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

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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

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].

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

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

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

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

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 child-hood 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, individu-alised 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 neurobehavio-ral 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

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

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, pre-morbid 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

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-

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 inter-nalising 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.

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