



Published in final edited form as:

*J Pain*. 2013 October ; 14(10): 1242–1249. doi:10.1016/j.jpain.2013.05.007.

## Persistent Pain in Adolescents Following Traumatic Brain Injury

See Wan Tham<sup>\*</sup>, Tonya M. Palermo<sup>\*†</sup>, Jin Wang<sup>‡</sup>, Kenneth M. Jaffe<sup>§</sup>, Nancy Temkin<sup>¶,||</sup>, Dennis Durbin<sup>#</sup>, and Frederick P. Rivara<sup>†,‡</sup>

<sup>\*</sup>Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, Washington

<sup>†</sup>Department of Pediatrics, University of Washington, Seattle, Washington

<sup>§</sup>Department of Rehabilitation Medicine, University of Washington, Seattle, Washington

<sup>||</sup>Department of Neurological Surgery, University of Washington, Seattle, Washington

<sup>‡</sup>Harborview Injury Prevention and Research Center, University of Washington, Seattle, Washington

<sup>¶</sup>Department of Biostatistics, University of Washington School of Public Health, Seattle, Washington

<sup>#</sup>Department of Emergency Medicine, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

### Abstract

Traumatic brain injury (TBI) is a leading cause of pediatric disability. Although persistent pain has been recognized as a significant postinjury complication, there is a paucity of data concerning the postinjury pain experience of youth. This study aimed to examine the prevalence of persistent pain in adolescents after TBI, identify risk factors for pain, and evaluate the impact of pain on adolescent health-related quality of life. Participants included 144 adolescents with mild to severe TBI who were followed over 36 months after injury. At 3-, 12-, 24-, and 36-month assessments, measures of pain intensity, depression, posttraumatic stress disorder, and health-related quality of life were completed by adolescents. Findings demonstrated that 24.3% of adolescents reported persistent pain (defined as usual pain intensity  $\geq 3/10$ ) at all assessment points after TBI. Female sex (odds ratio = 2.73, 95% confidence interval = 1.12–6.63) and higher levels of depressive symptoms at 3 months after injury (odds ratio = 1.26, 95% confidence interval = 1.12–1.43) were predictors of persistent pain at 36 months. Furthermore, mixed linear models indicated that early pain experience at 3 months following TBI was associated with a significantly poorer long-term health-related quality of life.

© 2013 by the American Pain Society

Address reprint requests to See Wan Tham, MBBS, Seattle Children's Research Institute, M/S-CW8-6, PO Box 5371, Seattle, WA 98145-5005. see.tham@seattlechildrens.org.

Part of this research was presented in Abstract form at the 31st American Scientific Meeting of the American Pain Society, Honolulu, Hawaii, May 16–19, 2012. Tham S, Palermo T, Jimenez N, Wang J, Vavilala M, Rivara F: Persistent pain following traumatic brain injury in a pediatric population. *J Pain* 13:S22, 2012.

The authors have no financial or other relationships that would lead to a conflict of interest.

**Perspective**—This is the first study to examine the prevalence of persistent pain over long-term follow-up in adolescents after TBI and its impact on health-related quality of life. These findings indicate that adolescents with TBI may benefit from timely evaluation and intervention to minimize the development and impact of pain.

### Keywords

Traumatic brain injury; adolescents; pain; longitudinal study; health-related quality of life

Traumatic brain injury (TBI) is a significant pediatric public health issue. The Centers for Disease Control and Prevention (CDC) estimates that 697,347 pediatric TBIs occur annually. Rates of TBI-related hospitalizations and deaths are higher in children than in adults.<sup>17</sup> Epidemiologic studies suggest that 31.6% of the population by 25 years of age has experienced at least 1 TBI requiring medical attention.<sup>13</sup> Approximately 25% of all pediatric TBIs occur during adolescence, with the most common causes including falls, motor vehicle crashes, and sports-related injuries.<sup>17</sup> Adolescence is a crucial developmental period, when an injurious event may contribute to the development of longer-term functional impairment. The most commonly identified comorbidities of TBI include neurocognitive dysfunction, physical impairment, and neurobehavioral disturbances.<sup>2,18,19</sup> Only recently has chronic and persistent pain been recognized as a complication after TBI. Research in the adult literature suggests that 22 to 95% of adults with TBI experience chronic pain after injury.<sup>4,24,26,32,39,50</sup> To date, there has been little research devoted to understanding the development of pain in pediatric TBI populations. In view of the high cumulative incidence of TBI during adolescence, there may be a sizable population who proceed to young adulthood with repercussions of chronic and persistent pain following a TBI.

Despite the significant numbers of children who experience head injuries, the prevalence of persistent pain in children and adolescents following TBI remains unknown. Several pediatric studies have examined headache pain in children after TBI and found a widely ranging prevalence of 8 to 71.5% up to 2 years after injury.<sup>6,7</sup> In the 2 studies that used longitudinal designs, there was a decline in children's headaches over time.<sup>30,33</sup> However, these studies focused only on headaches as a source of pain, used varying definitions of pain, and were limited by short-term follow-up assessment points and lack of assessment of the impact of pain.

Several risk factors have been reported in the development of chronic pain in otherwise healthy youth including older age, female sex, and depressive symptoms.<sup>10,15,27,28</sup> Only 1 study has reported risk factors in children and adolescents with TBI; Blume and colleagues found that older females reported a higher prevalence of severe headaches.<sup>7</sup> Apart from pain prevalence, the impact of pain on youth is important to evaluate in order to identify clinical needs of the population.

Research has documented that a subset of children and adolescents with chronic pain show decreased activity participation, high rates of school absenteeism, and poor health-related quality of life (HRQOL).<sup>22,25,35</sup> Although there are no studies evaluating the impact of pain after TBI in youth, it would be expected that pain that persists over time might impede recovery progress and compromise optimal daily functioning. The aims of this study were to

examine the prevalence of persistent pain over 36 months in adolescents following TBI, identify risk factors for pain over this interval (age, sex, severity of TBI, depressive symptoms), and examine the longitudinal association of persistent pain with long-term HRQOL.

## Methods

The study was approved by the institutional review boards of all the participating institutions. Secondary data analysis was conducted from the Child Health After Injury<sup>46</sup> study, a multicenter longitudinal study designed to assess disability in children during the 3 years after TBI. Data pertaining to the prevalence of headaches at 12 months after TBI have been published,<sup>7</sup> but this is the first report to examine pain complaints more broadly in the adolescent sample.

### Participants and Study Design

Details concerning recruitment and study design can be found in Rivara and colleagues.<sup>45</sup> In brief, between March 1, 2007, and September 30, 2008, children and adolescents who were eligible for the Child Health After Injury study were identified after admission to 1 of 10 hospitals in the Pacific Northwest and 1 hospital in the mid-Atlantic. From a computer-generated list of 2,940 eligible participants, 2,179 were randomly selected. Families were initially approached either in person or by letter and followed up with a telephone call. The final sample was composed of 729 children ages birth to 17 years who fulfilled the eligibility criteria and were interested in participation. Reasons for exclusion were inability to establish contact, refusals, or that the children and adolescents did not have the injury in question during the screening procedures. Compared to the sample that was selected but not enrolled, the final sample did not differ by age (109.7 months vs 106.3 months;  $P = .41$ ) or sex (34.3 vs 35%;  $P = .83$ ) but was more likely to have moderate or severe TBI (13.5 vs 2.5%;  $P = .001$ ) and less likely to have been seen at lower-level trauma centers (20.6 vs 36.7%;  $P < .0001$ ).<sup>45</sup>

Parents or caregivers provided written consent for the study, and adolescents provided assent. Assessments were conducted at enrollment and at 3, 12, 24, and 36 months after TBI. One parent and the adolescent (if 14 years or older) completed a battery of questionnaire measures on pain, depressive symptoms, posttraumatic stress disorder symptoms, and HRQOL by mail or via phone interview. For the purpose of this study, only data for adolescents who were 14 years or older obtained via self-report on questionnaires were included for analyses (total sample available = 188 youth). Of the 188 adolescents, 144 completed all the assessments over 36 months. In comparing the 144 adolescents to the sample of adolescents who did not ( $n = 44$ ), there were no significant differences by sex, severity of TBI, or household income. Adolescents who completed all assessments were more likely to be younger (mean = 15.7 years vs mean = 16.1 years,  $P = .03$ ) and Caucasian (70.8 vs 50%,  $P = .05$ ) and to have private insurance (79.2 vs 56.8%,  $P = .01$ ).

## Measures

**Demographics**—Questionnaires on demographics (age, sex, ethnicity, race), medical history, and socioeconomic status were completed by parents or guardians on enrollment.

**Pain Assessment**—Adolescents were asked 4 questions about pain. They were asked to rate the intensity of headache pain in the past week on an 11-point numerical rating scale (NRS), where 0 is no pain and 10 is worst pain imaginable. Following that, they were also asked to document other locations of pain with a question about whether there was pain “other than a headache that bothered” them. If the answer was yes, the follow-up question asked adolescents to identify the area of the body that bothered the adolescent the most. The 8 response options included the back, neck, face, chest, stomach, upper limbs (shoulder, arm, wrist, hand, or fingers), lower limbs (hips, knee, thigh, leg, ankle, foot, or toes), and an option to state an anatomic region that was not provided. Pain intensity for this anatomic region was then rated using an 11-point NRS based on the experience in the past week. The NRS has been validated for use in the pediatric population.<sup>53</sup>

For the purpose of this report, adolescents were identified as having persistent pain over the duration of 36 months if pain intensity was rated at 3/10 or more at every follow-up assessment point (3, 12, 24, and 36 months) after TBI. Research supports that a pain intensity rating of 3 or more has been associated with moderate pain and comparable to pain immediately after major surgery in children.<sup>11,14,52</sup> The adolescents who did not meet criteria for persistent pain were identified as an infrequent pain group.

**Depressive Symptoms**—Depressive symptoms were assessed using the Patient Health Questionnaire–9 depression module.<sup>31</sup> The Patient Health Questionnaire–9 includes 9 items representing diagnostic criteria for depression in the *Diagnostic and Statistical Manual of Mental Disorders, 4th ed, text revision*.<sup>1</sup> Each item is scored from 0 (not at all) to 3 (nearly every day), with higher scores indicating greater severity of depressive symptoms. The Patient Health Questionnaire–9 has been validated for use in the adolescent population<sup>44</sup> and in persons with TBI.<sup>16</sup> Internal reliability was  $\alpha = .85$  in the current study. The variable that was used in analyses was the total score at 3 months after TBI.

**Posttraumatic Stress Disorder (PTSD) Symptoms**—The University of California at Los Angeles Post-traumatic Stress Disorder Reaction Index was used to assess for PTSD symptomatology.<sup>49</sup> This is a well-established 22-item measure including 7 items on avoidance symptoms, 5 on hyperarousal symptoms, and 5 on reexperiencing symptoms. Adolescents reported on each item based on the frequency of symptom experienced in the last month, from 0 = none, 1 = a little (twice a month), 2 = some (twice a week), 3 = much (3 times a week), to 4 = most of the time. Higher scores indicate increased severity of PTSD symptoms. This measure has been validated for use in adolescents and has shown validity with PTSD interviews.<sup>49</sup> In the present sample, internal consistency was  $\alpha = .93$ . The total score assessing PTSD symptomatology at 3 months following TBI was used in analyses.

**HRQOL**—The Pediatric Quality of Life Inventory, version 4.0 (PedsQL), was used to assess HRQOL.<sup>51</sup> This is a 23-item questionnaire on which adolescents were asked to rate

physical, emotional, and social functioning over the last 4 weeks. The response options are based on a Likert-type scale with 0 indicating never to 5 indicating almost always. The summary scores are totaled and converted to a 0 to 100 range, with lower scores indicating poorer HRQOL. The total scores were used in analyses. The PedsQL has been validated in various pediatric medical populations, and specifically for children after TBI.<sup>38</sup> This measure demonstrated an internal reliability of  $\alpha = .91$  in the current sample.

**Assessment of TBI Severity**—To establish the diagnosis of TBI, the primary investigator (F.P.R.) or a trained research nurse conducted abstraction from medical records based on criteria established in 2002 by the CDC.<sup>37</sup> Criteria for TBI were the presence of a head injury that was associated with any of 1) a decreased level of consciousness, 2) amnesia, 3) neurologic/ neuropsychological abnormality, or 4) the presence of an intracranial lesion. TBI was further classified as mild, moderate, or severe by using the criteria from the CDC and the World Health Organization.<sup>9,43</sup> Mild TBI was defined by a worst Glasgow Coma Scale (GCS) score of 13 to 15 at initial evaluation and a GCS score of 15 at discharge or at 24 hours if hospitalized. This was further subclassified based on computed tomography (CT) findings: Mild I, no CT abnormalities or no CT scans were performed; Mild II, skull fracture but not intracranial hemorrhages; Mild III, intracranial hemorrhage. Moderate TBI was classified by the best motor GCS score of 4 to 6 at 24 hours after injury, if it did not meet Mild TBI criteria. Severe TBI was classified by a best motor GCS score of 1 to 3 at 24 hours after injury. This classification has been used in previous work.<sup>23,36</sup>

**GCS**—The GCS is a measurement of the level of consciousness as a part of the neurologic examination. One of the indications for use is in the assessment of head injury. The GCS is composed of 3 subscales assessing best eye opening, best verbal response, and best motor response. The scales range from 3 to 15, with higher scores indicating greater levels of consciousness. For this study, the total scores and the best motor response scores were used in part to classify severity of TBI. The use of the GCS for classification of TBI is widely accepted.<sup>23,36</sup>

**Assessment of Overall Injury Severity**—The severity of injury to the head and other anatomic regions were classified using the Abbreviated Injury Scale (AIS).<sup>3,12</sup> Injury severity by AIS was determined as follows: 1 = minor; 2 = moderate; 3 = severe, not life-threatening; 4 = severe and life-threatening; 5 = critical, survival uncertain; and 6 = not survivable, or untreatable. The AIS scores for each of the following body regions were coded: head, face, chest, abdomen, extremities (including pelvis), and soft tissue. The head AIS was used in analyses. The maximum AIS scores (MAXAIS) were identified among all the other anatomic regions and used in analyses. Use of the AIS in addition to GCS for the evaluation of injury severity has been shown to have increased predictive relationship with 12-month outcomes.<sup>21</sup>

## Statistical Analyses

The first aim examined the cross-sectional prevalence of pain intensity of 3/10 in adolescents at each time point in the total sample ( $n = 144$ ). Persistent pain status was

defined by the presence of pain at every assessment point over 36 months, with pain rated as 3 on an 11-point NRS. Between-group differences (persistent pain vs infrequent pain) were examined on demographic variables (age, sex, race, and ethnicity) and clinical factors (TBI severity, injury severity, pain intensity, and depressive and PTSD symptomatology) using either chi-square for categorical variables, or t-tests or Fisher exact tests for noncategorical variables.

To test the hypotheses concerning the risk factors that may predict persistent pain, a logistic regression model was utilized to determine if persistent pain status was associated with age, sex, severity of TBI, and depressive symptoms at 3 months after injury. As there were no significant differences between groups on ethnicity, household income, or insurance status, these variables were not included in the model. Finally, to examine the longitudinal association between persistent pain and HRQOL, a linear mixed model was used. Predictors of longitudinal HRQOL (baseline, 3, 12, 24, and 36 months after TBI) included in the model were pain intensity at 3 months after TBI, age, sex, severity of TBI, presence of depressive symptoms at 3 months after TBI, and PTSD symptomatology at 3 months after TBI. Tests of statistical significance were conducted using  $\alpha = .05$ .

Data were analyzed using SAS 9.2 (SAS Institute Inc, Cary, NC) and Stata software 10 (StataCorp LP, College Station, TX).

## Results

### Descriptive Statistics

Cross-sectional descriptive analyses examined the prevalence of pain rated at 3/10 by adolescents at each time point (see Fig 1). Contrary to hypothesis, the prevalence of pain did not decline over the period from 3 months to 36 months after TBI (Fig 1). For adolescents with mild TBI, the prevalence of reported pain remained stable from 3 to 36 months, with prevalence rates ranging from 55.5 to 57.1%. For adolescents with moderate or severe TBI, the range was from 36% at 3 months after TBI to 68% at 36 months after TBI ( $P = .01$ ). There were no significant differences between groups at each time point. About 40% of the sample had pain present at both 3- and 12-month assessments; 30% did at 3-, 12-, and 24-month assessments; and 24.3% had persistent pain (3-, 12-, 24-, and 36-month assessments). Only 14.6% of adolescents did not report pain at any of the assessment points.

Demographic characteristics of the participants who completed questionnaires at all time points included 144 adolescents, 69.4% male, mean age 15.7 years ( $SD = 1.2$ ). Of these, 119 were classified with mild TBI (82.6%), 22 with moderate TBI (15.3%), and 3 (2.1%) with severe TBI. Two subgroups of adolescents were examined, those who reported persistent pain at all assessments ( $n = 35$ ) and those adolescents with none or infrequent pain across 36 months ( $n = 109$ ). Demographic details comparing the 35 adolescents with 36-month persistent pain and the 109 with infrequent pain are shown in Table 1. There were significantly more females in the persistent pain group (54.3%) than in the infrequent pain group (22.9%;  $P = .001$ ). There were no significant differences in the other demographic factors (age, ethnicity, household income, and insurance status), mechanism of injury, and

severity of TBI or other injuries, or whether the injury sustained was isolated head injury or multiple injuries.

In this subgroup of adolescents with persistent pain, 30 (85.7%) reported post-TBI headaches, 15 (42.9%) reported back pain, and 4 (11.4%) reported pain in the lower limbs at 36 months after TBI. Twenty (57.1%) adolescents described pain involving more than 1 anatomic region. In comparison, for the adolescents with infrequent pain, about half (45.9%) had headaches, 10 (9.2%) had back pain, and 8 (7.3%) had lower limb pain. As expected, adolescents with persistent pain rated higher pain intensity (mean = 5.9, SD = 1.9) compared to the infrequent pain group, who rated lower usual pain intensity (mean = 2.2, SD = 2.5,  $P < .0001$ ). Table 2 compares the pain assessments at 36 months after TBI. At 3- and 36-month assessment points, adolescents with persistent pain endorsed significantly higher levels of depressive symptoms, PTSD symptomatology, and significantly poorer HRQOL compared to adolescents with infrequent pain ( $P$ 's  $< .0001$ ). Table 3 examines depressive symptoms, PTSD symptomatology, and HRQOL at 3 months and at 36 months after TBI between the persistent pain group and the group with infrequent pain. Data for the 12- and 24-month assessments on these variables are not presented because they are comparable to the 36-month assessment.

### Risk Factors for Persistent Pain

Age, sex, severity of TBI, and depressive symptoms were examined as predictors of persistent pain. As hypothesized, the 2 independent variables that emerged as significant predictors of persistent pain were female sex (odds ratio [OR] = 2.73, 95% confidence interval [CI] = 1.12–6.63) and increased symptoms of depression at 3 months after TBI (OR = 1.26, 95% CI = 1.12–1.43; see Table 4). Age and severity of TBI were not significantly associated with the presence of persistent pain.

### Longitudinal Association Between Pain and HRQOL

To examine the longitudinal association between pain and HRQOL, linear mixed models were used. Analyses demonstrated that HRQOL over the course of 36 months was predicted by pain intensity at 3 months after TBI ( $F[1, 181] = 5.88, P = .02$ ), TBI severity ( $F[1, 181] = 8.89, P = .003$ ), depressive symptoms at 3 months ( $F[1, 181] = 24.88, P < .0001$ ), and PTSD symptoms at 3 months ( $F[1, 181] = 31.01, P < .0001$ ) where higher early experience of pain, higher TBI severity, and greater depressive and PTSD symptoms predicted poorer longitudinal HRQOL.

### Discussion

Our findings demonstrated that pain is a common sequela following pediatric TBI and was reported frequently at each follow-up assessment. In adolescents with mild TBI, more than half the adolescents reported experiencing pain that remained fairly stable over 36 months. In contrast, in adolescents with moderate or severe TBI, pain complaints increased over the course of 36 months to involve the majority (68%) of these adolescents. We were also able to characterize a subgroup of youth (24.3%) for whom pain was present at each assessment point categorized as having persistent pain. To our knowledge, this is the first study to

describe the prevalence and longitudinal trajectory of pain following head injury in adolescents.

Our findings extend the literature on prevalence of headaches following TBI in children and adolescents by specifically documenting pain involving other anatomic regions in the pediatric TBI population. We found that pain was commonly reported in the head, back, and lower extremities. This association of chronic pain and TBI has been recognized in the adult population,<sup>4,24,26,32,39,50</sup> and although further studies are needed, our preliminary data show that pain is also common following pediatric TBI.

Several mechanisms have been proposed to link head injury and chronic pain, including that head injuries may be complicated by biomolecular and cellular alterations in the neuroanatomic vasculature.<sup>5,8,42</sup> Neuronal hyper-excitability, hyper-reactivity, and exaggerated wind-up sensation may contribute to the development of chronic pain syndromes. For example, studies using laboratory based evaluations demonstrated reductions in thermal and tactile sensations and high rates of allodynia and hyperpathia in adults with TBI.<sup>40</sup> Furthermore, there are changes in brain matter parenchymal volumes in adults following a TBI event, and such changes have been associated with the experience of chronic pain.<sup>34</sup>

In this study, we identified several predictors of persistent pain and poor long-term quality of life after TBI. The significant predictors of persistent pain were female sex and early presence of depressive symptoms, which have also been found to predict development and maintenance of chronic pain in otherwise healthy community samples of youth.<sup>41,48</sup> Moreover, we demonstrated that injury severity (moderate-severe TBI) and psychological symptoms (depressive and PTSD symptoms) along with pain following TBI were associated with poor HRQOL at long-term follow-up. Hoffman and colleagues found that in the adult population with TBI, increased pain intensity was associated with depression, lower community integration scores, and poorer satisfaction with life.<sup>24</sup> The cumulative impact of persistent pain over time may result in a significant deterioration in HRQOL. Our findings suggest that there may be a subgroup of adolescents with TBI who are at an increased vulnerability and risk for poorer outcomes. Thus, the identification of risk factors that can be targeted in prevention and intervention programs is an important future research direction.

The current study has several limitations. First, there is limited information of pain characteristics to further understand the type of pain experienced by these youth. The etiology of the pain is unclear, whether the pain is due to neuropathy, central pain, or secondary to direct tissue injury. Future studies will need to include prospective and comprehensive evaluation of pain characteristics following a TBI. In addition, the presence of preinjury pain was not examined in this study, and further research will need to address preinjury pain occurrence and its association with postinjury pain experience. Second, the majority of our adolescent sample had experienced mild TBI, and thus our ability to generalize findings to adolescents with moderate and severe TBI is limited. Larger sample sizes may allow further examination of the possible association between the severity of head injury and pain. Third, although we found that adolescents with persistent pain reported greater depressive and PTSD symptomatology compared to adolescents with infrequent



pain, we were not able to identify the directionality between pain and psychological symptoms (eg, depression, PTSD). Studies in adults following TBI corroborate the co-occurrence of pain and depression.<sup>20,47</sup> Additional research is required to examine the directionality and perpetuating factors in the relationship between pain and psychological factors. Finally, our study did not include a healthy comparison cohort and thus we are unable to compare the rates of pain to youth who did not experience a head injury. Population-based studies examining the prevalence rates of pediatric persistent and chronic pain vary considerably, with estimates ranging from 23 to 51%.<sup>29</sup> Methodological differences, lack of consistency on the operational definition of pain, and different pain characteristics (eg, duration, locations) account for the variability in prevalence reports.<sup>29</sup> Findings in this study suggest that adolescents with TBI may be a vulnerable population for the development of persistent pain; however, future work is needed to examine the prevalence and characteristics of chronic pain comparing adolescents with TBI to healthy adolescents.

Despite the limitations of this study, the findings of high rates of persistent pain after a head injury remain significant. Further research is needed to understand pain as an outcome after TBI and to investigate the etiology of pain after a head injury.

## Acknowledgments

Support for this project was provided by the National Institutes of Health grants 5T32GM086270-03 (S.W.T.) and K24HD060068 (T.M.P.) and National Center for Injury Prevention and Control, Centers for Diseases Control and Prevention, grant R49 CE 001021 (F.P.R.).

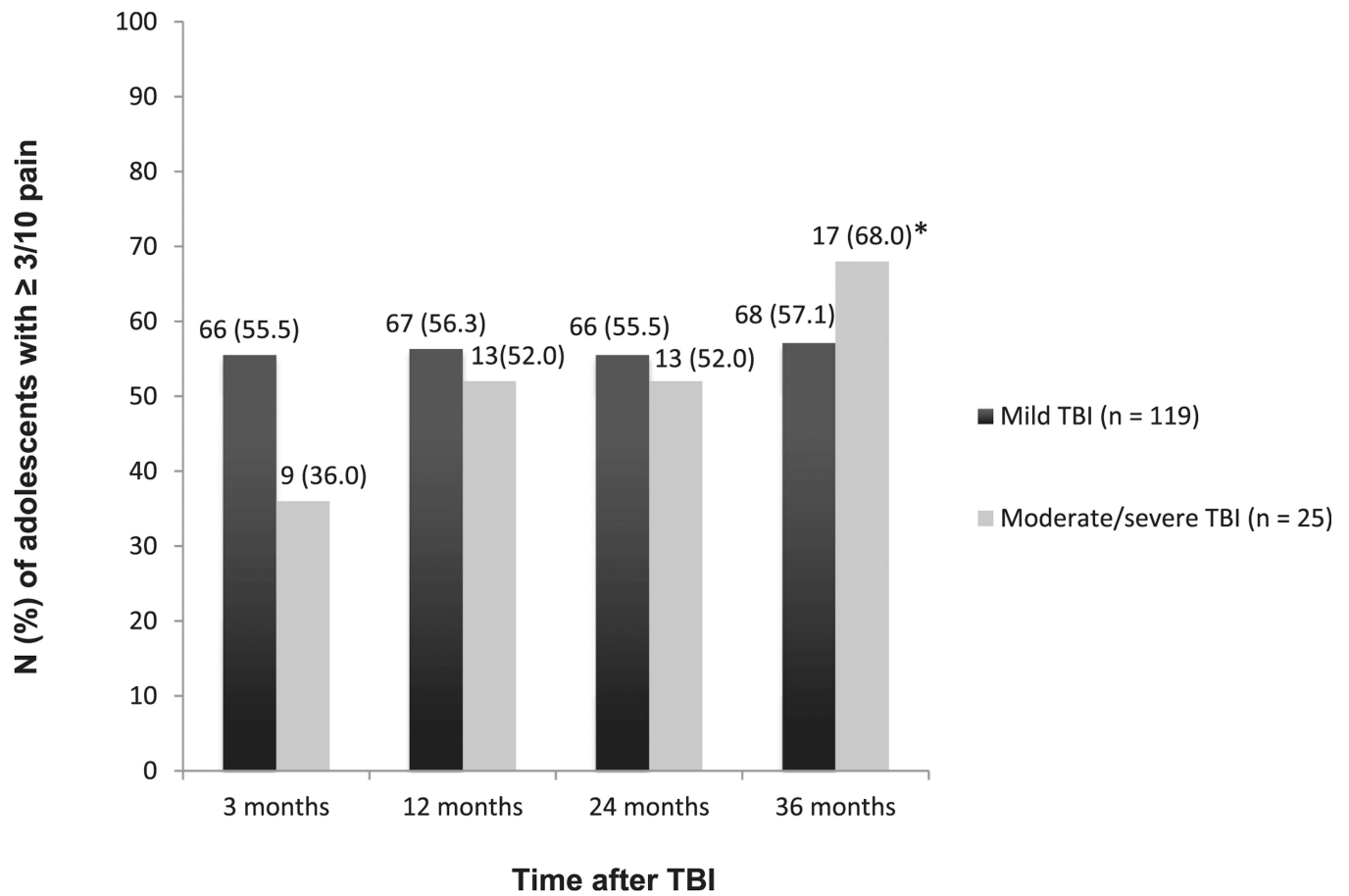
## References

1. American Psychiatric Association. Washington, DC: American Psychiatric Publishing; 2000. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision.
2. Babikian T, Asarnow R. Neurocognitive outcomes and recovery after pediatric TBI: Meta-analytic review of the literature. *Neuropsychology*. 2009; 23:283–296. [PubMed: 19413443]
3. Baker SP, O'Neill B, Haddon W Jr, Long WB. The injury severity score: A method for describing patients with multiple injuries and evaluating emergency care. *J Trauma*. 1974; 14:187–196. [PubMed: 4814394]
4. Beetar JT, Guilmette TJ, Sparadeo FR. Sleep and pain complaints in symptomatic traumatic brain injury and neurologic populations. *Arch Phys Med Rehabil*. 1996; 77:1298–1302. [PubMed: 8976315]
5. Belanger HG, Vanderploeg RD, Curtiss G, Warden DL. Recent neuroimaging techniques in mild traumatic brain injury. *J Neuropsychiatry Clin Neurosci*. 2007; 19:5–20. [PubMed: 17308222]
6. Blinman TA, Houseknecht E, Snyder C, Wiebe DJ, Nance ML. Postconcussive symptoms in hospitalized Tham et al The Journal of Pain 1247 pediatric patients after mild traumatic brain injury. *J Pediatr Surg*. 2009; 44:1223–1228. [PubMed: 19524745]
7. Blume HK, Vavilala MS, Jaffe KM, Koepsell TD, Wang J, Temkin N, Durbin D, Dorsch A, Rivara FP. Headache after pediatric traumatic brain injury: A cohort study. *Pediatrics*. 2012; 129:e31–e39. [PubMed: 22144708]
8. Buki A, Povlishock JT. All roads lead to disconnection? Traumatic axonal injury revisited. *Acta Neurochir (Wien)*. 2006; 148:181–193. discussion 193–194. [PubMed: 16362181]
9. Carroll LJ, Cassidy JD, Peloso PM, Borg J, von Holst H, Holm L, Paniak C, Pepin M. Prognosis for mild traumatic brain injury: Results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med* 2004. 2004; (43 Suppl):84–105.

10. Claar RL, Walker LS. Functional assessment of pediatric pain patients: Psychometric properties of the functional disability inventory. *Pain*. 2006; 121:77–84. [PubMed: 16480823]
11. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: What is moderate pain in millimetres? *Pain*. 1997; 72:95–97. [PubMed: 9272792]
12. Copes WS, Lawnick M, Champion HR, Sacco WJ. A comparison of Abbreviated Injury Scale 1980 and 1985 versions. *J Trauma*. 1988; 28:78–86. [PubMed: 3339666]
13. Corrigan JD, Bogner J, Holloman C. Lifetime history of traumatic brain injury among persons with substance use disorders. *Brain Inj*. 2012; 26:139–150. [PubMed: 22360520]
14. Demyttenaere S, Finley GA, Johnston CC, McGrath PJ. Pain treatment thresholds in children after major surgery. *Clin J Pain*. 2001; 17:173–177. [PubMed: 11444719]
15. Eccleston C, Crombez G, Scotford A, Clinch J, Connell H. Adolescent chronic pain: Patterns and predictors of emotional distress in adolescents with chronic pain and their parents. *Pain*. 2004; 108:221–229. [PubMed: 15030941]
16. Fann JR, Bombardier CH, Dikmen S, Esselman P, Warms CA, Pelzer E, Rau H, Temkin N. Validity of the Patient Health Questionnaire–9 in assessing depression following traumatic brain injury. *J Head Trauma Rehabil*. 2005; 20:501–511. [PubMed: 16304487]
17. Faul M, Xu L, Wald MM, Coronado VG. Traumatic brain injury in the United States: Emergency department visits, hospitalizations, and deaths 2002–2006. National Center for Injury Prevention and Control, Centers for Disease Control and Prevention. 2010
18. Fay GC, Jaffe KM, Polissar NL, Liao S, Rivara JB, Martin KM. Outcome of pediatric traumatic brain injury at three years: A cohort study. *Arch Phys Med Rehabil*. 1994; 75:733–741. [PubMed: 8024416]
19. Fay TB, Yeates KO, Wade SL, Drotar D, Stancin T, Taylor HG. Predicting longitudinal patterns of functional deficits in children with traumatic brain injury. *Neuropsychology*. 2009; 23:271–282. [PubMed: 19413442]
20. Fogelberg DJ, Hoffman JM, Dikmen S, Temkin NR, Bell KR. Association of sleep and co-occurring psychological conditions at 1 year after traumatic brain injury. *Arch Phys Med Rehabil*. 2012; 93:1313–1318. [PubMed: 22840828]
21. Foreman BP, Caesar RR, Parks J, Madden C, Gentilello LM, Shafi S, Carlile MC, Harper CR, Diaz-Arrastia RR. Usefulness of the abbreviated injury score and the injury severity score in comparison to the Glasgow Coma Scale in predicting outcome after traumatic brain injury. *J Trauma*. 2007; 62:946–950. [PubMed: 17426553]
22. Gauntlett-Gilbert J, Eccleston C. Disability in adolescents with chronic pain: Patterns and predictors across different domains of functioning. *Pain*. 2007; 131:132–141. [PubMed: 17267129]
23. Healey C, Osler TM, Rogers FB, Healey MA, Glance LG, Kilgo PD, Shackford SR, Meredith JW. Improving the Glasgow Coma Scale score: Motor score alone is a better predictor. *J Trauma*. 2003; 54:671–678. discussion 678–680. [PubMed: 12707528]
24. Hoffman JM, Pagulayan KF, Zawaideh N, Dikmen S, Temkin N, Bell KR. Understanding pain after traumatic brain injury: Impact on community participation. *Am J Phys Med Rehabil*. 2007; 86:962–969. [PubMed: 18090437]
25. Hunfeld JA, Perquin CW, Duivenvoorden HJ, Hazebroek-Kampschreur AA, Passchier J, van Suijlekom-Smit LW, van der Wouden JC. Chronic pain and its impact on quality of life in adolescents and their families. *J Pediatr Psychol*. 2001; 26:145–153. [PubMed: 11259516]
26. Jensen OK, Nielsen FF. The influence of sex and pre-traumatic headache on the incidence and severity of headache after head injury. *Cephalalgia*. 1990; 10:285–293. [PubMed: 2289229]
27. Kashikar-Zuck S, Goldschneider KR, Powers SW, Vaught MH, Hershey AD. Depression and functional disability in chronic pediatric pain. *Clin J Pain*. 2001; 17:341–349. [PubMed: 11783815]
28. Keogh E, Eccleston C. Sex differences in adolescent chronic pain and pain-related coping. *Pain*. 2006; 123:275–284. [PubMed: 16644131]
29. King S, Chambers CT, Hugué A, MacNevin RC, McGrath PJ, Parker L, MacDonald AJ. The epidemiology of chronic pain in children and adolescents revisited: A systematic review. *Pain*. 2011; 152:2729–2738. [PubMed: 22078064]

30. Kirk C, Nagiub G, Abu-Arafeh I. Chronic post-traumatic headache after head injury in children and adolescents. *Dev Med Child Neurol.* 2008; 50:422–425. [PubMed: 18422678]
31. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med.* 2001; 16:606–613. [PubMed: 11556941]
32. Lahz S, Bryant RA. Incidence of chronic pain following traumatic brain injury. *Arch Phys Med Rehabil.* 1996; 77:889–891. [PubMed: 8822679]
33. Lanser JB, Jennekens-Schinkel A, Peters AC. Headache after closed head injury in children. *Headache.* 1988; 28:176–179. [PubMed: 3384643]
34. Turner GR, Levine B. Augmented neural activity during executive control processing following diffuse axonal injury. *Neurology.* 2008; 71:812–818. [PubMed: 18779509]
35. Logan DE, Simons LE, Stein MJ, Chastain L. School impairment in adolescents with chronic pain. *J Pain.* 2008; 9:407–416. [PubMed: 18255341]
36. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, Salkever DS, Scharfstein DO. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med.* 2006; 354:366–378. [PubMed: 16436768]
37. Marr, AL.; Coronado, VG., editors. *Central Nervous system Injury Surveillance Data Submission Standards—2002.* Atlanta GA: Centers for Disease Control and Prevention; 2004.
38. McCarthy ML, MacKenzie EJ, Durbin DR, Aitken ME, Jaffe KM, Paidas CN, Slomine BS, Dorsch AM, Berk RA, Christensen JR, Ding R. The Pediatric Quality of Life 1248 The Journal of Pain Persistent Pain in Adolescents Following TBI Inventory: An evaluation of its reliability and validity for children with traumatic brain injury. *Arch Phys Med Rehabil.* 2005; 86:1901–1909. [PubMed: 16213229]
39. Nampiaparampil DE. Prevalence of chronic pain after traumatic brain injury: A systematic review. *JAMA.* 2008; 300:711–719. [PubMed: 18698069]
40. Ofek H, Defrin R. The characteristics of chronic central pain after traumatic brain injury. *Pain.* 2007; 131:330–340. [PubMed: 17689190]
41. Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA, Bohnen AM, van Suijlekom-Smit LW, Passchier J, van der Wouden JC. Pain in children and adolescents: A common experience. *Pain.* 2000; 87:51–58. [PubMed: 10863045]
42. Ray SK, Dixon CE, Banik NL. Molecular mechanisms in the pathogenesis of traumatic brain injury. *Histol Histopathol.* 2002; 17:1137–1152. [PubMed: 12371142]
43. National Center for Injury Prevention and Control. *Report to Congress on Mild Traumatic Brain Injury in the United States: Steps to Prevent a Serious Public Health Problem.* Atlanta GA: Centers for Disease Control and Prevention; 2003.
44. Richardson LP, McCauley E, Grossman DC, McCarty CA, Richards J, Russo JE, Rockhill C, Katon W. Evaluation of the Patient Health Questionnaire–9 Item for detecting major depression among adolescents. *Pediatrics.* 2010; 126:1117–1123. [PubMed: 21041282]
45. Rivara FP, Koepsell TD, Wang J, Temkin N, Dorsch A, Vavilala MS, Durbin D, Jaffe KM. Disability 3, 12, and 24 months after traumatic brain injury among children and adolescents. *Pediatrics.* 2011; 128:e1129–e1138. [PubMed: 22025592]
46. Ruperto N, Lovell DJ, Li T, Sztajn bok F, Goldenstein-Schainberg C, Scheinberg M, Penades IC, Fischbach M, Alcala JO, Hashkes PJ, Hom C, Jung L, Lepore L, Oliveira S, Wallace C, Alessio M, Quartier P, Cortis E, Eberhard A, Simonini G, Lemelle I, Chalom EC, Sigal LH, Block A, Covucci A, Nys M, Martini A, Giannini EH. Abatacept improves health-related quality of life, pain, sleep quality, and daily participation in subjects with juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken).* 2010; 62:1542–1551. [PubMed: 20597110]
47. Stalnacke BM. Postconcussion symptoms in patients with injury-related chronic pain. *Rehabil Res Pract* 2012. 2012; 2012:528265.
48. Stanford EA, Chambers CT, Biesanz JC, Chen E. The frequency, trajectories and predictors of adolescent recurrent pain: A population-based approach. *Pain.* 2008; 138:11–21. [PubMed: 18093737]
49. Steinberg AM, Brymer MJ, Decker KB, Pynoos RS. The University of California at Los Angeles Post-traumatic Stress Disorder Reaction Index. *Curr Psychiatry Rep.* 2004; 6:96–100. [PubMed: 15038911]

50. Uomoto JM, Esselman PC. Traumatic brain injury and chronic pain: Differential types and rates by head injury severity. *Arch Phys Med Rehabil.* 1993; 74:61–64. [PubMed: 8420522]
51. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: Reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care.* 2001; 39:800–812. [PubMed: 11468499]
52. Voepel-Lewis T, Burke CN, Jeffreys N, Malviya S, Tait AR. Do 0–10 numeric rating scores translate into clinically meaningful pain measures for children? *Anesth Analg.* 2011; 112:415–421. [PubMed: 21127278]
53. von Baeyer CL, Spagrud LJ, McCormick JC, Choo E, Neville K, Connelly MA. Three new datasets supporting use of the Numerical Rating Scale (NRS-11) for children’s self-reports of pain intensity. *Pain.* 2009; 143:223–227. [PubMed: 19359097]



**Figure 1.**

Prevalence of pain ( $\geq 3/10$ ) at each assessment by TBI groups. \*Significant change in the prevalence of pain from 3 to 36 months in adolescents with moderate and severe TBI ( $P = .01$ ).

**Table 1**

Descriptive Characteristics of Adolescents With Persistent Pain and With Infrequent Pain

|                              | <b>Persistent<br/>Pain<br/>(n = 35)</b> | <b>Infrequent<br/>Pain<br/>(n = 109)</b> | <b>P</b> |
|------------------------------|---|--|----------|
| Age (years), mean (SD)       | 15.9 (1.2)                              | 15.7 (1.2)                               | .53      |
| Sex (male), n (%)            | 16 (45.7)                               | 84 (77.1)                                | .001     |
| Ethnicity, n (%)             |   |  | .48*     |
| White                        | 23 (65.7)                               | 79 (72.5)                                |          |
| Black                        | 2 (5.7)                                 | 5 (4.6)                                  |          |
| Asian                        | 0 (.0)                                  | 2 (1.8)                                  |          |
| Hispanic                     | 1 (2.9)                                 | 8 (7.3)                                  |          |
| Other                        | 9 (25.7)                                | 14 (12.8)                                |          |
| Household income, n (%)      |   |  | .35*     |
| <\$30k                       | 6 (17.1)                                | 12 (11.0)                                |          |
| \$30–60k                     | 6 (17.1)                                | 20 (18.4)                                |          |
| \$60–100k                    | 11 (31.4)                               | 22 (20.2)                                |          |
| >\$100k                      | 12 (34.3)                               | 50 (45.9)                                |          |
| Unknown                      | 0 (.0)                                  | 5 (4.6)                                  |          |
| TBI severity, n (%)          |   |  | .97      |
| Mild                         | 29 (82.9)                               | 90 (82.6)                                |          |
| Moderate/severe              | 6 (17.1)                                | 19 (17.4)                                |          |
| Isolated brain injury, n (%) | 14 (40.0)                               | 40 (37.4)                                | .78      |
| Head MAXAIS, mean (SD)       | 2.0 (1.3)                               | 2.2 (1.3)                                | .28      |
| Non-Head MAXAIS, mean (SD)   | 1.2 (1.4)                               | 1.0 (1.1)                                | .29      |
| Mechanism of injury, n (%)   |   |  | .57      |
| Motor vehicle                | 7 (20.6)                                | 29 (26.6)                                |          |
| Pedestrian                   | 5 (14.7)                                | 9 (8.3)                                  |          |
| Fall                         | 10 (29.4)                               | 37 (33.9)                                |          |
| Struck by/against            | 12 (35.3)                               | 31 (28.4)                                |          |
| Insurance status, n (%)      |   |  | .40*     |
| None                         | 1 (2.9)                                 | 5 (4.6)                                  |          |
| Government insurance         | 6 (17.1)                                | 17 (15.6)                                |          |
| Private                      | 27 (77.1)                               | 87 (79.8)                                |          |
| Tricare                      | 1 (2.9)                                 | 0 (.0)                                   |          |

\* Fisher exact tests were used.

**Table 2**

Characteristics of Pain at 36 Months for Adolescents With Persistent Pain and Infrequent Pain

|                                   | <b>Persistent Pain<br/>(n = 35)</b> | <b>Infrequent Pain<br/>(n = 109)</b> | <b><i>P</i></b> |
|-----------------------------------|-------------------------------------|--------------------------------------|-----------------|
| Average pain intensity, mean (SD) | 5.9 (1.9)                           | 2.2 (2.5)                            | <.0001          |
| Pain sites, n (%)                 |                                     |                                      |                 |
| Head                              | 30 (85.7)                           | 50 (45.9)                            |                 |
| Neck                              | 3 (8.6)                             | 2 (1.8)                              |                 |
| Back                              | 15 (42.9)                           | 10 (9.2)                             |                 |
| Face                              | 0 (.0)                              | 0 (.0)                               |                 |
| Chest                             | 0 (.0)                              | 1 (.9)                               |                 |
| Stomach                           | 1 (2.9)                             | 4 (3.7)                              |                 |
| Upper limb                        | 2 (5.7)                             | 6 (5.5)                              |                 |
| Lower limb                        | 4 (11.4)                            | 8 (7.3)                              |                 |
| Other                             | 0 (.0)                              | 2 (1.8)                              |                 |

**Table 3**

Depression, PTSD, and HRQOL at 3 and 36 Months for Adolescents With Persistent Pain and Infrequent Pain After TBI

|                                   | <b>Persistent Pain<br/>(n = 35)<br/>Mean (SD)</b> | <b>Infrequent Pain<br/>(n = 109)<br/>Mean (SD)</b> | <b><i>P</i></b> |
|-----------------------------------|---|--|-----------------|
| Depressive symptoms at 3 months   | 5.7 (4.8)   | 2.2 (2.7)  | <.0001          |
| Depressive symptoms at 36 months  | 5.6 (4.0)   | 2.5 (3.0)  | <.0001          |
| PTSD symptoms at 3 months         | 20.4 (14.7)                                       | 10.4 (8.8)   | <.0001          |
| PTSD symptoms at 36 months        | 18.4 (12.5)                                       | 9.2 (9.8)  | <.0001          |
| PedsQL (total score) at 3 months  | 68.0 (21.2)                                       | 86.0 (12.5)  | <.0001          |
| PedsQL (total score) at 36 months | 70.4 (16.9)                                       | 86.1 (12.1)  | <.0001          |

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript



**Table 4**

## Adjusted Predictors of Persistent Pain for Adolescents With TBI

|   | OR    | 95% CI     |
|---|-------|------------|
| Age   | .993  | .96, 1.02  |
| Gender (females vs males)                       | 2.726 | 1.12, 6.63 |
| TBI severity (mild vs moderate/severe TBI)      | .930  | .30, 2.94  |
| Depressive symptomatology at 3 months after TBI | 1.263 | 1.12, 1.43 |

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript