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Depression and Depressive Symptoms in Pediatric Traumatic Brain Injury: A Scoping Review

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Abstract

Objective—This scoping review aimed to summarize the existing knowledge base regarding depression and depressive symptoms in pediatric TBI and to identify gaps in the literature in an effort to guide future research.

Method—Medline Ovid and PsycINFO Ovid databases were each searched by the authors using search terms intended to identify any original research study that examined depressive symptoms in children (i.e., ages 0–18 years) with TBI.

Results—A total of 14 published studies were included in the review. The studies included examined the prevalence of depression, risk factors associated with depression, and depression as a predictor of other TBI-related outcomes.

Conclusion—Existing research suggests that depressive symptoms are more common in a TBI population compared to a healthy or orthopedically injured population. Injury-related factors such as lesions in the brain and the presence of pain, as well as non-injury factors such as older age at injury and low socioeconomic status, may be predictive of depressive symptoms. Depression is likely a secondary outcome of pediatric TBI rather than a direct result of the injury itself. Overall, a relative dearth of research exists on this topic; thus, the review concludes by proposing future research directions.

Keywords

traumatic brain injury; depression; child; pediatric; outcome; review

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Introduction

Traumatic brain injury (TBI) is a significant health concern among children and adolescents.[1] Over half a million children present to the emergency department for TBI-related visits in the United States, annually,[2] with highest incident rates seen in children aged 0–4 years[3] and adolescents aged 15–19 years.[2] A large body of research has focused on understanding factors related to risk, prognosis, and outcomes following TBI in children and youth.

Pediatric TBI is associated with an array of negative outcomes, including impaired cognitive and academic abilities,[4] social impairments,[5] and behavioural problems.[6] Another outcome often associated with TBI in children is depression. Studies have estimated the rate of depression in children post-TBI to be as high as 33–50%.[7,8] Depression is characterized by chronic low mood that can be recurrent in nature.[9] Type and severity of symptoms of depression can vary widely, though often include low mood, feelings of worthlessness, weight loss/weight gain, anhedonia, sleeping more or less than usual, and/or recurrent thoughts of death.[10] Importantly, depression is a significant risk factor for suicide in children, and estimates indicate that suicide is the third leading cause of death among children aged 10–14 years.[11] With a lifetime prevalence of approximately 11% in children 13 to 18 years of age,[12] coupled with a high prevalence in children with TBI, depression represents a significant health concern in this population.

Research on depression in the general population suggests that an earlier age of onset results in greater severity and impairment,[13] and that more severe first episodes can result in recurrent depression.[14] Furthermore, depression is often complicated by a high comorbidity with other disorders. For example, anxiety and conduct disorder are associated with an estimated 4-fold increase in risk for major depressive disorder in adolescents.[12] The risk for comorbid disorders is further compounded within medical populations.

The relationship between TBI and depression, while not well understood in children, has been more widely studied among adults. Studies have suggested that the emergence of depression after adult TBI may be physiological in nature, perhaps due to the disruption of neural circuits (e.g., limbic-frontal circuitry[15]) or post-traumatic changes of neurotransmitters in the brain (see Jorge & Robinson[16] for a review). However, less is known regarding the mechanisms responsible for the occurrence of depression in children after TBI.

We identified only two systematic reviews that have been conducted to date that examine psychosocial outcomes, including depressive symptoms, in pediatric TBI. One examined outcomes within 2-years post-injury and identified only three studies that reported on depressive symptomatology.[17] The second review was limited to outcomes in children with mild TBI.[18] Notably, both reviews found depressive symptoms to be more common among children with TBI than non-head injured control groups. However, a review focusing exclusively on depressive symptoms in children across all TBI severities that includes studies examining long-term outcome (i.e., greater than 2 years) has yet to be published.

Therefore, the overall goal of this scoping review was to examine the literature pertaining to depression and depressive symptoms in childhood TBI in order to summarize the existing

knowledge base as well as to identify areas requiring further research. Specifically, we aimed to examine the rates of depressive disorder and/or depressive symptoms in this population, pre- and post-injury risk factors associated with depressive symptoms following TBI, the role of depressive symptoms as risk factors for other functional outcomes following TBI, and to elucidate whether depressive symptoms are a primary or secondary outcome following TBI.

One challenge to studying depression in children following TBI is the substantial overlap between symptoms that often occur after TBI, often called post-concussive symptoms (PCS), and those that define depression (e.g., difficulty concentrating, fatigue, and irritability). A second challenge in the study of depression in childhood TBI is the hetereogeneity in outcomes associated with TBI. TBI ranges in severity from mild to severe, and severity often predicts outcomes in a dose-response fashion; however, outcomes are also impacted by pre- and post-injury psychosocial factors.[19] Thus, our review attempts to explore whether depressive symptoms exceed or differ from those that occur after TBI, as well as whether depressive symptoms vary across TBI severities.

For the purposes of this review, depressive symptoms refer to any symptoms listed in the Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition[20] and/or Fifth Edition[21] under the category of Major Depressive Disorder (e.g., low mood, anhedonia, fatigue, feelings of worthlessness, difficulty thinking, thoughts of death or suicide). Depression, as described in this review, refers either to a diagnosis of a depressive disorder or to scores on self/parent report measures of depressive symptoms in the clinically significant range, as specified by the authors of the identified study.

Method

The review procedure adhered to Arksey and O'Malley's[22] methodological framework for scoping reviews. Specifically, the procedure was as follows: (1) identified the research question, (2) performed a literature search to locate relevant studies, (3) selected studies pertaining to our research question, (4) charted the data, and (5) collated, summarized, and reported the results.

In September 2016, searches of Medline Ovid and PsycINFO Ovid were conducted with the following keywords: ((depression OR mood disorder OR affective disorder OR low mood) AND (children OR adolescent OR pediatric OR paediatric) AND (TBI OR traumatic brain injury)) OR ((brain injuries OR brain concussion OR brain injury, chronic) AND (child, preschool OR child OR paediatric OR adolescent) AND (depression OR low mood)) OR ((traumatic brain injury OR brain injury) AND child AND (depression OR low mood)). Review articles (i.e., scoping reviews, systematic reviews, meta analyses) as well as articles written in languages other than English were excluded from the review.

Following the initial search, titles were scanned and articles were selected based on relevance to the topic. The selected studies were then exported from the database to an Excel file, where abstracts were read to ensure relevance to the review, based on the following inclusion criteria: (a) participants must be 18 years of age or younger at the time of study;

(b) participants must have suffered a TBI (i.e., no other type of acquired brain injury); (c) the study must have included a measure of depression, and (d) the study of depression must have pertained to children in the study (i.e., not parents). Studies for which a specific measure of depression was not derived (e.g., examined internalizing symptoms that encompassed both anxiety and depressive symptoms) were excluded. Following abstract review, 31 studies were selected for full text review. During the full text review, 17 were excluded due to not meeting inclusion criteria. Thus, the full text review resulted in a final inclusion of 14 articles. Figure 1 outlines the literature search process.

Results

Study characteristics

An overview of the aims, methodology, and key findings of each of the 14 studies is provided in Table 1. The countries where studies were conducted included the United States of America (9), Canada (2), United Kingdom (2), and Australia (1), and the dates of publication ranged from year 2000 to 2015. All publications were original research studies, of which 7 recruited participants retrospectively (4 studies with cross-sectional designs, 3 studies with longitudinal designs) and 7 employed a prospective, longitudinal design. Participants ranged in age from 0 to 18 years (one study specified an age range of 0–18 years in the study inclusion criteria but did not specify the exact age range of the sample analysed; the age range of all other studies was 5 to 18 years), and severity of TBI ranged from mild to severe. The Glasgow Coma Scale (GCS[23]) was used to classify injury severity in 13 studies (one study relied solely on self-report of history of a concussion). Mild TBI was defined as a GCS score of 13–15; moderate TBI was defined by (a) a GCS score of 9–12, or (b) a GCS score of 13–15 if accompanied by neuroimaging findings; severe TBI was defined as a GCS score of 8 or less, or (b) a GCS score of 6–12 with accompanied endotracheal intubation, mechanical ventilation, and admission to a pediatric intensive care unit. Five studies included a control group (orthopaedic injury or healthy control). Nine different parent/self-report measures were used to rate depression (see Table 1). Only one study utilized both self-and parent-report measures of depression, whereas 11 studies included self-report only and 2 studies included parent-report only.

Prevalence and risk of depression following TBI

Four studies reported the prevalence of depression among children between the ages of 8 to 18 years with a history of TBI at varying time points post-injury. Prevalence of depression in the TBI population was reported to range from 5.3 to 36%, depending on the time of assessment, assessment instrument, and TBI severity. Among children with mild TBI, prevalence was estimated to range from 5.3% at 4–26 weeks post-injury (M = 8.21, SD = 4.71[24]) to 36% at 5–12 months post-injury (M = 8.7, SD = 1.7[25]). Compared to risk rates for clinically elevated symptoms of depression in a normative sample, Peterson et al[24] reported no significant differences in parent-reported depression risk for those with mild TBI. Conversely, Chrisman et al[26] reported that a history of mild TBI corresponded with a 3.2-fold greater risk for depression, compared to those who had never sustained a mild TBI. Finally, O'Connor et al[27] reported slightly higher prevalence rates of depression in a mild TBI group (i.e., 6%, 4,%, 5% at 3, 12, and 24 months, respectively) in comparison to the

moderate/severe TBI or arm-injured groups, but group differences were not significant. Prevalence rates of depression were not reported in any study for children with TBI under the age of 8 years.

Injury factors associated with depression following TBI

Several studies addressed injury-related risk factors associated with the onset of depressive symptoms following TBI. Smyth et al[28] examined the association of the presence of post-concussive symptoms (PCS) with risk for depression in children across all ages (i.e., 0 to 18 years) and reported no group differences in rates of depression in those who reported elevated PCS compared to those who did not. On the contrary, Tham et al[29] found pain to be associated with significantly higher self-reported depressive symptoms among adolescents (ages 14 to 17 years) with TBI, regardless of severity (i.e., no group differences between mild, moderate, and severe TBI). Only one study examined structural brain changes associated with TBI and their relationship to risk of depression. Specifically, Max et al[30] reported lesions in the left inferior frontal gyrus, right frontal lobe white matter, left temporal pole, and left parietal regions to be predictive of depression in children, ages 5 to 14 years, with complicated mild (i.e., neuroimaging findings) to severe TBI. In sum, injury-related factors, such as pain and brain lesions, may be related to an increased risk of depression and/or depressive symptoms in adolescents or in cases of more severe injury (i.e., presence of neuroimaging findings). However, the literature is unclear whether this relationship exists for children of all ages and for TBI of all severities.

Non-injury factors associated with depression following TBI

Pre-injury and non-injury factors were considered in several studies as possible predictors of risk for depression following TBI. Peterson et al[24] did not find that a greater number of previous mild TBIs increases the risk for clinical depression. However, one study found age at injury to be predictive of depression. Specifically, Max and colleagues[30] reported the incidence of depression to be significantly greater in children who sustained a TBI when 12 years of age or older (18.2% prevalence), compared to those who sustained their injury before 9 years of age (3.5% prevalence). Similar findings were reported by Chrisman et al[26] who reported a 1.5-fold increased risk for depression in children aged 15–17 years compared to those aged 12–14 years, even after controlling for previous mild TBI. In children aged 5–14 years, pre-injury family and adaptive functioning, as well as non-injury factors, such as gender, race, and socioeconomic status (SES), were not found to be significantly predictive of the presence of depression among children with mild, moderate, or severe TBI.[30] On the contrary, Kirkwood et al[31] reported an association between SES and self-reported depressive symptoms among 6 to 12 year-old children with TBI and OI. Specifically, they reported higher SES to be related to fewer depressive symptoms, regardless of injury. They also reported a moderating effect of SES, wherein the presence of depressive symptoms in the severe TBI group relative to the comparison group was more pronounced among children from low SES homes. Additionally, Max et al[30] found that a family history of anxiety disorders, but not depressive disorders, was predictive of post-injury depression in children with TBI. In summary, the literature suggests that pre-injury factors may be related to the presence of depression following TBI, but that current environmental factors, such as SES,

may be a stronger predictor of depressive symptoms, although their contribution to depressive disorder is unclear.

Effect of depression on other outcomes following TBI

Four studied examined the role of depressive symptoms in predicting other outcomes following TBI. Tham et al[25] provided support for the role of self-reported depressive symptoms as a significant predictor of poorer sleep quality among adolescents with mild TBI. Additionally, increased self-reported symptoms of depression were found to be a significant predictor of persistent pain among adolescents with mild, moderate, or severe TBI at 3 months post-injury and poorer health-related quality of life at 36 months post-injury[29]. Furthermore, O'Connor et al[27] found that, among adolescents, increased self-reported depressive ratings 3 months post-injury were associated with poorer school functioning at 12 and 24 months post-injury. Finally, Kirkwood et al[31] did not find a significant relationship between self-reported depressive symptoms and intelligence scores at 6 and 12 months post-injury in children aged 6 to 12 years. Taken together, the evidence suggests that depressive symptoms following TBI may place a child at a greater risk for poorer functional outcomes.

Depression as a primary or secondary outcome following TBI

A key goal of this review was to elucidate whether depression is a primary or secondary outcome following TBI in children. That is, do depression/depressive symptoms arise due to changes in the brain related to the TBI itself, or as a result of changes in a child's experiences post-injury that may make them more prone to depressive symptoms (e.g., missing school, removal from sports teams, decreased interaction with peers)? Several studies included in the review addressed this question, but results were mixed. One approach to determining whether depression is a primary outcome due to brain changes as a result of injury is to compare depressive symptoms in children with differing levels of TBI severity. Max et al[30] found no significant differences in injury severity between those with and without depression. A similarly finding was reported by O'Connor et al[27], who reported no group differences in rates of depression among children with mild and moderate/severe TBI. In another study, raised intracranial pressure (ICP), a marker of injury severity, was shown to be unrelated to rates of depression among children with severe TBI several years post-injury (M = 3.9; Slawik et al[32]). Calvert et al[33] reported a significant correlation between scores on a measure of head injury severity and level of self-reported depressive symptoms shortly after injury, although the correlation was not significant at 3- and 6-month follow-up assessments. Furthermore, Mather et al[34] found no significant differences in self-reported depressive symptom ratings between children with and without mild TBI when assessed shortly after involvement in a traffic accident, suggesting that the role of a traumatic event may be more predictive of depressive symptoms than TBI. Although Max et al[30] found structural changes in the brain to be associated with depressive symptoms, it is difficult to know whether the structural differences were related to the injury itself, were pre-existing, or were related to non-injury factors. Thus, the existing research tends to suggest that depression is a secondary rather than primary outcome of TBI.

Discussion

The current scoping review sought to examine the state of the literature regarding depression and/or depressive symptoms in pediatric TBI. The quality of the studies included varied in terms of design (i.e., cross-sectional, longitudinal), sample size, comparison group, and measurement of depression. Overall, the relative dearth of research in this area reflects significant gaps in our understanding of depression after childhood TBI, although several key issues were elucidated by the existing research.

First, depressive symptoms do appear to be more common in children with TBI than in the general healthy or non-head injured population (e.g., Peterson et al[24]; Tham et al[25]). The question of whether depression as a clinical diagnosis (i.e., major depressive disorder; MDD) is more common, however, was not answered by this review, mainly because of inconsistencies in the definition of depression (i.e., symptoms vs. disorder). Few studies defined depression in terms of the DSM-5 definition of MDD (see APA[10]) or used structured psychiatric interviews to make a formal diagnosis. Given that symptoms of depression are so varied, studies of individual symptoms of depression can result in substantial variability in research results, hampering inferences regarding prevalence. Thus, although children with a history of TBI may be more likely to report increased depressive symptoms, we cannot conclude whether they are at a greater risk for a clinical diagnosis of MDD. Consequently, our findings should be taken to describe the risk of depressive symptoms associated with pediatric TBI, and not necessarily clinical depression. Additionally, little consensus exists regarding the risk for depression in the short-term (e.g., within the first year post-TBI) versus long-term (e.g., 5 years post-TBI). Future studies should therefore aim to examine the prevalence of MDD diagnoses in children following TBI by employing prospective, longitudinal designs using structured interviews at different times post-injury.

Secondly, several injury and non-injury factors were identified that contribute to the risk for depression or depressive symptoms following childhood TBI. Injury-related factors, such as presence of pain[29] or brain lesions,[30] were found to be associated with an increased risk for depressive symptoms, although relevant findings were limited to two studies and were contradicted by a third (i.e., Smyth et al[28]). Although older age at injury appears to be a risk factor for depression after TBI, other non-injury factors, such as SES and family history of psychiatric disorders, are less well understood in terms of their relationship to depression. Whether children from low SES environments or with a family history of psychiatric disorders who develop depression after TBI would have done so absent the TBI remains uncertain. Perhaps sustaining a TBI pushes them over the threshold between prodromal symptoms and clinical diagnosis. More research is needed to better understand both the injury and non-injury related factors associated with increased risk for depression after TBI, as well as their interactions with age and the mechanisms behind these relationships.

A third issue this review addressed was the relationship of depression to TBI as a primary versus secondary outcome. If depression were a primary outcome, then the level of depressive symptoms should be worse among those with more severe TBI (i.e., more brain damage); however, the available research does not support a strong relationship in this regard. Depression might be a primary outcome following TBI in the early stages post injury

(as reported by Calvert et al[33]), but the long-term associations remain unclear. Whether the risk for depression is due to interruptions of neural circuits[18] or hormonal changes,[19] as suggested in adult populations, or whether it is secondary to changes in the child's experiences or perceptions thereof, represents an area requiring further research. Studies that examined the relationship of depression to other outcomes of TBI (e.g., quality of life[29]; school functioning[27]) indicated that depression is predictive of other outcomes, but the causal direction of these relationships was not addressed. Mostly likely, the effects are bidirectional. Furthermore, factors such as age at injury and the family environment may interact with injury severity to predict depression. Nonetheless, taken together, the existing literature suggests that depression is largely a secondary outcome of childhood TBI, though further research is needed before any definitive conclusion can be drawn.

Several methodological limitations of the extant literature were highlighted by this review. One is the relative lack of attention to the effects of age on both symptoms of depression and the effects of TBI. Older age at injury was found to be predictive of greater risk for depression[30]. However, symptoms as well as etiology of depression likely differ between younger and older children.[35,36] Therefore, age at injury should be examined as a moderator of risk factors related to depression and depressive symptoms in TBI. Furthermore, children under the age of 8 years are scarcely represented in the existing literature; thus this population would benefit from future study. Another limitation involves the measures used to assess depression. These measures are not specifically normed on TBI populations; thus, the problem of overlap between TBI-related and depressive symptoms becomes a significant methodological challenge. Future studies would benefit from factoring out symptoms that may be related to TBI to better understand depression-specific symptomatology (e.g., persistent low mood, feelings of worthlessness) in TBI.

In summary, this scoping review provides insights into the status of existing research regarding depression and/or depressive symptoms in pediatric TBI. The results suggest that children who sustain a TBI are at an increased risk for depressive symptoms, and that several injury and non-injury factors may predict this risk. However, literature in this area is scarce, and several unanswered questions remain regarding the risk factors associated with depression, as well as the mechanisms behind these relationships. Furthermore, the quality of the existing studies is varied, and the use of combined multi-informant (e.g., parent and child ratings) and multimodal assessments (e.g., self-report and structured interview) to better inform findings is limited. More research is thus required to better understand these associations, particularly given the high prevalence of depressive symptoms associated with TBI in children, as well as the risk of suicidality associated with childhood depression in the general population.[37] Directing research towards untangling the complexities of this issue can help guide treatments with the goal of producing better functional outcomes for children who sustain a TBI.

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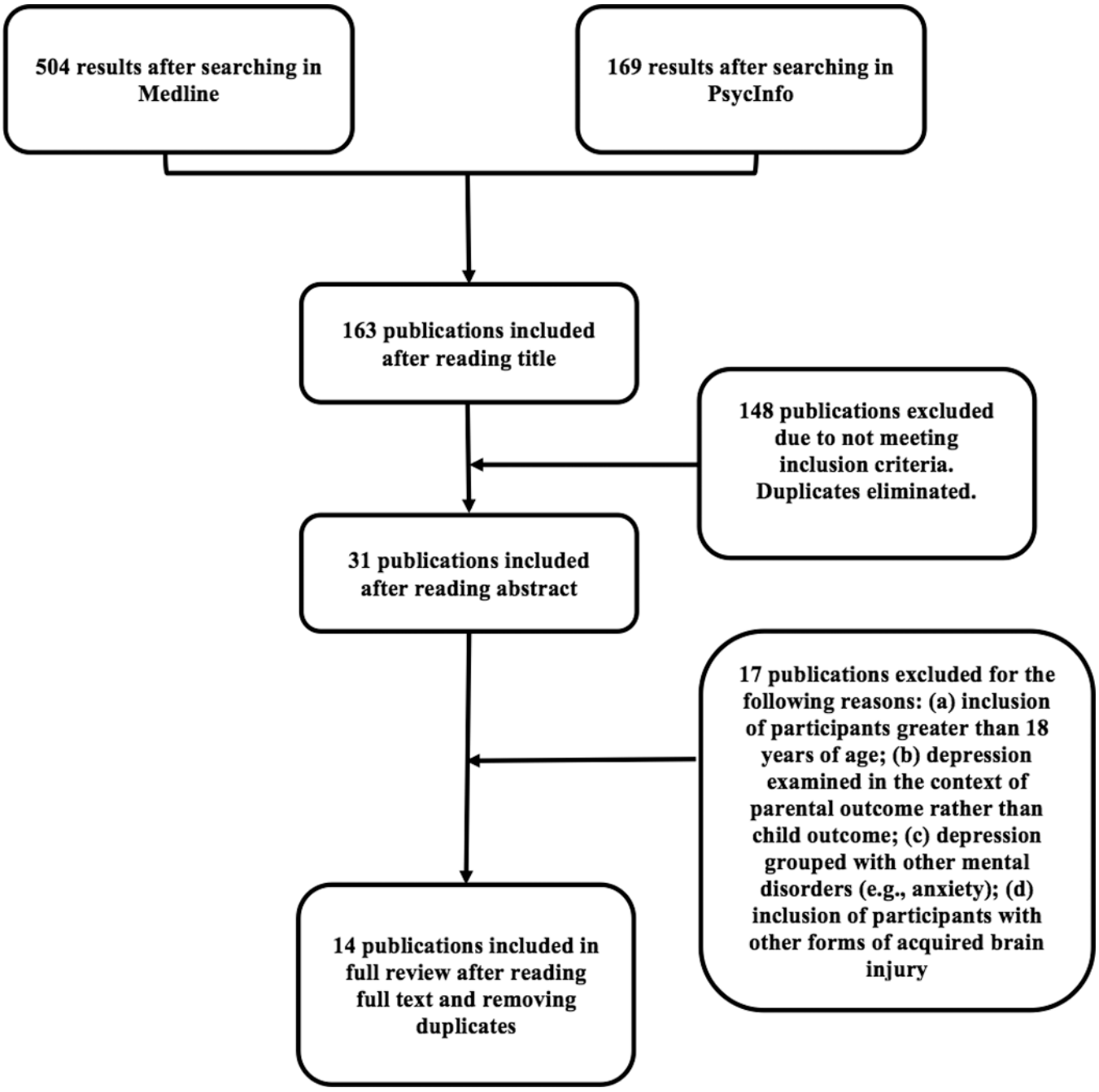

Figure 1.
Literature review process.

Table 1

Overview of studies included in scoping review

Author, year, country	Aims	Study design	Study population	Measured variables	Main findings*
Peterson et al[24], 2015; USA	**1** Characterize pre-injury emotional-behavioural functioning of children referred to an outpatient pediatric concussion program. **2** Investigate associations between emotional-behavioural problems and a history of mild TBI.	**1** Evaluated the proportion of mild TBI sample rated as falling in the clinical or at-risk range of the BASC-2 subscales compared to the norming sample (z-score comparison). **2** An ANOVA was conducted to compare the number of previous mild TBIs for groups falling in the normal, at-risk, and clinical ranges.	Children (N = 278) with mild TBI Age = 8–17 years (M = 14.63, SD = 2.24) Norming sample: normative rates of at risk or clinical range scores.	BASC-2 Depression Scale (parent report)	- 11.4% in the at-risk range, 5.3% in the clinical range of the BASC-2 Depression Scale (parent report). - A comparison between % of mild TBI group and normative sample in the at-risk and clinical ranges was non-significant. - Group differences of the number of previous mild TBIs for participants falling in the normal, at-risk, and clinical ranges for depression scale were non-significant.
Tham et al[25], 2015; USA	**1** Compare sleep in adolescents with mild TBI to healthy adolescents **2** Identify the clinical correlates associated with sleep problems.	Study materials (instructions, questionnaires, electronic sleep diary, and sleep watch) were mailed to participants. Sleep diary was completed twice daily. Sleep was monitored for 10 days.	Adolescents (N = 100) with mild TBI (n = 50) and healthy controls (n = 50) Age = 12–18 years (M = 15.6, SD = 2.0)	CES-D, NRS, ASWS, PSA, actigraphy sleep assessment	- In the mild TBI group, a higher proportion of adolescents met the criteria for depressive illness (CES-D) compared with healthy peers (36% vs. 12%). - Depressive symptoms predicted poorer sleep quality.
Keightley et al[38], 2014; Canada	Examine and compare working memory performance and related brain activity using fMRI in concussed youths and healthy age-matched controls.	Participants completed tasks assessing working memory while undergoing fMRI. Study included administration of a self-report measure of depression.	Adolescents (N = 30) with mild TBI (n = 15) and healthy controls (n = 15) Age = 10–17 years (mild TBI M = 14.47, SD = 2.29; healthy controls M = 14, SD = 2.3)	BDI total score	- mild TBI group did not endorse greater depressive symptoms than the control group.
Chrisman et al[26], 2013; USA	Examine the prevalence of depression in youth with a history of concussion using a nationally representative sample.	Phone survey asking parents if their child had ever been diagnosed with depression and/or brain injury or concussion.	Children (N = 36,060) Group 1: Age 12–14 years Group 2: Age 15–17 years	Presence of concussion and current diagnosis of depression, age, sex, parental mental health	- 2.7% of all children surveyed had a previous concussion, and 3.4% had a current depression diagnosis - A history of concussion was related to a 3.2-fold greater risk for current depression. - 1.5-fold greater risk of current depression in the 15–17 year old group compared to 12–14 after controlling for previous concussion.

Author, year, country	Aims	Study design	Study population	Measured variables	Main findings*
Smyth et al[28] 2013; Canada	Investigated the relationship between the HTR1A G (−1019) allele, depression, childhood life stressors, and PCS after pediatric mild TBI.	Participants recruited prospectively from a database. PCS, depression, stressful life events, and DNA were analyzed. PCSI was administered 7–10 days post injury and then again with all other questionnaires 1–3 years post-injury.	Children (N = 89) with symptomatic mild TBI (n = 47) or asymptomatic mild TBI (n = 42) Age = 0–18 years (symptomatic M = 14, SD = 3.3; asymptomatic M = 13.6, SD = 3.1)	CDI, PCSI	- No group differences in depressive symptoms between the asymptomatic and symptomatic groups. - Prevalence of depression found to be low (3%) following mild TBI.
Tham et al[29], 2013; USA	**1** Examine the prevalence of persistent pain over 36 months in adolescents following TBI. **2** Identify risk factors for pain over this interval (i.e., age, sex, TBI severity, depressive symptoms). **3** Examine the longitudinal association of persistent pain with long-term HRQOL.	Assessments were conducted at enrolment and at 3, 12, 24, and 36 months after TBI. One parent and the adolescent completed a battery of questionnaires on pain, depressive symptoms, posttraumatic stress disorder symptoms, and HRQOL by mail or via phone interview.	Adolescents (N = 144) with mild TBI (n = 119), moderate TBI (n = 22), or severe TBI (n = 3) Age = 14–17 years (M = 15.70, SD = 1.20)	PHQ-9, persistent pain, HRQOL	- At 3- and 36-month assessment points, adolescents with persistent pain endorsed significantly higher levels of depressive symptoms. - Increased symptoms of depression at 3 months after TBI were significant predictors of persistent pain. - TBI severity and depressive symptoms at 3 months predicted HRQL over the course of 36 months (higher TBI severity and greater depressive symptoms predicted poorer longitudinal HRQOL).
Max et al[30], 2012; USA	Examine the demographic, psychosocial, and lesion predictors, as well as the occurrence and phenomenology of new onset depressive symptomatology in children after TBI.	Measures were administered at baseline to record pre-injury diagnoses and repeated 6 months post-injury to record new-onset diagnoses. MRI was conducted 3 months post-injury.	Children (N = 141) with mild TBI (n = 69), moderate TBI (n = 18), or severe TBI (n = 54) Age = 5–14 years (M = 10.13, SD = 2.77)	Age at injury, family history of anxiety or mood disorder, personality change due to TBI, pre-injury anxiety disorder, lesions on MRI, K-SADS-PL, NPRS	- No significant differences between children with and without depression on demographic variables (gender, race, SES) and pre-injury psychosocial variables (family function, adaptive function). - No significant differences in injury severity between those with and without novel definite/subclinical depressive disorder. - Age at injury was significantly greater in children with depression (all) versus no depression (5-fold increase in the rate of depression for children with age of injury ≥12 years (18.2%) compared with age of injury <9 years (3.5%)). - Family history of anxiety disorder, left inferior frontal gyrus (IFG) lesions, and age at injury

Author, year, country	Aims		Study design	Study population	Measured variables	Main findings*
						significantly predicted novel depression. - Family history of a mood/ depressive disorders and pre-injury anxiety were not predictors for novel depression. - Comorbid personality change due to TBI at 6 months post injury was significantly correlated with novel anxious depression. - Depression was significantly correlated with lesions in the left IFG and right frontal lobe white matter. - Non-anxious depression was significantly correlated with lesions of the left IFG and the left temporal pole. - Anxious depression was significantly correlated with right frontal white matter lesions and left parietal lesions.
O'Connor et al[27], 2012; USA	**1**	Measures of PTSD and depression were used to compare mental health functioning between patients with differing levels of TBI severity and an arm-injured control group.	Baseline assessment battery administered by phone in the weeks following the injury (*median* = 37 days), in which parents and children were asked to rate pre-injury functioning. Phone or online follow-up assessments with parent and child were conducted at 3, 12, and 24 months post-injury.	Adolescents (N = 228) with mild TBI I (no intracranial haemorrhage, n = 125), mild TBI II (presence of intracranial haemorrhage, n = 33), moderate to severe TBI (n = 31), and arm-injured controls (n = 39) Age = 14–18 years (M = 15.88, SD = 0.93)	PHQ-9, UCLA PTSD reaction index for DSM-IV-R, PedsQL (parent report), FAD-GF (parent report)	- At 3, 12, and 24 months, 2%, 3%, and 0% of the arm-injured group, 6%, 4%, and 5% of the mild TBI group, and 3%, 4%, and 4% of the moderate/severe TBI group were identified as having probable depression. - No significant differences between TBI groups and the arm-injury group for depressive symptoms across 3, 12, and 24 months. - Greater PHQ-9 total score at 3 months was associated with poorer school functioning across 12 and 24 months.
	2	The association of PTSD and depressive symptoms at 3 months post-injury was examined.				
Slawik et al[32], 2009; UK	Examine whether individuals with severe TBI with raised intracranial pressure (ICP) immediately after the injury exhibit dysfunction in executive tasks.		At an average of 3.9 years post-injury, participants were administered a battery of neuropsychological tests focused on prefrontal function and underwent MRI.	Children (N = 33) with severe TBI who had ICP (n = 13) or no ICP (n = 20) Median age = 15.2 years, interquartile range = 8.4–13.0	BDI-Y	- There were no group differences on BDI-Y between the non-ICP and ICP groups.

Author, year, country	Aims	Study design	Study population	Measured variables	Main findings*
Calvert et al[33], 2008; UK	Determine if KOSCHI score at hospital discharge relates to measures of injury severity, cognition, behaviour/emotional status, health status, and HRQOL.	Participants were assessed for TBI severity at admission to hospital. Two follow-up assessments completed at 3- and 6- months post-injury.	Children (*N* = 81) with mild TBI (n = 37), moderate TBI (n = 15), or severe TBI (n = 29) Age = 5–16 years (*M* = 11.8)	KOSCHI, BDS	- Significant correlation between discharge KOSCHI (described as an indicator of injury severity) and level of depressive symptoms at first assessment, but not at follow-up assessments.
Wade et al[39], 2008; USA	**1** Can the Teen Online Problem Solving Intervention (TOPS) reduce behaviour problems and improve executive function skills following TBI? **2** Can the TOPS reduce parental depression and distress and improve family function?	Children with TBI and their families underwent a baseline assessment in the first session and then went on to complete 16 TOPS online, self-guided sessions (which required family involvement).	Children (*N* = 9) with moderate TBI (n = 7) or severe TBI (n = 2) sustained within the past 24 months, and their families Age = 11–18 years (*M* = 15.04)	CDI – 10 item short-form	- Depressive symptoms significantly decreased following the TOPS intervention.
Wade et al[40], 2005; USA	Examine the feasibility and efficacy of a self-guided web-based family intervention for children with TBI.	Children with TBI and their families underwent assessment in the first session and at the 6 week follow-up. The family completed the self-guided materials on the provided website and weekly sessions with a therapist were conducted.	Children (*N* = 6) with moderate TBI (n = 2) or severe TBI (n = 4) sustained within the past 15 months, and their families Age = 5–16 years (*M* = 10.5, *SD* = 3.62)	CDI – 10 item short-form	- Depressive symptoms did not significantly decrease following the web-based intervention.
Mather et al[34], 2003; Australia	Examine the frequency and course of PTSD and comorbid psychological symptomatology in children and adolescents with and without mild TBI as a result of traffic accidents.	Examined symptoms of depression and PTSD at 6 weeks post-accident and again at 13 weeks post-accident.	Children (*N* = 43) involved in traffic accidents with mild TBI (n = 14) and without mild TBI (n = 29) Age = 6–15 years (*M* = 9.7, *SD* = 2.5)	CDI	- No significant group differences in depression scores at initial assessment; group differences at follow-up not reported.
Kirkwood et al[31], 2000; USA	Examine the prevalence and correlates of depression following childhood TBI using child and parent ratings of depressive symptoms.	Children rated post-injury depressive symptoms at baseline (shortly after injury), as well as 6 and 12 months post-injury. Parents rated children's pre-injury functioning at baseline and their post-injury functioning at the 6 and 12 month follow-ups.	Children (*N* = 144) with moderate TBI (n = 51) or severe TBI (n = 38), and orthopedically-injured controls (n = 55) Age = 6–12 years (moderate TBI *M* = 9.87, *SD* =1.91; severe TBI *M* = 9.68, *SD* = 2.16; orthopaedic injury *M* = 9.40, *SD* =1.91)	Race, SES, FAD-GF, time since injury, CDI	- No significant main effect of group on CDI. - Significant group X time interaction in the prediction of CDI (the total score did not change over time in the TBI groups, but declined significantly in the OI group). - No group differences in the proportion of children who reported clinically significant depressive symptoms on the CDI at any occasion.

Author, year, country	Aims	Study design	Study population	Measured variables	Main findings*
					- Children from homes of higher SES reported fewer depressive symptoms in all groups and SES was a significant moderator of self-reported symptoms (the effect of severe TBI was more pronounced among children from more disadvantaged homes). - Family functioning moderated self reported depressive symptoms (children in the OI group from less dysfunctional families reported more symptoms at the initial assessment than those from more dysfunctional families, as well as more than children in either TBI group). - Self-reported ratings of depressive symptoms were unrelated to IQ scores at either 6 or 12 months post-injury.

ANOVA = analysis of variance; ASWS = Adolescent Sleep Wake Scale; BASC-2 = Behaviour Assessment System for Children – Second Edition; BDI = Beck Depression Inventory; BDI-Y = Beck Depression Inventory – Youth; BDS = Birleson Depression Scale; CDI = Children's Depression Inventory; CES-D = Center for Epidemiological Studies Depression Scale; DSM-IV-R = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Revised; FAD-GF = McMaster Family Assessment Device, General Functioning subscale; fMRI = functional magnetic resonance imaging; HRQOL = Health-Related Quality of Life; K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version; KOSCHI = King's Outcome Scale for Childhood Head Injury; NPRS = Neuropsychiatric Rating Schedule; NRS = Numerical Rating Scale; OI = orthopaedic injury; PCS = post-concussive symptoms; PCSI = Post-Concussion Symptom Inventory; PedsQL = Pediatric Quality of Life Inventory; PHQ-9 = Patient Health Questionnaire–9; PSA = Pre-Sleep Arousal; PTSD = post-traumatic stress disorder; SES = socioeconomic status; TBI = traumatic brain injury

* $p < .05$ interpreted as significant