ANXIETY DISORDERS FOLLOWING TRAUMATIC BRAIN INJURY IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS

Michelle Albicini, BPsych (Hons)

This thesis is submitted in partial fulfilment of the requirements for the Degree of Doctor of Psychology (Clinical Psychology)

School of Psychological Sciences

Faculty of Medicine, Nursing and Health Sciences

Monash University

Clayton, Victoria, Australia

December 2017

TABLE OF CONTENTS

DECLARATION

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes three original papers published in peer reviewed journals, one published abstract, and two unpublished publications. The core theme of this thesis is the nature of anxiety disorders and symptoms in children and adults following childhood TBI. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the School of Psychological Sciences, under the supervision of Dr Joanne Fielding and Dr Audrey McKinlay.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

In the case of chapters one, three, four, five, and six, my contribution to the work involved the following:

Thesis Chapter	**Publication Title**	**Status**	**Nature and % of student contribution**	**Co-authors names and % contribution**	**Co-authors, Monash student**
1	A systematic review of Anxiety Disorders following mild, moderate and severe TBI in children and adolescents	Published	70% Concept, write-up first draft	Dr Audrey McKinlay, manuscript input 30%	No
3	Internalizing disorders in adults with a history of childhood traumatic brain injury	Published	60% Data collection and analysis, manuscript preparation	Dr Audrey McKinlay, concept, manuscript input 40%	No
3	Internalizing disorders in adults with a history of childhood	Published abstract	80% Preparation, write-up,	Dr Audrey McKinlay, concept, abstract input 20%	No

	traumatic brain injury		presentation in conference		
4	The prevalence of traumatic brain injury, comorbid anxiety and other Psychiatric Disorders in an outpatient child and adolescent mental health service	Published	50% Data analysis, concept, manuscript preparation	Dr Audrey McKinlay, concept, manuscript input, 40% Dr Matthew Eggleston, manuscript input, 10%	No
5	Anxiety Disorders in adults with childhood traumatic brain injury: Evidence of difficulties more than 10 years post-injury	Published	60% Data analysis, concept, manuscript preparation	Dr Audrey McKinlay, concept, input into manuscript, 40%	No
6	Predictors of Long-Term Anxiety Disorders following Childhood Traumatic Brain Injury: The Role of Cognition and Frontal Lobe Functions	Submitted	60% Data analysis, concept, manuscript preparation	Dr Audrey McKinlay, concept, input into manuscript, 40%	No

I have renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Student Signature: [redacted] **Date:** 4/7/17

The undersigned hereby certify the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author I have consulted with the responsible author to agree on the respective contributions of the authors.

Main Supervisor Signature: [redacted] **Date:** 4/7/17

GENERAL ABSTRACT

Traumatic brain injury (TBI) is an injury to the head resulting from a bump or blow, which causes neurological impairment and disrupted consciousness or awareness. Severity of TBI ranges from mild to severe, with mild TBI being fairly common in young people between the ages of 0-25 years. While most young people will fully recover from TBI, a select group will continue to experience ongoing behavioural, physical and psychological problems. Childhood TBI can lead to difficulties with disruptive behaviours, inattention, hyperactivity, and drug and alcohol use. Less is known regarding how anxiety and other internalising difficulties (e.g. depression and withdrawal) manifest in such a population.

Individuals who have sustained a childhood TBI present with higher rates of most anxiety disorders, with particular emphasis paid towards post-traumatic stress symptoms given the traumatic nature of the injury. It appears that the risk of developing an anxiety disorder appears to increase in the presence of certain social factors (e.g. psychosocial adversity), biological factors (e.g. female gender, more severe injury), and psychological vulnerabilities (e.g. concurrent depression or anxiety). However, there are only a handful of research studies which focused on anxiety as an outcome of TBI in children and adolescents, and as such, there remains gaps in the literature for why a certain sub-group of individuals will develop anxiety later on in life, even after a seemingly minor injury.

Therefore, the present research aimed to examine the incidence and likelihood of ongoing anxiety and other internalising behavioural problems in young people and adults with a history of childhood TBI. The aim was to examine anxiety and other internalising behavioural issues among three groups to explore short-term and long-term outcomes of TBI that was sustained in childhood – that is, university students aged 18-25 years, children aged 5-15 years presenting in an outpatient mental health service, and a hospital-based sample of

adults older than 25 years who were admitted for an injury (head or orthopedic). Among these samples history of TBI was explored, either obtained via self-report or parent-report measures, or through hospital records, and ongoing problems were identified through information from self-report or parent-report behavioural questionnaires, mental health file reviews, or semi-structured interviews.

The present series of studies lend support to the existing literature which argues that TBI sustained in childhood, particularly more severe TBI but also including mild TBI, leads to ongoing anxiety (general, panic attacks, specific phobias), depression and somatic concerns. The findings indicated that in the more short-term phase of injury, ongoing anxiety is less apparent, as compared to long-term outcomes. Moreover, this finding highlights how anxiety-related outcomes following TBI may be dependent on the population from which the sample is derived. Examining long-term outcomes, individuals with a history of childhood moderate-severe TBI performed poorer on cognitive measures of attention and memory, and individuals with childhood mild TBI have worse executive functioning and overall frontal lobe functioning, in comparison to orthopedic controls. However, findings indicated that cognitive functioning was not related to anxiety disorders following TBI.

It appears that potential important predictors that increase the risk of developing anxiety disorders after childhood TBI are the severity of TBI, being female, and having overall deficits in frontal lobe functioning. Moreover, increased levels of apathy, behavioural disinhibition, and executive dysfunction may be slightly protective of anxiety when considered as individual factors. The thesis has examined outcomes and predictors for anxiety disorders following childhood TBI, across samples derived from varying populations, and has drawn together findings and conclusions for the development of an explanatory theory regarding why some young people who sustain a TBI experience ongoing anxiety later in life.

THESIS OVERVIEW

In line with Monash University guidelines, the experimental chapters are expanded written work based on manuscripts that have been submitted for publication, which were prepared separately for submission and expanded upon for inclusion in the thesis. As such there is some unavoidable repetition of introductory comments and methodology.

Full published manuscripts are presented in the appendices. Each manuscript's publication status and name of the corresponding journal is outlined at the beginning of each chapter where relevant. References are presented at the end of the thesis, rather than at the end of each chapter and formatted in accordance with APA formatting rather than what is required of each journal. Tables and headings have been re-numbered and structured to facilitate ease of reading of the thesis.

PUBLICATIONS AND CONFERENCE PRESENTATIONS

The following publications and presentations arose from research presented in this thesis:

Publications

Albicini, M. & McKinlay, A. (2015). A systematic review of Anxiety Disorders following Mild, Moderate and Severe TBI in Children and Adolescents, In A Fresh Look at Anxiety Disorders, Federico Durbano (Ed.), ISBN: 978-953-51-2149-7, *InTech Open, online*, 199-224. (See Appendix A for pdf chapter).

Albicini, M. & McKinlay, A. (2015). Internalizing disorders in adults with a history of childhood traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology, 37*(7), 776-784. (Appendix B)

Albicini, M. & McKinlay, A. (2017). Anxiety Disorders in adults with childhood traumatic brain injury: Evidence of difficulties more than 10 years postinjury. *Journal of Head Trauma Rehabilitation epub ahead of print.*

Albicini, M., Eggleston, M., & McKinlay, A. (2017). The prevalence of traumatic brain injury, comorbid anxiety and other psychiatric disorders in an outpatient child and adolescent mental health service. *Journal of Mental Health, Early Online, 1-7.*

Albicini, M. & McKinlay, A. Predictors of long-term anxiety following childhood TBI: Theoretical perspectives. *Journal of Head Trauma Rehabilitation, SUBMITTED.*

Conferences

Albicini, M. & McKinlay, A. Internalizing disorders in adults with a history of childhood traumatic brain injury. *Eleventh World Congress on Brain Injury, International Brain Injury Association,* The Hague, the Netherlands, 6th March 2016.

Published Abstracts

Albicini, M. & McKinlay, A. (2016). Internalizing disorders in adults with a history of childhood traumatic brain injury. *Brain Injury*, *30*(5-6), 509-509.

ACKNOWLEDGEMENTS

First I would like to acknowledge my wonderful, supportive supervisors, Dr Audrey McKinlay and Associate Professor Joanne Fielding, which without them I would not have been able to complete this thesis or have survived the past few years. To Jo, thank-you for your approachable and relaxed nature, your ever-present support, your availability and flexibility and your time. Thank-you for being readily available with ideas and advice, providing me with resources and examples, reviewing my work, and encouraging me to practice my presentations in a supportive environment. To Audrey, without you none of this would have been possible. Thank-you for sharing your wisdom, supporting my career advancement, and being a mentor and a friend through-out this entire process, I am forever grateful.

I am also grateful towards the participant's and their families who agreed to partake in this research and organisations which allowed recruitment and information sharing and gathering for the purposes of our work.

As for my fellow clinical DPsych students – thank-you for being such a supportive, fun, and approachable network of friends, since the first day of our course. Without our regular catch-ups, advice and conversations, I would have felt very lost, alone and confused much of the time!

And finally, my sincere thanks to my fiancé Paul, for being a never-ending source of support, love, advice and comfort. Your empathy, understanding and patience won't be forgotten and will always be appreciated. To my sister Rachael – thank-you for being a genuine support and best friend. And last, but never least, my loving parents Vito and Christine, your support for me began many, many years ago, and to this day I am eternally grateful for encouraging me to be in the position I am now.

ABBREVIATIONS

ADHD – Attention-Deficit/Hyperactivity Disorder

ASD – Acute Stress Disorder

ASR – Adult's Self Report

CD – Conduct Disorder

CIDI – Composite International Diagnostic Interview

CNS – Central Nervous System

CT – Computed Tomography

D-KEFS – Delis-Kaplan Executive Function System

DOT-A – Adaptive Digit Ordering Task

DCRS – Daneman and Carpenter Reading Span Test

DSM – Diagnostic and Statistical Manual for Mental Disorders

ED – emergency department

FrSBe – Frontal Systems of Behaviour Scale

GAD – Generalised Anxiety Disorder

GCS – Glasgow Coma Scale

JLOT – Judgement of Line Orientation Test

LOC – loss of consciousness

MANOVA – Multivariate Analysis of Variance

MR – magnetic resonance

PCS – post-concussive symptoms

PD – Panic Disorder

PTA – post-traumatic amnesia

PTSD – Post-Traumatic Stress Disorder

OCD – Obsessive-Compulsive Disorder

ODD – Oppositional Defiant Disorder

OFC – Orbitofrontal Cortex

OI – orthopedic injury

OSU TBI-ID – Ohio State University TBI Identification Method

ROF – Rey-Osterrieth Complex Figure

SAD – Separation Anxiety Disorder

SES – socioeconomic status

TOI – time of injury

TBI – traumatic brain injury

WASI-MR – Wechsler Abbreviated Scale of Intelligence's Matrix Reasoning

WMS-III PA - Wechsler Memory Scale-III Paired Associates I and II

CHAPTER ONE: SYSTEMATIC REVIEW OF ANXIETY DISORDERS FOLLOWING TBI

1.1.Introduction

Traumatic brain injury (TBI) is caused by a bump to the head, or by sudden movement to the head and/or neck, resulting in neurological changes that affect normal brain functioning (Albicini & McKinlay, 2014; Centers for Disease Control and Injury Prevention, 2013; Masel & DeWitt, 2010). Prevalence estimates vary depending on the source of the statistics, however rates of TBI have been reported to be as high as ~30% in individuals aged 0-25 years from a New Zealand birth cohort (McKinlay et al., 2008). Among children admitted to the emergency department (ED) of a Melbourne based hospital, TBI rates were reported to be as high as 20% for children aged 0-16 years (Crowe, Babl, Anderson, & Catroppa, 2009). Further, of these children, 89.1% were classified as mild, 7.9% as moderate and 3.0% as severe injuries (Crowe et al., 2009). Given the rate of TBI in young people, any accompanying negative effects associated with such an injury are likely to represent a significant health concern and burden, and such problems require further review and investigation to better understand what is required for rehabilitation and recovery.

There is consistent evidence that TBI can be accompanied by ongoing behavioural deficits. Research has demonstrated that children with TBI are at an increased risk of long-term externalising behaviour problems including increased hyperactivity, aggression and conduct problems (Hawley, 2003; Liu & Li, 2013; Massagli et al., 2004; McKinlay, Dalrymple-Alford, Horwood, & Fergusson, 2002; McKinlay, Grace, Horwood, Fergusson, & MacFarlane, 2009; Schwartz et al., 2003). In addition, a higher incidence of psychiatric disorders in children with TBI have been reported, including higher rates of Attention Deficit/Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), drug abuse,

and personality change disorders (Max et al., 2013; Max et al., 2012). While it has been established that TBI is associated with an increased rate of psychiatric disorders and behavioural problems in children, this focus has tended to be on externalising behaviours. By comparison, internalising disorders and in particular, anxiety disorders have been relatively ignored within the literature when exploring the negative outcomes associated with childhood TBI.

1.1.1. Definitions of TBI across severity levels

Severity of TBI refers to the extent of the disruption that has occurred to brain physiology and the amount of neuroanatomical damage as a result of the blow (Corrigan, Selassie, & Orman, 2010). It is most commonly assessed by the Glasgow Coma Scale (GCS), length of post-traumatic amnesia (PTA) and duration of loss of consciousness (LOC) (American Congress of Rehabilitation Medicine, 1993; Maas, Stochetti, & Bullock, 2008; McKinlay, 2010). The GCS is usually considered the best indicator of TBI severity, and measures severity across three domains – best motor and verbal responses, and eye opening, with 15 indicating lowest severity of injury (Greenwood, 2002).

TBI can be classified as mild, moderate or severe (Corrigan et al., 2010). A TBI is generally classified as severe when the patient presents with a GCS score of ≤8 (Baalen et al., 2003), PTA lasting over seven days, and LOC for more than 24 hours (Corrigan et al., 2010). Moderate TBI is defined by a GCS score of 9-13 (Baalen et al., 2003), PTA lasting between one and seven days and LOC lasting 30 minutes-24 hours (Corrigan et al., 2010). While there is poor consensus for the criteria associated with mild TBI (Albicini & McKinlay, 2014), it is generally indicated when LOC lasts less than 30 minutes, a GCS of 13-15 after 30 minutes is recorded, and PTA lasts less than one day (American Congress of Rehabilitation Medicine, 1993; Cassidy et al., 2004; Corrigan et al., 2010; McKinlay, 2010).

1.1.2. Research population groups

As mentioned above, prevalence rates of TBI will differ according to the participant sample they are derived from. Therefore, behavioural and psychiatric outcomes following TBI will also vary depending on different populations. TBI outcome studies generally draw participants from a community-based or hospital-based setting, and some recruit from clinical samples. Community-based samples include those which recruit participants from the general population utilising flyers and other advertisements (Hale, Raaijmakers, Muris, van Hoof, & Meeus, 2008; Hawley, Ward, & Magnay, 2004; Liu & Li, 2013; Vanderploeg, Curtiss, Luis, & Salazar, 2007), whereby TBI is recalled or identified based on retrospective accounts. Hospital-based samples utilise ED and hospital admission records to obtain medical information regarding TBI (Anderson, Brown, Newitt, & Hoile, 2009, 2011; Crowe et al., 2009; Max, Friedman, et al., 2015), which allows for more accurate identification of injury. Clinical samples include individuals presenting within a mental health service or other health-care facility (DeBellis et al., 2000; Kurowski et al., 2013; Max & Dunisch, 1997; Max, Sharma, & Qurashi, 1997), allowing for accurate and detailed diagnostic information regarding behavioural and psychological functioning. Among the research, the majority of childhood TBI outcome studies tend to use samples recruited from hospital admissions and community-based groups, with a lack of focus examining clinical samples. However, the method of recruitment is likely to highlight differing results, and though outside the scope of this chapter, these differences will be highlighted and discussed in later sections.

1.1.3. Rationale

As will be discussed, anxiety negatively affects all areas of function, which is particularly important in the case of children, who are in a rapid state of developmental

change. Research has shown that exposure to events that produce chronic anxiety can have long-term consequences by disrupting the developing architecture of the brain (Arnsten, 2009; Brinks, deKloet, & Oitzl, 2008). It is therefore important that we understand the impact of anxiety on outcomes following TBI in childhood as this will provide a platform for appropriate intervention to promote a more positive result. Based on the literature, this review will include three areas of research. The first will focus on internalising behaviour problems following TBI in children and adolescents, considering the comparative lack of interest in this area as compared to externalising problems. The second, and major part of the review, will systematically review all original research studies up until 2017 that have explored the relationship between TBI and anxiety disorders in children and adolescents. The merit of each study will also be critically analysed according to specified criteria outlined in a previous paper (Satz, 2001).

1.2. Internalising behaviour problems following TBI in children and adolescents

'Internalising behavioural problems' or 'internalising disorders' refer to psychiatric symptoms and behaviours which tend to manifest 'within the self', cause stress and impairment for the individual, and are usually dealt with internally, such as depression and anxiety (Bayer et al., 2012). This is in contrast to 'externalising behaviour problems' or 'externalising disorders', which are symptoms and behaviours that are directed outwards, and are usually visibly distressing, destructive and concerning for the individual, such as aggression and hyperactivity (Bayer et al., 2012).

As mentioned above, the incidence, rate and profile of internalising disorders following TBI in children has been relatively overlooked in the literature when compared to that of externalising disorders. This lack of extant research may be because internalising behaviours represent internal states of distress and therefore are not readily observed by others, whereas externalising behaviours are directed outwardly and therefore tend to be more

visibly distressing and observable (Bayer et al., 2012). This difference in presentation of difficulties may contribute to the lack of research in internalising disorders, given that externalising problems experienced by children following TBI may be more readily reported by parents. However, this does not explain why self-destructive internalising problems, such as self-harm and suicidal behaviours, are also overlooked. Alternatively, the fact that males present with higher rates of TBI than females (Crowe et al., 2009; McKinlay et al., 2008) may also be a factor, considering that externalising disorders tend to be more common in males (Bayer et al., 2012; Scott et al., 2015), while females are more likely to report internalising problems (Scott et al., 2015). Put together, these findings would likely bias the literature as externalising behaviours following TBI may be seen as a larger concern.

Some work has been conducted in the area of internalising disorders following TBI; however a number of methodological concerns exist in the research and, in comparison to studies investigating externalising behaviours, replication studies still need to be undertaken. The research exploring the incidence of psychiatric disorders in general following TBI have indicated that both symptoms and diagnoses of internalising behavioural problems, including anxiety, depression, emotional and social withdrawal symptoms, are elevated in children and adolescents post-injury (Karver et al., 2012; Liu & Li, 2013; Max et al., 2013; Max et al., 2012).

For instance, a longitudinal, prospective study investigating the rate of novel (new onset) psychiatric disorders three months after TBI in 141 children and adolescents (7-17 years when hospitalised) reported a rate of 49% suffering some novel disorder post-injury, compared to 13% of the orthopedic injury (OI) group (Max et al., 2012). Furthermore, when examining separate diagnoses, in the TBI group 15% had developed a novel anxiety disorder, 8% reported novel depressive disorder, and 18% reported novel internalising disorders (internally oriented distress and psychopathology), compared to the OI group with 7.5%, 2%

and 9%, respectively. Moreover, in this sample, novel internalising disorders and novel anxiety disorder were found to occur more frequently than ADHD and ODD (Max et al., 2012). In support of this, in a sample of children aged 5-15 years with mild TBI, at six months post-injury, novel psychiatric disorders occurred in 25/70 children, with 64% of these classified as internalising disorders, and 36% of these as specific anxiety disorders (Max et al., 2012). In contrast, McKinlay et al. (2009) also examined the rate of children suffering from psychiatric disorders following inpatient and outpatient mild TBI, however found no significant differences among TBI groups and the OI group in the number of children meeting diagnostic criteria for anxiety disorders. Differences among the studies may be due to the methodology, such that Max et al. (2012) focussed on short-term behavioural problems in children, whereas McKinlay et al. (2009) focussed on long-term effects of TBI; as such, length of time since injury and accompanying psychiatric outcomes will be a factor of further interest in this thesis.

Studies looking into behavioural functioning in general, without a focus on internalising problems, also present similar findings as above. Karver et al. (2012) assessed children, mean age of approximately five years, with mild to severe TBI over a 38 month period to examine the impact of age at time of injury (TOI) on the presence of persistent behavioural problems, compared to that of children with OI. Assessments were conducted at baseline and again at 38 months. Parent-report measures indicated that children with severe TBI had clinically elevated behaviour problems for externalising, ADHD, internalising and anxiety symptomatology at the extended follow-up (Karver et al., 2012). However, the study did find that this relationship was not as strong for anxiety disorders as compared to ADHD and other externalising behaviours (Karver et al., 2012). Liu and Li (2013) demonstrated that increased internalising problems including anxious/depressed, somatic complaints, and being

withdrawn, were evident for pre-school children with only mild TBI, compared to children with no injury (Liu & Li, 2013).

When reviewing studies which focus solely on the incidence of internalising disorders following TBI, it is evident that the literature is limited further. One study targeted internalising symptomatology of adolescents aged 12-17 years who had suffered from mild to severe TBI within the previous six months (Peterson et al., 2013). Parental and child ratings of internalising behavioural problems, via a behaviour rating scale were obtained, and the results revealed that while parental reports of internalising problems were within the normal range, 22-26% of the sample demonstrated clinically elevated internalising behaviour problems (Peterson et al., 2013). Further, for maternal reports, female gender was associated with higher levels of internalising problems, however this relationship did not exist for paternal reports (Peterson et al., 2013). Alternatively, a study of adult outcomes following pediatric TBI at age 1-17 years reports on increased rates of anxiety and internalising disorders in individuals with TBI compared to OI controls (Scott et al., 2015). Linking in with gender differences in rates of internalising problems post-TBI, this study found that females with moderate-severe TBI were more likely to develop lasting mood, anxiety and internalising disorders, and that females with mild TBI were more likely to report anxiety and internalising disorders (Scott et al., 2015), than males with TBI. These studies clearly highlight some gender difference in the presentation of long-term behavioural problems following TBI in children and adolescents.

Finally, within the literature assessing internalising disorders in individuals with a history of TBI, it is evident that anxiety disorders are among the problems experienced by such individuals. An early case study by Max et al. (1995) described one individual (of female gender) who, after sustaining a severe TBI at the age of 11 years, later developed symptoms of Obsessive-Compulsive Disorder (OCD). The patient was assessed at three, six

and 12 months post-TBI, and it was apparent that by the time of resolution of PTA, the patient started exhibiting compulsive hand washing, ordering, counting and arranging behaviours, which went on to require treatment (Max et al., 1995). Similarly, another case study reports on a 17 year old male patient with TBI requiring surgery, who reported the onset of Social Anxiety Disorder (SAD) following their injury (Chaves et al., 2012). Prior to his injury, the patient reported no history of shyness, fear or avoidance of social situations, which drastically changed following the TBI event (Chaves et al., 2012). However, despite this, studies exploring the incidence and predictors of specific anxiety disorders following mild, moderate and severe TBI in children and adolescents are still lacking. Considering this oversight within the literature, the next section of this review will focus more specifically, and in more detail, on anxiety disorders and symptomatology in children and adolescents following TBI.

1.3. Systematised literature search on studies involving anxiety disorders following TBI in children and adolescents.

1.3.1. Literature search methods

A systematised literature search was conducted using the following search engines: Google Scholar, Ovid Medline (1946 - Dec 2017), PsycINFO (1806 - Dec 2017), Comprehensive Journal Index and Additional Resources for Nursing and Allied Health Professionals (CINAHL) plus (1937 - Dec 2017), Cochrane database (2005 – Dec 2017) and Embase (1946 – Dec 2017). A search was conducted in each database using the terms “traumatic brain injury” or “brain injury” or “head injury” and “anxiety disorders” or “anxiety” and “pediatric” or “paediatric” or “children” or “child”. Returned articles were screened by title, abstract or full-text accordingly. Manual searching of articles based on the reference lists of relevant manuscripts was also conducted. Inclusion criteria for studies were

as follows: a) participants were children aged 0-18 years, b) the study included a TBI group, and c) anxiety symptoms or anxiety disorder diagnosis was included as an outcome measure. Exclusion criteria involved: a) adult participants or a mixture of children and adults, and b) participants with acquired brain injury.

1.3.2. Results of literature search

The initial search across all databases returned a total of 346 articles. Of these, 221 were screened by title (including duplicates), and 82 were screened based on the abstract. The full text was examined for 43 of the articles. Of the articles examined by full text, 32 of these were excluded for the following reasons: not an original research paper (n=6), case study (n=1), not specifically assessing anxiety as an outcome measure (n=21), not assessing TBI participants (n=3), or couldn't access the article (n=1). No further studies were found when conducting a manual search of additional studies using the reference lists of relevant papers. This search was repeated to include further research articles, which found one additional relevant paper. The final result included 12 research studies fitting the above criteria, for which study characteristics and findings are outlined in Table 1.1.

1.3.3. Critical examination of the literature

Examination of the merit of study methodology in accordance with Satz (2001)

In a review investigating the cognitive, behavioural and academic outcomes of mild TBI in children and adolescents, Satz (2001) analysed the merit of each study according to specified criteria. The basis of this was due to the wide variability in methodology for past studies involving mild TBI. The criteria of which studies were analysed will be listed following a display of studies in Table 1.1.

Table 1.1.

Characteristics of Studies from Literature Search

Authors	Participants	Diagnosing TBI	Inclusion/Exclusion Criteria	Anxiety Measures	General Results
[1] Max et al. (1998)	50 consecutively admitted TBI patients aged 6-14 years at time of injury (TOI) - 26 mild TBI, 9 moderate TBI, 15 severe TBI - 64% male	Severe injury = Glasgow Coma Scale (GCS) score ≤ 8 Moderate injury = GCS score 9-12 or 3-15 with positive computed tomography (CT) scan Mild injury = GCS score 13-15	Inclusion: admitted to tertiary care centre and 3 regional hospitals, CT scan on admission, English spoken language Exclusion: post-traumatic amnesia (PTA) > 3 months, penetrating TBI, documented history of child abuse and/or TBI involving hospital admission, history of Central Nervous System (CNS) disorders, pre-existing serious illness	Neuropsychiatry Rating Scale (NRS) Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) plus PTSD module Follow-ups: K-SADS plus sections on behaviour disorders, alcohol and substance abuse and PTSD module	2/50 with PTSD (resolved by 3 months) Increase in PTSD symptoms in first 3 months, then gradual decline 68% experienced ≥ 1 PTSD symptom at any point in first 3 months; 45%, 33%, 16% and 12% at 3, 6, 12 and 24 months Presence of internalising disorders, and severity of injury predictors of PTSD
[2] Levi & Drotar (1999)	Children 6-12 years at TOI 81 TBI - 44 moderate, 37 severe - 74% males 59 OI children - 61% males	Severe TBI = GCS score ≤ 8 Moderate TBI = GCS score 9-12, or >12 plus positive CT scans or loss of consciousness (LOC) > 15mins	Inclusion: hospitalised ⩾1 night, participants from a prospective study on impact of TBI, English as primary language Exclusion: history of child abuse, TBI or brain disease, children with brain injuries other than closed head injury (e.g. anoxic injuries)	Child PTSD Index (CPTSDRI) (child report) Post-Traumatic Stress Scale (PTSS) (parent report)	Parent reports for moderate TBI and OI in doubtful range for PTSD; mild levels PTSD reported for severe TBI at 6- and 12-months PTSD symptoms higher for severe TBI Younger age and higher social disadvantage associated with more PTSD symptoms Children displayed PTSD symptoms for >1 year post-TBI
[3] Gerring et al. (2002)	95 children aged 4-19 years with severe TBI and PTA - mean age at TOI 10.5 years -54 boys, 41 girls - 90 inpatient; 5 outpatient	GCS score of 3-8 indicated severe TBI	Inclusion: children admitted to neurorehabilitation unit of university-affiliated center Exclusion: previous hospitalisations for TBI, premorbid PTSD, premorbid mental retardation or CNS pathology, history of child abuse	Diagnostic Interview for Children and Adolescents parent and child form (DICA) Child Behaviour Checklist (CBCL) 1-year follow-up: DICA CBCL	13% sample developed PTSD within 1 year of TBI - 5 according to parent reports, 5 to child reports and 2 to both Risk factors for PTSD: female gender, high psychosocial adversity, greater injury severity, psychiatric disorders early after injury

[4] Herskovits et al. (2002)	94 participants aged 4-19 years with severe TBI - 53 boys, 41 girls - mean age TOI 10.5 years	GCS score of 3-8 indicated severe TBI	Inclusion: children referred from tertiary trauma centres to a university-affiliated center for neurological disorders Exclusion: previous hospitalisations for TBI, premorbid PTSD, premorbid mental retardation or CNS pathology, history of child abuse	Same procedure as Gerring et al. (2002) (above) Magnetic Resonance (MR) Imaging: - imaging at 3 months post-TBI - abnormalities included hematoma, contusion, infarct, axonal-shear injury	9 participants met full PTSD criteria; 41 re-experiencing criteria, 12 avoidance criteria, and 55 hyper-arousal criteria Participants with full PTSD criteria at 1 year post-TBI displayed lower lesion fractions in right medial frontal cortex and greater lesion fractions in left middle temporal gyrus High lesion burden was associated with lower probability of having PTSD
[5] Luis & Mittenberg (2002)	96 children aged 6-15 years - 42 mild (66.7% male), 19 moderate/severe (68.4% male), - 35 OI (74% male)	Reviewed medical charts GCS score on admission - mild TBI – GCS 13-15 and normal CT/neurological findings - moderate/severe TBI – GCS <13, abnormal CT, and/or skull fracture	Inclusion: children consecutively admitted to general hospital Exclusion: history of neurological disorders, history of abuse/neglect	Diagnostic Interview Schedule for Children (DISC-IV) Module A: Anxiety Disorders Diagnoses based on DSM-IV criteria Social Readjustment Rating Questionnaire (SRRQ) (stress)	Social Phobia: 10.5% moderate/severe Separation Anxiety Disorder (SAD): 7% mild, 21% moderate/severe Specific Phobia: 9.5% mild Panic Attacks: 4.7% mild Agoraphobia:7 % mild, 5.3% moderate/severe Generalised Anxiety Disorder (GAD): 16.7% mild, 15.8% moderate/severe Obsessive-Compulsive Disorder (OCD): 7% mild, 10.5% moderate/severe PTSD: 10% mild, 10.5% moderate/severe Acute Stress Disorder (ASD): 2.3% mild, 10.5% moderate/severe Overall Anxiety: 35.7% mild, 63.2% moderate/severe
[6] Vasa et al. (2002)	97 children aged 4-19 years with severe TBI - 58% male - mean age at TOI 10.56 years	GCS score of $\leq$8 taken at admission indicated severe TBI	Inclusion: referred from tertiary trauma centres and recruited from consecutive admissions from 1992-1996 to neurorehabilitation unit of university-affiliated center Exclusion: previous hospitalisations or emergency room visits for TBI, history of child abuse, premorbid mental retardation or CNS pathology	DICA-p assessed anxiety disorders at baseline and 1-year follow-up	Mean aggregate Anxiety score of 1.86 pre-injury and 3.73 post-injury - pre-TBI, 84% reported 0-3 anxiety symptoms, 13% reported 4-9, and 3 reported $\geq$10 - post-TBI, 66% reported 0-3, 22% reported 4-9 and 12% reported $\geq$10 - significant increases in amount that had 4-9 and more than 10 symptoms Pre-injury anxiety and younger age at injury risk factors for anxiety

[7] Mather et al. (2003)	43 children from Casualty section of Sydney hospital aged 6-16 years - 20 males, 23 females - 14 mild TBI, 29 no TBI	Mild TBI defined by: - witnessed LOC - GCS 13-15 taken from medical file - return to full GCS score after 24 hours	Inclusion: enrolled in normal stream school, involved in recent traffic accident, sustained an injury other than TBI or a TBI Exclusion: prior TBI history, current TBI of moderate or severe classification, limited English comprehension of families	CPTSDRI – children report of PTSD Revised Children's Manifest Anxiety Scale (RCMAS) PTSD module of Anxiety Disorders Interview Schedule-child version (ADIS-c) CBCL	No significant differences between groups for PTSD symptomatology 69% no-TBI and 85.7% TBI group suffered from PTSD Mean scores indicated improvements in PTSD symptoms Presence of PTSD strongly associated with anxiety Child and parent report of PTSD not significantly correlated
[8] Vasa et al. (2004)	97 children aged 4-19 years with severe TBI - 57% males - mean age at TOI 10.62 years	Initial GCS score on admission of ≤ 8 indicated presence of severe TBI	Inclusion: referred from tertiary trauma centres and recruited from consecutive admissions from 1992-1996 to neurorehabilitation unit of university-affiliated center Exclusion: previous hospitalisations or emergency room visits for TBI, history of child abuse, premorbid mental retardation or CNS pathology	MR Imaging conducted 3 months post-TBI DICA was given to parents of children to assess anxiety disorders and symptoms	12 subjects had 1 post-injury disorder, 1 had 2 disorders: 6 simple phobia, 5 overanxious disorder, 1 SAD and 1 OCD 7 subjects had post-injury PTSD; 1 had anxiety disorder and PTSD Mean number of anxiety symptoms: 1/88 pre- and 3.76 post-injury Inverse relationship between orbitofrontal damage and post-injury anxiety
[9] Grados et al. (2008)	72 children aged 6-18 years with severe TBI - mean age at TOI 10.5 years - 54% males	Initial GCS score on admission of ≤ 8 to indicate severe TBI Also monitored duration of coma	Inclusion: referred to neurorehabilitation unit of a university-affiliated hospital between 1992-1997 Exclusion: previous hospitalisations for TBI, premorbid PTSD, premorbid mental retardation or CNS pathology, history of child abuse	DICA-revised was used to determine OCD, OCS, mood, anxiety and behavioural problems MR Imaging 3 months after TBI	21 children had new onset OCS – 12 obsessions, 13 compulsions, 4 both Greater number of females in OCS group (70%) compared to non-OCS (37%) Those with OCS had higher number of SAD, specific phobia, PTSD, hyperarousal, mania, dysthymia and depressive symptoms Obsessions related to mesial prefrontal and temporal lesions; compulsions related to smaller orbitofrontal lesions

[10] Hajek et al. (2010)	251 children aged 8-15 years - 167 mild TBI (71% male), 84 OI (63% male)	Mild TBI – observed LOC ≤30 minutes, GCS of 13-14 or at least 2 symptoms of concussion OI – fracture injury within Abbreviated Injury Scale (AIS) ≤3	Inclusion: aged 8-15 years, recruited from Emergency Departments (ED) at selected hospitals, had suffered OI or mild TBI Exclusion: injury-related surgery, hypoxia or shock post-injury, previous TBI needing hospitalisation, premorbid neurological disorders, severe psychiatric disorder needing hospitalisation, AIS of greater than 3, injuries that would hinder assessment, child abuse/neglect	PTSD Checklist for Children/Parent Report (PCL-C/PR) to assess parent ratings of PTSD in children	PTSD diagnoses for Mild TBI: baseline 8%, 3 months 8% and 12 months 2% - OI: 7%, 7% and 7% respectively Across groups, PCS and PTSD ratings were correlated After controlling for PCS, OI group reported higher scores on PCL-C/PR than mild TBI group at baseline Symptoms of PTSD and PCS correlated more highly for OI group than mild TBI
[11] Max et al. (2011)	177 children aged 5-14 years with TBI - 86 mild, 27 moderate, 64 severe - mean age at TOI 10.13 years - 71% male	GCS scores of 3-8 for severe TBI, 9-12 for moderate TBI and 13-15 for mild TBI - also assessed MR scans	Inclusion: Consecutive admissions to 3 academic medical centres for TBI between 1998-2003 Exclusion: pre-existing autism, Attention-Deficit/Hyperactivity Disorder (ADHD) or schizophrenia, mental deficiency, injury due to child abuse or penetrating injury	DSM-IV diagnoses derived from KSADS present and lifetime version, and NRS MR Imaging scans at 3 months	8.5% developed novel clinical anxiety disorder and 17% developed novel subclinical anxiety disorder post-TBI - mild TBI: 11% clinical and 20% subclinical anxiety - moderate TBI: 0% clinical and 24% subclinical anxiety - severe TBI: 7% clinical and 11% subclinical anxiety 9 PTSD, 6 SAD, 4 simple phobia, 3 GAD, 3 adjustment disorder with anxious mood, 3 social phobia, 1 Panic Disorder (PD) Younger age at injury associated with novel anxiety disorder
[12] Max et al. (2015)	125 children aged 5-14 years with TBI - 63 mild, 16 moderate, 46 severe - mean age at TOI 9.99 years - 66.4% males	GCS scores of 3-8 for severe TBI, 9-12 for moderate TBI and 13-15 for mild TBI - also assessed MR scans	Inclusion: Consecutive admissions to 3 academic medical centres for TBI between 1998-2003 Exclusion: pre-existing autism, ADHD or schizophrenia, mental deficiency, injury due to child abuse or penetrating injury	DSM-IV diagnoses derived from KSADS present and lifetime version, and NRS MR Imaging scans at 3 months	10.4% presented with novel anxiety disorders in second 6-months after TBI - 6 simple phobia, 4 SAD, 4 GAD, 3 social phobia, 3 PTSD, 1 PD - 5/13 had >1 disorder

The key criteria set out as essential for studies in this area were as follows: a) use of a control group, b) longitudinal design with follow-up assessments, c) clear definition of mild TBI, d) inclusion of at least 20 participants with TBI, e) outcome measures involved standardised tests, and f) control for pre-injury factors (Satz, 2001). A study was concluded to have methodological merit if it met at least four of the previously listed criteria (Satz, 2001). For this review, the methodology of the selected papers was examined according to these criteria, with the inclusion of moderate and severe injuries for point a).

As is evident in Table 1.1, in accordance to the criteria set out by Satz (2001), all of the studies investigating anxiety disorders following TBI in children and adolescents had methodological merit, possessing at least four of the essential criteria. Three of the studies (see studies 2, 5, 10) included all of the listed criteria, and the most commonly missed criteria was a lack of a control group in eight out of the 12 papers (see studies 1, 3, 4, 6, 8, 9, 11, 12). All included studies showed evidence of criteria b), c) and e), indicating the use of longitudinal designs, well-defined TBI groups and standardised outcome measures and assessments. Only one study did not include more than 20 TBI participants or control for pre-injury characteristics (see study 7).

Of concern is the number of studies that did not include a non-TBI group. The research being discussed explores the rate of anxiety disorders following TBI in children and adolescents, and although this information can be obtained using only a TBI group, the strength of the results may be enhanced if authors could compare these rates to a non-injured or OI group of participants. It is also interesting to note that of the studies that did include a control group (see studies 2, 5, 7, 10), all utilised an OI group with injuries sustained to regions of the body other than the head or neck. There is therefore an absence of studies that have compared the incidence of anxiety disorders in children and adolescents with TBI and healthy control subjects, or a comparison of outcomes within clinical samples. While it is

useful to use an OI comparison group as it eliminates confounding variables associated with the nature of injury and exposure to hospital/rehabilitation services, the literature is in need of research which compares the incidence of anxiety following TBI to what is expected in the general child population, and clinical population seeking mental health support.

In addition, while all but one controlled for pre-injury characteristics and risk factors (see study 7), the validity of such measures is questionable given the timing of testing. In all cases, premorbid functioning such as behaviour scores, pre-existing psychiatric disorders and family functioning assessments were conducted at 'baseline' – meaning that they were assessed following the TBI event. This presents a large issue within the TBI literature as it is difficult to ascertain the validity of reports on child variables that were present before the TBI event when they are considered retrospectively. Psychological stress as a result of the injury, for both the child and the parent, is likely to affect the ability for the parent or child to recall incidents and functioning before the injury event. Furthermore, the child's current behaviour and functioning may change the child or parent's perspective of what occurred before the TBI. However, the authors do attempt to alleviate the effects of this issue in that testing at 'baseline' was always conducted as soon as possible, once major concussion symptoms (such as PTA) had resided.

A significant strength among the literature on anxiety disorders following TBI in children and adolescents is the use of a prospective, longitudinal design with follow-up assessments of behaviour and anxiety. Several studies conducted follow-ups up to one year after TBI (see studies 1-4, 6, 8-10, 12), which allowed for the examination of long-term effects of TBI and the persistence and chronicity of anxiety in such participants. Further, in fewer studies (see studies 1, 2, 10), participants were assessed at multiple time points, which is essential for exploring the pattern of anxiety disorders and symptomatology following TBI across time.

Well-defined severity groups are important when conducting TBI studies, particularly when comparing groups and when assessing the influence of injury severity on outcomes. Evidently, the studies presented in this paper all assessed and defined severity of TBI using the GCS (see Table 1.1, studies 1-12). As discussed previously, the GCS is regarded as the most common method of assessing TBI severity (Greenwood, 2002), and has been proven both useful and valid in multiple studies. In addition, in many cases other markers of TBI severity were also examined, such as positive CT scans (studies 1, 2, 5, 11, 12) and the duration of LOC (studies 2, 7, 9, 10).

Overall, when considering the methodological merit of the studies listed in this review, the results are in favour of existing research. While the absence of a control group for over half of the studies poses some concern for the generalisability of findings, their methodology is strengthened by the use of a longitudinal design with timely follow-up assessments post-TBI and well-defined and accurately assessed TBI severity for each injury group. In addition, all but one study (see study 7) had an adequately sized sample of TBI participants. Furthermore, outcome measures for all of the papers were assessed using standardised, common measures and procedures for examining the presence of anxiety disorders in children and adolescents. However, despite this, when exploring factors outside the main criteria set out by Satz (2001), other methodological issues across the literature are evident; they will now be discussed.

Other methodological issues within the literature

Upon examination, additional common methodological concerns arise across the featured studies. An important finding is that there is a lack of research which has included participants with mild TBI, with a large focus on children with severe TBI. Of the studies in this review, six included participants who had suffered mild TBI (studies 1, 5, 7, 10, 11, 12),

while ten of the studies also included moderate or severe TBI groups. Considering that studies on externalising disorders have indicated an increased incidence of psychiatric disorders such as ADHD, ODD, CD, drug and alcohol abuse/use and personality disorders in children with even mild TBI (Max et al., 2013; McKinlay et al., 2002; McKinlay et al., 2009), it remains just as important for mild TBI groups to be included in outcome studies, regardless of the lesser degree of injury compared to moderate or severe TBI.

In relation to this, it is often suggested within the PTSD literature that the diagnosis of PTSD following TBI is not valid due to the nature of the psychological events that follow such an injury (Levi, Drotar, Yeates, & Taylor, 1999; Mather, Tate, & Hannan, 2003; Max et al., 1998). This argument states that children who suffer from TBI and lose consciousness or experience PTA are unable to suffer the anxiety of PTSD that is associated with re-experiencing a traumatic event, as the event itself cannot be recalled and cannot therefore be subsequently emotionally suppressed (Levi et al., 1999; Max et al., 1998). The authors, however, do not discuss this argument in relation to children who suffer from a TBI mild enough that it does not result in LOC or PTA. However, instead they tended to utilise samples of children with more severe injuries (see studies 2-4), thereby contradicting their argument. Furthermore, over half of the research has focused on solely PTSD following TBI (studies 1-4, 7, 10) and excluded other anxiety disorders, due to the close relationship it has with trauma (Vasa et al., 2002). Moreover, one study (see study 7) applied more focus on PTSD in children following road traffic accidents, and utilised the TBI group as a control for confounds associated with such an injury, rather than exploring long-term anxiety outcomes following TBI.

Also interesting to note in regards to PTSD following TBI is the discrepancy that is often found between reports of PTSD symptomatology from the child versus the parents. For instance, studies by Levi et al. (1999) and Mather et al. (2003) utilised both parent and child

self-report questionnaires to assess PTSD. However, correlational analyses indicated a relatively low, non-significant relationship between reports from children and adults. The meaning of this is not well discussed, which poses a challenge to the methodology of papers which utilise only one source of PTSD symptom reporting. Such that, it may be impossible to know which method provides more accurate reports of PTSD symptomatology post-TBI, considering research findings differ according to the informant completing the questionnaires. In addition, it is not well-known whether the relationship (or lack thereof) between parent and child self-reports of PTSD symptomatology also exists for other anxiety measures. Indeed, Luis and Mittenberg (2002) question the validity of parent-report methods for assessing anxiety, arguing that these internal states can be reliably reported by the children themselves, without need for parental reports. Furthermore, parents may be a less reliable source of report as they are sometimes unable to see how a child is processing their inner thoughts and emotions. However, again, this issue is not well discussed or resolved within the literature. Given this discrepancy of results, it might be important for studies to examine the behavioural profile of children and adolescents with anxiety following TBI using more objective measures of assessment, including psychiatric assessment and observation of the child, rather than relying solely on the use of subjective parental reports.

While there have been advancements towards the study of internalising problems, including anxiety disorders, following TBI in children and adolescents, it is vital to note that of the 12 papers presented here, five of these utilised the same cohort of individuals (see studies 3, 4, 6, 8, 9). While the sample itself was derived from a large database of referrals from tertiary trauma centres over a relatively large period of time (years 1992-1996), the fact that these studies were replicated among the same cohort limits the generalisability of the results to anxiety and TBI literature. Moreover, studies by Max et al. (2011) and Max, Lopez, et al. (2015) also drew upon data from the same cohort of participants, albeit at different

time-points (six and 12 months). Although the studies provide useful information regarding the relationship between TBI and anxiety disorders (Gerring et al., 2002; Grados et al., 2008; Vasa et al., 2002) and also neural correlates associated with anxiety disorders after TBI (Herskovits, Gerring, Davatzikos, & Bryan, 2002; Vasa et al., 2004), the literature remains sparse in relation to different cohorts of children and adolescents being examined for such variables. In addition, the age range of participants across studies is quite large and variable. For instance, many of the studies utilised samples with children aged 4-19 years of age (Gerring et al., 2002; Herskovits et al., 2002; Vasa et al., 2002; Vasa et al., 2004). Internalised problems and behaviours experienced by a four year old are expected to be very different compared to that of a 19 year old. Moreover, a younger child of four years is developing and growing at a rapid rate, whereas a child of 19 years is more likely to have completed development at that age. This is something which may need to be considered in future research.

PTSD following TBI

As is evident in Table 1.1, results from the studies generally reveal a relationship between the development of anxiety disorders following TBI in children and adolescents. The majority of studies however have focused on correlates of PTSD following childhood TBI (see studies 1-4, 7, 10), due to the obvious relationship between such an injury event and trauma (Vasa et al., 2002). Main findings indicate that PTSD within one year following TBI can occur despite experiencing PTA (Levi et al., 1999; Max et al., 1998), and that PTSD symptomatology is more prominent in children with severe TBI than those with moderate TBI or OI (Levi et al., 1999).

In an early study of PTSD in children following TBI, Max et al. (1998) conducted psychiatric assessments at three, six, 12 and 24 month intervals to examine the predictors and

risk factors of children with mild, moderate and severe TBI on the likelihood to suffer from clinically significant PTSD symptomatology. Following comprehensive psychiatric interviews and evaluations, the results revealed that the incidence of PTSD was rare, however a definite increase in PTSD symptoms was noted in the first three months following TBI, with a steady decline thereafter (Max et al., 1998). Similarly, Levi et al. (1999) studied children from a prospective study of cognitive, academic, social and familial impacts of TBI in school-age children to explore the incidence of PTSD symptoms following TBI. In contrast to Max et al. (1998), this study utilised an OI control group, which enabled the authors to compare PTSD symptomatology in children with moderate and severe TBI to children with traumatic injuries sustained to other regions of their body. When comparing the participants, the results revealed significant differences between the three groups, in that parent reports of PTSD symptoms were in the doubtful range at six and 12 month follow-ups for children with moderate TBI and OI, whereas mild levels of PTSD were reported by parents of the severe TBI child group (Levi et al., 1999). Child reports of PTSD symptoms at 12 months were found to be higher for the severe TBI group when compared to moderate TBI and OI, however no group differences were observed at six months following their injury (Levi et al., 1999).

Two later studies further investigated the presence of PTSD following TBI, with a focus on children with severe TBI. Gerring et al. (2002) argued that children with TBI can go on to suffer PTSD symptomatology, despite experiencing neurological amnesia for the injury event. Children were recruited from an ongoing investigation of brain-behaviour relationships after severe TBI, and were assessed via psychiatric interviews and psychological rating scales. The authors reported an incident rate of 13% of children having fulfilled PTSD criteria by one year following their injury (Gerring et al., 2002). Utilising the same cohort of children in a brain imaging study, Herskovits et al. (2002) also explored the rate of PTSD

symptomatology, this time finding that 10% of the sample reported full PTSD criteria, 44% fulfilled re-experiencing criteria of PTSD, 13% reported avoidance symptoms of PTSD and 59% met criteria for the hyperarousal criterion of PTSD. Collectively, the studies provide evidence that PTSD can be experienced in children following severe TBI, regardless of neurological amnesia occurring in the child surrounding their injury event.

Conversely, two studies exploring the relationship between PTSD and TBI report different findings (see studies 7 and 10). One study explored PTSD following road traffic accidents in children with OI and mild TBI (Mather et al., 2003), and the other assessed the relationship between post-concussion symptoms (PCS) and PTSD in children with mild TBI and OI (Hajek et al., 2010). In contrast with the above studies, Mather et al. (2003) reported no significant difference between children with mild TBI and OI on PTSD symptomatology ratings. Moreover, Hajek et al. (2010) also found no significant main effect for group (type of injury) or for the group and time interaction for PTSD, indicating that there were no significant differences in reports of PTSD between children with mild TBI compared to those with OI. This result may suggest that those with milder TBI are not more likely to develop PTSD following their injury than children who have sustained an OI. However, differences in the presentation of PTSD symptomatology following injury were reported in the two papers. In Mather et al. (2003), children with mild TBI tended to report a more frequent occurrence of mild PTSD symptoms, whereas severe PTSD occurred at a higher rate in the OI group. Moreover, Hajek et al. (2010) found that those in the mild TBI group reported higher levels of hyperarousal at three and 12 months, but not when controlling for PCS. Alternatively, OI participants had higher levels of PTSD when controlling for baseline PCS, and were more likely to meet PTSD criteria (Hajek et al., 2010). Therefore, these findings suggest that while there were no differences in the rate of PTSD symptomatology and diagnoses between mild TBI and OI children, the clinical manifestations of such symptomatology may be quite

different across groups. Moreover, the hyperarousal aspect of PTSD appears to be more highly related to TBI than other PTSD symptomatology, which may reflect more of a general anxious response.

Given the above information, it appears that a 'dose-response' relationship may exist between the severity of TBI and the subsequent diagnosis of PTSD or development of PTSD symptoms in children. The research suggests that while there is a rare occurrence of PTSD following moderate or severe TBI in children, and a statistically significant difference in the frequency of this occurrence between children with moderate or severe TBI to children with OI, this relationship may not exist for children with only mild TBI.

Other anxiety disorders and TBI

When reviewing studies that focused specifically on the incidence and presentation of particular anxiety disorders in general, only five studies were found relevant in the literature (see studies 5, 6, 9, 11, 12). One study focused on the incidence of OCD and presence of OCD symptomatology following severe TBI in children and adolescents (Grados et al., 2008). Among those with severe TBI, this study identified 21 children with new onset OCD symptoms, and 51 with no OCD symptomatology. Of those with OCD symptoms, 12 experienced obsessions, 13 experienced compulsions and four suffered from both (Grados et al., 2008). It is therefore evident that the pattern of anxiety related experiences among individuals following TBI can be quite variable. In contrast to Grados et al. (2008), the remaining studies identified through the systematic literature search explored the relationship between mild, moderate and severe TBI and the incidence of disorders including Generalised Anxiety Disorder (GAD), Acute Stress Disorder (ASD), PTSD, Panic Disorder (PD), OCD, simple/specific phobia, social phobia and SAD (Luis & Mittenberg, 2002; Max et al., 2011; Max, Lopez, et al., 2015; Vasa et al., 2002).

Among the first to explore the relationship between TBI and new-onset anxiety disorders and mood disorders, Luis and Mittenberg (2002) evaluated predisposing factors such as developmental disorders, injury severity, environmental factors and individual historical factors on the likelihood of children suffering from such disorders following mild and moderate-severe TBI. Results revealed that children with TBI had a higher number of new-onset disorders than the OI comparison group, with no differences in these numbers between mild and moderate-severe TBI groups (Luis & Mittenberg, 2002). Further, the most common anxiety disorders that were generally reported by children with mild TBI were GAD (16.7%), PTSD (10%), and simple/specific phobia (9.5%), while the most commonly reported anxiety disorders for the moderate-severe TBI group were SAD (21%) and GAD (15.8%) (Luis & Mittenberg, 2002). In a similar study, Vasa et al. (2002) also explored the prevalence of new-onset anxiety disorders among children, however focussed on those who had suffered from severe TBI and included no comparison group. The authors reported that the overall net increase in anxiety disorders for this sample was minimal, with the net increase predominantly associated with 'overanxious disorder', however there was a statistically significant increase in the number of subjects who suffered from either four to nine, and 10 anxiety symptoms following their injury (Vasa et al., 2002). Similar to Luis and Mittenberg (2002), this study noted overanxious disorder, OCD, SAD and simple/specific phobia symptoms as the most common types of anxiety experienced by children following TBI (Vasa et al., 2002).

A more recent study by Max et al. (2011) also focused on the incidence of novel clinical and subclinical anxiety disorders, and included children with mild, moderate and severe TBI. Surprisingly, the results indicated that children with mild TBI had the highest incidence of novel anxiety disorders, while children with moderate TBI had the highest rate of novel subclinical anxiety disorders (Max et al., 2011). The authors contend that novel

anxiety disorders following TBI are heterogeneous in nature, such that they can include definite or subclinical PTSD, SAD, simple/specific phobia, GAD, social phobia and PD (Max et al., 2011). This finding is consistent with prior studies which also note this heterogeneity (Luis & Mittenberg, 2002; Vasa et al., 2002). The authors, in a follow-up study, further explored the nature of novel anxiety disorders in the same cohort of participants, at 12 months post-injury (Max, Lopez, et al., 2015). They found that children tended to present similarly to the six-month assessment, and that novel anxiety disorders present at 12 months were associated with affective dysregulation.

Generally, the results demonstrate that TBI in children and adolescents significantly increases the risk of developing subsequent anxiety disorders (Grados et al., 2008; Luis & Mittenberg, 2002; Max et al., 2011; Max, Lopez, et al., 2015; Vasa et al., 2002). Feeling overanxious was a commonly reported anxiety symptom in children with severe TBI (Vasa et al., 2002). When comparing children with mild TBI, moderate-severe TBI and OI, results suggest a potential relationship between degree of neurological insult and risk of developing subsequent anxiety disorders (Luis & Mittenberg, 2002) in that overall anxiety disorders were most common in children with moderate-severe TBI, followed by mild TBI and OI. However, similarly to research on PTSD after TBI, the pattern of results is often quite different among the sample groups.

Predictors of anxiety disorders following TBI

It is unsurprising that given the research on long-term psychiatric outcomes following childhood TBI, authors have sought to investigate the predictors and risk factors that will increase the likelihood a child will develop psychiatric disorders post-TBI. Among the research exploring anxiety disorders and TBI, several common findings have been reported. For instance, a number of the studies presented here assessed for premorbid psychosocial

adversity (see studies 3, 4, 6, 8, 9). These studies demonstrated that there are higher rates of anxiety and PTSD symptomatology and diagnoses in children that come from families with higher premorbid psychosocial adversity, including coming from a single parent household, being exposed to verbal/physical aggression between parents, or having parents with mental health and/or criminal problems (Gerring et al., 2002; Grados et al., 2008; Herskovits et al., 2002; Vasa et al., 2002; Vasa et al., 2004). In addition, when the impact of age was assessed (see studies 2, 3, 6, 11, 12), it was found that younger age at injury tended to be associated with a higher number of anxiety symptoms (Levi et al., 1999; Max et al., 2011; Max, Lopez, et al., 2015; Vasa et al., 2002). Alternatively, Gerring et al. (2002) found no support for age as a significant predictor of PTSD in their sample of children with severe TBI.

In addition to psychosocial adversity and age of injury, other factors have been noted to predict the development of PTSD in children following TBI. Studies have revealed that levels of PTSD symptoms may be related to social disadvantage and family social status (Gerring et al., 2002; Levi et al., 1999), such that higher levels of social disadvantage were related to higher parent reports of PTSD symptoms (Levi et al., 1999). Anxiety diagnoses and aggregate anxiety scores on the Diagnostic Interview for Children and Adolescents (parent and child forms) also have been found to significantly predict the probability of PTSD diagnosis and symptoms (Gerring et al., 2002), in addition to other internalising psychiatric diagnoses present at the TOI (Gerring et al., 2002; Max et al., 1998).

When examining the likelihood of children developing anxiety symptoms and specific anxiety diagnoses post-TBI, results are quite similar to that of research involving PTSD. The presence of OCD symptomatology following severe TBI was found to be significantly more common in females, and also in children with internalising psychiatric co-morbidities (Grados et al., 2008). Luis and Mittenberg (2002) reported a range of predictors for the development of new-onset anxiety disorders and symptoms, including pre-existing mood or

anxiety disorders, pre-injury history of ADHD or learning disabilities, parent education, post-injury stress scores and severity of TBI. Max et al. (2011) however, reported no association between novel anxiety disorders and severity of injury, yet did find a trend association for novel anxiety disorders and concurrent depressive disorder. See Table 1.2 for an outline of the predictors and risk factors associated with anxiety symptomatology in children and adolescents following TBI.

As evident in Table 1.2 below, it therefore may be apparent that while much research has focussed on identifying the predictors associated with PTSD following TBI, less is known in regards to specific anxiety disorders. Moreover, it is important to note that premorbid functioning is most always assessed post-injury, which clearly limits the ability to infer causation for the predictor variables in such studies.

Neurological explanations and brain lesion studies

In examining the brain regions associated with a higher risk of anxiety following childhood TBI, it is important to first review the areas of the brain that are commonly injured and implicated in TBI. Damage as a result of TBI can be either focal, whereby forces have caused localised damage, or diffuse, whereby damage has occurred to axonal networks across the brain (Levine et al., 2008; Povlishock & Katz, 2005). Due to the fact that TBI can occur under many different, individualised circumstances, damage to the brain is heterogeneous among individuals (Bigler et al., 2013). Despite this fact, it has been noted that the frontal and temporal regions are highly vulnerable to injury, due to the shape of the skull and the way the head is held (Bigler, 2007; Bigler et al., 2013; Levin, Williams, Eisenberg, High Jr, & Guinto Jr, 1992; Wilde et al., 2007). The frontotemporal susceptibility to damage from TBI has been noted as the major cause of the cognitive and neurobehavioural consequences of TBI that some go on to experience, including emotional regulation (Bigler, 2007).

Table 1.2.

Predictors and Risk Factors for Anxiety following Traumatic Brain Injury

Study	Predictors/Risk Factors
Max et al. (1998)	• Internalising disorders • Severity of traumatic brain injury (TBI)
Levi & Drotar (1999)	• Younger age at injury • Social disadvantage • Family social status
Gerring et al. (2002)	• High levels of premorbid psychosocial adversity • Social disadvantage • Family social status • Internalising disorders • Female gender • Severity of TBI
Herskovits et al. (2002)	• High levels of premorbid psychosocial adversity
Luis & Mittenberg (2002)	• Premorbid mood or anxiety disorders • Premorbid Attention-Deficit/Hyperactivity Disorder (ADHD) • Premorbid learning disabilities • Parent education • Post-injury stress scores • Severity of TBI
Vasa et al. (2002)	• High levels of premorbid psychosocial adversity • Younger age at injury
Vasa et al. (2004)	• High levels of premorbid psychosocial adversity
Grados et al. (2008)	• High levels of premorbid psychosocial adversity • Female gender • Internalising disorders
Hajek et al. (2010)	• Post-concussive symptoms (PCS)
Max et al. (2011)	• Younger age at injury • Concurrent depression • Concurrent personality change
Max et al. (2015)	• Younger age at injury • Concurrent depression • Concurrent personality change • Pre-injury anxiety disorder

Further, white matter tracts have been known to be more susceptible to damage due to the acceleration-deceleration forces and their direct exposure to shear and strain forces (Bigler et al., 2013; Povlishock & Katz, 2005; Rutgers et al., 2008), and this white matter

tract damage tends to occur more frequently again within the frontotemporal areas of the brain (Bigler et al., 2013).

Due to the diffuse damage likely to occur following TBI and the heterogeneity that occurs across individuals, research has sought to explore and highlight the most commonly affected regions within the brain that may be associated with long-term behavioural and emotional problems. Reports from a multicentre study of children with TBI have noted white matter hypersensitivities and focal atrophy distributed across frontotemporal areas of the brain (Bigler et al., 2013). More specifically, Magnetic Resonance (MR) imaging scans highlighted that among children with mild, moderate and severe TBI, there were lesions evident in frontal regions, temporal poles, and right medial temporal lobe, and damage was also evident to the amygdala, hippocampus, thalamus and basal ganglia (Bigler et al., 2013). MR imaging procedures were also used in another sample of children with moderate and severe TBI to evaluate brain volume differences in the whole brain and also prefrontal, temporal and posterior regions (Wilde et al., 2007). Imaging results indicated that children with TBI had significantly reduced whole brain, prefrontal and temporal regional tissue volumes compared to that of uninjured children. Further, there were also group differences on white matter and grey matter in superior medial and ventromedial prefrontal regions (Wilde et al., 2007). Additional research has also utilised MR imaging procedures to locate brain regions more commonly affected following TBI, with one study including individuals with mild to moderate TBI (Levin et al., 1992). In terms of number of lesions, results showed that the frontal and temporal areas had significantly more lesions than parietal and occipital areas of the brain.

Again, this is supported by the Toronto TBI study, which recruited individuals with chronic TBI across all levels of severity to undergo MR imaging one year following injury (Levine et al., 2008). The most reliable effects noted in the results were brain volume changes

within the frontal, temporal and cingulate regions, with focal lesions associated with greater volume loss in frontal and temporal regions (Levine et al., 2008). Finally, MR imaging has been used to examine reductions in fractional anisotropy (which reflects fibre density, axonal diameter and myelination in white matter) in adults with mild TBI (Rutgers et al., 2008). Results again demonstrated greater numbers of reductions in frontal and temporal regions, and also parietal regions, and among association bundles, fronto-temporal-occipital fibre bundles were most often involved (Rutgers et al., 2008). Table 1.3 provides a concise summary of the above findings within the literature.

Table 1.3.

Summary of Commonly Damaged Brain Regions following Traumatic Brain Injury

Study	Main results
Levin et al. (1992)	Number of lesions from Magnetic Resonance (MR) imaging: • Total = 145 • Frontal = 60 • Temporal = 55 • Parietal = 15 • Occipital = 10
Wilde et al. (2005)	MR volumetric findings: • Prefrontal regions smaller in those with traumatic brain injury (TBI) • Superior medial grey and white matter, lateral frontal white matter, and ventromedial grey matter smaller in TBI group Lesion volumes from MR imaging: • Majority lesions in frontal and temporal areas
Levine et al. (2008)	• Volume changes in ventral frontal and temporal regions • Cerebrospinal fluid increases in left medial frontal and posterior temporal regions • Grey matter volume changes in ventral frontal, middle frontal, superior frontal, bilateral posterior temporal, left medial temporal, left occipital and basal ganglia/thalamic regions
Rutgers et al. (2008)	Brain regions with reduced fractional anisotropy from MR imaging: • Frontal lobe = 42 individuals (22%) • Parietal lobe = 31 individuals (16%) • Temporal lobe = 28 individuals (15%) • Occipital lobe = 4 individuals (2%)
Bigler et al. (2013)	• Distribution of lesions was more frequent in frontal and temporal regions • Mean group volume differences for white matter, grey matter, hippocampus, amygdala, thalamus, basal ganglia • Focal signal abnormalities and white matter hypersensitivities located predominantly in frontal and temporal lobe regions

When looking into the neural regions implicated in those with anxiety following TBI, it may be possible to discover overlapping regions. However, only two studies have specifically attempted to delineate the neural correlates and brain regions involved in the development of anxiety disorders following TBI in children and adolescents (see studies 4 and 6). One of these studies focused on lesion burden in children with severe TBI and their relationship with PTSD symptomatology (see study 4). Data was obtained from the study by Gerring et al. (2002), which utilised participants with severe TBI, and no comparison group. MR imaging at three months following the TBI event revealed associations between lesion fractions in the right cingulum, right hippocampus, right medial frontal gyrus and left hippocampus at three months post-TBI, and the presence of PTSD re-experiencing symptoms at one year (Herskovits et al., 2002). In addition, assignment to the PTSD versus no-PTSD diagnosis group was dependent on lesions in the right medial frontal and left middle temporal gyri (Herskovits et al., 2002). Furthermore, a lower probability of suffering from PTSD hyperarousal correlated with higher lesion fraction in the left subcallosal gyrus, and avoidance symptoms were associated with lower lesion burden in the right medial frontal and left inferior temporal gyri and higher lesion burden in the left middle temporal gyrus (Herskovits et al., 2002). Interestingly, the researchers found no association between the re-experiencing criterion of PTSD and lesions in the right amygdala, despite research which has suggested that the amygdala is an important structure in the processing of fear and emotional signals (Baird et al., 1999), and in anxiety symptoms (DeBellis et al., 2000).

Again utilising the same cohort of participants, Vasa et al. (2004) explored anxiety disorders in general and their neural correlates in patients with severe TBI using MR imaging procedures. The study was unique in that it attempted to correlate specific brain lesions and their location, with different anxiety outcomes among children with severe TBI. In a one-year prospective study, with a focus on the orbitofrontal cortex (OFC), the imaging results

revealed that the presence of OFC lesions decreased the risk of anxiety disorders when including control variables in the analyses (Vasa et al., 2004). Therefore, an inverse relationship exists in that children with more lesions to the OFC as a result of TBI are less likely to develop anxiety disorders than those with fewer lesions. The OFC is stated to have reciprocal connections with the amygdala (Vasa et al., 2004), which again supports brain region studies which target the amygdala in having some role in anxiety disorders in children (Baird et al., 1999; DeBellis et al., 2000).

In addition, three other studies have included MR imaging procedures in their methodologies (see studies 9, 11 and 12). In examining the nature of OCD symptomatology in children and adolescents with a history of severe TBI, Grados et al. (2008) located specific areas that were associated with the onset of OCD symptomatology following TBI. MR imaging scans revealed relationships between OCD symptoms and lesions in the OFC and temporal lobe regions, and also thalamic lesions for males (Grados et al., 2008). Alternatively, Max et al. (2011) reported in their study of anxiety disorders in children and adolescents six months following severe TBI that a trend association exists between lesions to the superior frontal gyrus and the presence of novel anxiety disorders. Furthermore, a significant association was found between lesions to the superior frontal gyrus and novel subclinical anxiety disorder (Max et al., 2011). However, no other relationships between brain lesions and anxiety symptomatology were found. At a 12-month follow-up, the authors reported no group differences in brain imaging results (Max, Lopez, et al., 2015).

Therefore, the above studies implicate certain brain regions in relation to the elevated incidence of anxiety disorders following TBI in children and adolescents, with emphasis on structures such as the OFC, right medial frontal gyri and temporal gyri. While these studies provide some compelling initial evidence for the neurobiological basis of anxiety disorders following TBI, it is clear that the literature in this area is still sparse.

1.4. Overall discussion

Collectively, it is evident that children and adolescents with a history of mild, moderate and severe TBI are a group at risk of developing future internalising and anxiety problems. Behavioural studies have found a higher rate of depression, anxiety and somatic complaints in children and adolescents post-TBI (Karver et al., 2012; Liu & Li, 2013; Max et al., 2013; Max et al., 2012). Moreover, this relationship is stronger in females (Scott et al., 2015). When looking at anxiety in particular, higher rates of PTSD symptomatology have been identified in children and adolescents following TBI (Gerring et al., 2002; Levi et al., 1999; Max et al., 1998). Further to this, children and adolescents with a history of TBI also present with higher rates of GAD, ASD, OCD, PD, SAD and phobias (Grados et al., 2008; Luis & Mittenberg, 2002; Max et al., 2011; Max, Lopez, et al., 2015; Vasa et al., 2002).

The most common risk factors associated with the development of anxiety symptomatology following TBI in children and adolescents were severity of injury (Gerring et al., 2002; Luis & Mittenberg, 2002; Max et al., 1998), younger age at injury (Levi et al., 1999; Max et al., 2011; Max, Lopez, et al., 2015; Vasa et al., 2002) and high levels of premorbid psychosocial adversity (Gerring et al., 2002; Grados et al., 2008; Herskovits et al., 2002; Vasa et al., 2002; Vasa et al., 2004). Highlighting these premorbid risk factors for children and adolescents with anxiety following TBI enables a unique group to be identified, which can be the focus of clinical intervention and management for such individuals.

1.4.1. Clinical and theoretical implications

Given the findings reviewed in the literature, when assessing children who have been admitted for TBI, it may be important to screen for factors associated with family psychiatric history of internalising disorders, the individual's past psychiatric history of internalising disorders, and also to examine levels of psychosocial adversity. Furthermore, the increased

vulnerability of children with a younger age at injury to developing subsequent anxiety disorders should be considered in such assessments. Children who are younger at the time of TBI, have greater psychosocial adversity, and have some history of psychiatric internalising disorders may be at greater risk of developing anxiety disorders. If such children are targeted early, appropriate intervention practices may be put in place.

Intervention programs for children vulnerable to developing anxiety disorders following TBI may include relaxation procedures for the parent and the child, coping strategies, self-esteem building activities, or open communication between the parent and child regarding the child's anxiety symptoms or worries. Furthermore, those at high risk of developing anxiety disorders may benefit from a follow-up screen following their TBI to assess for any anxiety symptoms, and potentially undergo typical anxiety management procedures such as cognitive-behaviour therapy, behavioural assessment and psychotherapy. It is important that poor outcomes following TBI are targeted and managed early, to enhance quality of life and prevent the negative effects anxiety would have on both social and academic learning and development.

1.4.2. Future directions and conclusions

It is evident from the small number of studies identified in the above literature search that more work is required in specifically examining the incidence and rate of anxiety disorders following TBI in children and adolescents. Studies such as those by Gerring et al. (2002) and Vasa et al. (2002) should be replicated in different samples, with the inclusion of children with both mild and moderate TBI. Future studies should also include the use of control groups to compare against children with TBI, and utilise both healthy control participants and children with OI, as the presence and rate of anxiety disorders is expected to be different among each of these groups. Moreover, considering the influence of gender in

predicting the likelihood of developing anxiety post-TBI (Gerring et al., 2002; Vasa et al., 2002), and also findings that indicate differences in the type of behavioural and psychiatric problems suffered among males and females following childhood TBI (Scott et al., 2015), it is important that future studies further investigate the role of gender in mediating the relationship between anxiety disorders and TBI. Furthermore, the relationship between parent and child reports of anxiety disorders should be examined, considering the low correlation scores found among reports of PTSD in the extant literature (Levi et al., 1999; Mather et al., 2003). Finally, more studies should attempt to explore brain regions and lesion burdens associated with anxiety disorders in such a sample, as such studies are still lacking.

This research examined the existing literature assessing the presence of anxiety disorders following TBI in children and adolescents. While the literature to date is sparse, it may be concluded that children who have suffered from a TBI (mild, moderate or severe), are at a higher risk of developing subsequent anxiety disorders, even one year following the injury event. Moreover, children with more severe injuries, greater psychosocial adversity, and younger age at injury may be at the greatest risk, and are a group who would benefit from early intervention. Further studies are needed to replicate all the above findings and generate a more comprehensive view of the relationship between TBI and internalising disorders within the literature.

CHAPTER TWO: GENERAL METHODOLOGY

This chapter will outline a detailed methodology of the studies that comprise the thesis. This chapter will begin with an overall outline of the rationale and aims of the research, and will follow with more detailed information about ethical approval, participation rates, full protocols and description of the measures utilised. See Table 2.1 for an overview of each study, including information about participants, recruitment and comparison groups.

Table 2.1

Overview of Participant Groups and Samples across Studies

Study Title	Participants	Recruitment Location	Comparison Group
Internalising disorders in adults with a history of childhood traumatic brain injury	247 university students, 18-25 years 47 mild traumatic brain injury (TBI)	Monash University Melbourne, Australia	University students with no TBI history
The prevalence of traumatic brain injury, comorbid anxiety, and other psychiatric disorders in an outpatient child and adolescent mental health service	161 children 5-18 years presenting at a mental health service 42 mild TBI	Child and adolescent mental health outpatient setting Christchurch, New Zealand	Children and adolescents with no TBI history, presenting to a mental health service
Anxiety disorders in adults with childhood traumatic brain injury: Evidence of difficulties more than 10 years post-injury	169 adults who sustained an injury in childhood 65 mild TBI, 61 moderate-severe TBI	Hospital emergency department, outpatient Christchurch, New Zealand	43 adults with orthopedic injuries
Predictors of long-term anxiety following childhood traumatic brain injury: Theoretical perspectives	169 adults who sustained an injury in childhood 65 mild TBI, 61 moderate-severe TBI	Hospital emergency department, outpatient Christchurch, New Zealand	43 adults with orthopedic injuries

2.1. Outline of studies: Rationale, aims and hypotheses

This thesis comprises three major studies, each exploring internalising problems and anxiety following childhood TBI. The initial section includes an exploration of long-term

internalising behavioural problems in young adults with a childhood history of mild TBI. Following this, anxiety disorders in particular were given further focus, in children and adolescents with a history of TBI (predominantly mild), and more short-term outcomes of TBI were explored in this sample. Anxiety disorders were examined within the context of other psychiatric disorders for children and adolescents with and without TBI, presenting within the mental health system. The final two studies examined long-term anxiety-related outcomes following childhood TBI, including mild TBI, moderate to severe TBI, and a control group. These studies focused on anxiety in particular, and associated factors such as cognition, frontal lobe abilities, and other participant characteristics.

2.1.1. Participant samples

A feature of this thesis is the range of sample groups selected, which enabled discussion and exploration of the comparison of outcomes among three distinct participant groups. In the initial study, prevalence of TBI and accompanying behavioural and psychological outcomes was examined in a community-based sample. That is, the sample was drawn from posters and advertisements to recruit individuals within the general sub-population of a university. In the second study, children and adolescents were recruited from a specialised mental health service, thereby providing the opportunity to assess psychiatric outcomes and TBI prevalence within a clinically-based population. Finally, the third sample included individuals that were selected based on hospital records, thereby allowing the use of a hospital-based sample to explore psychiatric outcomes across levels of TBI severity. As will be explored throughout the thesis, particular outcomes following TBI are likely to be quite different across age groups, TBI severity, and participant populations. Therefore, the opportunity to examine and analyse outcomes of TBI, in children, adolescents, and adults, allows for greater scope, and further discussion of these differences will be outlined in the final chapter.

2.1.2. General rationale

As previously discussed, a TBI can disrupt the developing systems in the brain, with the predominant regions implicated being the frontal lobes (Bigler et al., 2013; Levin et al., 1992; Levine et al., 2008; Rutgers et al., 2008), temporal lobes (Levin et al., 1992; Rutgers et al., 2008; Wilde et al., 2007) and also areas of the amygdala, hippocampus and thalamus (Bigler et al., 2013; Levine et al., 2008). Damage to these regions is likely to result in a number of behavioural and emotional problems, including mood and anxiety. Moreover, chronic anxiety can have additional long-term consequences on an individual by disrupting the developing architecture of the brain (Arnsten, 2009; Brinks et al., 2008). Further, individuals with TBI and accompanying internalising and anxiety disorders are more likely to have poorer and complicated recovery following their injury (E. Moore, Terryberry-Spohr, & Hope, 2006). Those presenting with internalising problems, particularly anxiety and emotional dysregulation, may be less resilient to coping with the injury and its complications (Max et al., 2011), and as such, research in this area may highlight the need to screen for anxiety and internalising disorders at intake and follow-up for children and adolescents with TBI (Mather et al., 2003; Max et al., 2011). It is therefore important that the profile of anxiety and internalising problems following TBI in children and adolescents is better understood, particularly when considering intervention and treatment (Luis & Mittenberg, 2002; Mather et al., 2003; Peterson et al., 2013).

2.1.3. General aims

1) To examine the rate and profile of long-term internalising behavioural problems, including anxiety, depression, withdrawal, somatic complaints and avoidant personality problems, in young adults aged 18-25 years with a history of childhood TBI compared to young adults with no TBI history

2) To examine the incidence of TBI and an anxiety disorder diagnosis, in children and adolescents aged 5-18 years who are presenting within the mental health system, with a focus on more short-term outcomes
3) To compare the incidence of anxiety disorders with the incidence of other psychiatric disorders in children and adolescents with and without a history of TBI, investigating both long-term and short-term outcomes
4) To identify and explore predictors and risk factors associated with anxiety outcomes following childhood TBI, including the role of gender, age, age of injury, cognition, frontal lobe functioning, and other psychiatric symptomatology
5) To explore differences in findings dependent on the participant sample groups, including those recruited from hospitals, the community and mental health services

2.1.4. General hypotheses

1) Internalising behavioural problems, including anxiety, depression, withdrawal, somatic complaints and avoidant personality problems, will be reported in higher rates by young adults with a history of TBI than those without TBI
2) Children and adolescents within the mental health system with a history of TBI will have a higher incidence of anxiety diagnoses compared to children within the mental health system with no TBI
3) Younger age at injury, female gender, cognitive functioning, frontal lobe deficits and the presence of psychiatric symptomatology will significantly increase the risk of anxiety following TBI
4) Anxiety diagnoses will be accompanied by comorbid psychiatric disorders, particularly mood disorders

As discussed above, the thesis comprises three distinct areas of research focus. The specific methodology and design for each will now be discussed in turn, given that the studies utilise separate participant groups, research materials and data analyses.

2.2. Methodology: Internalising disorders in adults with a history of childhood TBI

2.2.1. Ethics

Ethical approval was granted by the Monash University Human Research Ethics Committee. All participants were fully informed of the study through the use of detailed participant information sheets, and provided implied consent by volunteering to participate. All participants were provided an incentive to participate in the study. In accordance with ethics requests, no identifiable information was collected from participants, apart from age and gender. The behavioural self-report measure was adapted for this study so no identifiable information could be collected from participants, by removing sections regarding the recording of ethnicity, birthdate and name.

2.2.2. Participants

Participants were recruited through the use of flyers placed around Monash University Clayton campus, and a booth set up in the University. Inclusion criteria involved individuals aged 18-25 years who were studying at or attending Monash University, and participants who could not speak English were excluded. Participants were not excluded based on socio-economic factors, or pre-existing psychological, physical or neurological disorders. These criteria were determined at the time of enquiry at the participation booth. In the initial study, of 259 students who enquired about the study, 247 participated (n=10 did not reply to follow up emails; n=2 did not return questionnaires), with an overall response rate of 95%. The final sample consisted of 103 males (M=20.60 years, SD=1.88 years) and 139 females (M=20.30

years, *SD*=1.99 years) aged 18-25 years, and five participants who did not record their sex or age. Fifty participants reported a history of TBI, with 47 mild TBI, two with moderate TBI, and one with severe TBI.

2.2.3. Procedure

Participants enquired about the study through email in response to advertisement flyers placed around the university, or to the study recruitment booth. The flyer requested "Healthy Volunteers for a TBI Study". Only participants fitting the inclusion/exclusion criteria (established through email or at the booth) were able to participate. Participants were required to approach the researcher at the booth to complete the study. Each participant completed self-report questionnaires regarding TBI status and behaviour. To ensure anonymity, questionnaires were handed to participants in an unsealed envelope which contained the explanatory statement, and questionnaires. The participants were required to complete the questionnaires at the time they were handed to them, and return them to the researcher in a sealed envelope. This procedure took approximately 20 minutes for the participants to complete.

2.2.4. Design

This study utilised a between-subjects, cross-sectional design whereby assessment of a participant's incidence of TBI and behaviour was evaluated at a single time point. The independent variable was whether or not participants had sustained a previous TBI, as determined by a self-report questionnaire examining history of TBI. The dependent variables were raw scores of behavioural outcomes, and converted *T*-scores for behaviour scales and syndromes according to the self-report behavioural assessment.

2.2.5. Materials

TBI history: The Ohio State University TBI Identification Method Short Form (OSU TBI-ID SF), adapted from the OSU TBI-ID (Corrigan & Bogner, 2007) was used as a self-report measure to screen lifetime TBI exposure. Five questions relate to past exposure to head and neck injuries caused by sources such as vehicle accidents, and if these injuries exist, a further three questions probe duration of LOC and loss of memory (Corrigan & Bogner, 2007). Inter-rater reliability is high, ranging from α=.85-.93 (Corrigan & Bogner, 2007), and test-retest reliability adequate with α>.60 (Bogner & Corrigan, 2009). In this study, mild TBI was defined by an injury with LOC <30 minutes, moderately-severe TBI by a LOC 30 minutes to 24 hours, and severe TBI by a LOC >24 hours. Participants who reported being dazed or having memory lapse resulting from a head injury were also classified as having mild TBI, as mild TBI has also been deemed present when an individual experiences loss of memory for events occurring near the injury, alongside alterations of mental state (Esselman & Uomoto, 1995; McKinlay, 2010). This measure has successfully been used in a number of studies to identify a history of TBI (e.g., Corrigan, Bogner & Holloman, 2012), and also is endorsed by the Ohio Valley Center for Brain Injury Prevention and Rehabilitation as a standardised procedure for indicating TBI history, being deemed the 'gold standard' for research and clinical use (Ohio Valley Center for Brain Injury Prevention and Rehabilitation, no date).

Internalising behaviours: To assess behavioural outcomes, the Adult's Self Report (ASR; Achenbach, Bernstein, & Dumenci, 2005) was used which measures adaptive functioning in individuals aged 18-59 years. The ASR consists of over 100 questions and assesses social, educational, recreational and occupational functioning (Achenbach et al., 2005). In addition, it examines behavioural problems across eight domains: Anxious/Depressed (Scale I) (e.g., "I feel lonely), Withdrawn (II) (e.g., "I would rather be

alone"), Somatic Complaints (III), Thought Problems (IV), Attention (V) (e.g., "I daydream a lot"), Aggressive Behaviour (VI), Rule-Breaking Behaviour (VII) (e.g., "I steal"), and Intrusiveness (VIII) (e.g., "I talk too much") (Achenbach et al., 2005). Participants may score statements as 0 (*not true*), 1 (*sometimes true*) or 2 (*very true*). The scores are summed, and the checklist derives Internalising (Scales I, II and III) and Externalising Behaviour scores (Scales VI, VII and VIII), and a Full Scale score (sum of Scale scores), with higher scores indicating more problems (Achenbach et al., 2005). Demographic information can also be obtained, and for the purposes of this study, age and gender were recorded. The measure has high internal consistency and test-retest reliability, with coefficients of α=.89 and α=.86, respectively (Achenbach et al., 2005). In the current study, the Chronbach Alpha coefficient was .85. Cross-informant reports yielded correlations of r=.3-.79 between scores on the ASR and the Adult Behaviour Checklist, demonstrating low to high convergent validity (Achenbach et al., 2005).

2.2.6. Data analysis

The data was analysed using SPSS version 20, and all statistical analyses were conducted using an alpha level of .05. Due to the small groups numbers for individuals with moderate (n=2) and severe (n=1) TBI, the cases were removed from statistical analyses. To examine group differences on demographic information, chi-square analyses were conducted for gender and education level, and independent-samples t-tests were conducted for age. A one-way multivariate analysis of variance (MANOVA) was conducted on raw scores of Anxious/Depressed, Withdrawn, Somatic Complaints and Internalising Disorders subscales to determine whether there were significant differences among those with and without a history of childhood TBI. To examine rates of clinically elevated and borderline ASR and DSM-oriented internalising disorders among the groups, raw scores from the above subscales were converted to standardised T-scores. Cut-off scores were T=65-70 for borderline and

T=70+ for clinically elevated cases. Percentages were calculated for each disorder in each group, and odds ratios were computed to determine differences in the likelihood of a person with and without childhood TBI of developing a disorder.

2.3. Methodology: The prevalence of TBI, comorbid anxiety, and other psychiatric disorders in an outpatient child and adolescent mental health service

2.3.1. Ethics

Ethical approval was obtained from the Royal Children's Hospital Human Research Ethics Committee, Monash University Human Research Ethics Committee and the Northern B Health and Disability Ethics Committee for the study. All participants were fully informed of the nature of the study, and parents/guardians and/or the children provided signed consent before initiating participation. One of two versions of the information and consent documents was used depending on the age of the young person. A parental consent version was used for individuals under 12 years of age and for children older than 12 years, in addition to the parental consent form, the child's consent was also obtained using a child version of the form. In the parental consent process, the parent/guardian was asked to confirm that their child has the capacity to consent to the study.

2.3.2. Participants

Participants were a random selection of children aged 5-18 years from two youth mental health services based in Melbourne, Australia (Royal Children's Mental Health Program) and Christchurch, New Zealand (Canterbury District Health Board). For new clients presenting to the service, a mail-out of study information, including participant information sheets and consent forms, was sent before their first appointment, which invited them to participate in the study. For all existing clients at the service, a mail out to all patients

attending each mental health centre was completed by the researcher. They were provided with the participant information sheets and consent forms, and also a cover letter briefly explaining the study and why they have been given the opportunity to participate. Inclusion criteria were children aged 5-18 years presenting for an assessment at a mental health facility. Participants were excluded if they did not speak English. Due to difficulties encountered within the Royal Children's Hospital mental health centres, and an extremely low response rate spanning over the course of two years, these participants were removed from the study (*n*=5). It is possible that the low response rate was due to the nature of the service in providing large quantities of initial information to new clients, which may have overloaded the individuals selected to participate in the study. The demographics of children and adolescents from Christchurch, New Zealand consisted of an overall sample of 161 participants (*M*=12.39 years, *SD*= 3.84 years), aged 5-18 years, with 85 males (*M*=11.40 years, *SD*=3.51 years) and 76 females (*M*=13.50 years, *SD*=3.12 years). Within the sample, 107 reported no TBI (*M*=12.37 years, *SD*=3.48 years) and 42 reported a history of TBI (*M*=12.46 years, *SD*=3.61 years); 12 participants failed to record TBI history.

2.3.3. Procedure

Participants enquired about the study based on information received in the mail, and were able to consent to participate when arriving for either their first or their next appointment at their respective mental health centre. Inclusion and exclusion criteria were established at the time of the mail out, based on client information. Upon receiving study information, participants were handed consent forms to reception at each mental health centre. Once consent was obtained, participants were handed an envelope with questionnaires examining TBI status history, parental stress and emotional behaviours and functioning (see below), and also a demographic questionnaire. Parents of the participants completed the questionnaires at their mental health centre before or after their appointments, and returned

the completed questionnaires to reception in a sealed envelope. The procedure took approximately 15-20 minutes.

In addition to information obtained from questionnaires, with consent from the participants, information from the mental health files of each client was also reviewed. Information within the files included demographic and socioeconomic data, reason for referral, any previous psychiatric diagnoses, any current psychiatric diagnoses, any substance and/or alcohol use, other behavioural and or/emotional problems, difficulties at home or school, contacts with the forensic system and offending behaviours, and other clinical information deemed important by the consulting clinician.. This information was accessed once the client's service with the mental health centre was terminated, and the review was conducted by a research assistant in New Zealand.

2.3.4. Design

A between-subjects, cross-sectional study design was used, with data collected over a two-year period. Incidence of TBI and mental health outcomes for each participant were evaluated at a single time point. The independent variable was whether or not participants had sustained a previous TBI, as determined by the OSU TBI-ID. The dependent variables were mental health outcomes and psychiatric disorders, including anxiety disorders, obtained from the mental health files.

2.3.5. Materials

A demographic questionnaire was used to record information about the participants including age, gender, ethnicity, developmental history, family dynamics, and school functioning. The questionnaire involves a yes/no format answer to each question, with the option to provide additional information when requested, formulated by researchers on the

study. The questions referred to: School difficulties, learning difficulties, educational assistance, behavioural problems, mental health problems, hospitalisations and previous medical diagnoses. It has been used in previous studies to gain background information about the participants that may influence outcomes of TBI.

TBI history: The OSU TBI-ID SF, adapted from the OSU TBI-ID (Corrigan & Bogner, 2007), was used as a self-report measure to screen lifetime TBI exposure. See above for more information on this identification measure.

Parental stress: The Parenting Stress Scale (Berry & Jones, 1995) was utilised to assess self-reported stress levels of parents of each child participant. The scale has demonstrated satisfactory levels of internal reliability (.83) and test-retest reliability (.81), and also convergent validity with other measures of stress (Berry & Jones, 1995). It is a useful tool for assessing stress of mothers and fathers of children both with and without clinical problems, and contains 18 statements which describe the parents' perceptions of their experience of being a parent. Participants rate each statement as "1=strongly disagree", "2=disagree', '3=undecided", "4=agree" or '5=strongly agree", with regards to emotions and role satisfaction such as guilt, marital satisfaction, and loneliness (Berry & Jones, 1995).

2.3.6. Data analysis

Descriptive statistical analyses were conducted for all variables within the dataset, utilising the split-file function for gender, TBI history, and anxiety diagnosis. A combined variable for TBI and anxiety diagnosis was also computed. To examine group differences on demographic information, chi-square analyses were conducted for gender, school and learning difficulties, behavioural problems, mental health problems, and medical history, and an independent-samples *t*-test was conducted for age. To examine the incidence of anxiety disorder diagnosis among participants with and without a history of TBI, frequencies and

descriptive statistical analyses were calculated to examine anxiety diagnoses, psychiatric comorbidities and other psychiatric diagnoses among the two groups.

2.4. Anxiety disorders in adults with childhood TBI: Evidence of difficulties more than 10 years post-injury

2.4.1. Ethics

Ethical approval for the study was obtained from the Upper South New Zealand Regional Ethics Committee, and was part of a larger study which investigated long-term neuropsychological outcomes of childhood TBI. All participants were fully informed of the nature of the study, and provided consent to participate.

2.4.2. Participants

Participants were recruited through an audit of hospital ED and admission records, and neurosurgical files. Additional recruitment was conducted by placing flyers within the community. General inclusion criteria for the study included having a history of an injury event (TBI or OI) during the ages 0-17 years which occurred at least five years prior to the study, and being 18 years or older. All participants spoke English. Sample groups were defined based on pre-existing criteria for TBI severity (Baalen et al., 2003; Borg et al., 2004; Centers for Disease Control and Injury Prevention, 2013).

Mild TBI

Inclusion criteria for individuals in the mild TBI group included: a) a medically confirmed diagnosis of mild TBI, b) LOC for less than 20 minutes, c) length of PTA less than one hour, d) GCS score of 13-15, e) stay in hospital no longer than 48 hours (due to injuries to the head only), and f) normal brain scan results.

Moderate-severe TBI

Individuals in the moderate-severe TBI were determined by the following inclusion criteria: a) a medically confirmed diagnosis of moderate or severe TBI, or b) skull fracture/evidence on brain scan, or c) cerebral haemorrhage, or d) PTA of more than 24 hours. Moderate TBI was specifically defined as a) GCS of 9-12 (or higher if there was evidence on brain scan results), b) PTA of less than one week, and c) length of LOC less than six hours. For severe TBI, the criteria were set as a) GCS score of < 9, b) PTA of more than one week, and c) length of LOC more than six hours.

OI controls

Individuals in the OI group were recruited from the audit of medical ED records and flyers placed in the community, and were defined as having experienced a fracture between the ages 0-17 years, more than five years prior to the study. Individuals were excluded if they had a history of TBI.

Final sample

The total sample consisted of 95 males (*M*=22.78 years, *SD*=3.44 years) and 74 females (*M*=22.27 years, *SD*=3.09 years), aged between 18 and 31 years. Within the sample, there were 65 with mild TBI (*M*=23.25 years, *SD*=3.58 years), 61 with moderate-severe TBI (*M*=22.34 years, *SD*=2.79 years) and 43 with OI (*M*=21.81 years, *SD*=3.36 years).

2.4.3. Procedure and materials

Participants were invited to attend a three hour assessment session at the University of Canterbury. To obtain information regarding background information, including age and gender, further information about the injury event, and associated symptomatology, a semi-structured interview was conducted. To obtain diagnostic information regarding psychiatric

symptoms, a structured interview was used to ask questions relating to a DSM-IV diagnosis of an anxiety disorder (GAD, panic attacks, PD, agoraphobia, social phobia, specific phobia, PTSD), depression, mania, and suicidal behaviours. Components of the Composite International Diagnostic Interview (CIDI; World Health Organisation, 1990) were used in a structured interview format, to ask questions relating to diagnostic criteria. This method of interview has been previously used and validated in earlier studies (D. Fergusson, Boden, & Horwood, 2007, 2009).

2.4.4. Design

A between-subjects, cross-sectional study design was used, utilising retrospective and current data from participants. The independent variable was injury group (mild TBI, moderate-severe TBI, or OI). The dependent variables were outcomes identified from unstructured and structured interviews, including age, gender, time since injury, and psychiatric diagnoses.

2.4.5. Data analysis

Descriptive statistical analyses were conducted, utilising the split-file function organising data by group (mild TBI, moderate-severe TBI, and OI), for background information including age, gender, time since injury, and age of treatment injury, and frequency analyses computed for psychiatric disorders. Chi-square and MANOVA tests were conducted to examine any group differences among the participant characteristics. A new variable was computed by combining mild and moderate-severe TBI groups to a general TBI group, to compare background information and psychiatric disorders in the same manner. For outcome variables, psychiatric disorders were coded as 0=no and 1=yes, and an overall anxiety disorders variable was computed by combining ‘yes’ values for all anxiety-related disorders (GAD, Panic Attacks, PD, Agoraphobia, Social Phobia, Specific Phobia, PTSD).

Finally, a variable was computed for multiple anxiety disorders, with 1=multiple disorders, and 0=none.

To analyse differences between participant groups on psychiatric disorders, a series of chi-square analyses were conducted, with rows set as participant group (1=mild TBI, 2=moderate TBI, 3=OI) and columns set as psychiatric disorders (0=no, 1=yes) and multiple anxiety disorders. This was repeated for the combined TBI group variable (1=TBI, 0=no TBI). To examine predictors for having a diagnosis of an anxiety disorder (any), a logistic regression was computed, with the dependent variable as overall anxiety disorders (0=no, 1=yes), and the independent variables as TBI group (1=TBI, 0=no TBI), age, gender, time since injury, and other psychiatric disorders. All data were analysed using SPSS version 22, and alpha levels were set to .05 for significance testing.

2.5. Predictors of long-term anxiety following childhood TBI: Theoretical perspectives

This paper was produced as an extension of the study outlined above (Section 2.4), however focussed solely on predictive factors associated with the development of anxiety following childhood TBI. Therefore, information regarding ethics, participants, procedures, materials and design match that already discussed. As such, for this study only information regarding data analysis will be provided, along with information regarding the assessment of potential predictors and risk factors.

2.5.1. Materials

Cognitive functioning

Memory function was examined using the Wechsler Memory Scale-III Paired Associates I and II (WMS-III PA) age adjusted scores (Wechsler, 1997), and the Rey-Osterrieth Complex Figure (ROF) memory trials (Lezak, 1995). In WMS-III PA, a list of

unrelated word pairs was read, and participants then were to provide the corresponding word when prompted with the first word. The WMS-III PA scores were derived from the sum of correct responses, with higher scores indicating better recall. In the ROF memory trials, participants were shown a figure, and asked to recall and draw the figure after a three- and 30-minute delay. The ROF scores were based on correctly remembered elements, with a maximum score of 36.

Visuospatial ability was measured using the Wechsler Abbreviated Scale of Intelligence's Matrix Reasoning subtest (WASI-MR) age adjusted scores (Wechsler, 1999), Judgement of Line Orientation Test (JLOT) (Benton, Sivan, & Hamsher, 1994), and ROF copy task (Lezak, 1995). Participants chose a response from options that would complete the matrix or series (WASI-MR), matched lines appropriately in accordance with position and direction (JLOT), and copied a complex figure (ROF copy). The tests were scored based on accuracy, and final scores were derived from the total number of correct responses.

Attention was assessed using the Daneman and Carpenter Reading Span Test (DCRS) (Daneman & Carpenter, 1980) and the Adaptive Digit Ordering Task (DOT-A) (Werheid et al., 2002). In DOT-A, participants recalled sequences of numbers in ascending order, with the maximum number of digits recalled in the appropriate order giving the final score. In DCRS, participants were presented with three trials of sets of sentences which were characterised with increasing difficulty. They read the sentences aloud, judged the veracity of the content, and recalled each sentence's last word. Trials were discontinued when the participants were unable to recall all sentences in a set, with scores derived from the total number of recalled words.

Processing speed was assessed using scores from the Delis-Kaplan Executive Function System (D-KEFS) verbal fluency and Stroop subtests – age adjusted (Delis, Kaplan, & Kramer, 2001). Participants were to produce words that start with letters F, A, and S within

60 seconds per letter, with the number of generated words creating the verbal fluency score. For the Stroop subtests, participants named the color patch, read the word, and identified the color in which the word is printed as quickly as possible. The correct responses provided a final score for each Stroop subtest.

Frontal lobe functioning

To assess behaviours associated with frontal lobe functioning, the Frontal Systems of Behaviour Scale (FrSBe) was utilised, in a self-report format (Grace & Malloy, 2001). The measure is a brief and valid tool in assessing behavioural aspects associated with frontal lobe functioning, including apathy, executive dysfunction and behavioural disinhibition, in adults aged 18-95 years. The FrSBe contains 46 self-report items, which are rated on a five point Likert scale, with 14 items pertaining to the Apathy subscale (e.g. lacking energy, loss of interest in things), 15 items for the Disinhibition subscale (e.g. laughing or crying too easily, hyperactivity) and 17 items pertaining to Executive Dysfunction (e.g. disorganisation, attentiveness) (Carvalho, Ready, Malloy, & Grace, 2013; Grace & Malloy, 2001). Raw scores were computed to *T*-scores for assessment of dysfunction comparative to norms, including norms associated with individuals with TBI (Grace & Malloy, 2001). Higher *T*-scores indicate more difficulties, with a cut-off of $T>50$ suggesting clinical concerns. The FrSBe has demonstrated good reliability, large-scale norms, and is effective in discriminating between individuals with frontal lesions versus non-frontal lesions in the brain (Malloy & Grace, 2005).

2.5.2. Design

A between-subjects, cross-sectional study design was used, utilising retrospective and current data from participants. The dependent variable was diagnosis of anxiety disorder (yes/no). The independent variables or predictors were outcomes identified from unstructured and structured interviews, including age, gender, time since injury, cognitive functioning

(memory, visuospatial functioning, processing speed, attention), and frontal lobe functioning (executive dysfunction, apathy, behavioural disinhibition).

2.5.3. Data analysis

For each of the cognitive domains described above, standardised *z*-scores were computed for individual test scores, and the standardised individual *z*-scores were combined to form the composite scores of each domain. For the frontal lobe functions, *T*-scores were derived from total scores for each subscale, and for overall functioning. Descriptive statistical analyses were conducted to obtain a frequency distribution of participant characteristics between the groups, utilising a split-file function for organisation of data by group (mild TBI, moderate-severe TBI group, OI group; anxiety, no anxiety). This was computed for the variables of age, gender, age at injury treatment, anxiety disorders, years since injury, cognitive performance, and frontal lobe functioning. The variable "anxiety disorders" refers to individuals with a diagnosis of GAD, panic attacks, PD, agoraphobia, social phobia, specific phobia, PTSD. Chi-square analyses and MANOVA tests were conducted to examine differences between groups for demographics (age, gender, age at injury treatment, years since injury), anxiety disorders, cognitive performance, and frontal lobe functioning. A logistic regression analysis was computed to assess significance of predictors for anxiety disorders following childhood TBI. All data were analysed using IBM SPSS version 24, and α levels were set to .05 for significance testing.

2.6. Final remarks

Following the current chapter outlining detailed methodology of each study that comprises the entire thesis, the remaining chapters will focus on each individual study. All studies were submitted as a peer reviewed article, which have been provided as appendices in the thesis. As such, the following chapters may be condensed and relatively brief in some

areas to account for publication regulations. The first study to be discussed will explore internalising disorders in adults following childhood TBI, given that previous research has placed major focus on short-term, externalising behaviour problems in this group.

CHAPTER THREE: INTERNALISING DISORDERS IN ADULTS WITH A HISTORY OF CHILDHOOD TBI

This chapter was written as a manuscript for publication, titled as above. The paper is available, currently published as an online first article in the Journal of Clinical and Experimental Neuropsychology. The full manuscript is attached as an appendix (Appendix B). A published abstract presented at the International Brain Injury Conference (Netherlands, 2016) associated with the work is attached as Appendix C.

Journal of Clinical and Experimental Neuropsychology, 2015
Vol. 37, No. 7, 776–784, http://dx.doi.org/10.1080/13803395.2015.1053843

Routledge
Taylor & Francis Group

Internalizing disorders in adults with a history of childhood traumatic brain injury

Michelle Albicini[1] and Audrey McKinlay[2]

[1]Faculty of Medicine, Nursing and Health Sciences, School of Psychology and Psychiatry, Monash University, Clayton, VIC, Australia
[2]School of Psychological Sciences, University of Melbourne, Melbourne, VIC, Australia

(*Received 12 November 2014; accepted 18 May 2015*)

Introduction: While the presence of externalizing behavioral problems following traumatic brain injury (TBI) has been well established in the literature, less is known regarding internalizing disorders, and more specifically anxiety disorders, in such a population. This study explored the presence, rate, and incidence of internalizing behavior problems, including anxiety, depression, somatic complaints, avoidant personality symptomatology, and overall internalizing behavior problems in university students aged 18–25 years. *Method*: A convenience sample of 247 university students (197 non-TBI, 47 mild TBI, 2 moderate TBI, 1 severe TBI) aged 18–25 years was utilized. Participants completed a self-report measure on behavioral functioning, the Adult Self Report (ASR), to identify internalizing behaviors, and a questionnaire to identify TBI history. *Results*: Raw scores of behavior indicated that participants with a history of childhood TBI reported significantly higher levels of withdrawal, somatic complaints, and internalizing behavioral problems than the non-TBI participants. When analyzing standardized *T*-scores for borderline and clinically elevated ASR syndromes and *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-oriented scales, individuals in the TBI group were significantly more likely to have higher rates of borderline anxiety, somatic complaints, avoidant personality problems, and overall internalizing disorders, and clinically elevated somatic complaints. Adults with a history of childhood TBI were also significantly more likely to report at least 1 or more DSM disorders. *Conclusion*: These results clearly suggest that individuals with a childhood history of TBI are at a heightened risk for a range of internalizing disorders in early adulthood, which is particularly troubling in a university sample pursuing tertiary education.

Keywords: Students; Traumatic brain injury; Behavioral problems; anxiety; Internalizing disorders.

Within the literature, it has been well established that traumatic brain injury (TBI) sustained in childhood is associated with a range of behavioral problems that develop later in life, such as hyperactivity and disorder, conduct disorder, oppositional defiant disorder, drug abuse, personality change disorders, and mood and anxiety disorders (Max et al., 2013; Max et al., 2012; McKinlay, Dalrymple-Alford,

3.1. Abstract

Introduction: While the presence of externalising behavioural problems following TBI has been well established, less is known regarding internalising disorders, and more specifically anxiety disorders, in such a population. This study explored the presence, rate, and incidence of internalising behaviour problems, including anxiety, depression, somatic complaints, avoidant personality symptomatology, and overall internalising behaviour problems in university students aged 18–25 years.

Method: A convenience sample of 247 university students (197 non-TBI, 47 mild TBI, two moderate TBI, and one severe TBI) aged 18–25 years was utilised. Participants completed a self-report measure on behavioural functioning, and a questionnaire to identify TBI history.

Results: Raw scores of behaviour indicated that participants with a history of childhood TBI reported significantly higher levels of withdrawal, somatic complaints, and internalising behavioural problems than the non-TBI participants. When analysing standardised *T*-scores for borderline and clinically elevated ASR syndromes and DSM-oriented scales, individuals in the TBI group were significantly more likely to have higher rates of borderline anxiety, somatic complaints, avoidant personality problems, and overall internalising disorders, and clinically elevated somatic complaints. Adults with a history of childhood TBI were also significantly more likely to report at least one or more DSM disorders.

Conclusion: These results clearly suggest that individuals with a childhood history of TBI are at a heightened risk for a range of internalising disorders in early adulthood, which might be particularly troubling in a university sample pursuing tertiary education, given the expected high levels of academic demands during this time.

3.2. Introduction and background

It has been previously established that a TBI that is sustained in childhood may be associated with a range of behavioural problems that develop later in life, such as hyperactivity and aggression, conduct problems, adaptive functioning skills, and social and emotional issues (Donders & Warschausky, 2007; Hawley et al., 2004; Schwartz et al., 2003; Sonnenberg, Dupuis, & Rumney, 2010). Moreover, it is also generally accepted that individuals with a childhood history of TBI may be at risk of developing psychiatric disorders, including ADHD, CD, ODD, drug abuse, personality change disorders, and mood and anxiety (Max et al., 2013; Max et al., 2012; McKinlay et al., 2002), which can persist even into adulthood (Anderson, Brown, et al., 2011; Anderson, Godfrey, Rosenfeld, & Catroppa, 2011). There is a vast literature on the incidence of behavioural problems and psychiatric disorders in individuals following TBI. However, the focus is often on externalising disorders and symptoms, with internalising problems rarely being specifically investigated in such a sample. Moreover, there is a lack of research that seeks to examine anxiety disorders in individuals with a history of TBI (Albicini & McKinlay, 2015).

Previous research examining long-term behavioural problems following childhood TBI have demonstrated that symptoms and diagnoses of internalising disorders, such as anxiety, depression, and emotional and social withdrawal symptoms, are elevated in some TBI samples (Karver et al., 2012; Max et al., 2013; Max et al., 2012). A handful of studies have highlighted that internalising problems may be a significant concern in a child and adolescent TBI sample, in that these individuals are more likely to have clinically elevated levels of anxiety and internalising problems, including depression, somatic complaints, and withdrawal, at long-term follow-ups (Karver et al., 2012; Liu & Li, 2013).

While there is an abundance of work exploring behavioural outcomes following TBI in general, research that has focused solely on the incidence and presentation of internalising behavioural problems and anxiety disorders in a TBI sample is limited (Albicini & McKinlay, 2015). Peterson et al. (2013) examined internalising symptomatology in 12–17-year-old TBI individuals with a history of TBI. Child and parental ratings of behaviour indicated that 22–26% of the TBI sample exhibited clinically elevated internalising problems (Peterson et al., 2013). In support of this, in a study of adult outcomes following childhood TBI, individuals with TBI reported higher rates of anxiety and internalising disorders than did OI controls (Scott et al., 2015). Furthermore, females with TBI were at higher risk of developing lasting mood, anxiety, and internalising disorders (Scott et al., 2015).

Finally, studies examining new-onset psychiatric disorders following childhood TBI also support the notion that internalising disorders may become a significant problem in such a sample. One study reports higher rates of novel anxiety, depression, and internalising disorders for children and adolescents with a history of TBI than for OI controls, which continued to be present three months following their injury (Max et al., 2012). Moreover, in this sample, novel internalising disorders and anxiety disorders occurred more frequently than ADHD and ODD (Max et al., 2012). Further, a later study looking at psychiatric disorders six months after mild TBI, also in children and adolescents, reported 64% of the sample to have internalising disorders, with 36% of these cases being anxiety disorders (Max et al., 2013).

When examining the above studies, it is apparent that anxiety may be an outcome of importance following childhood TBI. Again, this has been relatively overlooked in the literature (Albicini & McKinlay, 2015). Early accounts, however, indicate cases of new-onset OCD (Max et al., 1995), and SAD (Chaves et al., 2012), following childhood severe TBI. Such case studies highlight the need to explore anxiety symptomatology in larger TBI samples.

As such, one study has focused on the incidence of new onset compulsions and obsessions following severe pediatric TBI in children and adolescents (Grados et al., 2008), finding that 30% of the sample exhibited obsessive and compulsive symptomatology. Other studies have explored the rate of anxiety disorders including GAD, autism spectrum disorder, PTSD, PD, OCD, simple/specific phobia, social phobia, and SAD in TBI samples (Luis & Mittenberg, 2002; Max et al., 2011; Vasa et al., 2002) with results demonstrating that TBI in children and adolescents significantly increases the risk of developing subsequent anxiety disorders (Grados et al., 2008; Luis & Mittenberg, 2002; Max et al., 2011; Vasa et al., 2002). When comparing children with mild TBI, moderate-severe TBI, and OI, results suggest a potential relationship between degree of neurological insult and risk of developing subsequent anxiety disorders (Luis & Mittenberg, 2002) in that overall anxiety disorders were most common in children with moderate-severe TBI (Luis & Mittenberg, 2002).

In light of the above research and findings, it is important to explore the incidence and presentation of internalising disorders, with particular reference to anxiety, in individuals with a history of childhood TBI. While much of the above research has investigated acute behavioural problems following childhood TBI, it is also important to investigate long-term effects, given that structural changes have been noted in the brain even 10 years after childhood TBI (Beauchamp et al., 2011). The aim of this study was to examine the rate of internalising and anxiety disorders in a university student sample. It was hypothesised that university students with a history of childhood TBI would report higher rates of internalising disorders, including anxiety, depression, and somatic complaints, than university students with no TBI history.

3.3. Methods

3.3.1. Participants

The participants were from an existing study investigating TBI status and poor behavioural outcomes in university students. Inclusion criteria were individuals aged 18–25 years who were studying/attending Monash University. The exclusion criterion was non-English-speaking individuals. Of the 259 students who enquired about the study, 247 participated (*n*=10 did not reply to follow up emails; *n*=2 did not return questionnaires), with an overall response rate of 95%. The final sample consisted of 103 males (*M*=20.60 years, *SD*=1.88 years) and 139 females (*M* =20.30 years, *SD* =1.99 years) aged 18–25 years, and five participants who did not record their sex or age. Fifty participants reported a history of TBI, with 47 mild TBI, two moderate TBI, and one severe TBI. All participants were fully informed of the study and provided implied consent via completion of the questionnaires. All participants were provided an incentive to participate in the study. Ethics approval was obtained from Monash University human ethics committees.

3.3.2. Procedure

Each participant volunteered by enquiring at the booth and completed self-report questionnaires regarding TBI status and behaviour. The participants were required to complete the questionnaires at the time they were handed to them and to return them to the researcher in a sealed envelope. This procedure took approximately 20 minutes for the participants to complete.

3.3.3. Design

This study utilised a between-subjects, cross-sectional design whereby assessment of a participant's history of TBI and behaviour was evaluated at a single time point. The

independent variable was whether or not participants had sustained a previous TBI, as determined by the OSU TBI-ID (Corrigan & Bogner, 2007). The dependent variables were raw scores of behavioural outcomes, and incidence rates of converted *T*-scores for borderline and clinically elevated behaviour scales and syndromes according to the ASR (Achenbach et al., 2005).

3.3.4. Materials

The OSU TBI-ID SF, adapted from the OSU TBI-ID (Corrigan & Bogner, 2007) was used as a self-report measure to screen lifetime TBI exposure. Five questions relate to a history of exposure to head or neck injuries caused by events including vehicle accidents, and then a further three questions probe duration of LOC and loss of memory (Corrigan & Bogner, 2007). Participants who reported being dazed or having loss of memory resulting from a head injury were also classified as having mild TBI, as mild TBI has also been defined present when an individual experiences loss of memory for events occurring near the injury, alongside alterations of mental state (Esselman & Uomoto, 1995; McKinlay, 2010). Inter-rater reliability is high, ranging from α=.85 to α=.93 (Corrigan & Bogner, 2007), and test–retest reliability adequate with α>.60 (Bogner & Corrigan, 2009).

To assess behavioural outcomes, the ASR was used, which measures adaptive functioning in individuals aged 18–59 years (Achenbach et al., 2005). The ASR assesses social, educational, recreational, and occupational functioning and examines behavioural problems across eight domains. Participants score statements as 0 (not true), 1 (sometimes true), or 2 (very true). The scores are summed, and the checklist derives internalising and externalising behaviour scores and a full-scale score (Achenbach et al., 2005). The measure has high internal consistency and test–retest reliability, with coefficients of α=.89 and α=.86, respectively (Achenbach et al., 2005). Raw scores for the subscales Anxious/Depressed,

Withdrawn, Somatic Complaints, Internalising Disorders, Aggressive Behaviour, Rule-Breaking Behaviour, Intrusive Thoughts, and Externalising Disorders were calculated by summing scores for each scale. The internalising scale scores were converted to standardised *T*-scores. Additionally, the scale derives DSM-oriented subscales for which raw scores were also converted to standardised *T*-scores for Depression, Anxiety, Somatic Complaints, and Avoidant Personality Problems.

3.3.5. Data analysis

Due to the small groups numbers for individuals with moderate (n=2) and severe (n=1) TBI, the cases were removed from the statistical analyses. To examine group differences on demographic information, chi-square analyses were conducted for gender and education level, and independent-samples *t*-tests were conducted for age. First, a one-way MANOVA was conducted on raw scores of Aggressive Behaviour, Rule-Breaking Behaviour, Intrusive Thoughts, and Externalising Disorders subscales so a comparison of results could be examined between internalising and externalising problems. Then, a MANOVA was conducted on raw scores of Anxious/Depressed, Withdrawn, Somatic Complaints, and Internalising Disorders subscales to determine whether there are significant differences among those with and without a history of childhood TBI. Following this, a more detailed examination of internalising disorders was conducted by calculating rates of clinically elevated and borderline ASR and DSM-oriented internalising disorders among the groups. To do this, raw scores from the above subscales were converted to standardised *T*-scores. Percentages were calculated for each disorder in each group, and odds ratios were computed to determine differences in the likelihood of a person with and without childhood TBI of developing a disorder.

3.4. Results

3.4.1. Descriptive statistics

Demographic characteristics for individuals with TBI are shown in Table 3.1. Chi-square analyses indicated no significant association between the two groups in terms of gender, $\chi^2(1)=0.17$, $p=.68$, or education, $\chi^2(8)=4.62$, $p=.80$. Further, an independent-samples *t*-test revealed no significant differences in age between those with and those without TBI, $t(227)=-0.26$, $p=.79$.

Table 3.1.

Characteristics of Participants with Traumatic Brain Injury

Characteristic	**TBI group (*n*=50)**
Gender, *N*(%)	Male: 20 (40)
	Female: 30 (60)
Age (*M*)	20.36 years
Age at First Injury * (*M*)	14.80 years
TBI before/after 15 years *, *N*(%)	< 15 years: 20 (40)
	≥ 15 years: 15 (30)
	n/a: 15 (30)
TBI with any LOC, *N*(%)	36 (72)
TBI with LOC >30 mins, *N*(%)	5 (10)
Multiple TBI [a], *N*(%)	8 (16)

Note. *OSU-TBI-SF only provides this information for traumatic brain injury involving loss of consciousness

3.4.2. Raw scores for ASR syndromes

For the externalising scales, a MANOVA was conducted on raw scores for the syndrome scales Aggressive Behaviour, Rule-Breaking Behaviour, Intrusive Thoughts, and Externalising Disorders, to examine differences among students with and without a history of

TBI. The results revealed no significant differences between the two groups on aggression, $F(1, 242)=0.01$, $p=.94$, rule-breaking, $F(1, 242)=0.67$, $p=.41$, intrusive thoughts, $F(1, 242)=0.16$, $p=.69$, or externalising disorders, $F(1, 242)=0.5$, $p=.48$. A MANOVA was conducted on raw scores for the syndrome scales Anxiety/Depressed, Withdrawn, Somatic Complaints, and Internalising Disorders, to examine differences among students with and without a history of TBI. The results revealed a significant effect of TBI for somatic complaints, such that students with a TBI ($M=5.89$, $SD=5.02$) reported significantly more somatic problems than students without TBI ($M=3.56$, $SD=3.12$), $F(1, 242)=16.24$, $p<.001$, $\eta^2=.06$. There was also a main effect of TBI for internalising disorders, with those with a history of TBI ($M=21.66$, $SD=15.02$) endorsing significantly more internalising behavioural problems than those without TBI ($M=16.86$, $SD=11.80$), $F(1, 242)=5.62$, $p=.02$, $\eta^2=.02$. Further, scores on the Withdrawn subscale significantly differed between groups, with participants with TBI endorsing more problems ($M=4.79$, $SD=3.47$) than participants without TBI ($M=3.60$, $SD=3.21$), $F(1, 242)=5.04$, $p=.03$, $\eta^2=.02$. There was no significant difference in raw scores for the Anxious/Depressed subscale between the two groups, $F(1, 242)=1.24$, $p=.27$.

3.4.3. Converted *T*-scores

Raw scores from the ASR were converted into standardised *T*-scores, and rates of borderline and full internalising problems were examined in each group. Further, odds ratios were calculated to examine differences in the likelihood of developing a disorder among the two groups. Table 3.2 presents these rates and odds ratios for DSM-oriented syndromes among those with and without a history of TBI.

As is shown in Table 3.2, for DSM-oriented scales, those with TBI had a higher incidence of borderline cases of anxiety and depressive disorders, a higher incidence of full

Table 3.2.

Percentages and Odds Ratios for Clinically Elevated and Borderline DSM-Oriented Syndromes across Traumatic Brain Injury and Non-Traumatic Brain Injury Groups

	Group	***n***	**%**	**Odds Ratio**	**CI**	***p*-value**
Anxiety –	TBI	6/50	12	1.36	0.51-3.62	.54
borderline	Non-TBI	18/197	9			
Anxiety – full	TBI	4/50	8	1.34	0.41-4.35	.63
	Non-TBI	12/197	6			
Depression –	TBI	4/50	8	1.34	0.41-4.35	.63
borderline	Non-TBI	12/197	6			
Depression – full	TBI	7/50	14	1.62	0.64-4.12	.31
	Non-TBI	18/197	9			
Somatic complaints	TBI	4/50	8	0.92	0.29-2.87	.89
– borderline	Non-TBI	17/197	9			
Somatic complaints	TBI	6/50	12	5.24	1.53-17.94	.01*
- full	Non-TBI	5/197	3			
Avoidant	TBI	2/50	4	0.35	0.08-1.54	.10
personality –	Non-TBI	21/197	11			
borderline						
Avoidant	TBI	12/50	24	3.34	1.48-7.57	.004**
personality - full	Non-TBI	17/197	8			
≥1 DSM syndrome	TBI	24/50	48	2.57	1.36-4.88	.004**
	Non-TBI	52/197	26			

Note. TBI=traumatic brain injury; DSM=Diagnostic Statistical Manual; CI= confidence interval; *=significant at p<0.05, **=significant at p<.01

cases of anxiety, depression, somatic problems, and avoidant personality problems, and a higher rate of overall DSM syndromes, than non-TBI participants. Of these, the difference was significant for full somatic complaints, such that students with TBI were over five times more likely to report somatic complaints than students without TBI. Additionally, the difference for borderline avoidant personality problems was significant, in that students with TBI were over three times more likely to report avoidance problems than students without

TBI. Finally, students with TBI were 2.57 times more likely to endorse at least one DSM-oriented disorder than those without TBI, and this difference was significant. Table 3.3 presents rates of and odds ratios for borderline and elevated ASR syndrome scales among the groups.

Table 3.3.

Percentages and Odds Ratios for Clinically Elevated and Borderline Adult's Self Report Syndromes across Traumatic Brain Injury and Non-Traumatic Brain Injury Groups

	Group	***n***	**%**	**Odds Ratio**	**CI**	***p*-value**
Anxiety/Depressed –	TBI	6/50	22	4.35	1.79-10.57	.001**
borderline	Non-TBI	18/197	6			
Anxiety/Depressed –	TBI	4/50	10	0.67	0.25-1.84	.44
full	Non-TBI	12/197	14			
Withdrawn – borderline	TBI	4/50	22	2.03	0.92-4.50	0.07
	Non-TBI	12/197	12			
Withdrawn – full	TBI	7/50	12	1.93	0.69-5.36	.21
	Non-TBI	18/197	6			
Somatic complaints –	TBI	4/50	14	1.44	0.57-3.63	.44
borderline	Non-TBI	17/197	10			
Somatic complaints -	TBI	6/50	16	4.50	1.60-12.67	.004**
full	Non-TBI	5/197	4			
Internalising –	TBI	2/50	18	2.66	1.09-6.51	.03*
borderline	Non-TBI	21/197	7			
Internalising - full	TBI	12/50	28	1.39	0.69-2.82	.36
	Non-TBI	17/197	22			
≥1 ASR syndrome	TBI	24/50	48	1.79	0.96-3.36	.07
	Non-TBI	67/197	34			
Multiple Problems	TBI	25/50	50	2.58	1.37-4.88	.003**
	Non-TBI	55/197	28			

Note. CI= confidence interval; TBI=traumatic brain injury; ASR=Adult's Self Report; *=significant at $p<0.05$, **=significant at $p<.01$

As is evident in Table 3.3, those with TBI had higher rates of borderline anxiety/depression, withdrawal, somatic complaints, and internalising problems. The TBI

group also endorsed higher rates of full withdrawal, somatic complaints, and internalising problems. Finally, those with TBI also had a higher number of overall ASR syndromes and a higher rate of multiple problems. Odds ratio calculations indicated that students with TBI were over four times more likely to endorse borderline anxiety problems than non-TBI students, which was statistically significant. There was a significant difference among the groups for full somatic complaints, with students with a history of TBI being 4.5 times more likely to report such problems than the non-TBI group. Students with TBI were also significantly more likely to report borderline internalising problems, at a rate of almost three times more likely than the non-TBI group. Finally, the incidence of multiple problems was significantly higher for the TBI group, such that students with a history of TBI were over twice more likely to report multiple behavioural problems than students with no TBI.

3.5. Discussion

This study explored rates and differences in internalising symptomatology and disorders in university students aged 18–25 years with or without a history of childhood TBI. The study examined long-term, as opposed to acute, outcomes after predominately mild TBI. To examine whether participants' responses on the internalising behaviour scales reflected a response bias in those with TBI, mean scores for information on the externalising behaviour scales were also analysed. It was hypothesised that higher rates of anxiety, depression, withdrawal, somatic complaints, avoidant personality problems, and overall internalising behavioural problems would be significantly elevated in those with a history of TBI. The results of this study revealed that, in reference to raw behavioural scores, participants with a history of childhood TBI reported significantly higher levels of withdrawal, somatic complaints, and internalising behavioural problems than the non-TBI participants. When analysing standardised *T*-scores for borderline and clinically elevated syndromes and DSM-oriented diagnoses, individuals in the TBI group were significantly more likely to have higher

rates of borderline anxiety, somatic complaints, avoidant personality problems, and overall internalising disorders and clinically elevated somatic complaints. Students with TBI were also significantly more like to report at least one DSM disorder and multiple disorders.

The findings for the raw behaviour scores are in line with those of previous studies that have explored internalising problems following childhood TBI. For instance, Peterson et al. (2013) utilised the Child Behaviour Checklist, a child and adolescent form of the behaviour rating scale used in this study, and found that scores on the Withdrawn, Somatic Complaints, and Internalising Problems subscales were clinically elevated in childhood mild TBI compared to standardised norms. These results were in support of a similar study utilising the same assessment tool (Karver et al., 2012), with higher rates of internalising problems found in children with mild to moderate TBI and severe TBI than in an OI group. Unlike Peterson et al., this study found no differences in rates of problems for the Anxious/Depressed scale. However, the results were in line with Karver et al. (2012), who reported the same for their mild to moderate TBI group.

In reference to borderline and clinically elevated rates of internalising disorders, the study results also support past research. Scott et al. (2015) reported that participants aged 18–31 years with a childhood mild TBI were more likely to endorse symptoms of anxiety and internalising disorders, which is consistent with the current findings. Further, Luis and Mittenberg (2002) also reported higher rates of anxiety and mood problems following childhood TBI; however, this was a trend association and was found for children with moderate to severe injuries. Other studies have also reported clinically elevated levels of anxiety, depression, and withdrawal symptoms following childhood mild TBI (Hawley et al., 2004; Liu & Li, 2013; Max et al., 2013).

Explanations for the above results may involve the brain regions implicated in TBI and their effect on the emotion regulation system. MR imaging studies in children with TBI and subsequent internalising problems have identified regions such as the OFC, thalamus, temporal regions, amygdala, frontal gyri, and hippocampus to be implicated (Albicini & McKinlay, 2015; Grados et al., 2008; Herskovits et al., 2002; Max et al., 2011; Vasa et al., 2004). These systems are important for affect regulation and the generation of an appropriate affective state (Max et al., 2011), and so disruption to these areas in the event of TBI is likely to produce significant emotional problems.

Given a university-based sample was utilised, it may be assumed that the participants have a reasonable level of cognitive functioning to enable them to complete their academic studies. Cooper-Evans, Alderman, Knight, and Oddy (2008) reported that individuals with a history of TBI who have a higher level of cognitive function may possess more insight into their deficits, resulting in an increased risk of anxiety due to low self-esteem, thereby suggesting that university students may be more likely to report internalising behavioural problems because they are more aware of their dysfunctions following an injury. Additionally, this sample consisted of a higher number of females in the TBI group (60%), which is in contrast to research stating that males are at greater risk of TBI (Crowe et al., 2009; McKinlay et al., 2008). Countless studies have indicated that females experience internalising behavioural problems at higher rates (Feingold, 1994; Lewinsohn, Gotlib, Lewinsohn, Seeley, & Allen, 1998; McClean, Asnaani, Litz, & Hofmann, 2011). This has been attributed to hormonal differences including the role of estrogen and progesterone in enhancing stress responses (Seeman, 1997), a genetic predisposition such as the propensity to experience negative emotions (Feingold, 1994; Lewinsohn et al., 1998), internal locus of control and personality differences (Feingold, 1994), and the higher synthesis of serotonin within the brain in males (Nishizawa et al., 1997). The high prevalence of psychiatric symptoms in this

sample may also be attributed to the method of recruitment. For instance, the study description included reference to behavioural problems and head injury, and, as such, distressed individuals or students with pre-existing problems may have been more likely to participate in the study. However, considering that the results indicated no significant differences between the two groups on externalising behavioural problems, it is unlikely that there was a response bias.

3.5.1. Limitations

A limitation of the study was that all participants were university students attending the one campus, which may have biased the sample and decreased the external validity of the study. However, considering the sample was derived from a large and international institution, this is unlikely to be detrimental to the results. In addition, the self-report nature of the ASR may have led participants to respond in a socially desirable way. Further, the use of a retrospective and self-report measure of TBI may have resulted in misclassifying participants into the TBI/non-TBI groups due to the reliance on memory. The OSU TBI-ID does provide limited information regarding the nature of a TBI event, given that it is based on self-report, particularly in the case of participants who have suffered a TBI during childhood and do not recall the details of such an event. In addition, the measure was used as a rating form as opposed to an interview form, and, as such, it was not possible to ascertain and confirm information with the participants on the accuracy of their injuries. However, this measure has excellent psychometric properties, and the OSU TBI-ID has successfully been used in a number of studies to identify a history of TBI (e.g., Corrigan et al., 2012) and also is used clinically to screen for TBI exposure (Ohio Valley Center for Brain Injury Prevention and Rehabilitation, no date).

Another limitation is that premorbid behaviour and other individual characteristics such as psychiatric diagnoses, intellectual disabilities, or other pre-existing behavioural

problems were not assessed or controlled for, which will have likely affected the results of the current study. For instance, research has noted that premorbid anxiety symptoms and non-anxiety diagnoses (Gerring et al., 2002) and also internalising disorders at TOI (Max et al., 1998) significantly predict anxiety symptomatology following TBI. Moreover, non-neurological medical illnesses were also not examined or accounted for in the sample. Medical illnesses are also associated with symptoms of anxiety and depression (Katon, 2003; Roy-Byrne et al., 2008) and also somatic symptoms as a consequence of the illness itself. As such, elevated internalising disorders and symptoms evident in the study may be a function of the illness and not solely due to the TBI itself. Finally, to compute the overall internalising and externalising subscales, scores from the other subscales were summed. As such, this means that the data were not always independent in the analyses, which violates the statistical assumptions of the MANOVA.

3.5.2. Conclusions

This study sheds light on the limited knowledge regarding the profile of internalising disorders in a university sample with history of childhood TBI. Such a sample provides a snapshot of the type of long-term problems that may be experienced in young adulthood, an age group relatively ignored in the literature, who are pursuing tertiary education following an injury event. This study can direct future work into such behavioural problems and utilise objective assessment measures of TBI and MR imaging procedures to delineate structural brain dysfunction and correlates of internalising problems. It is concluded that university students with a history of childhood TBI are at risk of developing long-term internalising behavioural problems, including withdrawal, somatic complaints and avoidant personality problems. This is important to consider with regard to interventions that can aim to assist such individuals who may be struggling at university due to these long-term outcomes.

CHAPTER FOUR: THE PREVALENCE OF TBI, COMORBID ANXIETY, AND OTHER PSYCHIATRIC DISORDERS IN AN OUTPATIENT CHILD AND ADOLESCENT MENTAL HEALTH SERVICE

In the previous section, the chapter discussed and explored the long-term internalising outcomes of young adults who experienced a mild TBI in childhood, drawing from a community based sample. The study highlighted that indeed, some individuals with TBI reported higher rates of withdrawal, somatic complaints and internalising behavioural problems than individuals without TBI. To further examine this area of work, the current chapter sought to explore more acute outcomes of childhood TBI, instead drawing upon a clinical sample. This chapter was also written as a manuscript for publication, titled as above. The paper has been accepted in the Journal of Mental Health. The full-text manuscript is available in Appendix D.

Journal of MENTAL HEALTH

ISSN: 0963-8237 (print), 1360-0567 (electronic)

J Ment Health, Early Online: 1–7
 DOI: 10.1080/09638237.2017.1385733

Taylor & Francis
Taylor & Francis Group

Check for updates

ORIGINAL ARTICLE

The prevalence of traumatic brain injury, comorbid anxiety and other psychiatric disorders in an outpatient child and adolescent mental health service

Michelle Albicini[1,2], Matthew Eggleston[3], and Audrey McKinlay[2]

[1]Faculty of Medicine Nursing and Health Sciences, School of Psychological Sciences, Monash University, Clayton, Australia, [2]School of Psychological Sciences, University of Melbourne, Melbourne, Australia, and [3]Child and Family Specialty Service, Canterbury District Health Board, Christchurch, New Zealand

Abstract

Background: A history of traumatic brain injury (TBI) is prevalent in children and adolescents within the health system, which may be accompanied with higher rates of poor mental health outcomes including anxiety and other psychiatric disorders.
Aims: To explore rates of TBI and associated anxiety and other psychiatric diagnoses in children and adolescents aged 5–18 years within the mental health system.
Methods: Participants were recruited from an outpatient mental health service in Canterbury, New Zealand. The Ohio State University TBI Identification method was utilised to ascertain TBI history. Anxiety and other diagnoses were identified by a mental health file review.
Results: Over 28% of children in this study reported a history of TBI, the majority of which were mild. Review of mental health files revealed no significant differences between participants with and without TBI for anxiety and psychiatric diagnoses.

Keywords

Head injury, children, youth, psychiatric disorders, assessment

History

Received 6 December 2016
Revised 1 August 2017
Accepted 24 August 2017
Published online 4 October 2017

4.1. Abstract

Background: A history of TBI is prevalent in children and adolescents within the health system, which may be accompanied by higher rates of poor mental health outcomes including anxiety and other psychiatric disorders.

Aims: To explore rates of TBI and associated anxiety and other psychiatric diagnoses in children and adolescents aged 5-18 years within the mental health system.

Methods: Participants were recruited from an outpatient mental health service in Canterbury, New Zealand. The OSU TBI-ID was utilised to ascertain TBI history. Anxiety and other diagnoses were identified by a mental health file review.

Results: Over 28% of children in this study reported a history of TBI, the majority of which were mild. A review of mental health files revealed no significant differences between participants with and without TBI for anxiety and other psychiatric diagnoses.

Conclusions: A proportionately high number of children and adolescents within the mental health system reported a previous TBI. However, anxiety and other psychiatric problems were not over-represented in participants reporting history of TBI compared to those without. Further research is essential for examining the characteristics of children and adolescents with TBI within the mental health system, particularly those with more severe injuries, who may present a subgroup.

4.2. Introduction and background

TBI is accompanied by a range of ongoing difficulties, including behavioural, social, and cognitive problems, among children and adolescents (Donders & Warschausky, 2007; Hawley, 2003; Massagli et al., 2004; McKinlay et al., 2002). Worldwide, between 280-1373 per 100, 000 children have sustained some form of TBI (McKinlay & Hawley, 2014). In a

New-Zealand cohort, 790 per 100,000 cases were identified to have TBI, with 749 of these cases per 100,000 being of mild severity (Feigin et al., 2013). Children aged 0-14 years and young adults aged 18-34 years constituted 70% of all TBI cases (Feigin et al., 2013). In Australia, rates of hospitalisation for TBI in children aged 0-14 years were reported as 395.9 per 100,000, with 47.6 per 100,000 being 'high-threat-to-life' injuries (Berry, Jamieson, & Harrison, 2010). Considering these cases were only hospital-related, it is likely that rates are actually much higher when including non-reported cases. As such, any problems associated with such injuries are important to consider given the high number of individuals affected per year.

Research has now elucidated that TBI can be a precipitant of ongoing internalising and externalising behavioural issues reported by some children and adolescents (Karver et al., 2014; Liu & Li, 2013; McKinlay et al., 2009). For instance, parent ratings of their child's behaviour 18-months following TBI in children aged three to seven at TOI have revealed higher rates of behavioural problems compared to children with an OI, including problems with affect regulation, attention-deficit/hyperactivity issues, and overall behavioural problems (Karver et al., 2014). Moreover, these issues were reported to be described as 'unmet needs' in terms of access to clinical services, and were present in mild to moderate and severe TBI (Karver et al., 2014). Supporting this, in a large scale study of children aged six years with a history of mild TBI compared to healthy controls, parents of children with mild TBI reported higher rates of withdrawal, emotional reactiveness, and aggressive problems (Liu & Li, 2013). In adolescents aged 14-16 years, attention-deficit/hyperactivity, conduct and oppositional behavioural problems, substance abuse and mood problems have been reported to be significantly higher for individuals with a history of childhood mild TBI resulting in inpatient care, as compared to an outpatient mild TBI group, and healthy controls (McKinlay et al., 2009).

In addition to higher rates of behavioural issues, children and adolescents with a history of TBI also present with a higher incidence of psychiatric diagnoses including depression, anxiety, ADHD, CD, and substance use issues (Luis & Mittenberg, 2002; Massagli et al., 2004; Max et al., 2013; Max et al., 2012). For instance, in children aged 5-14 years with mild TBI, Max et al. (2013) found within the first six months following injury, 36% exhibited a novel psychiatric disorder, with highest numbers reporting ADHD, simple phobia, separation anxiety, and ODD (Max et al., 2013). In children aged 7-17 years with mild, moderate or severe TBI, similar results have been reported – in the initial three months following injury, 49% exhibited a novel psychiatric disorder, with the highest numbers reporting externalising disorder, anxiety disorder, and internalising disorder (Max et al., 2012).

Despite the aforementioned findings, anxiety appears to have been less of a focus when examining outcomes associated with TBI in children and adolescents (Albicini & McKinlay, 2015), with the majority of work examining externalising problems. A meta-analysis of the worldwide prevalence of psychiatric diagnoses in children and adolescents aged 6-18 years within the general population revealed 13.4% were diagnosed with a mental disorder, with a world-wide prevalence of 6.5% diagnosed with anxiety disorders, compared to that of 2.6% with depressive disorders and 3.4% with attention-deficit disorders (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015). Given these statistics, the elevated level of anxiety in the general child and adolescent population, and the high rate of TBI among children, it appears important that anxiety is examined in outcome studies for individuals with TBI (Albicini & McKinlay, 2015). This is particularly important considering the associations between anxiety and educational underachievement, co-morbid psychiatric disorders and functional impairment (Bennett & Walkup, 2016), and the long-term effects

chronic anxiety may have on the developing architecture of the brain (Arnsten, 2009; Brinks et al., 2008).

In one of the few studies to specifically examine anxiety, children and adolescents 6-12 months following mild to severe TBI exhibited novel anxiety disorders in over 10% of cases (Max, Lopez, et al., 2015). Previously, this has been supported by other studies, where among children 5-14 years with mild to severe TBI, 8.5% exhibited novel clinical anxiety disorders and 17% exhibited novel subclinical anxiety disorders (Max et al., 2011). Of those with mild TBI, 11% exhibited novel clinical anxiety disorders, and 20% exhibited subclinical anxiety disorders (Max et al., 2011). Anxiety disorders and symptomatology that have been more commonly reported in children and adolescents following TBI include PTSD (Hajek et al., 2010; Max et al., 2011; Vasa et al., 2004), separation anxiety (Luis & Mittenberg, 2002; Max et al., 2011), obsessions and compulsions (Grados et al., 2008; Luis & Mittenberg, 2002) and generalised anxiety (Luis & Mittenberg, 2002). At present, there is a lack of information regarding these aspects in clinical populations.

In an attempt to explain the above findings, predictor studies have sought to delineate the potential causes for these elevated rates of anxiety following TBI in children and adolescents. When considering internalising symptomatology (including anxiety, depression and withdrawal) in general, findings suggest that rates of parent psychiatric symptoms and female gender are predictors of internalising problems following TBI in adolescents (Peterson et al., 2013). Studies have also highlighted risk factors for the expression of affective lability in children with TBI, including elevated pre-injury affective lability, more psychosocial adversity, and greater damage to the OFC (Vasa et al., 2015). For anxiety more specifically, consensus falls among factors including higher levels of premorbid psychosocial adversity (Gerring et al., 2002; Grados et al., 2008; Herskovits et al., 2002; Vasa et al., 2002; Vasa et al., 2004), pre-existing mood and anxiety problems (Gerring et al., 2002; Grados et

al., 2008; Luis & Mittenberg, 2002; Max et al., 1998), and younger age of injury (Levi et al., 1999; Max et al., 2011; Vasa et al., 2002).

Collectively, outcome studies for children and adolescents with TBI suggest that there may be a growing need for services to account for the ongoing behavioural, social and emotional problems associated with these injuries. It is therefore likely that children and adolescents who have sustained a TBI may be over-represented within the mental health system to account for these needs. According to a large child and adolescent survey of mental health and well-being, in the general population, 17% of children and adolescents aged 4-17 years had utilised a service for mental health issues in the past 12 months (Lawrence et al., 2015). In comparison with children and adolescents with TBI, one study reports that around 24% of children ages 12-17 years received outpatient mental health services, 8.3% received school services, and 28.8% received any mental health service, one to six months after their injury (Kurowski et al., 2013). The higher rates of children and adolescents receiving mental health services following TBI is unsurprising, given findings that report on the poor outcomes that can be experienced following such an injury event. It appears important, therefore, to explore the particular outcomes and problems faced by children and adolescents with a history of TBI that are presenting within the mental health system, given that these children likely differ from children and adolescents with TBI in the general population.

This study has the following aims:

1) To identify the incidence of TBI and an anxiety disorder diagnosis, in children and adolescents aged 5-18 years who are presenting within the mental health system
2) To examine the incidence of anxiety disorders compared to that of other psychiatric diagnoses in children and adolescents aged 5-18 years who are presenting within the mental health system

3) To examine the comorbidities of psychiatric disorders among children and adolescents with a history of TBI and anxiety
4) To explore whether parental stress is heightened in families of children and adolescents with TBI compared to children and adolescents with no TBI history

It was hypothesised that:

1) Children and adolescents within the mental health system with a history of TBI will have a higher incidence of anxiety diagnoses compared to children within the mental health system with no TBI
2) Anxiety diagnoses will be accompanied by comorbid psychiatric disorders, particularly mood disorders, and comorbidities will be higher in the TBI group
3) Parental stress will be higher in the TBI group

4.3. Method

4.3.1. Participants

Participants were individuals aged 5-18 years from three child and adolescent mental health services based in Christchurch, New Zealand (Canterbury District Health Board). The sample was recruited from a larger study investigating criminal behaviours in children and adolescents presenting within the mental health system. The mental health service units included a child service (5-12 years), adolescent service (13-18 years) and rural service (5-18 years). Upon arrival at their mental health appointments, parents and their children were provided with forms briefly explaining the study and why they have been given the opportunity to participate. Inclusion criteria were children aged 5-18 years presenting for an assessment at one of the mental health services. Participants were excluded if they did not speak English. The overall sample consisted of 161 participants (M=12.39 years, SD=3.84 years), aged 5-18 years, with 85 males (M=11.40 years, SD=3.51 years) and 76 females

(*M*=13.50 years, *SD*=3.12 years). Within the sample, 107 reported no TBI (*M*=12.37 years, *SD*=3.48 years) and 42 reported a history of TBI (*M*=12.46 years, *SD*=3.61 years); 12 participants failed to record TBI history, resulting in 149 participants included in analysis of data.

4.3.2. Procedure

Following informed consent, participants were provided with an envelope with questionnaires examining TBI status history, parental stress, and also a demographic questionnaire. Parents of the children completed the questionnaires before or after their appointments, and returned the completed questionnaires to administration in a sealed envelope. The procedure took approximately 15-20 minutes.

In addition to information obtained from questionnaires, information from the mental health files of each client was also reviewed by research assistants in New Zealand. Information within the files included demographic and socioeconomic data, reason for referral, previous psychiatric diagnoses, current psychiatric diagnoses, substance and/or alcohol use, other behavioural and or/emotional problems, difficulties at home or school, contacts with the forensic system and offending behaviours, and other clinical information deemed important by the consulting clinician. For the purpose of this study, information regarding anxiety and other psychiatric diagnoses was of interest.

4.3.3. Design

A between-subjects, cross-sectional study design was used, with data collected over a two-year period. Incidence of TBI and mental health outcomes for each participant were evaluated at a single time point. The independent variable was whether participants had sustained a previous TBI, as determined by the OSU TBI-ID (Corrigan & Bogner, 2007) .

The dependent variables were mental health outcomes, including anxiety disorders and other psychiatric diagnoses, obtained from the mental health files.

4.3.4. Measures

A demographic questionnaire was used to record information about the participants including age, gender, developmental history, and school functioning. The questionnaire involved a yes/no format answer to each question, with the option to provide additional information when requested.

The OSU TBI-ID SF, adapted from the OSU TBI-ID (Corrigan & Bogner, 2007) was used as a self-report measure to screen lifetime TBI exposure, as described in previous sections of the thesis. In this study, mild TBI was defined by an injury with LOC <30 minutes, moderately-severe TBI by a LOC 30 minutes to 24 hours, and severe TBI by a LOC >24 hours. Participants who reported being dazed/having memory lapse resulting from a head injury were also classified as having mild TBI due to evidence of loss of memory for events occurring near the injury, and alterations of mental state (Esselman & Uomoto, 1995; McKinlay, 2010).

The Parenting Stress Scale (Berry & Jones, 1995) assessed self-reported stress levels of parents of each child participant. The scale has demonstrated satisfactory levels of internal reliability (.83) and test-retest reliability (.81), and also convergent validity with other measures of stress (Berry & Jones, 1995). It is a useful tool for assessing stress of mothers and fathers of children both with and without clinical problems, and explores domains related to emotions and role satisfaction such as guilt, marital satisfaction, and loneliness (Berry & Jones, 1995).

4.3.5. Data analysis

All statistical tests were performed using SPSS statistics version 22, with an alpha level set at .05. Descriptive statistical analyses were conducted for all variables within the dataset, utilising the split-file function for gender, TBI history, and anxiety diagnosis, to provide a frequency distribution of the data. A combined variable for TBI and anxiety diagnosis was also computed. To examine group differences on demographic information, chi-square analyses were conducted for gender, school and learning difficulties, behavioural problems, mental health problems, and medical history, and an independent-samples *t*-test was conducted for age. Outcomes of diagnoses were coded as 0=no, 1=yes. Co-morbid externalising, internalising and other disorders were defined as cases in which more than one diagnosis in each domain was present, and coded as 0=no comorbidities, 1=comorbidities. Percentages and chi-square tests were based on 'known' categories and values, and as such excluded missing cases. To examine the incidence of anxiety disorder diagnosis among participants with and without a history of TBI, frequencies and descriptive statistical analyses were calculated to examine anxiety diagnoses, psychiatric comorbidities and other psychiatric diagnoses among the two groups. Further chi-square analyses were conducted to compare rates of psychiatric disorders between children and adolescents with TBI, and Fisher's exact test to examine differences in psychiatric disorders for those with TBI and anxiety diagnosis, versus TBI and no anxiety diagnosis.

4.4. Results

4.4.1. Participant demographics

Descriptive statistics and frequencies were run to determine the demographic characteristics of children and adolescents with and without a history of TBI. Results are displayed in Table 4.1.

An independent-samples *t*-test was conducted to examine any differences in age for participants with and without a history of TBI, which revealed a non-significant result, $t(141)=-.014$, $p=.89$. Further, chi-square analyses were computed to examine group differences on categorical demographic data, revealing no significant differences for gender, $\chi^2(1) = 0.20$, $p=.27$, school difficulties, $\chi^2(1) =0.90$, $p=.34$, learning difficulties, $\chi^2(1) = 1.38$, $p=.24$, behavioural problems, $\chi^2(1) =0.08$, $p=.78$, mental health problems, $\chi^2(1) = 0.08$, $p=.78$, physical problems, $\chi^2(1) = 0.88$, $p=.35$, function-impairing medication use, $\chi^2(1) = 0.18$, $p=.67$, or medical diagnoses, $\chi^2(1) =1.14$, $p=.29$. There was a significant difference between the two groups for children needing educational assistance, $\chi^2(1) = 6.10$, $p=0.01$, with children with TBI requiring more assistance. To examine the TBI group further, an analysis of specific characteristics for children within the TBI group is presented in Table 4.2.

As is evident in Table 4.2, the majority of individuals reported their TBI incident to occur before the age of 15 years. Over half reported a LOC of any time length that occurred with their injury, and only a small minority reported a more severe TBI and multiple injuries.

4.4.2. Outcomes for mental health file review – TBI versus no-TBI

To identify rates of anxiety diagnoses and other psychiatric diagnoses for children and adolescents with and without a history of TBI, descriptive statistics and frequencies were analysed for outcomes derived from the file review. The results are displayed in Table 4.3.

As is evident in Table 4.3 below, individuals reporting a history of TBI also reported relatively high rates for suicidal/self-harm, anxiety disorders and mood disorders. Children and adolescents without a history of TBI also reported relatively high rates for anxiety disorders, suicidal/self-harm, and mood disorders. Those with TBI reported higher rates of mood disorders, suicidal/self-harm, and abuse history, than those without a history of TBI. Both groups presented with a moderate number of children and adolescents given no

Table 4.1.

Participant Characteristics for Traumatic Brain Injury and Non-Traumatic Brain Injury Groups

	TBI	**Non-TBI**
Characteristic	***n* (%)**	***n* (%)**
Total	42 (28.29) (*M*=12.46 years, *SD*=3.61)	107 (71.81) (*M*=12.37 years, *SD*=3.48)
Gender		
Male	24 (57.10)	50 (47.20)*
Female	18 (42.90)	56 (52.80)
School Difficulties		
Yes	28 (71.80)	62 (63.30)
No	11 (28.20)	36 (36.70)
Learning Difficulties		
Yes	13 (34.20)	23 (24.20)
No	25 (65.80)	72 (75.80)
Educational Assistance		
Yes	20 (52.60)	28 (29.80)
No	18 (47.40)	66 (70.20)
Behavioural Problems		
Yes	5 (13.20)	11 (11.50)
No	33 (86.80)	85 (88.50)
Mental Health Problems		
Yes	15 (39.50)	35 (36.80)
No	23 (60.50)	60 (63.20)
Any Hospitalisations		
Yes	15 (40.50)	31 (31.70)
No	22 (59.50)	67 (63.30)
Medical Diagnoses		
Yes	11 (31.40)	38 (41.80)
No	24 (68.60)	53 (58.20)

Note. N=149; TBI=traumatic brain injury;* = one participant failed to record gender.

Table 4.2.

Characteristics of Participants with Traumatic Brain Injury

Characteristic	**TBI group (*n*=42)**
Age at First Injury * (*M*)	7.47 years
TBI before/after 15 years *, *N* (%)	< 15 years: 12 (27.90) ≥ 15 years: 2 (4.70) n/a: 29 (67.40)
TBI with any LOC, *N* (%)	25 (59.52)
TBI with LOC >30 mins, *N* (%)	2 (4.76)
Multiple TBI *, *N* (%)	4 (9.53)

Note. *OSU TBI-ID only provides this information for TBI involving loss of consciousness; TBI=traumatic brain injury; LOC=loss of consciousness

diagnosis according to the file review, which was higher than expected given the nature of the sample. Chi-square analyses were conducted on variables of interest to determine any differences between the two groups on rates of diagnoses and mental health problems. These revealed no significant differences between anxiety, $\chi^2(1)=2.16$, $p=.14$, mood, $\chi^2(1)=0.4$, $p=.85$, behaviour disorder, $\chi^2(1)=0.17$, $p=.69$, pervasive developmental disorder, $\chi^2(1)=0.03$, $p=0.87$, drug and alcohol use, $\chi^2(1)=0.41$, $p=.52$, low IQ, $\chi^2(1)=0.45$, $p=.50$, or suicidal/self-harm, $\chi^2(1)=0.62$, $p=.89$.

Child versus parent reports of TBI and outcomes

Chi-square analyses were also conducted for parent report of their child's TBI diagnosis, and child report of their TBI diagnosis, to compare mental health outcomes. For parent reports of their child's diagnosis, chi-square analyses revealed a significant difference for anxiety, $\chi^2(1)=4.91$, $p=0.03$ and suicidal/self-harm, $\chi^2(3)=12.01$, $p=.01$.For child reports of a TBI diagnosis, no differences in mental health outcomes were found, with all $p>.05$.

4.4.3. Parental stress

To examine group differences on self-reported parental stress, independent-samples *t*-tests were conducted. Results revealed no significant differences for parental stress scores between those with children who had a history of TBI, $t(130)=0.35$, $p=.73$, and those without. When considering parent report of TBI and child self-report of TBI, and differences in parental stress, independent-samples *t*-tests further revealed no significant differences in parental stress scores for those with parent-reported TBI compared to no-TBI, $t(127)=0.23$, $p=.82$, or for those with child-reported TBI compared to no-TBI, $t(56)=-0.61$, $p=.55$.

Table 4.3.

Mental Health Concerns and Diagnoses for Individuals with and without History of Traumatic Brain Injury obtained from File Review

	TBI	**Non-TBI**
Characteristic	***n* (%)**	***n* (%)**
Total	42 (28.29) (*M*=12.46 years, *SD*=3.61)	107 (71.81) (*M*=12.37 years, *SD*=3.48)
Internalising Disorders (total)	*20 (47.60)*	*47 (43.90)*
Anxiety Disorder	8 (21.10)	32 (29.90)
Mood Disorder	7 (18.40)	16 (17.00)
Suicidal/Self-Harm	14 (36.80)	28 (29.80)
Comorbid Internalising Disorders	*8 (19.10)*	*21(20.60)*
Externalising Disorders (total)	*6 (14.30)*	*17 (15.90)*
Behaviour Disorder*	5 (13.20)	15 (16.00)
Drug and Alcohol	0	1 (1.10)
Comorbid Externalising Disorders	*5 (13.20)*	*2 (1.90)*
Pervasive Developmental Disorder	1 (2.60)	3 (3.20)
Other (total)	*11 (26.20)*	*27 (25.20)*
Low Intelligent Quotient**	1 (2.60)	5 (5.30)
Physical Disorder	5 (13.20)	13 (13.80)
Abuse History	5 (13.20)	10 (10.60)
Comorbid Other Disorders	*0*	*1 (1.10)*
No Diagnosis	21 (55.30)	44 (46.80)

Note. N=149; TBI=traumatic brain injury; * = behaviour disorders include Attention-Deficit/Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD); ** = low Intelligent Quotient refers to 70 or lower; Values refer to valid percent due to missing data (*n*=13 missing data non-TBI, *n*=5 missing data TBI).

4.4.4. Outcomes from mental health file review – Anxiety and TBI

As mentioned above, a combined variable for TBI and anxiety diagnosis (and TBI with no anxiety diagnosis) was also computed, to examine rates of other psychiatric disorders among the two groups. Descriptives and frequencies were analysed for each group for the computed variables, which are provided in Table 4.4.

Table 4.4.

Comorbidities and Participant Characteristics for Individuals with Anxiety Disorder Diagnosis and History of Traumatic Brain Injury compared to Individuals with Traumatic Brain Injury and No Anxiety Disorder

	TBI + Anxiety	TBI
Characteristic	*n* (%)	*n (*%)
Total	8 (19.05) (*M*=13.29 years, *SD*=3.45)	34 (80.95) (*M*=12.39 years, *SD*=3.67)
Gender		
Male	4 (50.00)	19 (55.90)
Female	4 (50.00)	14 (44.10)
Mood Disorder	1 (12.50)	6 (17.70)
Behaviour Disorder*	2 (25.00)	3 (8.80)
Drug and Alcohol	0	0
Pervasive Developmental Disorder	1 (12.50)	0
Low Intelligent Quotient**	0	1 (2.90)
Suicidal/Self-Harm	2 (25.00)	12 (3.50)
Physical Disorder	2 (25.00)	3 (8.80)
Abuse History	0	5 (14.70)

Note. N=42; TBI=traumatic brain injury;* = behaviour disorder includes Attention-Deficit/Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD); ** = low Intelligent Quotient refers to score of 70 or lower.

As shown in Table 4.4, children and adolescents with a history of TBI and anxiety disorder diagnosis also tended to show difficulties with behaviour disorders, suicidal/self-harm and physical disorders. For the TBI and no anxiety group, children and adolescents presented with the highest rates of mood disorders, abuse history, and physical disorders. To examine any potential comorbidities, chi-square analyses were conducted for the combined variables of anxiety and TBI, and TBI with no anxiety, for each of the above mental health outcomes. Utilising Fisher's exact test due to smaller group sizes, the results were non-significant for all variables, with $p>.05$.

4.5. Discussion

This study aimed to identify the incidence of TBI and an anxiety disorder diagnosis in children and adolescents aged 5-18 years who are presenting within the mental health system. It was of further interest to examine the incidence of anxiety disorders compared to that of other psychiatric diagnoses in the sample, and the potential comorbidities of psychiatric disorders among children and adolescents with a history of TBI and anxiety. It was hypothesised that children and adolescents with a history of TBI would have a higher incidence of anxiety diagnoses compared to children with no TBI, and that anxiety diagnoses would be accompanied by comorbid psychiatric disorders, particularly mood disorders, with comorbidities being higher in the TBI group.

The current study found that over 28% of children and adolescents presenting to mental health services reported a history of TBI, with the majority being of mild severity. This is in keeping with Kurowski et al. (2013), who reported that 24% of children and adolescents aged 12-17 years with TBI accessed outpatient mental health services, and 28% accessed any mental health service, versus 17% in children aged 4-17 years within the general population (Lawrence et al., 2015). In the general population, rates of TBI in children and adolescents has been reported as approximately 14% worldwide (McKinlay & Hawley, 2014) and approximately 8% in New Zealand for all severities of TBI, with mild TBI being the majority of cases (749/790) (Feigin et al., 2013). Considering this, it appears that children and adolescents with a history of TBI, particularly mild TBI, are over-presented within the mental health services of this sample.

In contrast to the previous literature, no significant group differences were found between children and adolescents with a history of TBI compared to those without for anxiety disorders. This is in contrast to samples recruited from hospital or rehabilitation admissions

which have recorded higher rates in TBI groups (Max et al., 2011; Max, Lopez, et al., 2015; Vasa et al., 2002). However, this finding is consistent with McKinlay et al. (2009), who reported that adolescents aged 14-16 years with a history of childhood TBI were not more likely to display symptoms of anxiety disorders. Further, no significant differences were found between the TBI and non-TBI groups for behavioural problems or any other psychiatric disorders, inconsistent with non-clinical studies (Karver et al., 2012; Massagli et al., 2004; Max et al., 2013; Max et al., 2012; McKinlay et al., 2002; McKinlay et al., 2009; Schwartz et al., 2003). When examining parental and child reports of previous TBI separately however, findings indicated a significant difference for anxiety disorder diagnosis and suicidal/self-harm, such that parent reports of TBI led to higher rates of such outcomes. Such discrepancies between child and parent reports of internalising problems are also evident within the existing TBI literature (Levi et al., 1999; Luis & Mittenberg, 2002; Mather et al., 2003).

When examining children and adolescents with history of TBI and anxiety disorder, despite smaller group numbers, relatively high rates of comorbid behavioural disorders, suicidal/self-harm and physical disorders were found within this group, however mood disorders did not appear to be a co-occurring problem. This is in contrast to studies finding that children and adolescents following TBI with anxiety disorders also tend to have concurrent mood and other internalising problems (Gerring et al., 2002; Grados et al., 2008; Luis & Mittenberg, 2002; Max et al., 1998).

4.5.1. Theoretical and practical explanations

When relying solely on parent reports of history of TBI, a significant difference for anxiety disorder diagnosis and suicidal/self-harm was highlighted, such that parent reports of TBI led to higher rates of such outcomes. However, this was not the case for TBI events

reported by children and adolescents themselves. Inconsistencies between reports from young people and their parents have been documented regarding rates of internalising disorders and PCS following TBI (Hajek et al., 2011; Levi et al., 1999; Luis & Mittenberg, 2002), however the nature of these reports are mixed, with young people reporting higher rates in some instances, and parents in others.

While past research has reported higher rates of anxiety disorders and symptomatology following TBI in children and adolescents (Max et al., 2011; Max, Lopez, et al., 2015; Max et al., 2012; McKinlay et al., 2009), the current findings are not consistent with this. For instance, this sample consisted of a higher number of males than females within the TBI group (not statistically significant), whereas the spread was more even for those without TBI. Therefore, the results may suggest a non-significant trend towards males being over-represented in the TBI group. Research maintains that anxiety symptomatology is more common in females than in males (Beesedo, Knappe, & Pine, 2009), with this gender difference reaching ratios of 2:1 and 3:1 for females to males as they reach adolescence (Wittchen, Nelson, & Lachner, 1998). These differences have been attributed to hormonal differences in responding to stress responses (Seeman, 1997), and potential genetic differences in the capacity to manage negative emotions (Feingold, 1994). Considering this, it is unsurprising that in children and adolescents with TBI, female gender also presents as a consistent predictor of the development of anxiety symptomatology (Gerring et al., 2002; Grados et al., 2008). For instance, in adult samples, research also shows a gender bias in anxiety disorders, such that adult females report higher rates of anxiety following childhood TBI (Scott et al., 2015).

The services from which the participants were recruited may also be another factor contributing to the unexpected findings. Anxiety disorders are noted to be the most frequent mental health disorder in children and adolescents (Beesedo et al., 2009), however in this

sample, there is a relatively low percentage of anxiety cases, both in those with TBI and those without, considering participants were recruited from a mental health service. Moreover, the small number of children and adolescents without a formal diagnosis is also surprisingly low. Given that the vast majority of mental health services are provided by public funding, the results may suggest that New Zealand clinicians may be somewhat reluctant to provide a diagnosis of anxiety and other disorders in children and adolescents. Moreover, considering that the mental health service from which the sample was obtained is a specialist service, there is exclusion criteria placed on client entry (e.g. CD not accompanied by co-morbid disorders, intellectual disability not accompanied by co-morbid disorders, sexual abuse cases) which is likely to have influenced the resultant participant characteristics.

Research suggests that risk factors associated with anxiety following TBI include higher levels of premorbid psychosocial adversity (Gerring et al., 2002; Grados et al., 2008; Herskovits et al., 2002; Vasa et al., 2002; Vasa et al., 2004), pre-existing mood and anxiety problems (Gerring et al., 2002; Grados et al., 2008; Luis & Mittenberg, 2002; Max et al., 1998), and younger age of injury (Levi et al., 1999; Max et al., 2011; Vasa et al., 2002). In addition, severity of injury also contributes to this risk, with more severe TBI associated with higher rates of anxiety (Gerring et al., 2002; Luis & Mittenberg, 2002; Max et al., 1998). Considering that this sample had mild TBI, and that the participant groups were similar so that they likely did not differ in pre-existing risk factors known to implicate the development of anxiety disorders post-TBI, it may be that history of TBI alone was not enough to indicate differences between the groups for anxiety-related outcomes.

An alternate consideration is the age and developmental period of children and adolescents within the sample, the age at TOI, and emergence of internalising symptomatology. Research suggests that ongoing problems following childhood TBI may arise from a combination of neurobiological and environmental factors (Anderson, Spencer-

Smith, & Wood, 2011). While there is evidence that children are vulnerable to the effects of early neurological insult of developing social and emotional skills (Ryan, Anderson, et al., 2014), it is possible that deficits or difficulties in these areas do not become noticed until a certain level of maturity (Ryan, Catroppa, et al., 2014). It has indeed been found that adults with a history of childhood TBI, even in less severe injury cases, report higher rates of internalising symptomatology (for instance, highlighted in chapter three of the thesis). Children and adolescents with a history of TBI, particularly milder TBI, may therefore appear to function normally relative to individuals without TBI until more complex social and emotional skills develop, whereby issues with anxiety and mood may become more apparent.

Developmental trajectories of anxiety in the general population also suggest both differences for females and males, and younger versus older children and adolescents. Research has identified that younger adolescent females present with stronger growth rates of GAD symptomatology, whereas middle adolescent females reported initially higher rates of GAD that remained stable across a five year period (Hale et al., 2008). Alternatively, males displayed a gradual decrease in anxiety symptomatology from early to middle adolescence (Hale et al., 2008). In comparing internalising disorders (e.g. anxiety, depression) and externalising disorders (e.g. inattention, defiance), it has been documented that while internalising disorders tend to increase with age, externalising disorders tend to decrease (Costello, Copeland, & Angold, 2011). Most notably is that internalising disorders have been found to increase from age 13 years and onwards, and that this increase is associated with low and very low rates of externalising disorders (Nivard et al., 2016). These patterns described in the literature have been associated with a number of factors, including structural changes in grey and white brain matter densities (Paus, Keshavan, & Giedd, 2008), hormonal changes and puberty (Paus et al., 2008) and social factors (Ahmed, Bittencourt-Hewitt, & Sebastian, 2015). Considering both the mean age (*M*=12.39 years) and higher number of

males within the present study, any group differences in anxiety may have been masked or otherwise identified if the sample more closely fit that of at-risk groups more commonly found in the literature.

An additional factor to consider is the nature of psychiatric disorder or mental health concern that parents perceive to require utilisation of mental health services for their children. A mental health survey for children and adolescents aged 4-17 years reported that the majority of individuals in the survey accessed mental health services for depression (79.6%), and CD (68.8), with anxiety coming in third (61.4). For younger age groups (4-11 years), this difference is more marked, with 73.2% using services for depression, 66.4% for CD and 53.6% for anxiety disorders (Lawrence et al., 2015). When identifying reasons for mental health service use by parents for their children, increased perceived burden is associated with a higher rate of service use, with anxiety and depressive disorders seen as less burdensome and causing less impairment (Angold, Messer, et al., 1998). Moreover a higher rate of mental health service use for young people is strongly associated with 'more severe mental health impairment' (Olfson, Druss, & Marcus, 2015). It is interesting to consider what parents of young people perceive as being 'more severe', and it is likely that psychiatric symptomatology that is more strongly associated with service use are those associated with externalising disorders, due to their nature of being more generally directed outwards, visibly distressing, destructive and concerning for the individual (Bayer et al., 2012).

4.5.2. Limitations

A limitation of the study was the reliance of self-report, from parents and children/adolescents, regarding the incidence and nature of TBI. Research indicates that adults aged 25 years recall their incidence of childhood TBI with only 84.5% accuracy (McKinlay & Horwood, 2016), and for 25 year-olds with a history of childhood TBI

requiring hospitalisation, only 59/101 were recalled. Considering this study utilised a self-report measure which relied on memory of TBI severity and incidence, the rate of TBI in this sample may have been higher. Furthermore, there was a reliance on the mental health file review for ascertaining psychiatric diagnosis, which is dependent on the clinical opinion of the consulting clinician. As such, although there are a number of children without a diagnosis in the sample, individuals with significant mental health issues may have been underrepresented in this study due to the nature of the mental health file review (i.e. dichotomous coding of yes/no diagnosis). It may be in fact that many children exhibited sub-threshold symptoms of a disorder and as such, many cases of significant anxiety and other psychiatric symptomatology that did not fit criteria for a full diagnosis may have been missed. This study also may have lacked sufficient power to identify any group differences, particularly considering the TBI cases were of mild severity. Further, there was no control for pre-existing mental health issues or other factors. However, when comparing groups for demographic data and participant characteristics, no significant group differences were identified.

4.5.3. Theoretical and practical implications

Theoretically speaking, this study implicates previous theories that describe the development and course of anxiety disorders and other internalising symptomatology in children and adolescents. Consequentially, the findings may also suggest that this trend of trajectory may influence the emergence of anxiety in young people following TBI. In a clinical setting, these theoretical implications might explain when young people are more likely to initiate service use for anxiety following TBI, in that they may be more likely to notice onset of symptomatology in middle-adolescence, despite an injury occurring in early to late childhood. As such, clinicians working with children with a TBI history may need to consider relevant risk factors, including gender, parental stress, family history of internalising

disorders and socioeconomic factors, in identifying potential ‘at-risk’ individuals who may require early intervention and management to support any future emergence of anxiety symptomatology and disorders.

4.5.4. Conclusions

While this study did not identify overall group differences in anxiety and other psychiatric disorders or symptomatology, it highlighted that children and adolescents presented with higher rates of suicidal/self-harm behaviours and anxiety disorder diagnosis for those with parent-reported TBI. Moreover, the study described characteristics of a sample within the mental health system, for children and adolescents with and without a history of TBI. Further, it was identified that children and adolescents may be overrepresented within the mental health system, as compared to rates of TBI within the general child and adolescent population, which suggests the need for early detection of individuals presenting with TBI and risk factors known to accompany ongoing psychiatric and behavioural problems.

CHAPTER FIVE: ANXIETY DISORDERS IN ADULTS WITH CHILDHOOD TBI: EVIDENCE OF DIFFICULTIES MORE THAN 10 YEARS POST-INJURY

Previously discussed were the findings regarding young adults with long-term internalising symptomatology following childhood TBI based in a community sample, and more short-term psychiatric outcomes following TBI in children and adolescents based on a clinical sample. Comparatively, long-term outcomes were highlighted in the community-based sample whereas generally, there were no differences among short-term psychiatric problems post-TBI for a clinically based sample. This chapter will focus on long-term outcomes utilising a hospital-based sample. This chapter was submitted for publication as a manuscript, which may be accessed online from the Journal of Head Trauma Rehabilitation. The manuscript is attached as an appendix at the end of the thesis (Appendix E)

J Head Trauma Rehabil

Anxiety Disorders in Adults With Childhood Traumatic Brain Injury: Evidence of Difficulties More Than 10 Years Postinjury

Michelle Albicini, BPSych Hons; Audrey McKinlay, A.Dip Clin Psyc, PhD

Objective: To explore long-term psychiatric outcomes in individuals with a history of childhood traumatic brain injury (TBI) or orthopedic injury (OI). **Setting:** Hospital emergency department, medical admission records and outpatient settings. **Participants:** There were 95 males ($M = 22.78$ years, SD = 3.44 years) and 74 females ($M = 22.27$ years, SD = 3.09 years), 65 with mild TBI ($M = 23.25$ years, SD = 3.58 years), 61 with moderate-severe TBI ($M = 22.34$ years, SD = 2.79 years), and 43 with OI ($M = 21.81$ years, SD = 3.36 years). **Design:** Longitudinal, between-subjects, cross-sectional design using retrospective and current data. **Main Measures:** Semistructured interview to obtain psychiatric diagnoses and background information, and medical records for identification of TBI. **Results:** Group with moderate-severe TBI presented with significantly higher rates of any anxiety disorder ($\chi^2_2 = 6.81$, $P = .03$) and comorbid anxiety disorder ($\chi^2_2 = 6.12$, $P < .05$). Group with overall TBI presented with significantly higher rates of any anxiety disorder ($\chi^2_1 = 5.36$, $P = .02$), panic attacks ($\chi^2_1 = 4.43$, $P = .04$), specific phobias ($\chi^2_1 = 4.17$, $P = .04$), and depression ($\chi^2_1 = 3.98$, $P < .05$). Prediction analysis revealed a statistically significant model ($\chi^2_7 = 41.84$, $P < .001$) explaining 23% to 37% of the variance in having any anxiety disorder, with significant predictors being group (TBI) and gender (female). **Conclusions:** Children who have sustained a TBI may be vulnerable to persistent anxiety, panic attacks, specific phobias, and depression, even 13 years after the injury event. **Key words:** *anxiety*, *anxiety disorders*, *brain injuries*, *child*, *concussion*

THE ARGUMENT that childhood traumatic brain injury (TBI) can result in ongoing challenges and issues, which persist into adulthood, continues to be debated.[1,2] Some suggest that the plasticity of the young brain functions as a buffer against any ongoing effects

Compounding this debate is the finding that long-term behavioral, cognitive, and emotional outcomes following childhood TBI are heterogeneous,[6] as is the brain damage that occurs as a result of diffuse injury.[5,7] Therefore, outcome studies investigating the long-term

5.1. Abstract

Objective: To explore long-term psychiatric outcomes in individuals with a history of childhood TBI or OI.

Setting: Hospital ED, medical admission records and outpatient settings.

Participants: There were 95 males (*M*=22.78 years, *SD*=3.44 years) and 74 females (*M*=22.27 years, *SD*=3.09 years), 65 with mild TBI (*M*=23.25 years, *SD*=3.58 years), 61 with moderate-severe TBI (*M*=22.34 years, *SD*=2.79 years) and 43 with OI (*M*=21.81 years, *SD*=3.36 years).

Design: Longitudinal, between-subjects, cross-sectional design using retrospective and current data.

Main Measures: Semi-structured interview to obtain psychiatric diagnoses and background information, and medical records for identification of TBI.

Results: The group with moderate-severe TBI presented with significantly higher rates of any anxiety disorder ($\chi^2(2)=6.81$, $p=0.03$), and comorbid anxiety disorder ($\chi^2(2)=6.12$, $p<0.05$). The group with overall TBI presented with significantly higher rates of any anxiety disorder ($\chi^2(1)=5.36$, $p=0.02$), panic attacks ($\chi^2(1)=4.43$, $p=.04$), specific phobias ($\chi^2(1)=4.17$, $p=.04$) and depression ($\chi^2(1)=3.98$, $p<.05$). Prediction analysis revealed a statistically significant model ($\chi^2(7)=41.84$, $p<.001$) explaining 23-37% of the variance in having any anxiety disorder, with significant predictors being group (TBI) and gender (female).

Conclusions: Children who have sustained a TBI may be vulnerable to persistent anxiety, panic attacks, specific phobias and depression, even 13 years after the injury event.

5.2. Introduction and background

The argument that childhood TBI can result in ongoing challenges and issues, which persist into adulthood, continues to be debated (Anderson et al., 2009; McKinlay et al., 2002). Some suggest that the plasticity of the young brain functions as a buffer against any ongoing effects of insult, while others describe an intrinsic vulnerability leading to ongoing problems following TBI (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005; Anderson, Spencer-Smith, et al., 2011), yet the distinct nature of how TBI affects the neurological structures of the brain is still not completely understood (Albicini & McKinlay, 2014). Compounding this debate is the finding that long-term behavioural, cognitive and emotional outcomes following childhood TBI are heterogeneous (Jonsson, Catroppa, Godfrey, Smedler, & Anderson, 2013), as is the brain damage that occurs as a result of diffuse injury (Albicini & McKinlay, 2014). Therefore, outcome studies investigating the long-term challenges faced by individuals following TBI report diverse findings, and assessment of these issues can be quite difficult.

Following TBI, a number of factors likely interact to influence the prognosis of recovery and outcomes following injury (Jonsson et al., 2013), including severity of TBI, age of injury, premorbid functioning, and psychosocial factors (Anderson et al., 2009). And what is known is that in the initial, acute stages of TBI recovery, children will experience a number of symptoms including inattention, learning and memory difficulties, fatigue, sleep disruption, social problems and slower information processing (Albicini & McKinlay, 2014; Anderson et al., 2005; Centers for Disease Control and Injury Prevention, 2006; Yeates et al., 2005). It has been suggested that acute problems faced by children with TBI will influence the acquisition of skills, such as social and academic skills, which is also accompanied by other factors as a result of the TBI including family stress and adjustment (Anderson, Brown, et al., 2011). This cascade of events is therefore likely to play some part in the development of long-term problems following childhood TBI, which may be evident even into adulthood.

The transition from childhood into adulthood comprises a number of biological, social and emotional changes (Rosema et al., 2015), and due to these changes, it is during this period that psychological and social impairments become more apparent (Angold, Costello, & Worthman, 1998; Susman et al., 1985). A model of psychosocial recovery after childhood TBI has been formulated (Anderson & Beauchamp, 2012; Beauchamp & Anderson, 2010), suggesting that adaptive social skills are developed as a result of normal brain maturation and development of cognition and behaviour within a secure environment. Moreover, a number of factors both internal and external to the child interact to influence behaviour and psychological well-being (Anderson & Beauchamp, 2012; Beauchamp & Anderson, 2010; Max et al., 2012). Therefore, a disruption to any part of this complex system is likely to result in negative outcomes for the child, which may be ongoing as they develop through life.

Research exploring outcomes following childhood TBI have reported on higher rates of social dysfunction (Yeates et al., 2004), behavioural issues (Hawley et al., 2004; Karver et al., 2012; McKinlay, 2014; McKinlay, Grace, Horwood, Fergusson, & MacFarlane, 2010; Schwartz et al., 2003), psychiatric disorders (Max, Friedman, et al., 2015; Max, Robin, et al., 1997), and neuropsychological deficits (Fay et al., 2009) up to five years following their injury event. While more severe TBI sustained in childhood tended to be related to poorer outcomes (Fay et al., 2009; Karver et al., 2012; Max, Robin, et al., 1997; Schwartz et al., 2003), mild TBI was also associated with ongoing issues in behavioural, attentional, executive, and psychiatric domains, with the most commonly reported predictors being family functioning, lower socioeconomic status (SES) and pre-injury functioning (Hawley et al., 2004; Karver et al., 2012; Max, Friedman, et al., 2015; Max, Robin, et al., 1997).

Looking into even longer-term outcomes following childhood TBI, approximately 10 years post-injury, much of the research has examined issues associated with quality of life, adaptive function, academic function, vocation, and neuropsychological and/or cognitive

functioning (Anderson et al., 2009; Anderson, Brown, et al., 2011; Jonsson et al., 2013), and general behavioural functioning such as the presence of internalising and externalising symptoms post-TBI (Rosema et al., 2014; Rosema et al., 2015), with little in the way of examining the rate of psychiatric and psychological disorders many years after TBI. One study explored rates of psychological disorders in adolescents aged 14-16 years who sustained a mild TBI in childhood, which either required inpatient or outpatient intervention (McKinlay et al., 2009). The authors indicated higher rates of ADHD, ODD, mood disorder and substance abuse in individuals with inpatient mild TBI.

Adult studies have also explored the long-term effects of TBI, one of which conducted a 30 year follow-up of individuals who sustained a TBI of any severity, finding increased psychiatric disorders (the majority being depression) with onset of disorders occurring after TBI (Koponen et al., 2002). In support of this, 66% of an adult sample of individuals who sustained a TBI of any severity seven years prior exhibited symptoms consistent with personality disorders including borderline personality disorder, avoidant personality disorder, paranoid personality disorder, narcissistic personality disorder and obsessive-compulsive personality disorder (Hibbard et al., 2000), and another sample presented with high rates of depression 14 years following severe TBI (Hoofien, Gilboa, Vakil, & Donovick, 2001).

While there is compelling evidence to inform that some individuals do go on to experience significant difficulties following childhood TBI, there remains to be weaknesses and gaps in the existing research. For instance, there is a lack of work which focusses on very long-term outcomes of childhood TBI, such as the exploration of outcomes more than five years post-injury, and many of the studies operate from the same cohort of participants. Those that have examined very long-term outcomes, 10 years or more post-injury, tended to utilise samples for which TBI occurred after 18 years of age. Additionally, outcomes are often based on parent-report of symptoms, which thereby may present issues regarding

subjectivity of answers. Moreover, longitudinal studies which have explored the longer-term consequences of TBI have examined neuropsychological functions including memory, language and intelligence; whereas there is extant literature on persisting anxiety, depression and other psychiatric disorders in child TBI cases. Finally, much of the existing work neglects to include individuals which have sustained a mild TBI in the study. As such, this chapter will explore long-term psychiatric outcomes, with a focus on anxiety disorders, in individuals with a history of TBI or OI, which occurred in childhood, based on medical records for indication of injury type and long-term follow-up assessing outcomes. The following was hypothesised:

1) Individuals with moderate-severe TBI will present with the highest number of psychiatric diagnoses, followed by those with mild TBI and then OI
2) Younger age at injury, female gender, and presence of internalising psychiatric symptomatology will significantly increase the risk of anxiety following TBI

5.3. Methods

5.3.1. Participants

Participants were recruited through an audit of hospital ED and admission records, and neurosurgical files. Additional recruitment was conducted by placing flyers within the community. General inclusion criteria included having a history of an injury (TBI or OI) during the ages 0-17 years which occurred at least five years prior to the study, and being 18 years or older. All participants spoke English. Sample groups were defined based on pre-existing criteria for TBI severity (Baalen et al., 2003; Borg et al., 2004; Centers for Disease Control and Injury Prevention, 2013).

Mild TBI

Inclusion criteria for individuals in the mild TBI group included: a) a medically confirmed diagnosis of mild TBI, b) LOC for less than 20 minutes, c) length of PTA less than one hour, d) GCS score of 13-15, e) stay in hospital no longer than 48 hours (due to injuries to the head only), and f) normal brain scan results.

Moderate-severe TBI

Individuals in the moderate-severe TBI were determined by the following inclusion criteria: a) a medically confirmed diagnosis of moderate or severe TBI, or b) skull fracture/evidence on brain scan, or c) cerebral haemorrhage, or d) PTA of more than 24 hours. Moderate TBI was specifically defined as a) GCS of 9-12 (or higher if there was evidence on brain scan results), and b) PTA of less than one week, and c) length of LOC less than six hours. For severe TBI, the criteria were set as a) GCS score of <9 points, and b) PTA of more than one week, and c) length of LOC more than six hours.

OI controls

Individuals in the OI group were also recruited through the ED admission and neurosurgical audits, and flyers placed in the community. They were defined as having experienced a fracture between the ages 0-17 years, more than five years prior to the study. Individuals were excluded if they had a history of TBI.

Final sample

The audit of hospital records, ED admissions and neurosurgical files resulted in an identification of 558 individuals fitting the above criteria. The total sample consisted of 95 males (*M*=22.78 years, *SD*=3.44 years) and 74 females (*M*=22.27 years, *SD*=3.09 years), aged between 18 and 31 years, resulting in a 32% response rate. Within the sample, there

were 65 with mild TBI (*M*=23.25 years, *SD*=3.58 years), 61 with moderate-severe TBI (*M*=22.34 years, *SD*=2.79 years) and 43 with OI (*M*=21.81 years, *SD*=3.36 years).

5.3.2. Procedure and materials

Ethical approval for the study was obtained from the Upper South New Zealand Regional Ethics Committee, and was part of a larger study which investigated long-term neuropsychological outcomes of childhood TBI. Participants were invited to attend a three hour assessment session at the University of Canterbury, which was conducted by a trained psychology post-doctoral fellow. To obtain information regarding age and gender, further information about the injury event, and associated symptomatology, a semi-structured interview was conducted. To obtain diagnostic information regarding psychiatric symptoms, components of the CIDI (World Health Organisation, 1990) were used in a structured interview format, to ask questions relating to a DSM-IV diagnosis of an anxiety disorder (GAD, panic attacks, PD, agoraphobia, social phobia, specific phobia, PTSD), depression, mania, and suicidal behaviours, as used in earlier studies (D. Fergusson et al., 2007, 2009). The CIDI reportedly has good to excellent Kappa coefficients for test-retest reliability and inter-rater reliability estimated based on validity studies (World Health Organisation, 1990).

5.3.3. Design

A between-subjects, cross-sectional study design was used, utilising retrospective and current data from participants. The independent variable was injury group (mild TBI, moderate-severe TBI, and OI). The dependent variables were outcomes identified from unstructured and structured interviews, including age, gender, time since injury, and psychiatric disorders.

5.3.4. Data analysis

Descriptive statistical analyses were conducted, utilising the split-file function organising data by group (mild TBI, moderate-severe TBI, OI), for background information including age, gender, time since injury, and age of treatment injury, and frequency analyses computed for psychiatric disorders. Chi-square MANOVA tests were conducted to examine any group differences among the participant characteristics. A new variable was computed by combining mild and moderate-severe TBI groups to a general TBI group, to compare background information and psychiatric disorders in the same manner. For outcome variables, psychiatric disorders were coded as 0=no and 1=yes, and an overall anxiety disorders variable was computed by combining 'yes' values for all anxiety-related disorders (GAD, Panic Attacks, PD, Agoraphobia, Social Phobia, Specific Phobia, PTSD). Finally, a variable was computed for multiple anxiety disorders, with 1=multiple disorders, and 0=none.

To analyse differences between participant groups on psychiatric disorders, a series of chi-square analyses were conducted, with rows set as participant group (1=mild TBI, 2=moderate-severe TBI, 3=OI) and columns set as psychiatric disorders (0=no, 1=yes) and multiple anxiety disorders. This was repeated for the combined TBI group variable (1=TBI, 0=no TBI). To examine predictors for having diagnosis of an anxiety disorder (any), a logistic regression was computed, with the dependent variable as overall anxiety disorders (0=no, 1=yes), and the independent variables as TBI group (1=TBI, 0=no TBI), age, gender, time since injury, and other psychiatric disorders. All data were analysed using SPSS version 22, and alpha levels were set to .05 for significance testing.

5.4. Results

5.4.1. Participant characteristics

Results of an analysis of descriptive statistics are outlined in Table 5.1. Injury characteristics of each participant group were compared for those with mild TBI, moderate-severe TBI, and OI, on variables including gender, years since injury and age when receiving injury treatment.

Table 5.1.

Injury Characteristics of Participants with Mild Traumatic Brain Injury, Moderate-Severe Traumatic Brain Injury and Orthopedic Injury

	Mild TBI	**Moderate-Severe TBI**	**Orthopedic Injury**
	***n* (%)**	***n* (%)**	***n* (%)**
Total	65 (38.50) *M*=23.25, *SD*=3.58	61 (36.10) *M*=22.34, *SD*=2.79	43 (25.40) *M*=21.81, *SD*=3.36
Gender			
Male	43 (66.20)	33 (54.10)	19 (44.20)
Female	22 (33.80)	28 (45.90)	24 (55.80)
Time Since Injury (years)	*M*=12.17, *SD*=5.31	*M*=15.13, *SD*=4.69	*M*=11.05, *SD*=4.69
Age of Injury Treatment (years)	*M*=10.86, *SD*=4.87	*M*=7.05, *SD*=4.03	*M*=10.47, *SD*=3.79

Note. *N*=169; TBI=traumatic brain injury.

A MANOVA was conducted to examine differences among the groups on participant demographics, which indicated no significant differences for age, $F(2, 166)=2.71$, $p=.07$, but highlighted a statistically significant difference for years since injury, $F(2, 166)=10.36$, $p<.01$, and age of injury treatment, $F(2, 166)=14.07$, $p<.01$. Post-hoc analyses revealed that more time had lapsed since their injury for the moderate-severe TBI group compared to those with OI and mild TBI, and that those with moderate-severe TBI were significantly younger than both groups when they first received injury treatment. A chi-square analysis further revealed no significant group differences for gender, $\chi^2(2)=5.25$, $p=.07$.

5.4.2. Psychiatric disorders among mild TBI, moderate-severe TBI and OI groups

Table 5.2. highlights the rates of psychiatric disorders, including specific anxiety disorders, overall anxiety disorders and comorbid anxiety disorders, according to each participant group.

Table 5.2.

Psychiatric Disorders among Participants with Mild Traumatic Brain Injury, Moderate-Severe Traumatic Brain Injury and Orthopedic Injury

	Mild TBI	**Moderate-Severe TBI**	**Orthopedic Injury**
	***n* (%)**	***n* (%)**	***n* (%)**
Depression	22 (33.80)	25 (41.0)	11 (25.60)
Mania	3 (4.60)	2 (3.30)	2 (4.70)
Suicide attempts	2 (3.10)	4 (6.60)	0
Generalised Anxiety	5 (7.70)	5 (8.20)	2 (4.70)
Panic Attacks	7 (10.80)	10 (16.40)	1 (2.30)
Panic Disorder	3 (4.60)	5 (8.20)	1 (2.30)
Agoraphobia	2 (3.10)	2 (3.30)	1 (2.30)
Social Phobia	3 (4.60)	5 (8.20)	1 (2.30)
Specific Phobia	4 (6.20)	7 (11.50)	1 (2.30)
Post-Traumatic Stress Disorder	1 (1.50)	2 (3.30)	1 (2.30)
Any Anxiety Disorder	12 (18.50)	16 (26.30)	3 (7.00)
Comorbid Anxiety	4 (6.20)	9 (14.80)	1 (2.30)

Note. N=169; TBI=traumatic brain injury

Comparison of anxiety disorders among participants with mild TBI, moderate-severe TBI and OI

To explore differences in rates of anxiety disorders and individuals with a history of mild TBI, moderate-severe TBI, and OI, a series of chi-square analyses were conducted. A significant difference for the grouping variable was found for any anxiety disorder,

$\chi^2(2)=6.81$, $p=0.03$, with the moderate-severe TBI exhibiting the highest rate of problems. There was also a significant difference between groups for comorbid anxiety disorders, $\chi^2(2)=6.12$, $p<0.05$, again with the moderate-severe TBI group presenting highest rates. There were no significant differences between the groups for GAD, $\chi^2(2)=0.62$, $p=.73$, panic attacks, $\chi^2(2)=5.6$, $p=.06$, PD, $\chi^2(2)=1.98$, $p=0.37$, agoraphobia, $\chi^2(2)=1.46$, $p=0.48$, social phobia, $\chi^2(2)=3.92$, $p=.14$, specific phobia, $\chi^2(2)=5.75$, $p=0.0.6$ or PTSD, $\chi^2(2)=1.66$, $p=.44$).

Comparison of other psychiatric disorders among participants with mild TBI, moderate-severe TBI and OI

Chi-square analyses were also conducted to compare participant groups on the rate of other psychiatric disorders. These indicated no significant differences for any of the psychiatric disorders between the three groups. That is, rates did not differ among those with mild TBI, moderate-severe TBI and OI for rates of suicide attempts, $\chi^2(2)=3.27$, $p=.20$, $\chi^2(2)=4.47$, $p=.11$, mania, $\chi^2(2)=0.14$, $p=.93$, or depression, $\chi^2(2)=5.89$, $p=.53$.

5.4.3. Outcomes for combined TBI (mild and moderate-severe TBI) and OI groups

As mentioned earlier, a new variable was computed by combining mild and moderate-severe TBI groups to a general TBI group. Injury characteristics for those with TBI and OI are outlined in Table 5.3.

As also conducted above, a comparison among rates of psychiatric disorders was conducted for participants with TBI and OI. Table 5.4 describes descriptive statistics for each of the groups.

Comparison of anxiety disorders among participants with TBI and OI

To explore rates of anxiety disorders for individuals with a history of TBI and OI, a series of chi-square analyses were conducted. A significant difference was found for having

Table 5.3.

Injury Characteristics of Participants within the Combined Traumatic Brain Injury Group and Orthopedic Injury Group

	TBI	**Orthopedic Injury**
	***n* (%)**	***n* (%)**
Total	126 (74.56) *M*=22.80, *SD*=5.22	43 (25.44) *M*=21.81, *SD*=3.36
Gender		
Male	76 (60.30)	19 (44.20)
Female	50 (39.70)	24 (55.80)
Time since injury (years)	*M*=13.60, *SD*=5.22	*M*=11.05, *SD*=4.69
Age of injury treatment (years)	*M*=9.02, *SD*=4.86	*M*=10.47, *SD*=3.79

Note. N=169; TBI=traumatic brain injury

Table 5.4.

Psychiatric Disorders among Participants with Traumatic Brain Injury and Orthopedic Injury

	TBI	**Orthopedic Injury**
	***n* (%)**	***n* (%)**
Depression	47 (37.30)	11 (25.60)
Mania	5 (4.00)	2 (4.70)
Suicide attempts	2 (1.60)	0
Generalised Anxiety	10 (7.90)	2 (4.70)
Panic Attacks	17 (13.50)	1 (2.30)
Panic Disorder	8 (6.30)	1 (2.30)
Agoraphobia	4 (3.20)	1 (2.30)
Social Phobia	8 (6.30)	1 (2.30)
Specific Phobia	11 (8.70)	1 (2.30)
Post-Traumatic Stress Disorder	3 (2.40)	1 (2.30)
Any Anxiety Disorder	28 (22.20)	3 (7.00)
Comorbid Anxiety	13 (10.30)	1 (2.30)

Note. N=169; TBI=traumatic brain injury.

any anxiety disorder, $\chi^2(1)=5.36$, $p=0.02$, with the TBI group presenting with more problems. There was also a significant difference between the groups for panic attacks, $\chi^2(1)=4.43$, $p=.04$, and specific phobia, $\chi^2(1)=4.17$, $p=.04$, again with the TBI group having higher rates for each. However, there were no significant difference among the groups for GAD, $\chi^2(1)=0.60$, $p=.44$, PD, $\chi^2(1)=1.11$, $p=.29$, agoraphobia, $\chi^2(1)=.45$, $p=.23$ or PTSD, $\chi^2(1)=1.08$, $p=.30$.

Comparison of other psychiatric disorders among participants with TBI and OI

Finally, the rates of other psychiatric disorders were compared for participants with TBI and OI using chi-square analyses. The results revealed a significant difference between groups for depression, $\chi^2(1)=3.98$, $p<.05$, with the TBI group presenting with higher rates. There were no significant differences found for mania, $\chi^2(1)=0.02$, $p=.90$ or suicide attempts, $\chi^2(1)=0.73$, $p=.39$.

5.4.4. Prediction analysis for having any anxiety diagnosis

To determine the impact of TBI, participant characteristics and other psychiatric disorders on the likelihood that participants have any anxiety diagnosis, a logistic regression was computed. The outcome variable was any anxiety diagnosis (yes or no), and the predictors were age, gender, group (TBI or OI), depression, mania, and suicide attempts. The full model containing all predictors was statistically significant, $\chi^2(7)=41.84$, $p<.001$, indicating the model was able to distinguish between individuals with any anxiety disorder and those without. The model as a whole explained between 23% (Cox and Snell R Square) and 37% (Nagelkerke R Square) of the variance in any anxiety disorder diagnosis, and correctly classified 81.4% of cases. Table 5.5 represents logistic regression parameters for predicting group membership to either having any anxiety disorder or no anxiety disorder.

Table 5.5.

Logistic Regression Predicting the Likelihood of Any Anxiety Disorder

Variable	*B*(S.E.)	Wald	df	Odds Ratio	95.0% C.I	
					Upper	Lower
Group	1.57* (0.74)	4.43	1	4.78	20.54	1.11
Age	0.01 (0.08)	0.02	1	1.01	1.19	0.86
Gender	1.48** (0.52)	8.15	1	4.39	12.10	1.59
Years post-injury	0.06 (0.05)	1.29	1	1.06	1.17	0.96
Depression	0.04 (0.68)	0.00	1	1.04	3.90	0.28
Mania	22.34 (4.97)	0.00	1	0	0	0
Suicide attempts	0.59 (2.15)	0.08	1	1.81	121.96	0.03

Note. *=p<.05, **= p<.01, S.E.= standard error, C.I= confidence interval.

Table 5.5 demonstrates that a significant predictor of having an anxiety disorder is participant group, and it is indicated that participant group membership raises the likelihood of having any anxiety disorder by almost five times. Moreover, gender also made a significant contribution to the variance in the model, such that it increases the likelihood of having any anxiety disorder by more than four times. Frequency analysis of rates of any anxiety disorder according to gender revealed that 31.5% of females reported any anxiety disorder versus 8.4% of males.

5.5. Discussion

This chapter sought to explore long-term psychiatric outcomes, with a focus on anxiety disorders, in individuals with a history of childhood TBI or OI, based on medical records for indication of injury type and long-term follow-up assessing outcomes. It was found that when comparing individuals with mild TBI, moderate-severe TBI and OI, individuals with moderate-severe TBI exhibited higher rates of any anxiety disorder, and

comorbid anxiety disorders. When the two groups with TBI were combined, it was found that individuals with TBI presented with higher rates of any anxiety disorder, panic attacks, specific phobia, and depression. Significant predictors for having any anxiety disorder included having a TBI and being female.

These findings are consistent with previous findings that have reported ongoing, long-term difficulties following childhood TBI (McKinlay et al., 2009; McKinlay, Grace, et al., 2010; Rosema et al., 2015). While there are few studies that have examined the presence of long-term psychiatric disorders following childhood TBI, other longitudinal outcome studies are in support of these findings. One study reported that individuals with childhood mild TBI were found to present with higher rates of internalising symptomatology even 10 years post-injury (Rosema et al., 2015), and another indicated long-term deficits in emotion perception for individuals who had sustained a childhood TBI 10-years prior (Ryan, Anderson, et al., 2014).

Given that TBI, of even mild severity, involves actual structural damage to the brain which can be either focal or diffuse (Albicini & McKinlay, 2014, 2015; Levine et al., 2008; Povlishock & Katz, 2005), a potential explaining factor for the higher rates of anxiety disorders and depression among those with TBI is due to the impacted neurobiological regions at the TOI. It has been suggested that the 'social brain' consists of the temporal pole, medial prefrontal cortex, OFC, amygdala, tempoparietal junction and inferior parietal cortex (Ryan, Anderson, et al., 2014), areas of which appear to be implicated in both TBI and anxiety disorders (Albicini & McKinlay, 2015). Moreover, the 'social brain' is purportedly responsible for functions such as emotion perception and affect recognition (Ryan, Anderson, et al., 2014), which are hypothesised to play a role in the vulnerability of developing anxiety disorders (Cisler & Olatunji, 2012; Cisler, Olatunji, Feldner, & Forsyth, 2010). Therefore, it may be that direct impact to these areas of the young and developing brain, and particularly

areas responsible for affect regulation (Max et al., 2011) such as the OFC, hippocampus, thalamus, temporal regions, amygdala and frontal gyri (Grados et al., 2008; Herskovits et al., 2002; Mather et al., 2003), results in ongoing mood and anxiety problems.

However, most children with mild, moderate and even severe TBI will go on to make a full recovery without experiencing ongoing psychiatric difficulties, so there is clearly other moderating factors associated with these long-term outcomes that go beyond neurological insult. What is known in the literature is that a number of factors serve to increase the likelihood that an individual will go on to experience problems after TBI, including the quality of the child's environment such as SES, parental warmth and parental mental health (Max, Robin, et al., 1997; Ryan, Anderson, et al., 2014). Studies exploring acute outcomes of TBI in children and adolescents have found that among the most common predictors of anxiety disorders are TBI severity, younger age of injury, and female gender (Luis & Mittenberg, 2002; Max et al., 2011). In this study, being female significantly predicted the likelihood of having an anxiety disorder, and the moderate-severe TBI group were the youngest at age of injury and presented with the highest rate of anxiety-related problems. This is unsurprising given that even in non-TBI samples, females tend to report higher rates of anxiety than males, with anxiety being over 1.5 times more common for females than males (McClean et al., 2011), affecting approximately one in three women in their lifetime (Beyond Blue, 2016). Gender differences in the development of anxiety disorders have been attributed to neurochemical and hormonal differences (Nishizawa et al., 1997; Seeman, 1997), and factors associated with genetics, personality and internal locus of control (Feingold, 1994; Lewinsohn et al., 1998).

A limitation of the study is that premorbid functioning was not assessed due to the nature of the longitudinal research design. As such, it was not possible to account for pre-existing behavioural, emotional, cognitive and psychological issues that may have been

apparent before the injury, which are noted to predict future ongoing psychiatric disorders after TBI (Max, Friedman, et al., 2015; Max, Robin, et al., 1997). Moreover, years of education was not examined among the participant groups, which may be a significant factor in participation of the study. In addition, diagnosis of psychiatric disorders, although was obtained through structured interview, was reliant on self-reported symptomatology. It may have been useful to obtain informant reports to corroborate participant's difficulties to ensure validity. Further, the methodology of recruitment resulted in a relatively low response rate (32%), and it was not possible to examine whether there were any differences between individuals who participated and those who declined. It may be likely that the individuals who participated in the study differed in terms of their injury characteristics or psychiatric outcomes. Finally, due to the response rate, the sample size was comparatively small, particularly considering the number of comparisons conducted in the analyses.

Strengths of the study include it being a longitudinal design whereby individuals with TBI were followed many years after their injury, considering the lack and underrepresentation of long-term follow-ups of psychiatric disorders (particularly anxiety) in childhood TBI within the literature. Moreover, participants were recruited from hospital admissions which would increase the validity of identification of TBI (as opposed to self-reported TBI, see McKinlay and Horwood (2016)). In addition, structured interviews were utilised, as per DSM criteria, to identify psychiatric disorders and therefore the study was not reliant on parent report of symptoms, which in the past have been considered unreliable in describing internalising difficulties of children and adolescents (Luis & Mittenberg, 2002; Rosema et al., 2014). Finally, the inclusion of an OI comparison group allowed some control over factors attributed to the experience of an early injury (e.g. family stress, adjustment, hospitalisation, missed school) that may have otherwise influenced results.

Considering the above, future directions for work in this area should involve a replication of a similar, longitudinal outcome study tracking psychiatric disorders, particularly anxiety considering the results of the present study, after childhood TBI (>10 years). In combination, brain imaging techniques would also be useful to identify the affected brain regions associated with post-injury anxiety disorders, in addition to the collection of pre-injury information to decipher predictors and risk factors for this group. This information put together could allow for the implementation of intervention programs targeted at children and adolescents, or parenting groups, to assist those at risk of developing ongoing anxiety and other psychiatric disorders following TBI.

In conclusion, this study highlights that children who have sustained a TBI of mild or moderate-severe severity may be vulnerable to ongoing symptoms of anxiety, panic attacks, specific phobias and depression, which can persist even 13 years after the injury event. Moreover, children who are female and have more severe TBI are at greater risk, and as such, early intervention for these individuals may be important to help lessen the burden associated with such an injury.

CHAPTER SIX: PREDICTORS OF LONG-TERM ANXIETY FOLLOWING CHILDHOOD TBI: THEORETICAL PERSPECTIVES

In the previous chapter, the research focus was the long-term psychological issues that adults who had sustained a childhood TBI many years prior may continue to face long after their injury. Specifically, anxiety disorders were present in higher rates for individuals with a history of mild and moderate-severe TBI. Further, participant characteristics were examined to determine whether they could predict the presence of anxiety after childhood TBI, and as such found that as well as having a history of TBI, being female also significantly increased the risk of having an anxiety disorder. This chapter extends on the previous chapter, seeking to examine additional factors that may predict anxiety disorders following TBI. This chapter was prepared for submission as a manuscript, submitted to The Journal of Head Trauma Rehabilitation, and is currently under review (see Appendix F for pdf proofs).

6.1. Abstract

Background and objectives: The manifestation and risk factors of anxiety in individuals with childhood TBI are not well understood. This study sought to explore the predictors associated with anxiety disorders after childhood TBI in an adult sample.

Methods: Longitudinal, between-subjects, cross-sectional design with retrospective and current data. Information about TBI was retrieved from hospital ED and medical records. The CIDI assessed anxiety disorders according to DSM-IV criteria. Neuropsychological assessments were conducted to obtain information about cognitive functioning, and the FrSBe examined frontal lobe functions (apathy, executive dysfunction, and disinhibition).

Participants: There were 95 males (*M*=22.78 years, *SD*=3.44 years) and 74 females (*M*=22.27 years, *SD*=3.09 years), 65 with mild TBI (*M*=23.25 years, *SD*=3.58 years), 61 with moderate-severe TBI (*M*=22.34 years, *SD*=2.79 years) and 43 with OI (*M*=21.81 years, *SD*=3.36 years).

Results: The TBI groups performed significantly worse for memory $F(2)=4.73$, $p=.01$ and attention $F(2)=4.79$, $p=.01$. Individuals with mild TBI had higher scores on executive dysfunction ($p=.004$) and total frontal lobe functioning ($p=.02$) than the OI group. A logistic regression revealed that significant predictors for anxiety disorders were severity of TBI, gender, apathy, disinhibition, executive dysfunction and overall frontal lobe abilities.

Conclusions: Moderate-severe TBI, female gender, and poorer frontal lobe functioning increased the risk of anxiety disorders following childhood TBI. Increased apathy, being disinhibited and having poorer executive functioning appeared to be protective of anxiety. However, these factors in combination serve to increase the likelihood of meeting diagnostic criteria for an anxiety disorder post-TBI.

6.2. Introduction and background

A handful of research studies have identified that children and adolescents recruited from hospital ED admissions and community-based samples have higher parent-report and assessment-based rates of anxiety disorders following mild to severe TBI (Gerring et al., 2002; Grados et al., 2008; Herskovits et al., 2002; Levi et al., 1999; Liu & Li, 2013; Luis & Mittenberg, 2002; Max et al., 1998). More specifically, these individuals tend to present with higher rates of PTSD (Herskovits et al., 2002; Mather et al., 2003; Max et al., 1998), OCD (Grados et al., 2008), and other anxiety disorders such as GAD, SAD, phobias and panic (Liu & Li, 2013; Luis & Mittenberg, 2002; Max et al., 2011; Max, Lopez, et al., 2015; Vasa et al., 2002). However, a limitation within the research is that studies have utilised the same samples of participants, which restricts the generalisability of results and lends to a lack of research which identifies strong predictors of anxiety after TBI. Thus far, the following predictors have been highlighted.

6.2.1. Predictors of anxiety disorders following TBI in children and adolescents

The disrupted neurobiology of the brain has a role in the development of anxiety after TBI, with particular focus on frontal areas involving the OFC and right medial frontal gyri, and also the temporal gyri (Albicini & McKinlay, 2015; Grados et al., 2008; Max et al., 2011; Vasa et al., 2004), however the damage is heterogeneous and no single brain structure can be identified as the cause of poor outcome (Albicini & McKinlay, 2015). Younger age at injury (Levi et al., 1999; McClean et al., 2011; Vasa et al., 2002) and being female (Gerring et al., 2002; Grados et al., 2008) have also been identified as biological factors which increase the risk.

Psychological functioning after TBI is also linked with ongoing anxiety disorders, including the presence of general internalising disorders, depression and personality change (Gerring et al., 2002; Grados et al., 2008; Max et al., 1998; Max et al., 2011). With regards to cognitive functioning, areas noted to be impaired or associated with anxiety after TBI include processing speed, memory and executive function even ten years post-injury (Ponsford, Draper, & Schonberger, 2008), and in the shorter-term, anxiety has been associated with poor attention, slowed information processing and executive dysfunction in adults (Barker-Collo et al., 2015; Gould, Ponsford, & Spitz, 2014).

Premorbid psychosocial adversity, which refers to single-parent households, exposure to parental aggression, and having parents with mental health or criminal problems (Gerring et al., 2002; Grados et al., 2008; Herskovits et al., 2002; Vasa et al., 2002; Vasa et al., 2004), is also linked with higher rates of anxiety after TBI. Moreover, those with social disadvantage or lower family status and parents with lower levels of completed education may also be vulnerable to experiencing anxiety disorders after childhood TBI (Gerring et al., 2002; Levi et al., 1999; Luis & Mittenberg, 2002).

As such, the presence of certain psychological and contextual factors, in combination with the biological damage suffered to the brain at a young age, operate together to help explain why certain young people with TBI may go on to experience anxiety after their injury. However, as mentioned above, the existing research is based on a small number of participant samples, decreasing the generalisability of results. In addition, the identified predictors appear to vary greatly dependent on the sample. As such, there is a lack of a general theoretical basis for why some individuals go on to experience anxiety after TBI, while the majority do not. To explore this, it is important to consider the existing theories for anxiety disorders in general. For instance, in terms of a biopsychosocial model of the development of anxiety, theories have identified risk factors for the development and maintenance of anxiety, and authors postulate that these factors create 'vulnerabilities' towards the development of anxiety (Barlow, 2000; Bouton, Mineka, & Barlow, 2001). All theories are outside the scope of this chapter, but briefly, biological, social and psychological factors will be discussed as they will inform the nature of the exploratory analyses.

6.2.2. Factors associated with the development of anxiety disorders

Biologically speaking, a family history of anxiety is known to increase the risk of a child developing some form of anxiety later in life (Moffitt et al., 2007). Attachment styles have also been identified as important, such as having an anxious or ambivalent style of attachment in infancy (Schimmenti & Bifulco, 2013). Biological aspects inherent to the individual also increase the risk, including being female (Barlow, 2000), having negative affect, behavioural inhibition, neuroticism and anxiety sensitivity traits, which tend to have a strong genetic component (Clark, Watson, & Mineka, 1994). Moreover, biological structures of the brain which have been linked to anxiety disorders and symptomatology include parts of the frontal lobes (prefrontal cortex, OFC, frontal gyri), amygdala, and temporo-parietal

regions (Albicini & McKinlay, 2015; Cisler & Olatunji, 2012; Cisler et al., 2010; Ryan, Anderson, et al., 2014).

Considering anxiety is an inherent, anticipatory emotional state (Bouton et al., 2001), a disruption to emotional regulatory systems is likely to increase one's propensity to have heightened anxiety (Mennin, Heimberg, & Fresco, 2002). Others discuss anxiety, particularly when considering PD and specific phobias, as a learned response which results from an initially neutral stimulus becoming a feared stimulus (Bouton et al., 2001). Cognition also appears to be a factor associated with anxiety disorders. Cognitive factors include the way individuals with anxiety process incoming information (Beck & Clark, 1997). Other cognitive factors involve avoidance (Behar, DiMarco, Hekler, Mohlman, & Staples, 2009), intolerance of uncertainty (Ladouceur, Gosselin, & Dugas, 2000), and positive or negative beliefs about worry (Barlow, 2000; Beck & Clark, 1997; Behar et al., 2009; Ladouceur et al., 2000). In terms of general cognitive functioning, childhood intellectual functioning has been associated with the risk of anxiety disorders later in life (Castaneda et al., 2011; Koenen et al., 2009), while subjective complaints of cognitive problems in individuals with anxiety is also noted (Castaneda et al., 2011; Moritz, Kuelz, Jacobsen, Kloss, & Fricke, 2006).

Collectively, the above factors are proposed to interact and contribute to an increase in an individual's risk of developing anxiety (Bouton et al., 2001). However, as discussed above, theoretical models for why some individuals go on to develop anxiety disorders after TBI has been an area of research which has received little interest. As such, the purpose of this chapter is to explore predictors in reference to cognitive factors, factors linked to frontal lobe functioning, and factors including gender, age of injury, and injury severity, which may contribute to an increased risk of developing long-term anxiety disorders in adults with a history of childhood mild and moderate-severe TBI. It was hypothesised that female gender, younger age of injury, and more severe TBI would predict an increased risk of anxiety

disorders. Further, it was hypothesised that cognitive functioning, including attention, processing speed, memory, visuospatial functioning, and frontal lobe functions including apathy, disinhibition and executive dysfunction, would also contribute to the risk of anxiety after childhood TBI.

6.3. Methods

6.3.1. Participants

Participants were recruited through an audit of hospital ED and admission records, neurosurgical files, and flyers within the community. General inclusion criteria included being injured when aged 0-17 years but at least five years prior to the study (TBI or OI), and being 18 years or older. All participants spoke English. Sample groups were defined based on pre-existing criteria for mild, moderate and severe TBI (Baalen et al., 2003; Borg et al., 2004; Centers for Disease Control and Injury Prevention, 2006, 2013).

TBI groups

Inclusion criteria for mild TBI included having: a) a medically confirmed diagnosis of mild TBI, b) LOC for less than 20 minutes, c) length of PTA less than one hour, d) GCS score of 13-15, e) stay in hospital no longer than 48 hours (due to injuries to the head only), and f) normal brain scan results. Individuals with moderate-severe TBI were those with: a) a medically confirmed diagnosis of moderate or severe TBI, or b) skull fracture/evidence on brain scans, or c) cerebral haemorrhage, or d) PTA of more than 24 hours. Moderate TBI was specifically defined as: a) GCS of 9-12 (or higher if there was evidence on brain scans), b) PTA of less than one week, and c) length of LOC less than six hours. For severe TBI, the criteria were set as a) GCS of less than 9, b) PTA of more than one week, and c) length of LOC more than six hours.

OI controls

Individuals in the OI group were defined as having experienced a fracture between the ages 0-17 years, more than five years prior to the study. Individuals were excluded if they had a history of TBI.

Final sample

The audit of hospital records, ED admissions and neurosurgical files resulted in an identification of 558 individuals fitting the above criteria, with 169 individuals participating in the study. The total sample consisted of 95 males (*M*=22.78 years, *SD*=3.44 years) and 74 females (*M*=22.27 years, *SD*=3.09 years), aged between 18 and 31 years, resulting in a 32% response rate. Within the sample, there were 65 with mild TBI (*M*=23.25 years, *SD*=3.58 years), 61 with moderate-severe TBI (*M*=22.34 years, *SD*=2.79 years) and 43 with OI (*M*=21.81 years, *SD*=3.36 years).

6.3.2. Procedure and materials

Ethical approval for the study was obtained from the Upper South New Zealand Regional Ethics Committee, and was part of a larger study which investigated long-term neuropsychological outcomes of childhood TBI. Methods are also outlined elsewhere in chapter five of the thesis. Participants attended a three hour assessment session at the University of Canterbury conducted by a trained psychology post-doctoral research fellow. Age and gender, information about the injury event, and associated symptomatology, were retrieved via a semi-structured interview.

Psychiatric symptoms and diagnoses

To obtain diagnostic information regarding psychiatric symptoms, components of the CIDI (World Health Organisation, 1990) were used to ask questions relating to a DSM-IV

diagnosis of an anxiety disorder (GAD, panic attacks, PD, agoraphobia, social phobia, specific phobia, PTSD), depression, mania, and suicidal behaviours. For the purpose of this study, anxiety disorders were of focus. This method of interview has been previously used and validated in earlier studies (D. Fergusson et al., 2007, 2009), and has been reported to hold good to excellent Kappa coefficients for test-retest and inter-rater reliability studies (World Health Organisation, 1990).

Cognitive functioning

Memory function was examined using the WMS-III PA age adjusted scores (Wechsler, 1997), and the ROF memory trials (Lezak, 1995). In WMS-III PA, a list of unrelated word pairs was read, and participants were to provide the corresponding word when prompted with the first word. The WMS-III PA scores were derived from the sum of correct responses, with higher scores indicating better recall. In the ROF memory trials, participants were shown a figure, and asked to recall and draw the figure after a three- and 30-minute delay. The ROF scores were based on correctly remembered elements, with a maximum score of 36.

Visuospatial ability was measured using the WASI-MR age adjusted scores (Wechsler, 1999), JLOT (Benton et al., 1994), and ROF copy task (Lezak, 1995). Participants chose a response from options that would complete the matrix or series (WASI-MR), matched lines appropriately in accordance with position and direction (JLOT), and copied a complex figure (ROF copy). The tests were scored based on accuracy, and final scores were derived from the total number of correct responses.

Attention was assessed using the DCRS (Daneman & Carpenter, 1980) and the DOT-A (Werheid et al., 2002). In DOT-A, participants recalled sequences of numbers in ascending order, with the maximum number of digits recalled in the appropriate order giving the final score. In DCRS, participants were presented with three trials of sets of sentences that were

characterised with increasing difficulty. They read the sentences aloud, judged the veracity of the content, and recalled each sentence's last word. Trials were discontinued when the participants were unable to recall all sentences in a set, with scores derived from the number of recalled words.

Processing speed was assessed using scores from the D-KEFS verbal fluency and Stroop subtests – age adjusted (Delis et al., 2001). Participants were to produce words that start with letters F, A, and S within 60 seconds per letter, with the number of generated words creating the verbal fluency score. For the Stroop subtests, participants named the color patch, read the word, and identify the color in which the word is printed as quickly as possible. The correct responses provided a final score for each Stroop subtest.

Frontal lobe functioning

To assess behaviours associated with frontal lobe functioning, the FrSBe was utilised, in a self-report format (Grace & Malloy, 2001). The measure is a brief and validated tool in assessing behavioural aspects associated with frontal lobe functioning, including apathy, executive functioning and behavioural disinhibition. The FrSBe contains 46 self-report items, which are rated on a five point Likert scale, with 14 items pertaining to the Apathy subscale, 15 items for the Disinhibition subscale and 17 items pertaining to Executive Dysfunction (Carvalho et al., 2013; Grace & Malloy, 2001). Raw scores were transformed to *T*-scores for assessment of dysfunction comparative to norms, including norms associated with individuals with TBI (Grace & Malloy, 2001). Higher *T*-scores indicate more difficulties, with a cut-off of $T>50$ suggesting clinical concerns. The FrSBe has demonstrated good reliability, large-scale norms, and is effective in discriminating between frontal and non-frontal lesioned patients (Malloy & Grace, 2005).

6.3.3. Design

A between-subjects, cross-sectional study design was used, utilising retrospective and current data from participants. The dependent variable was having a diagnosis of an anxiety disorder (GAD, panic attacks, PD, agoraphobia, social phobia, specific phobia, PTSD). The independent variables or predictors were outcomes identified from unstructured and structured interviews, including age, gender, time since injury, cognitive outcomes (memory, visuospatial functioning, processing speed, attention), and frontal lobe functioning (executive dysfunction, disinhibition, apathy).

6.3.4. Data analysis

For each of the cognitive domains described above, standardised *z*-scores were computed for individual test scores, and the standardised individual test *z*-scores were combined to form the composite scores of each domain. *T*-scores were derived from total raw scores for the subscales of the FrSBe (Apathy, Disinhibition, Executive Dysfunction), and for overall scores on the measure. Descriptive statistical analyses were conducted to obtain a frequency distribution of participant characteristics between the groups, utilising a split-file function for organisation of data by group (mild TBI, moderate-severe TBI group, OI group/anxiety, no anxiety). This was computed for the variables of age, gender, age at injury treatment, years since injury, cognitive performance, and frontal lobe functioning. The variable “anxiety disorders“ refers to individuals with a diagnosis of GAD, panic attacks, PD, agoraphobia, social phobia, specific phobia, PTSD. Chi-square analyses and MANOVA tests were conducted to examine differences between groups for demographics (age, gender, age at injury treatment, years since injury), anxiety disorders, cognitive performance, and frontal lobe functioning. A logistic regression analysis was also computed to assess significance of

predictors for anxiety disorders following childhood TBI. All data were analysed using IBM SPSS version 24, and α levels were set to .05 for significance testing.

6.4. Results

6.4.1. Participant group characteristics

Table 6.1 displays group characteristics for the mild TBI, moderate-severe TBI and OI groups, for age, gender, age of injury treatment, years since injury, and anxiety disorders. Characteristics were also compared across each of the groups utilising MANOVA and chi-square analyses to examine any statistically significant differences between the groups.

Table 6.1.

Characteristics for Individuals in the Mild Traumatic Brain Injury, Moderate-Severe Traumatic Brain Injury and Orthopedic Injury Participant Groups

	Mild TBI	**Moderate-Severe TBI**	**Orthopedic Injury**
	***n* (%)**	***n* (%)**	***n* (%)**
Total	65 (38.50) *M*=23.25, *SD*=3.58	61 (36.10) *M*=22.34, *SD*=2.79	43 (25.40) *M*=21.81, *SD*=3.36
Gender			
Male	43 (66.20)	33 (54.10)	19 (44.20)
Female	22 (33.80)	28 (45.90)	24 (55.80)
Time since injury (years)	*M*=12.17, *SD*=5.31	*M*=15.13, *SD*=4.69	*M*=11.05, *SD*=4.69
Age when treated (years)	*M*=10.86, *SD*=4.87	*M*=7.05, *SD*=4.03	*M*=10.47, *SD*=3.79
Anxiety disorders	12 (19.40)	16 (26.20)	3 (7.0)
Female	9 (13.80)	12 (19.70)	2 (4.60)
Male	3 (4.60)	4 (6.60)	1 (2.30)

Note. *N*=169; TBI=traumatic brain injury.

A MANOVA revealed no significant differences between the three groups for age, $F(2, 166)=2.71$, $p=.07$. There was a statistically significant difference however for time since injury $F(2, 166)=10.36$, $p<.01$, and age when treated for the injury, $F(2, 166)=14.07$, $p<.01$.

Post-hoc analyses revealed that the moderate-severe TBI group were significantly younger when they both sustained their injury and when treated for their injury, as compared to those with OI and mild TBI. Chi-square analyses revealed no significant group differences for gender, $\chi^2(2)=5.25$, $p=.07$, but identified a statistically significant difference between the groups for anxiety disorders, $\chi^2(2)=6.81$, $p=.03$, with the moderate-severe TBI group presenting with highest rates. Further analyses revealed that 23 females (31.5% of all females, 13.61% overall) in the overall sample had an anxiety disorder diagnosis, versus 8 males (9.1% of males, 5.3% overall), and for those with anxiety disorders, females presented with the highest rates within each injury group. A chi-square analysis revealed that the gender difference in this study is statistically significant $\chi^2(1)=12.90$, $p<.0001$.

6.4.2. Cognitive performance and frontal lobe functioning

Group means for individuals with mild TBI, moderate-severe TBI and OI, and also for individuals with and without anxiety disorders (irrespective of injury), for each of the cognitive domains examined (memory, visuospatial functioning, processing speed, and attention) and frontal lobe functioning (executive dysfunction, disinhibition, apathy) are outlined in Table 6.2. A MANOVA was also conducted to explore differences in cognitive performance and frontal lobe functioning across the TBI and OI groups, and also between individuals with and without an anxiety disorder.

A MANOVA revealed that significant differences in cognitive performance across the TBI and OI groups existed for memory $F(2)=4.73$, $p=.01$ and attention $F(2)=4.79$, $p=.01$. Post-hoc analyses utilising Bonferroni tests revealed that the mild TBI performed significantly worse than the OI group, and also that the moderate-severe TBI group performed worse than the OI group, on both cognitive domains (with $p<.01$).

Table 6.2.

Means for Cognitive Performance and Frontal Lobe Functioning among Participant Groups

	Mild TBI	Moderate-Severe TBI	Orthopedic Injury
	***M* (SD)**	***M* (SD)**	***M* (SD)**
Cognitive Domain			
Memory	-0.19 (0.87)	-0.06 (0.62)	0.39 (0.52)
Visuospatial Functioning	-0.20 (0.96)	-0.06 (0.53)	0.18 (0.58)
Processing Speed	-0.13 (0.93)	-0.05 (0.77)	0.13 (0.77)
Attention	-0.27 (0.79)	-0.07 (0.77)	0.44 (0.80)
	Mild TBI	**Moderate-Severe TBI**	**Orthopedic Injury**
	***M* (SD)**	***M* (SD)**	***M* (SD)**
Frontal Lobe Domain			
Apathy	59.70 (15.56)	59.49 (13.80)	55.84 (10.56)
Disinhibition	60.26 (15.33)	63.15 (14.22)	55.77 (8.79)
Executive Dysfunction	66.23 (16.99)	62.98 (15.07)	56.74 (12.36)
Total	65.32 (17.45)	64.07 (14.97)	57.07 (10.69)
	Anxiety	**No Anxiety**	
	***M* (SD)**	***M* (SD)**	
Cognitive Domain			
Memory	-0.11 (0.83)	0.08 (0.69)	
Visuospatial Functioning	0.11 (0.64)	0.04 (0.73)	
Processing Speed	-0.12 (0.71)	0.06 (0.78)	
Attention	0.001 (0.72)	0.07 (0.82)	
	Anxiety	**No Anxiety**	
	***M* (SD)**	***M* (SD)**	
Frontal Lobe Domain			
Apathy	59.53 (10.89)	58.12 (14.21)	
Disinhibition	62.90 (16.28)	58.99 (12.50)	
Executive Dysfunction	63.62 (14.87)	61.82 (15.54)	
Total	64.72 (14.92)	61.67 (14.96)	

Note. TBI=traumatic brain injury.

No significant differences were found for cognitive performance between individuals with or without an anxiety disorder, with all *p* values >.05. For the frontal lobe domains of function,

a MANOVA revealed no significant differences in behavioural functioning amongst individuals with mild TBI, moderate-severe TBI or OI, or between individuals with or without an anxiety disorder, with all *p* values >.05. However, post-hoc analyses revealed a significant difference between individuals with OI and mild TBI on executive dysfunction (p=.004) and total frontal lobe functioning (p=.02), with mild TBI presenting with higher *T*-scores.

6.4.3. Regression analysis for predicting anxiety disorders

A binary logistic regression analysis was computed to determine the impact of TBI, participant characteristics, and cognitive and frontal lobe functioning on the likelihood of participants having an anxiety disorder. The outcome variable was anxiety disorder (yes/no), and predictors were group (mild TBI, moderate-severe TBI, OI), gender, age, age of injury treatment, years since injury, apathy, disinhibition, executive dysfunction, overall frontal lobe functioning, memory, visuospatial functioning, attention and processing speed. The full model containing all predictors was statistically significant, $\chi^2(14)=44.68$, $p<.001$, indicating that it was able to distinguish between individuals with and without an anxiety disorder diagnosis. Using Cox & Snell and Nagelkerke R Square estimates indicated that between 26% and 42% of the variance in anxiety disorder diagnoses is explained by the model and it was able to correctly classify 83.7% of cases. Table 6.3 represents parameters of the logistic regression for predicting group membership for having an anxiety disorder diagnosis or no anxiety.

As displayed in Table 6.3, Group(1) was a significant positive predictor in the model, indicating that with increasing severity of TBI there is an increased likelihood of having an anxiety disorder, with the odds being almost 6 times for moderate-severe TBI compared to that of the OI group. Gender also significantly predicted having an anxiety disorder,

Table 6.3.

Logistic Regression Parameters for Predicting Anxiety Disorder Diagnosis

Variable	*B*(S.E.)	Wald	df	Odds Ratio	95.0% C.I	
					Upper	Lower
Group		4.65	2			
Group(1)	1.76 (0.86)*	4.27	1	5.90	31.78	1.10
Group(2)	1.69 (0.88)	3.69	1	5.43	30.52	0.97
Gender(1)	3.11 (0.74)**	17.76	1	0.05	0.19	0.01
Age	0.05 (0.19)	0.07	1	1.05	1.52	0.72
Age treated	0.06 (0.20)	0.09	1	1.06	1.57	0.72
Years since injury	0.17 (0.19)	0.77	1	1.18	1.71	0.82
Apathy	-0.26 (0.08)**	10.35	1	0.78	0.91	0.67
Disinhibition	-0.20 (0.07)**	8.27	1	0.82	0.94	0.71
Executive Dysfunction	-0.20 (0.08)*	6.45	1	0.82	0.96	0.70
Total FrSBe	0.56 (0.18)**	9.61	1	1.76	2.51	1.23
Memory	-0.23 (0.47)	0.24	1	0.80	1.98	0.32
Visuospatial Function	0.60 (0.56)	1.17	1	1.82	5.41	0.61
Attention	0.06 (0.43)	0.02	1	1.06	0.50	2.43
Processing Speed	-0.12 (0.40)	0.09	1	0.89	1.95	0.41

Note. TBI=traumatic brain injury; *=p<.05, **= p<.01, S.E.= standard error, C.I= confidence interval.

with a negative association, meaning that being male significantly decreases the likelihood of having anxiety by 0.05 times compared to that of females. In terms of frontal lobe functioning, apathy, disinhibition, and executive dysfunction also significantly contributed to the model with negative relationships with having an anxiety disorder, whereby having increased apathy, executive dysfunction and disinhibition decreases the likelihood of having an anxiety disorder by 0.78-0.82 times. Alternatively, overall frontal lobe functioning was a significant positive predictor in the model, and increased the likelihood of having an anxiety disorder by 1.76 times. The remainder of the variables in the model were not significant predictors for having an anxiety disorder.

6.5. Discussion

In this sample, individuals with a history of childhood mild and moderate-severe TBI had higher rates of anxiety disorders compared to individuals with a history of OI. A higher number of females had a diagnosis of anxiety both between and within participant groups. Moreover, individuals with mild TBI and moderate-severe TBI had significantly poorer attention and memory than the OI group, and the mild TBI group had significantly worse executive dysfunction and poorer overall frontal lobe abilities than the OI group. In keeping with the hypotheses, severity of TBI and gender significantly predicted the likelihood of having an anxiety disorder, with moderate-severe TBI increasing the risk, and being male decreasing the risk. Moreover, frontal lobe abilities were significantly associated with having an anxiety disorder, such that having higher levels of apathy, higher disinhibition and poorer executive functioning all decreased the likelihood of having anxiety, whereas overall frontal lobe functioning significantly increased the risk in this group.

The functions that the FrSBe aims to tap into when assessing individuals are those that are most frequently cited as consequential of frontal lobe damage (Stout, Ready, Grace, Malloy, & Paulsen, 2003). As such, its use in this study has highlighted the behavioural outcomes that are associated with the impact of TBI which has occurred many years prior. In terms of the biological effects of TBI, the injury is most often associated with frontal lobe diffuse damage (Bigler et al., 2013; Levin et al., 1992; Wilde et al., 2007). As such, the findings support the hypothesis that the diffuse frontal damage that occurs as a result of TBI is associated with poorer outcomes of apathy, executive dysfunction and disinhibition, which potentially have a role in the development or maintenance of anxiety disorders. Executive functions are described to encompass self-regulative abilities, and are related to the development of frontal neural networks which are vulnerable in childhood TBI (Levin & Hanten, 2005). Moreover, anxiety, neuroticism and executive functioning are also linked with

the prefrontal lobes, highlighted in research focussing on adults with history of TBI (Forbes et al., 2014). The finding that disinhibition was negatively associated with having an anxiety disorder may link with theories postulating that those with anxiety are more inhibited (Rosenbaum et al., 1993) and that in individuals with higher neuroticism (common in people with anxiety) (Clark et al., 1994), these neurotic tendencies have been associated with impulsivity and behavioural inhibition (Forbes et al., 2014).

When comparing individuals with anxiety disorders and no anxiety disorders, no significant differences were found regarding cognitive functioning and frontal lobe abilities. This is in contrast to previous work supporting a relationship between cognitive difficulties and anxiety. For instance, anxiety disorders in adults have been linked with significant impairments in episodic memory and executive functioning (Airaksinen, Larsson, & Forsell, 2005). However, as will be explored further, there are inconsistencies inherent in the research regarding the relationship between cognition and anxiety disorders.

There was also no significant association found for cognitive functions as a predictor of ongoing anxiety disorders. This is inconsistent with existing research which highlights that poor performance on domains such as processing speed, memory and executive function are evident following mild, moderate and severe TBI, and that these difficulties are associated with higher rates of self-reported anxiety (Ponsford et al., 2008). Other research has identified problems with attention, information processing, and executive functioning (but not memory) one year following TBI which were significant predictors for having an anxiety disorder (Gould et al., 2014). However, inconsistencies in the association between cognition and anxiety after TBI exist (Barker-Collo et al., 2015), and it appears that cognition tends to improve in the first year following TBI in some cases (Barker-Collo et al., 2015; Stenberg, Godbolt, de Boussard, Levi, & Stalnacke, 2015). Considering this study focussed on long-

term outcomes, any cognitive deficits that emerged following childhood TBI may have resolved by the follow-up assessments.

In non-TBI young adults with anxiety disorders, a lack of impairments in cognitive abilities across memory, attention, processing speed and executive functioning have also been previously highlighted (Castaneda et al., 2011). It may be that self-reported anxiety symptomatology is associated with cognitive deficits due to anxiety being a manifestation of coping with difficulties following TBI (Ponsford et al., 2008), however symptoms meeting diagnostic criteria may not be associated with cognitive problems. Moreover, in adolescents, mild anxiety has been associated with better attentive abilities (Jarros et al., 2017), meaning that using anxiety in a functional manner may actually be protective of cognitive dysfunction.

Another consideration is the severity and specific sub-type of the anxiety disorder an individual is experiencing. For instance, cognitive impairment has been noted only in young adults with anxiety disorders who were also taking anxiety medication (Castaneda et al., 2011). Moreover, the profile of anxiety-related cognitive deficits may depend on anxiety sub-type, with research highlighting OCD as having a stronger relationship with cognition (Castaneda, Tuulio-Henriksson, Marttunen, Suvisaari, & Lonnqvist, 2008). Further, GAD and specific phobias have been identified to be unrelated to cognition in a previous study (Airaksinen et al., 2005). In the present study, there is a lack of information about the severity of anxiety, and whether individuals were taking medication for their symptoms. Moreover, symptoms of OCD were not assessed, which is noted to have a stronger link with cognitive problems, and all sub-types of anxiety disorders were grouped.

6.5.1. Limitations

A limitation of the study is that premorbid functioning of the participants was not assessed, such as SES, education levels and family factors, and other biological,

psychological and cognitive factors. As such, any pre-existing contextual factors which may explain the above findings cannot be accounted for. In addition, the structured interview questions were reliant on self-report answers regarding anxiety symptoms and frontal lobe functioning, and diagnostic criteria for anxiety disorders were based on the DSM-IV rather than the newest version of the manual. However, the structured interview was detailed and conducted by a trained research fellow, and measures included in this study have been deemed to have adequate to very good psychometric properties. Finally, due to the methodology of recruitment, there was a low response rate of 32%, thereby potentially limiting the generalisability of the sample.

6.5.2. Implications and future directions

Theoretical implications associated with the aforementioned findings are that the relationship between cognitive functioning and anxiety following TBI continues to differ across research studies. Indeed, as mentioned above, inconsistencies are identified in the literature regarding the particular cognitive domains implicated in anxiety disorders and whether the direction of the relationship is positive or negative in nature. Moreover, the findings presented here support previous theories that individuals with more severe TBI and female gender are at an increased risk of ongoing anxiety disorders. However, these findings have provided further insight, such that specific domains of frontal lobe ability may operate differently than overall frontal lobe functioning in the risk of anxiety disorders.

As such, it may be important for clinicians and other professionals involved in the care of children and adolescents with TBI to conduct neuropsychological assessments to screen for any vulnerabilities that may require early intervention and scaffolding. This could include cognitive rehabilitation, particularly functions tapping into frontal lobe abilities, with the aim of reducing the risk of these children developing ongoing emotional difficulties later in life.

This also would be particularly important for children with TBI who are female and have sustained a more severe injury, who in this study presented with the greatest risk.

Future work could replicate the methodology of this study, in addition to assessing premorbid cognitive, psychological and other factors, in a similar sample. Moreover, in addition to the structured assessment of psychological and cognitive functioning conducted with participants, informant reports from family members, friends or other relevant people may be useful to corroborate and strengthen findings. Further assessment utilising measures which assess frontal lobe function is important in this sample considering the novelty of findings to examine whether findings can be replicated. Finally, mapping of brain regions with MR imaging or other techniques would also be useful to examine neural correlates associated with anxiety, childhood TBI and risk factors that may be moderating the relationship between these issues.

6.5.4. Conclusions

In conclusion, adults with a history of childhood TBI are at risk of developing anxiety disorders even many years after their injury. Individuals with more severe TBI, females, and those with poorer frontal lobe functioning may be at a higher risk. Increased apathy, being disinhibited and having poorer executive functioning appear to be slightly protective of developing an anxiety disorder following TBI. Therefore, these deficits may buffer an individual from experiencing anxiety disorders, potentially due to a lower level of insight or cognitive capacity or lack of motivation to ruminate or worry. However, these factors in combination increase the likelihood of meeting diagnostic criteria for an anxiety disorder. The findings associated with frontal lobe functioning are novel and provide further insight into how anxiety may manifest many years after childhood TBI, and such, these abilities should be explored further in future studies to examine whether findings may be replicated.

CHAPTER SEVEN: GENERAL DISCUSSION

This chapter will review the aims, hypotheses and rationale for the entire body of work presented within the thesis. It will present a summary of findings, with associated explanations and further considerations not already discussed in the previous text. The discussion introduces an explanatory diagram and discussion regarding the pathways involved in the development of anxiety disorders in individuals following childhood TBI.

7.1. Overview of aims

The overarching aims of the research were as follows. The first aim was to examine outcomes of childhood TBI with reference to internalising symptomatology, and then more specifically, explore the prevalence rates and predictors of anxiety disorders following childhood TBI utilising a systemic literature search. Following this, the objective was to explore the rates of internalising behavioural problems and symptomatology experienced by young adults with a history of childhood mild TBI, including issues associated with anxiety, depression, withdrawal, somatic symptoms, and avoidant personality problems, as compared to young adults with no TBI history. Moreover, this enabled the exploration of anxiety and other internalising problems within a community-based sample of individuals, and to assess the long-term effects of TBI.

Another overarching aim of the research was to examine the general incidence of anxiety disorders compared to other psychiatric disorders among individuals with a history of childhood TBI, looking both at short-term and long-term outcomes, across individuals selected from different populations. This was achieved utilising a child and adolescent sample, and adult samples.

A third general aim of the research was to examine the incidence of TBI, anxiety, and comorbid psychological issues in a younger sample of children and adolescents within an outpatient mental health service. This sample was utilised both to examine prevalence rates of TBI among children and adolescents within a mental health setting, and also prevalence rates among children and adolescents with an anxiety diagnosis. Within the mental health sample, a further aim was to examine rates of anxiety disorders and other psychiatric diagnoses in children and adolescents with TBI, and compare that to children and adolescents with no TBI, within a clinical sample.

A forth overarching objective was to highlight the potential risk factors and predictors associated with the development of anxiety disorders following childhood TBI, including the role of gender, age of injury and other psychosocial factors. This was achieved through the use of an adult sample of individuals who had sustained a TBI or OI in childhood, in comparing anxiety-related outcomes drawn from a hospital-based sample.

The final aim was to assess outcomes of childhood TBI, focussing on anxiety disorders, among three distinct samples (community-based, clinical, hospital-based). This allowed a comparison and discussion regarding how rates of anxiety disorders may differ depending on the sample of participants utilised, including the population they are recruited from and also the age of participants, and whether information about anxiety and TBI is collected via self-report measures or objective medical and clinical records.

7.2. Overview of brief rationale

7.2.1. Lack of research for internalising problems after TBI

Internalising behaviours, such as anxiety, depression and somatic symptoms (e.g. headaches, fatigue, stomach problems) are those that are directed inwards or into the self, and

may be less visibly seen by others, whereas externalising behaviours, such as aggression or hyperactivity, are more disruptive or visibly distressing (Bayer et al., 2012), particularly for parents. Within the TBI literature, a large focus is placed on externalising outcomes following TBI including hyperactivity, aggression, and oppositional behaviours. This may be due to the fact that those behaviours are quite distressing for parents and other significant people involved in the child's life (e.g. siblings, friends, teachers), as compared to issues such as anxiety and depression which may go unnoticed or are harder to detect in children. Indeed it has been noted that there are disagreements between children and adolescent self-report versus parental report of anxiety symptoms (Levi et al., 1999; Mather et al., 2003), and also across informant reports of internalising problems (Achenbach, McConaughy, & Howell, 1987; De Los Rayes & Kazdin, 2005; Peterson et al., 2013). It would be expected that where more severe depression (e.g. indication of suicidal ideation or self-harm) or anxiety (e.g. ritualistic behaviours in OCD) are present, that these disorders will be identified and that help would be sought. Whereas with more mild to moderate anxiety and depression, it may be dependent on the child or adolescent to inform their parents about their difficulties, which would further depend on that child's ability to articulate what is going on and their willingness to share this with others.

Within the TBI field, a number of studies have explored rates of externalising behaviours and problems following childhood TBI, including issues associated with drug and alcohol use (Corrigan et al., 2012; Felde, Westermeyer, & Thuras, 2009; McKinlay et al., 2009), hyperactivity (Konrad, Gauggel, Manz, & Scholl, 2000; McKinlay et al., 2009), offending behaviours and forensic involvement (McKinlay, Corrigan, Horwood, & Fergusson, 2014; W. Williams, Cordan, Mewse, Tonks, & Burgess, 2010), and aggression (Dooley, Anderson, Hemphill, & Ohan, 2008; Rao et al., 2009) . Less focus has been directed

towards anxiety and other internalising problems, potentially due to the perceived smaller burden or impact compared to that of externalising difficulties listed above.

7.2.2. Gender differences in the rates of anxiety disorders among males and females

Another reason the thesis focussed particularly on anxiety disorders following TBI is the gender difference that is associated with anxiety. In general, symptoms of anxiety are more common in females than in males. In childhood, females are twice as likely as males to develop anxiety symptoms or disorders, and this likelihood increases to three times when reaching adolescence (Wittchen et al., 1998). In TBI research in particular, following childhood TBI, female adults are more likely to report internalising problems (depression, anxiety) whereas male adults present with a higher rate of externalising problems (offending behaviour, substance abuse/dependence) (Scott et al., 2015).

In general, males present with higher rates of TBI than females (Crowe et al., 2009; McKinlay et al., 2008), which has been attributed to factors such as interpersonal violence and testosterone levels resulting in impulsive behaviours (Bruns Jr & Hauser, 2003). Considering males are at higher risk of TBI, and also tend to report higher rates of externalising symptomatology than females, this may be a factor for why anxiety has been overlooked in TBI research. However, females may be underrepresented within the TBI literature. For instance, when comparing females and males within similar sports, it has been highlighted that females actually have higher rates of concussion than males (Dick, 2009). Therefore, in some instances females may be at equal or greater risk of TBI than males. As such, focus should be given towards anxiety and other internalising problems that may be present after TBI given the inherent or greater risk for females.

7.2.3. Impact and burden of anxiety

Anxiety can have lasting and ongoing effects in individuals, which may impair young people throughout development. It has been noted that chronic anxiety can have long-term consequences through a disruption or interference with the developing architecture of the brain (Arnsten, 2009; Brinks et al., 2008). Anxiety disorders also have a marked impact on an individual's quality of life, with impairments evident even with sub-threshold disorders (Mendlowicz & Stein, 2000), and may also lead to premature withdrawal from school (Van Ameringen, Mancini, & Farvolden, 2003). Further difficulties associated with ongoing anxiety are alcohol abuse and/or dependence, particularly in adolescents and young adults with social phobia, panic attacks and PD (Zimmermann et al., 2003). Moreover, anxiety disorders in adolescence have been reported to lead to a later risk of depression, substance dependence (nicotine, alcohol, and illicit drugs), suicidal behaviour, education under-achievement, and early parenthood (Woodward & Fergusson, 2001). As such, if childhood TBI is associated with any increased risk regarding the development of anxiety symptomatology and disorders, then early identification of vulnerable individuals is required to allow for intervention and management.

7.2.4. Use of participant groups in comparing anxiety-related outcomes following TBI

A unique aspect of the thesis is the utilisation of three distinct groups of participants, including a university community-based sample, a clinical sample derived from an outpatient mental health service, and a sample based on hospital admission records. This approach was adopted because prevalence rates of TBI vary quite significantly according to the participant sample they are derived from, including the age range utilised and how TBI is defined (McKinlay et al., 2008). As such, it is expected

that the incidence of anxiety disorders and other post-injury issues will vary depending on the sample used.

For instance, the use of hospital-based samples with ED and hospital admission records to obtain medical information regarding TBI (Anderson et al., 2009; Anderson, Brown, et al., 2011; Crowe et al., 2009; Max, Friedman, et al., 2015) allows for more accurate identification of injury severity. Clinical samples such as individuals that are presenting within a mental health service or other health-care facility (DeBellis et al., 2000; Kurowski et al., 2013; Max & Dunisch, 1997; Max, Sharma, et al., 1997) may allow for more accurate and detailed diagnostic information regarding behavioural and psychological functioning, which is useful when examining and comparing psychiatric outcomes following TBI. The utilisation of hospital-based and clinical samples is ideal as they are not reliant on self-report measures for either TBI or behaviours. However, a limitation is access to participants and potentially smaller sample sizes, whereas using a community-based sample allows for larger sample sizes and more generalisable results. Therefore, in utilising three separate samples within the thesis, the relationship between anxiety disorders and TBI has been viewed from different perspectives. For instance, it was expected that anxiety would be more prevalent in individuals with childhood TBI drawn from a hospital-based sample, and also that individuals within a mental health clinic presenting with anxiety disorders would have higher rates of childhood TBI. The opportunity to assess the general research question (that is, are anxiety disorders and childhood TBI related) from different angles utilising different sample groups is unique and has provided good insight into how anxiety may manifest in individuals following TBI.

7.3. Overview of study findings

7.3.1. Internalising disorders in young adults with childhood mild TBI

In general, the findings were consistent with the hypotheses, which were that young adults with a history of childhood mild TBI would present or report higher rates of internalising behavioural problems, including depression, withdrawal, anxiety, somatic symptoms (e.g. fatigue, headaches, gastrointestinal concerns), and avoidant personality problems, compared to that of young adults with no TBI history. The study highlighted that having a history of mild TBI that occurred in childhood (before the age of 14 years) is associated with ongoing internalising symptomatology including anxiety, withdrawal, somatic symptoms and avoidant personality problems. More specifically, it was found that young adults with a history of mild TBI reported higher rates of somatic complaints and overall internalising symptoms than young adults without TBI. Moreover, compared to the non-TBI group, young adults with a history of childhood mild TBI also had higher rates of clinically elevated somatic complaints and avoidant personality problems, higher rates of sub-threshold anxiety, a higher incidence of having at least one DSM-related diagnosis, and higher rate of having multiple internalising problems. These findings are consistent with recent research which has indicated a high rate (35.3%) of anxiety disorders 'not otherwise specified', therefore sub-threshold and not meeting full diagnostic criteria, in individuals with a history of TBI (Gould, Ponsford, Johnston, & Schonberger, 2011).

7.3.2. Anxiety in children and adolescents within an outpatient mental health service

Findings differed in comparison to the expected outcomes for the study, which hypothesised that children and adolescents with a history of TBI would present with higher rates of anxiety and other psychiatric disorders, compared to individuals without TBI. The results were surprising and differed from what was found in the university, community-based

sample of young adults. The research highlighted that a high proportion (over 28%) of children and adolescents within a mental health service had a self-reported or parent-reported history of mild TBI. Overall, no differences were found between individuals with history of mild TBI and individuals without TBI history for anxiety disorders. However, when comparing outcomes according to child-reported TBI and parent-reported TBI, parent-reported TBI was associated with significantly higher rates of anxiety.

The results were generally inconsistent with most existing literature that reports higher rates of anxiety disorders in individuals with a history of TBI. The findings are discussed with reference to a number of factors, including the age and developmental period of the participants with relation to when anxiety disorders may be more likely to emerge, reasons for why parents utilise mental health services for their child, gender, and specific exclusion criteria of the mental health service. Additional factors to consider here are associated with the potential for there to have been anxiety disorders 'not otherwise specified' within the sample, that were not identified in the mental health file review as only full diagnoses of anxiety were coded. This is likely given that substantially high rates of anxiety disorders 'not otherwise specified' have been found in TBI groups (Gould et al., 2011). As will be outlined in more detail later, another important consideration is the pre-existing personality factors of the young people who go on to develop anxiety after TBI. Vulnerability factors known to play a role in future emergence of anxiety, such as being behaviourally inhibited, avoidant or timid (Clark et al., 1994; Rosenbaum et al., 1993), may result in a child being less likely to injure themselves, meaning anxiety is actually underrepresented in TBI outcome studies. This may account for the low incidence of anxiety in both the TBI and OI groups.

7.3.3. Long-term anxiety disorders following childhood mild and moderate-severe TBI

Assessing anxiety-related outcomes in adults with a history of childhood TBI enabled an exploration of whether there was evidence of ongoing or chronic difficulties. Findings associated with the adult group with childhood history of mild, and moderate-severe TBI ~10 years prior were in favour of the stated hypotheses. Generally, it was expected that adults with a history of childhood moderate-severe TBI would be associated with the highest rates of anxiety and other psychiatric disorders, followed by individuals with a history of mild TBI, and adults with a history of OI having the least number of issues. Further, it was hypothesised that certain factors would serve to increase the risk of having anxiety, including age, gender, age of injury, and other internalising psychiatric diagnoses. When comparing the mild TBI, moderate-severe TBI and OI groups, a significant difference was found for rates of overall anxiety disorders and comorbid anxiety disorders, such that the moderate-severe TBI group had the highest number of issues. When combining the TBI groups and exploring anxiety and other disorders between individuals with TBI or OI, higher rates of depression, panic attacks, specific phobias and overall anxiety disorders were present in adults with a history of childhood TBI. Finally, significant predictors associated with having an anxiety disorder were history of TBI, and gender, with females and more severe injury presenting a greater risk.

7.3.4. Predictors of anxiety disorders in adults following childhood mild and moderate-severe TBI

As an extension of the aforementioned study, further analyses were conducted to examine the predictors associated with anxiety following childhood mild and moderate-severe TBI, in accordance with existing theories and previous research. The predictors of interest included TBI severity, gender, age of injury and injury treatment, cognitive

functioning (memory, attention, processing speed and visuospatial abilities) and domains known to be associated with frontal lobe deficits (apathy, executive dysfunction and disinhibition). In general, a higher number of females had a diagnosis of an anxiety disorder both between and within participant groups, which was statistically significant. Moreover, individuals with mild TBI and moderate-severe TBI had significantly poorer attention and memory abilities than the OI group, and the mild TBI group had significantly worse executive dysfunction and poorer overall frontal lobe abilities than the OI group. In keeping with the hypotheses, severity of TBI and gender significantly predicted the likelihood of having an anxiety disorder, with moderate-severe TBI increasing the risk by six times, and being male slightly decreasing the risk. Moreover, frontal lobe abilities were significantly associated with having an anxiety disorder, such that having higher levels of apathy, higher disinhibition and poorer executive functioning all decreased the likelihood of having anxiety, whereas overall frontal lobe functioning significantly increased the risk in this group. Alternative to what was expected, when comparing individuals with and without anxiety disorders (regardless of injury type), cognitive performance and frontal lobe deficits did not differ. Further, cognitive functioning was not a significant predictor in the model explaining the likelihood of having an anxiety disorder diagnosis.

Table 7.1.displays the overall findings previously presented in the thesis. The table indicates participant characteristics, and the main findings relating to anxiety outcomes following TBI.

Table 7.1.

Summary of Overall Research Findings according to Chapter and Participant Group

	Participants	Main Findings
Chapter Three	• Convenient, community-based sample • 247 university students, 18-25 years • 47 mild traumatic brain injury (TBI), age of injury *M*=14.8 • 103 males (*M*=20.6); 139 females (*M*=20.3)	• Raw scores: TBI group higher rates of somatic complaints, overall internalising problems, and withdrawal • *T*-scores, borderline concerns: TBI group higher rates avoidant personality problems, anxiety and depression, overall internalising problems • *T*-scores, clinically elevated concerns: somatic complaints • TBI group 2.57 times more likely to report ≥ 1 disorder and multiple internalising problems
Chapter Four	• Child and adolescent mental health outpatient setting • 161 children 5-18 years; *M*=12.39 • 42 mild TBI, age of injury *M*=12.46 • 85 males (*M*=11.4); 76 females (*M*=13.5)	• Over 28% of sample reported history of TBI • Generally, no significant differences between TBI and non-TBI groups for psychiatric disorders or parental stress • Considering only parental report of TBI: significant differences in rates of anxiety and suicidal/self-harm (TBI group with more issues) • Eight participants with history of TBI and anxiety disorders
Chapter Five	• Longitudinal, between-subjects, cross-sectional • Hospital emergency department (ED) outpatient admission records • 169 individuals; 95 males (*M*=22.78), 74 females (*M*=22.27) • 65 mild TBI, 61 moderate-severe TBI, 43 orthopedic injury (OI); age of injury mild TBI *M*=10.86, moderate-severe TBI *M*=7.5, OI *M*=10.47	• TBI: 22.2% overall anxiety, 10.3% comorbid anxiety, 7.9% Generalised Anxiety Disorder (GAD), 13.5% panic attacks, 6.3% Panic Disorder (PD), 3.2% agoraphobia, 6.3% social phobia, 8.7% specific phobia, 2.40% Post-Traumatic Stress Disorder (PTSD) • OI: 7.0% overall anxiety, 2.3% comorbid anxiety, 4.7% GAD, 2.3% for panic attacks, PD, agoraphobia, social phobia, specific phobia, and PTSD • Moderate-severe TBI group: highest rates of overall anxiety and comorbid anxiety • TBI: higher rates of overall anxiety, panic attacks, specific phobia
Chapter 6	• Longitudinal, between-subjects, cross-sectional • Hospital ED outpatient admission records • 169 individuals; 95 males (*M*=22.78), 74 females (*M*=22.27) • 65 mild TBI, 61 moderate-severe TBI, 43 OI; age of injury mild TBI *M*=10.86, moderate-severe TBI *M*=7.5, OI *M*=10.47	• Mild and moderate-severe TBI group performed worst on measures of attention and memory • Mild TBI: higher scores of executive dysfunction and frontal lobe difficulties than OI group • Severity of TBI and gender predictive of anxiety disorders • Apathy, disinhibition and executive dysfunction negatively associated with anxiety disorders • Frontal lobe functioning positively associated with anxiety disorders • Cognitive functioning not significantly associated with anxiety disorders

7.3.5. Differences across sample groups

Currently, the research exploring TBI and anxiety among children and adolescents have utilised either hospital-based or rehabilitation service samples (Gerring et al., 2002; Grados et al., 2008; Hajek et al., 2010; Herskovits et al., 2002; Levi et al., 1999; Luis & Mittenberg, 2002; Mather et al., 2003; Max et al., 1998; Max et al., 2011; Max, Lopez, et al., 2015; Vasa et al., 2002; Vasa et al., 2004) apart from one which utilised a community-based cohort and relied on parent-report identification of TBI (Liu & Li, 2013). As such, there is little diversity among the existing research regarding the samples used, which limits the generalisability of findings and conclusions to some degree.

It is important to consider reasons for why there are differences in anxiety-related outcomes depending on the cohort of participants being studied. One factor worth noting is the differences in the length of time that had lapsed between the TBI and when behaviour or psychological functioning was assessed, given that the child and adolescent mental health service sample had sustained TBI more recently than the other two participant groups. This is in keeping with the idea that anxiety disorders do not emerge until the young person has developed into adulthood whereby many biological and psychological changes occur, and as they are placed under more complex social and emotional demands, this leads to more marked anxiety symptoms and impaired functioning (Angold, Costello, et al., 1998; Susman et al., 1985). This may help to explain why the younger sample did not have any differences between the TBI and non-TBI groups.

Additionally, another important factor is that within each study sample, different control groups were utilised due to the population from which the sample was derived. For instance, in the young adult community-based sample, individuals with a history of mild TBI were compared to that of individuals with no TBI history, or in other words a sub-sample of

the general population. In the clinical sample however, children and adolescents with mild TBI and mental health concerns were compared to children and adolescents with mental health concerns and no TBI history, therefore a sub-group of the clinical population. And finally, in the hospital-based sample, individuals with a history of childhood TBI were compared to individuals with a history of OI, therefore a sub-group of an injured population. Indeed, in existing TBI research, differences in anxiety and other internalising behavioural problems are noted for those with TBI compared to the general population (Hawley et al., 2004; Liu & Li, 2013), and also between TBI and OI samples (Karver et al., 2012; Max et al., 2012; Scott et al., 2015). However, when comparing TBI with a clinical sample across all diagnostic variables, including internalising disorders and externalising disorders (Max & Dunisch, 1997; Max, Sharma, et al., 1997), little to no differences in behavioural, emotional and psychological functioning have been noted.

Some have theorised that this may be due to the idea that ongoing difficulties after TBI are solely related to pre-existing problems already present within the individual (Brown, Chadwick, Shaffer, Rutter, & Traub, 1981; Max & Dunisch, 1997). However this theory has since been debated and argued in the literature, with numerous studies which are inconsistent with this conclusion. There is limited information as to why children and adolescents with TBI tend not to differ from children and adolescents without TBI within a mental health setting, with regards to psychiatric diagnostic information. However, considering what the research in this area has highlighted so far, perhaps further work could be conducted in the utility of a mental health sample as a comparison group for individuals with TBI.

7.4. Further theoretical and methodological explanations

7.4.1. Expectations about effects of TBI

An important factor that may be contributing to the higher rates of anxiety and other ongoing problems in individuals with TBI are an individual's expectations or beliefs about the injury event itself. Research has described that individuals with mild TBI tend to overestimate post-concussive change (including memory problems, irritability, fatigue, sleep difficulties, headaches, or anxiety) that is consistent with their negative expectations of the outcome of injury (R. Fergusson, Mittenberg, Barone, & Schneider, 1999). Others have highlighted poorer performance on neuropsychological tests when reminded about their history of mild TBI, compared to others with history of mild TBI who were not reminded (Suhr & Gunstad, 2002). Individuals with higher levels of cognitive function are also noted to possess more insight into their deficits following injury, resulting in increased anxiety (Cooper-Evans et al., 2008). Other factors hypothesised to contribute to poor outcome of mild TBI include lack of coping strategies, low positive appraisal and higher external locus of control (A. Moore & Stambrook, 1991, 1992). It is therefore proposed that the negative expectations some individuals hold regarding mild TBI symptoms results in a hypervigilance or increased focus on the experience of symptoms, resulting in higher levels of distress (R. Fergusson et al., 1999).

Another explanation or contributing factor for why some individuals experience persistent anxiety after childhood TBI, even of mild severity, might be due to personality and cognitive factors. Individuals with a higher level of insight regarding their current deficits compared to premorbid functioning may have resultant stress and potential avoidance of certain activities in case of failure or embarrassment. Those that hold negative beliefs or expectations about the potential prognosis or recovery from TBI, particularly those who may

be more inclined to undertake research about poor outcomes or educate themselves about what to expect, may experience higher levels of stress and anxiety and also be hypervigilant to even minor symptoms which they catastrophically attribute to the injury.

7.4.2. Premorbid functioning

An alternative explanation is whether there is an under-represented risk of anxiety following childhood TBI due to the nature of individuals who are more likely to sustain an injury when they are young. For instance, it is well documented that certain risk factors are associated with childhood TBI. These include male gender (Berney, Favier, & Froidevaux, 1994; McKinlay, Kyona, et al., 2010), exposure to adverse life events or poorer environmental conditions (Demellweek, Baldwin, Appleton, & Al-Kharusi, 2002; McKinlay, Kyona, et al., 2010), younger age (Berney et al., 1994; Lalloo, 2003), hyperactivity (Lalloo, 2003), conduct issues (Lalloo, 2003), and generally elevated behavioural issues (Brown et al., 1981). As such, the children who do sustain a TBI tend to be less inhibited, have lower levels of self-control, and may be behaviourally dysregulated.

When considering individuals or young children with anxiety-related traits and temperaments, in contrast to above, they may be more likely to present as timid, avoidant or behaviourally inhibited (Clark et al., 1994; Rosenbaum et al., 1993). Indeed, research into theories of how anxiety disorders develop suggest a number of factors associated with an increased risk, for instance family history of anxiety (Moffitt et al., 2007) and over-protective or over-involved parenting (Bowlby, 1973). These factors inherent to the child's temperament and personality, in combination with factors associated with the parents and the household, may buffer the child against actually sustaining a TBI due to the child's cautiousness and also parental cautiousness. Therefore, it could be theorised that there are low base rates for anxiety, meaning that current prevalence rates of anxiety disorders

following childhood TBI are actually under-representative of the actual risk in this population. However, on the other hand, anxiety has also been associated with a cold, critical parenting style or neglectful upbringing (Schimmenti & Bifulco, 2013), which in turn may be associated with a child's increase in risk-taking or lack of boundaries, potentially leading to a higher likelihood of TBI. Further research into the premorbid biopsychosocial functioning of children who sustain TBI is essential to further explore these hypotheses.

7.5. Outline and discussion of a diagrammatic representation for the manifestation of anxiety disorders following childhood TBI

What is clear is that in any case of TBI, whether mild, moderate or severe, there is an event involving a blow or knock to the head that has caused either local or diffuse damage to the brain, resulting in some sort of neurological impairment (Albicini & McKinlay, 2014; Centers for Disease Control and Injury Prevention, 2013). The extent of damage done to the brain may therefore be associated with the severity of injury, mode of impact, and area of the brain hit. For instance, it would be expected that less damage to neurological structures would occur when frontal regions are hit due to more bone and skull versus the temporal regions (Umile, Sandel, Alavi, Terry, & Plotkin, 2002), and that penetrating injury would cause more impairments than blunt force trauma (Williams, Ling & Tortella, 2006). In addition, brain imaging and lesion studies have indicated that areas of the brain implicated in TBI do in fact overlap with brain regions associated with anxiety, including the OFC, hippocampus, thalamus, temporal regions, amygdala and frontal gyri (Grados et al., 2008; Herskovits et al., 2002; Mather et al., 2003). Therefore it could be reasonably hypothesised that the impact to these areas of the brain when an individual is in childhood where the brain is continuing to develop, creates a vulnerability to ongoing anxiety. However, most individuals do go on to recover after TBI, so it is more likely that there are other moderating factors at play that serve to increase the risk of anxiety disorders beyond neurological insult. As such, merely

considering the neurobiological impact of TBI on functioning and ongoing outcome is incomplete, considering that even very mild injuries can result in lasting problems, and that what is known is that females present with a greater risk of developing anxiety than males.

7.5.1. Explanatory theory for individuals at increased risk of developing anxiety disorders after mild TBI

Figure 7.1. outlines a proposed biopsychosocial explanatory theory, including factors associated with the initial TBI, and also factors associated with the individual. The figure includes a number of interacting factors which are likely to increase the vulnerability of certain individuals to develop ongoing anxiety disorders following childhood mild TBI.

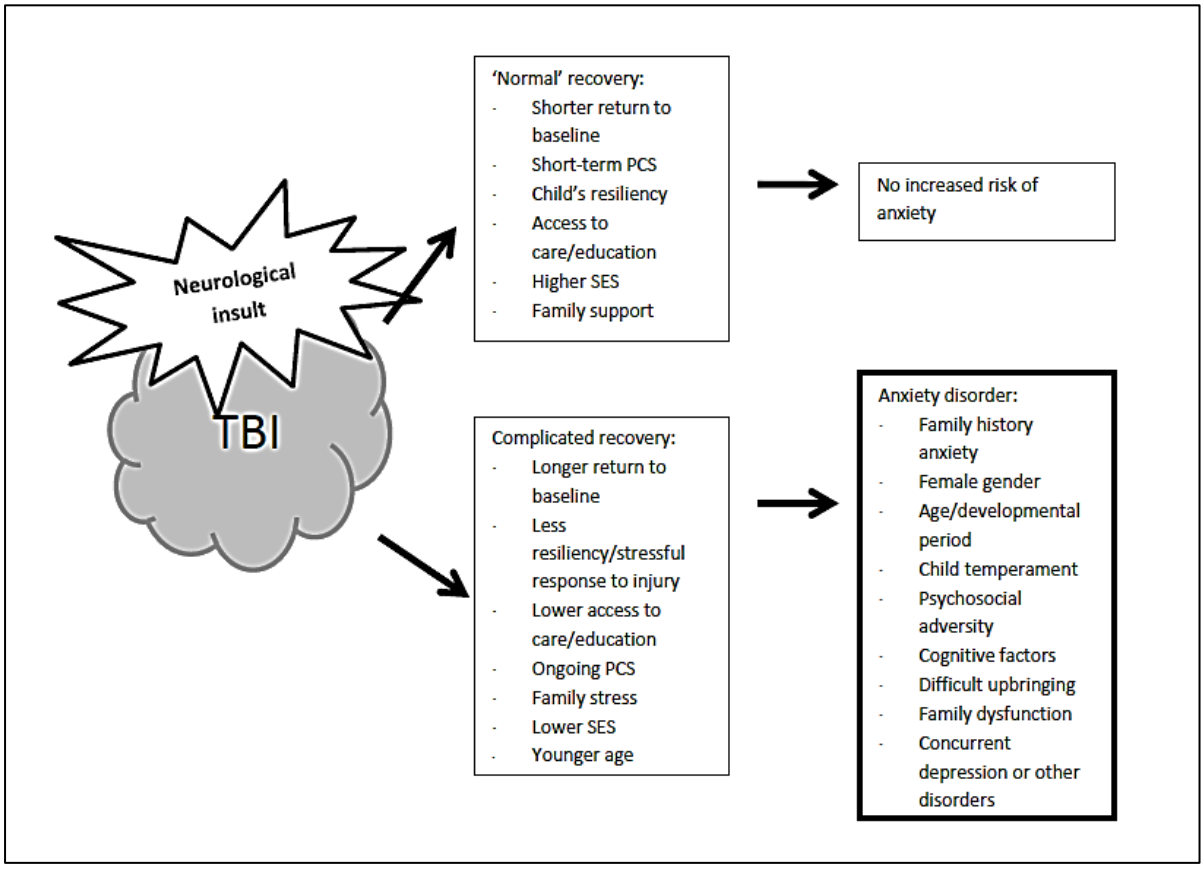

Figure 7.1. Mechanisms associated with the Development of Anxiety Disorders following Mild Traumatic Brain Injury. Legend: TBI=traumatic brain injury, PCS=post-concussive symptoms, SES=socioeconomic status

Generally speaking, following the initial blow to the head, acute, short-term symptoms are often associated with TBI, including nausea, disorientation, fatigue, sleep difficulties, poor concentration, inattention, and other somatic problems (Centers for Disease Control and Injury Prevention, 2006). The recovery process and trajectory thereafter may follow one of two courses. That is, a child who sustains a mild TBI might experience an uncomplicated, or 'normal' recovery, or a 'complicated' recovery. The terms 'normal' versus 'complicated' recovery might refer to the length of time or duration it takes to return to baseline functioning.

When considering 'normal' recovery from mild TBI, a number of factors will likely interact to contribute to and increase the chance of this recovery. These include a lower number or more short-term experience of PCS (Ganesalingam et al., 2008; Iverson, Lovell, Smith, & Franzen, 2000), a child's ability to be resilient and respond with less anxiety or stress in response to the injury (Schwartz et al., 2003), having easier or more access to medical or mental health care and education about TBI (Anderson, Spencer-Smith, et al., 2011), the family's level of SES (Ryan, Anderson, et al., 2014; Zonfrillo et al., 2014), and higher levels of family support (Pericall & Taylor, 2014; Schwartz et al., 2003).

However, with complicated recovery, these factors may be reversed and interact to have negative implications on the child's ability to adapt to their injury and return to baseline functioning. Such as being less resilient or unable to cope and adapt with the injury (Schwartz et al., 2003), having a lower SES (Ryan, Anderson, et al., 2014; Zonfrillo et al., 2014), having less or limited access to medical or mental health care or a lack of resources associated with education about TBI and what to expect (Anderson, Spencer-Smith, et al., 2011), experiencing longer-term or more severe PCS (Ganesalingam et al., 2008; Iverson et al., 2000), being exposed to high levels of family stress or poor family functioning (Anderson, Godfrey, Rosenfeld, & Catroppa, 2012; Schwartz et al., 2003), exaggerated parental response

to the injury and poor family adaptation (Pericall & Taylor, 2014; Peterson et al., 2013; Ryan, Anderson, et al., 2014), and being younger when the injury occurred (Taylor & Alden, 1997).

Therefore, individuals that do experience a more complicated recovery following their injury, in combination with all the factors described above, may be hypothesised to be more vulnerable to developing ongoing behavioural, emotional or psychological problems. The nature of these problems might be externalising or internalising, and therefore the presentation of difficulties is likely to be associated with further vulnerability factors, pre-existing or concurrent, that are inherent to the child and their environment, which serve to increase this risk even further. These factors could be considered with reference to anxiety theories which postulate certain vulnerabilities inherent in the development of anxiety disorders in the general population. These may include biological factors such as a family history of anxiety (Moffitt et al., 2007), being female (Barlow, 2000), and age given that it is proposed that anxiety disorders emerge when an individual transitions from adolescence to young adulthood (Costello et al., 2011; Nivard et al., 2016). Moreover, factors regarding the child's temperament also will play a significant role, including being more anxious or ambivalent in their attachment style (Schimmenti & Bifulco, 2013), and more shy or behaviourally inhibited (Clark et al., 1994). Also considering child-related factors, cognition and cognitive style also contributes to this risk in anxiety, including rumination, avoidance and beliefs about worry (Behar et al., 2009; Ladouceur et al., 2000). Finally, social and environmental factors play a large part in the vulnerability of developing anxiety disorders, including exposure to psychosocial adversity, having a difficult upbringing, and overall family dysfunction (Bowlby, 1973; Mineka & Zinbarg, 2006; Moffitt et al., 2007; Schimmenti & Bifulco, 2013).

As such, the factors associated with poorer recovery after mild TBI, combined with the vulnerability factors associated with anxiety disorders, may create an 'at risk' group, who

would be a target for intervention and support. It might be that individuals in the general population who are at more at-risk of developing anxiety disorders will have a lower threshold following a mild TBI with a complicated recovery. However, it is important to note a 'sliding scale' of impact based on the severity of the TBI. It is more likely that with moderate or severe TBI cases, the neurological insult and damage to the brain that has occurred will be having more of a direct impact on the risk of anxiety (particularly where regions overlap with those implicated in anxiety disorders), whereas in mild TBI cases, the psychological, social and environmental factors have a larger role. As such, it is important to note that these pathways may look different when considering moderate and severe TBI as the mechanisms are likely to vary quite significantly.

7.5.2. Considerations for moderate to severe TBI cases

There are a number of factors associated with moderate to severe TBI which will affect the process and trajectory of outcome, when compared to mild TBI. In the initial stages, a mild TBI is associated with a brief LOC (less than 30 minutes) and PTA lasting for no more than one day (Albicini & McKinlay, 2014; American Congress of Rehabilitation Medicine, 1993; Cassidy et al., 2004; McKinlay, 2010). With increasing severity of TBI comes increasing severity of initial symptomology. In the instance of moderate TBI, PTA may last for up to seven days and LOC up to 24 hours (Baalen et al., 2003; Corrigan et al., 2010), whereas in severe TBI, duration of PTA is more than seven days and LOC over 24 hours (Baalen et al., 2003; Corrigan et al., 2010). As such, it is expected that the recovery of a young person who has sustained a severe TBI and was unconscious for over a week will be vastly different to that of a young person who lost consciousness for less than 30 minutes. In fact, research describes subjective quality of life to be associated with duration of unconsciousness and PTA symptomatology (Teasdale & Enberg, 2005).

Therefore, the mechanisms associated with poor and ongoing outcomes after moderate and severe TBI will differ to that of mild TBI, and while mention of all possibilities and research in this area is outside the scope of this chapter, a brief discussion will be outlined here. In general, the length of physical recovery would likely be of longer duration in more severe TBI cases, including length of hospital stay and more medical procedures (Chua, Ng, Yap, & Bok, 2007; Popernack, Gray, & Reuter-Rice, 2015), and prolonged PCS (Sigurdardottir, Andelic, Roe, Jerstad, & Schanke, 2009). Associated with this therefore would be a longer time to return to usual activities including school, social activities and sports (Centers for Disease Control and Injury Prevention, 2016; Popernack et al., 2015). When considering theories by Anderson, Beauchamp and colleagues (Anderson & Beauchamp, 2012; Beauchamp & Anderson, 2010), these initial symptoms and difficulties may impair individuals from following a usual trajectory of development, which is likely to be more pronounced than in mild TBI.

However, associated with these prolonged symptoms and delayed return to 'normal' or baseline functioning, may be a number of protective factors when considering the risk of developing anxiety later on in life. For instance, a longer stay in hospital may mean that children and families are provided with more education about TBI and its potential ongoing effects, and also a higher level of medical support and rehabilitation (Andriessen et al., 2011; Chua et al., 2007; Popernack et al., 2015), which individuals who experience a mild TBI (particularly those with very brief LOC) may not receive. Furthermore, children who are instructed to remain at home and rest may receive more support, empathy from family members, and parental warmth, which is known to buffer against the development of anxiety (Schimmenti & Bifulco, 2013). Moreover, through this support, the child may experience increased validation and feel better understood which is comparative to individuals who sustain a mild TBI, who may be told that they should expect a full recovery and that any

ongoing poor outcomes are not related to their injury. In general, individuals tend to experience better and more positive outcomes after TBI when they have felt listened to and understood, and receive more social support (Rotondi, Sinkule, Balzer, Harris, & Moldovan, 2007). This is not to say however that individuals who sustain a moderate or severe TBI do not experience ongoing difficulties.

In families with a history of anxiety, parents may tend towards becoming overly distressed and therefore restrictive or overly protective in response to injury, which is a risk factor for anxiety disorders (Bowlby, 1973). There is also the hypothesis that children who experience more severe TBI, leading to deficits in cognition and higher-order processing of information, may have less insight into their injury and also into their deficits and change in function (Khan, Baguley, & Cameron, 2003; Teasdale et al., 1997), which could be protective in nature as they are not as knowledgeable about their issues which might be associated with less distress. Indeed, evidence suggests an increase in mental health difficulties as awareness regarding the injury increases (Schonberger, Humle, & Teasdale, 2006).

The hypotheses and theories presented here regarding the mechanisms involved in the development of anxiety after childhood TBI are speculative in nature, yet draw upon what has been discussed and highlighted thus far in the thesis. The importance of further research into how anxiety manifests after childhood TBI is therefore imperative, so that these mechanisms may be better defined and understood.

7.6. Overall limitations of the research

It is important to consider research in light of its limitations. Each chapter already outlines the limitations inherent in each research study discussed. One of which pertains to the low response rate (32%) of participants in chapters 5 and 6, which inevitably may have

biased the overall samples and limits generalisability of the results. Additionally, the main limitations of the work will be further outlined here to inform future research and directions.

7.6.1. Use of self-report measures

A limitation of chapters three and four is the use of self-report measures to record history of TBI and behavioural functioning. In chapter three, a self-report measure of TBI was utilised, where the correct identification of TBI (including severity) was dependent on the accurate memory of the participants. Due to the nature of the study, there was no opportunity to obtain any corroborative reports about TBI, such as from parents, siblings, family members or hospital records, to confirm the accuracy of reporting. Furthermore, considering the mean age of TBI was approximately 14 years, some participants were reporting an injury which had occurred 5-10 years prior. Previous research has identified the issues of utilising a self-report measure of TBI history, and has highlighted that people are actually quite poor at correctly reporting history of TBI. In particular, adults aged 25 years have been noted to recall their incidence of childhood TBI with only 84.5% accuracy (McKinlay & Horwood, 2016), and for 25 year-olds with a history of childhood TBI requiring hospitalisation, only 58.4% tend to be accurately recalled.

A further limitation is the use of a self-report measure of behavioural functioning and psychiatric symptomatology in the adult samples with childhood TBI. In chapter three, participants completed a self-report measure for internalising and externalising behavioural issues. This may have led individuals to either respond in a socially-desirable way, thereby minimising issues, or alternatively they may have over-reported symptoms considering how the study was advertised in recruitment information. This would have been relatively easy to do considering the face validity of the measure (Achenbach et al., 2005). For chapter five, diagnostic information regarding anxiety and other disorders was obtained via self-report in

an interview style. Again, informant reports for both studies regarding their experience and severity of internalising behavioural issues would have been useful to ensure validity and generalisability of results.

A final point to note is the use of parental and child reports, with reference to chapter four of the thesis. In the child and adolescent sample, self-report and parent-reported history of TBI was obtained, with the informant depending on the age of the child (above age 15 years, children were able to complete the measures themselves). When relying solely on parent reports of history of TBI, there was a significant difference for anxiety disorder diagnosis and suicidal/self-harm, such that parent reports of TBI led to higher rates of these outcomes. However, this was not the case for TBI events reported by children and adolescents themselves. Inconsistencies between reports from young people and their parents have been documented regarding rates of internalising disorders and PCS following TBI (Hajek et al., 2011; Levi et al., 1999; Luis & Mittenberg, 2002). Therefore, this confuses the results, because poor outcomes following TBI were dependent on whether it was the parent reporting history of TBI rather than the child. It is unclear in this study whether the discrepancy is due to parental or child inaccuracy or incorrect memory of TBI.

7.6.2. Assessment of premorbid functioning

Premorbid functioning of participants was not assessed or controlled for, which clearly limits the ability to make conclusions regarding ongoing problems after TBI. It is impossible to conclude that the ongoing issues participants' in the studies were reporting were not due to pre-existing psychiatric, intellectual, medical or behavioural problems. This is an issue because findings highlight that premorbid anxiety symptoms and disorders, as well as other internalising symptoms, significantly predict anxiety symptoms following TBI (Gerring et al., 2002; Max et al., 1998). However, it is important to note that the assessment

of premorbid functioning is difficult in itself, due to the fact that often individuals underestimate their premorbid difficulties or overestimate their functioning when retrospectively reporting (Iverson, Lange, Brooks, & Rennison, 2010; Lange, Iverson, & Rose, 2010). Moreover, each study included a control group for comparison, and analyses of demographic information (e.g. age and gender) revealed that participant groups were not significantly different. As such, while premorbid functioning was not assessed, the use of control groups controlled for any problems associated with premorbid functioning to some degree.

7.7. Discussion of research strengths

The research studies presented within this thesis have a number of strengths, which are important to note in reference to the ability to make valid conclusions and mark areas for future research. The areas of strength to be discussed include the measurement tools utilised for assessment and recording of TBI, behavioural functioning and psychiatric diagnoses, methodological strengths in reference to the study design, and novelty of the research in terms of adding to the existing literature.

7.7.1. Measurement tools

The studies presented within the thesis utilised well-validated, commonly used and reliable instruments to assess history of TBI, behavioural functioning and psychiatric symptomatology. For the assessment of internalising behavioural functioning, the ASR (Achenbach et al., 2005) has high internal consistency, construct validity, and test-retest reliability, with questions directly associated with DSM diagnostic categories. It has been widely used in research assessing anxiety and other psychiatric disorders in adult samples (Achenbach & Rescorla, 2003; Iverach et al., 2009; Neumann & Pardini, 2014). In chapters five and six, information regarding the diagnosis of anxiety and other psychiatric disorders

was obtained via a semi-structured interview, and while reliant on self-report responses regarding symptoms, the CIDI (World Health Organisation, 1990) is also well validated and provides excellent reliability estimates. It has been used in previous research to determine DSM related diagnostic information in adult samples aged 18-35 years (D. Fergusson et al., 2007, 2009; D. Fergusson et al., 2015), and is noted to be reliable and sensitive in detecting anxiety and other psychiatric disorders in relation to DSM diagnostic criteria (Reed et al., 1998; Wittchen, 1994).

In determining history and severity of TBI in both the young adult and also child and adolescent samples, the OSU TBI-ID SF (Corrigan & Bogner, 2007) was used. Although there are limitations inherent with using a self-report or parent-report measure for assessing and identifying history of TBI, the measure has high inter-rater reliability (Corrigan & Bogner, 2007) and good test-retest reliability estimates (Bogner & Corrigan, 2009). Moreover, the measure is widely used to identify prevalence rates of TBI (Corrigan et al., 2012) and is utilised in clinical assessments to examine TBI history (Ohio Valley Center for Brain Injury Prevention and Rehabilitation, no date). Further, self-report assessment tools for obtaining TBI information have the advantages of being cost-efficient while also holding the ability to provide insight into prevalence rates of TBI among different samples (Corrigan et al., 2010).

7.7.2. Further methodological strengths

Across the research studies, large sample sizes were utilised to assess outcomes following TBI, which allowed both for higher generalisability of the samples and also increased validity of results. Moreover, all studies obtained demographic and background information about participants, and statistical analyses were conducted between participant groups to establish differences. These analyses concluded that in each of the studies, the

participant groups (TBI versus no TBI) did not differ according to age, gender, and other characteristics (except for the case of chapter five and six whereby the moderate TBI group were significantly younger at age of injury). As such, this suggests that results or conclusions cannot be explained by pre-existing differences between participant groups. An additional strength to note is the use of hospital ED admission records, which allowed for accurate identification of TBI severity and OI in the sample, eliminating any issues associated with self-reported or parent-reported TBI incidence.

7.7.3. Novelty of research and additions to the literature

Most importantly, the methodologies and results presented here in the thesis contribute to existing literature regarding the development and incidence of anxiety disorders after childhood TBI, and the scope of the research provided the ability to present findings which add to the literature in a meaningful way. Chapters five and six included a longitudinal, between-subjects and cross-sectional design, with participants followed-up many years following a childhood injury and the ability to utilise current and retrospective data. This type of design with such a large time-frame between initial injury and outcome assessment is rare when exploring the incidence of anxiety disorders following childhood TBI, with the majority of studies examining factors such as quality of life, vocational status and cognition (Anderson, Brown, et al., 2011; Anderson et al., 2005; Anderson, Godfrey, et al., 2011; Anderson et al., 2012).

In addition, there have been few studies that have examined outcomes of TBI in a child and adolescent mental health outpatient sample. There is little diversity among the existing research regarding the samples used, which limits the generalisability of findings and conclusions to some degree. The thesis included the most recent study to investigate anxiety disorders specifically in children and adolescents and their association with TBI within a

clinical sample, apart from studies conducted in 1997, which also found a lack of psychiatric outcomes between a TBI and non-TBI groups (Max & Dunisch, 1997; Max, Sharma, et al., 1997). As such, the findings in chapter four are consistent with previous (and limited) research, which generally informs that children and adolescents within a mental health setting are virtually indistinguishable from their non-TBI counterparts.

Moreover, findings presented in chapter six shed further light into the inconsistent findings regarding the association between cognitive abilities and anxiety after TBI, given that the relationship between cognitive functioning and anxiety following TBI continues to differ across research studies. Inconsistencies are identified in the literature regarding the particular cognitive domains implicated in anxiety disorders, and whether the direction of the relationship is positive or negative in nature. The predictive analyses conducted in the thesis has allowed for further insight into the roles of cognitive and frontal lobe abilities in the development of anxiety after TBI. At this time, there does not appear to be specific research which has identified factors associated with frontal lobe functioning such as apathy, executive functioning, and disinhibition, and how they operate as risk factors for anxiety disorders after childhood TBI.

The thesis scope also allowed an opportunity to explore anxiety-related outcomes among three distinct participant samples with childhood TBI. The ability to assess incidence rates of TBI, anxiety and other psychiatric outcomes amongst young children, adolescents and young adults, utilising a mixture of self-report and hospital or clinical-based records, amongst diverse populations (community, clinical, hospital) is unique and has provided further understanding about how anxiety may manifest following childhood TBI. Furthermore, the study findings, reviews and discussion about existing literature allowed the formulation of theories to explain why some individuals may develop anxiety following childhood TBI. A diagram to outline the specific mechanisms and pathways involved in

anxiety disorders in relation to TBI has not been a major focus in past research, and as such, the findings and discussions presented here may highlight the need for intervention and further focus.

7.8. Theoretical and clinical implications of findings

Generally, the thesis outlines that childhood TBI, across all levels of severity, is associated with ongoing anxiety disorders and internalising symptomatology even ten years or more following injury. Although in the child and adolescent sample the TBI group did not present with higher rates of anxiety and other psychiatric disorders compared to a non-TBI group, this may be attributed to the population of which the sample was selected, but also may be due to the developmental period the young people were in. These findings lend support to existing theories which postulate that the impact of TBI (neurobiological, psychological and social) at a young age disrupts normal social, emotional and cognitive development, but that it is not until the child matures in adulthood where more complex skills are required, that these difficulties start to emerge more significantly and may be considered clinically relevant (Anderson & Beauchamp, 2012; Anderson, Brown, et al., 2011; Angold, Costello, et al., 1998; Max et al., 2012; Rosema et al., 2015).

In a clinical setting, these theoretical implications will influence when young people may initiate service use for anxiety following TBI, in that they may be more likely to notice onset of symptomatology in middle-adolescence to early adulthood, despite an injury occurring in early to late childhood. Moreover, as outlined in Figure 7.1, it might be that the sub-group of individuals who develop anxiety disorders following childhood TBI will a) experience a more complicated recovery accompanied by a number of negative consequences associated with the adaptation and response to their injury, which further interacts with problems in their environment such as lower SES and family dysfunction, and b) also have a

number of concurrent or pre-existing vulnerability factors associated with anxiety, including family history, female gender, cognitive factors, disrupted or neglectful upbringing and temperament or personality factors. Moreover, findings in chapter six indicate that some children with TBI may develop lasting difficulties in the domains of executive function, attention, frontal lobe difficulties and memory, and that ongoing frontal lobe deficits are associated with anxiety many years following injury.

Therefore, with this knowledge, clinicians working with children with a recent or past TBI history may need to consider these risk and vulnerability factors within a comprehensive assessment. As such, clinicians or professionals involved in the care of such children should conduct neuropsychological assessments to screen for any vulnerability that may require early intervention and scaffolding. This could include cognitive rehabilitation, particularly functions tapping into frontal lobe abilities, with the aim of reducing the risk of these children developing ongoing emotional difficulties later in life. The assessment of other current biopsychosocial and contextual factors would further allow for the identification of a specific 'at-risk' group of individuals who may require early intervention and management to support any future emergence of anxiety symptomatology and disorders.

Intervention and management after childhood TBI may directly involve one-on-one therapy for the individual to manage adaptation and cognitions regarding their injury and PCS, stress-related factors, or early intervention regarding anxiety management strategies. In addition, it could include parenting work and family therapy regarding psychoeducation about TBI and symptomatology, but also targeting the vulnerability factors associated with anxiety such as family functioning, parental stress and anxiety, and how to effectively manage and respond to any behavioural differences exhibited by the child which may occur as a consequence of TBI. Existing research supports the use of behavioural and cognitive interventions for emerging behavioural issues after childhood TBI (Feeney & Ylvisaker,

2003), in addition to intensive family support for optimal outcomes (Braga, Paz Junior, & Ylvisaker, 2004). For the management of anxiety disorders, modified cognitive-behavioural therapy is also endorsed as being effective in managing anxiety-related symptomatology following TBI (Bryant, Moulds, Guthrie, & Nixon, 2003; Ponsford et al., 2016; Soo & Tate, 2009; Tiersky et al., 2005), however evidence is currently limited in younger samples.

7.9. Future Directions

As such, future work in this area should consider a number of directions. Outcomes related to TBI should be assessed in child and adolescent clinical samples given that thus far, children with TBI appear similar to individuals without TBI in these settings. In addition, further exploration of the long-term effects of mild, moderate and severe childhood TBI should be replicated with the utilisation of objective assessment measures for identifying TBI history (e.g. medical ED records, MR/CT findings and GCS scores) and the inclusion of informant reports and comprehensive assessments of difficulties to provide accurate identification and diagnosis of ongoing anxiety disorders in these individuals. Moreover, a replication of a longitudinal outcome study tracking anxiety disorders after childhood TBI is important, in combination with brain imaging techniques to identify any implicated brain regions, and in addition to the collection of pre-injury information. Finally, the inclusion of cognitive functioning and frontal lobe abilities as predictors for anxiety disorders following childhood TBI should be replicated, given the novel findings presented in the thesis. This would hopefully provide even further insight into delineating and deciphering the particular predictors, moderating factors and vulnerabilities specific to individuals with childhood TBI and ongoing anxiety disorders, to assist with the implementation of early intervention and management for these individuals.

7.10. General conclusions

There is a clear, 'at risk' group of individuals who may benefit from early management and intervention following TBI, including those with early moderate-severe TBI, females, and individuals suffering from difficulties with frontal lobe functioning. Given the importance of contextual factors in the manifestation of anxiety disorders, education should be provided to families and parents regarding the management and prognosis of TBI. Moreover, support from health care professionals is required in reference to accessing care for the child and parent intervention strategies. Given the burden on health care systems in relation to TBI and anxiety disorders, the implementation of preventative or intervention practices is imperative. The findings presented in this thesis will hopefully motivate and guide further work into the field of anxiety-related outcomes following childhood TBI, despite a relative lack of focus in extant literature.

In conclusion, mild, moderate and severe TBI sustained in childhood is associated with ongoing anxiety and other internalising symptomatology in adults. As such, anxiety disorders are an important outcome when considering children and adolescents with TBI, given the obvious impacts chronic anxiety can have on an individual. Difficulties with anxiety following TBI were found across all levels of severity, highlighting that even minor injuries should not be discounted when considering those who may require early assessment and intervention. Moreover, it appears that anxiety disorders may not immediately manifest following childhood TBI, but that early intervention is unequivocally important in this group, with the addition of contextual supports to buffer against risk factors that may increase a child's risk of ongoing difficulties. When considering base rates and premorbid functioning of children who sustain TBI, it has been discussed previously that anxiety may be underrepresented in a TBI population. As such, further focus in the research is required to

replicate these findings and consolidate an appropriate model to explain the manifestation of anxiety disorders following childhood TBI.

REFERENCES

Achenbach, T., Bernstein, A., & Dumenci, L. (2005). DSM-oriented scales and statistically based syndromes for ages 18 to 59: Linking taxonomic paradigms to facilitate multitaxonomic approaches. *Journal of Personality Assessment, 84*(1), 49-63. doi: 10.1207/s15327752jpa8401_10

Achenbach, T., McConaughy, S. H., & Howell, C. T. (1987). Child/adolescent behavioural and emotional problems: Implications of cross-informant correlations for situational specificity. *Psychological Bulletin, 10*(2), 213-232. doi: 10.1037/0033-29090.101.2.213

Achenbach, T., & Rescorla, L. (2003). *Manual for the ASEBA adult forms & profiles*. Burlington: VT University of Vermont, Research Centre for Children, Youth and Families.

Ahmed, S. P., Bittencourt-Hewitt, A., & Sebastian, C. L. (2015). Neurocognitive bases of emotion regulation development in adolescence. *Developmental Cognitive Neuroscience, 15*, 11-25. doi: 10.1016/j.dcn.2015.07.006

Airaksinen, E., Larsson, M., & Forsell, Y. (2005). Neuropsychological functions in anxiety disorders in population-based samples: Evidence of episodic memory dysfunction. *Journal of Psychiatric Research, 39*(2), 207-214. doi: 10.1016/j.jpsychires.2004.06.001

Albicini, M., & McKinlay, A. (2014). Mild traumatic brain injury: A review of terminology, symptomatology, clinical considerations and future directions. In F. Sadaka (Ed.), *Traumatic brain injury* (pp. 3-22). doi: 10.5772/57208

Albicini, M., & McKinlay, A. (2015). A systematic review of anxiety disorders following mild, moderate and severe TBI in children and adolescents. In F. Durbano (Ed.), *A fresh look at anxiety disorders* (pp. 199-224). doi: 10.5772/60426

Albicini, M., & McKinlay, A. (2017). Anxiety disorders in adults with childhood traumatic brain injury: Evidence of difficulties more than 10 years postinjury. *Journal of Head Trauma Rehabilitation* (*epub ahead of print)*. doi: 10.1097/HTR.0000000000000312

American Congress of Rehabilitation Medicine. (1993). Definition of mild traumatic brain injury. *Journal of Head Trauma Rehabilitation, 8*(3), 86-87. Retreieved from http://acrm.org/wp-content/uploads/pdf/tbidef_english_10-10.pdf

Anderson, V., & Beauchamp, M. (2012). SOCIAL: A theoretical model of developmental social neuroscience. In V. Anderson & M. Beauchamp (Eds.), *Developmental social neuroscience and childhood brain insult: Theory and practice* (pp. 3-20). New York: The Guildford Press.

Anderson, V., Brown, S., Newitt, H., & Hoile, H. (2009). Educational, vocational, psychosocial, and quality-of-life outcomes for adult survivors of childhood traumatic brain injury. *Journal of Head Trauma Rehabilitation, 24*(5), 303-312. doi: 10.1097/HTR.0b013e3181ada830

Anderson, V., Brown, S., Newitt, H., & Hoile, H. (2011). Long-term outcome from childhood traumatic brain injury: Intellectual ability, personality and quality of life. *Neuropsychology, 25*(2), 176-184. doi: 10.1037/a0021217

Anderson, V., Catroppa, C., Morse, S., Haritou, F., & Rosenfeld, J. (2005). Functional plasticity or vulnerability following early brain injury?. *Pediatrics, 116(*6), 1374-1382. doi: 10.1542/peds.2004-1728

Anderson, V., Godfrey, C., Rosenfeld, J., & Catroppa, C. (2011). 10 years outcome from childhood traumatic brain injury. *International Journal of Developmental Neuroscience, 30*(3), 217-224. doi: 10.1016/j.ijdevneu.2011.09.008

Anderson, V., Godfrey, C., Rosenfeld, J., & Catroppa, C. (2012). Predictors of cognitive function and recovery 10 years after traumatic brain injury in young children. *Pediatrics, 129*(2), e254-e261. doi: 10.1542/peds.2011-0311

Anderson, V., Spencer-Smith, M., & Wood, A. (2011). Do children really recover better? Neurobehavioural plasticity after early brain insult. *Brain, 134*(8), 2197-2221. doi:10.1093/brain/awr103

Andriessen, T., Horn, J., Franschman, G., van der Naalt, J., Haitsma, I., Jacobs, B., . . . Vos, P. E. (2011). Epidemiology, severity classification, and outcome of moderate and severe traumatic brain injury: A prospective multicenter study. *Journal of Neurotrauma, 28*(10), 2019-2031. doi: 10.1089/neu.2011.2034

Angold, A., Costello, E., & Worthman, C. (1998). Puberty and depression: The role of age, pubertal status and pubertal timing. *Psychological Medicine, 28*, 51-61. doi: 10.1017/S003329179700593X

Angold, A., Messer, S., Stangl, D., Farmer, E., Costello, E., & Burns, B. (1998). Perceived parental burden and service use for child and adolescent psychiatric disorders. *American Journal of Public Health*, *88*(1), 75-80. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1508410/

Arnsten, A. (2009). Stress signalling pathways that impair prefrontal cortex structure and function. *Nature Reviews Neuroscience, 10*(6), 410-422. doi: 10.1038/nrn2648

Baalen, B., Odding, E., Maas, A., Ribbers, G., Bergen, M., & Stam, H. (2003). Traumatic brain injury: Classification of initial severity and determination of functional outcome. *Disability and Rehabilitation, 25*(1), 9-18. doi: 10.1080/09638280210142266

Baird, A. A., Gruber, S. A., Fein, D. A., Maas, L. C., Steingard, R. J., Renshaw, P. F., . . . Yurgelun-Todd, D. A. (1999). Functional magnetic resonance imaging of facial affect

recognition in children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 38*(2), 195-199. doi: 10.1097/00004583-199902000-00019

Barker-Collo, S., Jones, K., Theadom, A., Starkey, N., Dowell, A., McPherson, K., . . . Feigin, V. (2015). Neuropsychological outcome and its correlates in the first year after adult mild traumatic brain injury: A population-based New Zealand study. *Brain Injury, 29*(13-14), 1604-1616. doi: 10.3109/02699052.2015.1075143

Barlow, D. H. (2000). Unraveling the mysteries of anxiety and its disorders from the perspective of emotion theory. *American Psychologist, 55*(11), 1247-1263. doi: 10.1037/0003-066X.55.11.1247

Bayer, J., Ukoumunne, O., Mathers, M., Wake, M., Abdi, N., & Hiscock, H. (2012). Development of children's internalising and externalising problems from infancy to five years of age. *Psychiatry, 46*(7), 659-668. doi: 10.1177/0004867412450076

Beauchamp, M., & Anderson, V. (2010). SOCIAL: An integrative framework for the development of social skills. *Psychological Bulletin, 136*, 39-64. doi: 10.1037/a0017768

Beauchamp, M., Ditchfield, M., Maller, J., Catroppa, C., Godfrey, C., Rosenfeld, J., . . . Anderson, V. (2011). Hippocampus, amygdala and global brain changes 10 years after childhood traumatic brain injury. *International Journal of Developmental Neuroscience, 29*(2), 137-143. doi: 10.1016/j.ijdevneu.2010.12.003

Beck, A., & Clark, D. (1997). An information processing model of anxiety: Automatic and strategic processes. *Behaviour Research and Therapy, 35*(1), 49-58. doi: 10.1016/S0005-7967(96)00069-1

Beesedo, K., Knappe, S., & Pine, D. (2009). Anxiety and anxiety disorders in children and adolescents: Developmental issues and implications for DSM-V. *Psychiatric Clinics of North America, 32*(3), 483-524. doi: 10.1016/j.psc.2009.06.002

Behar, E., DiMarco, I., Hekler, E., Mohlman, J., & Staples, A. (2009). Current theoretical models of generalised anxiety disorder (GAD): Conceptual review and treatment implications. *Journal of Anxiety Disorders, 23(*8), 1011-1023. doi: 10.1016/j.janxdis.2009.07.006

Bennett, S., & Walkup, J. (2016). *Anxiety disorders in children and adolescents: Epidemiology, pathogenesis, clinical manifestations and course*. Retrieved from http://www.uptodate.com/contents/anxiety-disorders-in-children-and-adolescents-epidemiology-pathogenesis-clinical-manifestations-and-course

Benton, A. L., Sivan, A. B., & Hamsher, K. (1994). *Contributions to neuropsychological assessment: A clinical manual* (2nd ed.). New York: Oxford University Press.

Berney, J., Favier, A., & Froidevaux, C. (1994). Pediatric head trauma: Infleunce of age and sex. I. Epidemiology. *Child's Nervous System, 10*(8), 509-516. doi: 10.1007/BF00335073

Berry, J., Jamieson, L., & Harrison, J. (2010). Head and traumatic brain injuries among Australian children, July 2000-June 2006. *Injury Prevention, 16*(3), 198-202. doi: 10.1136/ip.2009.022442

Berry, J., & Jones, W. (1995). The Parental Stress Scale: Initial psychometric evidence. *Journal of Social and Personal Relationships, 12*(3), 463-472. doi: 10.1177/0265407595123009

Beyond Blue. (2016). *Who does it affect?* Retrieved from https://www.beyondblue.org.au/who-does-it-affect/women

Bigler, E. (2007). Anterior middle crania fossa in traumatic brain injury: Relevant neuroanatomy and neuropathology in the study of neuropscyhological outcome. *Neuropsychology, 21*(5), 515-531. doi: 0.1037/0894-4105.21.5.515

Bigler, E., Abildskov, T., Petire, J., Farrer, T., Dennis, M., Simic, N., . . . Yeates, K. (2013). Heterogeneity of brain lesions in pediatric traumatic brain injury. *Neuropsychology, 27*(4), 438-451. doi: 10.1037/a0032837

Bogner, J. A., & Corrigan, J. (2009). Reliability and predictive validity of the Ohio State University TBI Identification Method with prisoners. *Journal of Head Trauma Rehabilitation, 24*(4), 279-291. doi: 10.1097/HTR.0b013e3181a66356

Bogner, J. A., & Corrigan, J. D. (2009). Reliability and predictive validity of the Ohio State University TBI Identification Method with prisoners. *Journal of Head Trauma Rehabilitation, 24*(4), 279-291. doi: 10.1097/HTR.0b013e3181a66356

Borg, J., Holm, L., Cassidy, J., Peloso, P., Carroll, L., von Holst, H., & Ericson, K. (2004). Diagnostic procedures in mild traumatic brain injury: Results of the WHO collaborating task force on mild traumatic brain injury. *Journal of Rehabilitation Medicine, 43(*Suppl), 61-75. doi: doi:10.1080/16501960410023822

Bouton, M., Mineka, S., & Barlow, D. H. (2001). A modern learning theory perspective on the etiology of panic disorder. *Psychological Review, 108*(1), 4-32. doi: 10.1037//0033-295X.108.1.4

Bowlby, J. (1973). *Attachment and loss, Vol 2. Separation: Anxiety and anger*. New York: Basic Books.

Braga, L., Paz Junior, A., & Ylvisaker, M. (2004). Direct clinician-delivered versus indirect family-supported rehabilitation of children with traumatic brain injury: A randomized control trial. *Brain Injury, 19*(10), 819-831. doi: 10.1080/02969905050011016 5

Brinks, V., deKloet, E., & Oitzl, M. (2008). Strain specific fear behaviour and gluccocorticoid response to aversive events: Modelling PTSD in mice. *Progress in Brain Research, 167*, 257-261. doi: 10.1016/S0079-6123(07)67019-8

Brown, G., Chadwick, O., Shaffer, D., Rutter, M., & Traub, M. (1981). A prospective study of children with head injuries: III. Psychiatric sequelae. *Psychological Medicine, 11*(1), 63-78. doi: 10.1017/S0033291700053289

Bruns Jr, J., & Hauser, W. (2003). The epidemiology of traumatic brain injury: A review. *Epilepsia: Official Journal of the International League Against Epilepsy*, *44*(10), 2-10. doi: 10.1046/j.1528-1157.44.s10.3.x

Bryant, R., Moulds, M., Guthrie, R., & Nixon, R. (2003). Treating acute stress disorder following mild traumatic brain injury. *The American Journal of Psychiatry, 160*(3), 585-587. doi: 10.1176/appi.ajp.160.3.585

Carvalho, J. O., Ready, R. E., Malloy, P. F., & Grace, J. (2013). Confirmatory factor analysis of the Frontal Systems of Behaviour Scale (FrSBe). *Assessment, 20*(5), 632-641. doi: 10.1177/1073191113492845

Cassidy, J., Carroll, L., Peloso, P., Borg, J., von Holst, H., Holm, L., . . . Coronado, V. (2004). Incidence, risk factors and prevention of mild traumatic brain injury: results of the who collaborating centre task force on mild traumatic brain injury. *Journal of Rehabilitation Medicine, 36*(43), 28-60. doi: 10.1080/16501960410023732

Castaneda, A. E., Suvisaari, J., Marttunen, M., Perala, J., Saarni, S. I., Aalto-Setala, T., . . . Tuulio-Henriksson, A. (2011). Cognitive functioning in a population-based sample of young adults with anxiety disorders. *European Psychiatry, 26*(6), 346-353. doi: 10.1016/j.eurpsy.2009.11.006

Castaneda, A. E., Tuulio-Henriksson, A., Marttunen, M., Suvisaari, J., & Lonnqvist, J. (2008). A review on cognitive impairments in depressive and anxiety disorders with a

focus on young adults. *Journal of Affective Disorders, 106*(1-2), 1-27. doi: 10.1016/j.jad.2007.06.006

Centers for Disease Control and Injury Prevention. (2006). *Heads up: Facts for physicians about mild traumatic brain injury*. Retrieved from http://www.brainlinemilitary.org/concussion_course/course_content/pdfs/mtbi.pdf

Centers for Disease Control and Injury Prevention. (2013). *Traumatic brain injury.* Retrieved from http://www.cdc.gov/TraumaticBrainInjury/

Centers for Disease Control and Injury Prevention. (2016). *Traumatic brain injury and concussion: Recovery.* Retrieved from https://www.cdc.gov/traumaticbraininjury/recovery.html

Chaves, C., Trzesniak, C., Derenusson, G., Araujo, D., Wichert-Ana, L., Machado-De-Sousa, J., . . . Hallak, J. (2012). Late-onset social anxiety disorder following traumatic brain injury. *Brain Injury, 26*(6), 882-886. doi: 10.3109/02699052.2012.666373

Chua, K., Ng, Y., Yap, S., & Bok, C. (2007). A brief review of traumatic brain injury rehabilitation. *Annals of the Academy of Medicine, 36*(1), 31-42. doi: 10.1.1.471.5931

Cisler, J., & Olatunji, B. (2012). Emotion regulation and anxiety disorders. *Current Psychiatry Reports, 14*(3), 182-187. doi: 10.1007/s11920-012-0262-2

Cisler, J., Olatunji, B., Feldner, M., & Forsyth, J. (2010). Emotion regulation and anxiety disorders: An integrative review. *Journal of Psychopathology and Behavioural Assessment, 32*(1), 68-82. doi: 10.1007/s10862-009-9161-1

Clark, L., Watson, D., & Mineka, S. (1994). Temperament, personality and the mood and anxiety disorders. *Journal of Abnormal Psychology, 103*(1), 103-116. doi: 10.1037/0021-843X.103.1.103

Cooper-Evans, S., Alderman, N., Knight, C., & Oddy, M. (2008). Self-esteem as a predictor of psychological distress after severe acquired brain injury: An exploratory study.

Neuropsychological Rehabilitation, 18(5-6), 607-626. doi: 10.3109/02699052.2012.666373

Corrigan, J., & Bogner, J. (2007). Initial reliability and validity of the OSU TBI Identification Method. *Journal of Head Trauma Rehabilitation, 22*(6), 318-322. doi: 10.1097/01.HTR.0000300227.67748.77

Corrigan, J., Bogner, J., & Holloman, C. (2012). Lifetime history of traumatic brain injury among persons with substance abuse disorders. *Brain Injury, 26*(2), 139-150. doi: 10.3109/02699052.2011.648705

Corrigan, J., Selassie, A., & Orman, J. (2010). The epidemiology of traumatic brain injury. *Journal of Head Trauma Rehabilitation, 25*(2), 72-80. doi: 10.1097/HTR.0b013e3181ccc8b4

Corrigan, J. D., & Bogner, J. A. (2007). Initial reliability and validity of the OSU TBI Identification Method. *Journal of Head Trauma Rehabilitation, 22*(6), 318-329. Doi: 10.1097/01.HTR.0000300227.67748.77

Costello, E., Copeland, W., & Angold, A. (2011). Trends in psychopathology across the adolescent years: What changes when children become adolscents, and when adolescents become adults? *Journal of Child Psychology and Psychiatry, 52*(10), 1015-1025. doi: 10.1111/j.1469-7610.2011.02446.x

Crowe, L., Babl, F., Anderson, V., & Catroppa, C. (2009). The epidemiology of paediatric head injuries: Data from a referral centre in Victoria, Australia. *Journal of Paediatric and Child Health, 45*(6), 346-350. doi: 10.1111/j.1440-1754.2009.01499.x

Daneman, M., & Carpenter, P. A. (1980). Individual differences in working memory and reading. *Journal of Verbal Learning and Verbal Behavior, 19*(4), 450-466. doi: 10.1016/S0022-5371(80)90312-6

De Los Rayes, A., & Kazdin, A. (2005). Informant discrepancies in the assessment of childhood psychopathology: A critical review, theoretical framework and recommendations for further study. *Psychological Bulletin, 131*(4), 483-509. doi: 10.1037/0033-2909.131.4.483

DeBellis, M., Casey, B., Dahl, R., Birmaher, B., Williamson, D., Thomas, K., . . . Ryan, N. (2000). A pilot study of amygdala volumes in pediatric generalized anxiety disorder. *Society of Biological Psychiatry, 48*(1), 51-57. doi: 10.1016/S0006-3223(00)00835-0

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan Executive Function System (D-KEFS).* San Antonio, TX: The Psychological Corporation.

Demellweek, C., Baldwin, T., Appleton, R., & Al-Kharusi, A. (2002). A prospective study and review of premorbid characteristics in children with traumatic brain injury. *Pediatric Rehabilitation, 5*(2), 81-89. doi: 10.1080/136384902320807194

Dick, R. (2009). Is there a gender difference in concussion incidence and outcomes?. *British Journal of Sports Medicine, 43*(Suppl I), i46-i50. doi: 10.1136/bjsm.2009.058172

Donders, J., & Warschausky, S. (2007). Neurobehavioural outcomes after early versus late childhood traumatic brain injury. *Journal of Head Trauma Rehabilitation, 22*(5), 296-302. doi: 10.1097/01.HTR.0000290974.01872.82

Dooley, J., Anderson, V., Hemphill, S., & Ohan, J. (2008). Aggression after pediatric traumatic brain injury: A theoretical approach. *Brain Injury, 22*(11), 836-846. doi: 10.1080/02699050802425444

Esselman, P., & Uomoto, J. (1995). Classification of the spectrum of mild traumatic brain injury. *Brain Injury, 9*(4), 417-424. doi: 10.3109/02699059509005782

Fay, T., Yeates, K., Wade, S., Drotar, D., Stancin, T., & Taylor, G. (2009). Predicting longitudinal patterns of functional deficits in children with traumatic brain injury. *Neuropsychology, 23*(3), 271-282. doi: 10.1037/a0014936

Feeney, T., & Ylvisaker, M. (2003). Context-sensitive behavioural supports for young children with TBI: Short-term effects and long-term outcome. *Journal of Head Trauma Rehabilitation, 18*(1), 33-51. doi: 10.1080/02699050600744194

Feigin, V., Theadom, A., Barker-Collo, S., Starkey, N., McPherson, K., Kahan, M., . . . Ameratunga, S. (2013). Incidence of traumatic brain injury in New Zealand: A population-based study. *The Lancet Neurology, 12*(1), 53-64. doi: 10.1016/S1474-4422(12)70262-4

Feingold, A. (1994). Gender differences in personality: A meta-analysis. *Psychological Bulletin, 116*(3), 429-456. doi: 10.1037/0033-2909.116.3.429

Felde, A., Westermeyer, J., & Thuras, P. (2009). Co-morbid traumatic brain injury and substance use disorder: Childhood predictors and adult correlates. *Brain Injury, 20*(1), 41-49. doi: 10.1080/02699050500309718

Fergusson, D., Boden, J., & Horwood, J. (2007). Exposure to single parenthood in childhood and later mental health, educational, economic, and criminal behaviour outcomes. *Archives of General Psychiatry, 64*(9), 1089-1095. doi: 10.1001/archpsyc.64.9.1089

Fergusson, D., Boden, J., & Horwood, J. (2009). Tests of causal links between alcohol dependence and major depression. *Archives of General Psychiatry, 66*(3), 260-266. doi: 10.1001/archgenpsychiatry.2008.543

Fergusson, D., McLeod, G., Horwood, J., Swain, N., Chapple, S., & Poulton, R. (2015). Life satisfaction and mental health problems (18 to 35 years). *Psychological Medicine, 45*(11), 2427-2436. doi: 10.1017/S00332917150000422

Fergusson, R., Mittenberg, W., Barone, D., & Schneider, B. (1999). Postconcussion syndrome following sports-related head injury: Expectation as etiology. *Neuropsychology, 13*(4), 582-589. doi: 10.1037//0894-4105.13.4.582

Forbes, C., Poore, J., Krueger, F., Barbey, A., Solomon, J., & Grafman, J. (2014). The role of executive function and the dorsolateral prefrontal cortex in the expression of neuroticism and conscientiousness. *Social Neuroscience, 9*(2), 139-151. doi: 10.1080/17470919.2013.871333

Ganesalingam, K., Yeates, K., Ginn, M., Taylor, G., Dietrich, A., Nuss, K., & Wright, M. (2008). Family burden and parental distress following mild traumatic brain injury in children and its relationship to post-concussive symptoms. *Journal of Pediatric Psychology, 33*(6), 621-629. doi: 10.1093/jpepsy/jsm133

Gerring, J., Slomine, B., Vasa, R., Grados, M., Chen, A., Rising, W., . . . Ernst, M. (2002). Clinical predictors of Posttraumatic Stress Disorder after closed head injury in children. *Journal of the American Academy of Child and Adolescent Psychiatry, 41*(2), 157-165. doi: 10.1097/00004583-200202000-00009

Gould, K., Ponsford, J., Johnston, L., & Schonberger, M. (2011). The nature, frequency and course of psychiatric disorders in the first year after traumatic brain injury: a prospective study. *Psychological Medicine, 41*(10), 2099-2109. doi: 10.1017/S003329171100033X

Gould, K., Ponsford, J., & Spitz, G. (2014). Association between cognitive impairments and anxiety disorders following traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology, 36*(1), 1-14. doi: 10.1080/13803395.2013.863832

Grace, J., & Malloy, P. F. (2001). *Frontal Systems Behaviour Scale (FrSBe) professional manual*. Odessa, Florida: Psychological Assessment Resources.

Grados, M., Vasa, R., Riddle, M., Slomine, B., Salorio, C., Christensen, J., & Gerring, J. (2008). New onset obsessive-compulsive symptoms in children and adolescents with severe traumatic brain injury. *Depression and Anxiety, 25*(5), 398-407. doi: 10.1002/da.20398

Greenwood, R. (2002). Head injury for neurologists. *Journal of Neurology, Neurosurgery and Psychiatry, 73* (Suppl I), i8-i16. doi: 10.1136/jnnp.73.suppl_1.i8

Hajek, C., Yeates, K., Taylor, G., Bangert, B., Dietrich, A., Nuss, K., . . . Wright, M. (2010). Relationships among post-concussive symptoms and symptoms of PTSD in children following mild traumatic brain injury. *Brain Injury, 24*(2), 100-109. doi: 10.3109/02699050903508226.

Hajek, C., Yeates, K., Taylor, G., Bangert, B., Dietrich, A., Nuss, K., . . . Wright, M. (2011). Agreement between parents and children on ratings of post-concussive symptoms following mild traumatic brain injury. *Child Neuropsychology, 17*(1), 17-33. doi: 10.1080/09297049.2010.495058

Hale, W., Raaijmakers, Q., Muris, P., van Hoof, A., & Meeus, W. (2008). Developmental trajectories of adolescent anxiety disorder symptoms: A 5-year prospective community study. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*(5), 556-564. doi: 10.1097/CHI.0b013e3181676583

Hawley, C. (2003). Reported problems and their resolution following mild, moderate and severe traumatic brain injury amongst children and adolescents in the UK. *Brain Injury, 17*(2), 105-129. doi: 10.1080/0269905021000010131

Hawley, C., Ward, A., & Magnay, J. (2004). Outcomes following childhood head injury: A population study. *Journal of Neurology, Neurosurgery and Psychiatry, 75*(5), 737-742. doi: 10.1136/jnnp.2003.020651

Herskovits, E., Gerring, J., Davatzikos, C., & Bryan, R. (2002). Is the spatial distribution of brain regions associated with closed head injury in children predictive of subsequent development of Post-Traumatic Stress Disorder?. *Radiology, 224*(2), 345-351. doi: 10.1148/radiol.2242011439

Hibbard, M., Bogdany, J., Uysal, S., Kepler, K., Silver, J., Gordon, W., & Haddad, L. (2000). Axis II psychopathology in individuals with traumatic brain injury. *Brain Injury, 14*(1), 45-61. doi: 10.1080/0269905001209161

Hoofien, D., Gilboa, A., Vakil, E., & Donovick, P. (2001). Traumatic brain injury (TBI) 10-20 years later: A comprehensive outcome study of psychiatric symptomtology, cognitive abilities and psychosocial functioning. *Brain Injury, 15*(3), 189-209. doi: 10.1080/026990501300005659

Iverach, L., O'Brian, S., Jones, M., Block, S., Lincoln, M., Harrison, E., . . . Onslow, M. (2009). Prevalence of anxiety disorders among adults seeking speech therapy for stuttering. *Journal of Anxiety Disorders, 23*(7), 928-934. doi: 10.1016/j.janxdis.2009.06.003

Iverson, G., Lange, R., Brooks, B., & Rennison, V. (2010). "Good old days" bias following mild traumatic brain injury. *The Clinical Neuropsychologist, 24*(1), 17-37. doi: 10.1080/13854040903190797

Iverson, G., Lovell, M., Smith, S., & Franzen, M. (2000). Prevalence of abnormal CT scans following mild head injury. *Brain Injury, 14*(12), 1057-1061. doi: 10.1080/02699050050203559

Jarros, R., Salum, G., da Silva, C., Toazza, R., Becker, N., Agranonik, M., . . . Manfro, G. (2017). Attention, memory, visuoconstructive, and executive task performance in adolescents with anxiety disorders: A case-control community study. *Trends in Psychiatry and Psychotherapy, 39*(1), 5-11. doi: 10.1590/2237-6089-2016-0032

Jonsson, C., Catroppa, C., Godfrey, C., Smedler, A., & Anderson, V. (2013). Individual profiles of predictors and their relations to 10 years outcome after childhood traumatic brain injury. *Brain Injury, 27*(7-8), 831-838. doi: 10.3109/02699052.2013.775493

Karver, C., Kurowski, B., Semple, E., Stancin, T., Taylor, G., Yeates, K., . . . Wade, S. (2014). Utilization of behavioural therapy services long-term after traumatic brain injury in young children. *Archives of Physical Medicine and Rehabilitation, 95*(8), 1556-1563. doi: 10.1016/j.ampr.2014.03.030

Karver, C., Wade, S., Cassedy, A., Taylor, G., Stancin, T., Yeates, K., & Walz, N. (2012). Age at injury and long-term behavior problems after traumatic brain injury in young children. *Rehabilitation Psychology, 57*(3), 256-265. doi: 10.1037/a0029522

Katon, W. (2003). Clinical health services relationships between major depression, depressive symptoms and general medical illness. *Society of Biological Psychiatry, 54*(3), 216-226. doi: 10.1016/S00006-3223(03)00273-7

Khan, F., Baguley, I., & Cameron, I. (2003). Rehabilitation after traumatic brain injury. *MJA Practice Essentials: Rehabilitation Medicine, 178*(6), 290-295. Retrieved from https://www.mja.com.au/system/files/issues/178_06_170303/kha11095_fm.pdf

Koenen, K. C., Moffitt, T., Roberts, A., Martin, L., Kubzansky, L., Harrington, H., . . . Caspi, A. (2009). Childhood IQ and adult mental disorders: A test of the cognitive reserve hypothesis. *American Journal of Psychiatry*, *166*(1), 50-57. doi: 10.1176/appi.ajp.2008.08030343

Konrad, K., Gauggel, S., Manz, A., & Scholl, M. (2000). Inhibitory control in children with traumatic brain injury (TBI) and children with attention deficit/hyperactivity disorder. *Brain Injury*, *14*(10), 859-875. doi: 10.1080/0296990500445691

Koponen, S., Taiminen, T., Portin, R., Himanen, L., Isoniemi, H., Heinonen, H., . . . Tenovuo, O. (2002). Axis I and II psychiatric disorders after traumatic brain injury: A 30-year follow-up study. *American Journal of Psychiatry, 159*(8), 1315-1321. doi: 10.1176/appi.ajp.159.8.1315

Kurowski, B., Wade, S., Kirkwood, M., Brown, P., Stancin, T., & Taylor, G. (2013). Behavioural predictors of outpatient mental health service utilization within 6 months after traumatic brain injury in adolescents. *American Academy of Physical Medicine and Rehabilitation, 5*(12), 1026-1034. doi: 10.1016/j.pmrj.2013.08.589

Ladouceur, R., Gosselin, P., & Dugas, M. (2000). Experimental manipulation of intolerance of uncertainty: A study of a theoretical model of worry. *Behaviour Research and Therapy, 38*(9), 933-941. doi: 10.1016/S0005-7967(99)00133-3

Lalloo, R. (2003). Risk factors for major injuries to the face and teeth. *Dental Traumatology, 19*(1), 12-14. doi: 10.1034/j.1600-9657.2003.00139.x

Lange, R., Iverson, G., & Rose, A. (2010). Post-concussion symptom reporting and the "good old days" bias following mild traumatic brain injury. *Archives of Clinical Neuropsychology, 26*(2), 127-137. doi: 10.1093/arclin/acq031

Lawrence, D., Johnson, S., Hafekost, J., Boterhoven de Haan, K., Sawyer, M., Ainley, J., & Zubrick, S. (2015). *The mental health of children and adolescents: Report on the second Australian Child and Adolescent Survey of Mental Health and Wellbeing*. Canberra: Department of Health. Retrieved from https://www.health.gov.au/internet/main/publishing.nsf/Content/9DA8CA21306FE6EDCA257E2700016945/$File/child2.pdf

Levi, R., Drotar, D., Yeates, K., & Taylor, G. (1999). Posttraumatic stress symptoms in children following orthopedic or traumatic brain injury. *Journal of Clinical Child Psychology, 28*(2), 232-243. doi: 10.1207/s15374424jccp2802_10

Levin, H., & Hanten, G. (2005). Executive functions after traumatic brain injury in children. *Pediatric Neurology, 33*(2), 79-93. doi: 10.1016/j.pediatrneurol.2005.02.002

Levin, H., Williams, D., Eisenberg, H., High Jr, W., & Guinto Jr, F. (1992). Serial MRI and neurobehavioural findings after mild to moderate closed head injury. *Journal of Neurology, Neurosurgery and Psychiatry, 55*(4), 255-262. doi: 10.1136/jnnp.55.4.255

Levine, B., Kovacevic, N., Nica, E., Cheung, G., Gao, F., Schwartz, M., & Black, S. (2008). The Torronto traumatic brain injury study. *Neurology, 70*(10), 771-778. doi: 10.1212/01.wnl.0000304108.32283.aa

Lewinsohn, P., Gotlib, I., Lewinsohn, M., Seeley, J., & Allen, N. (1998). Gender differences in anxiety disorders and anxiety symptoms in adolescents. *Journal of Abnormal Psychology, 107*(1), 109-117. doi: 10.1037/0021-843X.107.1.109

Lezak, M. D. (1995). *Neuropsychological assessment* (3rd ed.). New York: Oxford University Press.

Liu, J., & Li, L. (2013). Parent-reported mild head injury history and behavioural performance in children at 6 years. *Brain Injury, 27*(11), 1263-1270. doi: 10.3109/02699052.2013.804205

Luis, C., & Mittenberg, W. (2002). Mood and anxiety disorders following pediatric traumatic brain injury: A prospective study. *Journal of Clinical and Experimental Neuropsychology, 24*(3), 270-279. doi: 10.1076/jcen.24.3.270.982

Maas, A., Stochetti, N., & Bullock, R. (2008). Moderate and severe traumatic brain injury in adults. *The Lancet Neurology, 7*(8), 728-741. doi: 10.1016/s1474-4422(08)70164-9

Malloy, P. F., & Grace, J. (2005). A review of rating scales for measuring behaviour change due to frontal systems damage. *Cognitive Behavioural Neurology, 18*(1), 18-27. doi: 10.1097/10.wnn.0000152232.47901.88

Masel, B., & DeWitt, D. (2010). Traumatic brain injury: A disease process, not an event. *Journal of Neurotrauma, 27*(8), 1529-1540. doi: 10.1089/neu.2010.1358

Massagli, T., Fann, J., Burington, B., Jaffe, K., Katon, W., & Thompson, R. (2004). Psychiatric illness after mild traumatic brain injury in children. *Archives of Physical Medicine and Rehabilitation, 85*(9), 1428-1434. doi: 10.1016/j.apmr.2003.12.036

Mather, F., Tate, R., & Hannan, T. (2003). Post-traumatic stress disorder in children following road traffic accidents: a comparison of those with and without mild traumatic brain injury. *Brain Injury, 17*(12), 1077-1087. doi: 10.1080/0269905031000114045

Max, J., Castillo, C., Robin, D., Lindgren, S., Smith, W., Sato, Y., & Arndt, S. (1998). Posttraumatic stress symptomatology after childhood traumatic brain injury. *The Journal of Nervous and Mental Disease, 186*(10), 589-596. doi: 10.1097/00005053-199810000-00001

Max, J., & Dunisch, D. (1997). Traumatic brain injury in a child psychiatry outpatient clinic: A controlled study. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*(3), 404-411. doi: 10.1097/00004583-199703000-00020

Max, J., Friedman, K., Wilde, E., Bigler, E., Hanten, G., Schachar, R., . . . Levin, H. (2015). Psychiatric disorders in children and adolescents 24 months after mild traumatic brain injury. *Journal of Neuropsychiatry and Clinical Neuroscience, 27*(2), 112-120. doi: 10.1176/appi.neuropsych.13080190

Max, J., Keatley, E., Wilde, E., Bigler, E., Levin, H., Schachar, R., . . . Yang, T. (2011). Anxiety disorders in children and adolescents in the first six months after traumatic brain injury. *The Journal of Neuropsychiatry and Clinical Neurosciences, 23*(1), 29-39. doi: 10.1176/jnp.23.1.jnp29

Max, J., Lopez, A., Wilde, E., Bigler, E., Schachar, R., Saunders, A., . . . Levin, H. (2015). Anxiety disorders in children and adolescents in the second six months after traumatic

brain injury. *Journal of Pediatric Rehabilitation Medicine, 1*(8), 345-355. doi: 10.3233/PRM-150352

Max, J., Robin, D., Lindgren, S., Smith Jr, W., Sato, Y., Mattheis, P., . . . Castillo, C. (1997). Traumatic brain injury in children and adolescents: Psychiatric disorders at two years. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*(9), 1278-1285. doi: 10.1097/00004583-199709000-00021

Max, J., Schachar, R., Landis, J., Bigler, E., Wilde, E., Saunders, A., . . . Levin, H. (2013). Psychiatric disorders in children and adolescents in the first six months after mild traumatic brain injury. *Journal of Neuropsychiatry and Clinical Neuroscience, 25*(3), 187-197. doi: 10.1176/appi.neuropsych.12010011

Max, J., Sharma, A., & Qurashi, M. (1997). Traumatic brain injury in a child psychiatry inpatient population: A controlled study. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*(11), 1595-1601. doi: 10.1016/S0890-8567(09)66570-9

Max, J., Smith Jr, W., Lindgren, S., Robin, D., Mattheis, P., Stierwalt, J., & Morrisey, M. (1995). Case study: Obsessive-compulsive disorder after severe traumatic brain injury in an adolescent. *Journal of the American Academy of Child and Adolescent Psychiatry, 34*(1), 45-49. doi: 10.1097/00004583-199501000-00012

Max, J., Wilde, E., Bigler, E., MacLeod, M., Vasquez, A., Schmidt, A., . . . Levin, H. (2012). Psychiatric disorders after pediatric traumatic brain injury: A prospective, longitudinal, controlled study. *Journal of Neuropsychiatry and Clinical Neuroscience, 24*(4), 427-436. doi: 10.1176/appi.neuropsych.12060149

McClean, C., Asnaani, A., Litz, B., & Hofmann, S. (2011). Gender differences in anxiety disorders: Prevalence, course of illness, comorbidity and burden of illness. *Journal of Psychiatric Research, 45*(8), 1027-1035. doi: 10.1016/j.psychires.2011.03.006

McKinlay, A. (2010). Controversies and outcomes associated with mild traumatic brain injury in childhood and adolescents. *Child Care and Health Development, 36*(1), 3-21. doi: 10.1111/j.1365-2214.2009.01006.x

McKinlay, A. (2014). Long-term outcomes of traumatic brain injury in early childhood. *Australian Psychologist, 49*(6), 323-327. doi: 10.1111/ap.12084

McKinlay, A., Corrigan, J., Horwood, J., & Fergusson, D. (2014). Substance abuse and criminal activities following traumatic brain injury in childhood, adolescence and early adulthood. *Journal of Head Trauma Rehabilitation, 29*(6), 498-506. doi: 10.1097/HTR.0000000000000001

McKinlay, A., Dalrymple-Alford, J., Horwood, J., & Fergusson, D. (2002). Long-term psychosocial outcomes after mild head injury in early childhood. *Journal of Neurology, Neurosurgery and Psychiatry, 73*(3), 281-288. doi: 10.1136/jnnp.73.3.281

McKinlay, A., Grace, R., Horwood, J., Fergusson, D., & MacFarlane, M. (2009). Adolescent psychiatric symptoms following preschool childhood mild traumatic brain injury: Evidence from a birth cohort. *Journal of Head Trauma Rehabilitation, 24*(3), 221-227. doi: 10.1097/HTR.0b013e3181a40590

McKinlay, A., Grace, R., Horwood, J., Fergusson, D., & MacFarlane, M. (2010). Long-term behavioural outcomes of pre-school mild traumatic brain injury. *Child Care and Health Development, 36*(1), 22-30. doi: 10.1111/j.1365-2214.2009.00947.x

McKinlay, A., Grace, R., Horwood, J., Fergusson, D., Riddler, E., & MacFarlane, M. (2008). Prevalence of traumatic brain injury among children, adolescents and young adults: Evidence from a birth cohort. *Brain Injury, 22*(2), 175-181. doi: 10.1080/02699050801888824

McKinlay, A., & Hawley, C. (2014). *Incidence rates for traumatic brain injury in children*. Retrieved from http://www.internationalbrain.org/incidence-rates-for-traumatic-brain-injury-in-children/

McKinlay, A., & Horwood, J. (2016). The accuracy of adult recall for early mild traumatic brain injury. *Disability and Rehabilitation, 39*(13), 1296-1299. doi: 10.1080/09638288.2016.1193905

McKinlay, A., Kyona, E., Grace, R., Horwood, J., Fergusson, D., & MacFarlane, M. (2010). An investigation of the pre-injury risk factors associated with children who experience traumatic brain injury. *Injury Prevention, 16*(1), 31-35. doi: 10.1136/ip.2009.022483

Mendlowicz, M., & Stein, M. (2000). Quality of life in individuals with anxiety disorders. *American Journal of Psychiatry, 157*(5), 669-682. doi: 10.1176/appi.ajp.157.5.669

Mennin, D. S., Heimberg, R., & Fresco, D. (2002). Applying an emotion regulation framework to integrative approaches to generalised anxiety disorder. *Clinical Psychology: Science and Practice, 9*(1), 85-90. doi: 10.1093/clipsy.9.1.85

Mineka, S., & Zinbarg, R. (2006). A contemporary learning theory perspective on the etiology of anxiety disorders. *American Psychologist, 61*(1), 10-26. doi: 10.1037/0003-066X.61.1.10

Moffitt, T., Caspi, A., Harrington, H., Milne, B., Melchior, M., Goldberg, D., & Poulton, R. (2007). Generalized anxiety disorder and depression: Childhood risk factors in a birth cohort followed to age 32. *Psychological Medicine, 37*(3), 441-452. doi: 10.1017/S0033291706009640

Moore, A., & Stambrook, M. (1991). Cognitive moderators in adjustment to chronic illness: Locus of control beliefs following traumatic brain injury. *Neuropsychological Rehabilitation, 1*(3), 185-198. doi: 10.1080/09602019108520164

Moore, A., & Stambrook, M. (1992). Coping strategies and locus of control following traumatic brain injury: Relationship to long-term outcome. *Brain Injury, 6*(1), 89-94. doi: 10.3109/02699059209008129

Moore, E., Terryberry-Spohr, L., & Hope, D. (2006). Mild traumatic brain injury and anxiety sequelae: A review of the literature. *Brain Injury, 20*(2), 117-132. doi: 10.1080/02699050500443558

Moritz, S., Kuelz, A., Jacobsen, D., Kloss, M., & Fricke, S. (2006). Severity of subjective cognitive impairment in patients with obsessive-compulsive disorder and depression. *Journal of Anxiety Disorders, 20*(4), 427-443. doi: 10.1016/j.janxdis.2005.04.001

Neumann, C., & Pardini, D. (2014). Factor structure and construct validity of the self-report psychopathology (SRP) scale and the youth psychopathic traits inventory (YPI) in young men. *Journal of Personality Disorders, 28*(3), 419-433. doi: 10.1521/pedi_2012_26_063

Nguyen, R., Fiest, K., McChesney, J., Kwon, C., Jette, N., Frolkis, A., . . . Gallagher, C. (2016). The international incidence of traumatic brain injury: A systematic review and meta-analysis. *Canadian Journal of Neurological Sciences, 43*(6), 774-785. doi: 10.1017/cjn.2016.290

Nishizawa, S., Benkelfat, C., Young, S., Leyton, M., Mzengeza, S., de Montigny, C., . . . Diksic, M. (1997). Differences between males and females in rates of serotonin synthesis in human brain. *Proceedings of the National Academy of Sciences, 94*(10), 5308-5313. Retrieved from http://www.pnas.org/content/94/10/5308.full.pdf

Nivard, M., Lubke, G., Dolan, C., Evans, D., Pourcain, B., Munafo, M., & Middledorp, C. (2016). Joint developmental trajectories of internalising and externalising disorders between childhood and adolescence. *Development and Psychopathology, 29*(3), 919-928. doi: 10.1017/S0954579416000572

Ohio Valley Center for Brain Injury Prevention and Rehabilitation. (no date). *Screening for TBI: A snap shot from OVC*. Retrieved from http://ohiovalley.org/informationeducation/screening/

Olfson, M., Druss, B., & Marcus, S. (2015). Trends in mental health care among children and adolescents. *The New England Journal of Medicine, 372*(21), 2029-2038. doi: 10.1056/NEJMsa1413512

Paus, T., Keshavan, M., & Giedd, J. (2008). Why do many psychiatric disorders emerge during adolescence?. *Nature Reviews Neuroscience, 9*(12), 947-957. doi: 10.1038/nm2513

Pericall, M., & Taylor, E. (2014). Family function and its relationship to injury severity and psychiatric outcome in children with acquired brain injury: A systematised review. *Developmental Medicine and Child Neurology, 56*(1), 19-30. doi: 10.1111/dmcn.12237

Peterson, R., Kirkwood, M., Taylor, G., Stancin, T., Brown, T., & Wade, S. (2013). Adolescents' internalising problems following traumatic brain injury are related to parents' psychiatric symptoms. *Journal of Head Trauma Rehabilitation, 28*(5), E1-12. doi: 10.1097/HTR.0b013e318263f5ba

Polanczyk, G., Salum, G., Sugaya, L., Caye, A., & Rohde, L. (2015). Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *Journal of Child Psychology and Psychiatry, 56*(3), 345-365. doi: 10.1111/jcpp.12381

Ponsford, J., Draper, K., & Schonberger, M. (2008). Functional outcome 10 years after traumatic brain injury: Its relationship with demographic, injury severity, and cognitive and emotional status. *Journal of the International Neuropsychological Society, 14*(2), 233-242. doi: 10.10170S1355617708080272

Ponsford, J., Lee, N., Wong, D., McKay, A., Haines, K., Downing, M., . . . O'Donnel, M. (2016). Efficacy of motivational interviewing and cognitive behavioural therapy for anxiety and depression symptoms following traumatic brain injury. *Psychological Medicine, 46*(5), 1079-1090. doi: 10.1017/S0033291715002640

Popernack, M., Gray, N., & Reuter-Rice, K. (2015). Moderate-to-severe traumatic brain injury in children: Complications and rehabilitation strategies. *Journal of Pediatric Health Care, 29*(3), e1-e7. doi: 10.1016/j.pedhc.2014.09.003

Povlishock, J., & Katz, D. (2005). Update of neuropathology and neurological recovery after traumatic brain injury. *Journal of Head Trauma Rehabilitation, 20*(1), 76-94. doi: 10.1097/00001199-200501000-00008

Rao, V., Rosenberg, P., Bertrand, M., Salehinia, S., Spiro, J., Vaishnavi, S., . . . Miles, Q. (2009). Aggression after traumatic brain injury: Prevalence and correlates. *The Journal of Neuropsychiatry and Clinical Neurosciences, 21*(4), 420-429. doi: 10.1176/appi.neuropsych.21.4.420

Reed, V., Gander, F., Pfister, H., Steiger, A., Sonntag, H., Trenkwalder, C., . . . Wittchen, H. (1998). To what degree does the Composite International Diagnostic Interview (CIDI) correctly identify DSM-IV disorders? Testing validity issues in a clinical sample. *Psychiatric Research, 7*(3), 142-155. doi: 10.1002.mpr/44

Rosema, S., Muscara, F., Anderson, V., Godfrey, C., Eren, S., & Catroppa, C. (2014). Agreement on and predictors of long-term psychosocial development 16 years post-childhood traumatic brain injury. *Journal of Neurotrauma, 31*(10), 899-905. doi: 10.1089/neu.2013.3226

Rosema, S., Muscara, F., Anderson, V., Godfrey, C., Hearps, S., & Catroppa, C. (2015). The trajectory of long-term psychosocial development 16 years following childhood

traumatic brain injury. *Journal of Neurotrauma*, *32*(13), 976-983. doi: 10.1089/neu.2014.3567

Rosenbaum, J., Biederman, J., Bolduc-Murphy, E., Faraone, S., Chaloff, J., Hirshfield, D., & Kagan, J. (1993). Behavioural inhibition in childhood: A risk factor for anxiety disorders. *Harvard Review of Psychiatry*, *1*(1), 2-16. doi: 10.3109/10673229309017052

Rotondi, A., Sinkule, J., Balzer, K., Harris, J., & Moldovan, R. (2007). A qualitative needs assessment of persons who have experienced traumatic brain injury and their primary family caregivers. *Journal of Head Trauma Rehabilitation*, *22*(1), 14-25. doi: 10.1097/0000119-200701000-00002

Roy-Byrne, P., Davidson, K., Kessler, R., Asmundson, G., Goodwin, R., Kubzansky, L., . . . Stein, M. (2008). Anxiety disorders and comorbid medical illness. *General Hospital Psychiatry*, *30*(3), 208-225. doi: 10.1016/j.genhosppsych.2007.12.006

Rutgers, D., Toulgoat, F., Cazejust, J., Fillard, P., Lasjaunias, P., & Ducreux, D. (2008). White matter abnormalities in mild traumatic brain injury: a diffusion tensor imaging study. *American Journal of Neuroradiology*, *29*(3), 514-519. doi: 10.3174/ajnr.A0856

Ryan, N., Anderson, V., Godfrey, C., Beauchamp, M., Coleman, L., Eren, S., . . . Catroppa, C. (2014). Predictors of very-long-term sociocognitive function after pediatric traumatic brain injury: Evidence for the vulnerability of the immature "social brain". *Journal of Neurotrauma*, *31*(7), 649-657. doi: 10.1089/neu.2013.3153

Ryan, N., Catroppa, C., Cooper, J., Beare, R., Ditchfield, M., Coleman, L., . . . Anderson, V. (2014). The emergence of age-dependent social cognitive deficits after generalised insult to the developing brain: A longitudinal prospective analysis using susceptibility-weighted imaging. *Human Brain Mapping*, *36*(5), 1677-1691. doi: 10.1002/hbm.22729

Satz, P. (2001). Mild head injury in children and adolescents. *Current Directions in Psychological Science, 10*(3), 106-109. doi: 10.1111/1467-8721.00127

Schimmenti, A., & Bifulco, A. (2013). Linking lack of care in childhood to anxiety disorders in emerging adulthood: The role of attachment styles. *Child and Adolescent Mental Health*, *20*(1), 41-48. doi: 10.1111/camh.12051

Schonberger, M., Humle, F., & Teasdale, T. (2006). Subjective outcome of brain injury rehabilitation in relation to the therapeutic working alliance, client compliance and awareness. *Brain Injury, 20*(12), 1271-1282. doi: 10.1080/02699050601049395

Schwartz, L., Taylor, G., Drotar, D., Yeates, K., Wade, S., & Stancin, T. (2003). Long-term behavior problems following pediatric traumatic brain injury: Prevalence, predictors and correlates. *Journal of Paediatric Psychology, 28*(4), 251-263. doi: 10.1093/jpepsy/jsg013

Scott, C., McKinlay, A., McLellan, T., Britt, E., Grace, R., & McFarlane, M. (2015). A comparison of adult outcomes for males compared to females following pediatric traumatic brain injury. *Neuropsychology, 29*(4), 501-508. doi: 10.1037/neu0000074

Seeman, M. (1997). Psychopathology in women and men: Focus on female hormones. *American Journal of Psychiatry*, *154*(4), 501-508. doi: 10.1176/ajp.154.12.1641

Sigurdardottir, S., Andelic, N., Roe, C., Jerstad, T., & Schanke, A. (2009). Post-concussion symptoms after traumatic brain injury at 3 and 12 months post-injury: A prospective study. *Brain Injury*, *23*(6), 489-497. doi: 10.1080/02699050902926309

Sonnenberg, L., Dupuis, A., & Rumney, P. (2010). Pre-school traumatic brain injury and its impact on social development at 8 years of age. *Brain Injury, 24*(7-8), 1003-1007. doi: 10.3109/02699052.2010.489033

Soo, C., & Tate, R. (2009). Psychological treatment for anxiety in people with traumatic brain injury (review). *Cochrane Database of Systematic Reviews, 18*(3), 1-22. doi: 10.1002/14651858.CD005239

Stenberg, M., Godbolt, A., de Boussard, C., Levi, R., & Stalnacke, B. (2015). Cognitive impairment after severe traumatic brain injury, clinical course and impact on outcome: A Swedish-Icelandic study. *Behavioural Neurology, 3,* 1-12. doi: 10.1155/2015/680308

Stout, J., Ready, R. E., Grace, J., Malloy, P. F., & Paulsen, J. (2003). Factor analysis of the Frontal Systems Behaviour Scale (FrSBe). *Assessment, 10*(1), 79-85. doi: 10.1177/1073191102250339

Suhr, J., & Gunstad, J. (2002). "Diagnosis threat": The effect of negative expectations on cognitive performance in head injury. *Journal of Clinical and Experimental Neuropsychology, 24*(4), 448-457. doi: 10.1076/jcen.24.4.448.1039

Susman, E., Nottelmann, E., Inoff-Germain, G., Dorn, L., Cutler, G., Loriaux, D., & Chrousos, G. (1985). The relation of relative hormonal levels and physical development and social-emotional behaviour in young adolescents. *Journal of Youth and Adolescence, 14*(3), 245-264. doi: 10.1007/BF02090322

Taylor, G., & Alden, J. (1997). Age-related differences in outcomes following childhood brain insults: An introduction and overview. *Journal of the International Neuropsychological Society, 3*(6), 555-567. Retrieved from https://www.researchgate.net/profile/H_Taylor/publication/13783081_Age-related_differences_in_outcomes_following_childhood_brain_insults_An_introduction_and_overview/links/5555e07908ae6fd2d82297d9/Age-related-differences-in-outcomes-following-childhood-brain-insults-An-introduction-and-overview.pdf

Teasdale, T., Christensen, A., Willmes, K., Deloche, G., Braga, L., Stachowiak, F., . . . Leclercq, M. (1997). Subjective experience in brain injured patients and their close relatives: A European Brain Injury Questionnaire study. *Brain Injury, 11*(8), 543-564. doi: 10.1080/026990597123250

Teasdale, T., & Enberg, A. (2005). Subjective well-being and quality of life following traumatic brain injury in adults: A long-term population-based follow-up. *Brain Injury, 19*(12), 1041-1048. doi: 10.1080/02699050500110397

Tiersky, L., Anselmi, V., Johnston, M., Kurtyka, J., Roosen, E., Schwartz, T., & DeLuca, J. (2005). A trial of neuropsychologic rehabilitation in mild-spectrum traumatic brain injury. *Archives of Physical Medicine and Rehabilitation, 86*(8), 1565-1574. doi: 10.1016/j.ampr.2005.03.013

Umile, E., Sandel, M., Alavi, A., Terry, C., & Plotkin, R. (2002). Dynamic imaging in mild traumatic brain injury: Support for the theory of medial temporal vulnerability. *Archives of Physical Medicine and Rehabilitation, 83*(11), 1506-1513. doi: 10.1053/apmr.2002.35092

Van Ameringen, M., Mancini, C., & Farvolden, P. (2003). The impact of anxiety disorders on educational achievement. *Journal of Anxiety Disorders, 17*(5), 561-571. doi: 10.1016/S0887-6185(02)00228-1

Vanderploeg, R., Curtiss, G., Luis, C., & Salazar, A. (2007). Long-term morbidities following self-reported mild traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology, 29*(6), 585-598. doi: 10.1080/13803390600826587

Vasa, R., Gerring, J., Grados, M., Slomine, B., Christensen, J., Rising, W., . . . Riddle, M. (2002). Anxiety after severe pediatric closed head injury. *Journal of the American Academy of Child and Adolescent Psychiatry, 41*(2), 148-156. doi: 10.1097/00004583-200202000-00008

Vasa, R., Grados, M., Slomine, B., Herskovits, E., Thompson, R., Salorio, C., . . . Gerring, J. (2004). Neuroimaging correlates of anxiety after pediatric traumatic brain injury. *Biological Psychiatry, 55*(3), 208-216. doi: 10.1016/s0006-3223(03)00708-x

Vasa, R., Suskauer, S., Thorn, J., Kalb, L., Grados, M., Slomine, B., . . . Gerring, J. (2015). Prevalence and predictors of affective lability after pediatric traumatic brain injury. *Brain Injury, 29*(7-8), 921-928. doi: 10.3109/02699052.2015.1005670

Wechsler, D. (1997). *Wechsler Memory Scale* (3rd ed.). San Antonio, TX: Pearson.

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence*. New York, NY: The Psychological Corporation, Harcourt Brace and Company.

Werheid, K., Hoppe, C., Thöne, A., Müller, U., Müngersdorf, M., & von Cramon, D. Y. (2002). The Adaptive Digit Ordering Test: Clinical application, reliability, and validity of a verbal working memory test. *Archives of Clinical Neuropsychology, 17*(6), 547-565. doi: 10.1016/S0887-6177(01)00134-2

Wilde, E., Bigler, E., Hunter, J., Fearing, M., Scheibel, R., Newsome, M., . . . Levin, H. (2007). Hippocampus, amygdala and basal ganglia morphometrics in children after moderate-to-severe traumatic brain injury. *Developmental Medicine and Child Neurology, 49*(4), 294-299. doi: 10.1111/j.1469-8749.2007.00294.x

Williams, A., Ling, G., & Tortella, F. (2006). Severity level and injury track determine outcome following a penetrating ballistic-like brain injury in the rat. *Neuroscience Letters, 408*(3), 183-188. doi: 10.1016/j.neulet.2006.08.086

Williams, W., Cordan, G., Mewse, A., Tonks, J., & Burgess, C. (2010). Self-reported traumatic brain injury in male young offenders: A risk factor for re-offending, poor mental health and violence?. *Neuropsychological Rehabilitation, 20*(6), 801-812. doi: 10.1080/09602011.2010.519613

Wittchen, H. (1994). Reliability and validity studies of the WHO-Composite International Diagnostic Interview (CIDI): A critical review. *Journal of Psychiatric Research, 28*(1), 57-84. doi: 10.1016./0022-3956(94)90036-1

Wittchen, H., Nelson, C., & Lachner, G. (1998). Prevalence of mental disorders and psychosocial impairments in adolescents and young adults. *Psychological Medicine, 28*(1), 109-126. doi: 10.1017/S0033291797005928

Woodward, L., & Fergusson, D. (2001). Life course outcomes of young people with anxiety disorders in adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry, 40*(9), 1086-1093. doi: 10.1097/00004583-200109000-00018

World Health Organisation. (1990). *Composite International Diagnostic Interview (CIDI)*. Geneva: World Health Organisation.

Yeates, K., Armstrong, K., Janusz, J., Taylor, G., Wade, S., Stancin, T., & Drotar, D. (2005). Long-term attention problems in children with traumatic brain injury. *Journal of the American Academy of Child and Adolescent Psychiatry, 44*(6), 574-584. doi: 10.1097/01.chi.0000159947.50523.64

Yeates, K., Swift, E., Taylor, G., Wade, S., Drotar, D., Stancin, T., & Minich, N. (2004). Short- and long-term social outcomes following pediatric traumatic brain injury. *Journal of the International Neuropsychological Society, 10*(3), 412-426. doi: 10.1017/S1355617704103093

Zimmermann, P., Wittchen, H., Hofler, M., Pfister, H., Kessler, R., & Lieb, R. (2003). Primary anxiety disorders and the development of subsequent alcohol use disorders: A 4-year community study of adolescents and young adults. *Psychological Medicine, 33*(7), 1211-1222. doi: 10.1017/S0033291703008158

Zonfrillo, M., Durbin, D., Koepsell, T., Wang, J., Temkin, N., Dorsch, A., . . . Rivara, F. (2014). Prevalence of and risk factors for poor functioning after isolated mild

traumatic brain injury in children. *Journal of Neurotrauma, 31*(8), 722-727. doi: 10.1089/neu.2013.3088

LIST OF APPENDICES

Chapter 10

A Systematic Review of Anxiety Disorders following Mild, Moderate and Severe TBI in Children and Adolescents

Michelle Albicini and Audrey McKinlay

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/60426

Abstract

The aim of this chapter is to systematically review the research exploring the relationship between TBI and anxiety disorders in children and adolescents. A literature search was conducted using Google Scholar, Ovid Medline (1946 - Dec 2013), PsycINFO (1806 - Dec 2013), CINAHL plus (1937 - Dec 2013), Cochrane database (2005 – Dec 2013) and Embase (1946 – Dec 2013). The search returned 346 articles, and 11 of these met the inclusion criteria. Anxiety disorders were often found to be a negative outcome following childhood TBI, with a higher incidence of disorders including GAD, ASD, PTSD, PD, OCD, simple/specific phobia, social phobia and SAD found in children following their injury. In most cases, this relationship was strongest for children with severe TBI who sustained their injury at a younger age. Psychosocial adversity was found to be a consistently significant predictor for the likelihood of children developing anxiety following TBI. It is concluded that children who have suffered from a TBI (mild, moderate or severe), are at a higher risk of developing subsequent anxiety disorders, even 1 year following the injury event, and children with more severe injuries, greater psychosocial adversity, and younger age at injury are considered to be the most vulnerable.

Keywords: traumatic brain injury, children, adolescents, anxiety disorders, risk factors

1. Introduction

Traumatic brain injury (TBI) is a common cause of morbidity and mortality worldwide, with prevalence estimates of 235 per 100,000 individuals in European countries having some form of TBI [1] and for children in particular, rates vary between 280-1373 per 100,000 across the world [2]. Considering the high rates of injury in children and young people, any accompanying long-term negative effects associated with such an injury are likely to represent a significant health concern and burden. Indeed, it is now well-documented that children with TBI may be at an increased risk of long-term, self-reported externalising behavioural problems including increased hyperactivity, aggression and conduct problems [3-8]. In addition to externalising behaviours, a higher incidence of diagnosed psychiatric disorders in children and adolescents following a TBI event has also been established, including Attention Deficit/Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), Conduct Disorder (CD), drug abuse, and personality change disorders [9-10], compared to healthy controls and children with orthopedic injury (OI; an injury, such as fracture or break, to the bones excluding the head, neck or spinal cord [11]). In light of these ongoing problems children and young people may face following their TBI, a review and investigation is required to better understand the need for rehabilitation and recovery, and to understand the children at risk of these long-term effects.

2. Defining traumatic brain injury

Traumatic brain injury (TBI) is defined as an injury to the head as a result of a blow or movement to the head and/or neck, following acceleration/deceleration impact, which causes neurological changes that affect normal brain functioning [12]. Severity of TBI therefore refers to the extent of neurological disruption that has occurred, and is classified as mild, moderate and severe [13]. The assessment of TBI severity is measured by the Glasgow Coma Scale (GCS), length of post-traumatic amnesia (PTA) and duration of loss of consciousness (LOC) [14-16]. The GCS is considered the best indicator of TBI severity, and evaluates three areas, including best motor and verbal responses, and eye opening [17]. Table 1 outlines the levels of severity for TBI and the respective definitions.

Mild TBI	Moderate TBI	Severe TBI
GCS = > 13 after 30 minutes	GCS = 9-13	GCS = ≤8
LOC = < 30 minutes	LOC = 30 minutes to 24 hours	LOC = > 24 hours
PTA = < 1 day	PTA = between 1 and 7 days	PTA = > 7 days

Note: Information in [13-14, 18]; GCS = Glasgow Coma Scale, LOC = loss of consciousness, PTA = post-traumatic amnesia.

Table 1. Defining severity levels of TBI

http://dx.doi.org/10.5772/60426

2.1. Research findings

While it has been established that TBI is associated with an increased rate of externalising behavioural problems, there is a lack in the research exploring the incidence of internalising disorders, and in particular anxiety, following TBI in children. A couple of case studies report on individuals who developed new-onset anxiety symptomatology following TBI, which highlight the need for research in the area. For instance, an 11 year-old girl sustained a severe TBI following a fall from her bicycle, resulting in a coma for 16 days, and following resolution of PTA symptoms, the patient had developed new-onset compulsive behaviours including hand-washing, ordering, arranging and counting rituals [19]. Moreover, the symptoms appeared to worsen at a 6 month follow-up, which was subsequently treated with antidepressant medication [19]. Similarly, another case study reports on a patient who suffered from TBI requiring surgery at the age of 17 years, who reported the onset of social anxiety disorder (SAD) following their injury [20]. The male was previously characterised as extroverted and displayed no evidence of social anxiety. However, following the injury he became socially anxious which worsened until he sought treatment at 21 years, reporting difficulties with authority figures, unknown persons and people of the opposite sex [20]. Both of these aforementioned studies above highlight the important role of the frontal regions of the brain in that their damage following injury may precipitate anxiety symptomatology that is ongoing and requiring treatment or intervention [19-20].

Research exploring the incidence of novel post-injury psychiatric disorders and behavioural problems following TBI in children suggests a greater need for information about the onset of anxiety disorders in the TBI population. There have been reports of rates of novel anxiety disorders in 15% of children with TBI compared to 7.5% of an OI control group [10]. Further, anxiety has been found to occur in higher rates than ADHD and ODD [10]. In children with mild TBI, up to 36% of individuals have been found to exhibit specific anxiety disorders 6-months post-injury [9]. This finding is also evident in other samples for children with mild-TBI, with increased rates on anxious/depressed self-report items on a behavioural rating scale as compared to children with no injury [4]. Others however have reported on different findings. For instance, in an assessment of long-term psychiatric outcomes following preschool mild TBI, no significant difference in the incidence of anxiety disorders were found between individuals with and without TBI when they reached adolescence [7]. Further, while parent reports of behaviour following severe TBI in children has indicated elevated rates of anxiety, the relationship was weak compared to that of ADHD and other externalising problems [21]. Differences in reported outcomes may be due to the length of time that assessments took place post-injury, or in differences in the tools used to evaluate problems. Despite the mixed results, there have been reports of heightened anxiety symptoms following TBI in children and adolescent samples [9-10, 21].

Brain imaging studies further support the potential relationship between an increased incidence of anxiety disorders following TBI in children and adolescents, however again the literature is sparse. While it has been stated that frontal and temporal regions are the most susceptible to impact during a TBI [22], it has been found that deep-brain structures such as the amygdala and hippocampus are also highly vulnerable to such an injury [22]. Indeed, the amygdala has been targeted as an important region in children for processing fearful facial

expressions and producing rapid protective responses [23]. Further, right and left amygdala volumes have been found to be significantly larger in children with anxiety [24]. These findings have potential implications for literature involving anxiety and TBI in children and adolescents. Considering the discrepancies in the research mentioned above, and the fact that specific anxiety disorders are rarely the focus of interest in studies exploring the long-term and acute effects of TBI, it is important to review the literature and examine avenues for future research.

2.2. Rationale and aims

It is clear that anxiety negatively affects all areas of function, which is particularly important in the case of children, who are in a rapid state of developmental change. As outlined above, a TBI event can disrupt the developing systems in the brain. Further, research has shown that exposure to events that produce chronic anxiety can have long-term consequences by disrupting the developing architecture of the brain [25-26]. It is therefore important that we understand the impact of anxiety on outcomes following TBI in childhood as this will provide a platform for appropriate intervention to promote a more positive result.

As stated above, the incidence, rate and profile of internalising disorders following TBI in children has been relatively overlooked in the literature when compared to that of externalising disorders. Internalising behaviours represent internal states of distress, whereas externalising behaviours are directed outwardly and therefore tend to be more visibly distressing [27]. This difference in presentation of difficulties may contribute to the lack of research in internalising disorders, given that externalising problems experienced by children following TBI may be more readily reported by parents. The fact that males present with higher rates of TBI than females [28-29] may contribute to this difference, considering that externalising disorders tend to be more common in males than females [27, 30], while females are more likely to report internalising problems [30]. It is evident therefore that there may be a bias in the literature with regards to female oriented behavioural outcomes following TBI, with internalising problems (particularly anxiety) being significantly overlooked.

Based on the literature, this chapter will systematically review original research studies up until 2013 that have explored the relationship between TBI and anxiety disorders in children and adolescents. A comprehensive review investigated the cognitive, behavioural and academic outcomes of mild TBI in children and adolescents, and the merit of each study was strategically analysed according to specified criteria [31]. The rationale behind this procedure was due to the wide variability in methodology for past studies involving mild TBI.

The key criteria set out as essential for studies in this area were as follows:

a. Use of control group,

b. longitudinal design with follow-up assessments,

c. clear definition of mild TBI,

d. inclusion of at least 20 participants with TBI,

e. outcome measures involved standardised tests, and

f. control for pre-injury factors [31].

http://dx.doi.org/10.5772/60426

A study was concluded to have methodological merit if it met at least four of the previously listed criteria [31]. For this review, the methodology of the selected papers was examined according to these criteria, with the inclusion of moderate and severe injuries. When considering anxiety disorders, this refers to disorders including Generalised Anxiety Disorder (GAD), Post-Traumatic Stress Disorder (PTSD), Social Anxiety Disorder (SAD), Obsessive-Compulsive Disorder (OCD), Acute Stress Disorder (ASD), simple/specific phobia, social phobia and Panic Disorder (PD). Search methods and results will be outlined, and methodological considerations and future directions will be discussed and explored.

2.3. Comparison of merit of studies with criteria from Satz (2001)

As mentioned above, a prior literature review examined research studies investigating behavioural problems following mild TBI, and set out criteria regarding what constitutes as a study that has 'methdological merit' [31]. This method was utilised here, and each paper generated from the literature search was analysed according to the review's criteria. The results of the analysis can be found in Table 2 below.

	a) Use of control group	b) Longitudinal design with follow-up	c) Clear definition of TBI	d) At least 20 TBI participants	e) Standardised tests used	f) Controlled for pre-injury factors
[11] Hajek et al. (2010)	√	√	√	√	√	√
[32] Max et al. (1998)		√	√	√	√	√
[33] Levi & Drotar (1999)	√	√	√	√	√	√
[34] Gerring et al. (2002)		√	√	√	√	√
[35] Herskovits et al. (2002)		√	√	√	√	√
[36]Mather et al. (2003)	√	√	√		√	
[37] Grados et al. (2008)		√	√	√	√	√
[38] Luis & Mittenberg (2002)	√	√	√	√	√	√
[39] Max et al. (2011)		√	√	√	√	√

	a) Use of control group	b) Longitudinal design with follow-up	c) Clear definition of TBI	d) At least 20 TBI participants	e) Standardised tests used	f) Controlled for pre-injury factors
[40] Vasa et al. (2002)		√	√	√	√	√
[41] Vasa et al. (2004)		√	√	√	√	√

Table 2. Literature search results based on research methodology criteria

As is evident in Table 2, in accordance to the criteria set out by the review [31], all of the studies involving anxiety disorders following TBI in children and adolescents had methodological merit, possessing at least four of the essential criteria. A discussion of this analysis will be provided later in the chapter.

3. Method

A systematised literature search was conducted using the following search engines: Google Scholar, Ovid Medline (1946 - Dec 2013), PsycINFO (1806 - Dec 2013), Comprehensive Journal Index and Additional Resources for Nursing and Allied Health Professionals (CINAHL) plus (1937 - Dec 2013), Cochrane database (2005 – Dec 2013) and Embase (1946 – Dec 2013). A search was conducted in each database using the terms "traumatic brain injury" or "brain injury" or "head injury" and "anxiety disorders" or "anxiety" and "pediatric" or "paediatric" or "children" or "child". Returned articles were screened by title, abstract or full-text accordingly. Manual searching of articles based on the reference lists of relevant manuscripts was also conducted.

Inclusion criteria for studies were as follows:

a. Participants were children aged 0-18 years,

b. the study included a TBI group, and

c. anxiety symptoms or anxiety disorder diagnosis was included as an outcome measure.

Exclusion criteria involved:

a. Adult participants or a mixture of children and adults, and

b. participants with acquired brain injury (ABI).

4. Results

The search returned a total of 346 articles. Of these, 221 were screened by title, and 82 were screened based on abstract. The full text was examined for 43 of the articles. Of the articles

http://dx.doi.org/10.5772/60426

examined by full text, 32 of these were excluded for the following reasons: not an original research paper (n=6), case study (n=1), not specifically assessing anxiety as an outcome measure (n=21), not assessing TBI participants (n=3), or couldn't access the article (n=1). Manual searching of additional studies using the reference lists of relevant articles was conducted, however no further studies were found. The final result included 11 research studies fitting the above criteria, for which study characteristics and findings are outlined in Table 3.

4.1. Anxiety disorders following TBI in children and adolescents

As is evident in Table 3, results from the studies generally reveal some relationship between the presence of anxiety disorders following TBI in children and adolescents. The majority of studies focused on correlates of PTSD following childhood TBI [11, 32-36], with generally mixed but similar findings. The focus on PTSD in such a sample is unsurprising given the close link between such an injury and trauma. Main findings indicate that PTSD within 1 year following TBI can occur despite experiencing post-traumatic amnesia (PTA) [32-33], and that PTSD symptomatology is more prominent in children with severe TBI than those with moderate TBI or OI [33]. Analysis of factors that can predict the development of PTSD in children following TBI reveal that levels of PTSD symptoms are related to social disadvantage/family social status [33-34], anxiety diagnoses and aggregate anxiety scores [34], other psychiatric diagnoses and symptoms [34] and the presence of internalising disorders at time of injury [32]. Furthermore, predicting the diagnosis of PTSD following TBI was significantly related to anxiety diagnoses and scores, depression symptoms and non-anxiety psychiatric diagnoses [34]. When examining gender differences, female gender was a significant predictor of PTSD in one study [34], however was not the case for other investigators [32]. It is interesting to note that gender was unexamined in one study [33] considering anxiety disorders are seen in higher rates in a female population, it would be beneficial to the literature to compare anxiety symptomatology among groups.

Conversely, two studies exploring the relationship between PTSD and TBI report on different findings. One study explored PTSD following road traffic accidents in children with OI and mild TBI [36], and the other assessed the relationship between post-concussion symptoms (PCS) and PTSD in children with mild TBI and OI [11], with both papers reporting no significant difference among the sample groups on levels of PTSD symptomatology. This result may suggest that those with milder TBI are no more likely to develop PTSD following their injury than children who have sustained an OI. However, differences in the presentation of PTSD symptomatology following injury were found among the two papers. In [11], children with mild TBI tended to report a more frequent occurrence of mild PTSD symptoms, whereas severe PTSD occurred at a higher rate in the OI group. Moreover, another found that those in the mild TBI group reported higher levels of hyperarousal at 3 and 12 months, but not when controlling for PCS, whereas OI participants had higher levels of PTSD when controlling for baseline PCS and were more likely to meet PTSD criteria [26]. Therefore, these findings indicate that while there were no differences in the rate of PTSD symptomatology and diagnoses between mild TBI and OI children, the clinical manifestations of such symptomatology may be quite different across groups. Again, neither study examined any influence of gender on the likelihood of developing PTSD following TBI.

Authors	Aims	Participants	Classifying TBI Severity	Inclusion/ Exclusion Criteria	Anxiety Measures	General Results
[32] Max et al. (1998)	Identify PTSD and PTSD symptomatology following TBI Determine predictors of PTSD following TBI	50 consecutively admitted TBI patients aged 6-14 years at TOI - 26 mild TBI, 9 moderate TBI, 15 severe TBI - 64% male	Severe injury = Glasgow Coma Scale (GCS) score ≤ 8 Moderate injury = GCS score 9-12 or 3-15 with positive CT scan Mild injury = GCS score 13-15	Inclusion: admitted to tertiary care centre and 3 regional hospitals, CT scan on admission, English spoken language Exclusion: PTA > 3 months, penetrating TBI, documented history of child abuse and/or TBI involving hospital admission, history of CNS disorders, pre-existing serious illness	Neuropsychiatry Rating Scale (NRS) Baseline: - Schedule for Affective Disorders and Schizophrenia for School-Age Children – Epidemiologic version (K-SADS-E) plus PTSD module Follow-ups: - K-SADS-E plus sections on ADHD, ODD, CD, alcohol and substance abuse and PTSD module	2/50 with PTSD (resolved by 3 months) Increase in PTSD symptoms in first 3 months, then gradual decline 68% experienced ≥ 1 PTSD symptom at any point in first 3 months; 45%, 33%, 16% and 12% at 3, 6, 12 and 24 months Presence of internalising disorders, and severity of injury were main predictors of PTSD
[33] Levi & Drotar (1999)	Explore PTSD symptoms in children who have experienced traumatic injuries Compare PTSD symptoms of children with TBI and OI	Children 6-12 years at TOI 81 TBI children - 44 moderate, 37 severe - 74% males 59 OI children - 61% males	Severe TBI = GCS score ≤ 8 Moderate TBI = GCS score 9-12, or >12 plus positive CT scans or LOC > 15mins	Inclusion: hospitalised ≥1 night, participants from a prospective study on impact of TBI, English as primary language Exclusion: history of child abuse, TBI or brain disease, children with brain injuries other than closed head injury (e.g. anoxic injuries)	Child PTSD Index (CPTSDRI) (child report) Post Traumatic Stress Scale (PTSS) (parent report)	Parent reports for moderate TBI and OI in doubtful range for PTSD; mild levels PTSD reported for severe TBI at 6- and 12-months PTSD symptoms reported as higher for severe TBI group Younger age and higher social disadvantage associated with more PTSD symptoms Children displayed PTSD symptoms for >1 year post-TBI
[34] Gerring et al. (2002)	Examine the presence and rate of PTSD diagnosis and PTSD symptomatology following TBI	95 children aged 4-19 years with severe TBI and PTA - mean age at TOI 10.5 years -54 boys, 41 girls - 90 inpatient; 5 outpatient	GCS score of 3-8 indicated severe TBI classification	Inclusion: children admitted to neurorehabilitation unit of university-affiliated center Exclusion: previous hospitalisations for TBI, premorbid PTSD, premorbid mental retardation or CNS	Baseline: - Diagnostic Interview for Children and Adolescents parent form (DICA-p) - Child Behavior Checklist (CBCL) -- parents reported retrospectively of premorbid behavior	13% sample developed PTSD within 1 year of TBI - 5 according to parent reports, 5 to child reports and 2 to both Premorbid anxiety symptoms predisposed participants to PTSD symptoms 1 year post TBI Risk factors for PTSD and PTSD symptoms: female gender, high psychosocial adversity, greater

Authors	Aims	Participants	Classifying TBI Severity	Inclusion/ Exclusion Criteria	Anxiety Measures	General Results
				pathology, history of child abuse	- DICA child form (DICA-c/a) 1-year follow-up: - DICA-p, DICA-c/a - CBCL	injury severity, psychiatric disorders early after injury
[35] Herskovits et al. (2002)	Explore PTSD symptomatology post-TBI Compare spatial distribution of brain lesions due to TBI among participants with and without PTSD	94 participants aged 4-19 years with severe TBI - 53 boys, 41 girls - mean age TOI 10.5 years	GCS score of 3-8 indicated severe TBI classification	Inclusion: children referred from tertiary trauma centres to a university-affiliated center for neurological disorders Exclusion: previous hospitalisations for TBI, premorbid PTSD, premorbid mental retardation or CNS pathology, history of child abuse	PTSD diagnosis and symptoms ascertained with same procedure as Gerring et al. (2002) (above) MR Imaging: - imaging at 3 months post-TBI - abnormalities included hematoma, contusion, infarct, axonal-shear injury	9 participants met full PTSD criteria; 41 had re-experiencing criteria, 12 had avoidance criteria, and 55 had hyper-arousal criteria Participants with full PTSD criteria at 1 year post-TBI displayed lower lesion fractions in right medial frontal cortex and greater lesion fractions in left middle temporal gyrus High lesion burden was associated with lower probability of having PTSD
[38] Luis & Mitten-berg (2002)	Investigate relationship between TBI and anxiety/ mood disorders Examine factors that predict children who will suffer from anxiety/ mood disorders following TBI	96 children aged 6-15 years - 42 mild (66.7% male), 19 moderate/severe (68.4% male), - 35 OI (74% male)	Reviewed medical charts GCS score on admission - mild TBI – GCS 13-15 and normal CT/ neurological findings - moderate/severe TBI – GCS <13, abnormal CT, and/or skull fracture	Inclusion: children consecutively admitted to general hospital Exclusion: history of neurological disorders, history of abuse/neglect	Diagnostic Interview Schedule for Children (DISC-IV) - Module A: Anxiety Disorders Diagnoses based on DSM-IV criteria Social Readjustment Rating Questionnaire (SRRQ) (stress)	OI groups reported less post-injury stress Anxiety diagnoses: - Social Phobia: 5.7% OI, 10.5% moderate/severe - SAD: 7% mild, 21% moderate/ severe - Specific Phobia: 9.5% mild - Panic Attacks: 4.7% mild - Agoraphobia:7 % mild, 5.3% moderate/severe - GAD: 5.7% OI, 16.7% mild, 15.8% moderate/severe - OCD: 5.7% OI, 7% mild, 10.5% moderate/severe - PTSD: 10% mild, 10.5% moderate/ severe

http://dx.doi.org/10.5772/60426

Authors	Aims	Participants	Classifying TBI Severity	Inclusion/ Exclusion Criteria	Anxiety Measures	General Results
						- ASD: 2.3% mild, 10.5% moderate/ severe - overall Anxiety Disorders: 11.4% OI, 35.7% mild, 63.2% moderate/severe
[40] Vasa et al. (2002)	Compare rate of pre- and post-TBI anxiety disorders and symptoms Examine relationship between risk factors and anxiety outcomes following TBI	97 children aged 4-19 years with severe TBI - 58% male - mean age at TOI 10.56 years	GCS score of ≤8 taken at admission indicated severe TBI	Inclusion: referred from tertiary trauma centres and recruited from consecutive admissions from 1992-1996 to neurorehabilitation unit of university-affiliated center Exclusion: previous hospitalisations or emergency room visits for TBI, history of child abuse, premorbid mental retardation or CNS pathology	DICA-p assessed anxiety disorders at baseline and 1-year follow-up - derived symptoms from each anxiety disorder in addition	Mean aggregate Anxiety score of 1.86 pre-injury and 3.73 post-injury - pre-TBI, 84% reported 0-3 anxiety symptoms, 13% reported 4-9, and 3 reported ≥10 - post-TBI, 66% reported 0-3, 22% reported 4-9 and 12% reported ≥10 - significant increases in amount that had 4-9 and more than 10 symptoms Pre-injury anxiety and younger age at injury risk factors for post-injury anxiety
[36] Mather et al. (2003)	Compare the presence of PTSD in children who have been in a traffic accident with and without mild TBI Compare child and parent reports of PTSD following the accident	43 children from Casualty section of Sydney hospital aged 6-16 years - 20 males, 23 females - 14 mild TBI, 29 no TBI	Mild TBI defined by: - witnessed LOC - GCS 13-15 taken from medical file - return to full GCS score after 24 hours	Inclusion: enrolled in normal stream school, involved in recent traffic accident, sustained an injury other than TBI or a TBI Exclusion: prior TBI history, current TBI of moderate or severe classification, limited English comprehension of families	CPTSDRI – children report of PTSD Revised Children's Manifest Anxiety Scale (RCMAS) – child report of anxiety PTSD module of Anxiety Disorders Interview Schedule-child version (ADIS-c) – parent report or PTSD CBCL	No significant differences between groups for PTSD symptomatology 69% no-TBI and 85.7% TBI group suffered from PTSD Mean scores indicated improvements in PTSD symptoms Presence of PTSD strongly associated with anxiety Child and parent report of PTSD not significantly correlated
[41] Vasa et al. (2004)	Examine whether damage to specific brain regions are associated	97 children aged 4-19 years with severe TBI - 57% males	Initial GCS score on admission of ≤ 8	Inclusion: referred from tertiary trauma centres and recruited from	MR Imaging conducted 3 months post-TBI	12 subjects had 1 post-injury disorder, 1 had 2 disorders: 6 simple

http://dx.doi.org/10.5772/60426

Authors	Aims	Participants	Classifying TBI Severity	Inclusion/ Exclusion Criteria	Anxiety Measures	General Results
	with anxiety in children with severe TBI	- mean age at TOI 10.62 years	indicated presence of severe TBI	consecutive admissions from 1992-1996 to neurorehabilitation unit of university-affiliated center Exclusion: previous hospitalisations or emergency room visits for TBI, history of child abuse, premorbid mental retardation or CNS pathology	DICA was given to parents of children to assess anxiety disorders and symptoms	phobia, 5 overanxious disorder, 1 SAD and 1 OCD 7 subjects had post-injury PTSD; 1 had anxiety disorder and PTSD Mean number of anxiety symptoms: 1/88 pre- and 3.76 post-injury Inverse relationship between OFC damage and post-injury anxiety
[37] Grados et al. (2008)	Identify prevalence of new onset obsessive-compulsive symptoms (OCS) after severe childhood TBI Assess risk factors and comorbidities of OCS post-TBI	72 children aged 6-18 years with severe TBI - mean age at TOI 10.5 years - 54% males	Initial GCS score on admission of ≤ 8 to indicate severe TBI Also monitored duration of coma	Inclusion: referred to neurorehabilitation unit of a university-affiliated hospital between 1992-1997 Exclusion: previous hospitalisations for TBI, premorbid PTSD, premorbid mental retardation or CNS pathology, history of child abuse	DICA-revised was used to determine OCD, OCS, mood, anxiety and behavioural problems MR Imaging 3 months after TBI	21 children had new onset OCS – 12 had obsessions, 13 had compulsions, 4 had both Greater number of females in OCS group (70%) compared to non-OCS (37%) Those with OCS had higher number of psychiatric disorders – SAD, specific phobia, PTSD hyperarousal, mania, dysthymia and depressive symptoms more common in those with OCS Obsessions related to mesial prefrontal and temporal lesions; compulsions related to smaller OFC lesions
[11] Hajek et al. (2010)	Examine the rate and the relationship between PCS and PTSD in children following TBI and OI	251 children aged 8-15 years - 167 mild TBI (71% male), 84 OI (63% male)	Mild TBI – observed LOC ≤30 minutes, GCS of 13-14 or at least 2 symptoms of concussion OI – fracture injury within Abbreviated Injury Scale (AIS) score of ≤3	Inclusion: aged 8-15 years, recruited from emergency departments at selected hospitals, had suffered OI or mild TBI Exclusion: injury-related surgery, hypoxia or shock post-injury,	PTSD Checklist for Children/Parent Report (PCL-C/PR) to assess parent ratings of PTSD in children	PTSD diagnoses for Mild TBI: baseline 8%, 3 months 8% and 12 months 2% - OI: 7%, 7% and 7% respectively Across groups, PCS and PTSD ratings were correlated

Authors	Aims	Participants	Classifying TBI Severity	Inclusion/ Exclusion Criteria	Anxiety Measures	General Results
				previous TBI needing hospitalisation, premorbid neurological disorders, severe psychiatric disorder needing hospitalisation, AIS of greater than 3, injuries that would hinder assessment, child abuse/neglect		After controlling for PCS, OI group reported higher scores on PCL-C/PR than mild TBI group at baseline Symptoms of PTSD and PCS correlated more highly for OI group than mild TBI
[39] Max et al. (2011)	Examine the rate and nature of novel anxiety disorders and novel subclinical anxiety disorders in children following TBI	177 children aged 5-14 years with TBI - 86 mild, 27 moderate, 64 severe - mean age at TOI 10.13 years - 71% male	GCS scores of 3-8 for severe TBI, 9-12 for moderate TBI and 13-15 for mild TBI - also assessed MR scans	Inclusion: Consecutive admissions to 3 academic medical centres for TBI between 1998-2003 Exclusion: pre-existing autism, ADHD or schizophrenia, mental deficiency, injury due to child abuse or penetrating injury	DSM-IV diagnoses derived from KSADS present and lifetime version, and NRS MR Imaging scans at 3 months	8.5% developed novel clinical anxiety disorder and 17% developed novel subclinical anxiety disorder post-TBI - mild TBI: 11% clinical and 20% subclinical anxiety - moderate TBI: 0% clinical and 24% subclinical anxiety - severe TBI: 7% clinical and 11% subclinical anxiety 9 PTSD, 6 SAD, 4 simple phobia, 3 GAD, 3 adjustment disorder with anxious mood, 3 social phobia, 1 panic disorder Younger age at injury associated with novel anxiety disorder

Note. PTSD = Post-Traumatic Stress Disorder; TBI = traumatic brain injury; TOI = time of injury; CT = computed tomography; PTA = post-traumatic amnesia; CNS = central nervous system; ADHD = Attention-Deficit/Hyperactivity Disorder; ODD = Oppositional Defiant Disorder; CD = Conduct Disorder; OI = orthopaedic injury; LOC = loss of consciousness; MR = magnetic resonance; DSM-IV = Diagnostic and Statistical Manual for Mental Disorders fourth edition; SAD = separation anxiety disorder, GAD = Generalised Anxiety Disorder; OCD = Obsessive-Compulsive Disorder; ASD = Acute Stress Disorder; OFC = Orbitofrontal Cortex; PCS = post-concussion symptoms

Table 3. Characteristics of studies from literature search presented in order of study recency

http://dx.doi.org/10.5772/60426

When focusing on the incidence and presentation of anxiety disorders in general, only four studies were found relevant. One study focused on the incidence of OCD and presence of OCD symptomatology following severe TBI in children and adolescents [37], while the remaining studies explored the relationship between TBI and the incidence of disorders including GAD, ASD, PTSD, PD, OCD, simple/specific phobia, social phobia and SAD [38-40]. Only two studies included participants with mild, moderate and severe TBI [38-39], while the rest focused on severe TBI [37, 40]. Generally, the results demonstrate that in children and adolescents who have sustained aTBI of any severity, there is a statistically significant higher risk of developing subsequent anxiety disorders [37-40].

Overanxious (heightened anxiety which is generalised and non-specific) was a commonly reported disorder in children with severe TBI [40], and the presence of OCD symptomatology following severe TBI was significantly more common in females. When comparing children with mild TBI, moderate/severe TBI and OI, results suggest a potential relationship between degree of neurological insult and risk of developing subsequent anxiety disorders [38], in that overall anxiety disorders were most common in children with moderate/severe TBI, followed by mild TBI and OI. However, similarly to research on PTSD after TBI, the pattern of results is often quite different among the sample groups, including differing age ranges, varying use of control groups, and severity of TBI. For instance, a few of the studies [37, 39-40] didn't use any comparison group when examining rates of anxiety symptomatology and diagnoses, and as such the conclusion that such diagnoses are heightened in a TBI sample is relatively weak, as compared to another study [38] which compared incidence of anxiety diagnoses to an OI comparison group. In terms of gender differences, among two of the studies, gender as a predictor was either not considered [38] or not discussed in any detail [39-40]. Only one study found that being female was associated with a higher number of obsessive compulsive symptoms, with a greater number of females reporting obsessive compulsive symptoms following TBI [37].

Predictors/Risk Factors
· Internalising disorders [32, 34, 37]
· Severity of TBI [32, 34, 38]
· Younger age at injury [33, 39, 40]
· Social disadvantage [33-34]
· Family social status [33-34]
· High levels of pre-morbid psychosocial adversity [34-35, 37, 40-41]
· Female gender [34, 37]
· Pre-morbid mood or anxiety disorders [32, 34, 37-38]
· Pre-morbid ADHD [38]
· Pre-morbid learning disabilities [38]
· Parent education [38]
· Post-injury stress scores [38]
· Post-concussive symptoms [11]
· Concurrent depression [39]
· Concurrent personality change [39]

Table 4. Predictors and risk factors for anxiety following TBI

Among the research, common themes exist in reference to the relationship between anxiety disorders and TBI in children and adolescents. A number of the studies presented here assessed for pre-morbid psychosocial adversity, with all studies reporting higher rates of anxiety and PTSD symptomatology and diagnoses in children from families with higher pre-morbid psychosocial adversity [34-35, 37, 40-41]. In addition, when the impact of age was assessed within the methodology, it was found that younger age at injury tended to be associated with a higher number of anxiety symptoms [33, 39-40] in such children. Alternatively however, there have been conflicting results, in that one found no support for age as a significant predictor of PTSD in their sample of children with severe TBI [34]. This is comparative to results found in a sample of children with mild, moderate and severe TBI, whereby younger age was associated with a higher number of PTSD symptoms [33]. This may be accounted for by the fact that in [34], the researchers utilised a large age range of participants (4-19 years), versus the other study which restricted their sample to children aged 6-12 years [33]. The implications of age ranges utilised in the study samples is discussed further below. See Table 4 for the predictors and risk factors for children and adolescents to develop anxiety disorders and symptomology following TBI.

4.2. Neural substrates and brain regions associated with anxiety following TBI

In examining the brain regions associated with a higher risk of anxiety following childhood TBI, it is important to first review the areas of the brain that are commonly injured and implicated in TBI. Damage as a result of TBI can be either focal, whereby forces have caused localised damage, or diffuse, whereby damage has occurred to axonal properties across the brain [42-43]. Due to the fact that TBI can occur under many different, individualised circumstances, damage to the brain is heterogeneous [44]. However, it has been noted that the frontal and temporal regions are highly vulnerable to injury, due to the shape of the skull and the way the head is held [22, 44-46]. The frontotemporal susceptibility to damage from TBI has been noted as the major cause of the cognitive and neurobehavioral consequences of TBI that some go on to experience, including emotional regulation [45]. Further, white matter tracts have been demonstrated to be more susceptible to damage due to the acceleration-deceleration forces and their direct exposure to shear and strain forces [43-44, 47], and this white matter tract damage tends to occur more frequently again within the frontotemporal areas of the brain [44].

Due to the diffuse damage likely to occur following TBI, and the heterogeneity that occurs across individuals, research has sought to explore and highlight the most commonly affected regions within the brain that may be associated with long-term behavioural and emotional problems. Reports from a multicentre study of children with TBI have noted white matter hypersensitivities and focal atrophy distributed across frontotemporal areas of the brain [44]. More specifically, Magnetic Resonance Imaging (MRI) scans highlighted that among children with mild, moderate and severe TBI, there were lesions evident in frontal regions, temporal poles, and right medial temporal lobe, and damage was also evident to the amygdala, hippocampus, thalamus and basal ganglia [44]. MRI procedures were also used in another sample of children with moderate and severe TBI, to evaluate brain volume differences in the

http://dx.doi.org/10.5772/60426

whole brain and also prefrontal, temporal and posterior regions [22]. Imaging results indicated that children with TBI had significantly reduced whole brain, prefrontal and temporal regional tissue volumes compared to that of uninjured children. Further, there were also group differences on white matter and grey matter in superior medial and ventromedial prefrontal regions [22]. Additional research has also utilised MRI procedures to locate brain regions more commonly affected following TBI, with one study including individuals with mild to moderate TBI [46]. In terms of number of lesions, results showed that the frontal and temporal areas had significantly more lesions than parietal and occipital areas of the brain. Again, this is supported by the Toronto TBI study, which recruited individuals with chronic TBI across all levels of severity to undergo MRI 1 year following injury [42]. The most reliable effects noted in the results were brain volume changes within the frontal, temporal and cingulate regions, with focal lesions associated with greater volume loss in frontal and temporal regions [42]. Finally, MRI has been used to examine reductions in fractional anisotropy (reflects fibre density, axonal diameter and myelination in white matter) in adults with mild TBI [47]. Results again demonstrated more reductions in frontal and temporal regions, and also parietal regions, and among association bundles, fronto-temporal-occipital fibre bundles were most often involved [48]. Table 5 provides a concise summary of the above findings within the literature.

As is evident, the frontal and temporal regions are highly implicated following TBI of all severities. In looking at the neural regions implicated in those with anxiety disorders following TBI, it may be possible to discover overlapping regions. However, only two studies have specifically attempted to delineate the neural correlates and brain regions involved in the development of anxiety disorders following TBI in children and adolescents [35, 40]. One of these studies focused on lesion burden in children with severe TBI and their relationship with PTSD symptomatology [35]. Data was obtained from a cohort from a pre-existing study [34], which utilised participants with only severe TBI, and did not include any comparison group. Magnetic Resonance Imaging (MRI) at 3 months following the TBI event revealed associations between lesion fractions in the right cingulum, right hippocampus, right medial frontal gyrus and left hippocampus at 3 months post-TBI, and the presence of PTSD re-experiencing symptoms at 1 year [35]. In addition, assignment to the PTSD versus no-PTSD diagnosis group was dependent on lesions in the right medial frontal and left middle temporal gryi [35]. Furthermore, a lower probability of suffering from PTSD hyperarousal correlated with higher lesion fraction in the left subcallosal gyrus, and avoidance symptoms were associated with lower lesion burden in the right medial frontal and left inferior temporal gyri and higher lesion burden in the left middle temporal gyrus [35]. Interestingly, the researchers found no association between the re-experiencing criterion of PTSD and lesions in the right amygdala, despite research which has suggested that the amygdala is an important structure in the processing of fear and emotional signals [23], and in anxiety symptoms [24].

Again utilising the same cohort of participants in [34], the incidence and presence of anxiety disorders in general and their neural correlates in patients with severe TBI was examined, using MRI procedures [41]. The study was unique in that it attempted to correlate specific brain lesions and their location, with different anxiety outcomes among children with severe TBI. In a 1-year prospective study, with a focus on the orbitofrontal cortex (OFC), imaging results

Study	Main results
[46] Levin et al. (1992)	Number of lesions from MRI: · Total = 145 · Frontal = 60 · Temporal = 55 · Parietal = 15 · Occipital = 10
[22] Wilde et al. (2005)	MRI volumetric findings: · Prefrontal regions smaller in those with TBI · Superior medial grey and white matter, lateral frontal white matter, and ventromedial grey matter smaller in TBI group · Lesion volumes from MRI: · Majority lesions in frontal and temporal areas
[42] Levine et al. (2008)	· Volume changes in ventral frontal and temporal regions · Cerebrospinal fluid increases in left medial frontal and posterior temporal regions · Grey matter volume changes in ventral frontal, middle frontal, superior frontal, bilateral posterior temporal, left medial temporal, left occipital and basal ganglia/thalamic regions
[47] Rutgers et al. (2008)	Brain regions with reduced fractional anisotropy from MRI: · Frontal lobe = 42 individuals (22%) · Parietal lobe = 31 individuals (16%) · Temporal lobe = 28 individuals (15%) · Occipital lobe = 4 individuals (2%)
[44] Bigler et al. (2013)	· Distribution of lesions was more frequent in frontal and temporal regions · Mean group volume differences for white matter, grey matter, hippocampus, amygdala, thalamus, basal ganglia · Focal signal abnormalities and white matter hypersensitivities located predominantly in frontal and temporal lobe regions

Table 5. Summary of commonly damaged brain regions following TBI

revealed that the presence of OFC lesions decreased the risk of anxiety disorders when control variables (demographics, psychosocial adversity, preinjury anxiety, injury severity, post-injury PTSD, whole brain volume) were included in the analyses [41]. Therefore, an inverse relationship exists in that children with more lesions to the OFC as a result of TBI are less likely to develop anxiety disorders than those with fewer lesions. This is said to be due to a disruption between the OFC and amygdala, which results in a disrupted ability to modify responses to cues based on processing the emotional valence of a stimulus [41].The OFC is purported to have important reciprocal connections with the amygdala [41], which again further supports the brain region studies which target the amygdala in having some role in anxiety disorders in children [23-24].

In addition, two other studies included MRI procedures in their methodology - however brain lesion analysis was not a major aim of their study [33, 37, 39]. In examining the nature of OCD symptomatology in children and adolescents with a history of severe TBI, some specific areas were located to potentially be associated with the onset of OCD symptomatology following TBI [37]. MRI scans revealed relationships between OCD symptoms and lesions in the OFC

http://dx.doi.org/10.5772/60426

and temporal lobe regions, and also thalamic lesions for males [37]. Alternatively, in their study of anxiety disorders in children and adolescents following severe TBI [39], it was reported that a trend association exists between lesions to the superior frontal gyrus and the presence of novel anxiety disorders. Furthermore, a statistically significant association was found between lesions to the superior frontal gyrus and novel subclinical anxiety disorder [39]. However, no other statistically significant relationships between specific brain lesions and anxiety symptomatology were found in the study.

The above studies implicate certain regions in relation to the elevated incidence of anxiety disorders following TBI in children and adolescents, with emphasis on structures such as the OFC, right medial frontal gyri and temporal gyri. Table 3 outlines the specific regions implicated in anxiety following TBI from the literature. Evidently, these findings highlight a link with commonly affected brain regions following TBI, where research has implicated areas associated with the frontal and temporal regions. While these studies provide some compelling initial evidence for the neurobiological basis of anxiety disorders following TBI, it is clear that the literature in this area is still very sparse and lacking.

Brain Regions Implicated
· Right cingulum [35]
· Right hippocampus [35]
· Frontal regions [35, 37, 39]
- Right medial frontal gyrus [35]
- Right medial frontal cortex [35]
- Mesial prefrontal cortex [41]
- Frontal lobes [37]
- Superior frontal gyrus [39]
· Left hippocampus [35]
· Temporal regions [35, 37, 41]
- Left temporal regions [37]
- Left middle temporal gyri [35]
- Temporal lobes [37]
· Right amygdala [35]
· Orbitofrontal cortex [37, 41]

Table 6. Brain regions associated with anxiety in children and adolescents with TBI

5. Discussion

The above literature demonstrates that the presence of mild, moderate and severe TBI in children and adolescents significantly increases the risk of developing subsequent anxiety disorders [37-40], with feeling overanxious being a commonly reported anxiety symptom in children with severe TBI [40]. When comparing children with mild TBI, moderate/

severe TBI and OI, overall results suggests a potential relationship between the degree of neurological insult that has occurred, and the risk of developing new-onset anxiety disorders [38]. In addition, it has been noted that there is a similar link found for those with PTSD following TBI. The research suggests that while there is a rare (yet, noted) occurrence of PTSD following moderate or severe TBI in children, and a statistically significant difference in the frequency of this occurrence between children with moderate or severe TBI to children with OI, this relationship may not exist for children with only mild TBI. Furthermore, the most important predictors for anxiety symptomatology following childhood TBI include social disadvantage/family social status, severity of TBI, psychosocial adversity and younger age of injury [33-35, 37, 40-41].

5.1. Methodological concerns

As indicated above in Table 2, the studies were analysed according to their methodological merit, as determined by set criteria [31]. Three of the studies [11, 33, 38] included all of the listed criteria, and the most commonly missed criteria was a lack of a control group in 7 out of the 11 papers [32, 34-35, 37, 39-41]. All included studies showed evidence of criteria b), c) and e), indicating the use of longitudinal designs, well-defined TBI groups and standardised outcome measures and assessments. Only one study did not include more than 20 TBI participants or control for pre-injury characteristics [36].

Of concern is the number of studies that did not include a non-TBI group. The research being discussed explores the rate of anxiety disorders following TBI in children and adolescents, and although this information can be obtained using only a TBI group, the strength of the results may be enhanced if authors could compare these rates to a non-injured or OI group of participants, particularly when anxiety is already evident in high rates in the general population. It is also interesting to note that of the studies that did include a control group [11, 33, 36, 38], all utilised an OI group with injuries sustained to regions of the body other than the head or neck. There is therefore an absence of studies that have compared the incidence of anxiety disorders in children and adolescents with TBI and healthy control subjects. While it is useful to use an OI comparison group as this eliminates confounding variables associated with the nature of injury and exposure to hospital/rehabilitation services, the literature is in need of research that compares the incidence of anxiety following TBI to what is expected in the general child population.

In addition, while all but one controlled for pre-injury characteristics and risk factors [36], issues pertain to the validity of such measures regarding the timing of testing. In all cases, premorbid functioning such as behavior scores, pre-existing psychiatric disorders and family functioning assessments were conducted at 'baseline' – meaning that they were assessed following the TBI event. This presents a large issue within the TBI literature as it is difficult to ascertain the validity of reports on child variables that were present before the injury when they are considered retrospectively. Psychological stress as a result of the injury, for both the child and the parent, is likely to affect the ability for the parent or child to recall incidents and functioning before the TBI event. Furthermore, the child's current behavior and functioning may change the child or parent's perspective of what occurred before the TBI. However, the

http://dx.doi.org/10.5772/60426

authors do attempt to alleviate the effects of this issue in that testing at 'baseline' was always conducted as soon as possible, once major concussion symptoms (such as PTA) had resided.

A major strength among the literature on anxiety disorders following TBI in children and adolescents is the use of a prospective, longitudinal design with follow-up assessments of behavior and anxiety. Several studies conducted follow-ups up to 1 year after TBI [11, 32-35, 37, 40-41], which allowed for the examination of long-term effects of TBI and the persistence and chronicity of anxiety in such participants. Furthermore, in fewer studies [11, 32-33], participants were assessed at multiple time points, which is essential for exploring the pattern of anxiety disorders and symptomatology following TBI across time. Additionally, well-defined severity groups are important when conducting TBI studies, particularly when comparing groups and when assessing the influence of injury severity on outcomes. Evidently, the studies presented in this paper all assessed and defined severity of TBI using the GCS. The GCS is regarded as the most common method of assessing TBI severity [17], and has been proven both useful and valid in multiple studies. In addition, in many cases other markers of TBI severity were also examined, such as positive CT scans [32-33, 38-39] and the duration of LOC [33, 36-37, 39].

Overall, when considering the methodological merit of the studies listed in this paper, the results seem quite positive. While the absence of a control group for over half of the studies poses some concern for the generalizability of findings, their methodology is strengthened by the use of a longitudinal design with timely follow-up assessments post-TBI and well-defined and accurately assessed TBI severity for each injury group. In addition, all but one study [36] had an adequately sized sample of TBI participants. Furthermore, outcome measures for all of the papers were assessed using standardised, common measures and procedures for examining the presence of anxiety disorders in children and adolescents.

5.2. Other concerns

Examining the literature, common methodological concerns arise across the featured studies. An important finding is that there is a lack of research which has included participants with mild TBI, with a large focus on children with severe TBI. Of the studies in this review, five included participants who had suffered mild TBI [11, 32, 36, 38-39], while the majority only included participants with moderate-severe TBI or severe TBI. Considering that studies on externalising disorders have indicated an increased incidence of psychiatric disorders such as ADHD, ODD, CD, drug and alcohol abuse/use and personality disorders in children with even mild TBI [6-7, 9], it surprising that such a sample has been relatively neglected in the literature.

In relation to this, it is often suggested within the PTSD literature that the diagnosis of PTSD following TBI is not valid due to the nature of the psychological events that follow such an injury [32-33, 36]. This argument states that children who suffer from TBI and lose consciousness or experience PTA are unable to suffer the anxiety of PTSD that is associated with re-experiencing a traumatic event, as the event itself cannot be recalled and subsequently emotionally suppressed [32-33]. The authors, however, do not discuss this argument in relation to children who suffer from a TBI mild enough that it does not result in loss of consciousness (LOC) or PTA. However, instead they tended to utilise samples of children with more severe

injuries [33-35], thereby contradicting their argument. Furthermore, over half of the research has focused on solely PTSD following TBI [11, 32-36] and excluded other anxiety disorders, due to the close relationship it has with trauma [40]. Moreover, one study [36] applied more focus on PTSD in children following road traffic accidents, and utilised the TBI group as a control for confounds associated with such an injury, rather than exploring long-term anxiety outcomes following TBI.

Also interesting to note in regards to PTSD following TBI is the discrepancy that is often found between reports of PTSD symptomatology from the child versus the parents. For instance, in [32] and [36], both studies utilised both parent and child report questionnaires to assess PTSD. However, correlational analyses indicated a relatively low relationship between reports from children and adults, and of which the relationship was non-significant in both cases. The meaning of this is not well discussed, which poses a challenge to the methodology of papers which utilise only one source of PTSD symptom reporting. In addition, it is not well-known whether this relationship (or lack thereof) also exists for other anxiety measures. Indeed, some have questioned the validity of parent-report methods for assessing anxiety, arguing that these internal states can be reliably reported by the children themselves, without need for parental reports [38]. Internalising disorders in children and adolescents are not as readily observable for parents, and as such, it may be difficult to report their presence or absence in their children. Further, younger children and children who have sustained a TBI and have developed cognitive deficits may not understand or be able to articulate the internalising problems they are experiencing. As such, this discrepancy between parent and child reports of internalising symptoms should be explored further to examine the best possible way to accurately assess difficulties such children and adolescents may exhibit following TBI.

The importance of gender as a predictor of anxiety disorders following TBI has been significantly neglected within this literature. Considering that a higher number of females experience and report internalising and anxiety problems compared to males in both a normal [48] and TBI [30] population, it is surprising that gender differences in these studies hasn't been thoroughly explored. Women are at greater risk of developing anxiety disorders including GAD, PD and PTSD [49], and also some phobias [50]. However, differences in the psychopathology of children following TBI is has rarely been compared across gender groups, as is evident in the above samples. Given that much work has been done exploring externalising behavioural outcomes of children post-TBI, such as attention, hyperactivity and aggressive behaviours [3-6], it is important that behaviours that are more likely to be seen in a female population are also as extensively explored.

Finally, while there have been some advancements towards the study of internalising problems, including anxiety disorders, following TBI in children and adolescents, it is vital to note that of the 11 papers presented here, 5 of these utilised the same cohort of individuals [34-35, 37, 40-41]. While the sample itself was derived from a large database of referrals from tertiary trauma centres over a relatively large period of time (years 1992-1996), the fact that these studies were replicated among the same cohort limits the generalizability of the results to anxiety and TBI literature. Although the studies provided useful information regarding the relationship between TBI and anxiety disorders [34, 37, 40] and also neural correlates associ-

http://dx.doi.org/10.5772/60426

ated with anxiety disorders after TBI [35, 41], the literature remains sparse in relation to different cohorts of children and adolescents being examined for such variables.

5.3. Practical implications

Given the findings in the literature, when assessing children who have been admitted for TBI, it may be important to screen for factors associated with family psychiatric history of internalising disorders, the individual's past psychiatric history of internalising disorders, and also to examine levels of psychosocial adversity. Furthermore, the increased vulnerability of children with a younger age at injury to developing subsequent anxiety disorders would be considered in such assessments. Children who are younger at the time of TBI, have greater psychosocial adversity and have some history of psychiatric internalising disorders may be at greater risk of developing anxiety disorders, and so if such children are targeted early, appropriate intervention practices may be put in place.

Intervention programs for children vulnerable to developing anxiety disorders following TBI may include relaxation procedures for the parent and the child, coping strategies, self-esteem building activities, or open communication between the parent and child regarding the child's anxiety symptoms or worries. Furthermore, those at high risk of developing anxiety disorders may benefit from a follow-up screen following their TBI to assess for any anxiety symptoms, and potentially undergo typical anxiety management procedures such as cognitive-behavior therapy, behavioural assessment and psychotherapy. It is important that such poor outcomes following TBI are targeted and managed early, to enhance quality of life and prevent the negative effects anxiety would have on both social and academic learning and development.

5.4. Limitations

One major limitation of this review is that only 11 papers have been reviewed for discussion. In addition, among these papers, 5 utilised the same cohort of participants. However, this fact highlights further the need for more work in the field of anxiety disorders following childhood TBI. As mentioned above, it is likely that there is less of a focus on internalising behaviours because males have been reported to be at greater risk of TBI than females [28-29], and that the more overt and distressing nature of externalising problems [27] are more readily reported by parents, and also more observable to the human eye.

5.5. Future directions and conclusions

It is clear from the small number of studies generated in this literature search that much work needs to be done in examining the incidence and rate of anxiety disorders following TBI in children and adolescents. Studies that have investigated the presence and rate of PTSD diagnoses and symptomatology [34], and the rate of pre- and post-TBI anxiety disorders and symptoms [40], should be replicated in different samples, with the inclusion of children with both mild and moderate TBI. Moreover, future studies should include the use of control groups to compare against children with TBI, and utilise both healthy control participants and children with OI, as the presence and rate of anxiety disorders is expected to be different among each

of these groups. Furthermore, the relationship between parent and child reports of anxiety disorders should be examined, considering the low correlation scores found among reports of PTSD in the present literature [33, 36]. Finally, more studies should attempt to explore brain regions and lesion burdens associated with anxiety disorders in such a sample, as such studies are severely lacking.

This chapter examined the current literature assessing the presence of anxiety disorders following TBI in children and adolescents. While the literature to date is sparse, it may be concluded that children who have suffered from a TBI (mild, moderate or severe), are at a higher risk of developing subsequent anxiety disorders, even 1 year following the injury event. Moreover, children with more severe injuries, greater psychosocial adversity, and younger age at injury may be at the greatest risk, and are a group who would benefit from early intervention. Further studies are needed to replicate all the above findings and generate a more comprehensive view of the relationship between TBI and internalising disorders within the literature.

Author details

Michelle Albicini[1*] and Audrey McKinlay[2]

*Address all correspondence to: michelle.albicini@monash.edu

1 Monash University; School of Psychological Sciences, Australia

2 The University of Melbourne, School of Psychological Sciences, Psychology Clinic, Australia

References

[1] Styrke J, Stalnacke B, Sojka P, Bjorstig. Traumatic brain injuries in a well-defined population: epidemiological aspects and severity. Journal of Neurotrauma 2007;24 1425-1436.

[2] McKinlay A, Hawley CA. Incidence rates for traumatic brain injury in children: International Brain Injury Association. http://www.internationalbrain.org/incidence-rates-for-traumatic-brain-injury-in-children/ (accessed 4 December 2014)

[3] Hawley CA. Reported problems and their resolution following mild, moderate and severe traumatic brain injury amongst children and adolescents in the UK. Brain Injury 2003;17(2) 105-129. doi: 10.1080/0269905021000010131

[4] Liu J, Li L. Parent-reported mild head injury history and behavioural performance in children at 6 years. Brain Injury 2013;27(11) 1263-1270. doi: 10.3109/02699052.2013.804205

[5] Massagli TL, Fann JR, Burington BE, Jaffe KM, Katon WJ, Thompson RS. Psychiatric illness after mild traumatic brain injury in children. Archives of Physical Medicine and Rehabilitation 2004;85(9), 1428-1434. doi: 10.1016/j.apmr.2003.12.036

[6] McKinlay A, Dalrymple-Alford J, Horwood J, Fergusson D. Long term psychosocial outcomes after mild head injury in early childhood. Journal of Neurology, Neurosurgery and Psychiatry 2002;73 281-288.

[7] McKinlay A, Grace R, Horwood J, Fergusson D, MacFarlane M. Adolescent psychiatric symptoms following preschool childhood mild traumatic brain injury: Evidence from a birth cohort. Journal of Head Trauma Rehabilitation 2009;24(3) 221-227.

[8] Schwartz L. Long-Term Behavior Problems Following Pediatric Traumatic Brain Injury: Prevalence, Predictors, and Correlates. Journal of Pediatric Psychology 2013;28(4) 251-263. doi: 10.1093/jpepsy/jsg013

[9] Max JE, Schachar R, Landis J, Bigler E, Wilde E, Saunders A... Levin H. Psychiatric disorders in children and adolescents in the first six months after mild traumatic brain injury. Journal of Neuropsychiatry and Clinical Neuroscience 2013;25(3) 187-197.

[10] Max JE, Wilde E, Bigler E, MacLeod M, Vasquez A, Schmidt A... Levin H. Psychiatric disorders after pediatric traumatic brain injury: A prospective, longitudinal, controlled study Journal of Neuropsychiatry and Clinical Neuroscience 2012;24(4) 427-436.

[11] Hajek CA, Yeates KO, Gerry TH, Bangert B, Dietrich A, Nuss KE... Wright M. Relationships among post-concussive symptoms and symptoms of PTSD in children following mild traumatic brain injury. Brain Injury 2010;24(2) 100-109. doi: 10.3109/02699050903508226

[12] Centers for Disease Control and Injury Prevention. CDC: Traumatic Brain Injury. http://www.cdc.gov/TraumaticBrainInjury/ (accessed 13 February 2014)

[13] Corrigan J, Selassie A, Orman J. The epidemiology of traumatic brain injury. Journal of Head Trauma Rehabilitation 2010;25(2) 72-80.

[14] American Congress of Rehabilitation Medicine. Definition of mild traumatic brain injury. Journal of Head Trauma Rehabilitation 1993;8(3) 86-87.

[15] Maas AIR, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. The Lancet Neurology 2008;7(8) 728-741. doi: 10.1016/s1474-4422(08)70164-9

[16] McKinlay A. Controversies and outcomes associated with mild traumatic brain injury in childhood and adolescences. Child Care and Health Development 2010;36(1) 3-21. doi: 10.1111/j.1365-2214.2009.01006.x

[17] Greenwood R. Head injury for neurologists. Journal of Neurology, Neurosurgery and Psychiatry 2002;73 (Suppl I) i8-i16.

[18] Baalen B, Odding E, Maas AIR, Ribbers G, Bergen M, Stam H. Traumatic brain injury: Classification of initial severity and determination of final outcome. Disability and Rehabilitation 2003;25(1) 9-18.

[19] Max JE, Smith W, Lindgren S, Robin D, Mattheis P, Stierwalt J, Morrisey M. Case study: Obsessive-Compulsive Disorder after severe traumatic brain injury in an adolescent. Journal of the American Academy of Child and Adolescent Psychiatry 1995;34(1) 45-49.

[20] Chaves C, Trzesniak C, Derenusson GN, Araujo D, Wichert-Ana L, Machado-De-Sousa JP....Hallak JEC. Late-onset social anxiety disorder following traumatic brain injury. Brain Injury 2012;26(6) 882-886.

[21] Karver CL, Wade SL, Cassedy A, Taylor HG, Stancin T, Yeates KO, Walz NC. Age at injury and long-term behavior problems after traumatic brain injury in young children. Rehabilitation Psychology 2012;57(3) 256-265. doi: 10.1037/a0029522

[22] Wilde EA, Bigler ED, Hunter JV, Fearing M, Scheibel R, Newsome M... Levin HS. Hippocampus, amygdala and basal ganglia morphometrics in children after moderate-to-severe traumatic brain injury. Developmental Medicine and Child Neurology 2007;49 294-299.

[23] Baird A, Gruber S, Fein D, Maas L, Steingard R, Renshaw P... Yurgelun-Todd D. Functional magnetic resonance imaging of facial affect recognition in children and adolescents. Journal of American Academy of Child and Adolescent Psychiatry 1999;38(2) 195-199.

[24] De Bellis M, Casey B, Dahl R, Birmaher B, Williamson D, Thomas K... Ryan N. A pilot study of amygdala volumes in pediatric Generalised Anxiety Disorder. Society of Biological Psychiatry 2009;48 51-57.

[25] Arnsten AF. Stress signaling pathways that impair prefrontal cortex structure and function. Nature Reviews Neuroscience 2009;10 410–422.

[26] Brinks V, de Kloet ER, Oitzl MS. Strain specific fear behaviour and glucocorticoid response to aversive events: modelling ptsd in mice. Progress in Brain Research 2008;167 257–261.

[27] Bayer JK, Ukoumunne OC, Mathers M, Wake M, Abdi N, Hiscock H. Development of children's internalising and externalising problems from infancy to five years of age. Psychiatry 2012;46(7) 659-668.

[28] Crowe L, Babl F, Anderson V, Catroppa C. The epidemiology of paediatric head injuries: data from a referral centre in Victoria, Australia. Journal of Paediatric and Child Health 2009;45(6) 346-350. doi: 10.1111/j.1440-1754.2009.01499.x

[29] McKinlay A, Grace RC, Horwood LJ, Fergusson DM, Ridder EM, MacFarlane MR. Prevalence of traumatic brain injury among children, adolescents and young adults: prospective evidence from a birth cohort. Brain Injury2008;22(2) 175-181. doi: 10.1080/02699050801888824

[30] Scott C, McKinlay A, McLellan T, Britt E, Grace R, McFarlane M. A comparison of adult outcomes for males compared to females following paediatric traumatic brain injury. Neuropsychology 2014. No Pagination Specified.

[31] Satz P. Mild Head Injury in Children and Adolescents. Current Directions in Psychological Science 2001;10(3) 106-109. doi: 10.1111/1467-8721.00127

[32] Max JE, Castillo C, Robin D, Lindgren S, Smith W, Sato Y, Arndt S. Posttraumatic stress symptomatology after childhood traumatic brain injury. The Journal of Nervous and Mental Disease 1998;186(10) 589-596.

[33] Levi RB, Drotar D, Yeates KO, Taylor HG. Posttraumatic stress symptoms in children following orthopedic or traumatic brain injury. Journal of Clinical Child Psychology 1999;28(2) 232-243. doi: 10.1207/s15374424jccp2802_10

[34] Gerring J, Slomine BS, Vasa RA, Grados MA, Chen A, Rising W... Ernst M. Clinical predictors of Posttraumatic Stress Disorder after closed head injury in children. Journal of the American Academy of Child and Adolescent Psychiatry 2002;41(2) 157-165.

[35] Herskovits EH, Gerring J, Davatzikos C, Bryan R. Is the spatial distribution of brain lesions associated with closed-head injury in children predictive of subsequent development of Posttraumatic Stress Disorder?. Radiology 2002;224 345-351.

[36] Mather FJ, Tate RL, Hannan TJ. Post-traumatic stress disorder in children following road traffic accidents: a comparison of those with and without mild traumatic brain injury. Brain Injury 2003;17(12) 1077-1087. doi: 10.1080/0269905031000114045

[37] Grados MA, Vasa RA, Riddle MA, Slomine BS, SalorioC, Christensen J, Gerring J. New onset obsessive-compulsive symptoms in children and adolescents with severe traumatic brain injury. Depression and Anxiety 2008;25(5) 398-407. doi: 10.1002/da.20398

[38] Luis CA, Mittenberg W. Mood and anxiety disorders following pediatric traumatic brain injury: a prospective study. Journal of Clinical and Experimental Neuropsychology 2002;24(3) 270-279. doi: 10.1076/jcen.24.3.270.982

[39] Max JE, Keatley E, Wilde E, Bigler E, Levin H, Schachar R... Yang T. Anxiety disorders in children and adolescents in the first six months after traumatic brain injury. The Journal of Neuropsychaitry and Clinical Neurosciences 2011;23 29-39.

[40] Vasa R, Gerring JP, Grados M, Slomine B, Christensen J, Rising W... Riddle MA. Anxiety after severe pediatric closed head injury. American Academy of Child and Adolescent Psychitry 2002;41(2) 148-156.

[41] Vasa RA, Grados M, Slomine B, Herskovits EH, Thompson RE, Salorio C... Gerring JP. Neuroimaging correlates of anxiety after pediatric traumatic brain injury. Biological Psychiatry 2004;55(3) 208-216. doi: 10.1016/s0006-3223(03)00708-x

[42] Levine B, Kovacevic N, Nica EI, Cheung G, Gao F, Schwartz ML, Black SE. The Torronto traumatic brain injury study. Neurology 2008;7 771-778.

[43] Povlishock JT, Katz DI. Update of neuropathology and neurological recovery after traumatic brain injury. Journal of Head Trauma Rehabilitation 2008;20(1) 76-94.

[44] Bigler ED, Dennis M, Taylor HG, Vannatta K, Gerhardt CA, Abildskov TJ.... Yeates KO. Heterogeneity of brain lesions in pediatric traumatic brain injury. Neuropsychology 2013;27(4) 438-451.

[45] Bigler ED. Anterior and middle cranial fossa in traumatic brain injury: Relevant neuroanatomy and neuropathology in the study of neuropsychological outcome. Neuropsychology 2007;21(5) 515-531.

[46] Levin HS, Williams DJ, Eisenberg HM, High WM Jr, Guinto FC Jr. Serial MRI and neurobehavioural findings after mild to moderate closed head injury. Journal of Neurology, Neurosurgery and Psychiatry 1992;55 255-262.

[47] Rutgers DR, Toulgoat F, Cazejust J, Fillard P, Lasjaunias P, Ducreux D. White matter abnormalities in mild traumatic brain injury : A diffusion tensor imaging study. American Journal of Neuroradiology 2008;29, 514-519.

[48] McLean CP, Asnaani A, Litz BT, Hofmann SG. Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. Journal of psychiatric research 2011;45(8) 1027-1035.

[49] Carr A, McNulty M., Editors. The handbook of adult clinical psychology: An evidence-based approach. London: Routledge; 2006.

[50] Seeman MV. Psychopathology in women and men: Focus on female hormones. American Journal of Psychiatry 1997;154 1641-1647.

Journal of Clinical and Experimental Neuropsychology
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/ncen20

Internalizing disorders in adults with a history of childhood traumatic brain injury

Michelle Albicini[a] & Audrey McKinlay[b]
[a] Faculty of Medicine, Nursing and Health Sciences, School of Psychology and Psychiatry, Monash University, Clayton, VIC, Australia
[b] School of Psychological Sciences, University of Melbourne, Melbourne, VIC, Australia
Published online: 24 Aug 2015.

To cite this article: Michelle Albicini & Audrey McKinlay (2015) Internalizing disorders in adults with a history of childhood traumatic brain injury, Journal of Clinical and Experimental Neuropsychology, 37:7, 776-784, DOI: 10.1080/13803395.2015.1053843

To link to this article: http://dx.doi.org/10.1080/13803395.2015.1053843

Journal of Clinical and Experimental Neuropsychology, 2015
Vol. 37, No. 7, 776–784, http://dx.doi.org/10.1080/13803395.2015.1053843

Internalizing disorders in adults with a history of childhood traumatic brain injury

Michelle Albicini[1] and Audrey McKinlay [2]

[1]Faculty of Medicine, Nursing and Health Sciences, School of Psychology and Psychiatry, Monash University, Clayton, VIC, Australia
[2]School of Psychological Sciences, University of Melbourne, Melbourne, VIC, Australia

(*Received 12 November 2014; accepted 18 May 2015*)

Introduction: While the presence of externalizing behavioral problems following traumatic brain injury (TBI) has been well established in the literature, less is known regarding internalizing disorders, and more specifically anxiety disorders, in such a population. This study explored the presence, rate, and incidence of internalizing behavior problems, including anxiety, depression, somatic complaints, avoidant personality symptomatology, and overall internalizing behavior problems in university students aged 18–25 years. *Method*: A convenience sample of 247 university students (197 non-TBI, 47 mild TBI, 2 moderate TBI, 1 severe TBI) aged 18–25 years was utilized. Participants completed a self-report measure on behavioral functioning, the Adult Self Report (ASR), to identify internalizing behaviors, and a questionnaire to identify TBI history. *Results*: Raw scores of behavior indicated that participants with a history of childhood TBI reported significantly higher levels of withdrawal, somatic complaints, and internalizing behavioral problems than the non-TBI participants. When analyzing standardized *T*-scores for borderline and clinically elevated ASR syndromes and *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-oriented scales, individuals in the TBI group were significantly more likely to have higher rates of borderline anxiety, somatic complaints, avoidant personality problems, and overall internalizing disorders, and clinically elevated somatic complaints. Adults with a history of childhood TBI were also significantly more likely to report at least 1 or more DSM disorders. *Conclusion*: These results clearly suggest that individuals with a childhood history of TBI are at a heightened risk for a range of internalizing disorders in early adulthood, which is particularly troubling in a university sample pursuing tertiary education.

Keywords: Students; Traumatic brain injury; Behavioral problems; anxiety; Internalizing disorders.

Within the literature, it has been well established that traumatic brain injury (TBI) sustained in childhood is associated with a range of behavioral problems that develop later in life, such as hyperactivity and aggression, conduct problems, adaptive functioning skills, and social and emotional issues (Donders & Warschausky, 2007; Hawley, Ward, Long, Owen, & Magnay, 2003; Schwartz 2003; Sonnenberg, Dupuis & Rumney, 2010). Moreover, it is also generally accepted that individuals with a childhood history of TBI may be at risk of developing psychiatric disorders, including attention-deficit/hyperactivity disorder, conduct disorder, oppositional defiant disorder, drug abuse, personality change disorders, and mood and anxiety disorders (Max et al., 2013; Max et al., 2012; McKinlay, Dalrymple-Alford, Horwood, & Fergusson, 2002), which can persist even into adulthood (Anderson, Brown, Newitt, & Hoile, 2011; Anderson, Godfrey, Rosenfield, & Catroppa, 2011). There is a vast literature on the incidence of behavioral problems and psychiatric disorders in individuals following TBI. However, the focus is often on externalizing disorders and symptoms, with internalizing problems rarely being

No potential conflict of interest was reported by the author(s).

Address correspondence to: Michelle Albicini, School of Psychology and Psychiatry, Faculty of Medicine, Nursing and Health Sciences, Monash University, Wellington Road, Clayton, Victoria 3800, Australia [redacted]

specifically investigated in such a sample. Moreover, there is a lack of research that seeks to examine anxiety disorders in individuals with a history of TBI (Albicini & McKinlay, in press)

Previous research examining long-term behavioral problems following childhood TBI have demonstrated that symptoms and diagnoses of internalizing disorders, such as anxiety, depression, and emotional and social withdrawal symptoms, are elevated in such individuals (Karver et al., 2012; Max et al., 2013; Max et al., 2012). A handful of studies have highlighted that internalizing problems may be a significant concern in a child and adolescent TBI sample, in that these individuals were more likely to have clinically elevated levels of anxiety and internalizing problems, including depression, somatic complaints, and withdrawal, at long-term follow-ups (Karver et al., 2012; Liu & Li, 2013).

While there is an abundance of work exploring behavioral outcomes following TBI in general, research that has focused solely on the incidence and presentation of internalizing behavioral problems and anxiety disorders in a TBI sample is limited (Albicini & McKinlay, in press). Peterson et al. (2013) examined internalizing symptomatology in 12–17-year-old TBI individuals with a history of TBI. Child and parental ratings of behavior indicated that 22–26% of the TBI sample exhibit clinically elevated internalizing problems (Peterson et al., 2013). In support of this, in a study of adult outcomes following childhood TBI, individuals with TBI reported higher rates of anxiety and internalizing disorders than did orthopedic injury (OI) controls (Scott et al., 2014). Furthermore, females with TBI were at higher risk of developing lasting mood, anxiety, and internalizing disorders (Scott et al., 2014).

Finally, studies examining new-onset psychiatric disorders following childhood TBI also support the notion that internalizing disorders may become a significant problem in such a sample. One study reports higher rates of novel anxiety, depression, and internalizing disorders for children and adolescents with a history of TBI than for OI controls, 3 months after injury (Max et al., 2012). Moreover, in this sample, novel internalizing disorders and anxiety disorder occurred more frequently than ADHD and ODD (Max et al., 2012). Further, a later study looking at psychiatric disorders 6 months after mild TBI, also in children and adolescents, reported 64% of the sample to have internalizing disorders, with 36% of these cases as anxiety disorders (Max et al., 2013).

When examining the above studies, it is apparent that anxiety may be an outcome of importance following childhood TBI. Again, this has been relatively overlooked in the literature (Albicini & McKinlay, in press). Early accounts, however, indicate cases of new-onset obsessive compulsive disorder (OCD; Max et al., 1995), and social anxiety disorder (SAD; Chaves et al., 2012), following childhood severe TBI. Such case studies highlight the need to explore anxiety symptomatology in larger TBI samples.

Following from this, one study has focused on the incidence of new onset compulsions and obsessions following severe pediatric TBI in children and adolescents (Grados et al., 2008), finding that 30% of the sample exhibited obsessive and compulsive symptomatology. Other studies have explored the rate of anxiety disorders including generalized anxiety disorder (GAD), autism spectrum disorder (ASD), posttraumatic stress disorder (PTSD), Parkinson's disease (PD), obsessive-compulsive disorder (OCD), simple/specific phobia, social phobia, and SAD in TBI samples (Luis & Mittenberg, 2002; Max et al., 2011; Vasa et al., 2002) with results demonstrating that TBI in children and adolescents significantly increases the risk of developing subsequent anxiety disorders (Grados et al., 2008; Luis & Mittenberg, 2002; Max et al., 2011; Vasa et al., 2002). When comparing children with mild TBI, moderate/severe TBI, and OI, results suggest a potential relationship between degree of neurological insult and risk of developing subsequent anxiety disorders (Luis & Mittenberg, 2002) in that overall anxiety disorders were most common in children with moderate/severe TBI (Luis & Mittenberg, 2002).

In light of the above research and findings, we believe that it is important to explore the incidence and presentation of internalizing disorders, with particular interest of anxiety, in individuals with a history of childhood TBI. While much of the above research has investigated acute behavioral problems following childhood TBI, it is also important to investigate long-term effects, given that structural changes have been noted in the brain even 10 years after childhood TBI (Beauchamp, et al., 2011). The aim of this study was to examine the rate of internalizing and anxiety disorders in a university student sample. It is hypothesized that university students with a history of childhood TBI will report higher rates of internalizing disorders, including anxiety, depression, and somatic complaints, than university students with no TBI history.

METHOD

Participants

The participants were from an existing study investigating TBI status and poor behavioral outcomes in university students. Participants were volunteers, recruited through the use of flyers and a booth set up in the University. Inclusion criteria were individuals aged 18–25 years who were studying/attending Monash University. The exclusion criterion was non-English-speaking individuals. Of the 259 students who enquired about the study, 247 participated (n = 10 did not reply to follow up emails; n = 2 did not return questionnaires), with an overall response rate of 95%. The final sample consisted of 103 males (M = 20.60 years, SD = 1.88 years) and 139 females (M = 20.30 years, SD = 1.99 years) aged 18–25 years, and five participants who did not record their sex or age. Fifty participants reported a history of TBI, with 47 mild TBI, 2 moderate TBI, and 1 severe TBI. All participants were fully informed of the study and provided implied consent via completion of the questionnaires. All participants were provided an incentive to participate in the study. Ethics approval was obtained from Monash University human ethics committees.

Procedure

Each participant volunteered by enquiring at the booth and completed self-report questionnaires regarding TBI status and behavior. The participants were required to complete the questionnaires at the time they were handed to them and to return them to the researcher in a sealed envelope. This procedure took approximately 20 min for the participants to complete.

Design

This study utilized a between-subjects, cross-sectional design whereby assessment of a participant's history of TBI and behavior was evaluated at a single time point. The independent variable was whether or not participants had sustained a previous TBI, as determined by the Ohio State University TBI Identification Method (Corrigan & Bogner, 2007; see below). The dependent variables were raw scores of behavioral outcomes, and incidence rates of converted (T) scores for borderline and clinically elevated behavior scales and syndromes according to the Adult's Self Report.

Materials

The Ohio State University TBI Identification Method Short Form (OSU TBI-ID SF), adapted from the OSU TBI-ID (Corrigan & Bogner, 2007) was used as a self-report measure to screen lifetime TBI exposure. Five questions relate to past exposure to head and neck injuries caused by sources such as vehicle accidents, and if these injuries are present, a further three questions probe duration of loss of consciousness (LOC) and loss of memory (Corrigan & Bogner, 2007). Participants who reported being dazed or having loss of memory resulting from a head injury were also classified as having mild TBI (mTBI), as mTBI has also been defined present when an individual experiences loss of memory for events occurring near the injury, alongside alterations of mental state (Albicini & McKinlay, 2014; Esselman & Uomoto, 1995; McKinlay, 2010). Interrater reliability is high, ranging from α = .85 to α = .93 (Corrigan & Bogner, 2007), and test–retest reliability adequate with α > .60 (Bogner & Corrigan, 2009). To assess behavioral outcomes, the Adult's Self Report (ASR; Achenbach, Bernstein, & Dumenci, 2005) was used, which measures adaptive functioning in individuals aged 18–59 years. The ASR assesses social, educational, recreational, and occupational functioning and examines behavioral problems across eight domains. Participants must score statements as 0 (*not true*), 1 (*sometimes true*), or 2 (*very true*). The scores are summed, and the checklist derives internalizing and externalizing behavior scores and a full-scale score (Achenbach et al., 2005). The measure has high internal consistency and test–retest reliability, with coefficients of α = .89 and α = .86, respectively (Achenbach et al., 2005). Raw scores for the subscales Anxious/Depressed, Withdrawn, Somatic Complaints, Internalizing Disorders, Aggressive Behavior, Rule-Breaking Behavior, Intrusive Thoughts, and Externalizing Disorders were calculated by summing scores for each scale. The internalizing scale scores were converted to standardized T-scores. Additionally, the scale derives *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-oriented subscales for which raw scores were also converted to standardized T-scores for Depression, Anxiety, Somatic Complaints, and Avoidant Personality Problems.

Data analysis

To examine group differences on demographic information, chi-square analyses were conducted for

gender and education level, and independent samples *t* tests were conducted for age. First, a one-way multivariate analysis of variance (MANOVA) was conducted on raw scores of Aggressive Behavior, Rule-Breaking Behavior, Intrusive Thoughts, and Externalizing Disorders subscales so a comparison of results could be examined between internalizing and externalizing problems. Then, a MANOVA was conducted on raw scores of anxious/depressed, withdrawn, somatic complaints, and internalizing disorders subscales to determine whether there are significant differences among those with and without a history of childhood TBI. Following this, a more detailed examination of internalizing disorders was conducted by calculating rates of clinically elevated and borderline ASR and DSM-oriented internalizing disorders among the groups. To do this, raw scores from the above subscales were converted to standardized *T*-scores. Percentages were calculated for each disorder in each group, and odds ratios were computed to determine differences in the likelihood of a person with and without childhood TBI of developing a disorder.

RESULTS

Descriptive statistics

Demographic characteristics for individuals with TBI are shown in Table 1. Chi-square analyses indicated no significant association between the two groups in terms of gender, $\chi^2(1) = 0.17$, $p = .68$, or education, $\chi^2(8) = 4.62$, $p = .80$. Further, an independent-samples *t* test revealed no significant differences in age between those with and those without TBI, $t(227) = -0.26$, $p = .79$.

TABLE 1
Characteristics of participants with TBI

	TBI group (n = 50)		
Characteristic	*N*	*%*	*M*
Gender			
Male	20	40	
Female	30	60	
Age (years)			20.36
Age at first injury[a] (years)			14.80
TBI before/after 15 years[a]			
<15 years	20	40	
≥15 years	15	30	
n/a	15	30	
TBI with any LOC	36	72	
TBI with LOC >30 min	5	10	
Multiple TBI[a]	8	16	

Note. TBI = traumatic brain injury; LOC = loss of consciousness.

[a]The Ohio State University TBI Identification Method Short Form (OSU TBI-ID SF) only provides this information for TBI involving LOC.

Raw scores for ASR syndromes

For the externalizing scales, a MANOVA was conducted on raw scores for the syndrome scales Aggressive Behavior, Rule-Breaking Behavior, Intrusive Thoughts, and Externalizing Disorders, to examine differences among students with and without a history of TBI. The results revealed no significant differences between the two groups on aggression, $F(1, 242) = 0.01$, $p = .94$, rule-breaking, $F(1, 242) = 0.67$, $p = .41$, intrusive thoughts, $F(1, 242) = 0.16$, $p = .69$, or externalizing disorders, $F(1, 242) = 0.5$, $p = .48$. A MANOVA was conducted on raw scores for the syndrome scales Anxiety/Depressed, Withdrawn, Somatic Complaints, and Internalizing Disorders, to examine differences among students with and without a history of TBI. The results revealed a significant effect of TBI for somatic complaints, such that students with a TBI ($M = 5.89$, $SD = 5.02$) reported significantly more somatic problems than students without TBI ($M = 3.56$, $SD = 3.12$), $F(1, 242) = 16.24$, $p < .001$, $\eta^2 = .06$. There was also a main effect of TBI for internalizing disorders, with those with a history of TBI ($M = 21.66$, $SD = 15.02$) endorsing significantly more internalizing behavioral problems than those without TBI ($M = 16.86$, $SD = 11.80$), $F(1, 242) = 5.62$, $p = .02$, $\eta^2 = .02$. Further, scores on the Withdrawn subscale significantly differed between groups, with participants with TBI endorsing more problems ($M = 4.79$, $SD = 3.47$) than participants without TBI ($M = 3.60$, $SD = 3.21$), $F(1, 242) = 5.04$, $p = .03$, $\eta^2 = .02$. There was no significant difference in raw scores for the Anxious/Depressed subscale between the two groups, $F(1, 242) = 1.24$, $p = .27$.

Converted *T*-scores

Raw scores from the ASR were converted into standardized *T*-scores, and rates of borderline and full internalizing problems were examined in each group. Further, odds ratios were calculated to examine differences in the likelihood of developing a disorder among the two groups. Table 2 presents these rates and odds ratios for DSM-oriented syndromes among those with and without a history of TBI.

As is shown in Table 2, for DSM-oriented scales, those with TBI had a higher incidence of borderline cases of anxiety and depressive disorders, a

TABLE 2
Percentages and odds ratios for clinically elevated and borderline DSM-oriented syndromes across TBI and non-TBI groups

DSM syndrome	*Severity*	*Group*	*n*	*%*	*Odds ratio*	*CI*	*p*
Anxiety	borderline	TBI	6/50	12	1.36	[0.51, 3.62]	.54
		Non-TBI	18/197	9			
	full	TBI	4/50	8	1.34	[0.41, 4.35]	.63
		Non-TBI	12/197	6			
Depression	borderline	TBI	4/50	8	1.34	[0.41, 4.35]	.63
		Non-TBI	12/197	6			
	full	TBI	7/50	14	1.62	[0.64, 4.12]	.31
		Non-TBI	18/197	9			
Somatic complaints	borderline	TBI	4/50	8	0.92	[0.29, 2.87]	.89
		Non-TBI	17/197	9			
	full	TBI	6/50	12	5.24	[1.53, 17.94]	.01*
		Non-TBI	5/197	3			
Avoidant personality	borderline	TBI	2/50	4	0.35	[0.08, 1.54]	.10
		Non-TBI	21/197	11			
	full	TBI	12/50	24	3.34	[1.48, 7.57]	.004**
		Non-TBI	17/197	8			
≥1 DSM syndrome		TBI	24/50	48	2.57	[1.36, 4.88]	.004**
		Non-TBI	52/197	26			

Note. TBI = traumatic brain injury; CI = confidence interval; DSM = *Diagnostic and Statistical Manual of Mental Disorders*. *$p < .05$. **$p < .01$.

higher incidence of full cases of anxiety, depression, somatic problems, and avoidant personality problems, and a higher rate of overall DSM syndromes, than non-TBI participants. Of these, the difference was significant for full somatic complaints, such that students with TBI were over five times more likely to report somatic complaints than students without TBI. Additionally, the difference for borderline avoidant personality problems was significant, in that students with TBI were over three times more likely to report avoidance problems than students without TBI. Finally, students with TBI were 2.57 times more likely to endorse at least one DSM-oriented disorder than those without TBI, and this difference was significant. Table 3 presents rates of and odds ratios for borderline and elevated ASR syndrome scales among the groups.

As is evident in Table 3, those with TBI had higher rates of borderline anxiety/depression, withdrawal, somatic complaints, and internalizing problems. The TBI group also endorsed higher rates of full withdrawal, somatic complaints, and internalizing problems. Finally, those with TBI also had a higher number of overall ASR syndromes and a higher rate of multiple problems. Odds ratio calculations indicated that students with TBI were over four times more likely to endorse borderline anxiety problems than non-TBI students, which was statistically significant. There was a significant difference among the groups for full somatic complaints, with students with a history of TBI being 4.5 times more likely to report such problems than the non-TBI group. Students with TBI were also significantly more likely to report borderline internalizing problems, at a rate of almost three times more likely than the non-TBI group. Finally, the incidence of multiple problems was significantly higher for the TBI group, such that students with a history of TBI were over twice as likely to report multiple behavioral problems than students with no TBI.

DISCUSSION

This study explored rates and differences in internalizing symptomatology and disorders in university students aged 18–25 years with or without a history of childhood TBI. The study examined long-term, as opposed to acute, outcomes after predominately mild TBI. To examine whether participants' responses on the internalizing behavior scales reflected a response bias in those with TBI, the authors also analyzed information on the externalizing behavior scales of the outcome measure. It was hypothesized that higher rates of anxiety, depression, withdrawal, somatic complaints, avoidant personality problems, and overall internalizing behavioral problems would be significantly elevated in those with a history of TBI. The results of this study

TABLE 3
Percentages and odds ratios for clinically elevated and borderline ASR syndromes across TBI and non-TBI groups

ASR syndrome	*Severity*	*Group*	*n*	*%*	*Odds ratio*	*CI*	*p*
Anxiety/Depressed	borderline	TBI	6/50	22	4.35	[1.79, 10.57]	.001**
		Non-TBI	18/197	6			
	full	TBI	4/50	10	0.67	[0.25, 1.84]	.44
		Non-TBI	12/197	14			
Withdrawn	borderline	TBI	4/50	22	2.03	[0.92, 4.50]	0.07
		Non-TBI	12/197	12			
	full	TBI	7/50	12	1.93	[0.69, 5.36]	.21
		Non-TBI	18/197	6			
Somatic complaints	borderline	TBI	4/50	14	1.44	[0.57, 3.63]	.44
		Non-TBI	17/197	10			
	full	TBI	6/50	16	4.50	[1.60, 12.67]	.004**
		Non-TBI	5/197	4			
Internalizing	borderline	TBI	2/50	18	2.66	[1.09, 6.51]	.03*
		Non-TBI	21/197	7			
	full	TBI	12/50	28	1.39	[0.69, 2.82]	.36
		Non-TBI	17/197	22			
≥1 ASR syndrome		TBI	24/50	48	1.79	[0.96, 3.36]	.07
		Non-TBI	67/197	34			
Multiple problems		TBI	25/50	50	2.58	[1.37, 4.88]	.003**
		Non-TBI	55/197	28			

Note. TBI = traumatic brain injury; ASR = Adult Self Report; CI = confidence interval.
*$p < .05$; **$p < .01$.

revealed that, in reference to raw behavioral scores, participants with a history of childhood TBI reported significantly higher levels of withdrawal, somatic complaints, and internalizing behavioral problems than the non-TBI participants. When analyzing standardized *T*-scores for borderline and clinically elevated syndromes and DSM-oriented diagnoses, individuals in the TBI group were significantly more likely to have higher rates of borderline anxiety, somatic complaints, avoidant personality problems, and overall internalizing disorders and clinically elevated somatic complaints. Students with TBI were also significantly more like to report at least one DSM disorder and multiple disorders.

Our findings for raw behavior scores are in line with those of previous studies that have explored internalizing problems following childhood TBI. For instance, Peterson et al. (2013) utilized the Child Behavior Checklist, a child and adolescent form of the behavior rating scale used in this study, and found that scores on the Withdrawn, Somatic Complaints, and Internalizing Problems subscales were clinically elevated in childhood mild TBI compared to standardized norms. These results were in support of a similar study utilizing the same assessment tool (Karver et al., 2012), with higher rates of internalizing problems found in children with mild to moderate TBI and severe TBI than in an OI group. Unlike Peterson et al., this study found no differences in rates of problems for the Anxious/Depressed scale. However, the results were in line with Karver et al. (2012), who reported the same for their mild to moderate TBI group.

In reference to borderline and clinically elevated rates of internalizing disorders, our results also support past research. Scott et al. (2014) reported that participants aged 18–31 years with a childhood mild TBI were more likely to endorse symptoms of anxiety and internalizing disorders, which is consistent with our findings. Further, Luis and Mittenberg (2002) also reported higher rates of anxiety and mood problems following childhood TBI; however, this was a trend association and was found for children with moderate to severe injuries. Other studies have also reported clinically elevated levels of anxiety, depression, and withdrawal symptoms following childhood mild TBI (Hawley et al., 2003; Liu & Li, 2013; Max et al., 2013).

Explanations for the above results may involve the brain regions implicated in TBI and their effect on the emotion regulation system. Magnetic resonance imaging (MRI) studies in children with TBI and subsequent internalizing problems have identified regions such as the orbitofrontal cortex, thalamus, temporal regions, amygdala, frontal gyri, and hippocampus to be

implicated (Albicini & McKinlay, in press; Grados et al., 2008; Herskovits, Gerring, Davatzikos, & Bryan, 2002; Max et al., 2011; Vasa et al., 2004). These systems are important for affect regulation and the generation of an appropriate affective state (Max et al., 2011), and so disruption to these areas in the event of TBI is likely to produce significant emotional problems.

Other explanations for our results may relate to the specific sample that we have selected. We utilized a university-based sample, which means that the participants are assumed to have a reasonable level of cognitive functioning to enable them to complete their academic studies. Cooper-Evans, Alderman, Knight, and Oddy (2008) reported that individuals with a history of TBI who have a higher level of cognitive function may possess more insight into their deficits, resulting in an increased risk of anxiety or low mood due to low self-esteem, thereby suggesting that university students may be more likely to report internalizing behavioral problems because they are more aware of their dysfunctions following an injury. Additionally, this sample consisted of a higher number of females in the TBI groups than males (60%), which is in contrast to research stating that males are at greater risk of TBI (Crowe, Babl, Anderson, & Catroppa, 2009; McKinlay et al., 2008). Countless studies have indicated that females experience internalizing behavioral problems at higher rates (Feingold, 1994; Lewinsohn, Gotlib, Lewinsohn, Seeley, & Allen, 1998; McLean, Asnaani, Litz, & Hofmann, 2011). This has been attributed to hormonal differences including the role of estrogen and progesterone in enhancing stress responses (Seeman, 1997), some sort of genetic predisposition such as the propensity to experience negative emotions (Feingold, 1994; Lewinsohn et al., 1998), internal locus of control and personality differences (Feingold, 1994), and the higher synthesis of serotonin within the brain in males (Nishizawa et al., 1997). The high prevalence of psychiatric symptoms in this sample may also be attributed to the method of recruitment—the study description included reference to behavioral problems and head injury, and, as such, distressed individuals or students with preexisting problems may have been more likely to participate in the study. However, considering that our results indicated no significant differences between the two groups on externalizing behavioral problems, it is unlikely that there was a response bias.

Limitations

A limitation of the study was that all participants were university students attending the one campus, which may have biased the sample and decreased the external validity of the study. However, considering the sample was derived from a large and international institution, this is unlikely to be detrimental to our results. In addition, the self-report nature of the ASR may have led participants to respond in a socially desirable way. Further, the use of a retrospective and self-report measure of TBI may have resulted in misclassifying participants into the TBI/non-TBI groups due to the reliance on memory. The OSU TBI-ID does provide limited information regarding the nature of a TBI event, given that it is based on self-report, particularly in the case of participants who have suffered a TBI during childhood and do not recall the details of such an event. In addition, the measure was used as a rating form as opposed to an interview form, and, as such, it was not possible to ascertain and confirm information with the participants on the accuracy of their injuries. However, this measure has excellent psychometric properties, and the OSU TBI-ID has successfully been used in a number of studies to identify a history of TBI (e.g., Corrigan, Bogner, & Holloman, 2012) and also is used clinically to screen for TBI exposure (Ohio Valley Center for Brain Injury Prevention and Rehabilitation, 2015).

Another significant limitation is that we did not control for premorbid behavior and other individual characteristics such as psychiatric diagnoses, intellectual disabilities, or other preexisting behavioral problems, which will have likely affected the results of the current study. For instance, research has noted that premorbid anxiety symptoms and nonanxiety diagnoses (Gerring et al., 2002) and also internalizing disorders at time of injury (Max et al., 1998) significantly predict anxiety symptomatology following TBI. Moreover, we did not control for non-neurological medical illnesses in our sample. Medical illness are also associated with symptoms of anxiety and depression (Katon, 2003; Roy-Byrne et al., 2008) and also somatic symptoms as a consequence of the illness itself. As such, the elevating internalizing disorders and symptoms evident in the study may be a

function of the illness and not solely due to the TBI itself. Finally, to compute the overall internalizing and externalizing subscales, scores from the other subscales are summed. As such, this means that the data were not always independent in the analyses, which violates the statistical assumptions of the MANOVA.

CONCLUSIONS

This study sheds light on the limited knowledge regarding the profile of internalizing disorders in a university sample with history of childhood TBI. Such a sample provides a snapshot of the type of long-term problems that may be experienced in young adulthood, an age group relatively ignored in the literature, who are pursuing tertiary education following an injury event. This study can direct future work into such behavioral problems and utilize objective assessment measures of TBI and MRI procedures to delineate structural brain dysfunction and correlates of internalizing problems. It is concluded that university students with a history of childhood TBI are at risk of developing long-term internalizing behavioral problems, including withdrawal, somatic complaints and avoidant personality problems. This is important to consider with regard to interventions that can aim to assist such individuals who may be struggling at university due to these long-term outcomes.

ORCID

Audrey McKinlay http://orcid.org/0000-0001-9846-8514

REFERENCES

Achenbach, T. M., Bernstein, A., & Dumenci, L. (2005). DSM-oriented scales and statistically based syndromes for ages 18 to 59: Linking taxonomic paradigms to facilitate multitaxonomic approaches. *Journal of Personality Assessment*, *84*(1), 49.

Albicini, M., & McKinlay, A. (2014). Mild traumatic brain injury: A review of terminology, symptomatology, clinical considerations and future directions. In F. Sadaka (Ed.), *Traumatic brain injury*. Retrieved from http://www.intechopen.com/books/traumatic-brain-injury/mild-traumatic-brain-injury-a-review-of-terminology-symptomatology-clinical-considerations-and-futur

Albicini, M., & McKinlay, A. (in press). A systematic review of anxiety disorders following mild, moderate and severe TBI in children and adolescents. In F. Durbano (Ed.), *A fresh look at anxiety disorders*. Intech Publishing.

Anderson, V., Brown, S., Newitt, H., & Hoile, H. (2011). Long-term outcome from childhood traumatic brain injury: Intellectual ability, personality and quality of life. *Neuropsychology*, *25*(2), 176–184.

Anderson, V., Godfrey, C., Rosenfield, J. V., & Catroppa, C. (2011). 10 Years outcome from childhood traumatic brain injury. *International Journal of Developmental Neuroscience*, *30*, 217–224.

Beauchamp, M. H., Ditchfield, M., Maller, J. J., Catroppa, C., Godfrey, C, Rosenfield, J. V., … Anderson, V. A. (2011). Hippocampus, amygdala, and global brain changes 10 years after childhood traumatic brain injury. *International Journal of Developmental Neuroscience*, *29*, 137–143.

Bogner, J. A., & Corrigan, J. D. (2009). Reliability and predictive validity of the Ohio State University TBI Identification Method with prisoners. *Journal of Head Trauma Rehabilitation*, *24*(4), 279–291.

Chaves, C., Trzesniak, C., Derenusson, G. N., Araujo, D., Wichert-Ana, L., Machado-de-Sousa, J. P., … Hallak, J. E. (2012). Late-onset social anxiety disorder following traumatic brain injury. *Brain Injury*, *26*(6), 882–886. doi:10.3109/02699052.2012.666373

Cooper-Evans, S., Alderman, N., Knight, C., & Oddy, M. (2008). Self-esteem as a predictor of psychological distress after severe acquired brain injury: An exploratory study. *Neuropsychological Rehabilitation*, *18*(5–6), 607–626.

Corrigan, J. D., Bogner, J., & Holloman, C. (2012). Lifetime history of traumatic brain injury among persons with substance abuse disorders. *Brain Injury*, *26*(2), 139–150.

Corrigan, J. D., & Bogner, J. A. (2007). Initial reliability and validity of the OSU TBI Identification Method. *Journal of Head Trauma Rehabilitation*, *22*(6), 318–329.

Crowe, L., Babl, F., Anderson, V., & Catroppa, C. (2009). The epidemiology of pediatric head injuries: Data from a referral centre in Victoria, Australia. *Journal of Pediatric and Child Health*, *45*(6), 346–350.

Donders, J., & Warschausky, S. (2007). Neurobehavioural outcomes after early versus late childhood traumatic brain injury. *Journal of Head Trauma Rehabilitation*, *22*, 296–302.

Esselman, P. C., & Uomoto, J. M. (1995). Classification of the spectrum of mild traumatic brain injury. *Brain Injury*, *9*, 417–424.

Feingold, A. (1994). Gender differences in personality: A meta-analysis. *Psychological Bulletin*, *116*(3), 429–456.

Gerring, J., Slomine, B. S., Vasa, R. A., Grados, M. A., Chen, A., Rising, W., … Ernst, M. (2002). Clinical predictors of posttraumatic stress disorder after closed head injury in children. *Journal of the American Academy of Child and Adolescent Psychiatry*, *41*(2), 157–165.

Grados, M. A., Vasa, R. A., Riddle, M. A., Slomine, B. S., Salorio, C., Christensen, J., & Gerring, J. (2008). New onset obsessive-compulsive symptoms in children and adolescents with severe traumatic brain injury. *Depression and Anxiety*, *25*(5), 398–407. doi:10.1002/da.20398

Hawley, C. A., Ward, A. B., Long, J., Owen, D. W., & Magnay, A. R. (2003). Prevelance of traumatic brain injury amongst children admitted to hospital in one health district: A population-based study. *Injury*, *34*, 256–260.

Herskovits, E. H., Gerring, J., Davatzikos, C., & Bryan, R. (2002). Is the spatial distribution of brain lesions associated with closed-head injury in children predictive of subsequent development of posttraumatic stress disorder? *Radiology*, *224*, 345–351.

Karver, C. L., Wade, S. L., Cassedy, A., Taylor, H. G., Stancin, T., Yeates, K. O., & Walz, N. C. (2012). Age at injury and long-term behavior problems after traumatic brain injury in young children. *Rehabilitation Psychology*, *57*(3), 256–265. doi:10.1037/a0029522

Katon, W. J. (2003). Clinical health services relationships between major depression, depressive symptoms and general medical illness. *Society of Biological Psychiatry*, *54*, 216–226.

Lewinsohn, P. M., Gotlib, I. H., Lewinsohn, M., Seeley, J. R., & Allen, N. B. (1998). Gender differences in anxiety disorders and anxiety symptoms in adolescents. *Journal of Abnormal Psychology*, *107*(1), 109–117.

Liu, J., & Li, L. (2013). Parent-reported mild head injury history and behavioural performance in children at 6 years. *Brain Injury*, *27*(11), 1263–1270. doi:10.3109/02699052.2013.804205

Luis, C. A., & Mittenberg, W. (2002). Mood and anxiety disorders following pediatric traumatic brain injury: A prospective study. *Journal of Clinical and Experimental Neuropsychology*, *24*(3), 270–279. doi:10.1076/jcen.24.3.270.982

Max, J. E., Castillo, C., Robin, D., Lindgren, S., Smith, W., Sato, Y., & Arndt, S. (1998). Posttraumatic stress symptomatology after childhood traumatic brain injury. *The Journal of Nervous and Mental Disease*, *186*(10), 589–596.

Max, J. E., Keatley, E., Wilde, E., Bigler, E., Levin, H., Schachar, R., … Yang, T. (2011). Anxiety disorders in children and adolescents in the first six months after traumatic brain injury. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *23*, 29–39.

Max, J. E., Schachar, R., Landis, J., Bigler, E., Wilde, E., Saunders, A., … Levin, H. (2013). Psychiatric disorders in children and adolescents in the first six months after mild traumatic brain injury. *Journal of Neuropsychiatry and Clinical Neuroscience*, *25*(3), 187–197.

Max, J. E., Smith, W., Lindgren, S., Robin, D., Mattheis, P., Stierwalt, J., & Morrisey, M. (1995). Case study: Obsessive-compulsive disorder after severe traumatic brain injury in an adolescent. *Journal of the American Academy of Child and Adolescent Psychiatry*, *34*(1), 45–49.

Max, J. E., Wilde, E., Bigler, E., MacLeod, M., Vasquez, A., Schmidt, A., … Levin, H. (2012). Psychiatric disorders after pediatric traumatic brain injury: A prospective, longitudinal, controlled study. *Journal of Neuropsychiatry and Clinical Neuroscience*, *24*(4), 427–436.

McKinlay, A. (2010). Controversies and outcomes associated with mild traumatic brain injury in childhood and adolescences. *Child: Care, Health and Development*, *36*, 3–21. doi:10.1111/j.1365-2214.2009.01006.x

McKinlay, A., Dalrymple-Alford, J., Horwood, J., & Fergusson, D. (2002). Long term psychosocial outcomes after mild head injury in early childhood. *Journal of Neurology, Neurosurgery and Psychiatry*, *73*, 281–288.

McKinlay, A., Grace, R. C., Horwood, L. J., Fergusson, D. M., Ridder, E. M., & MacFarlane, M. R. (2008). Prevalence of traumatic brain injury among children, adolescents and young adults: Prospective evidence from a birth cohort. *Brain Injury*, *22*(2), 175–181.

McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender differences in anxiety disorders: Prevalence, course of illness, comorbidity and burden of illness. *Journal of Psychiatric Research*, *45*(8), 1027–1035.

Nishizawa, S., Benkelfat, C., Young, S. N., Leyton, M., Mzengeza, S., de Montigny, C., … Diksic, M. (1997). Differences between males and females in rates of serotonin synthesis in the human brain. *Proceedings of the National Academy of Sciences*, *94*(10), 5308–5313.

Ohio Valley Center for Brain Injury Prevention and Rehabilitation. (2015). *Screening for TBI: A SynapShot from OVC*. Retrieved from http://ohiovalley.org/informationeducation/screening/

Peterson, R. L., Kirkwood, M. W., Taylor, H. G., Stancin, T., Brown, T. M., & Wade, S. L. (2013). Adolescents' internalizing problems following traumatic brain injury are related to parents' psychiatric symptoms. *Journal of Head Trauma Rehabilitation*, *28*(5), E1–E12. doi:10.1097/HTR.0b013e318263f5ba

Roy-Byrne, P. P., Davidson, K. W., Kessler, R. C., Asmundson, G. J. G., Goodwin, R. D., Kubzansky, L., … Stein, M. B. (2008). Anxiety disorders and comorbid medical illness. *General Hospital Psychiatry*, *30*(3), 208–225.

Schwartz, L. (2003). Long-term behavior problems following pediatric traumatic brain injury: Prevalence, predictors, and correlates. *Journal of Pediatric Psychology*, *28*(4), 251–263. doi:10.1093/jpepsy/jsg013

Scott, C., McKinlay, A., McLellan, T., Britt, E., Grace, R., & McFarlane, M. (2014). A comparison of adult outcomes for males compared to females following paediatric traumatic brain injury. *Neuropsychology*, *29*(4), 501–508.

Seeman, M. V. (1997). Psychopathology in women and men: Focus on female hormones. *American Journal of Psychiatry*, *154*(12), 1641–1647.

Sonnenberg, L. K., Dupuis, A., & Rumney, P. G. (2010). Pre-school traumatic brain injury and its impact on social development at 8 years of age. *Brain Injury*, *24*(7–8), 1003–1007. doi:10.3109/02699052.2010.489033

Vasa, R., Gerring, J. P., Grados, M., Slomine, B., Christensen, J., Rising, W., … Riddle, M. A. (2002). Anxiety after severe pediatric closed head injury. *American Academy of Child and Adolescent Psychiatry*, *41*(2), 148–156.

Vasa, R., Grados, M., Slomine, B., Herskovits, E. H., Thompson, R. E., Salorio, C., … Gerring, J. P. (2004). Neuroimaging correlates of anxiety after pediatric traumatic brain injury. *Biological Psychology*, *55*, 208–216.

DOI: 10.3109/02699052.2016.1162060

implanted drop foot stimulator system in chronic stroke patients.
Methods: [18F]-fluorodeoxyglucose-PET was prospectively acquired in 12 stroke patients with drop foot before and 1 year after the activation of a 4-channel stimulator, ActiGait, which selectively and directly stimulates the fibular nerve (five women, mean age = 47 ± 12 years, time since insult = 2 ± 1 year). Data were pre-processed and analysed by means of statistical parametric mapping (SPM8) with PET images of right-sided stroke patients being flipped.
Results: The implanted drop foot stimulator system improved walking endurance and the physiology of ankle joint kinematics. Prior to treatment, FDG-PET showed a significant decrease in metabolism in pre-motor and supplementary motor cortices, prefrontal cortex and left thalamus, contralateral to the paralysed side (FEW corrected). After 1 year of implanted fibular nerve stimulation, regional metabolism increased in pre-motor and supplementary motor cortices of ipsi- and contralateral hemisphere (0.001 uncorrected,).
Conclusions: Clinical improvement of gait after unilateral fibular nerve stimulation in chronic drop foot is parallelled by metabolic changes in the ipsi- and controlateral motor network. These results suggest a residual cortical plasticity occurring at the chronic state after a peripheral nerve stimulation.

0090 Internalizing disorders in adults with a history of childhood traumatic brain injury

Michelle Albicini[1], Audrey McKinlay[2]

[1]*Monash University, Melbourne, Australia,* [2]*University of Melbourne, Melbourne, Australia*

Objectives: There is a vast literature on the incidence of behavioural problems and psychiatric disorders in individuals following traumatic brain injury (TBI). However, the focus is often on externalizing disorders and symptoms, with internalizing problems rarely being specifically investigated in such a sample. Further, a large proportion of research in the TBI field utilizes child or older adult samples, with young adults being a relatively neglected age-group. This study explored the presence, rate and incidence of internalizing behaviour problems, including anxiety, depression, somatic complaints, avoidant personality symptomatology and overall internalizing behaviour problems in university students aged 18–25 years.
Methods: A conveniently selected sample of 247 university students (197 non-TBI, 47 mild TBI, two moderate TBI, one severe TBI) aged 18–25 years was utilized. Participants completed a self-report measure on behavioural functioning, the Adult Self Report (ASR), to identify internalizing behaviours. The internalizing scales include depression, anxiety, withdrawal, somatic complaints, avoidant personality problems and overall internalizing symptoms and clusters items into DSM-oriented scales and ASR syndromes. The Ohio State University TBI Identification Method was used as a self-report measure, which identified individuals with a history of TBI and obtains information regarding loss of consciousness and severity of injury.
Results: Due to the small group numbers ($n = 3$), individuals with moderate and severe TBI were excluded from the analyses. Mean age of TBI was 14.80 years and 57% of participants with TBI were injured before the age of 15 years. Raw scores were utilized and then converted to standardized *T*-scores to derive information on clinically significant problems. Raw scores of behaviour indicated that participants with a history of childhood TBI reported significantly higher levels of withdrawal, somatic complaints and internalizing behavioural problems than the non-TBI participants. When analysing standardized *T*-scores for borderline and clinically elevated ASR syndromes and DSM-oriented scales, individuals in the TBI group were significantly more likely to have higher rates of borderline anxiety, somatic complaints, avoidant personality problems and overall internalizing disorders and clinically elevated somatic complaints. Students with a history of childhood TBI were also significantly more like to report at least one or more DSM disorders.
Conclusions: This study sheds light on the limited knowledge regarding the profile of internalizing disorders in a university sample with a history of childhood mild TBI. This sample provides a snapshot of the long-term problems that may be experienced many years after a TBI event. It is concluded that students with a history of childhood mild TBI are at risk of developing long-term internalizing behavioural problems, including withdrawal, somatic complaints and avoidant personality problems. This is important to consider with regards to interventions which can aim to assist such individuals who may be struggling at university due to these long-term outcomes.

0091 The evaluation of cerebral blood flow in patients with traumatic head injury: A comparison of MRI ASL and Tc ECD SPECT

Yasushi Shibata, Ryota Mashiko

University of Tsukuba, Mito, Ibaraki, Japan

Objectives: Tc ECD SPECT is the standard method for evaluating cerebral blood flow (CBF); however, this method of examination is associated with some drawbacks, including high cost, radiation exposure and its limited availability for emergency patients. Arterial spin labelling (ASL) perfusion MRI is a method of CBF examination that does not involve the use of contrast media or radiation exposure and has become possible with the availability of 3T MRI. Because of its short image acquisition time, ASL can be performed in the course of a routine MRI examination. While CBF evaluation is known to be useful in the evaluation of cerebral function in cases of traumatic head injury, ASL perfusion MRI has not been fully evaluated in head injury patients. We performed ASL perfusion MRI and Tc ECD SPECT in patients with head injury and compared the imaging findings. Patients: A total of 21 patients (male: $n = 16$; female: $n = 5$; age from 18–90 years) were registered in this study. MRI and SPECT images were examined in 15 acute-phase (within 1 month after head injury), and six chronic-phase patients (more than 2 months). The final diagnoses were contusion ($n = 8$), ASDH ($n = 5$), CSDH ($n = 3$), concussion ($n = 3$), traumatic SAH ($n = 2$) and DAI ($n = 2$).
Methods: We intravenously injected Tc99m ECD 600MBq into the right cubital vein and acquired SPECT images using an E

Appendix D

Journal of Mental Health

ISSN: 0963-8237 (Print) 1360-0567 (Online) Journal homepage: http://www.tandfonline.com/loi/ijmh20

The prevalence of traumatic brain injury, comorbid anxiety and other psychiatric disorders in an outpatient child and adolescent mental health service

Michelle Albicini, Matthew Eggleston & Audrey McKinlay

To cite this article: Michelle Albicini, Matthew Eggleston & Audrey McKinlay (2017): The prevalence of traumatic brain injury, comorbid anxiety and other psychiatric disorders in an outpatient child and adolescent mental health service, Journal of Mental Health, DOI: 10.1080/09638237.2017.1385733

To link to this article: http://dx.doi.org/10.1080/09638237.2017.1385733

Journal of MENTAL HEALTH

http://tandfonline.com/ijmh
ISSN: 0963-8237 (print), 1360-0567 (electronic)

J Ment Health, Early Online: 1–7
 DOI: 10.1080/09638237.2017.1385733

Taylor & Francis
Taylor & Francis Group

Check for updates

ORIGINAL ARTICLE

The prevalence of traumatic brain injury, comorbid anxiety and other psychiatric disorders in an outpatient child and adolescent mental health service

Michelle Albicini[1,2], Matthew Eggleston[3], and Audrey McKinlay[2]

[1]Faculty of Medicine Nursing and Health Sciences, School of Psychological Sciences, Monash University, Clayton, Australia, [2]School of Psychological Sciences, University of Melbourne, Melbourne, Australia, and [3]Child and Family Specialty Service, Canterbury District Health Board, Christchurch, New Zealand

Abstract

Background: A history of traumatic brain injury (TBI) is prevalent in children and adolescents within the health system, which may be accompanied with higher rates of poor mental health outcomes including anxiety and other psychiatric disorders.
Aims: To explore rates of TBI and associated anxiety and other psychiatric diagnoses in children and adolescents aged 5–18 years within the mental health system.
Methods: Participants were recruited from an outpatient mental health service in Canterbury, New Zealand. The Ohio State University TBI Identification method was utilised to ascertain TBI history. Anxiety and other diagnoses were identified by a mental health file review.
Results: Over 28% of children in this study reported a history of TBI, the majority of which were mild. Review of mental health files revealed no significant differences between participants with and without TBI for anxiety and psychiatric diagnoses.
Conclusions: A proportionately high number of children and adolescents within the mental health system reported a previous TBI. However, anxiety and other psychiatric problems were not over-represented in this group. Further research is essential for examining the characteristics of children and adolescents with TBI within the mental health system, particularly those with more severe injuries, who may present a subgroup.

Keywords

Head injury, children, youth, psychiatric disorders, assessment

History

Received 6 December 2016
Revised 1 August 2017
Accepted 24 August 2017
Published online 4 October 2017

Introduction

Traumatic brain injury (TBI) is a lead predictor of ongoing difficulties, including behavioural, social, psychological and cognitive problems, among children and adolescents (Donders & Warschausky, 2007; Hawley, 2003; Massagli et al., 2004; McKinlay et al., 2002). Between 280 and 1373 per 100 000 children have sustained some form of TBI (McKinlay & Hawley, 2014). In a New-Zealand cohort, 790 per 100 000 cases were identified to have TBI, with 749 of these cases per 100 000 being of mild severity (Feigin et al., 2013). Moreover, children aged 0–14 years and young adults aged 18–34 years constituted 70% of all TBI cases (Feigin et al., 2013). It is important to consider any behavioural, emotional and social problems associated with such injuries, given the high number of individuals affected per year, and the potential burden this may have on individuals, their families, and mental health care systems.

According to a large Australian child and adolescent survey ($N = 2967$) of mental health and well-being, in the general population, 17% of children and adolescents aged 4–17 years utilised a service for mental health issues in the previous 12 month period (Lawrence et al., 2015). For those with TBI, 24% of children and adolescents aged 12–17 years received outpatient mental health services, 8.3% received school services, and 28.8% received any mental health service, 1–6 months after their injury (Kurowski et al., 2013). The higher rates of children and adolescents receiving mental health services following TBI is unsurprising, given findings that report on the poor outcomes that can be experienced (Hawley, 2003; McKinlay et al., 2002; McKinlay et al., 2009; Schwartz et al., 2003).

Research demonstrates that TBI may be accompanied by ongoing internalising and externalising behavioural issues in some children and adolescents (Karver et al., 2014; Liu & Li, 2013; McKinlay et al., 2009). Parent ratings of child behaviour 18-months following TBI in children aged 3–7 at the time of the injury have revealed elevated behavioural problems when compared to children with orthopaedic injury, including problems with affect, attention-deficit/hyperactivity issues, and overall behavioural problems (Karver et al., 2014). Moreover, these issues were reported to be 'unmet needs' in terms of access to clinical services, and were present in both mild to moderate and severe TBI (Karver et al., 2014).

Correspondence: Michelle Albicini, School of Psychological Sciences Monash University, 18 Innovation Walk, Clayton Campus, Wellington Road Monash University, VIC, 3800, Australia. E-mail: michelle.albicini@monash.edu

Supporting this, parents of children aged 6 years with TBI reported higher rates of withdrawal, emotional reactiveness, and aggressive problems (Liu & Li, 2013). In adolescents aged 14–16 years, attention-deficit/hyperactivity, conduct and oppositional behavioural problems, substance abuse and mood problems have been reported to be significantly higher for individuals with a history of childhood mild TBI resulting in inpatient care, as compared to a mild TBI outpatient group and healthy controls (McKinlay et al., 2009).

In addition to higher rates of behavioural issues, children and adolescents with a history of TBI may also present with a higher incidence of psychiatric or psychological diagnoses including depression, anxiety, attention-deficit/hyperactivity disorder (ADHD), conduct disorder and substance use issues (Luis & Mittenberg, 2002; Massagli et al., 2004; Max et al., 2013; Max et al., 2012). In children aged 5–14 years with mild TBI, Max et al. (2013) found that within the first 6 months following injury, 36% reported a novel psychiatric disorder, with highest numbers reporting ADHD, simple phobia, separation anxiety and oppositional defiant disorder (Max et al., 2013). In children aged 7–17 years with mild, moderate or severe TBI, similar results have been reported; in the initial three months following injury, 49% exhibited a novel psychiatric disorder, with highest numbers reporting externalising disorder, anxiety disorder and internalising disorder (Max et al., 2012). It is clear from the extant literature that for some children and adolescents, a history of TBI, regardless of severity, may lead to increased need for mental health services for support of ongoing psychological, behavioural, cognitive or social problems. Anxiety however, appears to have been less of a focus when examining outcomes associated with TBI in children and adolescents (Albicini & McKinlay, 2015), with the majority of work examining externalising problems (i.e. conduct disorder, hyperactivity or antisocial behaviour). This is particularly important to consider given the associations between anxiety and educational underachievement, co-morbid psychiatric disorders and functional impairment (Bennett & Walkup, 2016), and the long-term effects that chronic anxiety may have on the developing architecture of the brain (Arnsten, 2009; Brinks et al., 2008).

In children and adolescents 6–12 months following mild to severe TBI, novel anxiety disorders have been reported in over 10% of participants (Max et al., 2015). Similarly, in children 5–14 years with mild to severe TBI, 8.5% reported clinical anxiety disorders and 17% reported subclinical anxiety disorders (Max et al., 2011). Of those with mild TBI, 11% reported novel clinical anxiety disorders, and 20% reported subclinical anxiety disorders (Max et al., 2011). Anxiety disorders and symptomatology that have been more commonly reported in children and adolescents following TBI include post-traumatic stress disorder (Hajek et al., 2010; Max et al., 2011; Vasa et al., 2004), separation anxiety (Luis & Mittenberg, 2002; Max et al., 2011), obsessive-compulsive symptoms (Grados et al., 2008; Luis & Mittenberg, 2002) and generalised anxiety (Luis & Mittenberg, 2002). However, the data discussed above pertain to children and adolescents within hospital/rehabilitation based settings or the general community, and it is likely that numbers will differ if recruitment is drawn from a clinical or mental health setting.

At present, there is generally a lack of information regarding the rate of psychiatric and psychological outcomes of children with TBI within clinical populations. Early studies inform that children with TBI presenting in both inpatient (Max et al., 1997) and outpatient (Max & Dunisch, 1997) psychiatric settings are no different to children without TBI in these settings. However, considering the high rates of children and adolescents who have received any mental health service in the general population (Lawrence et al., 2015), and particularly those with TBI (Kurowski et al., 2013), our study aimed to further examine the incidence of TBI in children and adolescents aged 5–18 years presenting within the mental health system, and to explore rates of anxiety disorders and other psychiatric diagnoses, and any comorbidities that may be present.

Method

Participants

Participants were a selection of individuals aged 5–18 years from three child and adolescent mental health services based in Christchurch, New Zealand (Canterbury District Health Board), who volunteered to participate in the study. The mental health service units included a child service (5–12 years), adolescent service (13–18 years) and rural service (5–18 years). The mental health services from which the participants were recruited are specialist services, and there are general exclusion criteria placed on client entry (e.g. conduct disorder not accompanied by co-morbid disorders, intellectual disability not accompanied by co-morbid disorders, sexual abuse cases). Upon arrival at their mental health appointments, parents and their children were provided with the Participant Information Sheets and Consent Forms by administrative staff, briefly explaining the study and why they have been given the opportunity to participate. Inclusion criteria were children aged 5–18 years presenting for an assessment at a mental health facility. Participants were excluded if they did not speak English. The overall sample consisted of 161 participants ($M = 12.39$ years, $SD = 3.84$ years), aged 5–18 years, with 85 males ($M = 11.40$ years, $SD = 3.51$ years) and 76 females ($M = 13.50$ years, $SD = 3.12$ years). Within the sample, 107 reported no TBI ($M = 12.37$ years, $SD = 3.48$ years) and 42 reported a history of TBI ($M = 12.46$ years, $SD = 3.61$ years); 22 participants failed to record TBI history, resulting in an overall sample of 149 children and adolescents.

Procedure

Following informed consent, participants were handed an envelope with questionnaires examining TBI status history, and also a demographic questionnaire. Participants completed the questionnaires before or after their appointments, and returned the completed questionnaires to administration in a sealed envelope. The procedure took approximately 15–20 minutes.

In addition to information obtained from questionnaires, with consent from the participants and their parents, information from the mental health files of each client was also reviewed. Information within the files included demographic

and socioeconomic data, reason for referral, previous psychiatric diagnoses, current psychiatric diagnoses, substance and/or alcohol use, other behavioural and or/emotional problems, difficulties at home or school, contacts with the forensic system and offending behaviours, other clinical information deemed important by consulting clinician. For the purpose of this study, information regarding anxiety and other psychiatric diagnoses was of interest. Ethical approval was obtained from the Northern B Health and Disability Ethics Committee.

Design

A between-subjects, cross-sectional study design was used, with data collected over a two-year period. Incidence of TBI and mental health outcomes for each participant were evaluated at a single time point. The independent variable was whether participants had sustained a previous TBI, as determined by the Ohio State University TBI Identification Method (Corrigan & Bogner, 2007). The dependent variables were mental health outcomes, including anxiety disorders and other psychiatric diagnoses, obtained from the mental health files.

Measures

A demographic questionnaire was used to record information about the participants including age, gender, developmental history and school functioning. The questionnaire involved a yes/no format answer to each question, with the option to provide additional information as required.

The Ohio State University TBI Identification Method Short Form (OSU TBI-ID SF), adapted from the OSU TBI-ID (Corrigan & Bogner, 2007) was used as a self-report measure to screen lifetime TBI exposure. Five questions relate to past exposure to head and neck injuries caused by sources such as vehicle accidents, and if these injuries are present, a further three questions assess duration of loss of consciousness (LOC) and loss of memory (Corrigan & Bogner, 2007). Inter-rater reliability has ranged from $\alpha = 0.85$ to 0.93 (Corrigan & Bogner, 2007), and test-retest reliability adequate with $\alpha > 0.60$ (Bogner & Corrigan, 2009). In this study, mild TBI (mTBI) was defined by an injury with LOC <30 minutes, moderately-severe TBI by a LOC 30 minutes to 24 hours, and severe TBI by a LOC >24 hours. Participants who reported being dazed/having memory lapse resulting from a head injury were also classified as having mTBI due to evidence of loss of memory for events occurring near the injury, and alterations of mental state (Albicini & McKinlay, 2014b; Esselman & Uomoto, 1995; McKinlay, 2010).

Data analysis

Descriptive statistics analyses were conducted for all variables within the dataset, utilising the split-file function for gender, TBI history and anxiety diagnosis, to produce a frequency description of the data. A combined variable for TBI and anxiety diagnosis was also computed. To examine group differences on demographic information, chi-square analyses were conducted for gender, school and learning difficulties, behavioural problems, mental health problems, and medical history, and independent samples *t*-test was conducted for age. To examine the incidence of anxiety disorder diagnosis among participants with and without a history of TBI, frequencies and descriptive statistic analyses were calculated to examine anxiety diagnoses, psychiatric comorbidities and other psychiatric diagnoses among the two groups. Outcomes of diagnoses were coded as 0 = no, 1 = yes. Co-morbid externalising, internalising and other disorders were defined as cases in which more than one diagnosis in each domain was present, and coded as 0 = no comorbidities, 1 = comorbidities. Percentages and chi-square tests were based on 'known' categories and values, and as such missing cases were excluded.

Results

Participant demographics

Descriptive statistics and frequencies were used to determine demographic characteristics of children and adolescents with and without a history of TBI. Results are displayed in Table 1.

An independent samples *t*-test was conducted to examine any differences in age for participants with and without a history of TBI, which revealed a non-significant result, $t(141) = -0.014$, $p = 0.89$. Further, chi-square analyses were computed to examine group differences on categorical demographic data, revealing no significant differences for gender, $\chi^2(1) = 0.20$, $p = 0.27$, school difficulties, $\chi^2(1) = 0.90$, $p = 0.34$, learning difficulties, $\chi^2(1) = 1.38$, $p = 0.24$, behavioural problems, $\chi^2(1) = 0.08$, $p = 0.78$, mental health problems, $\chi^2(1) = 0.08$, $p = 0.78$, physical

Table 1. Participant characteristics for traumatic brain injury and non-traumatic brain injury groups.

	TBI	Non-TBI
Characteristic	*n* (%)	*n* (%)
Total	42 (28.29) (M = 12.46 years, SD = 3.61)	107 (71.81) (M = 12.37 years, SD = 3.48)
Gender		
Male	24 (57.10)	50 (47.20)[a]
Female	18 (42.90)	56 (52.80)
School difficulties		
Yes	28 (71.80)	62 (63.30.90)
No	11 (28.20)	36 (36.70)
Learning difficulties		
Yes	13 (34.20)	23 (24.20)
No	25 (65.80)	72 (75.80)
Educational assistance		
Yes	20 (52.60)	28 (29.80)
No	18 (47.40)	66 (70.20)
Behavioural problems		
Yes	5 (13.20)	11 (11.50)
No	33 (86.80)	85 (88.50)
Mental health problems		
Yes	15 (39.50)	35 (36.80)
No	23 (60.50)	60 (63.20)
Any hospitalisations		
Yes	15 (40.50)	31 (31.70)
No	22 (59.50)	67 (68.30)
Medical diagnoses		
Yes	11 (31.40)	38 (41.80)
No	24 (68.60)	53 (58.20)

$N = 149$; [a] = One participant failed to record gender.

problems, $\chi^2(1) = 0.88$, $p = 0.35$, function-impairing medication use, $\chi^2(1) = 0.18$, $p = 0.67$, or medical diagnoses, $\chi^2(1) = 1.14$, $p = 0.29$. There was a significant difference between the two groups for children needing educational assistance, $\chi^2(1) = 6.10$, $p = 0.01$, with children with TBI requiring more assistance. To examine the TBI group further, an analysis of specific characteristics for children within the TBI group is presented in Table 2.

Outcomes for mental health file review

To identify rates of anxiety diagnoses and other psychiatric diagnoses for children and adolescents with and without a history of TBI, descriptive statistics and frequencies were analysed for outcomes derived from the file review. The results are displayed in Table 3.

As is evident in Table 3, individuals reporting a history of TBI also reported high rates for suicidal/self-harm, anxiety disorders and mood disorders. Children and adolescents without a history of TBI also reported relatively high rates for anxiety disorders, suicidal/self-harm, and mood disorders. Those with TBI reported higher rates of mood disorders, suicidal/self-harm, and abuse history, than those without a history of TBI. Over 55% of the TBI group presented with 'no diagnosis', compared to 47% of individuals without TBI, which was higher than expected given the nature of the sample. However, when the variables in Table 3 were analysed using a chi-square analysis, there were no statistically significant results, given that individuals without TBI also reported high rates for psychiatric disorders.

As mentioned above, a combined variable for TBI and anxiety diagnosis (and TBI with no anxiety diagnosis) was also computed, to examine rates of other psychiatric disorders among the two groups. Descriptives and frequencies were analysed for each group for the computed variables, which are provided in Table 4.

As shown in Table 4, children and adolescents with a history of TBI and anxiety disorder diagnosis also tended to

Table 2. Characteristics of participants with TBI.

Characteristic	TBI group ($n = 42$)
Age at first injury[a] (M)	7.47 years
TBI before/after 15 years[a], *N*(%)	<15 years: 12 (27.90) ≥15 years: 2 (4.70) n/a: 29 (67.40)
TBI with any LOC, *N*(%)	25 (59.52)
TBI with LOC >30 mins, *N*(%)	2 (4.76)
Multiple TBI[a], *N*(%)	4 (9.53)

[a]OSU-TBI-SF only provides this information for TBI involving LOC.

Table 4. Comorbidities and participant characteristics for individuals with anxiety disorder diagnosis and history of TBI compared to individuals with TBI and no anxiety disorder.

	TBI + anxiety	TBI
Characteristic	*n* (%)	*n* (%)
Total	8 (19.05) (M = 13.29 years, SD = 3.45)	34 (80.95) (M = 12.39 years, SD = 3.67)
Gender		
Male	4 (50.0)	19 (55.90)
Female	4 (50.0)	14 (44.10)
Mood disorder	1 (12.50)	6 (17.70)
Behaviour disorder[a]	2 (25.0)	3 (8.80)
Drug and alcohol	0	0
Pervasive developmental disorder	1 (12.50)	0
Low IQ[b]	0	1 (2.90)
Suicidal/self-harm	2 (25.0)	12 (3.50)
Physical disorder	2 (25.0)	3 (8.80)
Abuse history	0 (0)	5 (14.70)

$N = 42$; Note [a] = behaviour disorder includes ADHD, ODD and CD; [b] = low IQ refers to borderline IQ or lower.

Table 3. Mental health concerns and diagnoses for individuals with and without history of TBI obtained from file review.

	TBI	Non-TBI
Characteristic	*n* (%)	*n* (%)
Total	42 (28.29) (M = 12.46 years, SD = 3.61)	107 (71.81) (M = 12.37 years, SD = 3.48)
Internalising disorders (total)	20 (47.60)	47 (43.90)
Anxiety disorder	8 (21.10) 4 males, 4 females	32 (29.90) 15 males, 17 females
Mood disorder	7 (18.40)	16 (17.0)
Suicidal/self-harm	14 (36.80)	28 (29.80)
Comorbid internalising disorders	8 (19.10)	21 (20.60)
Externalising disorders (total)	6 (14.30)	17 (15.90)
Behaviour disorder[a]	5 (13.20)	15 (16.0)
Drug and alcohol	0	1 (1.10)
Comorbid externalising disorders	5 (13.20)	2 (1.90)
Pervasive Developmental disorder	1 (2.60)	3 (3.20)
Other (total)	11 (26.20)	27 (25.20)
Low IQ[b]	1 (2.60)	5 (5.30)
Physical disorder	5 (13.20)	13 (13.80)
Abuse history	5 (13.20)	10 (10.60)
Comorbid other disorders	0	1 (1.10)
No diagnosis	21 (55.30)	44 (46.80)

$N = 149$; Note [a] = behaviour disorders include Attention-Deficit/Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD); [b] = low IQ refers to borderline IQ or lower. Values refer to valid percent due to missing data ($n = 13$ missing data non-TBI, $n = 5$ missing data TBI).

show difficulties with behaviour disorders, suicidal/self-harm and physical disorders. For the TBI and no anxiety group, children and adolescents presented with the highest rates of mood disorders, abuse history and physical disorders. However, Chi-square analyses indicated no statistically significant differences between the two participant groups.

Discussion

This study aimed to identify the incidence of TBI and an anxiety disorder diagnosis, in children and adolescents aged 5–18 years who are presenting within the mental health system. We also sought to examine the incidence of anxiety disorders compared to that of other psychiatric diagnoses in the sample, and also the potential comorbidity with psychiatric disorders among children and adolescents with a history of TBI and anxiety. We hypothesised that children and adolescents with a history of TBI would have a higher incidence of anxiety diagnoses compared to children with no TBI, and that anxiety diagnoses would be accompanied by comorbid psychiatric disorders, particularly mood disorders, with comorbidities being higher in the TBI group.

Our study found that over 28% of children and adolescents presenting to mental health services reported a history of TBI, with the majority being of mild severity. This is in keeping with Kurowski et al. (2013), who reported that 24% of children and adolescents with TBI aged 12–17 years accessed outpatient mental health services, and 28% accessed any mental health service, versus 17% in children aged 4–17 years within the general population (Lawrence et al., 2015). In the general population, rates of TBI in children and adolescents has been reported as approximately 14% worldwide (McKinlay & Hawley, 2014) and approximately 8% in New Zealand for all severities of TBI, with mild TBI being the majority of cases (749/790) (Feigin et al., 2013). Considering this, it appears that children and adolescents with a history of TBI, particularly mild TBI, are over-presented within the mental health services of this sample.

In contrast to the previous literature, we did not find group differences between children and adolescents with a history of TBI compared to those without for anxiety disorders, for which samples based on hospital or rehabilitation admissions have recorded higher rates in TBI groups (Max et al., 2011; Max et al., 2015; Vasa et al., 2002). However, this finding is consistent with McKinlay et al. (2009), whereby adolescents aged 14–16 years with childhood TBI were not more likely to display symptoms of anxiety disorders We also found no significant differences between the TBI and non-TBI groups for behavioural problems or any other psychiatric disorders, inconsistent with non-clinical sample studies (Karver et al., 2012; Massagli et al., 2004; Max et al., 2013; Max et al., 2012; McKinlay et al., 2002; McKinlay et al., 2009; Schwartz et al., 2003). However, our findings do support early work which suggests that children with TBI present in psychiatric settings are actually no different to children without TBI for outcomes including behavioural, anxiety, mood and developmental disorders (Max & Dunisch, 1997; Max et al., 1997).

When examining children and adolescents with history of TBI and anxiety disorder, despite smaller group numbers, we found relatively high rates of comorbid behavioural disorders, suicidal/self-harm and physical disorders within the group, however, mood disorders did not appear to be a co-occurring problem. This is in contrast to studies finding that children and adolescents following TBI with anxiety disorders, also tend to have concurrent mood and other internalising problems (Gerring et al., 2002; Grados et al., 2008; Luis & Mittenberg, 2002; Max et al., 1998).

Theoretical explanations

While past research has reported higher rates of anxiety disorders and symptomatology following TBI in children and adolescents (Max et al., 2011; Max et al., 2015; Max et al., 2012; McKinlay et al., 2009), our findings are not consistent with this. For instance, our sample consisted of a higher number of males than females within the TBI group (not statistically significant), whereas the spread was more even for the non-TBI group. Therefore, our results may suggest a non-significant trend towards males being over-represented in the TBI group. Research maintains that anxiety symptomatology is more common in females than in males (Beesedo et al., 2009), with this gender difference reaching ratios of 2:1 and 3:1 for females to males as they reach adolescence (Wittchen et al., 1998). These differences have been attributed to hormonal differences in responding to stress responses (Seeman, 1997), and potential genetic differences in the capacity to manage negative emotions (Feingold, 1994). Considering this, it is unsurprising that in children and adolescents with TBI, female gender also presents as a consistent predictor of the development of anxiety symptomatology (Gerring et al., 2002; Grados et al., 2008). Gender differences in post-TBI outcome research also shows that adult females report higher rates of anxiety following childhood TBI (Scott et al., 2015).

The services from which we recruited participants may also be another factor contributing to the unexpected findings. Anxiety disorders are noted to be the most frequent mental health disorder in children and adolescents (Beesedo et al., 2009), however in this sample, there was a relatively low percentage of anxiety cases, both in those with TBI and those without, considering participants were recruited from a mental health service. Given that the vast majority of mental health services are provided by public funding, the results may suggest that New Zealand clinicians may be somewhat reluctant to provide a diagnosis of anxiety and other disorders in children and adolescents. Moreover, the mental health service from which the sample was obtained is a specialist service, there are exclusion criteria placed on client entry (e.g. conduct disorder not accompanied by co-morbid disorders, intellectual disability not accompanied by co-morbid disorders, sexual abuse cases), which are likely to have influenced the resultant participant characteristics.

Research suggests that risk factors associated with anxiety following TBI include higher levels of pre-morbid psychosocial adversity (Gerring et al., 2002; Grados et al., 2008; Herskovits et al., 2002; Vasa et al., 2002; Vasa et al., 2004), pre-existing mood and anxiety problems (Gerring et al., 2002; Grados et al., 2008; Luis & Mittenberg, 2002; Max et al., 1998), and younger age of injury (Levi et al., 1999; Max

et al., 2011; Vasa et al., 2002). In addition, severity of injury also contributes to this risk, with more severe TBI associated with higher rates of anxiety (Gerring et al., 2002; Luis & Mittenberg, 2002; Max et al., 1998). Considering the children in this study presented with mild TBI, their family dynamics and rates of pre-existing mental health concerns, it may be that the absence of risk factors in more mild injuries reduce the incidence of anxiety.

Another consideration may relate to the age group of the children in the study, the age at time of injury and the emergence of internalising symptomatology. Research suggests that ongoing problems following childhood TBI may arise from a combination of neurobiological and environmental factors (Anderson et al., 2011). While there is evidence that children are vulnerable to the effects of early neurological insult of developing social and emotional skills (Ryan et al., 2014a), it is possible that deficits or difficulties in these areas do not become noticed until a certain level of maturity (Ryan et al., 2014b). It has indeed been found that adults with a history of childhood TBI, even in less severe injury cases, report higher rates of internalising symptomatology (Albicini & McKinlay, 2014a). Children and adolescents with a history of TBI, particularly milder TBI, may therefore appear to function normally relative to individuals without TBI until more complex social and emotional skills develop, whereby issues with anxiety and mood may become more apparent.

Limitations

A limitation of the study was the reliance of self-report, from parents and children/adolescents, regarding the incidence and nature of TBI. Research indicates that adults aged 25 years recall their incidence of childhood TBI with only 84.5% accuracy (McKinlay & Horwood, 2016), and for 25 year-olds with a history of childhood TBI requiring hospitalisation, only 59/101 were recalled. Considering we utilised a self-report measure, which relied on memory of TBI severity and incidence, the rate of TBI in this sample may have been higher. We also were reliant on mental health file review for ascertaining psychiatric diagnosis, which depends on the clinical opinion of the consulting clinician. As such, although there are a number of children without a diagnosis in the sample, individuals with significant mental health issues are likely underrepresented in this study due to the nature of the mental health file review (i.e dichotomous coding of yes/no diagnosis). It may be in fact that many children exhibited sub-threshold symptoms of a disorder and as such, many cases of significant anxiety and other psychiatric symptomatology that did not fit criteria for a full diagnosis may have been missed. Our study also may have lack sufficient power to identify any group differences, particularly considering the TBI cases were of mild severity. In addition, our exclusion of non-English speaking families may have influenced the results or limited our sample in terms of cultural background, income and disadvantaged populations. Further, we did not control for any pre-existing mental health issues or other factors, however, when comparing groups for demographic data and participant characteristics, we found no significant group differences.

Conclusions

This study explored the incidence of TBI in children and adolescents aged 5–18 years presenting within the mental health system, and the rate of anxiety and other psychiatric diagnoses that may be present in such a sample. While we did not find any significant group differences for any of the mental health outcomes, we did identify that a proportionately high number of children and adolescents within the mental health system have had a previous TBI. It appears that the sample from which individuals are recruited (clinical, hospital, community) serves as a large factor in identifying ongoing outcomes following TBI in children and adolescents. Further research is essential for examining outcomes and characteristics of children and adolescents with history of TBI within the mental health system, particularly for more severe injuries and from a larger sample size, as it is a potentially unique participant group within the literature.

Acknowledgements

The study received significant contribution from Dr Harith Swadi, University of Otago, Christchurch New Zealand.

Declaration of interest

No potential conflict of interest was reported by the authors.

The study was funded by Australian Research Council 10.13039/501100000923.

ORCID

Audrey McKinlay http://orcid.org/0000-0001-9846-8514

References

Albicini M, McKinlay A. (2014a). Internalising disorders in adults with a history of childhood traumatic brain injury. J Clin Exp Neuropsychol, 37, 776–84.

Albicini M, McKinlay A. (2014b). Mild traumatic brain injury: A review of terminology, symptomatology, clinical considerations and future directions. In: Sadaka F, ed. Traumatic Brain Injury. InTech Publishing, 3–22.

Albicini M, McKinlay A. (2015). A systematic review of anxiety disorders following mild, moderate and severe TBI in children and adolescents. In: Durbano F, ed. A Fresh Look at Anxiety Disorders. InTech Publishing, 199–224.

Anderson V, Spencer-Smith M, Wood A. (2011). Do children really recover better? Neurobehavioural plasticity after early brain insult. Brain, 134, 2197–221.

Arnsten A. (2009). Stress signalling pathways that impair prefrontal cortex structure and function. Nat Rev Neurosci, 10, 410–22.

Beesedo K, Knappe S, Pine D. (2009). Anxiety and anxiety disorders in children and adolescents: Developmental issues and implications for DSM-V. Psychiatr Clin North Am, 32, 483–524.

Bennett S, Walkup J. (2016). Anxiety disorders in children and adolescents: Epidemiology, pathogenesis, clinical manifestations and course. Available from: http://www.uptodate.com/contents/anxiety-disorders-in-children-and-adolescents-epidemiology-pathogenesis-clinical-manifestations-and-course [last accessed 5 Feb 2016].

Bogner J, Corrigan J. (2009). Reliability and predictive validity of the Ohio State University TBI identification method with prisoners. J Head Trauma Rehabil, 24, 279–91.

Brinks V, deKloet E, Oitzl M. (2008). Strain specific fear behaviour and glucocorticoid response to aversive events: modelling PTSD in mice. Prog Brain Res, 167, 257–61.

Corrigan JD, Bogner JA. (2007). Initial reliability and validity of the Ohio State University TBI identification method. J Head Trauma Rehabil, 22, 318–29.

Donders J, Warschausky S. (2007). Neurobehavioural outcomes after early versus late childhood traumatic brain injury. J Head Trauma Rehab, 22, 296–302.

Esselman P, Uomoto J. (1995). Classification of the spectrum of mild traumatic brain injury. Brain Inj, 9, 417–24.

Feigin V, Theadom A, Barker-Collo S, et al. (2013). Incidence of traumatic brain injury in New Zealand: A population-based study. Lancet Neurol, 12, 53–64.

Feingold A. (1994). Gender differences in personality: A meta-analysis. Psychol Bull, 116, 429–56.

Gerring J, Slomine B, Vasa R, et al. (2002). Clinical predictors of posttraumatic stress disorder after closed head injury in children. J Am Acad Child Adolesc Psychiatry, 41, 157–65.

Grados M, Vasa R, Riddle M, et al. (2008). New onset obsessive-compulsive symptoms in children and adolescents with severe traumatic brain injury. Depress Anxiety, 25, 398–407.

Hajek C, Yeates K, Taylor G, et al. (2010). Relationships among post-concussive symptoms and symptoms of PTSD in children following mild traumatic brain injury. Brain Inj, 24, 100–9.

Hawley C. (2003). Reported problems and their resolution following mild, moderate and severe traumatic brain injury amongst children and adolescents in the UK. Brain Inj, 17, 105–29.

Herskovits E, Gerring J, Davatzikos C, Bryan R. (2002). Is the spatial distribution of brain regions associated with closed head injury in children predictive of subsequent development of Post-Traumatic Stress Disorder? Radiol, 224, 345–51.

Karver C, Kurowski B, Semple E, et al. (2014). Utilization of behavioural therapy services long-term after traumatic brain injury in young children. Arch Phys Med Rehab, 95, 1556–63.

Karver C, Wade S, Cassedy A, et al. (2012). Age at injury and long-term behavior problems after traumatic brain injury in young children. Rehabil Psychol, 57, 256–65.

Kurowski B, Wade S, Kirkwood M, et al. (2013). Behavioural predictors of outpatient mental health service utilization within 6 months after traumatic brain injury in adolescents. Am Acad Phys Med Rehab, 5, 1026–34.

Lawrence D, Johnson S, Hafekost J, et al. (2015). The Mental Health of Children and Adolescents: Report on the second Australian Child and Adolescent Survey of Mental Health and Wellbeing Canberra: Department of Health.

Levi R, Drotar D, Yeates K, Taylor G. (1999). Posttraumatic stress symptoms in children following orthopedic or traumatic brain injury. J Clin Child Psych, 28, 232–43.

Liu J, Li L. (2013). Parent-reported mild head injury history and behavioural performance in children at 6 years. Brain Inj, 27, 1263–70.

Luis C, Mittenberg W. (2002). Mood and anxiety disorders following pediatric traumatic brain injury: a prospective study. J Clin Exp Neuropsychol, 24, 270–9.

Massagli T, Fann J, Burington B, et al. (2004). Psychiatric illness after mild traumatic brain injury in children. Arch Phys Med Rehabil, 85, 1428–34.

Max J, Castillo C, Robin D, et al. (1998). Posttraumatic stress symptomatology after childhood traumatic brain injury. J Nerv Ment Dis, 186, 589–96.

Max J, Dunisch D. (1997). Traumatic brain injury in a child psychiatry outpatient clinic: a controlled study. J Am Acad Child Adolesc Psychiatry, 36, 404–11.

Max J, Keatley E, Wilde E, et al. (2011). Anxiety disorders in children and adolescents in the first six months after traumatic brain injury. J Neuropsychiatr Clin Neurosci, 23, 29–39.

Max J, Lopez A, Wilde E, et al. (2015). Anxiety disorders in children and adolescents in the second six months after traumatic brain injury. PRM, 1, 345–55.

Max J, Schachar R, Landis J, et al. (2013). Psychiatric disorders in children and adolescents in the first six months after mild traumatic brain injury. JNP, 25, 187–97.

Max J, Sharma A, Qurashi M. (1997). Traumatic brain injury in a child psychiatry inpatient population: A controlled study. J Am Acad Child Adolesc Psychiatry, 36, 1595–601.

Max J, Wilde E, Bigler E, et al. (2012). Psychiatric disorders after pediatric traumatic brain injury: A prospective, longitudinal, controlled study. JNP, 24, 427–36.

McKinlay A. (2010). Controversies and outcomes associated with mild traumatic brain injury in childhood and adolescences. Child Care Health Dev, 36, 3–21.

McKinlay A, Dalrymple-Alford J, Horwood J, Fergusson D. (2002). Long-term psychosocial outcomes after mild head injury in early childhood. J Neurol Neurosurg Psychiatry, 73, 281–8.

McKinlay A, Grace R, Horwood J, et al. (2009). Adolescent psychiatric symptoms following preschool childhood mild traumatic brain injury: evidence from a birth cohort. J Head Trauma Rehabil, 24, 221–7.

McKinlay A, Hawley C. (2014). Incidence rates for traumatic brain injury in children. Available from: http://www.internationalbrain.org/incidence-rates-for-traumatic-brain-injury-in-children/ [last accessed 5 2016].

McKinlay A, Horwood J. (2016). The accuracy of adult recall for early mild traumatic brain injury. Disabil Rehab, 39, 1296–99.

Ryan N, Anderson V, Godfrey C, et al. (2014a). Predictors of very-long-term sociocognitive function after pediatric traumatic brain injury: Evidence for the vulnerability of the immature ''social brain''. J Neurotrauma, 31, 649–57.

Ryan N, Catroppa C, Cooper J, et al. (2014b). The emergence of age-dependent social cognitive deficits after generalised insult to the developing brain: A longitudinal prospective analysis using susceptibility-weighted imaging. Hum Brain Mapp, 36, 1677–91.

Schwartz L, Taylor G, Drotar D, et al. (2003). Long-term behavior problems following pediatric traumatic brain injury: prevalence, predictors and correlates. J Paediatr Psychol, 28, 251–63.

Scott C, McKinlay A, McLellan T, et al. (2015). A comparison of adult outcomes for males compared to females following pediatric traumatic brain injury. Neuropsychology, 29, 501–8.

Seeman M. (1997). Psychopathology in women and men: Focus on female hormones. AJP, 154, 4501–8.

Vasa R, Gerring J, Grados M, et al. (2002). Anxiety after severe pediatric closed head injury. J Am Acad Child Adolesc Psychiatry, 41, 148–56.

Vasa R, Grados M, Slomine B, et al. (2004). Neuroimaging correlates of anxiety after pediatric traumatic brain injury. Biol Psychiatry, 55, 208–16.

Wittchen H, Nelson C, Lachner G. (1998). Prevalence of mental disorders and psychosocial impairments in adolescents and young adults. Psychol Med, 28, 109–26.

J Head Trauma Rehabil

Anxiety Disorders in Adults With Childhood Traumatic Brain Injury: Evidence of Difficulties More Than 10 Years Postinjury

Michelle Albicini, BPSych Hons; Audrey McKinlay, A.Dip Clin Psyc, PhD

Objective: To explore long-term psychiatric outcomes in individuals with a history of childhood traumatic brain injury (TBI) or orthopedic injury (OI). **Setting:** Hospital emergency department, medical admission records and outpatient settings. **Participants:** There were 95 males ($M = 22.78$ years, SD = 3.44 years) and 74 females ($M = 22.27$ years, SD = 3.09 years), 65 with mild TBI ($M = 23.25$ years, SD = 3.58 years), 61 with moderate-severe TBI ($M = 22.34$ years, SD = 2.79 years), and 43 with OI ($M = 21.81$ years, SD = 3.36 years). **Design:** Longitudinal, between-subjects, cross-sectional design using retrospective and current data. **Main Measures:** Semistructured interview to obtain psychiatric diagnoses and background information, and medical records for identification of TBI. **Results:** Group with moderate-severe TBI presented with significantly higher rates of any anxiety disorder ($\chi_2^2 = 6.81$, $P = .03$) and comorbid anxiety disorder ($\chi_2^2 = 6.12$, $P < .05$). Group with overall TBI presented with significantly higher rates of any anxiety disorder ($\chi_1^2 = 5.36$, $P = .02$), panic attacks ($\chi_1^2 = 4.43$, $P = .04$), specific phobias ($\chi_1^2 = 4.17$, $P = .04$), and depression ($\chi_1^2 = 3.98$, $P < .05$). Prediction analysis revealed a statistically significant model ($\chi_7^2 = 41.84$, $P < .001$) explaining 23% to 37% of the variance in having any anxiety disorder, with significant predictors being group (TBI) and gender (female). **Conclusions:** Children who have sustained a TBI may be vulnerable to persistent anxiety, panic attacks, specific phobias, and depression, even 13 years after the injury event. **Key words:** *anxiety*, *anxiety disorders*, *brain injuries*, *child*, *concussion*

THE ARGUMENT that childhood traumatic brain injury (TBI) can result in ongoing challenges and issues, which persist into adulthood, continues to be debated.[1,2] Some suggest that the plasticity of the young brain functions as a buffer against any ongoing effects of insult, while others describe an intrinsic vulnerability leading to ongoing problems following TBI,[3,4] yet the distinct nature of how TBI affects the neurological structures of the brain is still not completely understood.[5] Compounding this debate is the finding that long-term behavioral, cognitive, and emotional outcomes following childhood TBI are heterogeneous,[6] as is the brain damage that occurs as a result of diffuse injury.[5,7] Therefore, outcome studies investigating the long-term challenges faced by individuals following TBI are important.

Following TBI, a number of factors likely interact to influence the prognosis of recovery and outcomes following injury,[6] including severity of TBI, age of injury, premorbid functioning, and psychosocial factors.[1] And what is known is that in the initial, acute stages of TBI recovery, children will experience a number of symptoms including inattention, learning and memory difficulties, fatigue, sleep disruption, social problems, and slower information processing.[3,5,8,9] It has been suggested that acute problems faced by children with TBI will influence the acquisition of skills, such as social and academic skills, which is also accompanied by other factors as a result of the TBI including family stress and adjustment.[10] This cascade of events is, therefore, likely to play some part in the development of long-term problems following childhood TBI, which may be evident even into adulthood.

Author Affiliations: *School of Psychological Sciences, Monash University Faculty of Medicine, Nursing and Health Sciences, and School of Psychology and Psychiatry, Monash University, Clayton, Melbourne, Victoria, Australia (Ms Albicini); and Melbourne School of Psychological Sciences, The University of Melbourne, Melbourne, Victoria, Australia (Dr McKinlay).*

The study was part of a larger study that was supported by a postdoctoral fellowship from the Health Research Council/Accident Compensation Corporation of New Zealand.

The authors declare no conflicts of interest.

Corresponding Author: *Michelle Albicini, (BPSych Hons), School of Psychological Sciences, Monash University Faculty of Medicine, Nursing and Health Sciences, Wellington Rd, Clayton, Melbourne, VIC 3800, Australia (michelle.albicini@monash.edu).*

DOI: 10.1097/HTR.0000000000000312

The transition from childhood into adulthood comprises a number of biological, social, and emotional changes,[11] and due to these changes, it is during this period that psychological and social impairments become more apparent.[12,13] A model of psychosocial recovery after childhood TBI was formulated,[14,15] suggesting that adaptive social skills are developed as a result of normal brain maturation and development of cognition and behavior within a secure environment. Moreover, a number of factors both internal and external to the child interact to influence behavior and psychological wellbeing.[14–16] Therefore, a disruption to any part of this complex system is likely to result in negative outcomes for the child, which may be ongoing as they develop through life.

Research exploring outcomes following childhood TBI has reported on higher rates of social dysfunction,[17] behavioral issues,[18–22] psychiatric disorders,[23,24] and neuropsychological deficits[25] up to 5 years following their injury event. While more severe TBI sustained in childhood tends to be related to poorer outcomes,[19,20,24,25] mild TBI is also associated with ongoing issues in behavioral, attentional, executive, and psychiatric domains, with the most commonly reported predictors being family functioning, lower socioeconomic status, and preinjury functioning.[18,19,23,24]

Looking into even longer-term outcomes following childhood TBI (~10 years postinjury), much of the research examines issues associated with quality of life, adaptive function, academic function, vocation, and neuropsychological and/or cognitive functioning,[1,6,10] and general behavioral functioning such as the presence of internalizing and externalizing symptoms post-TBI,[11,26] with little in the way of examining the rate of psychiatric and psychological disorders many years after TBI. One study explored rates of psychological disorders in adolescents aged 14 to 16 years who sustained a mild TBI in childhood, which required either inpatient or outpatient intervention.[27] The authors indicated higher rates of attention deficit/hyperactivity disorder, oppositional defiant disorder, mood disorder, and substance abuse in individuals with inpatient mild TBI. In a sample of university students aged 18 to 25 years with mild TBI sustained at mean age of 14 years,[7] higher rates were found for those with TBI than for those without TBI for borderline anxiety disorder, borderline avoidant personality disorder, borderline internalizing disorders, and clinically elevated somatic complaints.

Adult studies have also explored the long-term effects of TBI, with one that conducted a 30-year follow-up of individuals who sustained a TBI (any severity), finding increased psychiatric disorders (majority depression) with onset occurring after TBI.[28] In support of this, 66% of an adult sample of individuals who sustained a TBI (any severity) 7 years prior exhibited symptoms consistent with personality disorders including borderline personality disorder, avoidant personality disorder, paranoid personality disorder, narcissistic personality disorder, and obsessive-compulsive personality disorder,[29] and another sample presented with high rates of depression 14 years following severe TBI.[30]

There remains a lack of work that focusses on very long-term outcomes of childhood TBI (more than 5 years postinjury), with most of the studies operating from the same cohort. Those who have examined very long-term outcomes, 10 years or more postinjury, tended to utilize samples for which TBI occurred after 18 years of age. In addition, outcomes are often based on parent report of symptoms, which thereby may present issues regarding subjectivity of answers. Moreover, longitudinal studies that have explored the longer-term consequences of TBI have examined neuropsychological functions including memory, language, and intelligence, whereas there is extant literature on persisting anxiety, depression, and other psychiatric disorders in child TBI cases. Finally, much of the existing work neglects to include individuals who sustained a mild TBI. As such, this article will explore long-term psychiatric outcomes, with a focus on anxiety disorders, in individuals with a history of TBI or orthopedic injury (OI), which occurred in childhood, based on medical records for indication of injury type and long-term follow-up assessing outcomes. The following is hypothesized:

1. Individuals with moderate-severe TBI will present with the highest number of psychiatric diagnoses, followed by those with mild TBI and then OI.
2. Younger age at injury, female gender, and presence of internalizing psychiatric symptoms will significantly increase the risk of anxiety following TBI.

METHODS

Ethics

Ethical approval for the study was obtained from the Upper South New Zealand Regional Ethics Committee and was part of a larger study that investigated long-term outcomes of childhood TBI. All participants were fully informed of the nature of the study and provided consent to participate.

Participants

Participants were recruited through an audit of hospital emergency department and admission records and neurosurgical files. Additional recruitment was conducted by placing flyers within the community. General inclusion criteria for the study included having a history of an injury event (TBI or OI) during the ages 0 to 17 years, which occurred at least 5 years prior to the study, and being 18 years of age or older. All participants

spoke English. Sample groups were defined on the basis of preexisting criteria for TBI severity.[31–33]

Mild TBI

Inclusion criteria for individuals in the group with mild TBI were as follows: (*a*) a medically confirmed diagnosis of mild TBI, (*b*) loss of consciousness (LOC) for less than 20 minutes, (*c*) length of posttraumatic amnesia (PTA) less than 1 hour, (*d*) Glasgow Coma Scale score of 13 to 15, (*e*) stay in hospital for no longer than 48 hours (due to injuries to the head only), and (*f*) normal brain scan results.

Moderate-severe TBI

Individuals in the group with moderate-severe TBI were determined by the following inclusion criteria: (*a*) a medically confirmed diagnosis of moderate or severe TBI, (*b*) skull fracture/evidence on brain scan, (*c*) cerebral hemorrhage, or (*d*) PTA of more than 24 hours. Moderate TBI was specifically defined as having (*a*) Glasgow Coma Scale score of 9 to 12 (or higher if there was evidence on brain scan results), (*b*) PTA of less than 1 week, and (*c*) length of LOC less than 6 hours. For severe TBI, the criteria were set as (*a*) Glasgow Coma Scale score of less than 9, (*b*) PTA of more than 1 week, and (*c*) length of LOC more than 6 hours.

OI controls

Individuals in the group with OI were also recruited through the emergency department admission and neurosurgical audits, and flyers placed in the community. They were defined as having experienced a fracture between the ages of 0 and 17 years, more than 5 years prior to the study. Individuals were excluded if they had a history of TBI.

Final sample

The audit of hospital records, emergency department admissions, and neurosurgical files resulted in an identification of 558 individuals fitting the aforementioned criteria. The total sample consisted of 95 males (M = 22.78 years, SD = 3.44 years) and 74 females (M = 22.27 years, SD = 3.09 years), aged between 18 and 31 years, resulting in a 32% response rate. Within the sample, there were 65 with mild TBI (M = 23.25 years, SD = 3.58 years), 61 with moderate-severe TBI (M = 22.34 years, SD = 2.79 years) and 43 with OI (M = 21.81 years, SD = 3.36 years).

Procedure and materials

Participants attended a 3-hour assessment session at the University of Canterbury, which was conducted by a trained psychology postdoctoral fellow. To obtain information regarding background information, including age and gender, further information about the injury event, and associated symptoms, a semistructured interview was conducted. To obtain diagnostic information regarding psychiatric symptoms, components of the Composite International Diagnostic Interview[34] were used in a structured interview format to ask questions relating to a *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) diagnosis of an anxiety disorder [generalized anxiety disorder (GAD), panic attacks, panic disorder (PD), agoraphobia, social phobia, specific phobia, posttraumatic stress disorder]), depression, mania, and suicidal behaviors. Obsessive-compulsive disorder screening was not part of the diagnostic interview. This method of interview has been previously used and validated in earlier studies,[35,36] and the Composite International Diagnostic Interview reportedly has good to excellent κ coefficients for test-retest and interrater reliability studies.[34]

Data analysis

Descriptive statistic analyses were conducted, utilizing the split-file function organizing data by group (mild TBI, moderate-severe TBI, OI), for background information including age, gender, time since injury, and age of treatment injury, and frequency analyses computed for psychiatric disorders. The variable "overall anxiety disorders" refers to the grouping of subtypes of anxiety disorders, and the variable "comorbid disorders" includes cases that endorsed more than one anxiety disorder. Chi-square and multivariate analysis of variance tests were conducted to examine any group differences among the participant characteristics. Logistic regression was used to identify predictors of anxiety disorders. All data were analyzed using SPSS version 22, and α levels were set to .05 for significance testing.

RESULTS

Participant characteristics

Table 1 shows descriptive statistics. Injury characteristics of each participant group were compared for those with mild TBI, moderate-severe TBI, and OI, on variables including gender, years since injury, and age when receiving injury treatment. A multivariate analysis of variance was conducted to examine differences among the groups on participant demographics, which indicated no significant differences for age, $F_{2,166} = 2.71$; $P = .07$, but highlighted a statistically significant difference for years since injury, $F_{2,166} = 10.36$; $P < .01$, and age of injury treatment, $F_{2,166} = 14.07$; $P < .01$. Post hoc analyses revealed that more time had lapsed since their injury for those in the moderately severe TBI group than those with OI and mild TBI, and that those with moderately

TABLE 1 *Injury characteristics of participants*[a]

	Mild TBI *n* (%)	Moderate-severe TBI *n* (%)	Orthopedic injury *n* (%)
Total	65 (38.50)	61 (36.10)	43 (25.40)
	$M = 23.25$, SD = 3.58	$M = 22.34$, SD = 2.79	$M = 21.81$, SD = 3 .36
Gender			
Male	43 (66.20)	33 (54.10)	19 (44.20)
Female	22 (33.80)	28 (45.90)	24 (55.80)
Time since injury, y	$M = 12.17$, SD = 5.31	$M = 15.13$, SD = 4.69	$M = 11.05$, SD = 4.69
Age of injury treatment, y	$M = 10.86$, SD = 4.87	$M = 7.05$, SD = 4.03	$M = 10.47$, SD = 3.79

Abbreviation: TBI, traumatic brain injury.
[a] $N = 169$.

severe TBI were significantly younger than both groups when they first received injury treatment. A χ^2 analysis further revealed no significant group differences for gender, $\chi^2_2 = 5.25$, $P = .07$.

Psychiatric disorders among mild TBI, moderate-severe TBI, and OI groups

Rates of psychiatric disorders, including specific anxiety disorders, overall anxiety disorders, and comorbid anxiety disorders, according to each participant group, are outlined in Table 2.

Comparison of anxiety disorders among participants with mild TBI, moderate-severe TBI, and OI

To explore differences in rates of anxiety disorders and individuals with a history of mild TBI, moderate-severe TBI, and OI, a series of χ^2 analyses were conducted. A significant difference for the grouping variable was found for any anxiety disorder, $\chi^2_2 = 6.81$, $P = .03$, with the group with moderate-severe TBI exhibiting the highest rate of problems. There was also a significant difference between groups for comorbid anxiety disorders, $\chi^2_2 = 6.12$, $P < .05$, again with those in the moderate-severe TBI group presenting highest rates. There were no significant differences between the groups for GAD, $\chi^2_2 = 0.62$, $P = .73$; panic attacks, $\chi^2_2 = 5.6$, $P = .06$; panic disorder, $\chi^2_2 = 1.98$, $P = .37$; agoraphobia, $\chi^2_2 = 1.46$, $P = .48$; social phobia, $\chi^2_2 = 3.92$, $P = .14$; specific phobia, $\chi^2_2 = 5.75$, $P = .0.6$; or posttraumatic stress disorder, $\chi^2_2 = 1.66$, $P = .44$).

Comparison of other psychiatric disorders among participants with mild TBI, moderate-severe TBI, and OI

Chi-square analyses showed that rates of other psychiatric disorders did not differ for those with mild TBI, moderate-severe TBI and OI for suicide attempts, $\chi^2_2 = 3.27$, $P = .20$, $\chi^2_2 = 4.47$, $P = .11$, mania, $\chi^2_2 = 0.14$, $P = .93$, or depression, $\chi^2_2 = 5.89$, $P = .53$.

TABLE 2 *Psychiatric disorders among participants with mild TBI, moderate-severe TBI, and orthopedic injury*[a]

	Mild TBI *n* (%)	Moderate-severe TBI *n* (%)	Orthopedic injury *n* (%)
Depression	22 (33.80)	25 (41.0)	11 (25.60)
Mania	3 (4.60)	2 (3.30)	2 (4.70)
Suicide attempts	2 (3.10)	4 (6.60)	0
Generalized anxiety	5 (7.70)	5 (8.20)	2 (4.70)
Panic attacks	7 (10.80)	10 (16.40)	1 (2.30)
Panic disorder	3 (4.60)	5 (8.20)	1 (2.30)
Agoraphobia	2 (3.10)	2 (3.30)	1 (2.30)
Social phobia	3 (4.60)	5 (8.20)	1 (2.30)
Specific phobia	4 (6.20)	7 (11.50)	1 (2.30)
PTSD	1 (1.50)	2 (3.30)	1 (2.30)
Any anxiety disorder	12 (18.50)	16 (26.30)	3 (7.0)
Comorbid anxiety	4 (6.20)	9 (14.80)	1 (2.30)

Abbreviations: PTSD, posttraumatic stress disorder; TBI, traumatic brain injury.
[a] $N = 169$.

TABLE 3 *Injury characteristics of participants within the combined TBI group and orthopedic injury group*[a]

	TBI *n* (%)	Orthopedic injury *n* (%)
Total	126 (74.56)	43 (25.44)
	$M = 22.80$, SD = 5.22	$M = 21.81$, SD = 3.36
Gender		
Male	76 (60.30)	19 (44.20)
Female	50 (39.70)	24 (55.80)
Time since injury, y	$M = 13.60$, SD = 5.22	$M = 11.05$, SD = 4.69
Age of injury treatment, y	$M = 9.02$, SD = 4.86	$M = 10.47$, SD = 3.79

Abbreviation: TBI, traumatic brain injury.
[a] $N = 169$.

Outcomes for combined TBI group (mild and moderate-severe TBI) and OI groups

A new variable was computed by combining mild and moderate-severe TBI groups to a general TBI group. Injury characteristics for those with TBI and OI are outlined in Table 3.

As also conducted previously, a comparison among rates of psychiatric disorders was conducted for participants with TBI and OI. Table 4 describes descriptive statistics for each of the groups.

Comparison of anxiety disorders among participants with TBI and OI

To explore rates of anxiety disorders for individuals with a history of TBI and OI, a series of χ^2 analyses were conducted. A significant difference was found for having any anxiety disorder, $\chi^2_1 = 5.36$, $P = .02$, with participants in the TBI group presenting with more problems. There was also a significant difference between the groups for panic attacks, $\chi^2_1 = 4.43$, $P = .04$, and specific phobia, $\chi^2_1 = 4.17$, $P = .04$, again with individuals with TBI having higher rates for each. However, there were no significant differences among the groups for GAD, $\chi^2_1 = 0.60$, $P = .44$, panic disorder, $\chi^2_1 = 1.11$, $P = .29$, agoraphobia, $\chi^2_1 = .45$, $P = .23$, or posttraumatic stress disorder, $\chi^2_1 = 1.08$, $P = .30$.

TABLE 4 *Psychiatric disorders among participants with TBI and orthopedic injury*[a]

	TBI *n* (%)	Orthopedic injury *n* (%)
Depression	47 (37.30)	11 (25.60)
Mania	5 (4.0)	2 (4.70)
Suicide attempts	2 (1.60)	0
Generalized anxiety	10 (7.90)	2 (4.70)
Panic attacks	17 (13.50)	1 (2.30)
Panic disorder	8 (6.30)	1 (2.30)
Agoraphobia	4 (3.20)	1 (2.30)
Social phobia	8 (6.30)	1 (2.30)
Specific phobia	11 (8.70)	1 (2.30)
PTSD	3 (2.40)	1 (2.30)
Any anxiety disorder	28 (22.20)	3 (7.0)
Comorbid anxiety	13 (10.30)	1 (2.30)

Abbreviations: PTSD, posttraumatic stress disorder; TBI, traumatic brain injury.
[a] $N = 169$.

Comparison of other psychiatric disorders among participants with TBI and OI

Rates of other psychiatric disorders were compared for participants with TBI and OI using χ^2 analyses. The results revealed a significant difference between groups for depression, $\chi^2_1 = 3.98$, $P < .05$, with individuals with TBI presenting with higher rates. There were no significant differences found for mania, $\chi^2_1 = 0.02$, $P = .90$ or suicide attempts, $\chi^2_1 = 0.73$, $P = .39$.

Prediction analysis for having any anxiety diagnosis

A logistic regression was used to determine the impact of TBI, participant characteristics, and other psychiatric disorders on the likelihood that participants have any anxiety diagnosis. The outcome variable was any anxiety diagnosis (yes or no), and the predictors were age, gender, group (TBI or OI), depression, mania, and suicide attempts. The full model containing all predictors was statistically significant, $\chi^2_7 = 41.84$, $P < .001$, indicating that the model was able to distinguish between individuals with any anxiety disorder and those without. The model as a whole explained between 23% (Cox and Snell R^2) and 37% (Nagelkerke R^2) of the variance in any anxiety disorder diagnosis and correctly classified 81.4% of cases. Table 5 represents logistic regression parameters

TABLE 5 *Logistic regression predicting likelihood of any anxiety disorder*

Variable	*B* (SE)	Wald	*df*	Odds ratio	95.0% CI	
					Upper	Lower
Group	1.57[a] (0.74)	4.43	1	4.78	20.54	1.11
Age	0.01 (0.08)	0.02	1	1.01	1.19	0.86
Gender	1.48[b] (0.52)	8.15	1	4.39	12.10	1.59
Years postinjury	0.06 (0.05)	1.29	1	1.06	1.17	0.96
Depression	0.04 (0.68)	0.00	1	1.04	3.90	0.28
Mania	22.34 (4.97)	0.00	1	0	0	0
Suicide attempts	0.59 (2.15)	0.08	1	1.81	121.96	0.03

Abbreviations: CI, confidence interval; SE, standard error.
[a] $P < .05$.
[b] $P < .01$.

for predicting group membership to having either any anxiety disorder or no anxiety disorder.

Table 5 demonstrates that a significant predictor of having an anxiety disorder is participant group, and it is indicated that participant group membership raises the likelihood of having any anxiety disorder by almost 5 times. Moreover, gender also made a significant contribution to the variance in the model, such that it increases the likelihood of having any anxiety disorder by more than 4 times. Frequency analysis of rates of any anxiety disorder according to gender revealed that 31.5% of females reported any anxiety disorder versus 8.4% of males.

DISCUSSION

We explored long-term psychiatric outcomes, with a focus on anxiety disorders, in individuals with a history of childhood TBI or OI, based on medical records for indication of injury type and long-term follow-up assessing outcomes. We found that when comparing individuals with mild TBI, moderate-severe TBI, and OI, those with moderate-severe TBI exhibited higher rates of any anxiety disorder and comorbid anxiety disorders. When we combined the 2 groups with TBI, we found that individuals with TBI presented with higher rates of any anxiety disorder, panic attacks, specific phobia, and depression. Significant predictors for having any anxiety disorder included having a TBI and being female.

Our findings are consistent with previous findings that have reported ongoing, long-term difficulties following childhood TBI.[7,11,21,22,27] While there is a lack of studies that have examined the presence of long-term psychiatric disorders following childhood TBI, other longitudinal outcome studies are in support of our findings. One study reported that individuals with childhood mild TBI were found to present with higher rates of internalizing symptoms even 10 years postinjury,[11] and another indicated long-term deficits in emotion perception for individuals who had sustained a childhood TBI 10 years prior.[37]

Given that TBI, of even mild severity, involves actual structural damage to the brain that can be either focal or diffuse,[5,38–40] a potential explaining factor for the higher rates of anxiety disorders and depression among those with TBI is due to the impacted neurobiological regions at the time of injury. It has been suggested that the "social brain" consists of the temporal pole, medial prefrontal cortex, orbitofrontal cortex, amygdala, temporoparietal junction, and inferior parietal cortex,[37] areas of which appear to be implicated in both TBI and anxiety disorders.[38] Moreover, the "social brain" is purportedly responsible for functions such as emotion perception and affect recognition,[37] which are hypothesized to play a role in the vulnerability of developing anxiety disorders.[41,42] Therefore, it may be that direct impact to these areas of the young and developing brain, and particularly areas responsible for affect regulation[43] such as the orbitofrontal cortex, hippocampus, thalamus, temporal regions, amygdala, and frontal gyri,[44–46] results in ongoing mood and anxiety problems.

However, most children with mild, moderate, and sometimes even severe TBI will go on to make a full recovery without experiencing ongoing psychiatric difficulties, so there are clearly other moderating factors associated with these long-term outcomes that go beyond neurological insult. What is known in the literature is that a number of factors serve to increase the likelihood of an individual developing ongoing difficulties after TBI, including the quality of the child's environment such as socioeconomic status, parental warmth, and parental mental health.[24,37] Studies exploring acute outcomes of TBI in children and adolescents have found that among the most common predictors of anxiety disorders are TBI severity, younger age of injury, and female gender.[38,43,47] In our study, being female significantly predicted the likelihood of having an anxiety disorder, and our moderate-severe TBI group was the youngest

at age of injury and presented with the highest rate of anxiety-related problems. This is unsurprising given that even in non-TBI samples, females tend to report higher rates of anxiety than males, with anxiety being more than 1.5 times more common for females,[48] affecting approximately 1 in 3 women throughout their lifetime.[49] Gender differences in the development of anxiety disorders have been attributed to neurochemical and hormonal differences[50,51] and factors associated with genetics, personality, and internal locus of control.[52,53]

A limitation of the study is that we did not assess for premorbid functioning due to the nature of the longitudinal research design. As such, we could not account for preexisting behavioral, emotional, cognitive, and psychological issues that may have been apparent before the injury, which are noted to predict future ongoing psychiatric disorders after TBI.[23,24] Moreover, years of education was not examined among the participant groups, which may be a significant factor in participation of the study. In addition, diagnosis of psychiatric disorders, although was obtained through structured interview, was reliant on self-reported symptoms. It may have been useful to obtain informant reports to corroborate participant's difficulties to ensure validity. Furthermore, our methodology of recruitment resulted in a relatively low response rate (32%), and we did not examine whether there were any differences between those who participated and those who declined. It may be likely that the individuals who participated in the study differed in terms of their injury characteristics or psychiatric outcomes. Finally, due to the response rate, our sample size was relatively small, particularly considering the number of comparisons conducted in the analyses.

Strengths of our study include it being a longitudinal design whereby individuals with TBI were followed many years after their injury, considering the lack and underrepresentation of long-term follow-ups of psychiatric disorders (particularly anxiety) in childhood TBI within the literature. Moreover, participants were recruited from hospital admissions, which would increase the validity of identification of TBI (as opposed to self-reported TBI, see the study by McKinlay and Horwood[54]). In addition, we utilized structured interviews, as per *Diagnostic and Statistical Manual of Mental Disorders* criteria, to identify psychiatric disorders, and, therefore, we were not reliant on parent report of symptoms, which in the past have been considered unreliable in describing internalizing difficulties of children and adolescents.[26,47] Finally, the inclusion of an OI comparison group allowed some control over factors attributed to the experience of an early injury (eg, family stress, adjustment, hospitalization, missed school) that may have influenced results.

Considering the aforementioned text, future directions for work in this area should involve a replication of a similar, longitudinal outcome study tracking psychiatric disorders, particularly anxiety considering the results of the present study, after childhood TBI (>10 years). In combination, brain imaging techniques would also be useful to identify the affected brain regions associated with postinjury anxiety disorders, in addition to the collection of preinjury information to decipher predictors and risk factors for this group. This information put together could allow for the implementation of intervention programs targeted at children and adolescents, or parenting groups, to assist those at risk of developing ongoing anxiety and other psychiatric disorders following TBI.

CONCLUSION

In conclusion, our study highlights that children who have sustained a TBI of mild or moderate-severe severity may be vulnerable to ongoing symptoms of anxiety, panic attacks, specific phobias, and depression, which can persist even 13 years after the injury event. Moreover, children who are female and have more severe TBI are at greater risk, and as such, early intervention for these individuals may be important to help lessen the burden associated with such an injury.

REFERENCES

1. Anderson V, Brown S, Newitt H, Hoile H. Educational, vocational, psychosocial, and quality of life outcomes for adult survivors of childhood traumatic brain injury. *J Head Trauma Rehabil*. 2009;24(5):303–312.
2. McKinlay A, Dalrymple-Alford J, Horwood J, Fergusson D. Long-term psychosocial outcomes after mild head injury in early childhood. *J Neurol Neurosurg Psychiatry*. 2002;73(3):281–288.
3. Anderson V, Catroppa C, Morse S, Haritou F, Rosenfeld J. Functional plasticity or vulnerability following early brain injury? *Pediatrics*. 2005;116:1374–1382.
4. Anderson V, Spencer-Smith M, Wood A. Do children really recover better? Neurobehavioural plasticity after early brain insult. *Brain*. 2011;134:2197–2221.
5. Albicini M, McKinlay A. Mild traumatic brain injury: a review of terminology, symptomatology, clinical considerations and future directions. In:Sadaka F, ed. *Traumatic Brain Injury*. InTech Publishing; 2014:3–22.
6. Jonsson C, Catroppa C, Godfrey C, Smedler A, Anderson V. Individual profiles of predictors and their relations to 10 years outcome after childhood traumatic brain injury. *Brain Inj*. 2013;27(7–8):831–838.
7. Albicini M, McKinlay A. Internalising disorders in adults with a history of childhood traumatic brain injury. *J Clin Exp Neuropsychol*. 2014;37(7):776–784.
8. Centers for Disease Control and Injury Prevention. Heads up: facts for physicians about mild traumatic brain injury.

http://www.brainlinemilitary.org/concussion_course/course_content/pdfs/mtbi.pdf. Published 2006. Accessed November 2016.
9. Yeates K, Armstrong K, Janusz J, et al. Long-term attention problems in children with traumatic brain injury. *J Am Acad Child Adolesc Psychiatry*. 2005;44:574–584.
10. Anderson V, Brown S, Newitt H, Hoile H. Long-term outcome from childhood traumatic brain injury: intellectual ability, personality and quality of life. *Neuropsychology*. 2011;25(2):176–184.
11. Rosema S, Muscara F, Anderson V, Godfrey C, Hearps S, Catroppa C. The trajectory of long-term psychosocial development 16 years following childhood traumatic brain injury. *J Neurotrauma*. 2015;32:976–983.
12. Angold A, Costello E, Wortham C. Puberty and depression: the role of age, pubertal status and pubertal timing. *Psychol Med*. 1998;28:51–61.
13. Susman E, Nottelmann E, Inoff-Germain G, et al. The relation of relative hormonal levels and physical development and social-emotional behaviour in young adolescents. *J Youth Adolesc*. 1985;14:245–264.
14. Anderson V, Beauchamp M. SOCIAL: a theoretical model of developmental social neuroscience. In: Anderson V, Beauchamp M, eds. *Developmental Social Neuroscience and Childhood Brain Insult: Theory and Practice*. New York, NY: Guildford Press; 2012: 3–20.
15. Beauchamp M, Anderson V. SOCIAL: an integrative framework for the development of social skills. *Psychol Bull*. 2010;136:39–64.
16. Max J, Wilde E, Bigler E, et al. Psychiatric disorders after pediatric traumatic brain injury: a prospective, longitudinal, controlled study. *J Neuropsychiatry Clin Neurosci*. 2012;24(4):427–436.
17. Yeates K, Swift E, Taylor G, et al. Short- and long-term social outcomes following pediatric traumatic brain injury. *J Int Neuropsychol Soc*. 2004;10:412–426.
18. Hawley C, Ward A, Magnay J. Outcomes following childhood head injury: a population study. *J Neurol Neurosurg Psychiatry*. 2004; 75:737–742.
19. Karver C, Wade S, Cassedy A, et al. Age at injury and long-term behavior problems after traumatic brain injury in young children. *Rehabil Psychol*. 2012;57(3):256–265.
20. Schwartz L, Taylor G, Drotar D, Yeates K, Wade S, Stancin T. Long-term behavior problems following pediatric traumatic brain injury: prevalence, predictors and correlates. *J Paediatr Psychol*. 2003;28(4):251–263.
21. McKinlay A. Long-term outcomes of traumatic brain injury in early childhood. *Aust Psychol*. 2014;49(6):323–327.
22. McKinlay A, Grace R, Horwood J, Fergusson D, MacFarlane M. Long-term behavioural outcomes of pre-school mild traumatic brain injury. *Child Care Health Dev*. 2010;36(1):22–30.
23. Max J, Friedman K, Wilde E, et al. Psychiatric disorders in children and adolescents 24 months after mild traumatic brain injury. *J Neuropsychiatry Clin Neurosci*. 2015;27:112–120.
24. Max J, Robin D, Lindgren S, et al. Traumatic brain injury in children and adolescents: psychiatric disorders at two years. *J Am Acad Child Adolesc Psychiatry*. 1997;36(9):1278–1285.
25. Fay T, Yeates K, Wade S, Drotar D, Stancin T, Taylor G. Predicting longitudinal patterns of functional deficits in children with traumatic brain injury. *Neuropsychology*. 2009;23(3):271–282.
26. Rosema S, Muscara F, Anderson V, Godfrey C, Eren S, Catroppa C. Agreement on and predictors of long-term psychosocial development 16 years postchildhood traumatic brain injury. *J Neurotrauma*. 2014;31:899–905.
27. McKinlay A, Grace R, Horwood J, Fergusson D, MacFarlane M. Adolescent psychiatric symptoms following preschool childhood mild traumatic brain injury: evidence from a birth cohort. *J Head Trauma Rehabil*. 2009;24(3):221–227.
28. Koponen S, Taiminen T, Portin R, et al. Axis I and II psychiatric disorders after traumatic brain injury: a 30-year follow-up study. *Am J Psychiatry*. 2002;159:1315–1321.
29. Hibbard M, Bogdany J, Uysal S, et al. Axis II psychopathology in individuals with traumatic brain injury. *Brain Inj*. 2000;14(1): 45–61.
30. Hoofien D, Gilboa A, Vakil E, Donovick P. Traumatic brain injury (TBI) 10–20 years later: a comprehensive outcome study of psychiatric symptomatology, cognitive abilities and psychosocial functioning. *Brain Inj*. 2001;15(3):189–209.
31. Baalen B, Odding E, Maas A, Ribbers G, Bergen M, Stam H. Traumatic brain injury: classification of initial severity and determination of functional outcome. *Disabil Rehabil*. 2003;25(1): 9–18.
32. Borg J, Holm L, Cassidy J, et al. Diagnostic procedures in mild traumatic brain injury: results of the WHO collaborating task force on mild traumatic brain injury. *J Rehabil Med*. 2004;43:61–75.
33. Centers for Disease Control and Prevention. Traumatic brain injury. http://www.cdc.gov/TraumaticBrainInjury/. Published 2013. Accessed February 13, 2014.
34. World Health Organization. *Composite International Diagnostic Interview (CIDI)*. Geneva, Switzerland: World Health Organization; 1990.
35. Fergusson D, Boden J, Horwood J. Exposure to single parenthood in childhood and later mental health, educational, economic, and criminal behaviour outcomes. *Arch Gen Psychiatry*. 2007;64:1089–1095.
36. Fergusson D, Boden J, Horwood J. Tests of causal links between alcohol dependence and major depression. *Arch Gen Psychiatry*. 2009;66:260–266.
37. Ryan N, Anderson V, Godfrey C, et al. Predictors of very long-term sociocognitive function after pediatric traumatic brain injury: evidence for the vulnerability of the immature "social brain". *J Neurotrauma*. 2014;31:649–657.
38. Albicini M, McKinlay A. A systematic review of anxiety disorders following mild, moderate and severe TBI in children and adolescents. In: Durbano F, ed. *A Fresh Look at Anxiety Disorders*. InTech Publishing; 2015:199–224.
39. Levine B, Kovacevic N, Nica E, et al. The Toronto traumatic brain injury study. *Neurology*. 2008;70(10):771–778.
40. Povlishock J, Katz D. Update of neuropathology and neurological recovery after traumatic brain injury. *J Head Trauma Rehabil*. 2005;20(1):76–94.
41. Cisler J, Olatunji B. Emotion regulation and anxiety disorders. *Curr Psychiatry Rep*. 2012;14(3):182–187.
42. Cisler J, Olatunji B, Feldner M, Forsyth J. Emotion regulation and anxiety disorders: an integrative review. *J Psychopathol Behav Assess*. 2010;32(1):68–82.
43. Max J, Keatley E, Wilde E, et al. Anxiety disorders in children and adolescents in the first six months after traumatic brain injury. *J Neuropsychiatry Clin Neurosci*. 2011;23(1):29–39.
44. Grados M, Vasa R, Riddle M, et al. New onset obsessive-compulsive symptoms in children and adolescents with severe traumatic brain injury. *Depress Anxiety*. 2008;25(5):398–407.
45. Herskovits E, Gerring J, Davatzikos C, Bryan R. Is the spatial distribution of brain regions associated with closed-head injury in children predictive of subsequent development of post-traumatic stress disorder? *Radiology*. 2002;224:345–351.
46. Mather F, Tate R, Hannan T. Posttraumatic stress disorder in children following road traffic accidents: a comparison of those with and without mild traumatic brain injury. *Brain Inj*. 2003;17(12):1077–1087.
47. Luis C, Mittenberg W. Mood and anxiety disorders following pediatric traumatic brain injury: a prospective study. *J Clin Exp Neuropsychol*. 2002;24(3):270–279.

48. McClean C, Asnaani A, Litz B, Hofmann S. Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. *J Psychiatr Res*. 2011;45(8):1027–1035.
49. Beyond Blue. Who does it affect? https://www.beyondblue.org.au/who-does-it-affect/women. Published 2016. Accessed February 10, 2017.
50. Seeman M. Psychopathology in women and men: focus on female hormones. *Am J Psychiatry*. 1997;154(4):501–508.
51. Nishizawa S, Benkelfat C, Young S, et al. Differences between males and females in rates of serotonin synthesis in human brain. *Proc Natl Acad Sci*. 1997;94(10):5308–5313.
52. Feingold A. Gender differences in personality: a meta-analysis. *Psychol Bull*. 1994;116(3):429–456.
53. Lewinsohn P, Gotlib I, Lewinsohn M, Seeley J, Allen N. Gender differences in anxiety disorders and anxiety symptoms in adolescents. *J Abnorm Psychol*. 1998;107(1):109–117.
54. McKinlay A, Horwood J. The accuracy of adult recall for early mild traumatic brain injury. *Disabil Rehabil*. 2017;39(13):1296–1299.

Journal of Head Trauma Rehabilitation

Predictors of Long-Term Anxiety Disorders following Childhood Traumatic Brain Injury: The Role of Cognition and Frontal Lobe Functions

--Manuscript Draft--

Manuscript Number:	
Full Title:	Predictors of Long-Term Anxiety Disorders following Childhood Traumatic Brain Injury: The Role of Cognition and Frontal Lobe Functions
Article Type:	Original Article (unsolicited)
Section/Category:	Unsolicited (Focus on Clinical Research)
Keywords:	anxiety; anxiety disorders; brain injuries; frontal lobe functioning; cognition
Corresponding Author:	Michelle Albicini, BPsych (Hons) Monash University Faculty of Medicine Nursing and Health Sciences Melbourne, VIC AUSTRALIA
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	Monash University Faculty of Medicine Nursing and Health Sciences
Corresponding Author's Secondary Institution:	
First Author:	Michelle Albicini, BPsych (Hons)
First Author Secondary Information:	
Order of Authors:	Michelle Albicini, BPsych (Hons)
	Audrey McKinlay, A. Dip Clin Psyc, PhD
Order of Authors Secondary Information:	
Manuscript Region of Origin:	AUSTRALIA
Abstract:	Objective: Explore predictors associated with anxiety disorders after childhood traumatic brain injury (TBI) in an adult sample, compared to individuals with childhood orthopedic injury (OI). Setting: Hospital Emergency Department, medical admission records and outpatient settings. Participants: There were 95 males (M =22.78 years, SD=3.44 years) and 74 females (M=22.27 years, SD=3.09 years), 65 with mild TBI (M=23.25 years, SD=3.58 years), 61 with moderate-severe TBI (M=22.34 years, SD=2.79 years) and 43 with OI (M=21.81 years, SD=3.36 years). Design: Longitudinal, between-subjects, cross-sectional design using retrospective and current data. Main Measures: Semi-structured interview for anxiety diagnoses (Composite International Diagnostic Interview) and background information. Cognitive assessment measures for memory (Wechsler Memory Scale-III Paired Associates I and II , Rey-Osterrieth Complex Figure memory trials), visuospatial ability (Wechsler Abbreviated Scale of Intelligence's Matrix Reasoning, Judgement of Line Orientation Test, Rey-Osterrieth Complex Figure copy), attention (Daneman and Carpenter Reading Span , Adaptive Digit Ordering Task) and processing speed (Delis-Kaplan Executive Function System verbal fluency, Stroop). Frontal Systems of Behaviour scale to assess frontal lobe functions. Medical records reviewed for identification of TBI. Results: TBI groups performed significantly worse for memory F(2)=4.73, p=.01 and attention F(2)=4.79, p=.01. There was no main effect for group on frontal lobe functioning outcomes, however post-hoc analyses revealed the mild TBI group had higher scores on executive dysfunction (p=.004) and total frontal lobe functioning (p=.02) than the OI group. A logistic regression analysis revealed significant predictors for having an anxiety disorder were severity of TBI, gender, apathy, disinhibition, executive dysfunction and overall frontal lobe abilities. Conclusions: Individuals with more severe TBI, females, and those with poorer frontal

	lobe functioning may be at a higher risk of anxiety disorders following childhood TBI. Increased apathy, being disinhibited and having poorer executive functioning appeared to be protective of anxiety. However, these factors in combination serve to increase the likelihood of meeting diagnostic criteria for an anxiety disorder post-TBI.

To the Editorial Board,

Please see our uploaded manuscript entitled “Predictors of Long-Term Anxiety Disorders following Childhood Traumatic Brain Injury: The Role of Cognition and Frontal Lobe Functions”, by Ms Michelle Sarah Albicini (corresponding author) and Dr Audrey McKinlay. This paper is being submitted for exclusive consideration as an original research article to the Journal of Head Trauma Rehabilitation.

This paper explores the predictors of long-term anxiety outcomes in individuals with a history of childhood traumatic brain injury (TBI) or orthopaedic injury (OI) which occurred more than 10 years prior, through an audit of hospital emergency department admission records. We examined he rates of anxiety disorders among those with mild TBI, moderate-severe TBI and OI, and utilised a prediction analysis for the diagnosis of an anxiety disorder, using demographic variables, cognitive abilities and frontal lobe functioning. Our study highlighted that TBI groups presented with significantly worse memory and attention. Also, the mild TBI group had higher scores on executive dysfunction and total frontal lobe functioning than the OI group. A logistic regression analysis revealed significant predictors for having an anxiety disorder were severity of TBI, gender, apathy, disinhibition, executive dysfunction and overall frontal lobe abilities. Our findings may inform future intervention programs targeted at children and adolescents, or parenting groups, to assist those at risk of developing ongoing anxiety following TBI.

The main strengths of this paper include a longitudinal design, using semi-structured interviews for anxiety diagnoses and hospital records to identify history of TBI. Currently, the literature is sparse with regards to very long-term anxiety after childhood TBI. The findings related to frontal lobe functions as significant predictors in anxiety following childhood TBI is novel and adds to existing literature in this field.

We do not have any conflicts of interest to declare regarding this manuscript. All procedures described and outlined were in keeping with the Northern B Health and Disability Ethics Committee. This manuscript comprises original work and has not been published elsewhere, and all authors have contributed to the work. Thank-you for considering our work. Please address all correspondence concerning this manuscript to the corresponding author of the paper via email.

Sincerely,

The Authors

Title with affiliations

Predictors of Long-Term Anxiety Disorders following Childhood Traumatic Brain Injury: The Role of Cognition and Frontal Lobe Functions

Michelle Albicini (BPSych Hons) – School of Psychological Sciences, Monash University: Faculty of Medicine, Nursing and Health Sciences, School of Psychology and Psychiatry, Monash University, Clayton, VIC, Australia

Dr Audrey McKinlay (A. Dip Clin Psyc, PhD) - School of Psychological Sciences, University of Melbourne, Melbourne, VIC, Australia

Conflicts of interest: None.

Funding contributions: The study was part of a larger study which was supported by a postdoctoral fellowship from the Health Research Council/Accident Compensation Corporation of New Zealand.

Abstract

Objective: Explore predictors associated with anxiety disorders after childhood traumatic brain injury (TBI) in an adult sample, compared to individuals with childhood orthopedic injury (OI).

Setting: Hospital Emergency Department, medical admission records and outpatient settings.

Participants: There were 95 males (M =22.78 years, SD=3.44 years) and 74 females (M=22.27 years, SD=3.09 years), 65 with mild TBI (M=23.25 years, SD=3.58 years), 61 with moderate-severe TBI (M=22.34 years, SD=2.79 years) and 43 with OI (M=21.81 years, SD=3.36 years).

Design: Longitudinal, between-subjects, cross-sectional design using retrospective and current data.

Main Measures: Semi-structured interview for anxiety diagnoses (Composite International Diagnostic Interview) and background information. Cognitive assessment measures for memory (Wechsler Memory Scale-III Paired Associates I and II , Rey-Osterrieth Complex Figure memory trials), visuospatial ability (Wechsler Abbreviated Scale of Intelligence's Matrix Reasoning, Judgement of Line Orientation Test, Rey-Osterrieth Complex Figure copy), attention (Daneman and Carpenter Reading Span , Adaptive Digit Ordering Task) and processing speed (Delis-Kaplan Executive Function System verbal fluency, Stroop). Frontal Systems of Behaviour scale to assess frontal lobe functions. Medical records reviewed for identification of TBI.

Results: TBI groups performed significantly worse for memory $F(2)=4.73$, $p=.01$ and attention $F(2)=4.79$, $p=.01$. There was no main effect for group on frontal lobe functioning outcomes, however post-hoc analyses revealed the mild TBI group had higher scores on

executive dysfunction (p=.004) and total frontal lobe functioning (p=.02) than the OI group. A logistic regression analysis revealed significant predictors for having an anxiety disorder were severity of TBI, gender, apathy, disinhibition, executive dysfunction and overall frontal lobe abilities.

Conclusions: Individuals with more severe TBI, females, and those with poorer frontal lobe functioning may be at a higher risk of anxiety disorders following childhood TBI. Increased apathy, being disinhibited and having poorer executive functioning appeared to be protective of anxiety. However, these factors in combination serve to increase the likelihood of meeting diagnostic criteria for an anxiety disorder post-TBI.

Key Words: anxiety, anxiety disorders, brain injuries, frontal lobe functioning, cognition

Predictors of Long-Term Anxiety Disorders following Childhood Traumatic Brain Injury: The Role of Cognition and Frontal Lobe Functions

Emerging evidence suggests that individuals children and adolescents present with higher parent-report and assessment-based rates of anxiety disorders following mild to severe TBI (Gerring et al., 2002; Herskovits, Gerring, Davatzikos, & Bryan, 2002; Levi, Drotar, Yeates, & Taylor, 1999; Liu & Li, 2013; Luis & Mittenberg, 2002; Max et al., 1998). More specifically, these individuals tend to present with higher rates of Post-traumatic Stress Disorder (PTSD) (Herskovits et al., 2002; Max et al., 1998), Obsessive-Compulsive Disorder (OCD) (Grados et al., 2008), and other anxiety disorders such as generalised anxiety, separation anxiety, phobias and panic (Liu & Li, 2013; Luis & Mittenberg, 2002; Max et al., 2011; Max et al., 2015; Vasa et al., 2002). However, a limitation within this literature is that studies have utilised the same samples of participants, which restricts the generalisability of results and lends to a lack of research which identifies strong predictors of anxiety after TBI. Thus far, the following predictors have been highlighted.

Biological and psychosocial factors appear important with regards to identifying risk factors associated with anxiety following TBI. Brain regions implicated in anxiety disorders following TBI include frontal areas involving the orbitofrontal cortex and right medial frontal gyri (Albicini & McKinlay, 2015; Grados et al., 2008; Max et al., 2011; Vasa et al., 2004), however the damage is heterogeneous and no single brain structure can be identified as the cause of poor outcome (Albicini & McKinlay, 2015). With regards to cognitive functioning, processing speed, memory and executive function are noted to play a role in long-term anxiety following TBI (Ponsford, Draper, & Schonberger, 2008), and in the shorter-term, anxiety has been associated with poor attention, information processing and executive functioning in adults (Baker-Collo et al., 2015; Gould, Ponsford, & Spitz, 2014).

Contextual factors, such as premorbid psychosocial adversity (Gerring et al., 2002; Grados et al., 2008; Herskovits et al., 2002; Vasa et al., 2002; Vasa et al., 2004), and having social disadvantage or low family status (Gerring et al., 2002; Levi et al., 1999; Luis & Mittenberg, 2002), are also linked with higher rates of anxiety after TBI. As such, the presence of certain psychological and contextual factors, in combination with the biological damage suffered to the developing brain, may operate together to explain why some young people with TBI may experience anxiety after their injury. However the predictors identified in the research appear to vary dependent on the sample. As such, there is a lack of a general theoretical basis for why some individuals will go on to develop anxiety after TBI. To explore this, it is important to consider the aetiology of anxiety disorders in general.

For instance, biological aspects inherent to the individual are known to increase the risk, including being female (Barlow, 2000), and having negative affect, behavioural inhibition and neuroticism, which tend to have a strong genetic component (Clark, Watson, & Mineka, 1994). Cognition also appears to be a factor associated with anxiety disorders and symptomatology. Cognitive factors may involve avoidance (Behar, DiMarco, Hekler, Mohlman, & Staples, 2009) and beliefs about worry (Barlow, 2000; Beck & Clark, 1997; Behar et al., 2009). In terms of general cognitive functioning, childhood intellectual functioning has been associated with risk of anxiety disorders later in life (Castaneda et al., 2011; Koenen et al., 2009), while subjective complaints of cognitive problems in individuals with anxiety is also noted (Castaneda et al., 2011; Moritz, Kuelz, Jacobsen, Kloss, & Fricke, 2006).

Collectively, the above factors are proposed to interact and contribute to increase an individual's risk of developing anxiety later in life (Bouton et al., 2001). However, as discussed above, theoretical models of anxiety disorders after TBI has been an area of research which has received little interest. Therefore, the current study aimed to explore

predictors associated with cognition and frontal lobe functioning, and factors including gender, age of injury, and injury severity, which may contribute to an increased risk of developing long-term anxiety disorders in adults with a history of childhood mild and moderate-severe TBI. It was hypothesised that female gender, younger age of injury, and more severe TBI would predict an increased risk of anxiety disorders. Further, it was hypothesised that attention, processing speed, memory, visuospatial functioning, and frontal lobe functions including apathy, disinhibition and executive dysfunction, would also contribute to the risk of anxiety after childhood TBI.

Methods

Participants

Participants were recruited through an audit of hospital ED and admission records, neurosurgical files, and flyers within the community. General inclusion criteria included being injured when aged 0-17 years but at least five years prior to the study (TBI or orthopaedic injury/OI), and being 18 years or older. All participants spoke English. Sample groups were defined based on pre-existing criteria for mild, moderate and severe TBI (Baalen et al., 2003; Borg et al., 2004; Centers for Disease Control and Injury Prevention, 2006, 2013).

TBI groups

Inclusion criteria for mild TBI included having: a) a medically confirmed diagnosis of mild TBI, b) LOC for less than 20 minutes, c) length of PTA less than one hour, d) GCS score of 13-15, e) stay in hospital no longer than 48 hours (due to injuries to the head only), and f) normal brain scan results. Individuals with moderate-severe TBI were those with: a) a medically confirmed diagnosis of moderate or severe TBI, or b) skull fracture/evidence on

brain scan, or c) cerebral haemorrhage, or d) PTA of more than 24 hours. Moderate TBI was specifically defined as a) GCS of 9-12 (or higher if there was evidence on brain scan results), b) PTA of less than one week, and c) length of LOC less than six hours. For severe TBI, the criteria were set as a) GCS of less than 9, b) PTA of more than one week, and c) length of LOC more than six hours.

OI Controls

Individuals in the OI group were defined as having experienced a fracture between the ages 0-17 years, more than five years prior to the study. Individuals were excluded if they had a history of TBI.

Final Sample

The audit of hospital records, ED admissions and neurosurgical files resulted in an identification of 558 individuals fitting the above criteria, with 169 individuals participating in the study. The total sample consisted of 95 males (*M*=22.78 years, *SD*=3.44 years) and 74 females (*M*=22.27 years, *SD*=3.09 years), aged between 18 and 31 years, resulting in a 32% response rate. Within the sample, there were 65 with mild TBI (*M*=23.25 years, *SD*=3.58 years), 61 with moderate-severe TBI (*M*=22.34 years, *SD*=2.79 years) and 43 with OI (*M*=21.81 years, *SD*=3.36 years).

Procedure and Materials

Ethical approval for the study was obtained from the Upper South New Zealand Regional Ethics Committee, and was part of a larger study which investigated long-term neuropsychological outcomes of childhood TBI. Methods are also outlined elsewhere in a previous study (e.g. in Albicini & McKinlay, 2017). Participants attended a three hour assessment session at the University of Canterbury conducted by a trained psychology post-

doctoral research fellow. Age and gender, information about the injury event, and associated symptomatology, were retrieved via a semi-structured interview.

Psychiatric symptoms and diagnoses

To obtain diagnostic information regarding psychiatric symptoms, components of the Composite International Diagnostic Interview (CIDI; World Health Organisation, 1990) were used to ask questions relating to a Diagnostic and Statistical Manual for Mental Disorders forth edition (DSM-IV) diagnosis of an anxiety disorder (generalised anxiety, panic attacks, panic disorder, agoraphobia, social phobia, specific phobia, PTSD). This method of interview has been previously used and validated in earlier studies (Fergusson, Boden, & Horwood, 2007, 2009), and has been reported to hold good to excellent Kappa coefficients for test-retest and inter-rater reliability studies (World Health Organisation, 1990).

Cognitive functioning

Memory: The Wechsler Memory Scale-III Paired Associates I and II (WMS-III PA) age adjusted scores (Wechsler, 1997), and the Rey-Osterrieth Complex Figure (ROF) memory trials (Lezak, 1995) were used. In WMS-III PA, a list of unrelated word pairs was read, and participants provided the corresponding word when prompted with the first word. The WMS-III PA scores were derived from the sum of correct responses, with higher scores indicating better recall. In the ROF memory trials, participants were shown a figure, and asked recalled or drew the figure after a three- and thirty-minute delay. The ROF scores were based on correctly remembered elements, with a maximum score of 36.

Visuospatial ability: The Wechsler Abbreviated Scale of Intelligence's Matrix Reasoning (WASI-MR) age adjusted scores (Wechsler, 1999), Judgement of Line Orientation Test (JLOT; Benton, Sivan & Hamsher, 1994), and ROF copy task (Lezak, 1995) were utilised. Participants chose a response from options that would complete the matrix or series

(WASI-MR), matched lines appropriately in accordance with position and direction (JLOT), and copied a complex figure (ROF copy). The tests were scored based on accuracy, and final scores were derived from the total number of correct responses.

Attention: The Daneman and Carpenter Reading Span test (DCRS; Daneman & Carpenter, 1980) and the Adaptive Digit Ordering Task (DOT-A; Werheid et al., 2002) were used. In DOT-A, participants recalled sequences of numbers in ascending order, with the maximum number of digits recalled in the appropriate order giving the final score. In DCRS, participants were presented with three trials of sets of sentences that are characterized with increasing difficulty. Trials were discontinued when the participants were unable to recall all sentences in a set, with scores derived from the number of recalled words.

Processing speed: The Delis-Kaplan Executive Function System (D-KEFS) verbal fluency and Stroop subtests – age adjusted (Delis, Kaplan, & Kramer, 2001) scores were utilised. Participants produced words that started with letters F, A, and S within 60 seconds per letter, with the number of generated words creating the verbal fluency score. For the Stroop subtests, participants named the color patch, read the word, and identify the color in which the word is printed as quickly as possible. The correct responses provided a final score for each Stroop subtest.

Frontal Lobe Functioning

The Frontal Systems of Behaviour Scale (FrSBe) was utilised, in a self-report format (Grace & Malloy, 2001), which is a brief and valid tool in assessing behavioural aspects associated with frontal lobe functioning in adults aged 18-95 years. The FrSBe contains 46 self-report items, rated on a five point Likert scale, with 14 items pertaining to the Apathy subscale, 15 items for the Disinhibition subscale and 17 items pertaining to Executive Dysfunction (Carvalho, Ready, Malloy, & Grace, 2013; Grace & Malloy, 2001). Raw scores were transformed to *T*-scores for assessment of dysfunction comparative to norms, including

norms associated with individuals with TBI (Grace & Malloy, 2001). Higher *T*-scores indicated more difficulties, with a cut-off of $T>50$ suggesting clinical concerns. The FrSBe has demonstrated good reliability and is effective in discriminating between frontal and non-frontal lesioned patients (Malloy & Grace, 2005).

Design

A between-subjects, cross-sectional study design was used, utilising retrospective and current data from participants. The dependent variable was having a diagnosis of an anxiety disorder (generalised anxiety, panic attacks, panic disorder, agoraphobia, social phobia, specific phobia, PTSD). The independent variables or predictors were outcomes identified from unstructured and structured interviews, including age, gender, time since injury, cognitive outcomes (memory, visuospatial functioning, processing speed, attention), and frontal lobe functioning (executive dysfunction, disinhibition, apathy).

Data Analysis

For each of the cognitive domains, standardised *z*-scores were computed for individual test scores, and the standardised individual test *z*-scores were combined to form the composite scores of each domain. *T*-scores were derived from total raw scores for the subscales of the FrSBe (Apathy, Disinhibition, Executive Dysfunction), and for overall scores on the measure. Descriptive statistical analyses were conducted to obtain a frequency distribution of participant characteristics between the groups, utilising a split-file function for organisation of data by group (mild TBI, moderate-severe TBI group, OI group/anxiety, no anxiety). This was computed for the variables of age, gender, age at injury treatment, years since injury, cognitive performance, and frontal lobe functioning. The variable “anxiety disorders“ refers to individuals with a diagnosis of generalised anxiety, panic attacks, panic disorder, agoraphobia, social phobia, specific phobia, PTSD. Chi-square and Multivariate

Analysis of Variance (MANOVA) tests were conducted to examine differences between groups for demographics (age, gender, age at injury treatment, years since injury), anxiety disorders, cognitive performance, and frontal lobe functioning. A logistic regression analysis was also computed to assess significance of predictors for anxiety disorders following childhood TBI. All data were analysed using IBM SPSS version 24, and α levels were set to .05 for significance testing.

Results

Participant Group Characteristics

Table 1 displays group characteristics for the mild TBI, moderate-severe TBI and OI groups, for age, gender, age of injury treatment, years since injury, and anxiety disorders. Characteristics were also compared across each of the groups utilising MANOVA and chi-square analyses to examine any statistically significant differences that may be present.

**Table 1 here

A MANOVA revealed no significant differences between the three groups for age, $F(2, 166)=2.71$, $p=.07$. There was a statistically significant difference however for time since injury $F(2, 166)=10.36$, $p<.01$, and age when treated for the injury, $F(2, 166)=14.07$, $p<.01$. Post-hoc analyses revealed that the moderate-severe TBI group were significantly younger when they both sustained their injury and when treated for their injury, as compared to those with OI and mild TBI. Chi-square analyses revealed no significant group differences for gender, $\chi^2(2)=5.25$, $p=.07$, but identified a statistically significant difference between the groups for anxiety disorders, $\chi^2(2)=6.81$, $p=.03$, with the moderate-severe TBI group presenting with highest rates. Further analyses revealed that 23 females (31.5% of all females, 13.61% overall) in the overall sample had an anxiety disorder, versus 8 males (9.1%

of males, 5.3% overall), and for those with anxiety disorders, females presented with the highest rates within each injury group. A chi-square analysis revealed that the gender difference in this study is statistically significant $\chi^2(1)=12.90$, $p<.0001$.

Cognitive Performance and Frontal Lobe Functioning

Group means for individuals with mild TBI, moderate-severe TBI and OI, and also for individuals with and without anxiety disorders (irresepective of injury), for each of the cognitive domains examined and frontal lobe functioning are outlined in Table 2. A MANOVA was also conducted to explore differences in cognitive performance and frontal lobe functioning across the TBI and OI groups, and also between individuals with and without an anxiety disorder.

**Table 2 here

A MANOVA revealed that significant differences in cognitive performance across the TBI and OI groups existed for memory $F(2)=4.73$, $p=.01$ and attention $F(2)=4.79$, $p=.01$. Post-hoc analyses utilising Bonferroni tests revealed that the mild TBI performed significantly worse than the OI group, and also the moderate-severe TBI group performing worse than the OI group, on both cognitive domains (with $p<.01$). No significant differences were found for cognitive performance between individuals with or without an anxiety disorder, with all p values >.05. For the frontal lobe domains of function, a MANOVA revealed no significant differences in behavioural functioning amongst individuals with mild TBI, moderate-severe TBI or OI, or between individuals with or without an anxiety disorder, with all p values >.05. However, post-hoc analyses revealed a significant difference between individuals with OI and mild TBI on executive dysfunction ($p=.004$) and total frontal lobe functioning ($p=.02$), with mild TBI presenting with higher T-scores.

Regression analysis for predicting anxiety disorders

A binary logistic regression analysis was computed to determine the impact of TBI, participant characteristics, and cognitive and frontal lobe functioning on the likelihood of participants having an anxiety disorder. The outcome variable was anxiety disorder (yes/no), and predictors were group (mild TBI, moderate-severe TBI, OI), gender, age, age of injury treatment, years since injury, apathy, disinhibition, executive dysfunction, overall frontal lobe behavioural functioning, memory, visuospatial functioning, attention and processing speed. The full model containing all predictors was statistically significant, $\chi(14)=44.68$, $p<.001$, indicating that it was able to distinguish between individuals with and without an anxiety disorder diagnosis. Using Cox & Snell and Nagelkerke R Square estimates indicated that between 26% and 42% of the variance in anxiety disorder diagnoses is explained by the model, and it was able to correctly classify 83.7% of cases. Table 3 represents parameters of the logistic regression for predicting group membership for having an anxiety disorder diagnosis or no anxiety.

**Table 3 here

As displayed in Table 3, Group(1) was a significant positive predictor in the model, indicating that with increasing severity of TBI there is an increased likelihood of having an anxiety disorder, with the odds being almost 6 times for moderate-severe TBI compared to that of the OI group. Gender also significantly predicted having an anxiety disorder, with a negative association, meaning that being male significantly decreases the likelihood of having anxiety by 0.05 times compared to that of females. In terms of frontal lobe functioning, apathy, disinhibition, and executive dysfunction also significantly contributed to the model with negative relationships with having an anxiety disorder, whereby having increased apathy, executive dysfunction and disinhibition decreases the likelihood of having an anxiety

disorder by 0.78-0.82 times. Alternatively, overall frontal lobe functioning was a significant positive predictor in the model, and increased the likelihood of having an anxiety disorder by 1.76 times. The remainder of the variables in the model were not significant predictors for having an anxiety disorder.

Discussion

In this sample, individuals with a history of childhood mild and moderate-severe TBI had higher rates of anxiety disorders compared to individuals with a history of OI. A higher number of females had a diagnosis of an anxiety disorder both between and within participant groups. Moreover, individuals with mild TBI and moderate-severe TBI had significantly poorer attention and memory than the OI group, and the mild TBI group had significantly worse executive dysfunction and poorer overall frontal lobe abilities than the OI group. Severity of TBI and gender significantly predicted the likelihood of having an anxiety disorder, with moderate-severe TBI increasing the risk, and being male decreasing the risk. Moreover, frontal lobe abilities were significantly associated with having an anxiety disorder, such that having higher levels of apathy, higher disinhibition and poorer executive functioning all decreased the likelihood of having anxiety, whereas overall frontal lobe functioning significantly increased the risk in this group.

The functions of which the FrSBe taps into when assessing individuals is most frequently cited as those as a result of frontal lobe damage (Stout, Ready, Grace, Malloy, & Paulsen, 2003). In terms of the biological effects of TBI, it is well known that the injury is most often associated with frontal lobe diffuse damage (Bigler et al., 2013; Levin, Williams, Eisenberg, High Jr, & Guinto Jr, 1992; Wilde et al., 2007). As such, our findings support the hypothesis that the diffuse frontal damage resultant from TBI is associated with apathy, executive dysfunction and disinhibition, which potentially have a role in the development of anxiety

disorders. Executive functions are described to encompass self-regulative abilities, and are related to the development of frontal neural networks which are vulnerable in childhood TBI (Levin & Hanten, 2005). Moreover, anxiety, neuroticism and executive functioning are also linked with the prefrontal lobes, which was highlighted in research focussing on adults with history of TBI (Forbes et al., 2014). Our finding that disinhibition was negatively associated with having an anxiety disorder may link with theories postulating that those with anxiety are more inhibited (Rosenbaum et al., 1993) and that individuals with higher neuroticism common in people with anxiety disorders (Clark et al., 1994) is associated with impulsivity and behavioural inhibition (Forbes et al., 2014).

No significant differences were found regarding cognitive functioning and frontal lobe abilities for the anxiety groups. There was also no significant association found for cognitive functions as a predictor of ongoing anxiety disorders in this sample. This is inconsistent with existing research which highlights that poor performance on similar cognitive domains is evident following mild, moderate and severe TBI, and that these difficulties are associated with higher rates of self-reported anxiety (Gould et al., 2014; Ponsford et al., 2008). However, inconsistencies in the association between cognition and anxiety after TBI exist (Baker-Collo et al., 2015), and it appears that cognition tends to improve in the first year following TBI (Baker-Collo et al., 2015; Stenberg, Godbolt, de Boussard, Levi, & Stalnacke, 2015). Considering we examined long-term outcomes, any cognitive deficits that emerged following the childhood TBI may have resolved by follow-up assessments.

In non-TBI young adults with anxiety disorders, a lack of impairments in cognitive abilities across memory, attention, processing speed and executive functioning has also been highlighted (Castaneda et al., 2011). It may be that self-reported anxiety symptomatology is associated with cognitive deficits due to anxiety being a manifestation of coping with

difficulties following TBI (Ponsford et al., 2008), however symptoms meeting diagnostic criteria may not be associated with cognitive problems. Moreover, in an adolescent sample, mild anxiety has been associated with increased attentive abilities (Jarros et al., 2017), meaning that using anxiety in a functional manner may actually be protective of cognitive dysfunction.

Another consideration is the severity and sub-type of the anxiety disorder an individual is experiencing. Poor memory, slowed processing speed and executive dysfunction has been noted only in young adults with anxiety disorders who were also taking anxiety medication (Castaneda et al., 2011). Moreover, the profile of anxiety-related cognitive deficits may depend on anxiety sub-type, with research highlighting OCD as having a stronger relationship with cognition (Castaneda, Tuulio-Henriksson, Marttunen, Suvisaari, & Lonnqvist, 2008). Indeed generalised anxiety and specific phobias have been found to be unrelated to cognition (Airaksinen et al., 2005). In the present study, there is a lack of information about the severity of anxiety, and whether individuals were taking medication for their symptoms. Moreover, symptoms of OCD were not assessed, which is noted to have a stronger link with cognitive problems, and all sub-types of anxiety disorders were grouped.

Limitations

We did not assess or control for premorbid functioning of the participants, including socioeconomic status, education levels and family factors, and other biological, psychological and cognitive factors. As such, we cannot account for any pre-existing contextual factors which may explain the above findings. In addition, the structured interview questions were reliant on self-report answers regarding anxiety symptoms and frontal lobe functioning, and diagnostic criteria for anxiety disorders were based on the DSM-IV rather than the newest version of the manual. However, the structured interview was detailed and conducted by a

trained research fellow, and measures included in this study have been deemed to have adequate to very good psychometric properties. Finally, due to the methodology of recruitment, there was a low response rate of 32%, thereby potentially limiting the generalisability of the sample.

Implications

The relationship between cognitive functioning and anxiety following TBI continues to differ across research studies. Indeed, inconsistencies are identified in the literature regarding the particular cognitive domains implicated in anxiety disorders and whether the direction of the relationship is positive or negative. Moreover, the findings presented here support previous theories that individuals with more severe TBI and female gender are at an increased risk of ongoing anxiety disorders. However, further insight has been provided, such that specific domains of frontal lobe ability (apathy, executive functioning, disinhibition) may operate differently than overall frontal lobe functioning in the risk of anxiety disorders after childhood TBI.

As such, it may be important for clinicians and other professionals involved in the care of children and adolescents with TBI to conduct neuropsychological assessments to screen for any vulnerabilities that may require early intervention and scaffolding. This could include cognitive rehabilitation, particularly functions tapping into frontal lobe abilities, with the aim of reducing the risk of developing ongoing emotional difficulties later in life. This also would be particularly important for children with TBI who are female and have sustained a more severe injury, who in this study presented with the greatest risk.

Conclusions

In conclusion, adults with a history of childhood mild and moderate-severe TBI are at risk of developing anxiety disorders even many years after their injury. Individuals with more severe TBI, females, and those with poorer frontal lobe functioning may be at a higher risk. In this study, increased apathy, being disinhibited and having poorer executive functioning appeared to be slightly protective of developing an anxiety disorder following TBI. However, these factors in combination, serve to increase the likelihood of meeting diagnostic criteria for an anxiety disorder. Finally, in this study, cognitive functioning was not an important predictor for anxiety after childhood TBI. The findings associated with frontal lobe functioning are novel and provide further insight into how anxiety may manifest many years after childhood TBI, and such, these abilities should be explored further in future studies to examine whether findings may be replicated.

References

Airaksinen, E., Larsson, M., & Forsell, Y. (2005). Neuropsychological functions in anxiety disorders in population-based samples: evidence of episodic memory dysfunction. *Journal of Psychiatric Research, 39*(2), 207-214. doi: 10.1016/j.jpsychires.2004.06.001

Albicini, M., & McKinlay, A. (2014a). Internalising disorders in adults with a history of childhood traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology, 37*(7), 776-784. doi: 10.1080/13803395.2015.1053843

Albicini, M., & McKinlay, A. (2014b). Mild traumatic brain injury: A review of terminology, symptomatology, clinical considerations and future directions. In F. Sadaka (Ed.), Traumatic Brain Injury (pp. 3-22): InTech Publishing. doi: 10.5772/57208

Albicini, M., & McKinlay, A. (2015). A systematic review of anxiety disorders following mild, moderate and severe TBI in children and adolescents. In F. Durbano (Ed.), A Fresh Look at Anxiety Disorders (pp. 199-224): InTech Publishing. doi: 10.5772/60426

Albicini, M., & McKinlay, A. (2017). Anxiety disorders in adults with childhood traumatic brain injury: Evidence of difficulties more than 10 years postinjury. *Journal of Head Trauma Rehabilitation*, [epub ahead of print.]. doi: doi: 10.1097/HTR.0000000000000312

Baalen, B., Odding, E., Maas, A., Ribbers, G., Bergen, M., & Stam, H. (2003). Traumatic brain injury: Classification of initial severity and determination of functional outcome. *Disability and Rehabilitation, 25*(1), 9-18. doi: 10.1080/09638280210142266

Baker-Collo, S., Jones, K., Theadom, A., Starkey, N., Dowell, A., McPherson, K., . . . Feigin, V. (2015). Neuropsychological outcome and its correlates in the first year after adult

mild traumatic brain injury: A population-based New Zealand study. *Brain Injury, 29*(13-14), 1604-1616. doi: 10.3109/02699052.2015.1075143

Barlow, D. H. (2000). Unraveling the mysteries of anxiety and its disorders from the perspective of emotion theory. *American Psychologist, 55*(11), 1247-1263. doi: 10.1037/0003-066X.55.11.1247

Beck, A., & Clark, D. (1997). An information processing model of anxiety: Automatic and strategic processes. *Behaviour Research and Therapy, 35*(1), 49-58. doi: 10.1016/S0005-7967(96)00069-1

Behar, E., DiMarco, I., Hekler, E., Mohlman, J., & Staples, A. (2009). Current theoretical models of generalised anxiety disorder (GAD): Conceptual review and treatment implications. *Journal of Anxiety Disorders, 23*, 1011-1023. doi: 10.1016/j.janxdis.2009.07.006

Benton, A. L., Sivan, A. B., & Hamsher, K. (1994). *Contributions to Neuropsychological Assessment: A Clinical Manual* (2nd ed.). New York: Oxford University Press.

Bigler, E., Abildskov, T., Petire, J., Farrer, T., Dennis, M., Simic, N., . . . Yeates, K. (2013). Heterogeneity of brain lesions in pediatric traumatic brain injury. *Neuropsychology, 27*(4), 438-451. doi: 10.1037/a0032837

Borg, J., Holm, L., Cassidy, J., Peloso, P., Carroll, L., von Holst, H., & Ericson, K. (2004). Diagnostic procedures in mild traumatic brain injury: Results of the WHO collaborating task force on mild traumatic brain injury. *Journal of Rehabilitation Medicine, 43*, 61-75. doi: doi:10.1080/16501960410023822

Bouton, M., Mineka, S., & Barlow, D. H. (2001). A modern learning theory perspective on the etiology of panic disorder. *Psychological Review, 108*(1), 4-32. doi: 10.1037//0033-295X.108.1.4

Carvalho, J. O., Ready, R. E., Malloy, P. F., & Grace, J. (2013). Confirmatory factor analysis of the Frontal Systems of Behaviour Scale (FrSBe). *Assessment, 20*(5), 632-641. doi: 10.1177/1073191113492845

Castaneda, A. E., Tuulio-Henriksson, A., Marttunen, M., Suvisaari, J., & Lonnqvist, J. (2008). A review on cognitive impairments in depressive and anxiety disorders with a focus on young adults. *Journal of Affective Disorders, 106*, 1-27. doi: 10.1016/j.jad.2007.06.006

Clark, L., Watson, D., & Mineka, S. (1994). Temperament, personality and the mood and anxiety disorders. *Journal of Abnormal Psychology, 103*(1), 103-116. doi: 10.1037/0021-843X.103.1.103

Daneman, M., & Carpenter, P. A. (1980). Individual differences in working memory and reading. *Journal of Verbal Learning and Verbal Behavior, 19*(4), 450-466. doi: 10.1016/S0022-5371(80)90312-6

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan Executive Function System (D-KEFS)* San Antonio, TX: The Psychological Corporation.

Fergusson, D., Boden, J., & Horwood, J. (2007). Exposure to single parenthood in childhood and later mental health, educational, economic, and criminal behaviour outcomes. *Archives of General Psychiatry, 64*, 1089-1095. doi: doi:10.1001/archpsyc.64.9.1089

Fergusson, D., Boden, J., & Horwood, J. (2009). Tests of causal links between alcohol dependence and major depression. *Archives of General Psychiatry, 66*, 260-266. doi: doi:10.1001/archgenpsychiatry.2008.543

Forbes, C., Poore, J., Krueger, F., Barbey, A., Solomon, J., & Grafman, J. (2014). The role of executive function and the dorsolateral prefrontal cortex in the expression of neuroticism and conscientiousness. *Social Neuroscience, 9*(2), 139-151. doi: http://dx.doi.org/10.1080/17470919.2013.871333

Gerring, J., Slomine, B., Vasa, R., Grados, M., Chen, A., Rising, W., . . . Ernst, M. (2002). Clinical predictors of Posttraumatic Stress Disorder after closed head injury in children. *Journal of American Academy of Child and Adolescent Psychiatry, 41*(2), 157-165.

Gould, K., Ponsford, J., & Spitz, G. (2014). Association between cognitive impairments and anxiety disorders following traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology, 36*(1), 1-14. doi: 10.1080/13803395.2013.863832

Grace, J., & Malloy, P. F. (2001). *Frontal Systems Behaviour Scale (FrSBe) professional manual*. Odessa, Florida: Psychological Assessment Resources.

Grados, M., Vasa, R., Riddle, M., Slomine, B., Salorio, C., Christensen, J., & Gerring, J. (2008). New onset obsessive-compulsive symptoms in children and adolescents with severe traumatic brain injury. *Depression and Anxiety*, *25*(5), 398-407. doi: 10.1002/da.20398

Herskovits, E., Gerring, J., Davatzikos, C., & Bryan, R. (2002). Is the spatial distribution of brain regions associated with closed head injury in children predictive of subsequent development of Post-Traumatic Stress Disorder? *Radiology, 224*, 345-351. doi: http://dx.doi.org.ezproxy.lib.monash.edu.au/10.1148/radiol.2242011439

Jarros, R., Salum, G., da Silva, C., Toazza, R., Becker, N., Agranonik, M., . . . Manfro, G. (2017). Attention, memory, visuoconstructive, and executive task performance in adolescents with anxiety disorders: A case-control community study. *Trends in Psychiatry and Psychotherapy, 39*(1), 5-11. doi: 10.1590/2237-6089-2016-0032

Koenen, K. C., Moffitt, T., Roberts, A., Martin, L., Kubzansky, L., Harrington, H., . . . Caspi, A. (2009). Childhood IQ and adult mental disorders: A test of the cognitive reserve hypothesis. *American Journal of Psychiatry*, *166*(1), 50-57. doi: 10.1176/appi.ajp.2008.08030343

Levi, R., Drotar, D., Yeates, K., & Taylor, G. (1999). Posttraumatic stress symptoms in children following orthopedic or traumatic brain injury. *Journal of Clinical Child Psychology, 28*(2), 232-243. doi: 10.1207/s15374424jccp2802_10

Levin, H., & Hanten, G. (2005). Executive functions after traumatic brain injury in children. *Pediatric Neurology, 33*(2), 79-93. doi: 10.1016/j.pediatrneurol.2005.02.002

Levin, H., Williams, D., Eisenberg, H., High Jr, W., & Guinto Jr, F. (1992). Serial MRI and neurobehavioural findings after mild to moderate closed head injury. *Journal of Neurology, Neurosurgery and Psychiatry, 55*(4), 255-262. doi: dx.doi.org/10.1136/jnnp.55.4.255

Lezak, M. D. (1995). *Neuropsychological Assessment* (3rd ed.). New York: Oxford University Press.

Liu, J., & Li, L. (2013). Parent-reported mild head injury history and behavioural performance in children at 6 years. *Brain Injury, 27*(11), 1263-1270. doi: 10.3109/02699052.2013.804205

Luis, C., & Mittenberg, W. (2002). Mood and anxiety disorders following pediatric traumatic brain injury: a prospective study. *Journal of Clinical and Experimental Neuropsychology, 24*(3), 270-279. doi: 10.1076/jcen.24.3.270.982

Malloy, P. F., & Grace, J. (2005). A review of rating scales for measuring behaviour change due to frontal systems damage. *Cognitive Behavioural Neurology, 18*(1), 18-27.

Max, J., Castillo, C., Robin, D., Lindgren, S., Smith, W., Sato, Y., & Arndt, S. (1998). Posttraumatic stress symptomatology after childhood traumatic brain injury. *The Journal of Nervous and Mental Disease, 186*(10), 589-596.

Max, J., Keatley, E., Wilde, E., Bigler, E., Levin, H., Schachar, R., . . . Yang, T. (2011). Anxiety disorders in children and adolescents in the first six months after traumatic

brain injury. *The Journal of Neuropsychiatry and Clinical Neurosciences, 23*(1), 29-39.

Max, J., Lopez, A., Wilde, E., Bigler, E., Schachar, R., Saunders, A., . . . Levin, H. (2015). Anxiety disorders in children and adolescents in the second six months after traumatic brain injury. *Journal of Pediatric Rehabilitation Medicine, 1*(8), 345-355.

Mineka, S., & Zinbarg, R. (2006). A contemporary learning theory perspective on the etiology of anxiety disorders. *American Psychologist, 61*(1), 10-26. doi: 10.1037/0003-066X.61.1.10

Moritz, S., Kuelz, A., Jacobsen, D., Kloss, M., & Fricke, S. (2006). Severity of subjective cognitive impairment in patients with obsessive-compulsive disorder and depression. *Journal of Anxiety Disorders, 20*(4), 427-443. doi: 10.1016/j.janxdis.2005.04.001

Ponsford, J., Draper, K., & Schonberger, M. (2008). Functional outcome 10 years after traumatic brain injury: Its relationship with demographic, injury severity, and cognitive and emotional status. *Journal of the International Neuropsychological Society, 14*, 233-242. doi: 10.10170S1355617708080272

Rosenbaum, J., Biederman, J., Bolduc-Murphy, E., Faraone, S., Chaloff, J., Hirshfield, D., & Kagan, J. (1993). Behavioural inhibition in childhood: A risk factor for anxiety disorders. *Harvard Review of Psychiatry, 1*(1), 2-16.

Stenberg, M., Godbolt, A., de Boussard, C., Levi, R., & Stalnacke, B. (2015). Cognitive impairment after severe traumatic brain injury, clinical course and impact on outcome: A Swedish-Icelandic study. *Behavioural Neurology, 3*, 1-12. doi: 10.1155/2015/680308

Stout, J., Ready, R. E., Grace, J., Malloy, P. F., & Paulsen, J. (2003). Factor analysis of the Frontal Systems Behaviour Scale (FrSBe). *Assessment, 10*(1), 79-85. doi: 10.1177/1073191102250339

Vasa, R., Gerring, J., Grados, M., Slomine, B., Christensen, J., Rising, W., . . . Riddle, M. (2002). Anxiety after severe pediatric closed head injury. *Journal of American Academy of Child and Adolescent Psychiatry, 41*(2), 148-156. doi: 10.1097/00004583-200202000-00008

Vasa, R., Grados, M., Slomine, B., Herskovits, E., Thompson, R., Salorio, C., . . . Gerring, J. (2004). Neuroimaging correlates of anxiety after pediatric traumatic brain injury. *Biological Psychiatry, 55*(3), 208-216. doi: 10.1016/s0006-3223(03)00708-x

Wechsler, D. (1997). *Wechsler Memory Scale* (3rd ed.). San Antonio, TX: Pearson.

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence*. New York, NY: The Psychological Corporation, Harcourt Brace and Company.

Werheid, K., Hoppe, C., Thöne, A., Müller, U., Müngersdorf, M., & von Cramon, D. Y. (2002). The Adaptive Digit Ordering Test: Clinical application, reliability, and validity of a verbal working memory test. *Archives of Clinical Neuropsychology, 17*(6), 547-565. doi: 10.1016/S0887-6177(01)00134-2

Wilde, E., Bigler, E., Hunter, J., Fearing, M., Scheibel, R., Newsome, M., . . . Levin, H. (2007). Hippocampus, amygdala and basal ganglia morphometrics in children after moderate-to-severe traumatic brain injury. *Developmental Medicine and Child Neurology, 49*(4), 294-299.

World Health Organisation. (1990). *Composite International Diagnostic Interview (CIDI)*. Geneva: World Health Organisation.

Tables

Table 1. *Characteristics for individuals in the mild TBI, moderate-severe TBI and OI participant groups*

	Mild TBI	Moderate-Severe TBI	Orthopedic Injury
	n (%)	*n* (%)	*n* (%)
Total	65 (38.50) *M*=23.25, *SD*=3.58	61 (36.10) *M*=22.34, *SD*=2.79	43 (25.40) *M*=21.81, *SD*=3.36
Gender			
Male	43 (66.20)	33 (54.10)	19 (44.20)
Female	22 (33.80)	28 (45.90)	24 (55.80)
Time since injury (years)	*M*=12.17, *SD*=5.31	*M*=15.13, *SD*=4.69	*M*=11.05, *SD*=4.69
Age when treated (years)	*M*=10.86, *SD*=4.87	*M*=7.05, *SD*=4.03	*M*=10.47, *SD*=3.79
Anxiety disorders	12 (19.40)	16 (26.20)	3 (7.0)
Female	9 (13.80)	12 (19.70)	2 (4.60)
Male	3 (4.60)	4 (6.60)	1 (2.30)

N=169

Table 2. *Means for cognitive performance and frontal lobe functioning among participant groups*

	Mild TBI	Moderate-Severe TBI	Orthopedic Injury
	M (SD)	*M* (SD)	*M* (SD)
Cognitive Domain			
Memory	-0.19 (0.87)	-0.06 (0.62)	0.39 (0.52)
Visuospatial Functioning	-0.20 (0.96)	-0.06 (0.53)	0.18 (0.58)
Processing Speed	-0.13 (0.93)	-0.05 (0.77)	0.13 (0.77)
Attention	-0.27 (0.79)	-0.07 (0.77)	0.44 (0.80)

	Mild TBI	Moderate-Severe TBI	Orthopedic Injury
	M (SD)	*M* (SD)	*M* (SD)
Frontal Lobe Domain			
Apathy	59.70 (15.56)	59.49 (13.80)	55.84 (10.56)
Disinhibition	60.26 (15.33)	63.15 (14.22)	55.77 (8.79)
Executive Dysfunction	66.23 (16.99)	62.98 (15.07)	56.74 (12.36)
Total	65.32 (17.45)	64.07 (14.97)	57.07 (10.69)

	Anxiety	No Anxiety
	M (SD)	*M* (SD)
Cognitive Domain		
Memory	-0.11 (0.83)	0.08 (0.69)
Visuospatial Functioning	0.11 (0.64)	0.04 (0.73)
Processing Speed	-0.12 (0.71)	0.06 (0.78)
Attention	0.001 (0.72)	0.07 (0.82)

	Anxiety	No Anxiety
	M (SD)	*M* (SD)
Frontal Lobe Domain		
Apathy	59.53 (10.89)	58.12 (14.21)
Disinhibition	62.90 (16.28)	58.99 (12.50)
Executive Dysfunction	63.62 (14.87)	61.82 (15.54)
Total	64.72 (14.92)	61.67 (14.96)

Table 3. *Logistic Regression parameters for predicting anxiety disorder diagnosis*

Variable	*B*(S.E.)	Wald	df	Odds Ratio	95.0% C.I	
					Upper	Lower
Group		4.65	2			
Group(1)	1.76 (0.86)*	4.27	1	5.90	31.78	1.10
Group(2)	1.69 (0.88)	3.69	1	5.43	30.52	0.97
Gender(1)	3.11 (0.74)**	17.76	1	0.05	0.19	0.01
Age	0.05 (0.19)	0.07	1	1.05	1.52	0.72
Age treated	0.06 (0.20)	0.09	1	1.06	1.57	0.72
Years since injury	0.17 (0.19)	0.77	1	1.18	1.71	0.82
Apathy	-0.26 (0.08)**	10.35	1	0.78	0.91	0.67
Disinhibition	-0.20 (0.07)**	8.27	1	0.82	0.94	0.71
Executive Dysfunction	-0.20 (0.08)*	6.45	1	0.82	0.96	0.70
Total FrSBe	0.56 (0.18)**	9.61	1	1.76	2.51	1.23
Memory	-0.23 (0.47)	0.24	1	0.80	1.98	0.32
Visuospatial Function	0.60 (0.56)	1.17	1	1.82	5.41	0.61
Attention	0.06 (0.43)	0.02	1	1.06	0.50	2.43
Processing Speed	-0.12 (0.40)	0.09	1	0.89	1.95	0.41

Note. *=$p<.05$, **= $p<.01$, S.E.= standard error, C.I= confidence interval