 1998; Catroppa et al., 2007).

Also, Ginstfeldt and Emanuelson (2010) also report divided attention to be one of the most vulnerable domains to impairment post-TBI. Children who sustain severe TBIs are reported to perform significantly more poorly than control participants up to 5, but not at 10 years post injury (Beauchamp et al., 2011; Nadebaum et al., 2007). The fact that these deficits do not persist up to 10 years post-injury may imply that these skills may recover over time following severe TBI.

There have been some negative findings, however. Fenwick and Anderson (1999) reported that differences in performance on mental flexibility tasks were not discernible for children who had sustained TBIs and healthy controls.

Response inhibition and impulsivity. Response inhibition and impulsivity are often operationalized by counting errors of commission on a relevant task (e.g., *d2 Test of attention*; Brickenkamp & Zillmer, 1998; Wassenberg et al., 2004)

Studies in this domain demonstrate impairment in children and adolescents following moderate-to-severe TBI (V. Anderson et al., 1998; Fenwick & Anderson, 1999). A dose-response relationship is also demonstrated with children and adolescents, with those who experienced a severe TBI showing a slower recovery trajectory over the first 2 years post-injury in one study (Wassenberg et al., 2004 (6-14 year olds)) and making more impulsive

errors at each evaluation in another (Catroppa & Anderson, 2005). In their meta-analysis, Babikian and Asarnow (2009) also provide evidence from case-control studies for impairment in inhibition at more than 24 months post-TBI.

Attentional control. Studies specifically investigating this attentional component among 8-12-year-old children do not report significant differences as a function of severity at 2, 5 and 10 years post-injury (V. Anderson & Catroppa, 2005; Beauchamp et al., 2011; Nadebaum et al., 2007). In the 2005 study, V. Anderson and Catroppa do however report that the different severity groups were similar with regards to accuracy, but did differ on the rate of task completion. Children with severe injuries did perform worse as the complexity of the task increased.

Information processing. A number of studies focusing on this domain consistently demonstrate a dose-response relationship between severity and outcome for children and adolescents post-TBI (V. Anderson & Pentland, 1998; Catroppa & Anderson, 2005; Catroppa et al., 2007, 1999), even though initial research studies on this domain failed to demonstrate this trend (Catroppa & Anderson, 1999a; Fenwick & Anderson, 1999). These effects may persist up to 2 and 5 years post-injury for some school- and younger-aged children respectively (Catroppa et al., 2007; Catroppa & Anderson, 2005; Nadebaum et al., 2007), although some improvements have been reported during the first two years following severe TBI (Babikian & Asarnow, 2009). Babikian and Arsarnow (2009) also report impairments in processing speed at < 6 months post-injury, > 6 months to < 24 months post-injury, and > 24 months post-injury following severe TBI.

Other longitudinal studies report consistent findings with those described above. At long-term follow-up (3-12 years post-injury), Van Heugten et al., (2006) report that mental speed is an area in which most problems are exhibited for children with severe TBI. It is therefore not surprising that impairments in other attentional domains (e.g., shifting attention) can continue to occur as a function of deficits in speed of information processing (Catroppa et al., 2007; Ewing-Cobbs et al., 1998b). These impairments among children who sustain severe injuries before 7 years of age persist at 10 years post-injury (Beauchamp et al., 2011).

Thus, slowed information processing and consequent slowing in response rates do contribute substantially to the attentional impairments that occur post-TBI. The frequency of impairment in this attentional domain is such that some researchers describe it as an 'inevitable' outcome (Wood, 1988).

Working memory. Although there is some evidence for impairment in WM following moderate-to-severe TBI, even at 2 years post-injury (H. Levin et al., 2002; Roncadin, Guger,

Archibald, Barnes, & Dennis, 2004), some studies do not support this result (e.g., V. Anderson & Catroppa, 2007; Warschausky, Kewman, & Selim, 1996). These inconsistent findings may be as a result of the sensitivity of the different measures (e.g. *n*-back vs. digit span tasks, respectively) employed in these sets of studies.

Inconsistencies in findings in studies of attention and related constructs stem mainly from the fact that TBI may have a unique impact on each individual superimposed on the equally heterogeneous social and developmental progress of that individual (Babikian & Asarnow, 2009; Ewing-Cobbs et al., 1998b). In addition, differences in measures and methodologies used in various studies only add to inconsistencies in outcomes. Owing to its multidimensional nature, studies of attentional impairment often focus on different aspects of attention and with that, different measures, amount of time since injury and different aged samples are investigated. In spite of these inconsistencies, it is clear that attentional impairment can persist, especially following severe TBI.

Bearing in mind the important role of attention in the optimal functioning of other important cognitive domains, attentional difficulties following TBI is concerning. Because of the interdependence between a number of neural systems, impairment in attention due to pTBI could result in generalized residual deficits in a number of cognitive abilities. Intact attentional abilities are critical to normal cognitive development and learning, as attentional impairment could interfere with knowledge acquisition and learning (V. Anderson & Pentland, 1998).

Those skills developing or emerging at the time of injury are more compromised and may not develop at a normal rate post-injury. Skills that develop early are most robust. Depending on the specific cerebral region impacted, the developmental trajectory disrupted and the attentional domain investigated, different outcomes may be evident (Catroppa et al., 2007). Regardless of the component or subcomponent, these persistent attentional deficits post TBI underscore the need for efficacious and effective attention remediation.

Cognitive rehabilitation strategies for attention deficits following TBI. Attention remediation is one of the cognitive rehabilitation strategies showing most potential for both adults and children. In adults, a commonly used direct intervention for attention remediation is Sohlberg and Mateer's (1987) Attention Process Training (APT). This program is based on and derives its theoretical framework from Sohlberg and Mateer's (1987; 1989) clinical model of attention, outlined above. APT tasks are organized hierarchically and proceed from basic to higher order attention tasks (sustained and selective attention to alternating and divided attention), with increasing levels of difficulty.

A more child-friendly, pediatric version of APT is called 'Pay Attention!' (Thomson et al., 2005). It includes more colourful and age-appropriate tasks designed for children aged 4 to 11 years of age.

A number of studies and reviews provide support for these and other direct attention remediation strategies for adults (Cappa et al., 2003, 2005; Cernich et al., 2010; Cicerone et al., 2000, 2005; Gordon et al., 2006; Park & Ingles, 2001; Pero, Incoccia, Caracciolo, Zoccolotti, & Formisano, 2006; Rohling et al., 2009; Sohlberg, McLaughlin, Pavese, Heidrich, & Posner, 2000) and children (Butler & Copeland, 2002; Galbiati et al., 2009; Kerns, Eso, & Thomson, 1999; Laatsch et al., 2007; Penkman, 2004; Sjö, Spellerberg, Weidner, & Kihlgren, 2010; Van't Hooft et al., 2005).

Kerns et al. (1999) implemented the pediatric 'Pay Attention!' intervention with children aged 7 to 11 years with ADHD. In this study, children who received the intervention showed improvements in sustained, selective, and higher-order components of attention. These improvements also generalized: children diagnosed with ADHD showed more improved efficiency on academic tasks, as compared to the improvement shown by the control participants. Penkman (2004) reported on a case study in which the 'Pay Attention!' intervention was implemented with a 6-year-old child with high-risk acute lymphoblastic leukemia. Post-intervention, the child showed improvement in arithmetic, reaction time and ADHD-related tasks over and above what might be accounted for by practice effects. Galbiati et al., (2009) also provided support for direct attention interventions with children and adolescents (6-18 years) who had sustained severe TBI. In this sample, the intervention group improved significantly more than the severe TBI control group on measures of sustained attention and adaptive functioning measures.

Some studies report limited improvement in attention and associated domains, however. For example, although Sjö et al. (2010) reported improvements in learning and memory following the implementation of the Amsterdam Memory and Attention Training for Children (Amat-c) program, these effects did not extend to attention and executive functions.

In spite of the fact that not all studies on attention-training interventions report improvement in attention post-intervention, the weighted outcome of attention remediation studies has resulted in practice guidelines and standards in the adult and pediatric literature (Cicerone et al., 2000, 2005; Laatsch et al., 2007). Hence, the potential for this intervention and continued investigation thereof is duly warranted.

One may also consider interventions designed for improving functioning in related domains, such as WM, given the interrelationship between attention and executive function

domains (Barkley, 1996). One such intervention that has received considerable interest from researchers in recent years, and that therefore requires specific mention, is Pearson's Cogmed Working Memory Training (CWMT) program. CWMT is a computerised training programme that is available commercially. It is marketed as a tool for improving WM and related domains, such as attention (Cogmed, 2013). There are three programs: Cogmed JM, RM, and QM, designed for preschoolers, older children, and adults, respectively. The program is used for 5 weeks (40 minutes per day, 5 days a week). The program can be adapted, depending on the user's performance. In other words, the tasks can be made increasingly difficult (e.g., adding more words to a memory list) if the user is performing well (Shipstead, Hicks, & Engle, 2012a). Evidence of near transfer (to other untrained WM tasks) and far transfer (to tasks in related cognitive domains like attention and reasoning) of effects are required to demonstrate efficacy (e.g., Klingberg, Forssberg, & Westerberg, 2002).

Several studies (some of which were led by the program's co-founders) report favourable findings for the CWMT program, primarily for children and adolescents with ADHD or undiagnosed attention and hyperactivity problems (e.g., Beck, Hanson, Puffenberger, Benninger, & Benninger, 2010; Green et al., 2012; Klingberg, 2010; Klingberg et al., 2005, 2002; Mezzacappa & Buckner, 2010). There are also reported positive findings with other pediatric populations (e.g., preterm born children with very low birth weight, school going children and adolescents with social, emotional, and behavioural difficulties, pre-school children, children with brain tumours and acute lymphoblastic leukemia and low achieving children; Grunewaldt, Løhaugen, Austeng, Brubakk, & Skranes, 2013; Hardy, Willard, Allen, & Bonner, 2013; Holmes & Gathercole, 2013; Roughan & Hadwin, 2011; Thorell, Lindqvist, Bergman Nutley, Bohlin, & Klingberg, 2009).

There are few published studies in which CWMT is implemented specifically with children with TBI, however. Two studies report on its implementation in adults with ABI (Johansson & Tornmalm, 2012; Lundqvist, Grundström, Samuelsson, & Rönnberg, 2010). These studies included 5/18 and 1/21 adults with TBI, respectively. Both studies reported favourable outcomes on trained WM tasks (i.e., they showed evidence of near transfer) and self-report far transfer tasks (i.e., transfer of learned skill to tasks in related cognitive domains, such as attention and reasoning), although the former study did not include a control group.

However, in spite of these reports of favourable results, outcome studies for CWMT are not consistently positive. In a recent review, Shipstead et al. (2012) question the efficacy

of CWMT, highlighting methodological concerns about existing studies (e.g., sample sizes, inclusion of control groups, and generalizability) as well as the potential for replication of outcomes. These researchers state that the positive outcomes advertised by CogMed are therefore "largely unsubstantiated" (p.185). They also criticize the program for lacking a theory-driven approach, although researchers are beginning to explore relevant WM theories (e.g., Gibson, Gondoli, Johnson, Steeger, & Morrissey, 2012). The conclusions put forward by Shipstead et al. (2012) are supported by other researchers in the field (e.g., Hulme & Melby-Lervåg, 2012; Morrison & Chein, 2012).

Studies published after this review also appear to present discrepant findings to those presented by Klingberg and colleagues. For example, some studies report a lack of generalization to non-WM tasks, for example, in related domains or real-world (e.g., classroom) activities of WM with non-clinical samples of children with low working memory performance (Dunning, Holmes, & Gathercole, 2013). Other researchers report a similar lack of generalization to both near and far transfer tasks with older children and adolescents with severe learning disability and cormorbid ADHD (Gray et al., 2012). Similar mixed findings are reported for school-age children with ADHD, with researchers concluding that CWMT is only "possibly efficacious for youth with ADHD" (Chacko et al., 2013, p. 37). For attention specifically, Shipstead, Hicks, and Engle (2012b) suggest that given the inconsistency in findings and concerns raised in their earlier review, there is insufficient evidence to suggest that CWMT will improve attention and that the program remains "a work in progress" (p. 217). Also, besides concerns regarding efficacy, there are practical concerns related to using this program. CWMT is a web-based program, and hence may not be easily available to samples of children from low-SES backgrounds who do not have access to, or who do not have experience with, computers.

CHAPTER 8:
STUDY 3: IMPLEMENTING AN ATTENTION-TRAINING INTERVENTION IN A SEVERE PEDIATRIC TBI SAMPLE

Restitution and substitution mechanisms of recovery have provided a platform for cognitive rehabilitation efforts and for the development of various interventions. However, according to a recent review of literature pertaining to these mechanisms, there is little conclusive evidence for their benefit for the developing brain, especially following severe TBI (V. Anderson et al., 2011). Following generalized cerebral insults, such as often occurs with severe TBI, research has shown that recovery may be slower and outcome may be poorer for children compared to adults with insults of a similar nature (V. Anderson & Moore, 1995; Giza et al., 2007; Hessen, Nestvold, & Anderson, 2007; Taylor & Alden, 1997).

This element of inconclusiveness about the mechanisms of recovery, upon which the success of cognitive rehabilitation might be based, has also prevailed in the cognitive rehabilitation literature. This inconclusiveness in the field of cognitive rehabilitation has generally been attributed to a lack of evidence for the efficacy of interventions and to methodological limitations, rather than to a lack of support for the theoretical framework subserving it.

The methodological limitations commonly reported in cognitive rehabilitation reviews pertain to participant-related variables, such as heterogeneity and lack of representativeness of participants, small sample sizes, and lack of control groups; to treatment-related variables, such as heterogeneity in frequency and duration of interventions, and in standardization and target of treatment; and to outcome-related variables, such as variability in outcome measures and a lack of blind outcome evaluations (Cappa et al., 2003, 2005; Gordon et al., 2006; Laatsch et al., 2007; Limond & Leeke, 2005; Rohling et al., 2009). In children, there are also the added complications that come along with developmental factors such as variability in age at injury and in age at intervention among participants (Slomine & Locascio, 2009). Confounding variables such as test-retest effects and the impact of SES on neuropsychological test performance also contribute to difficulties in evaluating outcomes and are often not controlled for (Laatsch et al., 2007; Rohling et al., 2009).

Despite these identified problems, the state of cognitive rehabilitation efficacy appears to have improved over time. There has been a move away from the initial conclusion, made in a pediatric cognitive rehabilitation review, of "no conclusive evidence for the efficacy for cognitive rehabilitation in pediatric ABI" (Limond & Leeke, 2005, p. 341) to

increasing support and emerging evidence for some forms of cognitive rehabilitation for children (Laatsch et al., 2007; Slomine & Locascio, 2009).

Attention remediation is among those interventions consistently reported as potentially efficacious for improving cognitive functioning post-TBI. Attentional abilities are integral to optimal everyday functioning, but are vulnerable to the effects of (especially severe) TBI (Babikian & Asarnow, 2009; Wassenberg et al., 2008). The frequency of attention deficits following TBI is not surprising given that part of the neuroanatomical networks underlying attention, the prefrontal cortex, is an area most vulnerable to the impact of TBI (Babikian & Asarnow, 2009). Furthermore, diffuse axonal injury (DAI) is often the hallmark of severe TBI, especially following MVAs, and there is an established association between DAI and attentional and executive-related impairments (Meythaler et al., 2001; Wozniak et al., 2007).

These deficits may be apparent acutely, and can persist even 5 and 10 years post-injury (Beauchamp et al., 2011; Catroppa et al., 2007, 2011; Park et al., 2009; Yeates et al., 2005). However, studies demonstrate consistently that there are variations in the ways that attention and related executive skills are affected post-TBI. These variations arise due to a number of factors, including age at injury and injury severity (V. Anderson et al., 1998; V. Anderson & Pentland, 1998; Babikian & Asarnow, 2009; Catroppa & Anderson, 2005; Ewing-Cobbs et al., 1998; Ginstfeldt & Emanuelson, 2010).

Attention remediation for such impairments is recommended as a practice guideline in the treatment of children with ABI (Laatsch et al., 2007). The two studies upon which this recommendation was based include one on children who underwent radiation treatment for cancer and brain resections (Butler & Copeland, 2002), and one on a sample of children with mixed injury etiologies, including trauma, infection, and brain tumors (Van't Hooft et al., 2005).

In the study by Van't Hooft et al., eight of the total number of participants ($N = 38$) had sustained severe TBI (GCS < 8). Five of these participants were assigned to the intervention group and participated in a 17-week attention-training programme (The Amsterdam Memory and Attention Training for Children (Amat-c)) and three to a control group. The control participants ($N = 20$) spent the same amount of time as the intervention participants ($N = 18$) engaging in non-intervention interactive activities with an adult, to control for the effects of the stimulation and interaction received during the intervention. The intervention group showed positive gains on measures of sustained and selective attention.

Although the studies by Butler and Copeland (2002) and Van't Hooft et al. (2005) were both well-designed, neither focused specifically on severe TBI in middle childhood. Hence, the question about whether this practice guideline applies to that injury condition, or to that age group, remains open. It is this open question that the current study attempted to address.

Athough some earlier studies appear to provide support for attention training interventions, they differ from the current study in terms of design. Many of them were multiple-baseline single-case experimental designs (SCEDs) and case studies with no control groups (Butler, 1998; Thomson, 1995; Thomson & Kerns, 2000; Van't Hooft, Andersson, Sejersen, Bartfai, & Von Wendt, 2003).

Although randomized controlled trials are regarded as the gold standard approach to evaluating treatment efficacy, a number of researchers do provide support for *n*-of-1trials (SCEDs) provided that these are well-designed and evaluated against recognized criteria (e.g., Perdices & Tate, 2009; Tate et al., 2008 (RoBiN-T scale)). Unfortunately, again, none of these studies on attention training interventions focused exclusively on children who had sustained severe TBIs, as the current study does.

Attention training studies that specifically and solely focus on children who have sustained severe TBIs are limited in number. Among those that have been conducted, there are often other limitations in terms of the design or age range. Studies often include children of mixed severities and/or different etiologies. For example, in the Van't Hooft et al. (2005) study reviewed above, the sample included children with ABIs (trauma, infection, or malignancy). Those who had sustained TBIs had GCS scores of a wide range, both ≤ or > 8. Galbiati et al. (2009) included only children who had sustained severe TBIs, but they ranged from 6 to 18 years in age. Such a wide age range may be problematic given the different developmental trajectories for various aspects of attention. The inclusion of children with different etiologies and/or wide age range is most likely an effort to boost sample sizes, but it introduces difficulties related to generalization and external validity. Further, given the varying developmental trajectories of cognitive abilities from early to middle childhood and adolescence, the inclusion of children from a wide age range could drown out specific effects at various ages.

Despite a number of positive findings and consequent growth in the field, there are some published studies that do not report positive gains on attention or on a broader set of neurocognitive outcome measures following ABI. For instance, Brett and Laatsch (1998) reported on a computer-based attention-training programme implemented with 10 teenage

participants with ABI. The participants showed improvements on memory and EF measures, but not on basic attentional measures. Butler et al. (2008) reported on a randomized clinical trial with children treated for cancer. Participants were assigned to either an attention training intervention group ($N = 80$) or to a wait-listed control group ($N = 52$). There were no significant between-group differences on measures of neurocognitive functions. The groups only differed on parental reports of attentional functioning and in academic achievement.

In summary, although there is some evidence supporting the use of attention training programs in children with ABI, it is not entirely clear whether this is the case for children with severe TBI specifically. Also, individuals with severe TBI may not always be considered first for standard rehabilitation programs, given the degree of disability and the protracted nature of recovery associated with this degree of injury (Gray, 2000). It is also not clear whether positive effects of such an intervention on a severe TBI sample would hold after some important confounding effects (e.g., SES of participants or time spent with participants) and test-retest effects are controlled for. Therefore, although attention training is recommended as a practice guideline (Laatsch et al., 2007) in the treatment of children following ABI, the efficacy of this type of intervention for children who sustain severe TBI is unclear.

This study attempted to remedy the methodological deficits described above. I report on the outcomes for a group of children aged 7-10 years following severe TBI while attempting to control for the effects of the stimulation or attention provided, for practice effects, and for the effects of SES in this South African context.

The context in which this study is based is also important. The vast majority of children in South Africa and other LAMICs do not have access to cognitive rehabilitation post-ABI (Abdullah et al., 2005; K. Levin, 2004). This lack of access to cognitive rehabilitation is due not only to a lack of evidence to support the implementation of interventions, but also due to a lack of financial and human resources to offer the recommended approaches. Even though TBI and the associated human and economic cost is greatest in LAMICs (De Silva et al., 2009), most of the cognitive rehabilitation literature, and therefore the cognitive rehabilitation programs being evaluated, emanate from HICs. These programs may often not be suitable to implement in LAMICs, in which there are greater social and economic considerations. Therefore, studies of cognitive rehabilitation that are based in LAMICs are needed.

Aims

I investigated a pediatric attention-process training (APT) intervention with a group of 7- to 10-year-old South African children who had sustained severe TBIs. There were two aims in doing so: (1) to examine the efficacy of this intervention programme with the named sample, and (2) to explore the applicability of this program in the context of a LAMIC.

The scope of this study is such that it did not measure or evaluate the *effectiveness* of this intervention, but rather its *efficacy.* The latter type of enquiry (efficacy studies) is used in research settings for evaluating interventions of a limited duration and scope with specific, homogenous samples. In contrast, effectiveness studies are conducted in clinical settings and evaluate treatment protocols that involve and can be modified based on continued clinical evaluation and judgment (Cicerone et al., 2000).

Methods

Design and Setting

The setting for this study was two public hospitals and four low-SES schools situated in the Cape Town area.

I employed a quasi-experimental case-controlled trial using a pretest-posttest design, with four independent groups (n = 4 each). The pre- and post-testing sessions were approximately 3 months apart.The four groups were: (a) children who had sustained a severe TBI and who received the 'Pay Attention!' intervention (*TBI-intervention group*), (b) healthy children who received the 'Pay Attention!' intervention (*Control-intervention group*), (c) healthy children who did not receive the 'Pay Attention!' intervention, but who participated in regular play sessions with research assistants (*Play group*) and, (d) healthy children who neither received the 'Pay Attention!' intervention nor participated in play sessions, but were only tested during pre- and post-testing sessions (*Test-only group*). The participants in each of the three control groups were matched to the participants in the TBI-intervention group on age, race, sex, and SES. Healthy children were assigned randomly to the Control-intervention, Play, and Test-only groups by an individual not involved in this study.

Purpose of, and participant assignment to, control groups. The purpose of the Control-intervention group was to control for the effects of low SES on the participants' performances on the cognitive outcome measures. As outlined in Chapter 7, low SES affects various neurocognitive systems differently (see Hackman & Farah, 2009, for a review), with executive/attentional function systems being one of the systems most vulnerable to such effects.

The purpose of the Play group was to control for the effects of the one-on-one time that the TBI-intervention participants spent with the researcher. Given their SES backgrounds, the participants in this study would not always have had access to prolonged periods of individual attention with an older sibling or adult. The participants in this group spent an equal amount of time with research assistants as the TBI intervention participants spent engaging in the intervention program. They played outdoor games or engaged in interactive activities that did not require long periods of concentration.

The purpose of the *Test-only* group was to control for maturation and test-retest effects. Rohling et al. (2009) highlight the importance of controlling for such potential confounding effects.

Administration and testing of control participants. Two postgraduate psychology students conducted the control component of this study under my supervision. I contacted the schools and assisted them in setting up this part of the study protocol. I trained these students in the administration of the intervention and of the neuropsychological tests. The students reported to me after every intervention session and I provided feedback on how to proceed at the next session. These researchers were blind to group assignment at the pre-test. However, due to limited human resources, the same researchers were involved in post-testing, and were at that stage familiar with which children had participated in the intervention program. The researchers did not administer the post-tests with the same control participants with whom they had carried out the intervention, however.

Administration and testing of the TBI intervention group. As I had conducted the pre-intervention testing, I recruited post-graduate neuropsychology interns and clinicians, not otherwise involved in the study, to conduct the post-testing sessions for this group. However, one participant was not tested by an intern or clinician, because the intervention was conducted before those for the other three participants. I tested this participant on both occasions. The neuropsychology interns and clinicians were blind to the identities of the intervention participants.

In summary, the same researchers did not test the participants at both pre- and post-intervention testing sessions, except in one case. Assessments were blind at post-test for the TBI intervention participants and at pre-test for the control participants.

Participants

Recruiting and demographic characteristics of the TBI intervention participants. I recruited participants through retrospective inspection of clinic and hospital records (trauma registers) of children admitted to RXH for severe TBI. Once a list of suitable children was

compiled, medical files were investigated for contact details and inclusion and exclusion criteria. The identified children's families were then contacted telephonically and a brief verbal description of the study given to them. Once the level of interest was gauged, I scheduled an initial meeting with them at RXH, where a more detailed description of the research was given. If the parent was willing to participate and to allow their child to participate, the child's suitability and eligibility for the study was further assessed at that initial meeting. Those children who met the inclusion criteria, including the provision of informed consent by the parents and assent by the child, were assessed neuropsychologically.

Table 21 outlines the sociodemographic characteristics of the TBI-intervention group participants. All participants in this group were at least 1 year post-injury, an inclusion criterion consistent with other TBI studies (Cope, 1995; Van't Hooft et al., 2005). Although recovery in some patients may continue for several years post-injury, for many the peak in this recovery trajectory occurs in the first year post-injury, and is followed by a plateau after that time (Ginstfeldt & Emanuelson, 2010; Yeates et al., 2002). However, there does not appear to be a cutoff point after which cognitive rehabilitation can no longer be useful to individuals (Cernich et al., 2010). In other words, the timing of any intervention should not be limited to the first year post-injury (Tsaousides & Gordon, 2009).

Table 21
Demographic Characteristics of TBI Participants (N = 4)

	Participant 1	Participant 2	Participant 3	Participant 4
Sex	Female	Male	Male	Male
Age at injury[a]	6 : 6	6 : 8	7 : 6	9 : 1
Age at assessment[a]	7 : 7	8 : 10	9 : 6	10 : 10
Time since injury[a]	1 : 1	2 : 2	2 : 0	1 : 9
GCS	7	3	7	7
Motor GCS	5	1	4	4
Cause of injury	MVA passenger	Struck by an object	MVA pedestrian	MVA pedestrian

Note. [a]Years : months; GCS = Glasgow Coma Scale; MVA = motor vehicle accident.

The TBI participants were learners at four different schools in the Cape Town area. They were recruited through referral or through perusal of medical records obtained at RXH.

Besides the requirement that participants be at least 1 year post-injury, other inclusion criteria for the TBI intervention participants were: (a) that they had sustained a closed, severe

TBI (GCS ≤ 8), (b) that they were able to converse fluently in English, (c) that they were 6 to 10 years of age at the start of the intervention, (d) that their parents provided informed consent for their participation, and (e) that they provided assent for their participation. These inclusion criteria were put in place (a) because most pTBIs are closed, rather than open (V. Anderson, Northam, Hendy, et al., 2001), (b) so that a uniform neuropsychological test battery could be utilized across the sample (Hemp, 1989) and because the intervention materials were only available in English, and (c) because the intervention programme employed was designed for children aged 4 to 11 years and a number of tests in the assessment battery were designed for children from 6 years of age. Inclusion criteria (d) and (e) were of course mandatory for ethical reasons.

Other exclusion criteria included any previous head injuries (prior to the severe TBI) that resulted in hospitalisation or loss of consciousness, and any formally diagnosed premorbid learning, psychiatric, neurological, or developmental disorders. The latter were screened for using parental reports.

Recruiting and demographic characteristics of the control participants.

Recruitment of control participants took place after the intervention programs with the TBI intervention participants had been completed. I approached the relevant schools and set up preliminary meetings with the school principal or deputy principal. After obtaining permission to continue the study, I submitted two documents to those school administrators: (a) a sheet detailing profiles of suitable candidates for the study, and (b) a letter explaining the study for the parents of learners who matched the criteria (see Appendices T and U). I asked class teachers of the relevant grades to generate lists of students who matched these profiles and who met the study's inclusion and exclusion criteria. The research assistants then sent informed consent documents to these parents (e.g, see Appendix V).

The eligible and recommended children were included only if their parents provided informed consent. The two postgraduate researchers who assisted with the control component of this study then contacted the parents of these participants to introduce and explain the study. However, the number of participants was insufficient following this initial recruitment phase. Therefore, more participants were selected randomly from the list of possible learners and these parents were contacted. Once the total number of matched participants was recruited and the pre-intervention assessment sessions were completed, an independent researcher, blind to the nature of the study, assigned participants randomly to one of the three control groups.

The control participants were selected from two of the four schools that the TBI intervention participants attended. The two schools were selected based on proximity to the University of Cape Town (UCT): They were located less than 15 minutes away from UCT, whereas the other two schools were located more than 30 minutes away. The selection of the two closest schools was to facilitate ease of access to the eight Control-intervention and Play group participants in this part of the study. The intervention and play activities required a large number of hours and resources to complete over an extended period of time.

I consulted a report by the Information and Knowledge Management Department of the City of Cape Town (Gie & Romanovky, 2006) to acsertain the SES of the suburbs in which the schools were based. The SES index provided in the report was based on the following factors: income and level of education, rates of unemployment, and percentages of unskilled labourers. The indices are presented as percentages, with higher scores representing poorer outcomes. The areas in which the four schools of the TBI participants were located could be grouped into two pairs, each with similar index scores: 22.73 and 29.01, and 43.70 and 46.20. One school from each pair was included in this part of the study, for the proximity reason described above. Hence, for two of the TBI participants, I recruited the control participants from the same schools that they (the TBI participants) attended. For the two remaining TBI particpants, I recruited the control participants from the schools based in the suburbs with the more similar SES index.

Each TBI intervention participant was matched to three control group participants on age, race, sex, and SES. Hence, for every TBI intervention participant, there was a matched individual in each of the three control groups. The SES of the participants' families was confirmed through the use of a demographic questionnaire and asset index given to their parents (Appendix W).

Inclusion criteria for control participants were that they were fluent in English, that they matched the demographics of one of the intervention participants, that they provided assent for the study, and that their parents provided informed consent. Exclusion criteria included any previous head injuries that resulted in hospitalisation or loss of consciousness, and any formally diagnosed learning, psychiatric, neurological or developmental disorders. The latter were screened for using parental or teacher reports.

Measures

Below, I briefly review the various measures, as well as the attention training program, used in this study.

Clinical and demographic information, and neuropsychological measures. These measures are identical to those described in Study 2 (see Appendix C), with one exception: the Design Fluency subtest of the NEPSY-II was included in this assessment battery. The reason it was included here and not in Study 2 is because age-based norms for this subtest are only available for children aged 5 to 12, and the ages of the Study 2 participants ranged from 6 to 16 years.

Design Fluency. This is a generativity task and a measure of behavioural productivity. The participant is given 60 seconds to produce as many unique designs as he/she can, by joining from two up to five dots. The task includes a structured and a random array, presented in that order. These arrays are presented as symmetric or asymmetric arrangements of dots, respectively.

Attention training program: 'Pay Attention!' This programme was designed by (Thomson et al., 2005). It is an adapted pediatric version of the adult Attention Process Training (APT) programme (Sohlberg & Mateer, 1989), which is based on a hierarchical, clinical model of attention. Because it is designed for children, however, the materials have been adapted to make it more suitable for them; for example, Pay Attention! uses visual and auditory stimuli that are engaging to children, as well as concepts that are familiar to them.

The Pay Attention! training program is divided into four attentional domains organized hierarchically from, at the bottom, sustained, to selective, to alternating and then, at the top, divided attention (Thomson et al., 2005). There are four different tasks in the program: *Card Sort, House Search, Card Flip* and *Attention CD*. Card Sort, House Search and Card Flip are visual attention tasks, whereas Attention CD is an auditory attention task. The same four tasks are used across attentional domains, but are adapted to suit each domain. Within each task there are a number of parameters or stimuli on which to vary the task and make it increase in difficulty (see Kerns et al., 1999). These tasks, parameters, and stimuli are described in greater detail below.

Regarding the Card Sort task, for the sustained attention domain, it requires participants to use various criteria to sort cards into piles. These criteria begin with a single feature, for example, families (blue, black, or green) or hair colour, and then progress to multiple features such as blonde coloured hair and glasses (or no glasses). For the selective attention domain, the same sustained attention task is used, but a tape is played in the background with auditory distractors (e.g., the sound of a heartbeat, someone telling a story, or a baby crying). For the alternating attention domain, the child is required to switch between sorting the cards into two piles using two different sorting rules (e.g., glasses vs. no

glasses and hats vs. no hats) at the examiner's instruction. For the divided attention domain, the participant is again required to sort the cards into piles, but he/she also has to perform an additional task at the same time (e.g., sorting the cards into different families and placing the boys face down).

Regarding the House Search task, for the sustained attention domain, it requires that participants mark various stimuli on or around a picture of a house using a marker. The task begins with a single feature, for example, red things or flowers, and then progresses to multiple features, such as red things and things on the walls. For the selective attention domain, the same sustained attention task is used, but this time distracting visual overlays (e.g., transparent sheets with curved or intersecting lines) are placed over the house stimuli. For the alternating attention domain, the participants are required to start searching for and marking one target, and to then switch to and mark a different target, using a different coloured pen marker, on the examiner's instruction. For the divided attention domain, a tape is played while participants mark off target stimuli. Participants are required to, for example, mark off all of the red things in the house while listening for words beginning with the letter B.

Regarding the Card Flip task, for the sustained attention domain, it requires that participants press a clicker in response to seeing target stimuli (e.g., people with brown hair and glasses or blonde followed by a brunette) on a card. For the selective attention domain, the same sustained attention task is used and similar auditory distractors are used as for the selective attention Card Sort tasks. For the alternating attention domain, participants have to switch between responding to two stimuli at the examiner's instruction. The divided attention Card Flip and Attention CD tasks are combined.

Regarding the Attention CD task, for the sustained attention domain, it requires that participants press a clicker in response to hearing the target stimuli (e.g., red, among a number of different colour names). For the selective attention task, the same sustained attention task is used, but additional distracting stimuli (e.g., the sound of a heartbeat or a baby crying) are played in the background. For the alternating attention domain, the participants listen for two target words (e.g., red or cow) and must switch between these on the examiner's instruction. For the divided attention domain, participants sort cards into stacks while pressing a clicker each time a target word is heard on the CD.

In general, difficulty of tasks increases with more complex criteria as well as the speed at which the participant must respond. How participants perform relative to these criteria determines their progression (Kerns et al., 1999). Participants progress from one

parameter to the next, within each task, after showing improvement on that parameter for three consecutive intervention sessions.

Procedure

In this section, I describe the pre- and post-intervention testing of the TBI-intervention and control participants. I also decribe the implementation of the intervention programme with the TBI-intervention and Control-intervention participants, and the procedure for the Play and Test-only groups.

Pre-intervention assessments. All participants were administered the neuropsychological test battery. The pre-intervention testing sessions were necessary to establish baseline attentional and general neurocognitive functioning of participants. Each session lasted approximately 3.5 hours.

Upon arrival at the testing session, researchers asked parents to sign a consent form. Participants were reminded that their involvement in the study was voluntary and that they could withdraw at any time and for any reason, without penalty. They were then asked to read and sign an assent form (e.g., see Appendix X). Participants could take regular breaks and were provided with refreshments.

For the TBI intervention participants, these assessments took place at RXH (the three male participants) and at Tygerberg Hospital (the one female participant). Although this female participant was admitted to RXH and followed up there by staff at the Division of Neurosurgery, other medical assessments were conducted at Tygerberg Hospital because the participant and her family had moved following her injury and lived closer to that hospital. For control participants, pre-intervention testing sessions were conducted in quiet rooms in the Psychology Department at the University of Cape Town.

Implementing the 'Pay Attention!' intervention. The training manual guided the administration of the 'Pay Attention!' intervention. The programme was administered in two 45-minute sessions per week, for 10 weeks. This timeframe was adopted from other studies in which "Pay Attention!" has been implemented (see Limond & Leeke, 2005).

The intervention program was conducted at the participants' schools, in the hope that this would lead to less attrition. The decision to implement the programme at schools was also considered in light of the fact that the majority of patients admitted to the RXH are from low SES areas in and around South Africa (Dodd, 2006). Thus, expecting parents and their children to travel to the hospital (probably relying on public transport) on a such regular basis, for such an extended period of time, might not have been feasible even if they were compensated for travelling costs.

The participants in the TBI-intervention and Control-intervention groups were seen individually, for two 45-minute sessions per week. The participants moved from one exercise of attention to the next based on two main criteria: first, number of errors, and, second, task completion time. If participants decreased their number of errors or improved their completion time on a task, while maintaining the same level of accuracy for three consecutive trials, more difficult task criteria were used in the following session. Sessions commenced with tasks in the first attentional component (i.e., sustained attention). No one session included tasks from more than two attention components.

Procedure for the Play and Test-only groups. The research assistants recruited volunteers to participate in the play sessions with Play group participants. These volunteers were UCT Psychology undergraduate students who were awarded course credits for their help. Volunteers spent the same amount of time playing with the Play group participants as the researchers spent implementing the intervention with the TBI-intervention participants. The games played aimed to tap physical rather than cognitive abilities, in an attempt to avoid confounding attention or concentration effects. Therefore, games such as hop-scotch, jump rope, and hula-hooping were played.

Regarding participants in the Test-only group, neither researchers nor volunteers spent any time with these participants during the 10-week period over which the intervention was implemented.

Post-intervention testing sessions. All participants underwent post-testing following the completion of the 10-week intervention period. The same neuropsychological tests administered at pre-testing were re-administered. The only exception was the WASI subtests, as the general intellectual functioning of participants was not expected to change over such a short period.

Ethical Considerations

UCT's Department of Psychology Research Ethics Committee and Faculty of Health Sciences Ethics Committee, and the University of Stellenbosch's Health Sciences Ethics Committee (Appendices Y and Z), granted ethical approval for the various components of this study. Permission to include the school learners and to use the school facilities for both the TBI-intervention and the control groups was obtained from the Western Cape Education Department (Appendix D).

Informed consent and assent. Verbal and written informed consent were obtained from the participants' parents (see Appendices V and AA). Participants were asked for both verbal and written assent (see Appendices X and BB).

Confidentiality, voluntary participation, and deception. All information obtained throughout this study is confidential and will only be used for research purposes. In obtaining assent, both the prinicipal investigator and the assistant researchers emphasized to participants that their involvement was voluntary and that they could withdraw from the study at any point. They were told they would not incur a penalty from the hospital or school as a result, and that their medical treatment and academic experience would not be affected. This study did not make use of any deception.

Risks and benefits. There were no physical, social, or emotional risks to participants. However, participants may have experienced fatigue during testing sessions or during the implementation of the intervention or the assessment sessions. Hence, they were given regular breaks.

Participants did not benefit directly from their involvement. However, parents may have benefitted indirectly by gaining an increased understanding of their child's functioning. The parents of the intervention participants were compensated ZAR400 for their participation and completion of the intervention. All parents of participants were compensated ZAR50 for travelling expenses related to the pre- and post-intervention testing sessions. Participants were rewarded with a choice of sweets after each session.

Debriefing and feedback. The researcher conducting the assessment debriefed parents and children fully after testing. They were allowed to ask questions and they were given the contact details of the principal researcher. The results were made available to participants' parents upon request.

Data Analysis

I analysed all data using SPSS 19.0 and 20.0.

Deriving composite scores. The derivation of composite scores for this study followed the same premise and procedure as in Study Two. I reduced the number of dependent variables from 20 to 8 by creating composite scores using the hybrid method described before (see Ferrett et al., 2010; Medina et al., 2007).

Pre-intervention between- and within-group comparisons. I compared the pre-intervention composite scores of the TBI and the three control groups. I used one-way ANOVAs to compute these comparisons where assumptions of normality and homogeneity were upheld, and the nonparametric equivalents where assumptions were violated. I used the the Kruskal-Wallis *H* test for the between-group and the Wilcoxon signed rank test for the within-group comparisons. I used Chi-square or Fisher's exact test to assess differences

between categorical variables. I used Fisher's exact test in instances where the sample was small and where the cells of the variables in the analyses had expected counts of less than 5.

Effect size. I used the *r*-statistic as a measure of effect size. This statistic is a commonly used measure of effect size. Values of .10, .30, and .50, represent small, medium and large effect sizes, respectively (Field, 2009). The use of this statistic also allowed for the calculation of effect sizes for nonparametric statistical analyses. In practice, the *r*-statistic and Cohen's *d* can be used interchangeably; both can be employed when using a dichotomous and a continuous variable in analyses. Under certain circumstances, however, *r* and *d* are not equivalent; outcomes for these effect size estimates can vary depending on whether sample sizes are equal and on the variance of the dichotomous variable (McGrath & Meyer, 2006).

Reliable Change Index. To ascertain whether any of the changes in individual participants' scores from pre- to post-testing sessions were clinically meaningful, I used the Reliable Change Index (RCI*;* Jacobson & Truax, 1991). In neuropsychological assessment, and particularly in study contexts such as this, it is important to assess whether change in performance from one testing occasion to the next is meaningful or not (Parsons, Notebaert, Shields, & Guskiewicz, 2009). I calculated the individual RCI scores using a reliable change generator, developed by Devilly (2004). I compared these scores among the participants within each age group. This clinical tool is based on the original Jacobson and Truax (1991) RCI model and generates the degree of change at three different confidence intervals: 68.26%, 95%, and 99%. The data input into the program were pre- and post-test scores, the subtest's test-retest reliability coefficient (obtained from the relevant test manuals), and the standard deviation of the normative sample for that subtest. An RCI of above 1.96 (corresponding to a 95% confidence interval) is considered a significant difference between pre- and post-test scores.

The RCI is based on the following formula:

$$SEd = \sqrt{2}(Se)^2, \text{ where } Se = s(\sqrt{1} - rxx),$$

where *s* is the standard deviation and *rxx* is the test-retest reliability coefficient. The standard error of difference (*SEd*) gives the change from the time of pre-test to the time of post-test, using the test-retest reliability coefficient. This measure indicates whether these scores have changed more than fluctuations on tests of imprecise measurement (Jacobson & Traux, 1991).

Case studies. Finally, I report on two illustrative case studies of two participants in the TBI-intervention group. The reason for selecting these two cases is because there seemed to be a number of overlapping injury-related characteristics, and yet their outcomes were so

disparate. Hence, these case studies provided an opportunity to explore, in greater depth, the influence of various pre- and post-morbid factors on the intervention outcomes.

Results

Sample Demographic Characteristics

The TBI-intervention and control groups were evenly matched on sex, with three males and one female in each group. All participants were of mixed race and fluent in English. Regarding age and IQ, there were no significant between-group differences (see Table 22). There were also no significant between-group differences on any of the SES measures or on Asset Index scores (see Table 23).

Table 22
Demographic Characteristics of the Sample (N = 16)

	Group										
	TBI-intervention (n = 4)		Control-intervention (n = 4)		Play (n = 4)		Test-only (n = 4)		F/H	p	r
Variable	M (SD)	Range	M (SD)	Range	M (SD)	Range	M (SD)	Range			
Age at assessment[a]	110.25 (16.26)	91-130	108.50 (11.45)	94-121	105.75 (13.23)	90-122	107.25 (16.68)	88-124	0.07	.98	.13
Verbal IQ	77.75 (4.35)	74-84	87.00 (14.65)	76-108	95.25 (12.34)	77-104	85.00 (14.58)	73-106	1.39	.30	.51
Performance IQ	88.50 (12.34)	77-106	83.75 (2.06)	81-86	80.25 (9.00)	72-93	81.50 (5.45)	75-86	0.79	.52	.41
Full Scale IQ	81.00 (8.76)	75-94	83.25 (6.85)	78-93	86.25 (9.61)	73-96	81.50 (10.85)	71-96	1.08[b]	.78	.22

Note. [a]Age at assessment in months. [b]Kruskal-Wallis H statistic. The r value presented here is an estimate of effect size.

Table 23

Demographic Questionnaire and Asset Index Data (N = 16)

	Group				
	TBI-intervention (*n* = 4)	Control-intervention (*n* = 4)	Play (*n* = 4)	Test-only (*n* = 4)	*p*
Household income per year[a]					.540
0	0	0	0	1	
1 - 5 000	4	1	0	1	
5 001 - 25 000	0	2	1	0	
25 001 - 100 000	0	1	3	1	
100 001 +	0	0	0	1	
Parental education (father: mother)					.550; .650
0 years	-	-	-	-	
1-6 years	-	-	-	-	
7 years	1: 0	0: 0	0: 1	0: 0	
8-11 years	1: 2	0: 3	2: 2	1: 4	
12 years	0: 2	3: 1	1: 1	1: 0	
13 years +	0: 0	1: 0	1: 0	1: 0	
Unknown	2: 0	0: 0	0: 0	1: 4	
Parental employment (father: mother)					.330; .170
Higher executives, major professionals	0: 0	0: 0	0: 0	0: 1	
Business managers of medium businesses, lesser professions	0: 0	0: 1	0: 1	0: 1	
Administrative personnel, managers, minor professionals	-	-	-	-	
Clerical and sales, technicians, small businesses	0: 0	1: 2	1: 2	0: 0	
Skilled manual (with training)	0: 0	0: 1	1: 0	0: 2	
Semi-skilled	0: 1	2: 0	0: 0	0: 0	
Unskilled, unemployed	1: 0	0: 0	2: 1	1: 0	
Homemaker	0: 1	1: 0	0: 0	2: 0	
Student, no occupation	1: 2	0: 0	0: 0	0: 0	
Unknown/incomplete	2: 0	0: 0	0: 0	1: 0	
Material and financial resources (Asset Index)					.650
0-5 assets (low)	-	-	-	-	
6-12 assets (medium)	2	1	0	0	
13-17 assets (high)	2	3	4	4	

Note. [a]Presented in South African Rands (ZAR). At the time of the study, the US$: ZAR exchange rate was 1 : 9.01.

Pre-intervention Between-group Comparisons

I did not apply a Bonferroni correction to the results for the same reason as noted for Study 2: Public health researchers raise more concern about missing important effects (Type II errors) rather than concern for the strict control of alpha values (Jacobson & Jacobson, 2005). Hence, employing a Bonferroni adjustment may result in an underestimation of the effects of TBI on neuropsychological and behavioural outcomes.

Cognitive measures. At pre-intervention testing, there was a significant between-group difference on the Executive Function composite (see Table 24).

Post-hoc Mann-Whitney *U* tests showed that the TBI-intervention group differed significantly from the Control-intervention group on this composite score, $U < .001$, $p = .014$, $r = -.82$, with a large effect size. Although the TBI group also performed more poorly than the Play and the Test-only groups on the Executive Function composite, these differences were not significant, $U = 3.00$, $p = .10$, $r = -.51$; $U = 1.00$, $p = .06$, $r = -.63$, respectively. As can be seen, however, there were large effect sizes associated with these comparisons.

Although the between-group differences for the other four composite measures were not statistically significant, the results were in the expected direction, with the TBI group performing more poorly than the control groups. There were small to moderate effect sizes associated with these comparisons.

For between-group differences for the subtests making up these composites, see Appendix CC.

Table 24

Between-group Analyses for Neuropsychological Composites: TBI-intervention vs. Control Groups (N = 16)

	Groups												Test statistics		
	TBI intervention (n = 4)			Control intervention (n = 4)			Play control (n = 4)			Test-only control (n = 4)					
Composite variable	*M (SD)*	Range	Mean rank	*M (SD)*	Range	Mean rank	*M (SD)*	Range	Mean rank	*M (SD)*	Range	Mean rank	*F* / *H*	*p*	*r*
Basic attention (α = 0.773)	-0.19 (0.95)	-1.05- -1.12	6.75	-0.19 (0.37)	-0.09-0.72	10.00	0.20 (0.76)	-0.60-1.05	9.25	-0.20 (0.72)	-1.27-0.27	8.00	1.08[b]	.810	.22
Higher-order attention (α = 0.817)	-0.54 (0.79)[a]	-1.08-0.36	4.67	-0.65 (0.52)	0.18-1.10	11.00	0.22 (0.81)	-0.67-1.23	9.00	-0.24 (0.58)	-0.98-0.42	6.50	0.96[b]	.260	.16
Verbal memory (α = 0.798)	-0.61 (1.62)	1.83-1.69	5.50	0.36 (0.61)	0.31-1.03	10.38	-0.06 (0.44)	-0.48-0.52	7.63	0.32 (0.39)	0.02-0.86	10.50	0.96	.440	.44
Visual memory (α = 0.923)	-0.53 (1.19)	-1.85-0.64	6.38	0.37 (0.68)	-0.51-1.04	10.50	-0.04 (1.14)	-1.18-1.44	7.63	0.20 (0.75)	-0.55-1.11	9.50	0.66	.600	.38
Executive functions (α = 0.676)	- 0.79 (0.67)	-1.54-0.01	3.50	0.62 (0.45)	0.15-1.19	12.25	0.09 (0.59)	-0.34-0.96	7.50	0.11 (0.25)[a]	-0.18-0.27	9.00	7.86[b]	.029*	.47

Note. [a]*n = 3* in these cases. [b]Kruskal Wallis *H*. Values presented are *z*-scores (for M, SD, range). The *r* value presented here is an estimate of effect size.

* $p < 0.05$.

Behavioural measures. Between-group differences were significant for the Emotional Control and Plan / Organization indices of the BRIEF (see Table 25).

Post-hoc Mann-Whitney *U* tests show that the significant between-group differences for the Emotional Control Index might be accounted for by significant differences between the TBI-intervention group and both the Play, $U < 0.01$, $p = .014$, $r = -.84$, and the Test-only groups, $U < 0.01$, $p = .014$, $r = -.84$, with the TBI-intervention group scoring significantly higher (and hence reportedly showing significantly poorer functioning in this domain) than the control groups. There were large effect sizes associated with these comparisons. A post-hoc Tukey's test showed that, on the Plan / Organization index, there were significant differences between the TBI-intervention group and the Play group ($p = .01$), with the TBI-intervention group reportedly showing poorer functioning in this domain.

There were no other significant between-group differences for the remainder of the BRIEF parent and teacher reports (see Table 26), nor for the CBCL parent and teacher reports (see Tables 27 and 28). The trends in the results were, however, in the expected direction, with the TBI-intervention group scoring higher (and hence reportedly functioning more poorly) than the control groups. Effect sizes ranged from moderate to large for the BRIEF parent report, and from small to moderate for the other behavioural measures.

Pre- and Post-intervention Within-group Analyses

There were no significant within-group differences in performance from pre- to post-intervention (see Appendix DD).

Table 25
Between-group Comparisons: Pre-intervention BRIEF Indices (Parent Report) (N = 16)

	Group								Test statistics		
	TBI-intervention (n = 4)		Control-intervention (n = 4)		Play (n = 4)		Test-only (n = 4)				
Brief index	*M* (*SD*)	Range	*M* (*SD*)	Range	*M* (*SD*)	Range	*M* (*SD*)	Range	*F*/*H*	*p*	*r*
Inhibit	66.25 (17.27)	41-80	59.00 (12.52)	46-75	51.25 (12.29)	37-65	48.50 (9.75)	40-62	1.47	.270	.52
Shift	61.25 (11.33)	50-71	56.60 (11.50)	45-71	47.50 (10.97)	36-60	45.75 (10.81)	36-57	1.75	.210	.55
Emotional control	68.25 (6.50)	65-78	61.75 (11.09)	53-78	45.25 (12.31)	36-62	53.75 (7.18)	45-62	8.76[a]	.020*	.54
BRI	67.75 (10.56)	53-78	61.00 (13.29)	48-79	48.25 (9.57)	35-57	49.50 (9.47)	39-58	3.00	.070	.65
Initiate	62.75 (10.34)	55-78	54.75 (8.02)	47-66	54.00 (13.35)	35-66	50.50 (16.68)	39-75	0.68	.580	.38
Working memory	69.75 (5.74)	65-78	53.00 (10.86)	40-65	47.00 (10.17)	36-60	50.75 (18.96)	36-78	2.64	.100	.63
Plan/organization	72.25 (7.68)	67-84	51.00 (10.80)	37-63	44.75 (12.07)	33-61	51.25 (11.30)	38-65	5.35	.010*	.76
Org. of materials	54.75 (10.87)	39-64	52.00 (10.99)	36-61	50.25 (12.58)	33-61	39.75 (7.27)	33-49	1.53	.260	.53
Monitor	70.50 (1.73)	69-72	53.25 (10.60)	47-69	43.75 (13.53)	28-56	49.50 (17.66)	34-72	6.36[a]	.090	.34
MI	70.00 (7.44)	62-80	53.25 (11.15)	41-68	47.25 (13.30)	30-62	55.00 (22.06)	34-76	4.84[a]	.190	.22
GEC	70.75 (8.50)	59-79	56.75 (12.37)	46-74	47.25 (12.26)	30-59	48.75 (14.20)	37-67	3.21	.060	.67

Note. For each comparison presented here, degrees of freedom = (3, 12). BRI = Behaviour Regulation Index; MI = Metacognition Index; GEC Global Executive Composite; Org = Organization. The *r* value presented here is an estimate of effect size. [a]Kruskal-Wallis *H*; for Emotional Control, mean rank of the TBI-intervention group = 13.63, of the Control-intervention group = 9.63, of the Play group = 4.38, and of the Test-only group = 6.38; for Monitor, mean rank of the TBI-intervention group = 3.50, of the Control-intervention group = 7.50, of the Play group = 5.63, and of the Test-only group = 7.38; for MI, mean rank of the TBI-intervention group = 12.63, of the Control-intervention group = 7.38, of the Play group = 5.50, and of the Test-only group = 8.50
* $p < 0.05$.

Table 26
Between-group Comparisons: Pre-intervention BRIEF Indices (Teacher Report) (N = 16)

	Group												Test statistics		
	TBI intervention (n = 3)[a]			Control intervention (n = 4)			Play control (n = 4)			Test-only control (n = 4)					
Brief index	*M* (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*H*	*p*	*r*
Inhibit	61.67 (22.50)	44-87	9.17	55.00 (18.07)	44-82	7.63	54.75 (16.92)	44-80	7.75	57.00 (15.71)	44-78	7.75	0.26	.970	.48
Shift	66.67 (17.04)	47-77	10.67	59.25 (16.36)	44-82	9.00	52.75 (13.82)	42-73	6.25	52.00 (8.87)	43-63	6.75	2.21	.560	.04
Emotional control	62.67 (16.62)	45-78	9.83	58.50 (22.13)	44-91	7.25	58.25 (23.20)	45-93	8.63	51.25 (7.85)	44-59	6.75	1.03	.820	.23
BRI	63.00 (20.66)	44-85	9.00	58.00 (20.94)	43-89	8.38	56.00 (20.69)	45-87	7.75	54.00 (12.28)	43-69	7.13	0.35	.960	.44
Initiate	66.00 (15.88)	48-78	11.33	51.00 (12.25)	42-69	6.50	48.75 (7.14)	41-57	6.25	57.75 (18.55)	42-84	8.75	2.88	.440	.04
Working memory	68.67 (22.59)	45-90	10.67	53.75 (18.21)	43-81	6.75	52.75 (13.91)	38-69	6.50	62.25 (16.17)	44-83	8.75	1.96	.620	.08
Plan/organization	67.33 (19.14)	47-85	10.17	62.25 (21.09)	43-81	7.50	50.75 (9.11)	38-59	6.13	60.50 (16.11)	47-83	8.75	1.58	.700	.13
Org. of materials	65.33 (21.46)	51-90	11.17	50.75 (9.00)	44-64	7.13	51.50 (12.29)	42-69	6.50	57.00 (18.39)	44-83	8.00	2.15	.580	.05
Monitor	69.67 (20.21)	48-88	11.67	51.75 (13.25)	41-71	6.13	55.25 (15.71)	43-78	7.75	55.25 (11.93)	46-71	7.38	2.84	.450	.03
MI	68.67 (21.03)	47-89	10.83	54.75 (15.09)	44-76	6.88	52.25 (11.59)	40-67	6.50	59.25 (16.98)	44-83	8.50	1.98	.610	.07
GEC	68.67 (22.03)	46-90	10.33	56.25 (18.32)	43-83	7.63	54.00 (15.23)	42-76	6.50	57.75 (16.24)	43-80	8.13	1.31	.760	.18

Note. [a] Missing data; the BRIEF teacher report form was not returned for a TBI-intervention participant. For each comparison presented here, degrees of freedom = (3, 11). BRI = Behaviour Regulation Index; MI = Metacognition Index; GEC Global Executive Composite; Org = Organization. The *r* value presented here is an estimate of effect size.

Table 27
Between-group Comparisons: Pre-intervention CBCL Syndrome Profiles (Parent Report) (N = 16)

CBCL syndrome profile	Group												Test statistics		
	TBI intervention (n = 4)			Control intervention (n = 4)			Play control (n = 4)			Test-only control (n = 3)[a]					
	M (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*H*	*p*	*r*
Anxious / depressed	66.25 (14.20)	53-86	11.75	58.00 (10.17)	50-72	8.13	53.00 (6.00)	50-62	4.88	53.00 (3.46)	51-57	7.00	5.05	.170	.24
Withdrawn / depressed	69.75 (12.71)	56-82	11.50	59.00 (8.25)	50-66	7.63	52.00 (2.31)	50-54	4.25	62.00 (10.58)	50-70	8.83	5.57	.130	.28
Somatic complaints	65.25 (6.19)	57-70	10.63	58.75 (6.70)	50-64	6.63	59.00 (6.16)	50-64	6.25	61.33 (10.26)	50-70	8.67	5.57	.500	.00
Internalizing problems	68.50 (9.33)	58-80	11.50	56.25 (16.40)	33-70	7.50	48.75 (11.24)	34-61	4.75	58.33 (13.32)	43-67	8.33	2.57	.210	.21
Rule-breaking behaviour	67.00 (11.49)	50-74	11.13	54.25 (6.65)	50-64	5.88	59.25 (6.40)	50-64	8.13	54.33 (4.93)	51-60	6.50	3.27	.380	.08
Aggressive behaviour	71.25 (13.07)	57-87	11.88	61.00 (18.71)	50-89	7.25	57.50 (6.76)	50-65	7.88	51.33 (1.16)	50-52	4.00	5.61	.130	.28
Externalizing problems	68.75 (11.03)	54-79	12.00	52.75 (17.35)	34-76	6.13	55.75 (10.91)	40-64	8.00	50.67 (0.58)	50-51	5.17	5.15	.160	.25

Note. For each comparison presented here, degrees of freedom = (3, 11). [a] Missing data; the pre-intervention CBCL parent report form was only returned post-intervention for a test-only participant. The CBCL parent data for this participant was therefore excluded from this analysis. The *r* value presented here is an estimate of effect size

Table 28
Between-group Comparisons: Pre-intervention CBCL Syndrome Profiles (Teacher Report) (N = 16)

CBCL syndrome profile	Group												Test statistics		
	TBI intervention (n = 3)[a]			Control intervention (n = 4)			Play control (n = 4)			Test-only control (n = 4)					
	M (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*M* (*SD*)	Range	Mean rank	*H*	*p*	*r*
Anxious / depressed	63.67 (7.77)	55-70	12.33	56.00 (10.10)	50-71	7.75	54.75 (5.85)	50-62	7.50	50.75 (0.96)	50-52	5.50	4.40	.230	.19
Withdrawn depressed	63.67 (12.34)	50-74	11.17	53.50 (7.00)	50-64	6.63	55.75 (5.62)	50-63	8.75	53.25 (6.50)	50-63	6.25	3.07	.410	.06
Somatic complaints	63.33 (11.55)	50-70	10.83	50.00 (0.00)	50-50	5.50	59.50 (12.37)	50-76	9.50	52.00 (4.00)	50-58	6.88	4.49	.210	.20
Internalizing problems	65.33 (12.50)	51-74	12.33	48.00 (14.63)	38-69	6.00	54.50 (12.61)	38-68	8.63	46.25 (7.14)	38-55	6.13	4.48	.220	.19
Rule-breaking behaviour	62.67 (21.94)	50-88	8.67	58.50 (17.00)	50-84	7.63	55.00 (10.00)	50-70	7.38	53.75 (5.68)	50-62	8.50	0.32	.970	.48
Aggressive behaviour	61.67 (10.41)	50-70	9.67	59.25 (15.35)	50-82	8.00	57.00 (13.34)	50-77	7.50	53.50 (4.12)	50-58	7.25	0.64	.910	.33
Externalizing problems	60.67 (18.61)	41-78	9.67	54.75 (18.91)	41-82	8.38	51.25 (16.17)	41-75	6.75	49.50 (8.85)	41-59	7.63	0.82	.870	.28

Note. For each comparison presented here, degrees of freedom = (3, 11). [a] Missing data; the CBCL teacher report form was not returned for a TBI-intervention participant. The CBCL teacher data for this participant was therefore excluded from this analysis.The *r* value presented here is an estimate of effect size.

Individual Comparisons: RCI Analyses

Tables 29 to 32 present a summary of the results from the RCI analyses for 7-, 8-, 9- and 10-year olds, respectively. The tables provide a summary of only the improvements in the test scores for both the cognitive and behavioural domains for individual participants in the TBI-intervention and control groups.

Table 29

RCI Analyses: Cognitive and Behavioural Domains: 7-year-olds (N = 4)

Domain	Subtest	Group			
		TBI-intervention	Control-intervention	Play	Test-only
Cognitive measures					
Attention and concentration[a]	Sky Search Timing		Δ Δ	Δ	
	Sky Search Attention Score			Δ	
	Opposite Worlds				Δ
	Numbers Forward		Δ		
Memory	Word List Delayed			Δ Δ Δ	
	Dot Locations Delayed		Δ		
Executive functions	Numbers Backward	Δ			
	Inhibition-Inhibition	Δ Δ Δ	Δ Δ Δ	Δ Δ Δ	
	Inhibition-Switching	Δ Δ Δ	Δ Δ Δ	Δ	Δ
	Inhibition-Inhibition CT	Δ Δ	Δ Δ		Δ
	Inhibition-Switching CT	Δ Δ	Δ		Δ
	Inhibition Errors	Δ Δ Δ	Δ	Δ	Δ
	Design Fluency			Δ	
Behavioural measures					
BRIEF parent report	Shift			Δ Δ Δ	
	Emotional control	Δ			
	BRI		Δ		
	Initiate			Δ	
	Plan / organize	Δ	Δ		
	Monitor			Δ	
BRIEF teacher report	Shift		Δ Δ Δ		
	Emotional control	Δ Δ			
	BRI		Δ		
	Initiate		Δ		
	Working memory	Δ			
	Plan / organize	Δ	Δ Δ Δ		
	MI	Δ	Δ		
	GEC	Δ	Δ		
CBCL parent report	Externalizing behaviours				Δ Δ Δ
CBCL teacher report	Internalizing behaviours				Δ
	Externalizing behaviours	Δ			

Note. Δ = a positive change of at least 1 standard deviation with a confidence interval of 68.26%; Δ Δ = a positive change of at least 1.96 standard deviations with a confidence interval of 95%; Δ Δ Δ = a positive change of at least 2.58 standard deviations with a confidence interval of 99%. [a]Test-retest reliability coefficients were only available for the following TEA-Ch subtests included in the test battery: Sky Search Time per Target, Sky Search Attention Score, Score, Sky Search DT, and Opposite Worlds. CT = Completion time; BRI = Behaviour Regulation Index; MI = Metacognition Index; GEC Global Executive Composite.

Table 30

RCI Analyses: Cognitive Domains: 8-year-olds (N = 4)

		Group			
Domain	Subtest	TBI-intervention	Control-intervention	Play	Test-only
Cognitive measures[a]					
Attention and concentration[b]	Sky Search Timing		Δ Δ Δ		Δ Δ Δ
	Sky Search Attention Score		Δ Δ		Δ Δ Δ
	Opposite worlds				Δ
Memory	Word list delayed	Δ			
Executive functions	Numbers backward		Δ		
	Inhibition-Inhibition		Δ		
	Inhibition-Switching			Δ	Δ
	Inhibition-Inhibition CT		Δ		
	Inhibition-Switching CT				Δ
	Inhibition Errors		Δ		
	Design fluency	Δ	Δ		

Note. Δ = a positive change of at least 1 standard deviation with a confidence interval of 68.26%; Δ Δ = a positive change of at least 1.96 standard deviations with a confidence interval of 95%; Δ Δ Δ = a positive change of at least 2.58 standard deviations with a confidence interval of 99%. [a]Results for only the cognitive measures are presented here because the BRIEF and CBCL parent report forms were not completed post-intervention, and the BRIEF and CBCL teacher report forms were not returned both pre- and post-intervention, for the 8-year-old TBI-intervention participant. [b]Test-retest reliability coefficients were only available for the following TEA-Ch subtests included in the test battery: Sky Search Time per Target, Sky Search Attention Score, Score, Sky Search DT, and Opposite Worlds.

Table 31

RCI Analyses: Cognitive and Behavioural Domains: 9-year-olds (N = 4)

		Group			
Domain	Subtest	TBI-intervention	Control-intervention	Play	Test-only
Cognitive measures					
Attention and concentration[a]	Sky Search Timing	Δ	Δ Δ Δ		Δ Δ Δ
	Sky Search Attention Score		Δ Δ Δ		Δ Δ Δ
Memory	Word List Delayed			Δ Δ	
	Dot Locations Delayed			Δ	
Executive functions	Numbers Backward		Δ Δ Δ		
	Inhibition-Inhibition			Δ Δ Δ	
	Inhibition-Inhibition CT	Δ		Δ	
	Inhibition-Switching CT	Δ Δ Δ			Δ
Behavioural measures					
BRIEF parent report	Inhibit	Δ Δ Δ			
	Shift	Δ Δ Δ			
	Emotional control	Δ Δ Δ			
	BRI	Δ Δ Δ			
	Initiate	Δ Δ Δ	Δ Δ		
	Working memory	Δ Δ Δ			
	Plan / organize	Δ Δ Δ			Δ
	Organization of materials	Δ Δ			
	Monitor	Δ Δ Δ			
	MI	Δ Δ Δ			
	GEC	Δ Δ Δ			
BRIEF teacher report	Shift	Δ	Δ		
	Emotional control	Δ Δ	Δ Δ		
	BRI	Δ	Δ Δ		
	Initiate			Δ	
	Working memory	Δ			Δ Δ
	Organization of materials	Δ Δ Δ			
	Monitor	Δ Δ		Δ Δ	
	MI	Δ		Δ	
	GEC	Δ			
CBCL parent report	Internalizing behaviours	Δ Δ Δ			Δ Δ Δ
	Externalizing behaviours	Δ Δ Δ		Δ	Δ Δ Δ
CBCL teacher report	Externalizing behaviours		Δ Δ		

Note. Δ = a positive change of at least 1 standard deviation with a confidence interval of 68.26%; Δ Δ = a positive change of at least 1.96 standard deviations with a confidence interval of 95%; Δ Δ Δ = a positive change of at least 2.58 standard deviations with a confidence interval of 99%. [a]Test-retest reliability coefficients were only available for the following TEA-Ch subtests included in the test battery: Sky Search Time per Target, Sky Search Attention Score, Score, Sky Search DT, and Opposite Worlds.CT = Completion time; BRI = Behaviour Regulation Index; MI = Metacognition Index; GEC Global Executive Composite.

Table 32

RCI Analyses: Cognitive and Behavioural Domains: 10-year-olds (N = 4)

		Group			
Domain	Subtest	TBI-intervention	Control-intervention	Play	Test-only
Cognitive measures					
Attention and concentration[a]	Sky Search Timing		Δ Δ		Δ Δ Δ
	Sky Search Attention Score		Δ Δ Δ		Δ Δ Δ
	Opposite Worlds			Δ Δ Δ	Δ Δ
Memory	Word List Delayed		Δ Δ		Δ Δ Δ
	Dot Locations Delayed				Δ Δ Δ
Executive functions	Numbers Backward			Δ	
	Inhibition-Inhibition				Δ Δ Δ
	Inhibition-Switching		Δ Δ		Δ
	Inhibition-Inhibition CT	Δ			Δ
	Inhibition-Switching CT				Δ
	Inhibition Errors		Δ		
	Design Fluency	Δ		Δ	
Behavioural measures					
BRIEF parent report	Inhibit				Δ Δ
	Shift		Δ		Δ Δ
	Emotional control				Δ Δ
	BRI				Δ Δ Δ
	Working memory		Δ Δ		Δ Δ
	Plan / organize	Δ			Δ
	Org. of materials			Δ	Δ
	Monitor				Δ Δ Δ
	MI				Δ Δ Δ
	GEC				Δ Δ Δ
BRIEF teacher report	Inhibit				Δ
	Plan / organize		Δ	Δ	
	Org. of materials			Δ	
	MI			Δ	
CBCL parent report	Internalizing behaviours			Δ Δ Δ	MD
	Externalizing behaviours			Δ Δ	MD
CBCL teacher report	Externalizing behaviours				Δ

Note. Δ = a positive change of at least 1 standard deviation with a confidence interval of 68.26%; Δ Δ = a positive change of at least 1.96 standard deviations with a confidence interval of 95%; Δ Δ Δ = a positive change of at least 2.58 standard deviations with a confidence interval of 99%. [a]Test-retest reliability coefficients were only available for the following TEA-Ch subtests included in the test battery: Sky Search Time per Target, Sky Search Attention Score, Score, Sky Search DT, and Opposite Worlds.MD = Missing data; CT = Completion time; BRI = Behaviour Regulation Index; MI = Metacognition Index; GEC Global Executive Composite.

RCI analyses: cognitive results. Regarding the 7-year-old TBI-intervention participant, there was only one domain of functioning (inhibitory control) in which she showed significant change from pre- to post-intervention testing but in which the 7-year-old Play and Test-only control participants did not. As Table 29 shows, this participant showed reliable change on the NEPSY-II Inhibition-Switching, Inhibition-Inhibition Completion Time, Inhibition-Switching Completion Time, and Inhibition Errors subtests. Of note here, however, is that the 7-year-old Control-intervention participant also showed significant changes from pre- to post-intervention testing on the NEPSY-II Inhibition-Inhibition Completion Time and Inhibition-Switching outcome variables.

Regarding the 8-year-old TBI-intervention participant, there were no domains of functioning on which he showed significant change from pre-to post-intervention testing but in which the 8-year-old control participants did not (see Table 30).

Regarding the 9-year-old TBI-intervention participant, there was only one subtest, NEPSY-II Inhibition-Switching Completion Time, on which he showed significant change from pre- to post-intervention testing, but on which the 9-year old control participants did not (see Table 31).

Regarding the 10-year-old TBI-intervention participant, there were no domains of functioning on which he showed significant change from pre-to post-intervention testing but in which the 10-year-old control participants did not (see Table 32).

Also of interest in the data presented in Tables 30, 31, and 32 is that there were two TEA-Ch outcome variables, Sky Search Time per Target and Sky Search Attention Score, on which the 8-, 9-, and 10-year-old Test-only and Control-intervention participants showed reliable change but on which the TBI-intervention and Play participants did not. This pattern of data suggests the presence of practice/carryover effects on those subtests, but clearly it is in need of replication in light of the fact that the pattern was not present in the Play participants.

RCI analyses: behavioural results. Regarding the 7-year-old TBI-intervention participant, there was only one BRIEF Index, Emotional Control, on which she reportedly showed significant change from pre- to post-intervention testing, but on which the 7-year old control participants reportedly did not (see Table 29).

Regarding the 8-year-old TBI intervention participant, the behavioural results could not be analysed using the RCI because the BRIEF and CBCL parent report forms were not completed post-intervention, and the BRIEF and CBCL teacher report forms were not returned both pre- and post-intervention.

Regarding the 9-year-old TBI-intervention participant, there were several BRIEF indices on which he reportedly showed significant change from pre- to post-intervention testing, but on which the 9-year old control participants reportedly did not. As Table 31 shows, the BRIEF parent report suggested that this participant showed reliable change on all indices of the measure; these changes were not matched by the 9-year-old Play and Test-only participants. The BRIEF Teacher report also suggested significant change for this participant, but this change was limited to the Organization of Materials and the Emotional Control and Monitor indices.

There was a similar trend for the CBCL (parent report) of the 9-year-old TBI-intervention participant, with significant change in both Internalizing and Externalizing behaviour syndrome scales. However, the 9-year-old Test-only participant also reportedly showed similar gains in these syndrome scales.

Of note here is that the parents of the 9-year-old Control-intervention participant also reported significant change on the Initiate index of the BRIEF, and that that child's teacher reported significant change on the Emotional Control and BRI indices of the measure. These reported changes were not matched by similar changes in the control participants. The same child's teacher also reported significant positive changes from pre- to post-testing sessions on the Externalizing behaviours syndrome scales of the CBCL (see Table 31).

Regarding the 10-year-old TBI-intervention participant, there were no BRIEF or CBCL indices on which parents or teachers reported significant change from pre-to post-intervention testing but in which the parents or teachers of the 10-year-old control participants did not report such change (see Table 32).

According to his parent, the 10-year-old Test-only control participant showed significant change on all of the BRIEF indices, except Plan / Organize and Organization of Materials. These reported changes were not matched by similar reported changes in the TBI-intervention and other control participants, except in the case of Working Memory for the Control-intervention participant.

Case Studies

I now present two case studies, both for participants in the TBI-intervention group. The first focuses on a 7-year-old female, CB. She appeared to show some improvement from pre- to post-intervention in performance on the NEPSY-II Inhibition subtests, as described in the RCI Analyses section above. The second case study focuses on an 8-year-old male, JL. He did not show any improved performance from pre- to post-intervention on the cognitive measures.

CB and JL were of a similar age at the time of their injuries. In both cases, the injuries were classified as severe. They were both from low-SES backgrounds, and both attended mainstream schools prior to their accidents. In both cases, there were no reports of diagnosed, or possible but undiagnosed, premorbid problems. Both participants had no prior access to cognitive rehabilitation. Hence, it is of interest to explore possible reasons for their disparate outcomes post-intervention.

Case study 1: CB.

Medical history.

Injury-related details. I obtained this information from CB's parents and from her RXH medical folder. CB sustained a TBI when she was 6 years and 6 months old. She was a backseat (unrestrained) passenger in an MVA. Her initial GCS score was 6T / 15, which indicates a severe TBI. She was admitted to RXH. Some of the main concerns at the time, as noted in an occupational therapist's report, were "inconsistent concentration, emotional lability and the ability to return to school".

CB's CT scan showed mild swelling, corpus callosum contusions, and a small extradural haematoma anterior to the left temporal tip. In addition, the neurosurgeon involved in CB's care also reported diffuse axonal injury. CB also sustained facial lacerations.

Brain oxygenation monitoring. I obtained this information from the Head of the Division of Pediatric Neurosurgery at RXH. The duration of CB's monitoring was 74 hours. Her highest ICP reading was 16, and her lowest CPP reading 45. She had four episodes of CPP < 40. Her lowest $PbtO_2$ reading was 26.8. She did not experience any episodes of $PbtO_2$ < 20. In summary, there were no major episodes of concern during her monitoring period.

Developmental history. CB's parents provided this information during their screening interview for this study. I gleaned additional information from an occupational therapist's report. There were no noted complications during the pre- or perinatal periods. CB was 3.7 kg at birth. Her developmental milestones were reported to be normal. CB began to walk unassisted at approximately 11-12 months of age, and said her first word at approximately 7-8 months of age. She was able to write her own name by 5 years of age. CB's parents reported no notable concerns about their daughter and her development or behaviour prior to the accident.

However, CB's parents did report behavioural problems following the accident. Specifically, they reported that she showed mood swings, that she raised her voice at her two younger siblings more often than before, and with little provocation, that she cried more

easily than before, and that she was more aggressive than before the accident. CB had also acquired spectacles since the accident.

Some of the behavioural and emotional problems noted by CB's parents above were also described in an occupational therapist's report. In addition, CB was described by that therapist as 'distractible', which led to poor task completion.

Academic history. CB sustained her TBI when she was in Grade 1, halfway through the school year. She was unable to complete two out of the four examinations at the end of that year, but did, however, proceed to Grade 2. CB changed schools at this stage due to her parents moving residences. CB was more than halfway though Grade 2 at her new school at the time of the study. CB's class teacher of 8 months at that time described CB's general ability and her abilities in writing, mathematics, art, and sports, as below average and her reading and spelling abilities as average. She also reported that CB was 'insecure', that she lacked confidence, and that she was easily 'distractible'. CB attended sessions with an educational psychologist during the course of her Grade 2 year. Reports from that individual were not available at the time of this study.

Current social status. CB lived with her parents and two younger sisters, who were 5 and 2 years of age at the time, in a low-SES suburb in the Cape Town area. Both her parents were unemployed at the time of the study. They had recently moved residence as a result of financial difficulties. CB's parents had also separated for a period of time as a result of these difficulties. The family received a state grant.

Assessment results. CB was 7 years and 7 months at the time of her pre-intervention assessment. It had been 1 year and 1 month since she sustained her TBI.

Table 33
General Intellectual Functioning: WASI Scores for CB and her Controls (N = 4)

	Participants			
Measure	CB	Control-intervention	Play	Test-only
Vocabulary[a]	36	50	45	51
Similarities[a]	31	60	57	57
VIQ[b]	76	108	101	106
Block Design[a]	39	38	39	39
Matrix Reasoning[a]	41	37	34	43
PIQ[b]	85	81	79	86
FSIQ[b]	78	93	88	96

Note. [a]*T*-scores are presented. [b] IQ index scores are presented. WASI = Wechsler Abbreviated Scale of Intelligence.

General intellectual functioning. CB's FSIQ was lower than that of her control counterparts (see Table 33). This disparity can be traced, mainly, to her relatively low VIQ. CB scored poorly on both verbal subtests, but she was especially weak, compared to controls, on the Similarities subtest. Her results on the Performance subtests were more comparable to those of her control counterparts.

Attention / concentration. CB tended to perform more poorly than the matched controls on most tests of attention / concentration at both pre- and post-intervention assessment (see Table 34). There were, however, exceptions. For instance, her performance was largely consistent with control participants' for the Numbers Forward subtest. Her age-adjusted scaled scores tended to increase or remain relatively consistent from pre- to post-intervention, except for the Sky Search Timing and hence the Sky Search Attention score (selective attention), as the score of the former subtest is used in the calculation of the latter.

Memory. CB tended to perform relatively consistently with the matched controls on tests of verbal and visual memory at both pre- and post-intervention assessment (see Table 34).

Executive functions. Regarding working memory, CB performed more poorly than two of the three matched controls at pre-intervention testing (see Table 34). Her performance was largely consistent with that of the matched controls at post-intervention testing, however, suggesting improvement in this domain over the intervention period.

Regarding inhibitory control, CB tended to perform more poorly than the matched controls on all of the NEPSY-II inhibition subtests at pre-intervention testing. At post-

intervention testing, however, CB tended to perform more consistently with matched control participants on these subtests. Although the control participants showed improvement in their scores on some of the subtests, CB tended to show greater overall gains.

Regarding performance on the NEPSY-II Design Fluency subtest, CB showed no change from pre- to post-intervention testing (see Table 34). She tended to perform more poorly than two of the three matched controls at both pre- and post-intervention testing.

Table 34

Attention, Memory and EF Outcomes for CB and her Controls (N = 4)

		Participants							
		CB		Control-intervention		Play		Test-only	
Domain	Subtest / Battery	T1	T2	T1	T2	T1	T2	T1	T2
Attention and concentration	TEA-Ch								
Selective attention	Sky Search Target	4	9	14	14	8	8	11	14
	Sky Search Timing	8	2	4	8	2	5	7	8
	Sky Search Attention Score	8	3	6	8	2	5	7	8
	Map Mission	3	5	5	9	4	5	4	5
Sustained attention	Score!	4	6	7	11	9	7	6	11
Selective/ divided attention	Sky Search DT	1	4	13	9	4	11	4	9
Attentional control	Opposite Worlds	4	4	12	7	6	5	6	8
Concentration	Numbers Forward	10	11	7	9	10	7	10	11
Memory	CMS								
Verbal memory	Word List Learning	14	8	13	13	12	15	12	13
	Word List Delayed	17	12	14	14	9	16	9	12
Visual memory	Dot Locations Learning	10	14	9	12	10	11	10	10
	Dot Locations Total	11	15	8	11	10	11	9	10
	Dot Locations Delayed	13	13	9	12	11	11	9	11
Executive Functions	CMS								
Working memory	Numbers Backward	7	11	15	10	7	7	11	9
	NEPSY II								
Inhibition	Naming	5	9	11	12	8	11	8	7
	Inhibition	3	11	7	15	7	13	8	7
	Switching	5	12	7	12	10	12	7	10
Inhibition – CT	Naming	4	6	11	13	8	11	8	10
	Inhibition	6	11	8	14	9	11	7	10
	Switching	3	8	10	13	9	8	5	9
Inhibition errors	Total Errors	4	13	8	13	10	14	9	9
Generativity	Design Fluency	5	5	8	5	5	8	6	8

Note. T1 = Time 1, or pre-intervention; T2 = Time 2, or post-intervention; DT = Dual task; CT = Completion time.

Behavioural outcomes: BRIEF. Regarding the parent report form (see Figure 8), CB's scores were comparable to those of the matched controls at pre-intervention testing on a number of indices, including the three major ones: BRI, MI, and GEC. She did, however, score in the clinical range on the Emotional Control, Working Memory, Planning / Organization, and Monitor Indices, unlike her matched controls. CB's scores on the Emotional Control and Planning / Organization indices of the BRIEF parent report form shifted from the clinical to the normal range at post-intervention testing. Scores for matched controls were largely in the normal range on all indices of the BRIEF parent form at pre- and post-intervention testing sessions. In sum, although CB's parents reported some positive change on the BRIEF indices from pre- to post-testing assessments, her parents largely reported poorer behaviour (e.g., less emotional control and poorer planning and organization) for her compared to her controls at both pre- and post-testing sessions.

Regarding the BRIEF teacher report form (see Figure 9), CB reportedly scored more poorly than the Control-intervention and Test-only participants on all of the indices except Inhibit and Organization of Materials at pre-intervention testing, and on the Shift, Initiate, and Monitor indices at post-intervention testing. According to the BRIEF teacher report forms, CB scored more poorly than the Play participant on the Initiate and Planning / Organization indices at pre-intervention testing, and on the Initiate index at post-intervention testing. In sum, although CB's teacher reported some positive change on the BRIEF indices from pre- to post-testing assessments, her teacher largely reported poorer behaviour (e.g., intiating and monitoring behaviour) for her compared to the Control-intervention and Test-only controls at both pre- and post-testing sessions.

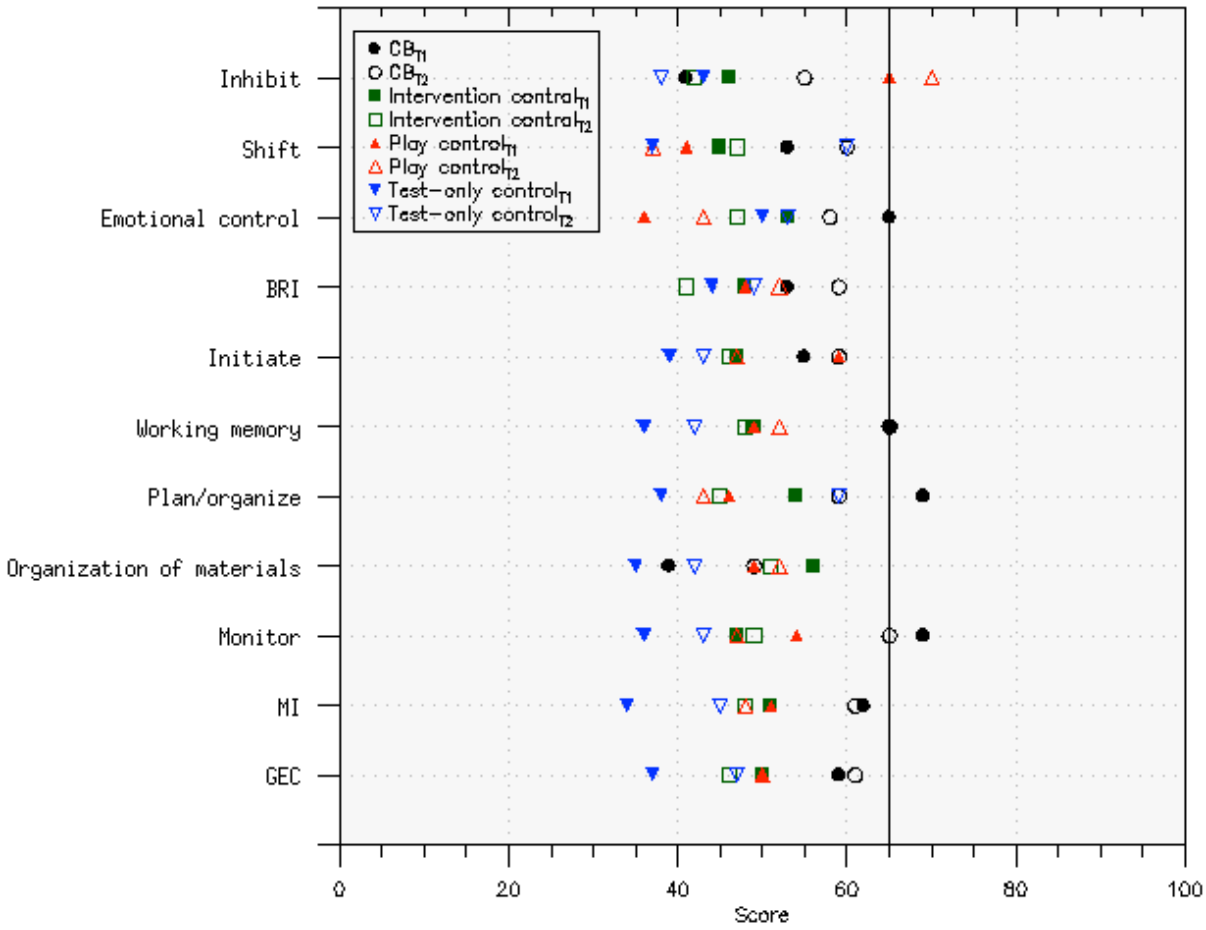

Figure 8. Pre- and post-intervention BRIEF parent report form for CB and matched controls. BRI = Behavioural Regulation Index. MI = Metacognition Index. GEC = Global Executive Composite. Scores > 65 are considered to be in the Clinical range (Gioia, Isquith, Guy, & Kenworthy, 2000). T1 = Time 1, or pre-intervention; T2 = Time 2, or post-intervention.

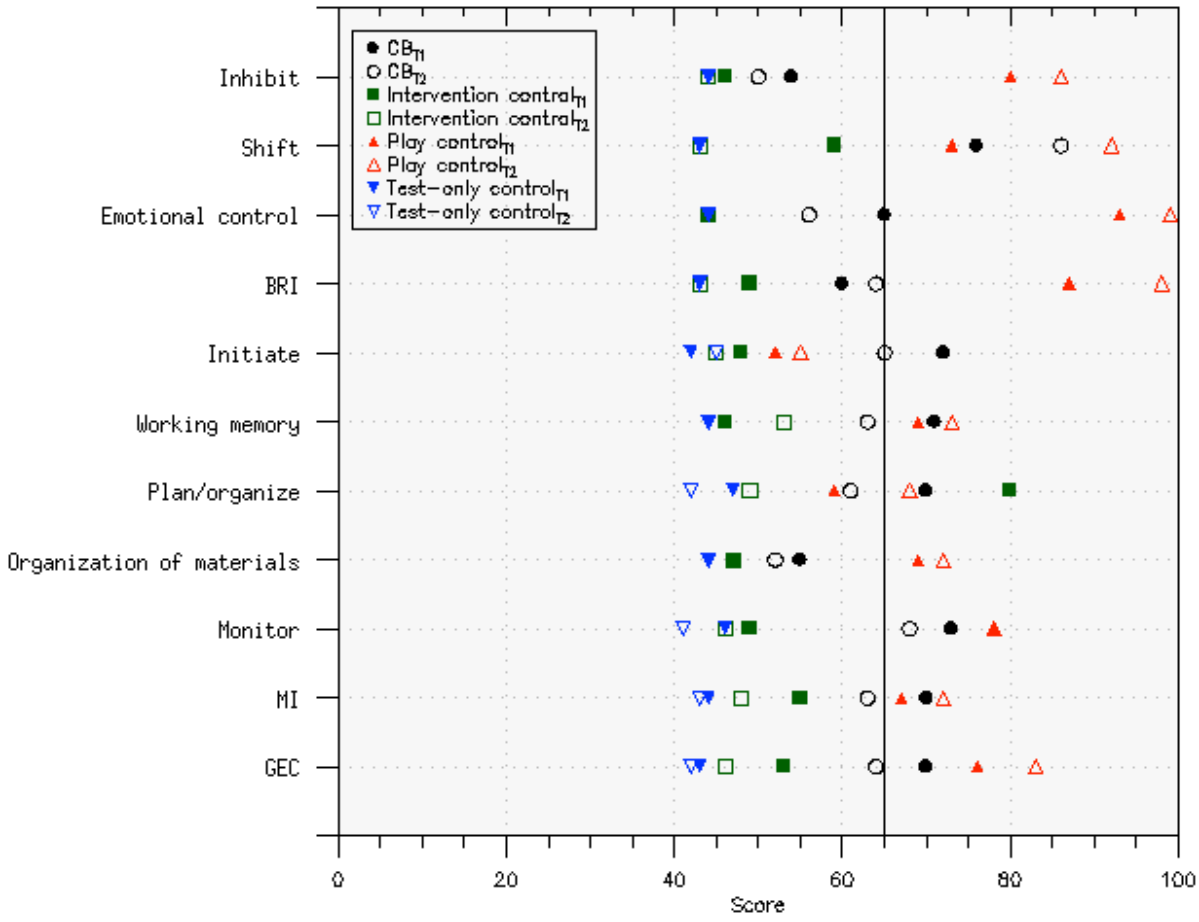

Figure 9. Pre- and post-intervention BRIEF teacher report form for CB and matched controls. BRI = Behavioural Regulation Index. MI = Metacognition Index. GEC = Global Executive Composite. Scores > 65 are considered to be in the Clinical range (Gioia, et al. 2000). T1 = Time 1, or pre-intervention; T2 = Time 2, or post-intervention.

Behavioural outcomes: CBCL. Regarding the CBCL parent report form, CB scored more poorly than the matched controls on the Internalizing and Externalizing Problems subscales at both pre- and post-intervention testing (see Figure 10). The only exception was the comparison with the Play participant at pre-intervention testing. CB's scores on both subscales did not improve post-intervention.

Regarding the CBCL teacher report form (see Figure 11), CB scored more poorly than the Control-intervention and the Test-only participants on both the Internalizing and Externalizing Problems subscales at pre- and post-intervention testing. However, according to the teacher report form, CB's scores on the Externalizing Behaviour syndrome grouping improved after the intervention.

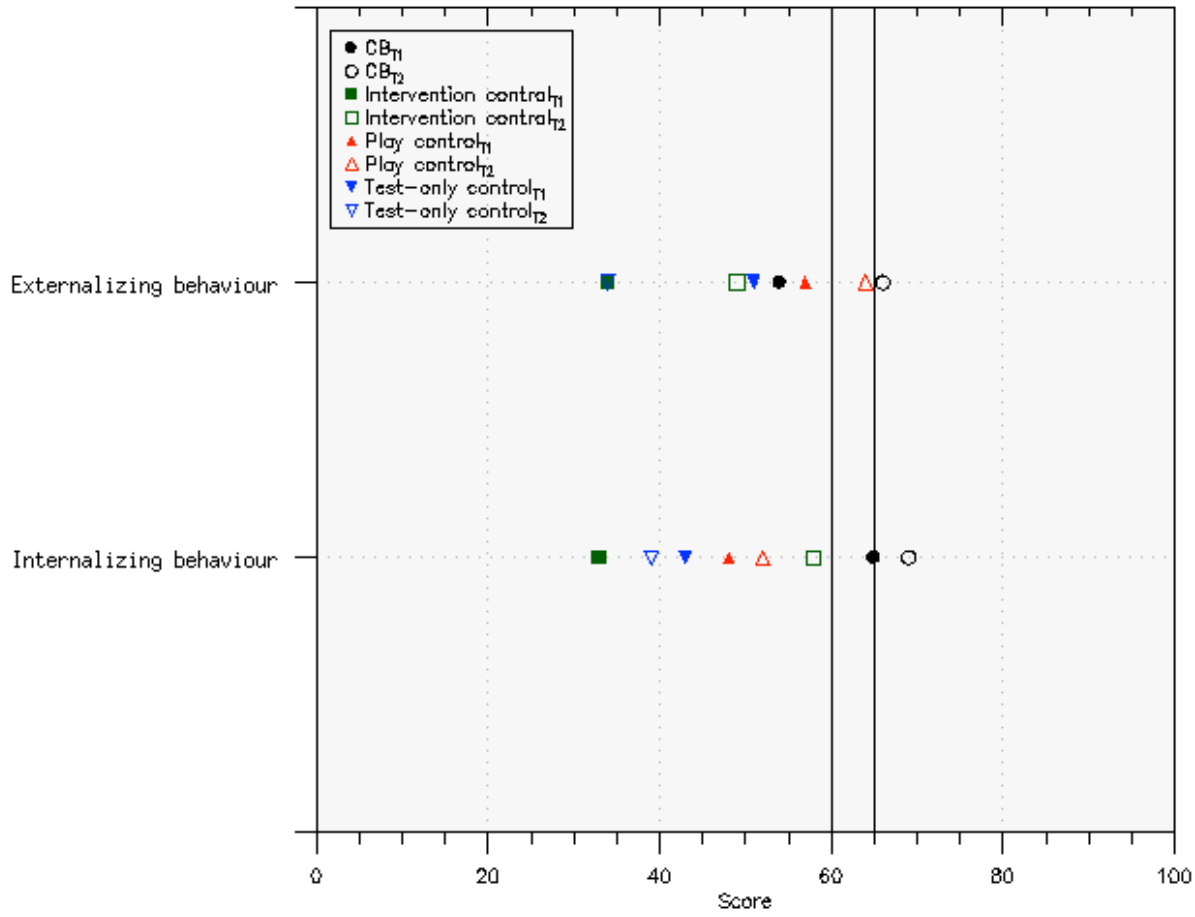

Figure 10. Pre- and post-intervention CBCL parent report form for CB and matched controls. Scores < 60 are considered in the Normal range, scores from 60 to 65 Borderline, and scores > 65 in the Clinical range (Achenbach, 1991).). T1 = Time 1, or pre-intervention; T2 = Time 2, or post-intervention.

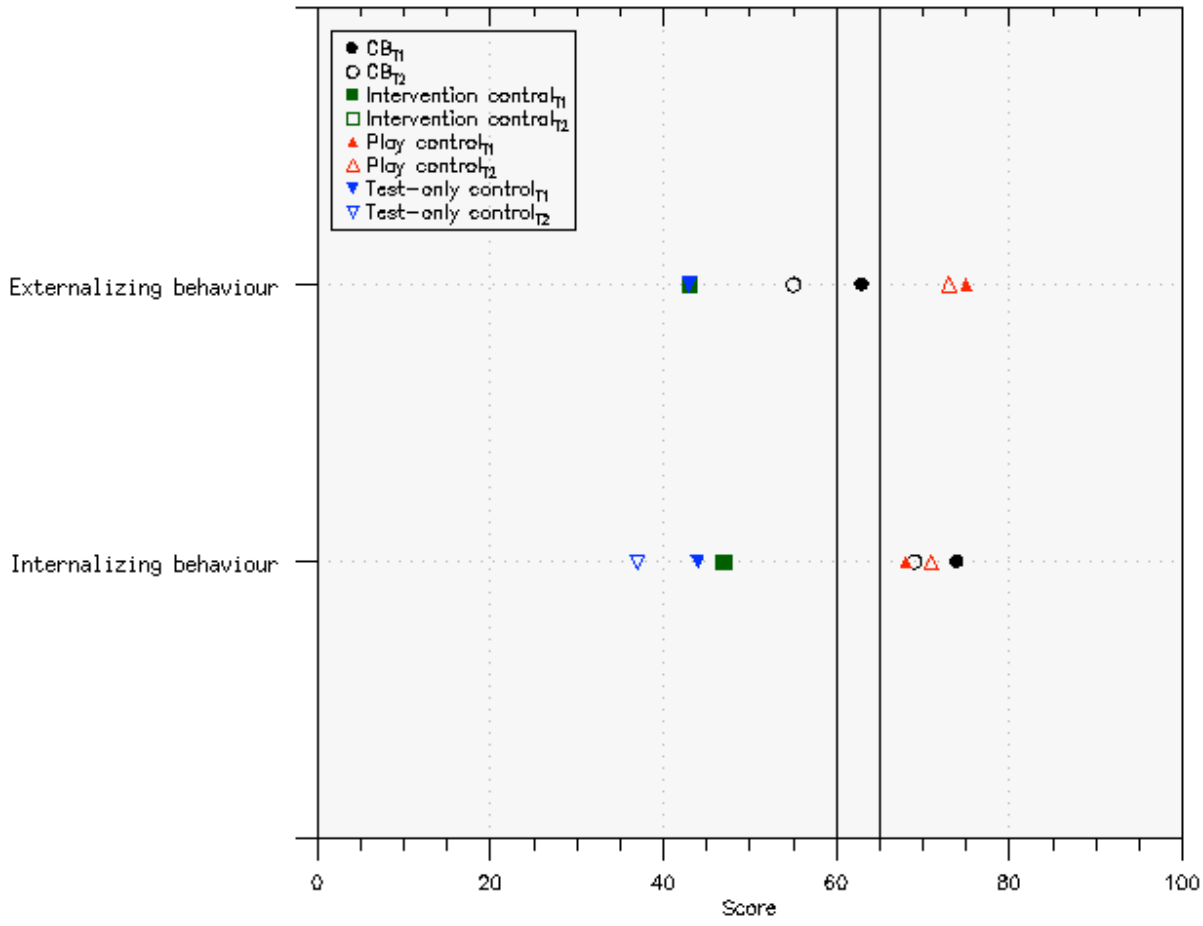

Figure 11. Pre- and post-intervention CBCL teacher report form for CB and matched controls. Scores < 60 are considered in the Normal range, scores from 60 to 65 Borderline, and scores > 65 in the Clinical range (Achenbach, 1991). T1 = Time 1, or pre-intervention; T2 = Time 2, or post-intervention.

Summary and interpretation of findings. At the pre-intervention assessment, CB presented as a shy but cooperative girl, despite documented concerns regarding her behavior (e.g., mood swings, increased aggression, crying more easily than before the accident). This pre-intervention assessment provided a map of possible areas of strengths and weaknesses. Despite previously documented concerns about CB's distractibility, she still performed comparably to her controls on the Numbers Forward (concentration) subtest. She also performed similarly on the visual memory tasks, and even better than her controls on the verbal memory tasks. Of note is that none of the aforementioned tasks were timed, however.

In general, results at the pre-intervention assessment show that most of the tasks that CB struggled with were timed tasks. Speed of processing is also an important element in P. Anderson's (2002) model of EF. It is deemed essential for the efficient operation of the system, and some researchers purport that it is the fundamental problem underlying the

attentional problems in individuals who have sustained TBIs (Catroppa & Anderson, 2005; Meythaler et al., 2001).

On the TEA-Ch Sky Search subtest, which assessed selective attention, CB's performance fluctuated in terms of time and accuracy across the two assessment sessions. It appeared as though CB either focused on finding all or most of the targets at the expense of time, or worked quickly through the tasks at the expense of accuracy. Although she performed better than two of the matched control participants on the timing component of the task at the pre-intervention assessment, these control participants seemed to improve at the post-intervention assessment, rather than fluctuating in performance as CB did.

In addition to speed of information processing, other areas of concern, as reflected by her performance on the test battery, mainly appeared to fall within the domains of attention, and executive functioning. This pattern of data is not surprising, given her etiology and the significant functional overlap across these domains.

Given CB's difficulties on the selective attention task, it is not surprising that she also struggled with the selective/divided attention task. CB also appeared to perform more poorly on the attentional control task. These attentional problems were also reflected in the parent and teacher BRIEF reports.

During the intervention training, CB was cooperative but remained reserved. Despite her quiet and shy nature, she attended the intervention sessions readily and participated actively during them. CB did appear distracted at times during these sesssions, however. Furthermore, she made more omission than commission errors in the visual and auditory attention tasks, which, according to some researchers (e.g., Wassenberg et al., 2004) represents inattentiveness rather than impulsiveness.

There were two major changes at the post-intervention assessment. The first was CB's improvement in performance on the NEPSY-II Inhibition subtests. This improvement could potentially be linked to the intervention training. Note that Control-intervention participants improved similarly. Inhibition forms part of the attentional control domain in P. Anderson's (2002) model of executive functions. It is possible that the regular and repeated attention training sessions and tasks, some of which do require a degree of inhibitory control (e.g., the Card Flip tasks where participants need to press a clicker only in response to particular stimuli and to inhibit responses inbetween) could have helped facilitate this improvement.

However, competing explanations, such as practice effects, cannot be ruled out. First, although the RCI analyses were significant largely for the intervention participants, there were some gains for the Test-only participant. These gains were, however, small relative to

CB's and it was not in the same domains (i.e. they were not in the domain of inhibition) . Second, CB's change in performance could be a function of her becoming more accustomed to the test-taking environment and materials (i.e., overcoming, to a degree, the effects of her low-SES background). However, one function of the control participants was to account for this factor. These participants were also from a low-SES background and would therefore similarly become more accustomed to the test-taking environment with time.

The second major change at post-intervention assessment was CB's teacher's description of the changes in her comportment, behaviour, attitude towards schoolwork, and overall grades. In fact, both parents and teacher reported improvements in emotional control and planning / organization on the BRIEF at post-intervention assessment. Post-intervention, CB's teacher described her as becoming more independent and more positive about her schoolwork. CB's grades also improved: At the end of the first semester (pre-intervention) they were 2, 1 and 3[1] for Language, Numeracy and Life Skills, respectively. In the third term, during the intervention period, CB received scores of 3, 2, and 3 for the same subjects, respectively; for the last term, post-intervention, CB scored 3 on all tasks. Although the intervention was not directly linked to the latter changes decribed by CB's teacher, these changes could be associated with an improvement in performance on the Inhibition subtests.

There may once again be competing explanations to account for these changes, however. As mentioned earlier, CB was also attending sessions with an educational psychologist prior to and during the intervention period. Her attendance at these sessions could be a link to the behavioural outcomes. In addition, CB began attending a new school shortly before the intervention began, and so her adaptation to this new environment could have improved with time, with the intervention taking place during the second half of the year. Also, it is possible that all of the children in her class at school showed similar improvement due to common maturation effects.

In summary, there is no strong evidence that the attention training intervention altered the performance of CB on the objective measures of attention, or on the behavioural reports regarding attentional functioning. There appeared to be some gains on tests of inhibitory controland in her behaviour at school, but these results are best interpreted with caution.

[1] 1 indicates that the ability or skill is not achieved; 2, that it is partially achieved; 3, that there is satisfactory achievement; and 4, that there excellent achievement of the ability or skill.

Case study 2: JL.

Medical history.

Injury-related details. I obtained this information from JL's mother and from his RXH medical folder. JL sustained a severe TBI when he was 6 years and 8 months old. He was assaulted with a blunt object (iron pole) by an older child. His GCS score upon hospital admission was 3/15. He was initially referred to a hospital closer to his home and then transferred to RXH.

JL's CT scan showed he had sustained a large left parietal haemorrhagic contusion and a depressed skull fracture. There was a substantial midline shift to the right, with partial effacement of the left lateral ventricle and a posterior cerebral artery (PCA) territory infarct. PCA distribution areas include the thalamus and parietal cortices, which are some of the brain regions implicated in attention in Posner and Peterson's (1990) model.

Brain oxygenation monitoring. I obtained this information from the Head of the Division of Pediatric Neurosurgery at RXH. The duration of JL's monitoring was 134 hours. His highest ICP reading was 77 and his lowest CPP reading 19. He had nine episodes of CPP < 40, and nine episodes of CPP < 50. His lowest $PbtO_2$ reading was 1.7. JL had six episodes of $PbtO_2 < 20$, five episodes of $PbtO_2 < 10$, and four episodes of $PbtO_2 < 5$. In summary, there were several major episodes of concern during his monitoring period.

***Developmental history*.** According to JL's mother, he was born prematurely via caesarian section when she was 7.5-8 months pregnant. She attributed JL's premature birth to her high blood pressure. JL was incubated for 2 weeks following his birth. He weighed 2.8 kg at birth. JL's mother also noted some difficulties with feeding and with bonding during the 2-3 weeks immediately following birth. She attributed the difficulties with bonding to JL's father "not being around". These feeding and bonding difficulties resolved over time.

Despite JL's premature arrival, his mother reported that he reached his developmental milestones normally. He began to walk unassisted at approximately 10 months of age, and said his first word even earlier. He was able to write his own name by 4.5 years of age. Premorbidly, JL's mother described him as a "very clever, respectable" boy with "good manners", who "wasn't naughty". She added that even before he attended school, he could "teach other children" presumably around the neighbourhood.

However, JL's mother reported changes following the TBI. Specifically, she noted that he was more emotional, that she found that he was "rude" and that he fought with other children around him.

Academic history. JL was in Grade 1 at a mainstream co-ed school at the time of the TBI. After the accident, he was enrolled in a special needs school that does not cater specifically for children who have sustained TBIs.

Pre-assessment information received from one of JL's teachers was that he could communicate well and that he was able to deliver messages from one person to another, although he was forgetful at times. She also reported that he was at times disobedient and disruptive in the classroom (e.g., he bothered his classmates while they were trying to work). There was also an issue with regular absenteeism. Unfortunately, this teacher left the school shortly after providing the initial information, and despite repeated attempts to obtain a formal school report, I did not receive it. The temporary teacher from whom I requested information post-assessment was unable to comment on JL's performance.

Current social status. At the time of the pre-intervention assessment, JL lived with his mother and other family members (four adults and three children) in a low-SES suburb in the Cape Town area. His mother was unemployed at the time of this study.

Assessment results. JL was 9 years and 6 months old at the time of his pre-intervention assessment. It had been 2 years and 1 month since he had sustained his TBI. JL's mother described him as "slow", at the pre-intervention assessment meeting.On testing, JL scored more poorly on attention tasks than tasks in other areas of functioning.

Table 35
General Intellectual Functioning: WASI Scores for JL and his Controls (N = 4)

	Participants			
Measure	JL	Control-intervention	Play	Test-only
Vocabulary[a]	29	36	42	31
Similarities[a]	34	45	63	46
VIQ[b]	74	86	104	83
Block Design[a]	47	41	36	44
Matrix Reasoning[a]	34	38	33	38
PIQ[b]	86	84	77	86
FSIQ[b]	77	83	88	83

Note. [a]*T*-scores are presented. [b] IQ index scores are presented. WASI = Wechsler Abbreviated Scale of Intelligence.

General intellectual functioning. JL's FSIQ was in the borderline range relative to standardized normative data, whereas his control counterparts all scored within the low-average range (see Table 35). This difference in FSIQ is primarily accounted for by the differences in VIQ scores and the subtest scores constituting it, as JL performed more comparably to his control counterparts on PIQ. JL performed more poorly than two of the controls on the Vocabulary subtest, but he was especially weak, compared to controls, on the Similarities subtest (see Table 35).

Attention / concentration. JL tended to perform more poorly than the matched controls on most tests of attention / concentration at both pre- and post-intervention testing (see Table 36). He did, however, obtain a scaled score of 9 on the target finding component of the Sky Search task at pre-intervention testing. This performance was not sustained at the post-intervention assessment, however.

Memory. JL tended to perform more poorly than the matched controls on tests of verbal and visual memory at both pre- and post-intervention assessments (see Table 36). His age-adjusted scaled scores tended to increase from pre- to post-intervention testing on both verbal memory subtests, but remained largely consistent for the visual memory subtests.

Executive functions. Regarding working memory, JL tended to perform more poorly than the matched controls at both pre- and post-intervention testing (see Table 36). His performance in this domain remained largely consistent from pre- to post-intervention.

Regarding inhibition, JL also tended to perform more poorly than the matched controls at both testing sessions (see Table 36). He did not show any pre- to post-intervention improvements in his age-adjusted scaed scores in this domain.

Regarding design fluency, JL performed more poorly than the matched controls at pre-intervention testing and more poorly than the intervention control and test-only control participants at the post-intervention assessment (see Table 36). On this test, his age-adjusted scaled scores increased from pre- to post-intervention.

Table 36

Attention, Memory and Executive Function Outcomes for JL and his Controls (N = 4)

		Participants							
		JL		Control-intervention		Play		Test-only	
Domain	Subtest / Battery	T1	T2	T1	T2	T1	T2	T1	T2
Attention and concentration	TEA-Ch								
Selective attention	Sky Search Target	9	5	6	8	10	10	10	10
	Sky Search Timing	1	1	3	8	6	7	6	12
	Sky Search Attention Score	1	1	4	9	7	7	7	13
	Map Mission	4	3	8	5	9	8	9	8
Sustained attention	Score!	3	2	8	7	12	7	6	8
Selective/ divided attention	Sky Search DT	1	3	7	5	7	6	9	6
Attentional control	Opposite Worlds	1	1	8	8	2	3	3	6
Concentration	Numbers Forward	3	4	9	8	7	7	4	4
Memory	CMS								
Verbal memory	Word List Learning	3	9	10	12	7	14	9	14
	Word List Delayed	7	10	11	12	12	14	14	14
Visual memory	Dot Locations Learning	4	5	13	6	7	13	10	12
	Dot Locations Total	5	5	15	6	8	13	11	13
	Dot Locations Delayed	5	7	10	6	10	9	12	12
Executive Functions	CMS								
Working memory	Numbers Backward	2	3	6	10	6	6	13	10
	NEPSY II								
Inhibition	Inhibition	1	1	9	12	7	8	2	3
	Switching	3	1	12	12	8	10	5	10
Inhibition – CT	Inhibition	2	1	11	15	6	7	5	6
	Switching	6	1	14	14	7	8	8	11
Inhibition errors	Total Errors	1	1	8	11	6	8	1	2
Generativity	Design Fluency	3	6	7	10	5	5	10	11

Note. T1 = Time 1, or pre-intervention; T2 = Time 2, or post-intervention; DT = Dual task; CT = Completion time.

Summary of findings. At the pre-intervention assessment, JL presented as a reserved but cooperative boy. The outcome of this assessment showed that, similar to CB, JL's relatively lower FSIQ was mainly attributable to his performance on the Verbal subtests, and on the Similarities subtest (a measure of abstract reasoning) in particular. This relatively poor performance on an executive function test was a pervasive feature of JL's assessment.

JL also scored lower than controls on most attention-related subtests at both pre- and post-intervention sessions. Although not measured directly, JL appeared to perform poorly on most timed tasks (e.g. Sky Search Timing and completion time on Inhibition subtests). This is a common outcome post-TBI (Catroppa & Anderson, 2005; Meythaler et al., 2001). In individual cases, TBI sequelae are unlikely to be limited solely to impairment in speed of information processing, however. Attention and executive functions are also often affected concomitantly (Babikian & Asarnow, 2009; Van Heugten et al., 2006). Thus, it is not surprising that JL also performed poorly on some untimed tasks such as the CMS Numbers Forward and Backward subtests, measures of concentration and working memory, respectively. Performance on other executive function subtests, such as NEPSY-II Inhibition and Design Fluency followed similar suit.

At this point, it is important to note that JL was born pre-term at 2.8kgs when his mother was 7.5-8 months pregnant. Hence, JL's birth could be classified as a late-preterm (Sutton & Darmstadt, 2013). Late-preterm births have previously been associated with increased internalizing and attention problems, as well as borderline IQ at 6 years of age. Whether the underlying mechanism for such potential cognitive effects can be attributed to the actual gestational age or to perinatal complications is unclear, however (Sutton & Darmstadt, 2013; Talge et al., 2010). Hence, JL's preterm status might also have contributed to his performance on IQ and attention tests.

JL performed relatively well on tests of memory, especially verbal memory. His scores on both the learning and delayed components of the memory task improved from pre- to post-intervention testing sessions.

During the intervention training, JL was cooperative and participated actively in the sessions. He appeared to try hard during these sessions. He made more omission than commission errors in the visual and auditory attention intervention tasks. According to researchers (e.g, Wassenberg et al., 2004), such errors represent inattentiveness rather than impulsiveness.

At post-intervention assessment, JL showed some positive but non-significant change on the memory and design fluency subtests. The improvement in test scores from pre- to

post-intervention testing for JL was, however, matched by similar improvement in performance by the Play, Test-only, and Control-intervention participants.

Thus, JL appeared to present with a dysexecutive syndrome, with a major contributing factor being his slowed speed of information processing. Given JL's history, not only of the TBI but also of the multiple episodes of critical $PbtO_2$, this outcome was not unexpected.

As discussed in Chapter 4, secondary brain hypoxia-ischemia may exacerbate an already injured or vulnerable brain. Executive dysfunction, including impulsivity and disinhibition, is among the deficits associated with hypoxia ischemia (V. Anderson, Northam, Hendy, et al., 2001; Lezak et al., 2004). Also outlined in that chapter is a study by Hopkins et al. (2005), who investigated and compared neuropsychological outcomes in a group of participants who had sustained moderate-severe TBIs and another group of participants who had sustained anoxic brain injury (ABI). There were no detectable between-group differences. Neuropsychological sequelae for both groups included impairment in memory, attention and EF, as well as in speed of information processing.

In summary, the intervention did not appear to benefit JL. Even though he had experienced a longer time since injury than CB, he showed a poorer outcome post-TBI. In addition to the TBI, JL also experienced several hypoxic episodes as compared to CB, who did not experience any. These hypoxic episodes would likely have exacerbated JL's already-injured brain, potentially leaving little redundant tissue to maintain the damaged tissue. As outlined in Chapter 6, intrahemispheric maintenance is the mechanism of anatomical reorganization purported to occur most often following severe TBI, as injuries of this nature are often associated with generalized and diffuse lesions. Owing to the nature of this mechanism, that is, of an ongoing maintenance of functions by damaged tissue, intrahemispheric maintenance is associated with the least favourable outcome (V. Anderson et al., 2011). These conjectures are likely to be even truer in a brain that has sustained a severe TBI and then several episodes of hypoxia.

Discussion

Cognitive rehabilitation is a relatively young field, particularly in terms of efficacy studies. Pediatric cognitive rehabiliation is an even younger field, and in even greater need of further empirical demonstration of efficacy and effectiveness. Both adult and pediatric reviews of cognitive rehabilitation present positive evidence for some types of interventions and, in some cases, practice guidelines or recommendations. These reviews also, however,

consistently highlight the host of methodological flaws that so often plague this research. Cognitive rehabilitation is also a young field in terms of access to and availability of interventions around the world, but especially in LAMICs like South Africa. Again, pediatric cognitive rehabilitation is even less accessible and available. Both of these factors (lack of efficacy, and limited access to, and availability of, cognitive rehabilitation) provided the impetus for this study.

The study described the implementation of an attention-training program with a group of low-SES South African children who had sustained severe TBI. Cognitive rehabilitation post-TBI, or other ABIs, is not standard practice in South Africa, and especially not in low-SES communities in this country. No study of this nature has been conducted or evaluated in this context, previously. In addition, no pediatric attention-training study has focused specifically on children with severe TBI, using a sample with such a restricted age range. Published literature in this field rarely focuses exclusively on severe TBI, even though the dose-response relationship between severity and outcome is well documented.

I chose to focus on the rehabilitation of attention for two reasons. First, it is one of the most common cognitive deficits reported post-TBI. Second, there are recommendations for attention process training in both the adult and pediatric reviews of cognitive rehabilitation following TBI. Reports in the literature suggest that attention-training programs are indeed efficacious for adults and children with ABIs. In a context where formal cognitive rehabilitation is not standard practice following TBI, this seemed like a fair place to start.

Because the study had dual aims (examining efficacy overall and examining applicability of the program in a specific context), I present separate sections focusing on each of those aims first. Thereafter, I highlight some limitations of the study and suggest ideas for future research.

Aim 1: Examining Overall Efficacy of the Intervention

Results for the within-group comparisons from pre- to post-intervention testing were non-significant. Results for the RCI analyses showed that there were no significant improvements on any of the TEA-Ch subtests for the TBI-intervention group. There were, however, significant changes on the NEPSY-II Inhibition and BRIEF outcome measures from pre- to post-intervention testing sessions for the 7-year-old female and 9-year-old male TBI-intervention participants, respectively, that were not matched by changes in the matched controls. I elaborate briefly on each of these participant's changes, below.

The 7-year-old TBI participant, CB, showed some significant improvement on the NEPSY-II Inhibition subtests and also in terms of her school performance (as indicated by her grades and positive feedback from her teacher).

There is significant functional overlap between attention and executive function (which includes inhibition) domains (P. Anderson., 2002). Therefore, if the attention-training intervention did contribute in any way to the significant change in CB's scores on the inhibition measures, then an investigation of what aspects of the intervention might effect such changes requires further exploration. One idea might be around the Card Flip and Attention CD tasks, which form part of the attention-training program across attentional domains in the hierarchy. These tasks require that participants press a clicker each time they see or hear a specific stimulus card or word, respectively, and that they hold (or inhibit) their response when these cards or words do not match the target criterion. In this task, the examiner notes both omission and commission errors, with the latter purported to indicate impulsivity. This indirect training on impulsivity might serve as the connection between the intervention and the inhibition outcome measure.

Also, although all of the participants were at least 1 year post-injury, CB had the shortest time since injury. If this is an effect of the intervention, then perhaps time since injury played a facilitating role in CB's outcomes. Perhaps being earlier in that recovery trajectory, only just past the 1-year mark where recovery is often reported to plateau, benefitted her in some way.

Lastly, CB was the youngest participant in the TBI intervention group. It may well be that the intervention materials were more appealing to her than to the other older participants, which might have facilitated greater engagement with the intervention materials. These pieces of speculation all require further investigation.

Regarding the 9-year old TBI (SC) participant's improvement on the BRIEF, these results are less convincing. The two BRIEF indices on which his mother and teacher reported significant change (Emotional Control and Organization of Materials), and where there were no similar changes for the control participants, might be regarded with interest. However, his teacher did not corroborate the changes reported by SC's mother on the remaining BRIEF indices, and there were no significant changes on the cognitive measures to support these reports. The bias in self-report data is widely known (Holden & Troister, 2009; A. Williamson, 2007), and therefore these results should be interpreted with caution.

Also, a later hospital referral for this participant post-intervention once again noted behavioural problems. Thus, even if the intervention did have some effect, this effect was

transient or it did not generalize to all contexts / situations. We do not yet have follow-up data on SC. Again, I acknowledge that there could be uncontrolled factors (e.g., self-report bias) that contributed to SC's outcome. This is part of the challenge in conducting this research. However, in this study, I made an effort to control for two major confounding variables (SES and time spent with participants) and for test-retest effects, all of which are often not accounted for or controlled in cognitive rehabilitation research.

Thus, despite the limited evidence for the efficacy of the Pay Attention! Programme with the participants in this study, this attempt to control for potentially confounding variables and for test-retest effects is an important strength of the study. The results of the two case studies offer additional points for consideration. These include the possibility of a broader set of predictors of outcome, including neurosurgical monitoring data and the need for individualized intervention programmes. I briefly outline each of these points below.

Controlling for potential confounding variables and test-retest effects. I attempted to control for the one-on-one time spent with intervention participants, for SES, and for test-practice effects. Regarding time spent with participants, there were a number of instances of significant pre- to post-intervention changes for participants of the Play group on the cognitive and behavioural measures. These findings show that time spent engaging with participants can be an important confounding factor that should be considered in pre- and post-test design studies, especially when including a low-SES sample, where children may not be afforded regular one-on-one attention.

Regarding control for the effects of SES on cognition and behaviour, as discussed previously the association between low-SES environments and poor cognitive outcome is well established (see, e.g., Hackman et al., 2010; Noble et al., 2007, 2005). Besides IQ, executive function / attentional systems are particularly vulnerable to SES-related variation. In low-SES samples, specific impairments have been reported for selective attention, inhibitory control, cognitive flexibility, and working memory (Farah et al., 2006; Lipina et al., 2005; Sarsour et al., 2011; Stevens et al., 2009). In this study, all of the groups were of low SES. The test scores across the groups demonstrate that it is important not to compare study participants, and especially those from low-SES backgrounds, to historical controls or to internationally based normative data.

Regarding the Test-only group, there were a number of instances of significant pre- to post-intervention changes for the participants of this group on the cognitive and behavioural measures (e.g, Sky Search Timing and Attention Score for the 8-, 9- and 10-year-old participants, and Externalising Behaviours reported by the parent for the 7-year-old

participant). Improved performance by the Test-only controls showed that any improvement by the TBI-intervention group needs to be interpreted cautiously, in light of the demonstrated effect of maturation and test-retest effects.

Case study implications. The two participants described in the case studies shared the following characteristics: They were of a similar age at the time of their injuries; they had both sustained severe TBIs; they were both from low-SES backgrounds; and they had both attended mainstream schools prior to their accidents. In both cases, there were no reports of diagnosed, or possible but undiagnosed, premorbid problems (although JL's preterm birth and the potential effects are noted), and neither participant had prior access to cognitive rehabilitation. They differed in the following respects: JL had a longer time since injury, the mechanisms of injury differed, and JL experienced more episodes of low $PbtO_2$.

A longer time since injury did not benefit JL. This finding is in keeping with V. Anderson et al.'s (2011) report that neurobiological mechanisms of recovery do not necessarily advantage the immature brain. There were markedly different secondary injury outcomes in terms of ICP, CPP and most notably, $PbtO_2$, which could contribute to outcome quite significantly (see Study 2, Chapter 4). These results once again highlight the important role that secondary injuries can play in determining outcome, even at this post-acute intervention stage of recovery.

The different intervention outcomes for CB and JL, despite apparent similarities in some of the common predictors of outcome, present a case for individual assessment and possible intervention design suited to specific individual needs. Although RCTs are recommended as the gold standard design and approach to evaluating studies such as the current one (Cope, 1995), a single-case experimental design (or *n*-of-1 trials) would better suit such individualised assessment and intervention. The single-case design may have been criticized previously and disparaged for its apparent lack of rigor, mainly as a result of a number of poorly designed studies. However, in recent years, criteria for well-designed *n*-of-1 trials and review mechanisms for studies with this design have been proposed (Perdices & Tate, 2009; Tate et al., 2008).

In summary , the first part of this discussion responded to the primary aim of this study: examining the overall efficacy of the Pay Attention! programme. The results show limited efficacy for the programme with the study sample.

Aim 2: Applicability of the Program in a Specific Context

The next leg of the discussion, in relation to the aims of this study, has to do with context. The second aim of the study was to evaluate the efficacy of an attention-training

program in a South African context. The implementation of the current study demonstrated that intervention programs of this nature are possible in LAMICs like South Africa, where the infrastructure for such programs may not be in place. However, the ethical question to consider is whether such programs should be run if they have only limited efficacy?

One point of view might be that the costs involved in running interventions with low efficacy are not warranted. Hence, only interventions with proven high efficacy should be run. Another view, however, might be that even if an intervention programme has limited efficacy and benefits only a few people (e.g., one in every 10 or even 15 people), the economic burden of TBI (e.g., in terms of the potential future loss of productivity) dictates that one should implement such a programme. Further, implementing and building on programmes with limited efficacy will also allow the opportunity to develop and refine new intervention programmes, suitable for specific contexts. The current study presents such an opportunity and already offers ideas for such development and refinement.

For example, what one of the case studies in the current study served to demonstrate, even if by chance, was that multidisciplinary efforts could be set up using the school setting. CB, for example, was afforded access to the services of an educational psychologist, through the school system, during the course of the intervention. There were, however, no a priori common goals between the teams involved.

Such a model can, however, be used in future and seems to offer a lot of potential. This structure, with the possible participation of the parents and with real-world goals directly linked to the intervention activities, could begin to create a more holistic intervention approach. This approach is endorsed by a number of practitioners in the field of cognitive rehabilitation (Ben-Yishay et al., 1985; Cernich, Kurtz, Mordecai, & Ryan, 2002; Cernich et al., 2010; Marcantuono & Prigatano, 2008).

Limitations and Directions for Future Research

The first, and primary, limitation of the study, is its small sample size. This limited sample size was primarily a function of available human, time, and financial resources for assessment, intervention, and Play-group purposes. Previous studies (e.g., Galbiati et al., 2009; Van't Hooft et al., 2005) included larger sample sizes, with $n = 40$ and $n = 18$ experimental participants, respectively. However, those studies included participants from a wider age range and included participants with mixed etiologies, including TBI, respectively. Hence, the small sample size in this study was, in part, a result of a desire to keep tight control in this regard. I will aim to recruit larger samples in follow-up studies, where resources (particularly time) will not be as limited.

A second limitation of the study was that both the pre-and post-intervention assessments were not blind. This limitation was largely due to available human resources. I will aim to include blind assessments at both pre- and post-intervention testing sessions in follow-up studies.

A third limitation was that test-retest reliability coefficients were not available for all of the subtests used. Therefore, RCI analyses (of the form used for other subtests) could not be performed for these subtests or properly considered in the two case studies.

In spite of attempts to control for the effects of a number of potentially confounding variables by including the three control groups, a fourth limitation of this study was the non-inclusion of a severe TBI no-intervention control group. This group would be administered identical procedures to the Test-only group. They would, however, be a wait-listed intervention group. Such a TBI no-intervention group would have controlled for maturation effects, test-retest effects, or recovery of patients, and will be included in a future study.

A fifth limitation of the study was that I did not include a real-world task as an outcome variable. One of the outcome measures investigated for the intervention participants was their school reports, but these reports were not directly linked to the intervention training skills. Also, schools and grades can differ in terms of the assessment criteria used. The BRIEF and CBCL were included in order to measure whether changes in attention or executive-related domains generalized to everyday behaviour in the home and school setting, although, as noted earlier, there are limitations to self-report measures. Future studies might also include the Vineland Adaptive Behaviour Scale (VABS; Sparrow, Balla, & Cicchetti, 1984) as an outcome measure, which is recommended as an ecologically valid measure in cognitive rehabilitation studies (Limond & Leeke, 2005).

The non-holistic approach in the current study might be regarded as a sixth limitation. Some of the studies reviewed above that have shown positive outcomes have employed multicomponent interventions (Galbiati et al., 2009; Van't Hooft et al., 2003, 2005). Holistic, multicomponent interventions are regarded as an ideal approach to cognitive rehabilitation and hence a method to strive towards. The current study did not include a multicomponent intervention strategy, but rather an APT intervention on its own. There were two reasons for this. First, as noted earlier, resources were limited. Second, this study was the first of its kind in a context where no formal cognitive rehabilitation is offered and the suitability of the setting and access were still being evaluated alongside the intervention. Part of the purpose of this study was for it to serve as a building block for future studies. With limited resources and time, the aim of the research was to implement a well-controlled study, addressing some of

the methodological flaws often highlighted in cognitive rehabilitation literature. Future studies will aim to adopt a multicomponent, holistic approach.

A final limitation of the study was that, due to limited resources, the number of weeks that the intervention was implemented had to be slightly reduced from the optimal 12 to 10 weeks. Given the general results of the study, it is not likely that the extra two weeks of the the intervention might have made a difference to the end results, however.

In spite of these limitations, there are no studies with which to compare these findings directly, as few studies have been conducted that focused solely on attention training with children with severe TBI over such a limited age range (7-10 years). The study by Galbiati et al. (2009) is one of the few to examine an attention-training intervention with severe TBI participants exclusively. However, besides the differences in sample size and age range noted before, other differences between that study and this one include the inclusion of a severe TBI control group in that one, different outcome measures, intervention and follow-up periods, different forms of intervention (computerized vs. table top), and the inclusion of metacognitive strategies as part of the intervention in that one.

The limitations noted above will serve as guidelines for follow-up studies on attention-training interventions in South Africa. Cognitive rehabilitation studies of this nature (i.e. focused on attention) remain limited in number, even though there appear to be a fair number of these studies relative to studies on other constructs (e.g., executive functions). Therefore, more research that explores the efficacy of attention-training interventions is needed. For example, more studies are needed that specifically explore the optimal intervention strategy for attention deficits in middle childhood following severe TBIs, as was the case in this study. Besides the improvements already noted, follow-up studies could also improve on the current study by employing a longer intervention period and a greater array of outcome measures. Certain successful elements of the current study could be maintained (e.g., implementation of the intervention at schools, and including numerous control groups).

Multicenter studies are also needed. These studies should implement and assess the same design, the same intervention program, and the same outcome measures across centers.

Besides addressing the dual aims of this research and raising some important points for consideration in future studies, this study also highlights a theoretical challenge in the cognitive rehabilitation literature. Cognitive rehabilitation and its associated theoretical framework present a problematic picture in the context of restorative approaches following severe pTBI. Mechanisms of recovery such as restitution and substitution mechanisms are often alluded to as the basis for cognitive rehabilitation; a recent review, however, outlines

evidence that these mechanisms may not provide a greater advantage in terms of recovery potential for the immature brain (V. Anderson et al., 2011).

The specific substitution mechanism that is most associated with severe TBI is intrahemispheric maintenance (see Chapter 6) and, owing the lowered levels of redundancy in the severely injured brain, it is not associated with favourable outcome (V. Anderson et al., 2011). Thus, an important dilemma not often highlighted in the published literature is that if the mechanisms upon which cognitive rehabilitation is based do not appear to benefit a specific population (e.g., children who have sustained severe TBIs), then how would this uncertainty translate in terms of the outcomes of the interventions purported to be based on those mechanisms? Although the purpose of this research was not to explore this question, it is important to bear it in mind when considering the results of this study and the implications for future research.

Summary and Conclusions

Between- and within-group analyses suggested that the attention-training program conducted in this study did not result in significant changes on either cognitive or behavioural measures. Some change was detectable via RCI analyses. These individual analyses pointed to only a few specific positive changes for selected subtests in individual participants, but these findings should be interpreted cautiously.

In the published literature, there appears to be a general dearth of research on cognitive rehabilitation for children following TBI, especially severe TBI. The dearth is even greater in LAMICs like South Africa. The answer to this problem is not to sit back and allow things to remain as they are. The implementation of this research may be difficult and it can be intensive and frustrating, especially without the necessary infrastructure. However, I hope this study demonstrated that with the necessary resources and willingness, practical interventions of this nature can be administered in this context. Therefore, this work helps advocate and appeal for greater attention and efforts aimed at cognitive rehabilitation for children following TBI in South Africa.

GENERAL DISCUSSION AND CONCLUSION

In this dissertation, I aimed to investigate topics related to severe TBI in South Africa. These topics included a) examining a snapshot of the profile of children admitted for severe TBI to the RXH in Cape Town, South Africa (Study 1), (b) investigating the relationship between the burden of secondary injury as manifest by brain oxygenation ($PbtO_2$) with neuropsychological and behavioural outcomes in children following severe TBI (Study 2), and (c) investigating the implementation and efficacy of an attention-training intervention program with children who had experienced severe TBI (Study 3).

Results from Study 1 showed that closed TBIs in children (mean age of 6 years) that lead to severe injuries and death occur most often as a result of road traffic accidents and, specifically, MVA-pedestrian related accidents. The sample demographics included mostly males and 0-4 year old children, from low-income families. English, Afrikaans and Xhosa were the dominant languages spoken by participants.

Results from Study 2 showed that, as may be expected, the TBI participants (n = 11) performed significantly more poorly than matched healthy controls (n = 11) on a number of cognitive and behavioural outcome measures. The cognitive measures were in the domains of IQ, attention, memory, executive functions, visuospatial functioning and expressive language. The behavioural outcome measures were all of the BRIEF parent indices and the externalizing syndrome scales of the CBCL parent form. The TBI participants were then separated into two groups: those who had experienced at least one hypoxic episode following injury and those who had not. Although the topic of brain oxygenation has been investigated frequently in the neurosurgical literature, no study to date has investigated both the neuropsychological and behavioural outcomes in relation to brain oxygenation following severe TBI in this age group. Results showed significant differences between the groups on measures of VIQ and FSIQ as well as on the basic and higher order attention composites, verbal memory, executive functioning, visuospatial and expressive language composites. Participants with the Lowest PbtO2 < 10 mmHg preformed more poorly than those for whom the Lowest PbtO2 > 10mmHg. Thus, episodes of hypoxia (a secondary injury) following severe TBI may be detrimental to cognitive outcomes. This study therefore highlights the importance of secondary injuries in relation to cognitive outcomes, and encourages investigation on a broader scale.

Results from Study 3 showed that the attention-training intervention was not effective at a group level. There were no within-group changes for the TBI intervention or the three matched control groups from pre- to post-intervention testing on measures of attention,

memory and executive functions. However, changes in specific domains could be detected on an individual level using RCI analyses. Study 3 is unique in the terms of the inclusion of multiple matched control groups and also with it being implemented in a LAMIC like South Africa. Of the three studies, the area of cognitive rehabilitation in South Africa is perhaps where most development in the TBI field is needed. Conducting such a study where the necessary support and infrastructure was lacking made it challenging. However, the results of Study 3 showed that the implementation of an intervention program of this nature is possible even in a context where cognitive rehabilitation is not standard practice.

Together, these three studies contribute unique information to our understanding of pTBI and its management in South Africa. The results of Studies 2 and 3 can also contribute to the general knowledge base of TBI globally. The first study showed where many of the children with severe TBI stem from, who they are demographically, and therefore who to target in terms of prevention strategies. The second demonstrated the importance of aggressive secondary injury management to cognitive outcomes after children have been admitted. The third demonstrated the need for individualized intervention programs for children once recovery has stabilized. From these results, it seems that our energy or hope should be pinned, firstly, on prevention, secondly on maximizing the window of opportunity provided by the amelioration of secondary injuries, and thirdly on intervention post-injury.

Each study informs one or more of the others. For example, generating current knowledge of the profile of pTBI is crucial for prevention and intervention efforts. Knowing the history of hypoxic episodes can help understand and explain cognitive outcomes post-TBI. Understanding these cognitive outcomes is important when planning intervention programs. Knowing the challenges associated with the intervention program and cognitive rehabilitation generally provide motivation for greater efforts at prevention.

Each of these areas of research requires serious and urgent attention. First, a greater focus on communities at risk and a campaign for prevention of injuries is needed. Formal incidence rates and monitoring strategies are needed to inform such prevention campaigns, which should include public awareness drives. Second, the field of neurosurgery appears to acknowledge the seriousness of secondary injuries, but neuropsychologists need to become involved in interdisciplinary work in investigating outcomes beyond the scope of mortality or survival of children. There is important work to be done in uncovering the neuropsychological sequelae that result from these injuries. Finally, neuropsychologists need to work at building and expanding on intervention programs in schools and in contexts /

environments where cognitive rehabilitation is lacking. Efforts aimed at remediating such injuries in a variety of ways are of paramount importance.

However, major funding is needed for this research to truly flourish and contribute on a greater scale. It remains an incredible paradox that pediatric traumatic brain injury is repeatedly described as a leading cause of mortality and morbidity and yet it remains underfunded ("Traumatic brain injury: time to end the silence," 2010). This issue of underfunding in TBI research is a problem globally and across disciplines. In a recent article, the need for recognition and support if TBI is to become something other than a 'silent epidemic', is emphasized ("Traumatic brain injury: time to end the silence.," 2010). In this paper, specific areas of research that are particularly underfunded are highlighted. One of these areas of research is rehabilitation. Research foci on secondary injuries and intervention is also encouraged, especially given the increasing rates of road traffic accident related TBIs. Thus, the research reported in this dissertation fits the descriptions of those areas of research deemed a priority for funding and investigation. This paper also highlights the need for multidisciplinary team efforts and focus, as I hope to have advocated in this dissertation also.

The three studies in this dissertation are not without limitations, however. I have highlighted the specific limitations for each study in the relevant chapters. There are however broad areas of improvement that cut across more than one study. For example, implementing a prospective design would improve both studies 1 and 2 and the issue of a small sample size is an important limitation for both studies 2 and 3. Both studies 2 and 3 would benefit from large multicentre studies in the future. Many of the noted limitations across the three studies were primarily a function of available human, time, and financial resources. Perhaps one aspect of the dissertation as a whole that may be considered a limitation, but which is not attributable to availability of resources, is the fact that it is largely descriptive. Although I touch on some theoretical issues, such distinguishing between a TBI vs hypoxic effect in Study 2 and the issue of limited evidence for mechanisms of recovery following severe TBI in the developing brain and how this affects the basis for cognitive rehabilitation in Study 3, these studies were not designed to address those issues. Future studies can be designed to address specific theoretical issues such as these. Despite this potential limitation, the three studies in this dissertation provide the groundwork for at least three important future studies in the field of pTBI in South Africa, with two of these studies (2 and 3) having global application.

Although South Africa appears to have higher rates of TBI and lags behind the developed world in terms of the availability of cognitive rehabilitation, as outlined in Studies

1 and 3, it is clear from Study 2 that this is not the entire picture. South Africa is not a classic developing world country. In some regards (e.g., socially and economically) it lags behind and yet in others (e.g., in terms of infrastructure), it seems ahead of the game (Layne, 1998). In spite of our developing world status, our primary intervention levels (e.g., our neurosurgical facilities at RXH), are a model of excellence in terms of the level of health care provided. These services are on par with international standards, especially in the provision of neurophysiological monitoring. This enabled the first study of brain oxygenation and neuropsychological and behavioural outcomes following severe TBI, hosted by this division. Hence, the idea is to maximize on the country's existing strengths, by becoming aware of and harvesting all available resources (as K. Levin, 2004, suggested).

At this stage we need more epidemiological studies, more neuropsychological outcome studies, for example in relation to neurosurgical interventions, which are on par with international standards and an extreme injection of energy and attention in the field of cognitive and neuropsychological rehabilitation for children who have sustained TBI.

TBI and especially pTBI is a silent epidemic that requires a voice and this research has endeavored to do so, even on a small scale. There are various ways that we could potentially begin to address this long-standing, growing problem by maximizing on what is and actively advocating for what needs to be done, even in a developing world context like South Africa.

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APPENDIX A

ETHICAL APPROVAL FOR STUDIES 1 AND 2 FROM THE UNIVERSITY OF CAPE TOWN'S FACULTY OF HEALTH SCIENCES

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
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01 April 2009

REC REF: 166/2009

Dr AA Fagaji
Paediatric Neurosurgery
Red Cross Children's Hospital
Rondebosch

Dear Dr Fagaji

PROJECT TITLE: REGISTRY FPR PAEDIATRIC NEUROTRAUMA

Thank you for submitting your study to the Research Ethics Committee for review.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study.

Approval is granted for one year till the 01st April 2010.

Please submit an annual progress report if the research continues beyond the expiry date. Please submit a brief summary of findings if you complete the study within the approval period so that we can close our file.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

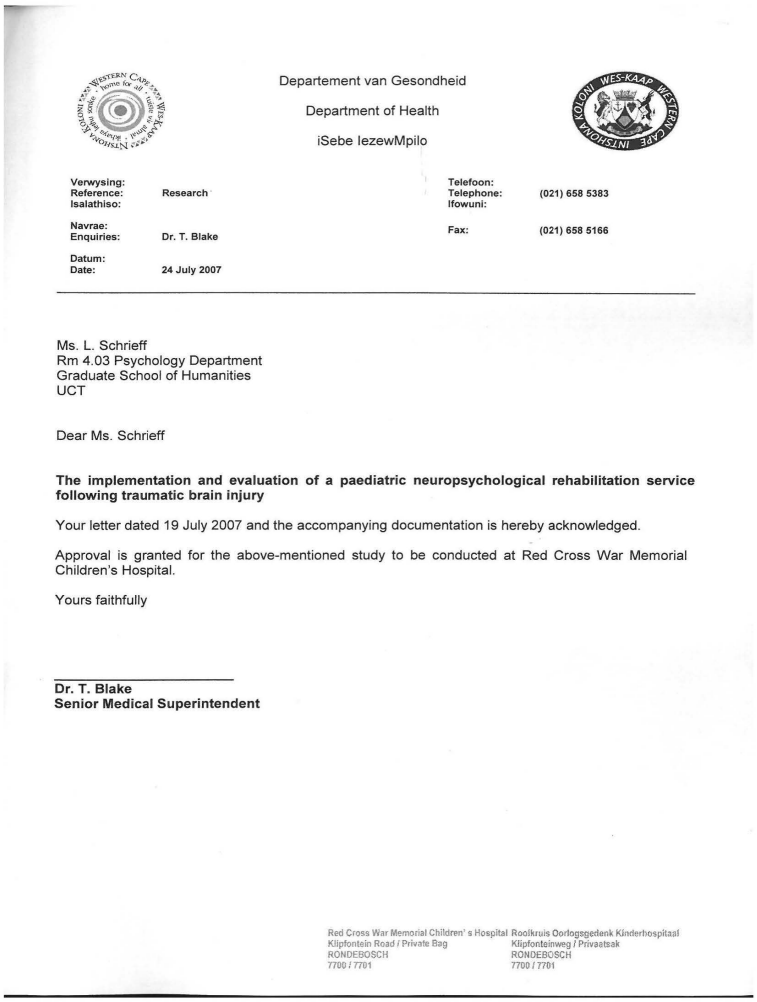
PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

kmjedi

Note. Ethical approval is renewed annually. This is an ongoing study.

APPENDIX B
PERMISSION TO ACCESS RXH FOLDERS



Departement van Gesondheid
Department of Health
iSebe lezewMpilo

Verwysing:
Reference: Research
Isalathiso:

Navrae:
Enquiries: Dr. T. Blake

Datum:
Date: 24 July 2007

Telefoon:
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Fax: (021) 658 5166

Ms. L. Schrieff
Rm 4.03 Psychology Department
Graduate School of Humanities
UCT

Dear Ms. Schrieff

The implementation and evaluation of a paediatric neuropsychological rehabilitation service following traumatic brain injury

Your letter dated 19 July 2007 and the accompanying documentation is hereby acknowledged.

Approval is granted for the above-mentioned study to be conducted at Red Cross War Memorial Children's Hospital.

Yours faithfully

Dr. T. Blake
Senior Medical Superintendent

Red Cross War Memorial Children's Hospital
Klipfontein Road / Private Bag
RONDEBOSCH
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APPENDIX C
MEASURES

Severity

The attending medical team determined the injury severity on admission, using the Glasgow Coma Scale (GCS) (Teasdale & Jennett, 1974). The GCS is used widely used measure of injury severity (Bruns & Hauser, 2003) and is commonly reported in the TBI literature (e.g., Anderson et al., 2009; Hawley, Ward, Long, Owen, & Magnay, 2003; H. S. Levin et al., 1990). Scores ≤ 8 out of 15 indicates a severe TBI (see Chapter 1).

Demographic Questionnaire

This questionnaire was designed to measure demographic information, the SES and the asset index of the participants. This measure incorporates methods put forward by Myer, Stein, Grimsrud, Seedat, and Williams (2008). It captures demographic details about parental education, occupation, and income, as well as information about the home living environment (e.g., the type of dwelling and participants' residence and neighbourhood). In addition, it also includes an asset index in addition to more traditional measures of SES, which, according to Myer, Ehrlich, and Susser (2004), may not adequately suit the SES strata found in developing world settings. These assets include material resources in the household such as running water, a flush toilet and a domestic worker, for example. They also include financial resources that the family has access to, such as a bank account, retail accounts or credit cards. Using this measure, asset ownership is divided into three groups, based on the total asset score: 0-5 (low asset ownership), 6-12 (medium asset ownership), and 13-17 (high asset ownership) (Myer et al., 2008).

Neuropsychological Measures

The test battery outlined below includes a selection of subtests from standardized neuropsychological batteries, developed and normed in Australia, the United States, Canada, and the United Kingdom. The selection of tests was guided by published literature on pediatric neuropsychological measures and on studies employing these measures (e.g., Anderson et al., 2010; Baron, 2001; Hawley, 2005; Hawley, Ward, Magnay, & Mychalkiw, 2004; Kramer et al., 2008; Lajiness-O'Neill, Erdodi, & Bigler, 2010; McNally et al., 2013; Nadebaum, Anderson, & Catroppa, 2007).

General Intellectual Functioning. The Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) was used as a measure of general intellectual functioning. The WASI can be used with individuals aged 6-89 years. It was standardized and normed in the United States. All four WASI subtests (Vocabulary, Similarities, Block Design, Matrix

Reasoning) were administered to obtain a measure of participants' Full Scale IQ (FSIQ). The two subtests used to derive a measure of Verbal IQ (VIQ) were *Vocabulary* and *Similarities*. The two subtests used to derive a measure of Performance IQ (PIQ) were *Block Design* and *Matrix Reasoning* (Stano, 2004; Wechsler, 1999).

Psychometric properties. Test-retest reliability coefficients for VIQ and PIQ range from .92 to .95, as per the WASI test administration and scoring manual. For children specifically, the reliability coefficients for the various subtests range from .81 to .97 (Stano, 2004; Wechsler, 1999).

Content validity for the WASI is verified by examining similar items of corresponding subtests of other Wechsler batteries (e.g., WISC-III), while factor analyses and intercorrelations between the subtests and other IQ scores are used to examine construct validity. Both the WASI and the WISC III include the Vocabulary, Similarities, and Block Design subtests, although there is no overlap in terms of the items included in these subtests. These subtests of the WISC (Vocabulary, Similarities, and Block Design subtests) are statistically significantly correlated with the corresponding WASI subtests, with correlation coefficients of .72, .69, and .74, respectively. The correlation coefficients for VIQ, PIQ, and FSIQ, for the two test batteries are .82, .76, and .87, respectively. Therefore the subtests and IQ scales of these measures appear to measure similar constructs (Wechsler, 1999).

There are at least moderate significant intercorrelations between the WASI subtests, largely ranging from .50 to .70 for younger and older samples. The highest correlations were between the Vocabulary and Similarities subtests, and the Matrix Reasoning and Block Design subtests. Correlation coefficients ranged from .55 to .85, and from .36 to .70, for these associations, respectively.

With two verbal and two performance subtests, the WASI is structured as a two-factor model. The factor analyses demonstrates that this structure is most appropriate for the normative data of the total sample on which the norms are based, including both the children (6-16 years) and adult (17-89 years) samples as well as for all of the six normative age bands (6-9, 10-13, 14-16, 17-34, 35-69, and 70-89) (Wechsler, 1999).

VIQ subtests.

Vocabulary. This subtest assesses crystallized intelligence, and is a strong correlate of general intellectual functioning (*g*; Wechsler, 1999). Specifically, it measures the knowledge of words and development of language ability. It includes 42 items, along an increasing gradient of difficulty. Items 1-4 require that participants name the pictures presented to them. Items 5-42 require that participants provide definitions of words presented orally, and

visually for certain age groups. Reliability coefficients for this subtest range from .86 to .93.

Similarities. This subtest assesses verbal concept formation and categorical reasoning. It includes 26 items. For items 1-4, participants are presented with two rows of pictures. The top row includes three pictures, which are thematically related. The bottom row also includes three pictures, only one of which relates to the pictures in the top row. Participants must then decide which one of the pictures in the bottom row most closely matches those in the top row. For the rest of the items, participants are asked to explain how the two words presented to them are similar. Reliability coefficients for this subtest range from .81 to .91.

PIQ subtests.

Block Design. This 13-item subtest assesses perceptual organization, spatial visualization, visual-motor coordination, and abstract conceptualization. Participants are required to reproduce designs made up of red- and white-coloured cubes within a given amount of time. These designs are constructed and / or presented, from models printed in a stimulus booklet, by the test administrator. Reliability coefficients range from .86 to .93.

Matrix Reasoning. This 35-item subtest assesses nonverbal fluid reasoning and the ability to mentally manipulate and perceive relationships among abstract symbols. Participants are presented with a matrix of patterns consisting of four to nine components. One of the components is omitted; participants must select the missing part from a choice of five items presented at the bottom of the page. Reliability coefficients range from .86 to .96.

Cross-cultural use / use in South Africa

Abu-Hilal, Al-Baili, Sartawi, Abdel-Fattah, and Al-Qaryouti (2011) investigated the psychometric properties of the WASI with a sample of 1721 individuals aged 6-28 years from the United Arab Emirates. Some test items were developed, while others were translated or adapted to fit the Arab sample. The results showed satisfactory stability and reliability estimates. Clinically, the subtests showed discrimination among normally developing individuals and those with special needs, and among the different age groups (individual groups for each age from 6 to 17, and an additional group for those older than 17).

Razani, Murcia, Tabares, and Wong (2007) compared the performances of a group of ethnically diverse individuals from Hispanic, Asian, and Middle-Eastern backgrounds who were fluent in English, to a group of Anglo-American individuals who spoke only English, on the WASI. The Anglo-American group performed better than the ethnically diverse group only on the verbal subtests. Performances on the verbal subtests and the Block Design subtest were predicted by the number of years of education outside of the US for the ethnically diverse group. Scores on the verbal subtests correlated with degree of acculturation and the

percentage of English spoken (both currently and while growing up). Hence, the WASI can be used in ethnically diverse populations, but issues of language and culture need to be considered, especially with the verbal subtests.

The WASI has previously been used in published research with South African samples (e.g., Ferrett, Carey, Thomas, Tapert, & Fein, 2010; J. Hoare et al., 2012; Thornton et al., 2008). However, in the Thornton et al. study, the original WASI Vocabulary subtest was replaced by the Human Science Research Council South African standardization of the Vocabulary subtest from the Wechsler Adult Intelligence Scale-3rd version (WAIS-III, Wechsler, 1997; Claassen, Kraynauw, Paterson, & Mathe, 2001).

Working Memory & Attention. The *Numbers* subtest of the Children's Memory Scale (CMS; Cohen, 1997) and various subtests of the Test of Everyday Attention for Children (TEA-Ch; Manly, Robertson, Anderson, V., & Nimmo-Smith, 1999) were used to assess these cognitive processes.

Children's Memory Scale (CMS). The CMS battery was standardized and normed in the United States. It is designed for children and adolescents from 5 to 16 years of age.

Psychometric properties. The reliability coefficients for the core subtests of the battery range from .61 to .93 and from .65 to .93 for the supplemental subtests. The subtests can be administered to children and adolescents aged 5 to 16 years.

The process of establishing content validity included evaluations of trial versions of the CMS subtests. These evaluation phases served to eliminate certain subtests that were found to be redundant or unsatisfactory in terms of the degree of child-friendliness, content, bias and psychometric properties. Structure and content validity were evidenced by Pearson correlation coefficients ranging from .06 to .96 across all ages. Finally, support for criterion validity stemmed from studies of clinical populations (epilepsy, TBI, and brain tumours). *T*-test analyses showed that participants drawn from these populations displayed poorer performances than matched controls the CMS indices (Cohen, 1997) .

Numbers subtest of the CMS. The first component of this subtest, *Numbers Forward*, is a measure of simple attentional capacity. It requires that the participant repeat a string of random digits in the same sequence as read out loud by the examiner. The second component, *Numbers Backward*, requires participants to repeat the digits read by the examiner in the reverse order. This component measures working memory ability.

Both Numbers Forward and Numbers Backward are supplemental subtests. Reliability coefficients range from .71 to .83 and from .66 to .82 for these subtests,

respectively (Cohen, 1997).

Cross-cultural use / use in South Africa. Although subtests of the CMS are increasingly being employed in South African research (e.g., see Ferrett et al., 2010) and clinical practice in pediatric neuropsychology, there is still a paucity of published work using this battery with South African samples. Abroad, however, the CMS battery is employed more frequently in brain injury research (e.g., see Hawley, 2005; Hawley, 2004; Vella et al., 2007).

Cash (2008) investigated the performances of ethnically diverse groups (including Hispanic and African American students) on CMS subtests. Specifically, performances on short-term and working memory subtests were associated with ethnicity (used as a proxy for culture). However, this association was largely facilitated by parents' level of education.

The Test of Everyday Attention for Children (TEA-Ch). The brief screening version of the TEA-Ch (Manly et al., 1999) was used as the measure of attention. The TEA-Ch was developed, normed, and standardized in Australia for children and adolescents from 6 to 16 years of age. This battery consists of nine subtests that measure selective, sustained, and divided attention, as well as attentional control. The brief screening version of the instrument includes four of the nine subtests from each of the attentional domains listed above. These include: *Sky Search, Score!, Creature Counting,* and *Sky Search Dual Task (DT)*.

The Creature Counting subtest relies on the participants being able to count backwards from 10 to 0. It could not be administered if participants were unable to do so. This is a task that many children with severe TBI struggle with. Therefore, an additional subtest from the remaining 5 subtests of the TEA-Ch, the *Same World / Opposite World* subtest, was administered to all participants. This subtest also measures attentional control, but does not rely on the ability to count backwards from 10 to 0.

Psychometric properties. The reliability coefficients for the nine subtests of the TEA-Ch range from .57 to .87. Inter-correlations between the subtests are reportedly strong.

The test developers investigated the validity of the TEA-Ch by examining the fit between observed performances on the TEA-Ch subtests and three latent variables: selective attention, sustained attention, and attentional control, using a Structural Equation Model. Regression coefficients are high with CFI (Comparative Fit Index) = .937; NFI (Normed Fit Index) = .913; and NNFI (Non-Normed Fit Index) = .96. These indices are well above the fit index value of .90, where values ≥ .90 represent a good fit to the data. Hence, these statistics and psychometric properties depict a good fit between the major constructs measured by the TEA-Ch (i.e., selective attention, attentional control/switching, and sustained attention) and

the observed patterns of performance (Manly et al., 1999).

Sky Search. This subtest assesses selective and focused attention. It is divided into two parts, an attention and a motor control component. In the attention component, participants are required to circle as many pairs of target spaceships as possible on a sheet filled with pairs of both target and distractor ships, as quickly as they can. In the control component, participants are once again required to circle as many pairs of target spaceships as quickly as they can on a page that contains only those target spaceships and no distractor stimuli. The score of the motor control component is subtracted from the score of the attention component. This provides a final attention score for this subtest that is not confounded by motor slowness. The test-retest reliability coefficients for the time per target and attention score components of this subtest are .80 and .75, respectively.

Score! This subtest measures sustained attention. It requires that participants keep a mental count of the number of scoring sounds heard on a soundtrack, "as if (they) were keeping score by counting the number of scoring sounds in a computer game" (Manly et al., 1999, p. 10). The lengths of the pauses between sounds vary from very short to fairly long intervals, with no other stimuli, making this an appropriate measure of a participant's ability to sustain his/her own attention. The test-retest reliability coefficient for this subtest is 76.2%.

Creature Counting. This subtest is a measure of attentional control/switching. Participants are required to count the number of creatures in a burrow. However, while counting, they need to switch between counting upwards (1,2,3) and downwards (3, 2, 1). This switching is cued by up or down arrows placed at varying intervals in the burrow. There are two practice rounds and seven testing rounds. The test administrator records both the time taken to complete the task and the accuracy thereof. The test-retest reliability coefficients for the accuracy and timing components of this subtest are .71 and .57, respectively.

Same world / Opposite world. This task requires that participants are able to identify and name the numbers one and two. In the *same world* component, participants are simply required to read a random array of the numbers one and two as the examiner points to each number. In the *opposite world* component, participants complete a similar task; however this time, one is read as two and two is read as one. Both components are timed. There are two 'same world' and two 'opposite world' components in this subtest. The test-retest reliability coefficients for the Same World and Opposite World components of this subtest are .87 and .85, respectively.

Sky Search Dual Task (DT). This subtest is a measure of sustained and divided attention. Participants are required to complete a task that incorporates the attention

component of the Sky Search subtest and the '*Score!'* task (as described above), simultaneously. The test-retest reliability coefficient for this subtest is .81.

Cross-cultural use / use in South Africa. Chan, Wang, Ye, Leung, and Mok (2008) evaluated a Chinese version of the TEA-Ch in a sample of 232 healthy children. Psychometric properties, in terms of construct validity and test-retest reliability, remained acceptable, demonstrating cross-cultural application of the TEA-Ch.

Although the TEA-Ch has been used for research and clinical purposes in a number of published studies (Bellgrove et al., 2005; Heaton et al., 2001; Manly et al., 2001), there are none that have included South African samples. The TEA-Ch has however been used in unpublished South African work (Malgas, 2010; Schoeman, 2011) in the field of pediatric neuropsychology.

Verbal and visual memory. Verbal and visual/nonverbal memory were assessed using selected subtests from the *CMS* (Cohen, 1997). The Word List CMS subtest was used to assess verbal/auditory learning and memory, and the Dot Locations CMS subtest was used to assess visual memory. Visual memory was also assessed using the *Rey Complex Figure Test* (*RCFT*; Osterreith, 1944).

CMS subtests.

Word List. This subtest measures the child's ability to learn and recall a list of semantically unrelated words. On the immediate recall component, participants are read a list of words and are then asked immediately to recall as many words as they can remember. There are four such trials. On the subsequent three trials, the participant is reminded only of those words that he/she has forgotten, and then asked again to recall as many words as possible. A distracter list of words is then presented and participants are asked to recall as many words as possible from that list. On the next trial, participants are once again required to recall as many words as from the first list as they can remember, without being reminded of those particular words. The delayed recall component of the task is conducted approximately 25-30 minutes later. Participants are once again asked to recall as many words from the first list of words as they can remember.

Word Lists is a supplemental subtest. Reliability coefficients range from .66 to .89 for the different components of this subtest (Cohen, 1997).

Dot Locations. This subtest measures the child's ability to learn and remember the spatial layout of an array of dots. As with the CMS Word List subtest, this subtest consists of three phases. In the immediate recall component, the participant is presented with a picture of

an array of blue dots for 5 seconds. Following this presentation, the participant is asked to reproduce the distribution on either a 3x4 or 4x4 grid, depending on his/her age, using blue plastic chips. There are three such trials. A distractor array with red dots is then displayed for 5 seconds, and the participant has to reproduce this new distribution using the same grid and the same blue chips. Thereafter, the participant is asked once again to reproduce the first array of blue dots, without exposure to the original array. The delayed recall component of the task is conducted approximately 25-30 minutes later. Participants are once again asked to reproduce the first array of blue dots.

Dot Locations is primarily a core battery subtest. Reliability coefficients for this subtest ranges from .61 to .82. The short delay component of the task forms part of the supplemental subtests, however. The reliability coefficients for this component range from .52 to .57 (Cohen, 1997).

Rey Complex Figure Test (RCFT). The immediate and delayed recall components of the RCFT (Osterreith, 1944) assessed visual memory. Although it was standardized and normed in the Canada, RCFT normative data from many countries are available for age groups ranging from 6 to 89 years (Meyers & Meyers, 1995; Mitrushina, Boone, & DíElia, 1999).

In this test, the child is presented with a copy of the two-dimensional figure and asked to reproduce it on a sheet of paper provided as accurately as possible, using a pencil. The time taken to complete the copy was recorded. The child was then required to recall the figure 3 minutes and 30 minutes after completing the copy. These were the immediate and delayed components of the task, respectively. These recall components provided an assessment of a more complex figural form of visual memory that the Dot Locations subtest.

I used the Rey (1941) 36-point scoring system to assess the recalled figures, which measures the accuracy and placement of 18 details of the figure. Each of these details is scored from 0.5 to 2; hence the highest score is 36 (Lezak, Howieson, Loring, Hannay, & Fischer, 2004).

Psychometric properties. Poulton and Moffitt, (1995) investigated the construct and predictive validity of the RCFT in a nonclinical sample of 13-year-old children in New Zealand. In their correlation analyses, they found that poor performances on the RCFT were matched by poor performances on the Block Design and Object Assembly subtests of the Wechsler Intelligence Scale for Children-Revised (WISC-R; Wechsler, 1974).

Stern, Singer, Duke, and Singer (1994) reported on internal consistency and interrater reliabilities for the RCFT. These data were collected in an adolescent and adult sample and

using the Boston Qualitative Scoring System (BQSS) to score the RCFT. Internal consistency and interrater reliability coefficients ranged from 0.7774 to 0.9128, and from 0.6342 to 0.9919, respectively.

Cross-cultural use / use in South Africa. Although no specific South African norms exist, this test is commonly used in clinical neuropsychological practice and research in South Africa (e.g., Ferrett et al., 2010; J. Hoare et al., 2012). Further, Demsky, Carone Jr., Burns, and Sellers (2000) investigated the test validity of the RCFT in a sample of 6- to 11-year-olds ($N = 432$) of various ethnicities, including White, Black and Hispanic. These authors found that test performance was independent of race or sex of participants.

Visuoconstructional Abilities. I used the copy component of the RCFT (Osterreith, 1944) to assess visuoconstructional abilities. The scoring procedure for this component of the RCFT is the same as described in the previous section.

Executive functions. I assessed inhibition using the relevant subtest from the NEPSY-II (Korkman, Kirk, & Kemp, 2007). This test battery was developed for individuals aged 5 to 16 years of age and was normed and standardized in the United States.

Psychometric properties. The NEPSY-II test developers used inter-rater and inter-scorer agreement, subtest internal consistency, and test-retest stability to determine test reliability. Stability coefficients range from .62 to .89, demonstrating the stability of the test across time and age groups. Studies of content validity showed that the test is able to distinguish between healthy children and those with known neurodevelopmental disorders (including learning disabilities, attention deficit/hyperactivity disorder, TBI, autistic disorders, and speech and learning impairment). Construct validity is also reported, based on concurrent validity studies with other measures and clinical group studies (Korkman et al., 2007).

Inhibition. This subtest measures the participants' capacity to inhibit prepotent responses in favour of those responses that the task requires. The subtest also measures the ability to switch between these response types. There are three conditions to this subtest: *Naming*, *Inhibition*, and *Switching.*

These conditions are repeated over two trials using black and white shapes (squares and circles) in the first trial and the direction in which arrows are pointing (up or down) in the second trial. In the Naming condition, the participant is required to name the black and white stimuli (either shapes or the direction of the arrows). In the Inhibition condition, he/she is required to provide the alternate response, depending on the colour of the shape or direction of the arrow. For example, the participant is required to say "circle" for "square" and vice-

versa, or "up" when he/she sees a "down" arrow, and vice-versa. Finally, in the Switching condition, participants are required to say the shape or arrow's correct name when it is black and the alternate response when it is white. For example, he/she would say "square" when he/she sees a black square and "circle" when he/she sees a white square (Korkman et al., 2007).

Cross-cultural use / use in South Africa.

Mulenga, Ahonen, and Aro (2001) compared the performances of Zambian and American children using the original NEPSY. Their results showed that the NEPSY was relatively unaffected by language and cultural factors, although these factors should always be taken into account in cross-cultural application of Western based assessment instruments. Hence, one might assume it suitable for use in the multi-cultural South African context. Although the NEPSY battery is being used more frequently in clinical practice, there are, however, limited published studies using either the NEPSY or NEPSY-II with South African populations (J. Hoare et al., 2012). It has been used in unpublished research studies in pediatric neuropsychology (Malgas, 2010; Schoeman, 2011).

Behavioural measures

I used the Child Behaviour Checklist (CBCL; Achenbach, 1991) and the Behaviour Rating Inventory of Executive Functions (*BRIEF;* Gioia, Isquith, Guy, & Kenworthy, 2000) to measure behaviour.

The selection of tests was also guided by published literature employing these measures (Dooley, Anderson, Hemphill, & Ohan, 2008; Ganesalingam et al., 2011; Karver et al., 2012; Mangeot, Armstrong, Colvin, Yeates, & Taylor, 2002; Wilson, Donders, & Nguyen, 2011).

The Child Behaviour Checklist (CBCL). The CBCL (Achenbach, 1991) is used to assess behavioural problems and competencies in children and adolescents aged 6 to 18 years. There are both parent / guardian and teacher versions of this measure, as the measure relates to both home and school environments. I used the parent / guardian version for Study 2 and both the parent / guardian and teacher versions for Study 3.

The CBCL measures competence in various functional domains, using different scales or profiles. I used the externalizing and internalizing syndrome groupings. These groupings are commonly reported in TBI research (Cole et al., 2008; Fletcher, Ewing-Cobbs, Miner, Levin, & Eisenberg, 1990; Wassenberg, Max, Koele, & Firme, 2004). Internalizing scales provide information about depression / withdrawal, anxiety and other somatic behaviors. The externalizing scales determine the presence of cruel, aggressive, or delinquent behaviors

(Achenbach, 1991).

Responses are scored on a Likert-type scale. There are three possible responses: "very often true"; "somewhat or sometimes true"; or "never true". *T*-scores for these scales ranging from 60 to 65 are classified as 'borderline' and *t*-scores above 65 are classified as being in the 'clinical' range.

Psychometric properties. The CBCL has sound psychometric properties, including test-retest reliability coefficients of 0.95-1.00, inter-rater reliability coefficients from 0.93 to 0.96 and internal consistency of 0.78-0.97. These properties hold for the numerous translated versions of this measure (Albores-Gallo et al., 2007).

Cross-cultural use / use in South Africa. Although the CBCL is being used more frequently in clinical practice, there are limited published (e.g., Cluver, Gardner, & Operario, 2007; Shields, Nadasen, & Pierce, 2008) and unpublished (e.g., Cheesman, 2011; Fischer, 2009) studies using the CBCL with South African populations. The CBCL has also been used in the broader African context. Appoh (2004) used this measure in investigating the effects of malnutrition in a sample of Ghanaian children (n = 54), 8-16 years of age, and their matched controls. Those children who were malnourished in the first three years of life reported more internalizing behaviour problems than those who were not.

The Behaviour Rating Inventory of Executive Functions (*BRIEF).*

The *BRIEF* (Gioia, Isquith, Guy, & Kenworthy, 2000) is used to assess behavioural aspects of executive functions in children aged 5 to 18 years of age. It provides a measure of participants' everyday behaviours, including their ability for self-regulation in problem solving situations. There are both parent / guardian and teacher versions of this measure, as the measure relates social functioning in both in the home and the school context (Gioia & Isquith, 2008; Malloy & Grace, 2005).

There are 86 items in the questionnaires. These combine to form two indices, with several subscales. The two main indices are the Behavioural Regulation Index (BRI) and the Metacognition Index (MI). The BRI includes the Inhibit, Shift, and Emotional Control subscales and the MI includes the Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor subscales. The BRI and MI can also be combined to form a Global Executive Composite (GEC) score (Gioia et al., 2000).

Psychometric properties. In terms of the BRIEF's psychometric properties, both high internal consistency and test-retest reliability have been reported. In terms of internal consistency, coefficients ranged from .80 to .98 for both parent and teacher forms across both clinical and normative samples. In terms of test-retest reliability, correlations ranged from .72

to .92 for parent and teacher form normative samples and the parent form clinical sample (Baron, 2000; Gioia et al., 2000; Malloy & Grace, 2005).

Cross-cultural use / use in South Africa. Although the BRIEF is being used more frequently in clinical practice, there is, however, no published literature using the instrument with South African populations. However, the cross-cultural application of the BRIEF has been demonstrated. Qian, Shuai, Cao, Chan, and Wang (2010) compared the executive functioning of Han Chinese children with ADHD (n = 89) to those with ADHD and OCD (n = 53) using the parent BRIEF form. Both groups performed worse than controls and ADHD and OCD group performed worse than ADHD group. These findings are consistent with findings in Western-based studies.

APPENDIX D
PERMISSION TO ACCESS SCHOOLS FROM THE WESTERN CAPE EDUCATION DEPARTMENT

Navrae
Enquiries
IMibuzo **Dr RS Cornelissen**

Telefoon
Telephone
IFoni **(021) 467-2286**

Faks
Fax
IFeksi **(021) 425-7445**

Verwysing
Reference
ISalathiso **20090428-0002**

Wes-Kaap Onderwysdepartement

Western Cape Education Department

ISebe leMfundo leNtshona Koloni

Miss Leigh Schrieff
Department of Psychology
University of Cape Town
Private Bag
RONDEBOSCH
7700

Dear Miss L. Schrieff

RESEARCH PROPOSAL: THE IMPLEMENTATION AND EVALUATION OF A COGNITIVE REHABILITATION SERVICE FOR CHILDREN FOLLOWING TRAUMATIC BRAIN INJURY.

Your application to conduct the above-mentioned research in schools in the Western Cape has been approved subject to the following conditions:

1. Principals, educators and learners are under no obligation to assist you in your investigation.
2. Principals, educators, learners and schools should not be identifiable in any way from the results of the investigation.
3. You make all the arrangements concerning your investigation.
4. Educators' programmes are not to be interrupted.
5. The Study is to be conducted from **6th May 2009 to 30th September 2009**.
6. No research can be conducted during the fourth term as schools are preparing and finalizing syllabi for examinations (October to December).
7. Should you wish to extend the period of your survey, please contact Dr R. Cornelissen at the contact numbers above quoting the reference number.
8. A photocopy of this letter is submitted to the principal where the intended research is to be conducted.
9. Your research will be limited to the list of schools as forwarded to the Western Cape Education Department.
10. A brief summary of the content, findings and recommendations is provided to the Director: Research Services.
11. The Department receives a copy of the completed report/dissertation/thesis addressed to:

    The Director: Research Services
    Western Cape Education Department
    Private Bag X9114
    CAPE TOWN
    8000

We wish you success in your research.

Kind regards.

Signed: Ronald S. Cornelissen
for: **HEAD: EDUCATION**
DATE: 6th May 2009

APPENDIX E
STUDY 2: ASSENT FORM

University of Cape Town
Department of Psychology

Assent form for Child/Adolescent Participants

1. Name of Participant ("Study Subject")

I am going to be asked to play some games and do some puzzles. I will also be asked some questions about myself, my feelings, and my thoughts, and some problems I might be having. The person who is going to ask me the questions has told me that I can stop if I am feeling tired and need to take a break, and that nobody else will be told my answers to the questions.

_____ _____
Signature of Child Date

_____ _____
Signature of Researcher Date

APPENDIX F
STUDY 2: CONSENT FORM

Informed Consent to Participate in Research and Authorization for Collection, Use, and Disclosure of Cognitive Performance and Other Personal Data

You are being asked to take part in a research study. This form provides you with information about the study and seeks your authorization for the collection, use and disclosure of your cognitive performance data, as well as other information necessary for the study. The Principal Investigator (the person in charge of this research) or a representative of the Principal Investigator will also describe this study to you and answer all of your questions. Your participation is entirely voluntary. Before you decide whether or not to take part, read the information below and ask questions about anything you do not understand. By participating in this study you will not be penalized or lose any benefits to which you would otherwise be entitled.

1. Name of Participant ("Study Subject")

_____

2. Title of Research Study

Cognitive Function in Children with Head Injury

3. Principal Investigator(s) and Telephone Number(s)

Kevin G. F. Thomas, Ph.D.
Senior Lecturer
Department of Psychology
University of Cape Town
021-650-4608

Leigh Schrieff, M.A.
Ph.D. Candidate
Department of Psychology
University of Cape Town
078-559-2997

4. Source of Funding or Other Material Support

None

5. What is the purpose of this research study?

The purpose of this research study is to better understand cognitive functioning (thinking and reasoning and remembering) in children who have experienced a head injury.

5. What will be done if your child takes part in this research study?

In this study, your child will be administered a series of paper-and-pencil cognitive tests. These tests measure attention, memory, thinking, problem-solving, and reasoning.

Your child's testing sessions will be held at a location of your preference. Possible locations are the University of Cape Town's Department of Psychology or Red Cross War Memorial Hospital. Each testing session will be individually conducted by either the principal investigators or a trained member of their research team. You or another caregiver may be present at the testing session.

After the testing sessions are over, you will be informed in detail about the design of the study and the research questions we hope to answer. You will also have the opportunity to ask questions and thus learn more about psychological research.

If you have any questions now or at any time during the study, you may contact the Principal Investigators listed in #3 of this form.

6. If you choose to allow your child to participate in this study, how long will he/she be expected to participate in the research?

The study consists of 2 sessions, both of which will last longer approximately 2.5 hours. If at any time during the experiment you or your child finds any of the procedures uncomfortable, you are free to discontinue participation without penalty.

7. How many children are expected to participate in the research?

20

8. What are the possible discomforts and risks?

There are no known risks associated with participation in this study. The only possible discomfort your child may experience is slight fatigue. If he/she becomes tired during any of the procedures, we will take a break. Your child will be allowed to take breaks whenever requested. You may find out that some of your child's thinking and memory abilities are worse than you expected, and this may cause some sadness or distress. If this happens, we will talk with you and give a referral for care.

If you wish to discuss the information above or any discomforts you or your child may experience, you may ask questions now or call the Principal Investigators listed on the front page of this form.

10a. What are the possible benefits to you and your child?

You and your child may or may not personally benefit from participating in this study. Participation in this study may, however, improve your child's mental test performance due to training and practice.

By you and your child partaking in the neuropsychological assessment, this will provide you with a deeper understanding of the functioning of your child.

10b. What are the possible benefits to others?

The information from this study may help improve our understanding of head injuries in children, particularly with regard to the effects of head injury on memory, thinking, reasoning, and attention. Because the study aims to understand how head-injured children compare to children with no history of head injury, any information we obtain might benefit the future diagnosis and treatment of head injury.

Additionally, this research will allow us to gather information about how healthy children perform on the administered tests. This research can then be applied to people who have experienced a traumatic brain injury.

11. If you choose to take part in this research study, will it cost you anything?

Participating in this study will not cost you anything.

12. Will you receive compensation for taking part in this research study?

You will receive R100.00 for taking part in this study. R25.00 will be paid to you after your first visit, and R75.00 will be paid to you after the second visit.

13a. Can you withdraw your child from this study?

You are free to withdraw your consent and to stop participating in this research study at any time. If you do withdraw your consent, there will be no penalty.

If you have any questions regarding your child's rights as a research participant, and your rights as the individual granting consent for research participation, you may phone the Psychology Department offices at 021-650-3430.

13b. If you withdraw your child from this study, can information about you still be used and/or collected?

Information already collected may be used.

14. Once personal and performance information is collected, how will it be kept secret (confidential) in order to protect your privacy?

Information collected will be stored in locked filing cabinets or in computers with security passwords. Only certain people have the right to review these research records. These people include the researchers for this study and certain University of Cape Town officials. Your research records will not be released without your permission unless required by law or a court order.

15. What information about your child may be collected, used and shared with others?

The information gathered from your child will be demographic information and records of his/her performance on cognitive tests. If you agree that your child can be in this research study, it is possible that some of the information collected might be copied into a "limited data set" to be used for other research purposes. If so, the limited data set may only include information that does not directly identify you or your child. For example, the limited data set cannot include your or your child's name, address, telephone number, ID number, or any other photographs, numbers, codes, or so forth that link you or your child to the information in the limited data set.

The results of the research will be presented as part of an Honours research project for the University of Cape Town. Also, the results may be submitted for publication in a peer-reviewed journal. In both instances neither you nor your child will be identified in any way.

16. What should you tell your child?

You may wish to discuss the study with your child to find out determine whether he/she feels comfortable taking part. Your child should know that he/she can choose not to participate in the study. Your child should also know that if he/she does choose to participate, he/she can withdraw at any time during the study with no negative consequences.

17. How will the researcher(s) benefit from your being in the study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator and others attached to this research project may benefit if the results of this study are presented at scientific meetings or in scientific journals.

18. Signatures

As a representative of this study, I have explained to the parent/guardian of the participant the purpose, the procedures, the possible benefits, and the risks of this research study; and how the participant's performance and other data will be collected, used, and shared with others:

_____ _____
Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; and how your child's performance and other data will be collected, used and shared with others. You have received a copy of this form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

You voluntarily consent to allow your child to participate in this study. You hereby authorize the collection, use and sharing of your child's performance and other data. By signing this form, you are not waiving any of your legal rights.

_____ _____
Signature of Person Consenting and Authorizing Date

Please indicate below if you would like to be notified of future research projects conducted by our research group:
_____ (initial) Yes, I would like to be added to your research participation pool and be notified of research projects in which I or my child might participate in the future.

Method of contact:

Phone number: _____
E-mail address: _____
Mailing address: _____
_____
_____

APPENDIX G

BETWEEN-GROUP COMPARISONS FOR IQ VARIABLES AND NEUROPSYCHOLOGICAL COMPOSITES AFTER THE REMOVAL OF OUTLIERS: TBI VS. CONTROLS

Table G1

IQ Variables and Neuropsychological Composites: Between-group comparisons for TBI vs. Controls (N = 22) after the removal of outliers

	TBI			Controls			Test statistics		
	n	Range	*M* (*SD*)	*n*	Range	*M* (*SD*)	*F/U*	*p*	*r*
General Intellectual Functioning									
VIQ	9	70-89	77.22 (6.02)	11	66-119	86.45 (15.28)	32.00[a]	.097	-.28
PIQ	10	67-86	79.40 (5.74)	9	79-91	85.00 (3.87)	6.07	.013*	.51
FSIQ	9	66-84	75.78 (5.17)	9	74-88	81.33 (4.58)	5.82	.014*	.52
Verbal Memory Composite (α = .929)	11	-2.20-1.37	-0.40 (1.15)	9	0.14-0.76	0.40 (0.24)	29.50[a]	.068	-.32
Executive Functions Composite (α =.774)	10	-1.83-0.65	-0.42 (0.69)	10	-0.36-1.18	0.36 (0.41)	9.41	.004**	.59
Visuospatial Skills Composite (α = .626)	10	-1.17-0.71	-0.16 (0.55)	10	-0.54-1.39	0.23 (0.54)	2.51	.066	.35

Note. For qualitative descriptions for VIQ, PIQ and FSIQ, see Appendix I. [a]Mann-Whitney *U*; for VIQ, mean rank of the TBI group = 8.56 and of the Control group = 12.09; for Verbal Memory Composite, mean rank of the TBI group = 8.68 and of the Control group = 12.72. The *r* value presented here is an estimate of effect size.

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

APPENDIX H

STUDY 2: SUBTESTS MAKING UP COMPOSITES: TBI vs. CONTROLS

Table H1

Subtests making up Neuropsychological Composites: Between-group Comparisons for TBI vs. Controls (*N* = 22)

	TBI			Controls			Test statistics		
	n	Range	*M* (*SD*)	*n*	Range	*M* (*SD*)	*F/U*	*p*	*r*
Basic Attention Composite (α = .753)									
Sky search targets	11	2-13	8.45 (3.86)	11	6-14	10.64 (2.84)	2.28	.146	.320
Sky search time per target	11	1-9	4.09 (3.62)	11	2-11	6.64 (2.94)	33.5[a]	.037*	-.383
Attention score	11	1-13	5.36 (4.55)	11	2-13	7.73 (3.38)	40.0[a]	.092	-.289
Map mission	10	1-9	4.60 (2.37)	11	2-10	6.27 (2.69)	2.27	.148	.327
Score	11	2-13	6.36 (3.64)	11	3-13	8.91 (2.95)	3.25	.087	.374
Numbers forward	11	2-10	5.64 (2.73)	11	4-12	8.27 (2.41)	5.76	.026*	.473
Higher-Order Attention Composite (α =.828)									
Sky search DT	10	1-8	2.70 (2.36)	11	1-11	7.18 (2.75)	14.00[a]	.001**	-.625
Opposite worlds	10	1-6	2.80 (1.99)	11	1-10	5.82 (2.64)	19.00[a]	.004**	-.546

Inhibition switching combined	9	1-10	5.22 (2.68)	11	1-12	7.36 (3.47)	2.294	.147	.336
Inhibition switching CT	9	2-8	5.78 (1.99)	11	3-14	8.55 (3.27)	23.5[a]	.023*	-.425
Inhibition total errors	9	1-8	3.56 (2.92)	11	1-11	6.82 (3.34)	21.00[a]	.014*	-.467
Verbal memory composite (α =0.929)									
Word list learning	11	1-14	7.82 (4.79)	11	6-16	10.64 (2.42)	45.00[a]	.160	-.219
Word list delayed	11	1-17	8.82 (4.71)	11	8-16	12.45 (2.51)	5.115	.035*	.451
Visual memory composite (α =0.771)									
Dot locations learning	11	3-13	7.91 (3.35)	11	2-14	10.73 (3.44)	33.5[a]	.038*	-.381
Dot locations total	11	4-13	8.45 (3.39)	11	4-15	11.27 (3.13)	4.103	.056	.413
Dot locations delayed	11	7-13	9.55 (2.38)	11	8-13	11.36 (1.75)	4.167	.055	.415
REY immediate recall	10	28-50	34.5 (6.29)	11	36-65	50 (10.32)	6.5[a]	.000**	-.730
REY delayed recall	10	22-48	35.3 (8.54)	11	34-67	48.45 (11.23)	10.67	.004**	.600
Executive functions composite (α = 0.774)									
Numbers backward	11	2-13	6.45 (3.62)	11	2-13	7.82 (3.74)	0.757	.395	.191

Inhibition-Inhibition combined	10	1-8	3.80 (2.39)	11	2-11	7.45 (2.81)	10.199	.005**	.591
Inhibition-Inhibition CT	10	1-8	5.00 (2.31)	11	5-12	8.18 (2.14)	10.761	.004**	.601
WASI similarities	11	20-56	37.27 (9.67)	11	28-62	43.73 (11.51)	2.029	.170	.304
WASI matrix reasoning	11	20-43	32.82 (6.84)	11	34-48	42.09 (5.24)	12.738	.002**	.624
Visuospatial skills composite (α =0.626)									
REY copy	11	3-30.5	19.68 (8.89)	11	20-35	29.09 (4.97)	9.381	.006**	.565
REY copy timing (sec)	11	111-571	281.73 (167.57)	10	139-386	252.20 (89.58)	53.00[a]	.452	-.042
WASI block design	11	23-48	37.18 (7.51)	11	35-63	42.91 (9.12)	42.00[a]	.117	-.260
Expressive language composite (α =0.683)									
Inhibition-naming combined	11	1-12	3.64 (3.56)	11	1-10	6.82 (2.56)	25.5[a]	.009**	-.496
Inhibition-naming CT	11	1-7	3.55 (2.34)	11	3-10	7.55 (2.34)	16.080	.001**	.668
WASI Vocabulary	11	20-51	31.55 (9.90)	11	20-61	36.91 (11.18)	1.421	.247	.258

Note. [a]Mann-Whitney *U*. The *r* value presented here is an estimate of effect size.

*$p < 0.05$. **$p < 0.01$.

APPENDIX I

QUALITATIVE DESCRIPTIONS OF WASI IQ SCORES

Qualitative Descriptions of WASI Scores

IQ Scores	Classification
130 and above	Very Superior
120 – 129	Superior
110 – 119	High Average
90 – 109	Average
80 – 89	Low Average
70 – 79	Borderline
69 and below	Extremely Low

Note. Taken from Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999).

APPENDIX J

BETWEEN-GROUP COMPARISONS FOR BRIEF INDICES AFTER THE REMOVAL OF OUTLIERS: TBI VS. CONTROLS

Appendix J1
BRIEF Indices: Between-group comparisons for TBI vs. Controls (N = 22) after the removal of outliers

	Group								
	TBI			Controls					
Indices	*n*	Range	*M* (*SD*)	*n*	Range	*M* (*SD*)	*F*/*U*	*p*	*r*
Inhibit	8	66-94	75.00 (9.26)	11	42-65	54.18 (7.40)	0.00[a]	< .001***	.78
Shift	11	53-80	67.64 (7.83)	10	41-60	49.20 (6.03)	35.98[b]	< .001***	.81
BRI	8	65-86	74.63 (6.12)	11	39-62	52.09 (7.62)	47.44[d]	< .001***	.86
Initiate	11	53-80	64.45 (9.52)	10	38-63	51.10 (7.59)	15.00[a]	.002**	.61
Working memory	10	65-84	72.10 (5.97)	10	40-63	52.30 (7.54)	42.36[c]	< .001***	.84
Plan/organization	10	63-84	71.20 (5.77)	11	37-69	51.18 (10.69)	27.67[b]	< .001***	.77
Monitor	11	47-84	65.27 (11.15)	10	43-72	54.40 (8.18)	6.38[b]	.011*	.50
MI	9	64-80	72.00 (6.04)	10	41-64	52.00 (6.57)	47.37[d]	< .001***	.86
GEC	9	69-85	75.44 (4.88)	11	36-67	51.91 (8.93)	50.00[c]	< .001***	.77

Note. BRI = Behaviour Regulation Index; Org. of materials = Organization of materials; MI = Metacognition Index; GEC Global Executive Composite. [a]Mann-Whitney *U*; for Inhibit, mean rank of the TBI group = 15.50 and of the Control group = 6.00; for Initiate, mean rank of the TBI group = 14.64 and of the Control group = 7.00. [b]degrees of freedom = (1, 19); [c]degrees of freedom = (1, 18); [d]degrees of freedom = (1, 17). The *r* value presented here is an estimate of effect size.
*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

APPENDIX K

BETWEEN-GROUP COMPARISONS FOR CBCL SYNDROME PROFILES AFTER THE REMOVAL OF OUTLIERS: TBI VS. CONTROLS

Table K1

CBCL Syndrome Profiles: Between-group comparisons for TBI vs. Controls (N = 22) after the removal of outliers

	Group								
	TBI group			Healthy control group					
CBCL syndrome profiles	*n*	Range	*M* (*SD*)	*n*	Range	*M* (*SD*)	*F/U*	*p*	*r*
Anxious/Depressed	10	51-69	60.50 (5.36)	10	50-65	55.70 (5.25)	4.09[b]	.029*	.43
Somatic Complaints	11	50-74	60.73 (8.39)	9	57-72	64.44 (4.42)	35.00[a]	.137	-.24
Internalizing Problems	10	54-71	63.50 (5.15)	10	48-77	62.30 (8.02)	0.16[b]	.329	.09
Aggressive Behaviour	10	57-76	67.60 (6.26)	10	50-55	52.60 (1.43)	0.00[a]	<.001**	-.81

Note. [a]Mann-Whitney *U*; for Somatic Complaints, mean rank of the TBI group = 9.18 and of the Control group = 12.11; for Aggressive Behaviour, mean rank of the TBI group = 15.50 and of the Control group = 5.50. [b]Degrees of freedom = (1, 18). The *r* value presented here is an estimate of effect size.
*$p < 0.05$. **$p < 0.01$.

APPENDIX L

BETWEEN-GROUP DIFFERENCES IN TIME SINCE INJURY AFTER THE REMOVAL OF OUTLIERS: HYPOXIA vs. NO HYPOXIA GROUPS

The figure below shows that there was one outlier for the Time since injury variable for the pTBI/hypoxia group. The between-group difference was still significant even after the removal of this outlier, however, $F(1, 8) = 7.89$; $p = .02$).

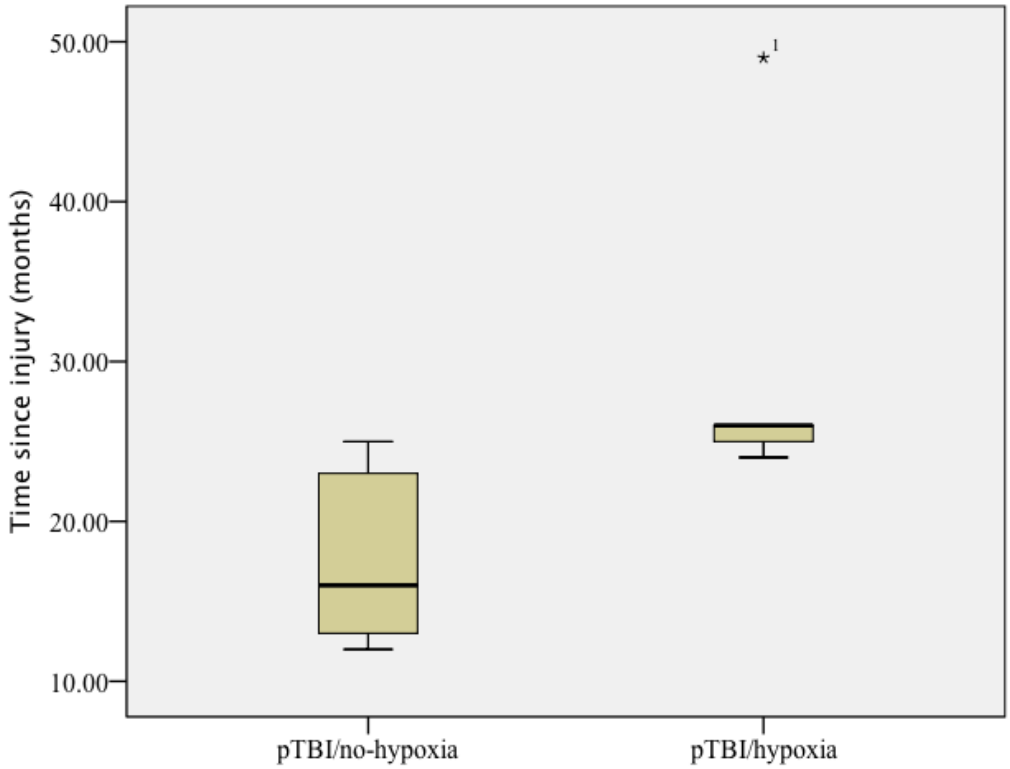


Figure L1. Box plot for *Time since injury* variable.

APPENDIX M

BETWEEN-GROUP COMPARISONS FOR CONTINUOUS NEUROSURGICAL VARIABLES: HYPOXIA vs. NO HYPOXIA

Table M1

Descriptive Statistics for Continuous Neurosurgical Variables: Hypoxia vs. No Hypoxia, after the removal of outliers

	Group									
	Hypoxia				No Hypoxia					
Variable	*n*	*M* (*SD*)	Range	Mean rank	*n*	*M* (*SD*)	Range	Mean rank	*F* /*U*	*p*	*r*
Mean ICP value > 20	4	27.40 (3.44)	23-31	8.00	6	11.72 (12.88)	0-25	3.83	2.00	.033*	-.65
Number of episodes: $PbtO_2$ < 10	4	2.75 (2.06)	1-5	8.50	6	0.00 (0.00)	0-0	3.50	0.00	.005**	-.87
Lowest PaO_2 value	4	9.63 (0.51)	9.1-10.2	3.50	6	13.16 (3.37)	8-16.7	6.83	4.00	.114	-.51
Lowest $PbtO_2$	4	6.83 (1.20)	6-8		5	15.00 (2.73)	12-18		30.37 [a]	.001**	.90

Note. Means and ranges are presented with standard deviations in parentheses.[a] *F*-statistic; degrees of freedom were (1, 7) in this case. The *r* value presented here is an estimate of effect size.

*$p < 0.05$. **$p < 0.01$.

APPENDIX N

SPEARMAN'S RHO CORRELATIONS FOR NEUROSURGICAL VARIABLES

Table N1

Spearman's Rho Correlation Matrix for Neurosurgical Variables.

		Initial MAP	Initial hypoxia	Initial SBP<90	Poly-trauma	ICP > 20	Mean ICP > 20	Mean ICP first 24	Mean ICP
	ρ	1.00	-0.40	-0.84**	0	-0.35	-0.15	-0.13	-0.21
Initial MAP	*p*	.	.222	.001	1.000	.288	.656	.698	.544
Initial	ρ		1.00	0.42	-0.29	-0.41	-0.40	-0.30	-0.50
hypoxia	*p*		.	.200	.389	.217	.218	.369	.116
Initial SBP	ρ			1.00	0.07	-0,03	-0.12	-0,21	-0,09
< 90	*p*			.	.840	.930	.724	.536	.793
	ρ				1.00	0.03	0	-0.15	0.15
Poly-trauma	*p*				.	.932	1.000	.671	.671
	ρ					1.00	.71*	.75**	.81**
ICP > 20	*p*					.	.014	.008	.003
Mean ICP	ρ						1.00	.92**	.82**
> 20	*p*						.	0	.002
Mean ICP	ρ							1.00	.85**
first 24	*p*							.	.001
	ρ								1.00
Mean ICP	*p*								.
	ρ								
Highest ICP	*p*								
	ρ								
Lowest CPP	*p*								
	ρ								
CPP < 40	*p*								
	ρ								
CPP < 50	*p*								
	ρ								
PaO2 < 8	*p*								
Lowest	ρ								
PaO_2	*p*								
	ρ								
Mean PaO_2	*p*								
	ρ								
Lowest Hb	*p*								
	ρ								
Mean Hb	*p*								
	ρ								
Sats < 90	*p*								
Lowest	ρ								
$PbtO_2$	*p*								
	ρ								
$PbtO_2$ < 5	*p*								
	ρ								
$PbtO_2$ < 10	*p*								
	ρ								
$PbtO_2$ < 20	*p*								

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

		Highest ICP	Lowest CPP	CPP < 40	CPP < 50	PaO_2 < 8	Lowest PaO_2	Mean PaO_2
	ρ	-0.24	-0.28	0	0.27	0.35	0.06	-0.39
Initial MAP	*p*	.483	.399	1.000	.426	.289	.873	.239
Initial	ρ	-0.30	0.50	-0.19	-0.41	-0.15	0.10	-0.10
hypoxia	*p*	.370	.116	.574	.212	.663	.770	.770
Initial SBP	ρ	-0.18	0.54	-0.46	-0.37	-0.36	0,06	0,12
< 90	*p*	.598	.087	.159	.268	.285	.861	.726
	ρ	-0.12	0.20	-0.15	0.09	0.51	-0.06	-0.17
Poly-trauma	*p*	.735	.550	.667	.796	.106	.866	.611
	ρ	.88**	-.62*	0.71*	0.39	0.19	-0.45	0,23
ICP > 20	*p*	<.001	.042	.014	.239	.574	.169	.496
Mean ICP	ρ	.90**	-.81**	0.57	0.52	0.11	-0,44	-0.09
> 20	*p*	<.001	.003	.066	.105	.750	.175	.788
Mean ICP	ρ	.93**	-.82**	0.66*	0.40	0.06	-0.34	-0,05
first 24	*p*	<.001	.002	.027	.229	.859	.304	.884
	ρ	.81**	-0.58	0.66*	0.28	0.06	-0.19	0.10
Mean ICP	*p*	.002	.060	.027	.398	.859	.582	.780
	ρ	1.00	-.82**	0.79**	0.52	0.19	-0.54	0.06
Highest ICP	*p*	.	.002	.004	.105	.578	.089	.873
	ρ		1.00	-0.60	-0.74**	-0.31	0.58	0.13
Lowest CPP	*p*		.	.053	.009	.352	.060	.709
	ρ			1.00	0,39	0.28	-0.36	0.12
CPP < 40	*p*			.	.236	.399	.271	.735
	ρ				1.00	0.63*	-0.89**	-0.14
CPP < 50	*p*				.	.036	0	.683
	ρ					1.00	-0.67*	-0.54
PaO2 < 8	*p*					.	.023	.087
Lowest	ρ						1.00	0.22
PaO_2	*p*						.	.519
	ρ							1.00
Mean PaO_2	*p*							.
	ρ							
Lowest Hb	*p*							
	ρ							
Mean Hb	*p*							
	ρ							
Sats < 90	*p*							
Lowest	ρ							
$PbtO_2$	*p*							
	ρ							
$PbtO_2$ < 5	*p*							
	ρ							
$PbtO_2$ < 10	*p*							
	ρ							
$PbtO_2$ < 20	*p*							

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

		Lowest Hb	Mean Hb	Sats < 90	Lowest $PbtO_2$	$PbtO_2$ < 5	$PbtO_2$ < 10	$PbtO_2$ < 20	Mean $PbtO_2$ 24hrs
	ρ	-0.24	-.87**	-0.06	0.51	-0,05	-0.37	-.81**	0.32
Initial MAP	*p*	.469	.001	.870	.113	.884	.261	.003	.332
Initial hypoxia	ρ	0.50	0.50	-0.05	0.10	-0.10	-0.27	0.10	-0.20
	p	.116	.117	.881	.770	.770	.416	.769	.555
Initial SBP < 90	ρ	0.42	.66*	-0.09	-0.18	-0.24	0.20	0.54	-0.30
	p	.199	.028	.787	.598	.479	.563	.087	.372
	ρ	-0.38	-0.23	-0.12	0.23	-0.29	-0.19	-0.12	0.40
Poly-trauma	*p*	.254	.494	.728	.494	.389	.577	.735	.218
	ρ	-0,15	0.39	0,27	-0.72*	0.25	0.50	0.71*	-0.06
ICP > 20	*p*	.660	.235	.423	.012	.453	.119	.014	.851
Mean ICP > 20	ρ	-0.44	0	0.23	-0.75**	0.51	0.64*	0,34	0.19
	p	.179	1.000	.503	.008	.113	.033	.306	.570
Mean ICP first 24	ρ	-0.31	0.08	0.24	-0.69*	0.50	0.45	0.35	-0.06
	p	.349	.821	.484	.019	.116	.164	.299	.852
	ρ	-0.23	0.06	-0.06	-0.55	0.50	0.35	0.33	-0.11
Mean ICP	*p*	.495	.863	.853	.079	.116	.297	.320	.749
	ρ	-0.28	0.25	0.34	-0.85**	0.50	0.62*	0.56	0
Highest ICP	*p*	.408	.467	.311	.001	.117	.043	.076	1.000
	ρ	0.47	0.25	-0,33	0.59	-0.40	-0.51	-0.15	-0.22
Lowest CPP	*p*	.149	.466	.321	.055	.222	.106	.668	.518
	ρ	-0.06	0.15	0.07	-0,567	0.64*	0.29	0.28	-0.03
CPP < 40	*p*	.859	.672	.835	.069	.035	.386	.397	.933
	ρ	-0.39	-0.33	0.02	-0.49	0.36	0.55	0.09	0.40
CPP < 50	*p*	.238	.315	.950	.124	.281	.083	.796	.230
	ρ	-0.10	-0.26	0.09	-0,04	-0.15	-0.05	-0.07	0.39
PaO2 < 8	*p*	.767	.447	.792	.906	.663	.880	.828	.234
Lowest PaO_2	ρ	0.11	-0.07	-0.21	0.65*	-0.20	-0.61*	-0.41	-0.23
	p	.749	.832	.544	.032	.555	.048	.216	.502
	ρ	-0.21	0.28	-0.22	-0.14	0.30	0.18	0.34	-0.16
Mean PaO_2	*p*	.545	.401	.525	.689	.370	.588	.311	.631
	ρ	1.00	0.48	-0.17	0.09	-0,15	-0.23	0.17	-0.64*
Lowest Hb	*p*	.	.132	.620	.790	.659	.493	.615	.035
	ρ		1.00	0.32	-0.48	-0.10	0.26	0.86**	-0.46
Mean Hb	*p*		.	.341	.133	.770	.434	.001	.160
	ρ			1.00	-0.37	-0,36	0.34	0.40	0.03
Sats < 90	*p*			.	.257	.277	.310	.219	.924
Lowest $PbtO_2$	ρ				1.00	-0.50	-0.89**	-0.75**	0.10
	p				.	.117	0	.008	.770
	ρ					1.00	0.44	0	-0.10
$PbtO_2$ < 5	*p*					.	.179	1.000	.770
	ρ						1.00	0.59	0.08
$PbtO_2$ < 10	*p*						.	.055	.828
	ρ							1.00	-0.28
$PbtO_2$ < 20	*p*							.	.408

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

APPENDIX O

BETWEEN-GROUP COMPARISONS FOR IQ VARIABLES AND NEUROPSYCHOLOGICAL COMPOSITES AFTER THE REMOVAL OF OUTLIERS: HYPOXIA vs. NO HYPOXIA GROUPS

Table O1

Between-group Comparisons for General Intellectual Functioning and Neuropsychological Composites: Hypoxia vs. No Hypoxia Groups, after the removal of outliers

	No Hypoxia			Hypoxia			Test statistics		
	n	Range	*Mean* (*SD*)	*n*	Range	*Mean* (*SD*)	*F/U*	*p*	*r*
General intellectual functioning									
VIQ	6	76-106	84.67 (11.59)	4	70-77	73.00 (3.16)	3.73	.045*	.56
FSIQ	5	76-84	78.80 (3.03)	4	66-77	72.00 (4.97)	1.00[a]	.016*	-.68
Verbal memory composite (α = 0.957)	6	0.15-1.53	0.72 (0.52)	4	-1.54-(-0.69)	-1.09 (0.35)	36.30	<.001***	.91
Visual memory composite (α = 0.686)	5	0.26-1.00	0.63 (0.28)	4	-0.62-0.04	-0.39 (0.29)	28.27	.001**	.90
Visuospatial skills composite (α = 0.572)	6	0.13-0.73	0.37 (0.25)	3	-0.58-0.33	-0.46 (0.13)	0.00[a]	.012*	-.70

Note. For qualitative descriptions for VIQ and FSIQ, see Appendix I_. [a]Mann-Whitney *U;* for FSIQ, mean rank of the No Hypoxia group = 6.80 and of the Hypoxia group = 2.75; for Visuospatial skills composite, mean rank of the No Hypoxia group = 6.50 and of the Hypoxia group = 2.00. The *r* value presented here is an estimate of effect size.

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

APPENDIX P

STUDY 2: SUBTESTS MAKING UP COMPOSITES: HYPOXIA vs. NO HYPOXIA GROUPS

Table P1

Subtests making up Neuropsychological Composites: Between-group Comparisons for No Hypoxia and Hypoxia groups (N = 11)

	No Hypoxia			Hypoxia			Test statistics		
	n	Range	*M* (*SD*)	*n*	Range	*M* (*SD*)	*F/U*	*p*	*r*
Basic Attention Composite (α = .726)									
Sky search targets	6	4-13	9.00 (4.15)	5	2-11	7.80 (3.83)	.244	.633	.162
Sky search time per target	6	1-9	5.83 (3.76)	5	1-6	2.00 (2.24)	6.00[a]	.045*	-.546
Attention score	6	1-13	7.50 (4.85)	5	1-7	2.80 (2.68)	5.50[a]	.048*	-.537
Map mission	5	3-9	5.80 (2.39)	5	1-6	3.40 (1.82)	3.20	.111	.535
Score	6	4-13	8.17 (3.66)	5	2-8	4.20 (2.39)	4.309	.068	.569
Numbers forward	6	4-10	7.33 (2.34)	6	2-6	3.60 (1.52)	9.364	.014*	.714
Higher-Order Attention Composite (α =.831)									
Sky search DT	6	1-8	3.67 (2.66)	4	1-1	1.00 (>.001)	4.00[a]	.071	-.580

Opposite worlds	5	2-6	4.40 (1.52)	5	1-2	1.20 (0.45)	0.50[a]	.008**	-.785
Inhibition switching combined	6	4-10	6.17 (2.40)	3	1-6	3.33 (2.52)	3.50[a]	.107	-.432
Inhibition switching CT	6	3-8	6.17 (1.72)	3	2-7	5.00 (2.65)	6.00[a]	.274	-.242
Inhibition total errors	6	1-8	4.83 (2.79)	3	1-1	1.00 (>.001)	1.50[a]	.048*	-.613
Verbal memory composite (α =0.957)									
Word list learning	6	8-14	11.33 (2.16)	5	1-8	3.40 (2.70)	29.41	>.001***	.875
Word list delayed	6	8-17	12.00 (3.16)	5	1-9	5.00 (3.08)	13.67	.005**	.777
Visual memory composite (α =0.686)									
Dot locations learning	6	5-13	10.17 (2.79)	5	3-8	5.20 (2.17)	10.51	.010*	.734
Dot locations total	6	6-13	10.83 (2.48)	5	4-7	5.60 (1.52)	2.50[a]	.013*	-.696
Dot locations delayed	6	7-13	10.67 (2.58)	5	7-10	8.20 (1.30)	3.71	.086	.541
REY immediate recall	6	28-37	33.67 (3.20)	4	29-50	35.75 (9.91)	.241	.637	.171
REY delayed recall	6	27-46	37.34 (6.71)	4	22-48	32.25 (11.09)	.835	.388	.307
Executive functions composite (α = 0.840)									

Numbers backward	6	6-13	9.00 (2.45)	5	2-6	3.40 (1.95)	0.50[a]	.004**	-.809
Inhibition-Inhibition combined	6	3-8	5.17 (2.14)	4	1-2	1.75 (0.50)	0.00[a]	.005**	-.783
Inhibition-Inhibition CT	6	5-8	6.50 (1.05)	4	1-5	2.75 (1.71)	18.95	.002**	.839
WASI similarities	6	31-56	40.67 (9.89)	5	20-44	33.20 (8.56)	1.75	.219	.403
WASI matrix reasoning	6	25-43	35.83 (6.40)	5	20-35	29.20 (5.98)	3.12	.112	.507
Visuospatial skills composite (α =0.572)									
REY copy	6	13.50-30.50	25.34 (6.06)	5	3-19	12.90 (6.82)	3.00[a]	.013*	-.662
REY copy timing (sec)	6	111-571	303.50 (171.53)	5	128-570	255.60 (178.50)	11.00[a]	.268	-.212
WASI block design	6	33-48	39.83 (5.19)	5	23-47	34.00 (9.17)	1.77	.216	.406
Expressive language composite (α =0.622)									
Inhibition-naming combined	6	1-12	5.67 (3.78)	5	1-2	1.20 (0.45)	3.00[a]	.013*	-.693
Inhibition-naming CT	6	2-7	5.00 (2.00)	5	1-4	1.80 (1.30)	2.50[a]	.015*	-.704
WASI Vocabulary	6	25-51	38.00 (8.32)	5	20-29	23.60 (3.51)	12.88	.006**	.767

Note. [a]Mann-Whitney *U*. The *r* value presented here is an estimate of effect size.

*$p < 0.05$. **$p < 0.01$. ***$p < 0.01$

APPENDIX Q

BETWEEN-GROUP COMPARISONS FOR BRIEF INDICES AFTER THE REMOVAL OF OUTLIERS: HYPOXIA vs. NO HYPOXIA

Table Q1

BRIEF Indices: Between-group comparisons for Hypoxia vs. No Hypoxia, after the removal of outliers

	Group								
	No Hypoxia			Hypoxia					
Indices	*n*	Range	*M* (*SD*)	*n*	Range	*M* (*SD*)	*F*/*U*	*p*	*r*
Inhibit	6	41-103	70.50 (25.23)	3	71-73	71.67 (1.16)	7.00	.357	-.16
Working memory	5	65-74	69.20 (4.27)	5	67-84	75.00 (6.40)	2.84[a]	.065	.51
Plan/Organization	6	50-74	66.00 (8.97)	3	67-84	71.67 (1.16)	6.00	.262	-.24
Org. of materials	6	39-72	56.00 (13.37)	3	58-58	58.00 (0.00)	9.00	.560	.00

Note. [a] *F*-statistic; degrees of freedom were (1, 8). BRI = Behaviour Regulation Index; Org. of materials = Organization of materials; MI = Metacognition Index; GEC Global Executive Composite. For Inhibit, mean rank of the No Hypoxia group = 4.67 and of the Hypoxia group = 5.67; for Plan / Organization, mean rank of the No Hypoxia group = 4.50 and of the Hypoxia group = 6.00; for Org. of Materials, mean rank of the No Hypoxia group = 5.00 and of the Hypoxia group = 5.00. The *r* value presented here is an estimate of effect size.

APPENDIX R

BETWEEN-GROUP COMPARISONS FOR CBCL SYNDROME PROFILES AFTER THE REMOVAL OF OUTLIERS: HYPOXIA vs. NO HYPOXIA GROUPS

Table R1

CBCL Syndrome Profiles: Between-group comparisons for Hypoxia vs. No Hypoxia, after the removal of outliers

	Group								
	No Hypoxia			Hypoxia					
Syndrome Profile	*n*	Range	*M* (*SD*)	*n*	Range	*M* (*SD*)	*F/U*	*p*	*r*
Anxious/Depressed	5	60-69	62.80 (4.09)	4	55-66	60.00 (4.97)	7.00	.270	-.23
Rule-breaking Behaviour	5	50-62	54.20 (4.60)	4	67-78	73.25 (4.57)	38.26[a]	<.001*	.92

Note. For Anxious / Depressed, mean rank of the No Hypoxia group = 5.60 and of the Hypoxia group = 4.25; for Rule-breaking Behaviour, mean rank of the No Hypoxia group = 3.00 and of the Hypoxia group = 7.50; [a] *F*-test, degrees of freedom were (1, 7). The *r* value presented here is an estimate of effect size.
*$p < .001$

APPENDIX S

ANCOVA RESULTS

Covariate	Dependant variables (residuals)		Sum of Squares	df	Mean Square	*F*	*p*
Mean ICP >20	VIQ	Between Groups	3.455	1	3.455	.723	.417
		Within Groups	43.025	9	4.781		
		Total	46.479	10			
	FSIQ	Between Groups	7.003	1	7.003	1.510	.250
		Within Groups	41.737	9	4.637		
		Total	48.741	10			
	Basic attention composite	Between Groups	12.384	1	12.384	2.899	.127
		Within Groups	34.176	8	4.272		
		Total	46.560	9			
	Higher Order attention composite	Between Groups	13.371	1	13.371	3.779	.100
		Within Groups	21.231	6	3.538		
		Total	34.601	7			
	Verbal memory composite	Between Groups	10.106	1	10.106	2.324	.162
		Within Groups	39.144	9	4.349		
		Total	49.250	10			
	Executive function composite	Between Groups	6.368	1	6.368	2.171	.179
		Within Groups	23.466	8	2.933		
		Total	29.834	9			
	Visuospatial composite	Between Groups	19.520	1	19.520	3.343	.101
		Within Groups	52.554	9	5.839		
		Total	72.074	10			
	Expressive language composite	Between Groups	26.492	1	26.492	4.219	.070
		Within Groups	56.508	9	6.279		
		Total	83.000	10			
Highest ICP	VIQ	Between Groups	13.766	1	13.766	2.077	.183
		Within Groups	59.652	9	6.628		
		Total	73.418	10			
	FSIQ	Between Groups	15.884	1	15.884	2.855	.125
		Within Groups	50.080	9	5.564		
		Total	65.964	10			
	Basic attention composite	Between Groups	17.720	1	17.720	4.267	.073
		Within Groups	33.221	8	4.153		
		Total	50.942	9			
	Higher Order attention composite	Between Groups	10.528	1	10.528	3.111	.128
		Within Groups	20.307	6	3.385		
		Total	30.835	7			
	Verbal memory composite	Between Groups	21.077	1	21.077	4.046	.075
		Within Groups	46.886	9	5.210		
		Total	67.964	10			

	Executive function composite	Between Groups	11.936	1	11.936	3.125	.115
		Within Groups	30.554	8	3.819		
		Total	42.491	9			
	Visuospatial composite	Between Groups	21.688	1	21.688	4.109	.073
		Within Groups	47.503	9	5.278		
		Total	69.191	10			
	Expressive language composite	Between Groups	38.148	1	38.148	6.328	.033*
		Within Groups	54.252	9	6.028		
		Total	92.400	10			
Lowest PbtO2	VIQ	Between Groups	7.805	1	7.805	1.044	.334
		Within Groups	67.311	9	7.479		
		Total	75.116	10			
	FSIQ	Between Groups	5.219	1	5.219	.909	.365
		Within Groups	51.645	9	5.738		
		Total	56.864	10			
	Basic attention composite	Between Groups	8.030	1	8.030	1.634	.237
		Within Groups	39.308	8	4.913		
		Total	47.338	9			
	Higher Order attention composite	Between Groups	2.904	1	2.904	.809	.403
		Within Groups	21.541	6	3.590		
		Total	24.444	7			
	Verbal memory composite	Between Groups	8.352	1	8.352	1.488	.253
		Within Groups	50.511	9	5.612		
		Total	58.864	10			
	Executive function composite	Between Groups	3.290	1	3.290	.755	.410
		Within Groups	34.855	8	4.357		
		Total	38.145	9			
	Visuospatial composite	Between Groups	6.552	1	6.552	1.262	.290
		Within Groups	46.711	9	5.190		
		Total	53.264	10			
	Expressive language composite	Between Groups	13.807	1	13.807	2.150	.177
		Within Groups	57.784	9	6.420		
		Total	71.591	10			
Lowest PaO2	VIQ	Between Groups	28.073	1	28.073	3.887	.080
		Within Groups	65.007	9	7.223		
		Total	93.080	10			
	FSIQ	Between Groups	29.044	1	29.044	4.726	.058
		Within Groups	55.311	9	6.146		
		Total	84.355	10			
	Basic attention composite	Between Groups	25.716	1	25.716	6.078	.039*
		Within Groups	33.847	8	4.231		
		Total	59.564	9			
	Higher Order attention composite	Between Groups	6.763	1	6.763	2.302	.180
		Within Groups	17.627	6	2.938		
		Total	24.390	7			

	Verbal memory composite	Between Groups	31.713	1	31.713	5.855	.039*
		Within Groups	48.751	9	5.417		
		Total	80.464	10			
	Executive function composite	Between Groups	17.067	1	17.067	3.698	.091
		Within Groups	36.924	8	4.616		
		Total	53.991	9			
	Visuospatial composite	Between Groups	39.659	1	39.659	6.984	.027*
		Within Groups	51.105	9	5.678		
		Total	90.764	10			
	Expressive language composite	Between Groups	37.404	1	37.404	6.631	.030*
		Within Groups	50.769	9	5.641		
		Total	88.173	10			
Lowest CPP	VIQ	Between Groups	18.084	1	18.084	2.755	.131
		Within Groups	59.085	9	6.565		
		Total	77.169	10			
	FSIQ	Between Groups	26.024	1	26.024	4.350	.067
		Within Groups	53.846	9	5.983		
		Total	79.870	10			
	Basic attention composite	Between Groups	13.417	1	13.417	5.955	.041*
		Within Groups	18.025	8	2.253		
		Total	31.442	9			
	Higher Order attention composite	Between Groups	8.937	1	8.937	3.490	.111
		Within Groups	15.362	6	2.560		
		Total	24.299	7			
	Verbal memory composite	Between Groups	30.184	1	30.184	5.656	.041*
		Within Groups	48.026	9	5.336		
		Total	78.210	10			
	Executive function composite	Between Groups	17.803	1	17.803	5.384	.049*
		Within Groups	26.453	8	3.307		
		Total	44.256	9			
	Visuospatial composite	Between Groups	35.044	1	35.044	6.275	.034*
		Within Groups	50.262	9	5.585		
		Total	85.306	10			
	Expressive language composite	Between Groups	28.536	1	28.536	5.473	.044*
		Within Groups	46.923	9	5.214		
		Total	75.459	10			
Time since injury	VIQ	Between Groups	6.680	1	6.680	1.051	.332
		Within Groups	57.221	9	6.358		
		Total	63.901	10			
	FSIQ	Between Groups	8.138	1	8.138	1.518	.249
		Within Groups	48.257	9	5.362		
		Total	56.394	10			
	Basic attention composite	Between Groups	12.265	1	12.265	2.661	.141
		Within Groups	36.872	8	4.609		
		Total	49.137	9			

	Higher Order attention composite	Between Groups	13.094	1	13.094	3.697	.103
		Within Groups	21.248	6	3.541		
		Total	34.342	7			
	Verbal memory composite	Between Groups	4.134	1	4.134	1.500	.252
		Within Groups	24.802	9	2.756		
		Total	28.936	10			
	Executive function composite	Between Groups	14.408	1	14.408	2.852	.130
		Within Groups	40.408	8	5.051		
		Total	54.816	9			
	Visuospatial composite	Between Groups	14.982	1	14.982	2.659	.137
		Within Groups	50.704	9	5.634		
		Total	65.686	10			
	Expressive language composite	Between Groups	14.693	1	14.693	2.626	.140
		Within Groups	50.353	9	5.595		
		Total	65.046	10			

Note: * Significance at $p \leq 0.05$

APPENDIX T

STUDY 3: LETTERS TO TEACHERS: PROFILES OF SUITABLE CANDIDATES FOR CONTROLS

Dear Miss Francis,

Thank you for being willing to host our research at your school again this year. The letter to parents and the consent form that explains the study is attached. The ages of the children that I need to participate in this study are:

3 coloured, English speaking female children aged 7 years 6 months – 7years 11 months

3 coloured, English speaking male children aged 10 years 6 months to 10 years 11 months

3 coloured, English speaking male children aged 12 years to 12 years 06 months

The children who had head injuries who we tested before were from low socio-economic circumstances, so it would be best if we could also match these children on those criteria too please.

If you could please give the invitation letter and consent form to a few learners matching these criteria, that would be great!

Thanks so much for your help.

Kind regards,

Leigh Schrieff

Lecturer
ACSENT Lab, Dep. of Psychology
University of Cape Town
South Africa

Tel: 078 559 2997

Email: leigh.schrieff@uct.ac.za

Dear Miss October,

Thank you for being willing to host our research at your school again this year. The letter to parents and the consent form that explains the study is attached. The ages of the children that I need to participate in this study are:

3 coloured, English speaking male children aged 9 years – 9 years 6 months

3 coloured, Eng/Afr speaking male children aged 8 years 6 months to 8 years 11 months

The children who had head injuries who we tested before were from poor socio-economic circumstances, so it would be best if we could also match these children on those criteria too please.

If you could please give the invitation letter and consent form to a few learners matching these criteria, that would be great!

Thanks so much for your help.

Kind regards,

Leigh Schrieff

Lecturer
ACSENT Lab, Dep. of Psychology
University of Cape Town
South Africa

Tel: 078 559 2997

Email: leigh.schrieff@uct.ac.za

APPENDIX U

STUDY 3: LETTER TO PARENTS: INVITATION TO PARTICIPATE IN STUDY

30 March 2011

Dear parent / guardian,

My name is Leigh Schrieff and I am a lecturer at the University of Cape Town's Psychology Department. My students and I would like to invite your child to participate in a research study.

The main purpose of this research is to investigate the effectiveness of a neuropsychological rehabilitation service for children who have experienced a head injury. This research was undertaken because of a **need of such services in South Africa**. We have already collected some of the information needed for this study with children who have had a head injury in the past. For this part of the study, however, **we need to collect information from healthy children who have not had a head injury before.**

If you allow your child to participate in this research, two sets of neuropsychological tests (for example, tests of memory and attention) will be carried out with your child, one at the beginning of the study, and one three months later. You, as the parent/caregiver, will also be asked to complete two forms so that the investigator can know more about your child's performance. The test performances will then be compared with other information that has been collected in the study.

The study will not cost you anything and you will be compensated for any travelling expenses and for your participation.

We may also invite your child to participate in an intervention program, but we will contact you with further details about this, should we invite your child to participate in that part of the study.

The form attached, gives you more details about this study. If you would like your child to participate in this study, please sign and return that form. **Please also provide your contact details so that we can get in touch with you.**

Thank you for taking the time to read this letter.

Regards,

Leigh Schrieff

Lecturer
ACSENT Lab, Dep. of Psychology
University of Cape Town
South Africa

Tel: 076 559 2997

Email: leigh.schrieff@uct.ac.za

APPENDIX V

STUDY 3: PARENTAL CONSENT FORM FOR CONTROLS

Parental Consent Form

UNIVERSITY OF CAPE TOWN

DEPARTMENT OF PSYCHOLOGY

Informed Consent to for you and your child to participate in research and authorization for collection, use, and disclosure of cognitive performance, and other personal data

You are being asked to allow your child to take part in a research study. This form provides you with information about the study and seeks your permission for the collection, use and disclosure of your child's cognitive performance data, as well as other information necessary for the study. The Principal Investigator (the person in charge of this research) or a representative of the Principal Investigator will also describe this study to you and answer all of your questions. Your child's participation is entirely voluntary. Before you decide whether or not to allow your child to take part, read the information below and ask questions about anything you do not understand. By allowing your child to participate in this study you will not be penalized or lose any benefits to which you would otherwise be entitled.

1. **Name of Participant ("Study Subject" – the child)**

   _____

2. **Title of Research Study**

   The implementation and evaluation of a neuropsychological rehabilitation service following paediatric traumatic brain injury

3. **Principal Investigator and Telephone Number(s)**

   Leigh Schrieff, PhD candidate

   Department of Psychology, office 4.30

   University of Cape Town

   Contact number: 078 5592997

4. **Source of Funding or Other Material Support**

   None

5. **What is the purpose of this research study?**

   The main purpose of this research is to investigate the effectiveness of a neuropsychological rehabilitation service for children who have experienced a traumatic brain injury. This research was undertaken because of a need of such services in South Africa.

6. What will be done if you take part in this research study?

Two sets of neuropsychological tests will be carried out with your child, one at the beginning of the study, and one three months later. You, as the parent/caregiver, will also be asked to complete two short forms so that the investigator can know more about your child's performance. The test performances will then be compared with other information that is collected in the study. We may also invite your child to participate in an intervention program, but we will contact you with further details about this, should we invite your child to participate in that part of the study.

7. If you choose to participate in this study, how long will you be expected to participate in the research?

On two occasions you will be required to bring your child to Red Cross War Memorial Children's Hospital for testing. Each visit should last for approximately 2 hours.

8. How many people are expected to participate in the research?

15

9. What are the possible discomforts and risks for you or your child?

There are no known risks associated with participation in this study.
One possible area of discomfort that you or your child may experience is that you may get tired during the testing and interview periods. You will be allowed to take breaks whenever you want to. We will also serve refreshments halfway through the assessments.
If you wish to discuss the information above or any discomforts you may experience, you may ask questions now or call the Principal Investigator listed on the front page of this form.

10a. What are the possible benefits to your child?

Your child may or may not personally benefit from participating in this study.
By you and your child partaking in the neuropsychological assessment, this will provide you with a deeper understanding of the functioning of your child.

10b. What are the possible benefits to others?

The information collected from these neuropsychological assessments will serve as important information that can be compared with children who have sustained traumatic brain injuries.
Additionally, this research will allow us to gather information about how healthy children perform on the administered tests. This research can then be applied to people who have experienced a traumatic brain injury.

11. If you choose to take part in this research study, will it cost you anything?

Participating in this study will not cost you anything.

12. Will you and your child receive compensation for taking part in this research study?

You will be compensated for travelling costs to and from Red Cross Hospital for both testing sessions.

13a. Can you and your child withdraw from this research study?

You are free to withdraw your consent and to stop participating in this research study at any time. If you do withdraw your consent, there will be no penalty.

If you have any questions regarding you or your child's rights as a research subject, you may phone the Psychology Department, University of Cape Town on 021-650-3430.

13b. If you withdraw, can information about you and your child still be used and/or collected?

Information already collected may be used.

14. Once personal and performance information is collected, how will it be kept secret (confidential) in order to protect your privacy?

Information collected will be stored in locked filing cabinets or on computers with security passwords. Only certain people have the right to review these research records. These people include the researchers for this study and certain University of Cape Town officials. Your research records will not be released without your permission unless required by law or a court order.

15. What information about you or your child may be collected, used and shared with others?

This information gathered from you will be demographic information and records of your responses, or your child's performance on the neuropsychological tests. If you agree to be in this research study, it is possible that some of the information collected might be copied into a "limited data set" (a computer file) to be used for other research purposes. If so, the limited data set may only include information that does not directly identify you or your child. For example, the limited data set cannot include your or your child's name, address, telephone number, ID number, or any other photographs, numbers, codes, or so forth that link you to the information in the limited data set.

16. How will the researcher(s) benefit from your being in the study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator and others attached to this research project may benefit if the results of this study are presented at scientific meetings or in scientific journals. This study is being undertaken for the Principal Investigator's doctoral degree.

17. This study has been approved by the Research Ethics Committee of the Department of Psychology at the University of Cape Town and the Western Cape Education Department.

18. Signatures

As a representative of this study, I have explained to the participant's (child's) parent/guardian the purpose, the procedures, the possible benefits, and the risks of this research study; and how the participant's performance and other data will be collected, used, and shared with others:

_____

_____

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; and how your responses and your child's performance and other data will be collected, used and shared with others. You have received a copy of this

form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

You voluntarily agree for you and your child to participate in this study. You hereby authorize the collection, use and sharing of your performance and other data. By signing this form, you are not waiving any of your legal rights.

_____

_____

Signature of Person Consenting and Authorizing (your signature)
Date

Authorization for _____ (your child's name) to participate in the study.
Relationship to child participating in the study: mother / father / legal guardian

---

_____

If you do consent to your child participating in this research, could you please provide us with your contact details so that we can contact you to tell you more about this study.

Method of contact:
Phone number: _____
E-mail address: _____
Mailing address: _____
_____
_____

Please indicate below if you would like to be notified of future research projects conducted by our research group:

_____ (initial) Yes, I would like to be added to your research participation pool and be notified of research projects in which I might participate in the future

APPENDIX W

DEMOGRAPHIC QUESTIONNAIRE AND ASSET INDEX

PARENT QUESTIONNAIRE AND ASSET INDEX

GENERAL INFORMATION

Full name (Parent):	
Telephone:	Work: ( ) Home: ( ) Cell:
How would you describe your ethnicity / race?	1. Black 2. Coloured 3. White 4. Asian 5. Other(specify):
Home Language:	
Full name (Child):	
Gender:	M F
Date of Birth:	
Grade:	

HOUSEHOLD INCOME: (Please circle appropriate number)

Household income per year:	1. R0 2. R1 – R5 000 3. R5001 – R25 000 4. R25 000 – R100 000 5. R100 001+

PARENTAL EDUCATION: (Please circle appropriate number)

	Biological mother	Biological father	Guardian
Highest level of education reached? Mark one response for each person as follows:			
1. 0 years (No Grades / Standards) = No formal education (never went to school)	1.	1.	1.
2. 1-6 years (Grades 1-6 / Sub A-Std 4) = Less than primary education (didn't complete primary school)	2.	2.	2.
3. 7 years (Grade 7 / Std 5) = Primary education (completed primary school)	3.	3.	3.
4. 8-11 years (Grades 8-11 / Stds 6-9) = Some secondary education (didn't complete high school)	4.	4.	4.
	5.	5.	5.
	6.	6.	6.

5. 12 years (Grade 12 / Std 10) = Secondary education (completed senior school) 6. 13+ years = Tertiary education (completed university / technikon / college) 7. Don't know	7.	7.	7.

PARENTAL EMPLOYMENT: (Please circle appropriate number)

Hollingstead categories:	Biological mother	Biological father	Guardian
1. Higher executives, major professionals, owners of large businesses)	1.	1.	1.
2. Business managers of medium sized businesses, lesser professions (e.g. nurses, opticians, pharmacists, social workers, teachers)	2. 3.	2. 3.	2. 3.
3. Administrative personnel, managers, minor professionals, owners / proprietors of small businesses (e.g. bakery, car dealership, engraving business, plumbing business, florist, decorator, actor, reporter, travel agent)	4.	4.	4.
4. Clerical and sales, technicians, small businesses (e.g. bank teller, bookkeeper, clerk, draftsperson, timekeeper, secretary)	5.	5.	5.
5. Skilled manual – usually having had training (e.g. baker, barber, chef, electrician, fireman, machinist, mechanic, painter, welder, police, plumber, electrician)	6.	6.	6.
6. Semi-skilled (e.g. hospital aide, painter, bartender, bus driver, cook, garage guard, checker, waiter, machine operator)	7.	7.	7.
7. Unskilled (e.g. attendant, janitor, construction helper, unspedified labour, porter, unemployed) 8. Homemaker 9. Student, disabled, no occupation	8. 9.	8. 9.	8. 9.

MATERIAL AND FINANCIAL RESOURCES (ASSET INDEX): (Please circle appropriate number)

Which of the following items, in working order, does your household have?

Items	Yes	No
1. A refrigerator or freezer	1.	1.
2. A vacuum cleaner or polisher	2.	2.

3. A television	3.	3.
4. A hi-fi or music center (radio excluded)	4.	4.
5. A microwave oven	5.	5.
6. A washing machine	6.	6.
7. A video cassette recorder or dvd player	7.	7.

Which of the following do you have in your home?

Items	Yes	No
1. Running water	1.	1.
2. A domestic servant	2.	2.
3. At least one car	3.	3.
4. A flush toilet	4.	4.
5. A built-in kitchen sink	5.	5.
6. An electric stove or hotplate	6.	6.
7. A working telephone	7.	7.

Do you personally do any of the following?

Items	Yes	No
1. Shop at supermarkets	1.	1.
2. Use any financial services such as a bank account, ATM card or credit card	2.	2.
3. Have an account or credit card at a retail store	3.	3.

APPENDIX X

STUDY 3: ASSENT FORM: CONTROLS

Assent Form for Participants

Name of Participant ("Study Subject")

_____

I am going to be required to complete some tests. The person who is going to administer the tests has told me that I can stop if I am feeling tired and need to take a break, that I may end my participation at any stage during the test period, and that nobody else will be told my answers to the questions in the tests.

_____ _____

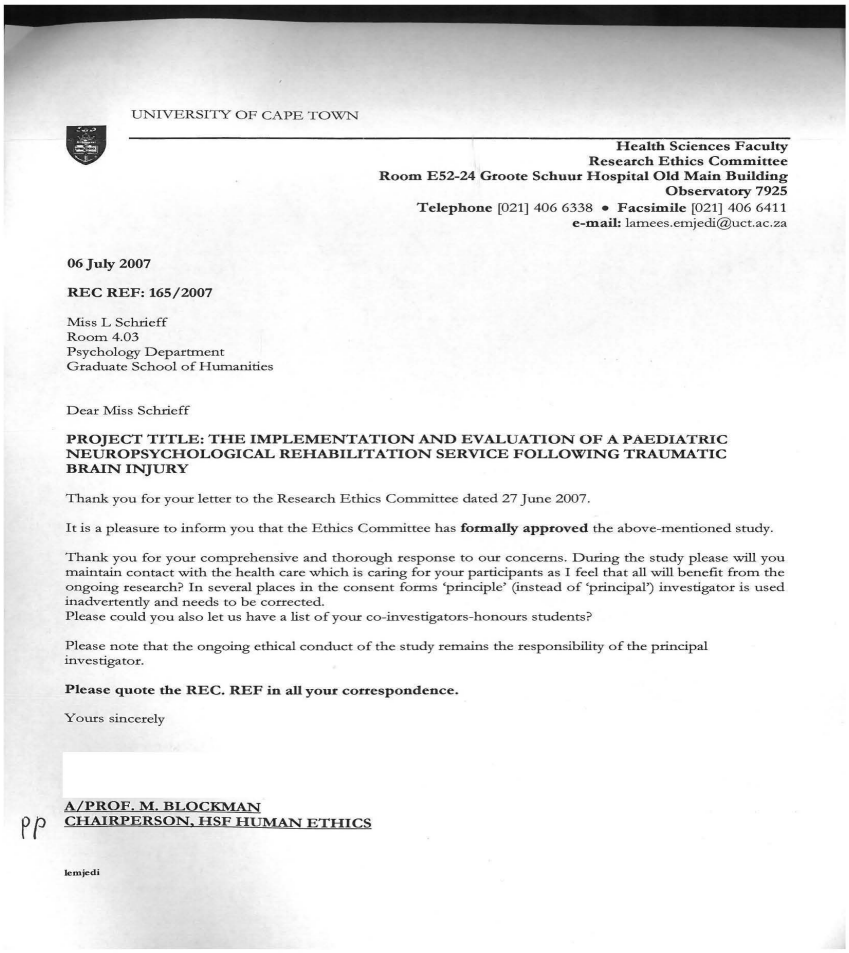
Signature of Child Date

_____ _____

Signature of Researcher Date

APPENDIX Y

ETHICAL APPROVAL FOR STUDY 3 FROM THE UNIVERSITY OF CAPE TOWN'S FACULTY OF HEALTH SCIENCES



UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
e-mail: lamees.emjedi@uct.ac.za

06 July 2007

REC REF: 165/2007

Miss L Schrieff
Room 4.03
Psychology Department
Graduate School of Humanities

Dear Miss Schrieff

PROJECT TITLE: THE IMPLEMENTATION AND EVALUATION OF A PAEDIATRIC NEUROPSYCHOLOGICAL REHABILITATION SERVICE FOLLOWING TRAUMATIC BRAIN INJURY

Thank you for your letter to the Research Ethics Committee dated 27 June 2007.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study.

Thank you for your comprehensive and thorough response to our concerns. During the study please will you maintain contact with the health care which is caring for your participants as I feel that all will benefit from the ongoing research? In several places in the consent forms 'principle' (instead of 'principal') investigator is used inadvertently and needs to be corrected.
Please could you also let us have a list of your co-investigators-honours students?

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

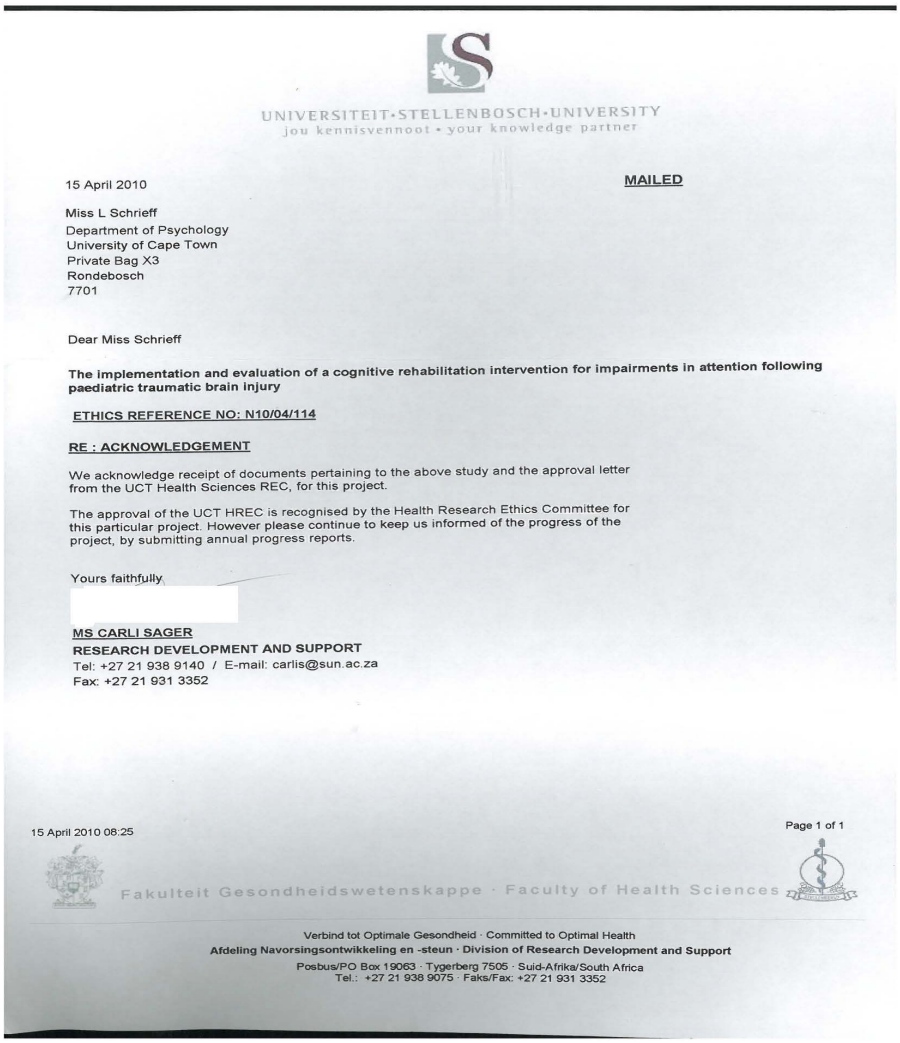
pp **A/PROF. M. BLOCKMAN**
CHAIRPERSON, HSF HUMAN ETHICS

lemjedi

Note. Ethical approval is renewed annually.

APPENDIX Z

ETHICAL APPROVAL FOR STUDY 3 FROM STELLENBOSCH UNIVERSITY'S FACULTY OF HEALTH SCIENCES



UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot • your knowledge partner

15 April 2010

MAILED

Miss L Schrieff
Department of Psychology
University of Cape Town
Private Bag X3
Rondebosch
7701

Dear Miss Schrieff

The implementation and evaluation of a cognitive rehabilitation intervention for impairments in attention following paediatric traumatic brain injury

ETHICS REFERENCE NO: N10/04/114

RE : ACKNOWLEDGEMENT

We acknowledge receipt of documents pertaining to the above study and the approval letter from the UCT Health Sciences REC, for this project.

The approval of the UCT HREC is recognised by the Health Research Ethics Committee for this particular project. However please continue to keep us informed of the progress of the project, by submitting annual progress reports.

Yours faithfully

MS CARLI SAGER
RESEARCH DEVELOPMENT AND SUPPORT
Tel: +27 21 938 9140 / E-mail: carlis@sun.ac.za
Fax: +27 21 931 3352

15 April 2010 08:25

Page 1 of 1

Fakulteit Gesondheidswetenskappe · Faculty of Health Sciences

Verbind tot Optimale Gesondheid · Committed to Optimal Health
Afdeling Navorsingsontwikkeling en -steun · Division of Research Development and Support
Posbus/PO Box 19063 · Tygerberg 7505 · Suid-Afrika/South Africa
Tel.: +27 21 938 9075 · Faks/Fax: +27 21 931 3352

APPENDIX AA

STUDY 3: PARENTAL CONSENT FORM FOR TBI-INTERVENTION PARTICIPANTS

Experimental group T1
UNIVERSITY OF CAPE TOWN
DEPARTMENT OF PSYCHOLOGY

Informed Consent for you and your child to participate in research and authorization for collection, use, and disclosure of neuropsychological rehabilitation and cognitive performance, and other personal data

You are being asked to allow your child to take part in a research study. This form provides you with information about the study and seeks your permission for the collection, use and disclosure of your child's neuropsychological rehabilitation and cognitive performance data, as well as other information necessary for the study. The Principal Investigator (the person in charge of this research) or a representative of the Principal Investigator will also describe this study to you and answer all of your questions. Your child's participation is entirely voluntary. Before you decide whether or not to allow your child to take part, read the information below and ask questions about anything you do not understand. By allowing your child to participate in this study you will not be penalized or lose any benefits to which you would otherwise be entitled.

1. **Name of Participant ("Study Subject" – the child)**

   _____

2. **Title of Research Study**
   The implementation and evaluation of a cognitive rehabilitation service following paediatric traumatic brain injury

3. **Principal Investigator and Telephone Number(s)**
   Leigh Schrieff, PhD candidate
   Department of Psychology, office 4.03.3
   University of Cape Town
   Contact number: 078 559 2997

4. **Source of Funding or Other Material Support**
   None

5. **What is the purpose of this research study?**
   The main purpose of this research is to investigate the effectiveness of a cognitive rehabilitation service for children who have experienced a traumatic brain injury. This research was undertaken because of a need of such services in South Africa.

6. **What will be done if you take part in this research study?**
   Firstly, a number of neuropsychological tests will be carried out with your child to find out his/her strengths and weaknesses, for example in the way they remember, pay attention or problem solve. You, as the parent/caregiver, will also be asked to participate in a few of these tests so that the investigator can know more about your child's performance at home or at school.

   Once these strengths and weaknesses are determined, the 'Pay Attention' program will be introduced to you and your child. This program is used if your child has problems concentrating, and it aims to teach your child to pay attention. These strategies will be discussed with you, the parent/caregiver, as well as with the child's school teacher.

   With this, we will request your permission to obtain a comprehensive report from your child's school teacher.

   The principle researcher and/or her research assistants will implement this rehabilitation strategy. However, some of the applications of the intervention strategies will require your involvement as the parent/caregiver. For example, you may be asked to help your child practice the intervention strategies at home.

   The principle researcher will monitor the children's progress over a maximum period of 10 weeks.

   At the end of the 10-week program, the same neuropsychological tests will be carried out with your child. You, as the parent/caregiver will again be asked to participate in the completion of some of the tests.

7. **If you choose to participate in this study, how long will you be expected to participate in the research?**
   In order to assess whether the interventions are effective, it will be necessary for the intervention to be monitored for at least 8 weeks. Thus, participation could last for up to 12 weeks, including the two neuropsychological assessments before and after the intervention.

   However, if at any time during the experiment you feel that you do not wish to continue, you are free to discontinue your participation without penalty.

8. **How many people are expected to participate in the research?**
   16, 8 of whom will be involved in the rehabilitation.

9. **What are the possible discomforts and risks for you or your child?**
   There are no known risks associated with taking part in this study.

   One possible area of discomfort that you or your child may experience is that you may become tired during the testing and interview periods. You will be allowed to take breaks whenever you want to. Light refreshments will be served halfway through the testing session.

During the testing period we may find that your child may need assistance in other areas of functioning not covered by the neuropsychological service. If this happens, we will talk with you and give a referral for the necessary care.

If you wish to discuss the information above or any discomforts you may experience, you may ask questions now or call the Principal Investigator listed on the front page of this form.

10a. What are the possible benefits to you and your child?

The general aim of the research is improvement in the quality of life for you and your child. More specifically, the intervention strategies chosen are aimed at improving specific areas of functioning for your child. As one of the aims of this study is to investigate how effective the intervention strategies are, it is not guaranteed that the rehabilitation interventions will result in improved functioning or performance for your child. It is important to bear this in mind at the outset of the study. However, part of the neuropsychological rehabilitation service is to provide you, the parent/caregiver, with useful advice regarding the management of your child in line with his/her areas of strengths and weaknesses.

By you and your child partaking in the neuropsychological assessment, this will provide you with a deeper understanding of the neuropsychological functioning of your child.

10b. What are the possible benefits to others?

Should the intervention strategies that are used prove to be effective, this will be an important contribution to future neuropsychological rehabilitation services offered to other children who have sustained traumatic brain injuries. In other words, this research can then be applied to other children, or families of children, who have experienced a traumatic brain injury. It will also help to motivate the need for formal development of such services in South Africa.

11. If you choose to take part in this research study, will it cost you anything?

Participating in this study will not cost you anything financially. The principle investigator will be carrying out the weekly intervention with your child at his/her school. In addition, the principle investigator or one of the research assistants may contact you in order to monitor your child's progress and to answer any questions that you may have or that may arise.

12. Will you and your child receive compensation for taking part in this research study?

You will receive financial compensation of the amount of R400 for your participation in the study. You will receive R50 at each neuropsychological testing session and the remaining R300 at the end of the intervention period.

13a. Can you and your child withdraw from this research study?

You are free to withdraw your consent and to stop participating in this research study at any time. If you do withdraw your consent, there will be no penalty.

If you have any questions regarding you or your child's rights as a research subject, you may phone the Psychology Department, University of Cape Town on 021-650-3430.

13b. If you withdraw, can information about you and your child still be used and/or collected?
Information already collected may be used.

14. Once personal and performance information is collected, how will it be kept secret (confidential) in order to protect your privacy?
Information collected will be stored in locked filing cabinets or on computers with security passwords. Only certain people have the right to review these research records. These people include the researchers for this study and certain University of Cape Town officials. Your research records will not be released without your permission unless required by law or a court order.

15. What information about you or your child may be collected, used and shared with others?
This information gathered from you will be demographic information, records of your responses, or your child's performance on the neuropsychological tests, and records of your child's progress in terms of the intervention strategies. If you agree to be in this research study, it is possible that some of the information collected might be copied into a "limited data set" (a computer file) to be used for other research purposes. If so, the limited data set may only include information that does not directly identify you or your child. For example, the limited data set cannot include you or your child's name, address, telephone number, ID number, or any other photographs, numbers, codes, or so forth that link you to the information in the limited data set.

16. How will the researcher(s) benefit from your being in the study?
In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator and others attached to this research project may benefit if the results of this study are presented at scientific meetings or in scientific journals. This study is being undertaken for the Principal Investigator's doctoral degree.

17. This study has been approved by the Research Ethics Committee of the Health Sciences Faculty at UCT. You can contact Professor Marc Blockman (021 406 6496) if you have any concerns about your own or your child's rights or welfare as a research participant.

18. Signatures

As a representative of this study, I have explained to the participant's (child's) parent the purpose, the procedures, the possible benefits, and the risks of this research study; and how the participant's performance and other data will be collected, used, and shared with others:

_____ _____

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; and how your responses and your child's performance and other data will be collected, used and shared with others. You have received a copy of this form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

You voluntarily agree for you and your child to participate in this study. You hereby authorize the collection, use and sharing of your performance and other data. By signing this form, you are not waiving any of your legal rights.

_____ _____

Signature of Person Consenting and Authorizing Date

Authorization for _____ to participate in the study.

Relationship to child participating in the study: parent / legal guardian

_____

Please indicate below if you would like to be notified of future research projects conducted by our research group:

_____ (initial & surname) Yes, I would like to be added to your research participation pool and be notified of research projects in which I might participate in the future.

Method of contact:

Phone number: _____
E-mail address: _____
Mailing address: _____
_____
_____

APPENDIX BB

STUDY 3: ASSENT FORM: TBI-INTERVENTION PARTICIPANTS

ASSENT TO PARTICIPATE IN RESEARCH

We are inviting you to be in our research study because we would like to learn more about children with head injuries and ways to help them.

If you agree to be in this study we will visit you at your school a few times a month to do some activities with us.

For example, we may ask you to try to remember things, to draw or read things. We will also ask your family to do the activities with you at home, and your teacher to do them with you at school.

These exercises and activities will not hurt you, but some of them may be long and you may feel tired at times. If you do, you can stop and rest at any time.

Signing this paper means that you want to be in the study. If you don't want to be in the study, don't sign the paper. No one will be cross if you don't sign this paper, and no one will be cross if you change your mind later and want to stop.

You can ask any questions that you have about the study. If you have a question later that you didn't think of now, you can call me on 083 477 6875 or ask me next time.

Signature of Participant _____ Date _____

Signature of Investigator _____ Date _____

APPENDIX CC

STUDY 3: SUBTESTS MAKING UP COMPOSITES: TBI-INTERVENTION vs. CONTROLS

Table CC1

Subtests making up Neuropsychological Composites: Between-group Comparisons for TBI-intervention and Controls groups (N = 16)

	TBI intervention			Control intervention			Play control			Test-only control			Test statistics		
	n	Range	*Mean* (*SD*)	*n*	Range	*Mean* (*SD*)	*n*	Range	*Mean* (*SD*)	*n*	Range	*Mean* (*SD*)	*F / H*	*p*	*r*
Basic attention composite ($\alpha = 0.773$)															
Sky search targets	4	4-13	9.25 (3.86)	4	6-14	10.50 (3.32)	4	8-11	9.25 (1.50)	4	4-13	9.50 (3.87)	.13	.94	.178
Sky search time per target	4	1-10	5.00 (4.69)	4	3-9	5.00 (2.71)	4	2-9	5.00 (3.16)	4	1-7	4.75 (2.63)	.01	.99	.037
Attention score	4	1-12	6.50 (4.93)	4	4-9	6.00 (2.16)	4	2-12	6.25 (4.35)	4	1-7	5.25 (2.87)	.07[a]	.10	.67
Map mission	4	1-9	4.25 (3.40)	4	2-8	5.50 (2.65)	4	1-9	4.50 (3.32)	4	4-9	5.25 (2.50)	.93[a]	.84	.25
Score	4	3-10	5.50 (3.12)	4	6-10	7.75 (1.71)	4	9-13	11.00 (1.83)	4	3-6	4.75 (1.50)	6.94	.006*	.796
Numbers forward	4	3-10	6.50 (2.89)	4	7-11	8.75 (1.71)	4	4-11	8.00 (3.16)	4	4-10	7.00 (3.46)	1.74[a]	.66	.11

Higher order attention composite (α = 0.817)														
Sky search DT	3	1-5	2.33 (2.31)	4	7-13	9.00 (2.83)	4	1-7	4.75 (2.87)	4	4-9	6.50 (2.08)	7.51[a]	.039*	.44
Opposite worlds	4	1-6	3.00 (2.45)	4	1-12	7.00 (4.55)	4	1-6	3.50 (2.38)	4	1-8	4.50 (3.12)	1.21	.35	.481
Inhibition switching combined	4	3-8	4.75 (2.36)	4	6-12	8.25 (2.63)	4	8-14	10.00 (2.83)	4	2-8	5.50 (2.65)	3.46	.051	.681
Inhibition switching CT	4	3-12	7.00 (3.74)	4	8-14	10.50 (2.52)	4	7-12	8.75 (2.36)	4	5-8	6.50 (1.73)	5.17[a]	.16	.25
Inhibition total errors	4	1-6	3.00 (2.45)	4	4-10	7.50 (2.52)	4	3-15	8.50 (5.20)	4	1-9	4.75 (4.35)	1.74	.21	.551
Verbal memory composite (α = 0.798)															
Word list learning	4	3-14	7.50 (4.80)	4	10-13	11.00 (1.41)	4	7-12	9.25 (2.22)	4	9-12	10.75 (1.50)	1.30	.32	.495
Word list delayed	4	6-17	9.75 (4.99)	4	9-14	12.00 (2.45)	4	9-14	11.25 (2.22)	4	9-14	12.00 (2.45)	.43	.74	.312
Visual memory composite (α = 0.923)															
Dot locations learning	4	4-11	7.75 (3.30)	4	9-13	10.50 (1.92)	4	6-13	9.00 (3.16)	4	9-13	10.50 (1.73)	1.02	.42	.451
Dot locations total	4	5-11	8.50	4	8-15	11.25	4	7-13	9.50	4	9-13	10.50	.80	.52	.409

			(3.00)			(2.99)			(2.65)			(1.92)		
Dot locations delayed	4	7-13	9.50	4	9-12	10.75	4	8-14	10.75	4	8-12	10.25	.28	.84	.257
			(2.65)			(1.50)			(2.50)			(2.06)			
Executive functions composite ($\alpha = 0.676$)															
Numbers backward	4	2-7	4.75	4	5-15	9.75	4	5-10	7.00	4	5-13	10.50	2.31	.13	.605
			(2.06)			(4.99)			(2.16)			(3.79)			
Inhibition-Inhibition	4	1-7	3.25	4	7-10	8.75	4	2-14	7.50	3	2-8	5.00	6.18[a]	.09	.33
combined			(2.63)			(1.26)			(4.93)			(3.00)			
Inhibition-Inhibition CT	4	2-10	5.25	4	7-13	9.75	4	4-12	7.75	3	4-7	5.33	4.96[a]	.18	.23
			(3.59)			(2.75)			(3.50)			(1.53)			
Design fluency	4	3-6	4.50	4	7-8	7.75	4	5-11	6.75	4	5-10	7.25	6.42[a]	.08	.35
			(1.29)			(.50)			(2.87)			(2.22)			

Note. [a]Kruskal-Wallis H . The r value presented here is an estimate of effect size

* $p \leq 0.05$. ** $p \leq 0.01$.

APPENDIX DD

PRE- AND POST-INTERVENTION WITHIN-GROUP ANALYSES: TBI-INTERVENTION AND CONTROLS

Table DD1

Neuropsychological Composites: Within-group Comparisons for TBI-intervention and Controls groups from pre- to post-intervention (N = 16)

	TBI intervention (*n* = 4)		Control intervention (*n* = 4)		Play control (*n* = 4)		Test-only control (*n* = 4)	
	Range	*Mean* (*SD*)	Range	*Mean* (*SD*)	Range	*Mean* (*SD*)	Range	*Mean* (*SD*)
Basic attention composite								
Pre-intervention	-1.05-1.12	-0.188 (0.95)	-0.09-0.72	0.189 (0.37)	-0.60-1.05	0.197 (0.76)	-1.27-0.27	-0.198 (0.72)
Post-intervention	-1.56-0.64	-0.622 (0.98)	-0.04-0.88	0.482 (0.45)	-1.14-0.86	-0.146 (0.84)	-0.18-0.77	0.286 (0.41)
Z	-1.826		-1.826		-1.826		-1.826	
p	.063		.063		.063		.063	
Higher order attention composite								
Pre-intervention	-1.08-0.36	-0.544 [b] (0.79)	0.18-1.10	0.645 (0.52)	-0.67-1.23	0.216 (0.81)	-0.98-0.42	-0.238 (0.58)
Post-intervention	-0.10-0.11	0.004[c] (0.15)	-0.36-0.80	0.297 (0.50)	-0.35-1.04	0.399 (0.57)	-0.83-0.44	-0.106 (0.59)
Z	-0.447		-1.461		0.000		-1.095	
p	.500		.125		.563		.188	
Verbal memory composite								
Pre-intervention	-1.83-1.69	-0.611 (1.62)	-0.31-1.03	0.359 (0.61)	-0.48-0.52	-0.064 (0.44)	0.02-0.86	0.316 (0.39)
Post-intervention	-2.06-(-0.78)	-1.301 (0.56)	-0.09-0.46	0.156 (0.28)	0.64-1.19	0.915 (0.24)	-0.64-0.83	0.229 (0.66)

Z	-0.730		-1.095		-1.826		0.000	
p	.313		.188		.063		.563	
Visual memory composite								
Pre-intervention	-1.85-0.64	-0.528 (1.19)	-0.51-1.04	0.373 (0.68)	-1.18-1.44	-0.040 (1.14)	-0.55-1.11	0.196 (0.75)
Post-intervention	-1.95-0.88	-0.524 (1.16)	-2.01-1.24	-0.131 (1.36)	-0.19-1.24	0.358 (0.64)	-0.41-0.91	0.298 (0.54)
Z	0.000		0.000		-0.730		-0.365	
p	.563		.563		.313		.438	
Executive functions composite								
Pre-intervention	-1.54-0.01	-0.789 (0.67)	0.15-1.19	0.620 (0.45)	-0.34-0.96	0.092 (0.59)	-0.18-0.27	0.112[b] (0.25)
Post-intervention	-1.59-0.19	-0.677 (0.76)	0.56-1.01	0.739 (0.21)	-0.64-1.11	0.156 (0.75)	-0.54-0.07	-0.218 (0.28)
Z	-0.365		-0.730		-0.730		-1.604	
p	.438		.313		.313		.125	

Note. [a]Kruskal-Wallis *H*. [b]$n = 3$; [c]$n = 2$.