A Scoping Review of Pain in Children after Traumatic Brain Injury: Is There More Than Headache?

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Abstract

Headache is a common source of pain in children after traumatic brain injury (TBI); however, relatively little is known about nonheadache pain in this pediatric population. The present review seeks to map the extant literature to determine the prevalence, characteristics, and impact of nonheadache pain in children post-TBI of all severities. We found that of 109 studies published on pain in children after a TBI, 95 (87%) were focused exclusively on headache pain and only 14 (13%) reported on nonheadache pain or overall pain, with half ($n = 7$) in the form of case studies. Overall, the level of evidence was low, with only three level 1 high-quality prospective studies. In one study, over half (57.1%) of adolescents who experienced persistent pain post-TBI reported pain in *multiple* body sites (e.g., back, lower limb, and neck).¹ For each additional noncephalic pain site, the risk for developing chronic migraine is also increased. Nevertheless, pain in body regions other than the head is often not assessed systematically in pediatric TBI research. Findings of the current review suggest that pain assessment in children post-TBI needs improvement, given that pain is linked to worse recovery, poorer quality of life, and can be long-lasting. More rigorous examination of nonheadache pain and its role in impeding recovery in children post-TBI is imperative and has the potential to improve the care and management of children with TBI. We conclude with recommendations for pain assessment, discuss gaps in the literature, and highlight directions for future research.

Keywords: pain assessment; pediatrics; traumatic brain injury

Introduction

HEADACHE IS A COMMON SYMPTOM after pediatric traumatic brain injury (TBI).^{1,2} A systematic review concluded that chronic headache pain is a common complication after pediatric TBI, even for minor injuries.³ This raises concerns given that children with pain are likely to grow up to become adults with chronic pain⁴ and to develop associated mental health problems,⁵ resulting in enormous economic,⁶ psychological,⁷ and social costs⁸ for individuals and society. Indeed, post-injury headache is an important area of research. However, headache is not the only type of pain that may be present after a TBI. Any biological tissue that contains nociceptive fibers is a potential source of pain in persons with TBI.⁹ Noncephalic pain is commonly comorbid in people with headache or migraine.² Recent research found that after controlling for demographics, individuals were 15% more likely to have persistent chronic migraine for each additional noncephalic pain site (e.g., face, neck or shoulders, and back).² Nevertheless, to the best of our knowledge, no published reviews have examined the prevalence and impact of nonheadache pain in children post-TBI.

A systematic review of pain in adult TBI reported an alarmingly high chronic pain prevalence of 57.8%, and discussed other non-headache pain syndromes as potential sequelae, such as complex regional pain syndrome, heterotopic ossification, peripheral neuropathic pain, and neuromuscular spasticity.¹⁰ Few studies have investigated mechanisms of pain after a TBI. The pathogenic etiologies of chronic pain post-TBI are thought to include musculoskeletal, vascular, neurogenic, visceral, and iatrogenic mechanisms.¹¹ However, these findings from adult studies may or may not generalize to children, given that numerous important differences characterize TBI in youth compared to adulthood. For instance, children show an increased propensity for apoptosis (programmed/regulated cell death), different age-dependent parameters for cerebral blood flow and metabolism, and an increased likelihood of early post-traumatic seizures.¹² Given the dissimilarities noted in pathophysiology, pain experiences post-TBI may differ across development.

The purpose of the current review was to map the nonheadache pain literature in the context of pediatric TBI based on several factors: study design, types of pain investigated, and methods used for pain assessment. Our goal was to elucidate what is known about

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the types of nonheadache pain that are present in children post-TBI. This is an important goal because both TBI and chronic pain are linked to poor outcomes across nearly every domain of functioning, from cognitive, social, and physical, to economic and familial.⁷ Therefore, pain may further complicate and exacerbate poor outcomes post-TBI in these vulnerable youths.

Methods

Study inclusion and exclusion criteria

Published studies were included that fulfilled three main criteria: 1) The study was specific to the pediatric population (between the ages 0 and 18 years, or participants of those ages were analyzed separately if older participants were included); 2) participants had a history of TBI; and 3) the study provided quantitative and/or qualitative information about pain (nonheadache pain or overall pain) whether from child or parent report. We included all study designs, including descriptive case studies, case series, cohort studies, case-control studies, and clinical trials. Pain could be measured using any method. Articles were excluded if they did not specifically examine pain in children after a TBI or only reported on headache pain. Studies were also excluded if they were not written in English. No restriction was imposed on sex, race, geographical residence, or source of population (e.g., community, hospital, registry, or health administrative data).

The primary outcomes of interest were pain characteristics reported in children at any time point before or after TBI. Preferably, the diagnosis of TBI was based on internationally recognized criteria, such as the World Health Organization Collaborating Center Task Force on Mild Traumatic Brain Injury,¹³ although studies using other methods (e.g., self-report) or local clinical judgment were also included.

Search strategy

The search for relevant publications included studies up to October 2016. The search strategy was developed using MeSH terms in MEDLINE (OvidSP), as well as relevant keywords. The terms “traumatic brain injury” or “concussion” or “brain injury” were exploded and searched in the title and/or abstract. The term “pain” was exploded, and “child” or other synonymous terms (e.g., adolescent, infant, and pediatrics) were searched in the title and/or abstract. In consultation with a librarian, the search strategy was adapted for use in other databases (EMBASE, PsycINFO, CINAHL, SportDiscus, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews). The full search strategy can be viewed in the Appendix.

Study selection

We selected studies in three stages (title screen, abstract screen, and full text screen) completed by two independent reviewers (V.K. and M.V.) based on the inclusion/exclusion criteria described above. Any disagreement was resolved between the two reviewers. Further, the citation lists of all included articles were scanned for any articles that may have been missed. The two reviewers (V.K. and M.V.) extracted data from included studies using a standardized data collection form. The level of the evidence was assessed using the “Levels of Evidence for Primary Research” for prognostic studies.¹⁴

Results

The search strategy yielded 1563 papers. The number was reduced to 450 and then 334 following the title screen and abstract screen, respectively. Full text reviews of the 334 studies further reduced the number to 109 (Fig. 1). Of the 109 studies published from the year 1806 to 2016 examining pain in children post-TBI,

only 14 (13%) reported on nonheadache pain or overall pain (pain anywhere in the body and not specifying the location of this pain). Almost half of these 14 studies ($n=6$; 43%) were descriptive case studies. The details of each study can be found in Table 1.

One study assessed pain intensity by body region (level 1), three studies measured pain using an overall score spanning the entire body (two level 1 and one level 3), three studies used a symptom questionnaire or checklist to assess specific types of pain such as neck pain (two level 2 and one level 3), and seven case studies relied on unspecified clinical assessment (seven level 4 evidence).

Pain rating by body region ($n=1$)

A cohort study of 144 adolescents between the ages of 0 and 17 years with TBI of all severities provided pain ratings using the Numerical Rating Scale-11 (anchors, 0=no pain; 10=worst pain imaginable).¹ Moderate pain was defined as a rating of 3 or higher out of 10. This definition was chosen because it is comparable to pain experienced by children immediately after major surgery.¹⁵ Results from this study showed that pain ratings in adolescents with mild TBI remained stable from 3 (55% reported significant pain) to 36 months (57.1% reported significant pain). Adolescents with moderate or severe TBI showed a significant increase in pain prevalence from 3 (36% reported significant pain) to 36 months (68% reported significant pain).

Persistent pain was defined as pain rated as ≥ 3 of 10 at all assessment time points (i.e., at enrollment and 3, 12, 24, and 36 months post-TBI). Among the participants, 24% ($n=35$) met the criteria for persistent pain. In this subgroup, sites of pain most commonly reported were the head (85.7%), back (42.9%), lower limb (11.4%), neck (8.6%), upper limb (5.7%), and stomach (2.9%). Among the persistent pain group ($n=20$), 57.1% of youth reported pain involving more than one anatomic region. To the best of our knowledge, this is the only study examining pain by location continuously over the long-term (e.g., >3 months) in youth post-TBI.

Overall pain rating ($n=3$)

Three studies examined overall pain. Two of the studies used the parent form of the Child Health Questionnaire (CHQ) to assess overall bodily pain (intensity and frequency).^{16,17} The CHQ assesses pain intensity (“During the past four weeks, how often has your child had bodily pain or discomfort?”) and pain frequency (“During the past four weeks, how often has your child had bodily pain or discomfort?”) on a scale from 1 to 6. Research has shown acceptable internal consistency, negligible floor and ceiling effects for the bodily pain subscale, convergent and discriminant validity, and equal item variance for the CHQ.¹⁸

In the study by Batailler and colleagues (2014), which included 127 children ages 0–16 with mild or moderate TBI, parents rated the recovery status of their child with five response options: “fully recovered,” “improved but not recovered,” “stabilized,” “deteriorated,” or “unknown.” Results showed that 77.5% of the children who had not fully recovered had bodily pain.¹⁶ Further, a significant correlation was found between the CHQ bodily pain subscale and recovery status ($r=0.482$; $p<0.001$) at 1 year post-injury. Recovery status correlated with the CHQ pain subscale more strongly than all other CHQ subscales (physical functioning, general health, mental health, social limitation, parental impact-time, parental impact-emotional, self-esteem, behavior, and family cohesion) but one (social-physical; $r=0.502$; $p<0.001$).¹⁶

In the other study using the CHQ, Brown and colleagues (2014) recoded the CHQ score into a transformed score ranging from 0 to

FIG. 1. Flow diagram of studies identified for possible inclusion. Source: from Moher D, Liberati A, Tetzlaff J, Altman DG; The PRISMA Group. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097. TBI, traumatic brain injury.

100, where lower scores indicate higher levels of pain (intensity and frequency) on the CHQ bodily pain or discomfort scale.¹⁷ Among 195 children ages 6–15 with mild, moderate, or severe TBI, mean ratings were 77.23 at 3 months, 80.01 at 6 months, and 83.92 at 18 months post-TBI. The researchers also analyzed the bodily pain scale score data using structural equation modeling to investigate the relationship between pain (CHQ pain subscale) and post-traumatic stress (Clinician Administered Posttraumatic Stress Disorder [PTSD] Scale for Children and Adolescents).¹⁹ The “Perpetual Avoidance Model,” where PTSD is theorized to facilitate the maintenance of pain, which, in turn, prolongs PTSD, fit the

data well (root mean square error of approximation=0.05 and $\chi^2_{(3)}=4.57$; $p=0.206$).

The other study of overall pain ratings utilized the Medical Outcomes Short Form (MOSF), which assesses pain intensity (“How much bodily pain have you had during the past 4 weeks?”) and pain-related impact (“During the past 4 weeks, how much did pain interfere with your normal work?”).²⁰ The adolescents rated their pain intensity on a scale from 1 (“none”) to 6 (“very severe”) and the impact of pain on functioning on a scale from 1 (“not at all”) to 5 (“extremely”). A bodily pain subscale score is then computed, ranging from 0 to 100, with a

TABLE 1. RESULTS OF PUBLISHED STUDIES (N=14) EVALUATING PAIN IN CHILDREN AFTER TRAUMATIC BRAIN INJURY, SORTED BY METHOD OF PAIN ASSESSMENT

Author, year, location	Study design	Case/control (n)	Case severity	Source of cases	Source of controls	Age of cases (years)	Sex of cases (M/F)	Time post-injury	Pain assessment method	Findings	Level of evidence ^a
Pain by body region (n=1) Tham and colleagues, 2013, USA	Prospective cohort	144/NA	Mild to severe TBI	10 Washington study hospitals and 1 hospital in Pennsylvania	NA	M=15.7; SD=±1.2	100/44	3, 12, 24, 36 months	4 questions about pain in the past week (child report): 1) Numerical rating scale, 0–10 2) Pain “other than a headache that bothered you” 3) If yes, identify where (8 options) 4) Numerical rating scale of the pain intensity in the other identified area(s)	Pain prevalence did not decline over the period from 3 months to 36 months after TBI. In the persistent pain subgroup, 57.1% endorsed pain involving more than 1 anatomic region. Adolescents with persistent pain had significantly higher levels of depressive symptoms, PTSD symptomatology, and poorer HRQOL compared to the infrequent pain subgroup ($p < 0.0001$).	1
Overall pain rating (n=3) Batailler and colleagues, 2014, France	Prospective cohort	127/1283 Selected out of 1283 persons in the database, but not analyzed as a control	Mild or moderate TBI (M-AIS) attributed to a road accident	Pediatric ESPARR cohort	Rhone registry	n=31 (age 0–5); n=87 (age 6–11); n=99 (age 12–16)	82/45	6 months and 1 year	Child Health Questionnaire (parents form)-50: bodily pain	Significant correlation between body pain and quality of life ($r=0.482$; $p < 0.001$) 77.5% of children who had not fully recovered by 1 year post-injury had body pain; 10.8% had body pain in the children who did recovery completely.	1
Brown, Kenardy and Dow, 2014, Australia	Prospective cohort	195/NA	Mild to severe TBI	3 Australian hospitals	NA	M=10.78; SD=±2.49 (range, 6–15 years)	137/59	3, 6, 18 months	Child Health Questionnaire (parent form): bodily pain	CHQ mean pain score (standardized) was 77.23 at 3 months, 80.01 at 6 months, and 83.92 at 18 months post-TBI. Structural equation modeling supports PTSD as driving pain. PTSD predicted pain, but only in the short term.	1
McLeod, Bay and Snyder, 2010, USA	Retrospective case-control	140/126 Football athletes with concussion matched to athletes without concussion	Mild TBI	5 local high schools in Arizona	5 local high schools in Arizona	Concussion group: M=15.0; SD=±1.3 Control group: M=14.6; SD=±1.2	266M	66.1% > 1 year, 19.1% within 1 year, 7% within the past 6 months, 6.1% within the past 3 months, and 1.4% within 1 month	Medical Outcomes Short Form-36 (child report):	The concussion group reported significantly lower mean scores/higher pain ($p < 0.001$) on the bodily pain (52.86 ± 6.9) compared to the control group (55.56 ± 7.3), with an effect size of 0.35.	3
Symptom questionnaire (n=3) Haran and colleagues, 2016, Australia	Prospective cohort	93/NA	Mild TBI	Emergency department at The Royal Children's Hospital Melbourne	NA	M=12.7; SD=±0.27	77/16	Not specified but average follow-up at 32 (± 5.2) days after initial ED visit	Follow-up phone call assessing post-concussive symptoms. The exact questionnaire for assessing “Concussive signs and symptoms” is not specified, but is said to be adapted from validated measures. Not specified whether child or parent report	85 children completed follow-up; 65 children experienced post-concussive symptoms; fatigue (57.6%), headache (56.5%), and neck pain (25.9%) were the top three main symptoms.	2

(continued)

TABLE 1. (CONTINUED)

Author, year, location	Study design	Case/control (n)	Case severity	Source of cases	Source of controls	Age of cases (years)	Sex of cases (M/F)	Time post-injury	Pain assessment method	Findings	Level of evidence ^a
Heyer and colleagues, 2016, USA	Retrospective cohort	1953/NA	Mild TBI	Pediatric Sports Medicine Clinic	NA	M = 14.1; SD = ±2.09	1229/724 (M/F)	Median 9 days, range 1–30 days	Symptom questionnaire (includes headache and neck pain) adapted from other sources (not present) to 6 (severe) Child report	Neck pain reported by 37.1% of the sample, with a mean score of 0.86, and a related headache probability of 0.89. Principal component analysis found strong correlations for a “cephalic” component consisting of neck pain, headache, nausea, photophobia, phonophobia, and dizziness.	2
Necajauskaite and colleagues, 2005, Europe	Retrospective case-control	102/102 Matched to other mild body injury	Mild TBI	Kaunas University of Medicine Hospital and Kaunas Red Cross Hospital	Kaunas University of Medicine Hospital and Kaunas Red Cross Hospital	M = 11; SD = ±3.1	74/28 (M/F)	Median = 27 months and not shorter than 1 year	Standardized questionnaire of previous (year before inquiry) and present (last month before inquiry) health status and symptoms concomitant to headaches and dizziness Parent report	6 children with mild TBI (9.4%) reported pain felt with headache in other body sites. This was higher than the control group of children with other mild body injury without head trauma ($n = 4$, 8%), although not significant ($p > 0.05$).	3
Unspecified clinical assessment (e.g., based on patient report or physical exam; $n = 7$)											
Ellis and McDonald, 2015, Canada	Case study	1/NA	Not specified	Pan Am Clinic/Concussion Program	NA	13 years old	1 M	2 days, 2 weeks, 6 weeks, 2 months	Unclear. Patient endorsement	3 days post-injury, patient endorsed headache and neck pain. Full and painless range of motion achieved. Cleared for return to sports at 2 months. Diagnosis was coexistent sports-related concussion and cervical spinal cord injury without radiographic abnormality.	4
Kwon and Jang, 2014, Korea	Case study	1/NA	Mild TBI	Yeungnam University	NA	14 years old	1 F	Initial, 29 days, 2 months, 10 weeks	Not specified, patient report	Patient involved in car accident, began to suffer posterior neck pain and back pain radiating to the right leg. Neurological examination at 10 weeks post-injury revealed quadriparesis and memory impairment. Diffusion tensor tractography showed discontinuation of both corticoreticular pathways at the midbrain level.	4
Lim and colleagues, 2007, UK-raine	Case study	1/NA	Severe TBI	Department of Pediatric Neurosurgery, Republic Crimea Children Clinical Hospital	NA	5 years old	1 M	2 weeks	Patient history examination; clinical assessment	Patient had mandibular fractures and underwent Maxillo-mandibular surgery with a Kirschner's knitting needle. After the surgery, the patient reported throbbing generalized headache, abrupt pain on his face and jaw, which was described as a burning and stabbing sensation. Radiologic films showed that Kirschner's knitting needle mobilized from the extracranial cavity into the middle cranial cavity, resulting in iatrogenic TBI.	4

(continued)

TABLE 1. (CONTINUED)

<i>Author, year, location</i>	<i>Study design</i>	<i>Case/control (n)</i>	<i>Case severity</i>	<i>Source of cases</i>	<i>Source of controls</i>	<i>Age of cases (years)</i>	<i>Sex of cases (M/F)</i>	<i>Time post-injury</i>	<i>Pain assessment method</i>	<i>Findings</i>	<i>Level of evidence^a</i>
Litt, 1995, USA	Case study	1/NA	Not specified. GCS score of 5 at 17 days post-collision	Columbus State Community College	NA	16 years old	1 M	Findings approx. 17 days after the first TBI and on the same day as the second TBI	Physical examination	The patient complained of left elbow pain, dizziness, and headache with vomiting, pallor, and unresponsiveness shortly after. CT scan showed an acute right-sided subdural hematoma with a midline shift.	4
Logan and colleagues, 2001, USA	Case study	1/NA	Not specified. GCS score of 15 upon arrival at ED	University of Illinois; Carle Sports Medicine	NA	18 years old	1 M	Initial assessment, 24 h, 1 week, 12 days, 1 month post-injury	Clinical exam; patient report	12 days post-TBI, patient complained of nocturnal neck pain. Clinical exam revealed an area of tenderness beneath the left occipital protuberance. Pain increased when patient turned his head to the right. One month later, the nocturnal neck pain from the cervical ligament sprain had ceased.	4
Meoded and colleagues, 2011, USA	Retrospective cohort (n=5)	10/NA	Mild to severe TBI	Johns Hopkins Hospital, Baltimore, Maryland	NA	M=7.18; SD=±4.37	4/6	Not specified	Clinical assessment on admission	A 6-year-old female with GCS=15 presented with cervical pain. MRI showed retroclival epidural hematoma, and associated tectorial membrane disruption, and minor compression of the brainstem; 5 other patients in the cohort had "minor pain."	4
Zaremski and colleagues, 2015, USA	Case study	1	"Concussion"	Sports Medicine Clinic	NA	17 years old	0/1	Continuous follow-up	Physical examination and patient report	Patient developed neck pain 5 weeks after concussion and showed a positive Tinel sign at the left craniocervical junction. Interventional pain management (e.g., greater occipital nerve [ON], lesser ON, and third ON block) relieved the pain, but the procedures needed to be repeated and managed long term.	4

^aLevel of evidence was assessed using "Levels of Evidence for Primary Research Question (prognostic studies)" by the Center for Evidence-Based Medicine (Oxford, UK). The scores range from 1 to 5, where a higher score indicates a weaker/lower level of evidence. Level 1 corresponds to high-quality prospective studies with sufficiently high follow-up rate (≥70%); level 2 for retrospective studies of lower quality or lesser-quality prospective studies; level 3 for case-control studies; and level 4 for case studies (Howick and colleagues, 2011). Level 5 is expert opinion, which was not encompassed by the reviewed studies.

NA, not applicable; TBI, traumatic brain injury; M-AIS, Maximum Abbreviated Injury Scale; GCS, Glasgow Coma Scale; ED, emergency department; M, mean; SD, standard deviation; M/F, male/female; approx., approximately; PTSD, post-traumatic stress disorder; HRQOL, health-related quality of life; CHQ, Child Health Questionnaire; CT, computed tomography; MRI, magnetic resonance imaging.

lower score indicating lower health-related quality of life. The psychometric properties of the MOSF-36 have revealed strong convergent validity in the bodily pain scale with physical-health factorial tests as expected.²¹ McLeod and colleagues (2010) found that in 140 high school athletes (age range not reported), those with a history of concussion reported a significantly lower score (higher pain intensity and pain-related impact) than those without a history of concussion (52.86 ± 6.9 in concussion group and 55.56 ± 7.3 in control group; $p < 0.001$), with a medium effect size of $d = 0.35$.²⁰

Symptom questionnaire (n = 3)

Three studies used nonstandardized or unreferenced symptom checklists or questionnaires to assess various symptoms of pain.^{22–24} The psychometric properties of these questionnaires were not reported. The questionnaires included neck pain as a possible symptom, in addition to headache, similar to other standardized concussion assessment tools (e.g., symptom checklist included in the Sport Concussion Assessment Tool).²⁵ Most other symptom questionnaires used in TBI only assesses headache pain (e.g., Post-concussive Symptoms Scale,²⁶ Post-Concussive Symptom Inventory,²⁷ and Health and Behavior Inventory)²⁸ and not pain in other anatomic regions.

Two studies reported on neck pain after mild TBI within the first month of injury. Haran and colleagues (2016) reported neck pain in 25.9% of 93 children between the ages of 5 and 18 years approximately 1 month after mild TBI (parent or child report not specified),²² and Heyer and colleagues (2016) reported child endorsement of neck pain in 37.1% of 1953 children ages 6–22 at a median of 9 days after mild TBI.²³ This rate of neck pain (25.9% to 37.1%) is higher than the rate (1.8% to 8.6%) reported by Tham and colleagues (2013) at 36 months post-TBI (all injury severities)¹; the difference may be attributed to the timing of assessment of pain, as well as the source of participants (prospective emergency department vs. clinic-based).

Studies using symptom questionnaires also provided information about how symptoms cluster together. Heyer and colleagues (2016) found that six symptoms (neck pain, headache, sensitivity to light, sensitivity to noise, nausea, and dizziness) loaded onto a “cephalic” component.²³ When neck pain was present, the probability of headache was 0.89 (lower probability than most of the other post-concussion symptoms evaluated). When a subcohort of patients with pre-morbid headaches were analyzed, neck pain no longer loaded onto the cephalic component. Instead, neck pain clustered with a “somatic” (rather than emotional or cognitive) component along with numbness in extremities and weakness in extremities.²³ Necajauskaite and colleagues (2005) also examined symptom clusters. Headache was associated with pain in other body sites in 9.4% ($n = 6$) of the mild TBI group and 8% ($n = 4$) of the matched control group (without head trauma).²⁴

Unspecified pain assessment (n = 7)

Many of the case studies described pain (along with other clinical features) as a sign of more serious central nervous system or cranial injury. For example, a case of an individual with neck pain was posited to be related to spinal cord injury, although no radiographic abnormality was detected.²⁹ In other cases, neck and back pain radiating to the right leg presented with impairments in the corticoreticular pathways³⁰; jaw and face pain was related to dislocation of a neurosurgical needle leading to iatrogenic TBI,³¹ and nocturnal neck pain was related to cervical ligament sprain.³²

Discussion

To our knowledge, this is the first scoping review on non-headache and overall pain in children post-TBI. Of studies that examined pain post-TBI, 95 of 109 (87%) reported on headache pain, but not on any other types of pain. Among the 14 included studies that reported on nonheadache pain, half were case studies (7 of 14; 50%). The level of evidence was generally low, with few high-quality prospective studies. Overall, three main findings are supported by this review: 1) Despite emerging evidence that non-head pain is common in children post-TBI,¹ few studies ($n = 7$) have been published on nonheadache or overall pain; 2) the assessment of pain in the TBI literature is problematic; and 3) how pain is assessed in children post-TBI needs improvement given research showing that pain is linked to worse recovery, poorer quality of life, and can be long-lasting.^{1,2,16,17,20} Thus, more rigorous examination of nonheadache pain and its role in impeding recovery in children post-TBI is imperative.

The neural mechanisms for nonheadache pain in children are not clearly understood, although some insights are available from research on adult TBI. A study of 15 adult patients post-TBI with chronic pain noted interesting features. These included: pain that tended to be unilateral/nonsymmetric, delayed development of pain (average = 6.6 months), reduced threshold for sensation of thermal and tactile stimulation, allodynia (normally nonpainful stimulation leading to pain), and hyperpathia (abnormally elevated levels of pain).³³ Interestingly, touch and graphesthesia remained intact, as compared to pain-free patients post-TBI and healthy controls. These findings suggest selective damage to the pain and temperature systems underlying the development of central pain in TBI patients.³³ This is supported by a recent diffusion tensor tractography study of the spinothalamic tract, which found decreased fractional anisotropy, increased mean diffusivity, and a lower tract volume in a mild TBI group presenting with neuropathic pain (must have developed after the TBI) as compared to two control groups (mild TBI without pain and healthy controls).¹¹

Concurrent orthopedic injuries likely also play a role. Heterotopic ossification (i.e., presence of bone in soft tissue where bone does not normally exist), neuromuscular spasticity, peripheral nerve injuries, and fractures have been reported in adults post-TBI. An estimated 21–50% of individuals with a TBI also have concurrent orthopedic injuries, thus pain attributed to orthopedic injuries may be present in TBI patients.^{34–36} Unfortunately, of the seven cohort studies, only one study by Necajauskaite and colleagues (2005) clearly differentiated isolated TBI from injuries to other parts of the body and no TBI.²⁴ All other studies did not clearly state whether concurrent orthopedic injuries were also present in their sample.

Measurement issues

In studies investigating pain in children post-TBI, numerous measurement issues are evident. These include a lack of systematic assessment of pain in different parts of the body, reliance on parental report of pain in young children who are capable of providing self-report (i.e., after 4 years of age), and the use of symptom rating scales that have not yet been shown to be reliable or valid in youth post-TBI.

The diversity of commonly painful locations post-TBI (headache, back, lower limb, neck, upper limb, and stomach)¹ are not reflected by many rating scales routinely administered in the pediatric TBI population. Most symptom rating scales assess headache pain only (e.g., Post-concussive Symptoms Scale,³⁷ Post-Concussive Symptom Inventory,³⁸ and the Health and Behavior

Inventory).²⁸ Although overall pain ratings are simpler, they do not allow for a fine-grained understanding of what types of pain are contributing to the overall score. This point is not trivial. Research shows that individuals with chronic generalized or widespread pain differ significantly from those with located/localized pain. Multiple pain sites imply higher pain intensity, longer pain duration, and reduced working capacity (i.e., more sick leave).³⁹ Thus, the assessment of pain using an overall measure is problematic because it omits important information about pain localization, which is likely to be highly relevant to recovery post-TBI.

The two studies reviewed that included children <8 years of age^{16, 17} relied on parent ratings rather than validated child pain assessment tools (e.g., Faces Pain Scale Revised for children ≥4 years).⁴⁰ Other simplified tools have been recently developed to facilitate self-report in young children.⁴¹ Previous research has found that parents can misperceive their child's pain and may overestimate or underestimate their child's pain experience.⁴² Thus, although little is known about pain after childhood TBI, this is especially true for young children <8 years of age.

In studies using symptom-rating scales, many of the scales used were not standardized, not referenced, and not included as supplementary material. The scales were described rather vaguely as: "Concussive signs and symptoms"; "Symptom questionnaire"; and "Standardized questionnaire of previous and present health status." Thus, it is unclear as to what exactly is being assessed in these scales, and whether all items were reported.

Recommendations for pain assessment

We believe that thorough pain assessment should encompass: 1) pain intensity, 2) pain duration and frequency, 3) pain location, and 4) impact of pain on functioning. Prospective assessment of pain intensity is ideal (e.g., The Headache Diary and The Pain Diary)^{43,44} to minimize recall bias. The Pain Questionnaire is frequently used in chronic pain studies and assesses pain frequency, location, duration, intensity, emotional distress, and interference.⁴⁵ Two other pain assessment questionnaires frequently used in chronic pain literature are the Abu-Saad Pediatric Pain Assessment Tool (PPAT)⁴⁶ and the Varni/Thompson Pediatric Pain Questionnaire (PPQ).⁴⁷ The PPAT assesses multiple aspects of pain (e.g., triggers, medication, descriptors of pain qualities, present pain, and worse pain).⁴⁶ The PPQ measures pain intensity, location, and the sensory, evaluative, and affective qualities of pain.⁴⁷ Both are well-established pain instruments.⁴⁸ The Patient-Reported Outcomes Measurement Information System also recently developed a new Pediatric Pain Interference Scale, which assesses the impact of pain on daily activities over the past week.⁴⁹

Response bias is important to consider as part of assessment and score interpretation. Young children, especially <5 years of age, tend to use the bottom and top extremes of scales rather than rate in the middle.⁵⁰ Whenever possible, steps should be taken to mitigate response biases. Overall, pain assessment can be strengthened through: using multiple methods, obtaining data from multiple informants, and assessing multiple dimensions of pain (intensity, affective reaction, cognitive appraisal, sensory qualities, impairment, location, etc.). We recommend choosing age-appropriate and validated tools⁵¹ and interpreting ratings by children <5 years of age with caution (e.g., for research, results could be analyzed with and without ratings from participants <5 years of age). The anchors in any given scale may be a major influence on a child's pain rating and should be taken into consideration for score interpretation. Scales with lower anchors depicting a neutral face prompt lower pain ratings than scales with

lower anchors depicting a smiling face.⁵² In addition, it is advisable to complement self-report ratings with observational measures (e.g., Face Legs Activity Cry and Consolability scale⁵³) and to consider the context for pain assessment (i.e., a child's motivation and expectations—do they think a high pain rating will result in more time away from school and sports?). When a child's ability to use a pain scale is unclear, offering the child a chance to practice using the scale for painful and nonpainful hypothetical situations (e.g., opening a birthday present vs. stepping on a sharp nail) may be helpful.^{50,54} Obtaining scores from multiple informants (e.g., child, parent, and clinician) makes it possible to observe, discuss, and resolve any discrepancies that may arise across the scores.^{54, 55}

Future research on pain in traumatic brain injury

This review highlights important avenues for future research on pain and TBI in the pediatric population. Future research should explore whether different aspects of recovery post-TBI differ depending on whether children experience only headache pain as compared to nonheadache pain, or pain in multiple locations. This is supported by past research that found noncephalic pain to be a risk factor for the onset of chronic and persistent migraine.² Other research shows that recurrent complaints of pain in children were associated with chronic health problems, frequent change of residence, poor school performance, frequent television watching, and rarely playing with other children.⁵⁶ In a general population of 6636 Dutch children between the ages of 0 and 18 years, multiple pains were common (endorsed by half of respondents who experienced pain) and also related to higher pain intensity.⁵⁷

Longitudinal research to study changes in pain, pre- and post-injury, should be prioritized. Mounting evidence suggests that headache post-TBI often involves a continuation or exacerbation of pre-existing headache. Among children who experienced chronic headaches after mild TBI, 47% had a previous history of migraines and 82% either had a pre-existing headache disorder or a family history of migraine.⁵⁸ It is unknown whether non-headache pain, or pain in multiple locations, is also likely to have pre-existed the TBI.

Future research with orthopedic injury controls and chronic pain controls (e.g., with no TBI history) will enhance TBI studies. We do not currently know whether individuals that have the same type of pain (e.g., shoulder), but from different injury mechanisms (e.g., TBI vs. orthopedic injury), are impacted equally. Based on ongoing work by the authors, however, the impact of pain may differ in these populations. In a large prospective study of children after mild TBI or orthopedic injury recruited from the emergency department, preliminary analyses showed that higher pain ratings were more strongly related to post-concussive symptoms in children after mild TBI than in children following mild orthopedic injury.⁵⁹

The study of psychosocial factors is also essential for understanding how acute pain transitions into chronic pain post-TBI. This is supported by findings in childhood TBI showing that PTSD symptoms facilitate continued pain.¹⁷ Pain catastrophizing in children and adolescents has been found to be a strong predictor of pain-related disability, over and above characteristics of pain.⁶⁰ Research has also shown that maternal catastrophizing is significantly related to the child's pain intensity.⁶¹ Thus psychosocial factors, including internalizing behaviors and parent's response to their child's pain, may drive the interference and chronicity of symptoms and are therefore an important area for future research in pediatric TBI.

Limitations

Half of our included articles were case studies, which may not necessarily generalize to the wider population. Although the focus of the review is on nonheadache pain, we included studies assessing overall pain, where pain attributed to headaches can be expected to contribute to the rating.

Conclusion

Pain left untreated post-TBI may have negative and long-lasting consequences on pain sensitivity, immune functioning, neurophysiology, attitudes, and healthcare behavior. Findings of this scoping review suggest that nonheadache pain is present in youth post-TBI and is linked to poorer recovery and outcomes. Yet, we found almost no studies that assessed pain comprehensively in terms of intensity, location, frequency, and interference with the child's daily functioning post-TBI. Future research examining how different profiles of pain are related to other outcomes has the potential to improve the care and management of children with TBI.

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APPENDIX

MEDLINE/OvidSP (1946 to present; 667 results)

1. exp brain injuries/

2. brain injur*.mp.

3. exp brain concussion/

4. concuss*.mp.

5. exp post-concussion syndrome/

6. post-concuss*.mp.

7. postconcuss*.mp.

8. exp pain/

9. pain*.mp.

10. exp Headache Disorders/ or exp Headache/ or exp Post-Traumatic Headache/

11. headache*.mp.

12. exp Migraine Disorders/

13. migraine*.mp.

14. exp child/

15. child*.mp.
16. exp adolescent/
17. adolescen*.mp.
18. exp infant/
19. infant*.mp.
20. exp pediatrics/
21. pediatric*.mp.
22. paediatric*.mp.
23. exp child, preschool/
24. preschool*.mp.
25. toddler*.mp.
26. youth*.mp.
27. teen*.mp.
28. TBI*.mp.
29. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 28
30. 8 or 9 or 10 or 11 or 12 or 13
31. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
32. 29 and 30 and 31
33. remove duplicates from 32
34. limit 33 to english language

EMBASE/OvidSP (1974 to June 2016; 1611 vs 8403 prior limit)

1. exp brain injuries/
2. brain injur*.mp.
3. exp brain concussion/
4. concuss*.mp.
5. exp post-concussion syndrome/
6. post-concuss*.mp.
7. postconcuss*.mp.
8. exp pain/
9. pain*.mp.
10. exp Headache Disorders/ or exp Headache/ or exp Post-Traumatic Headache/
11. headache*.mp.
12. exp Migraine Disorders/
13. migraine*.mp.
14. exp child/
15. child*.mp.
16. exp adolescent/
17. adolescen*.mp.
18. exp infant/
19. infant*.mp.
20. exp pediatrics/
21. pediatric*.mp.
22. paediatric*.mp.
23. exp child, preschool/
24. preschool*.mp.
25. toddler*.mp.
26. youth*.mp.
27. teen*.mp.
28. TBI*.mp.
29. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 28
30. 8 or 9 or 10 or 11 or 12 or 13
31. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
32. 29 and 30 and 31
33. remove duplicates from 32
34. limit 33 to english language

PsycINFO/OvidSP (1806 to June 2016; 171 vs 1299)

1. exp traumatic brain injury/
2. traumatic brain injur*.mp.

3. exp brain concussion/
4. concuss*.mp.
5. post-concuss*.mp.
6. postconcuss*.mp.
7. TBI*.mp.
8. exp pain/
9. pain*.mp.
10. exp MIGRAINE HEADACHE/ or exp HEADACHE/
11. headache*.mp.
12. migraine*.mp.
13. child*.mp.
14. adolescen*.mp.
15. infant*.mp.
16. exp pediatrics/
17. pediatric*.mp.
18. paediatric*.mp.
19. exp preschool students/
20. preschool*.mp.
21. toddler*.mp.
22. youth*.mp.
23. teen*.mp.
24. 1 or 2 or 3 or 4 or 5 or 6 or 7
25. 8 or 9 or 10 or 11 or 12
26. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
27. 24 and 25 and 26
28. remove duplicates from 27
29. limit 28 to english language

CINAHL/EBSCO (1937 to June 2016; 282 vs 1010)

- S32 S29 AND S30 AND S31
- S31 S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27
- S30 S8 OR S9 OR S10 OR S11 OR S12 OR S13
- S29 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S28
- S28 TBI*
- S27 teen*
- S26 youth*
- S25 toddler*
- S24 preschool*
- S23 (MH "Child, Preschool")
- S22 paediatric*
- S21 pediatric*
- S20 (MH "Pediatrics+")
- S19 infant*
- S18 (MH "Infant+")
- S17 adolescen*
- S16 (MH "Adolescence+")
- S15 child*
- S14 (MH "Child+")
- S13 migraine*
- S12 (MH "Migraine")
- S11 headache*
- S10 (MH "Headache+")
- S9 pain*
- S8 (MH "Pain+")
- S7 postconcuss*
- S6 post-concuss*
- S5 (MH "Postconcussion Syndrome")
- S4 concuss*
- S3 (MH "Brain Concussion+")
- S2 "brain injur*"
- S1 (MH "Brain Injuries+")

SportDiscus/EBSCO (1985 to June 2016; 89 vs 614)

S39 AND S40 AND S41 Search modes - Find all my search terms

S41 S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37

S40 S26 OR S27 OR S28

S39 S22 OR S23 OR S24 OR S25 OR S38

S38 TBI*

S37 teen*

S36 youth

S35 toddler*

S34 preschool*

S33 paediatric*

S32 pediatric*

S31 infant*

S30 adolescen*

S29 child*

S28 migraine*

S27 headache*

S26 pain*

S25 post-concuss*

S24 postconcuss*

S23 concuss*

S22 "traumatic brain injur**"

S21 S18 AND S19 AND S20

S20 S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16

S19 S5 OR S6 OR S7

S18 S1 OR S2 OR S3 OR S4 OR S17

S17 TBI*

S16 teen*

S15 youth

S14 toddler*

S13 preschool*

S12 paediatric*

S11 pediatric*

S10 infant*

S9 adolescen*

S8 child*

S7 migraine*

S6 headache*

S5 pain*

S4 post-concuss*

S3 postconcuss*

S2 concuss*

S1 "traumatic brain injur**"

Cochrane Central Register of Controlled Trials/OvidSP (Dates? 47 vs 121)

1. exp Brain Injuries/

2. exp Brain Concussion/

3. exp Post-Concussion Syndrome/

4. brain injur*.mp.

5. concuss*.mp.

6. postconcuss*.mp.

7. post-concuss*.mp.

8. exp Pain/

9. exp Post-Traumatic Headache/ or exp Headache/ or exp Tension-Type Headache/

10. exp Migraine Disorders/

11. pain*.mp.

12. headache*.mp.

13. migraine*.mp.

14. exp Child/

15. exp Adolescent/

16. exp Infant/

17. exp Pediatrics/

18. exp Child, Preschool/

19. child*.mp.

20. adolescen*.mp.

21. infant*.mp.

22. pediatric*.mp.

23. paediatric*.mp.

24. preschool*.mp.

25. youth.mp.

26. teen*.mp.

27. toddler*.mp.

28. TBI*.mp.

29. 28 or 1 or 2 or 3 or 4 or 5 or 6 or 7

30. 8 or 9 or 10 or 11 or 12 or 13

31. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27

32. 29 and 30 and 31

33. remove duplicates from 32

34. limit 33 to english language

Cochrane Database of Systematic Reviews/OvidSP (Dates? 67 vs 118)

1. concuss*.mp.

2. postconcuss*.mp.

3. post-concuss*.mp.

4. pain*.mp.

5. headache*.mp.

6. migraine*.mp.

7. child*.mp.

8. adolescen*.mp.

9. infant*.mp.

10. pediatric*.mp.

11. paediatric*.mp.

12. preschool*.mp.

13. youth.mp.

14. teen*.mp.

15. toddler*.mp.

16. traumatic brain injur*.mp.

17. TBI*.mp.

18. 1 or 2 or 3 or 16 or 17

19. 4 or 5 or 6

20. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15

21. 18 and 19 and 20

22. remove duplicates from 21