

Prevalence of Chronic Pain After Traumatic Brain Injury

A Systematic Review

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THE CENTERS FOR DISEASE CONTROL and Prevention estimates that approximately 1.4 million US individuals sustain traumatic brain injuries (TBIs) per year.¹ The diagnosis can be made subjectively by assessing patients for loss of consciousness (LOC), altered consciousness after a head injury, or post-traumatic amnesia.² These head injuries can be sustained either when the head forcefully hits an object, when an object penetrates the skull, or when brain tissue undergoes a sudden acceleration, deceleration, or both.

Since 2001, the United States has deployed more than 1.5 million military personnel to Iraq and Afghanistan.³ A higher percentage of these soldiers are now able to survive injuries that would have been fatal in previous wars.⁴ Among combatants who have returned to the United States, the prevalence of head injuries is estimated at 15.1%.³ Multiple studies have highlighted the importance of brain injuries to US military personnel in Iraq and Afghanistan. Studies of selected military units in Iraq reported that 88% to 97% of their soldiers have sustained blast injuries while in combat^{5,6} and that 47% to 59% of these soldiers have sustained injuries to the head and neck

Context The Centers for Disease Control and Prevention estimates that approximately 1.4 million US individuals sustain traumatic brain injuries (TBIs) per year. Previous reports suggest an association between TBI and chronic pain syndromes (eg, headache) thought to be more common in patients with mild TBI and in those who have sustained brain injury from violent rather than unintentional trauma. Comorbid psychiatric disorders such as posttraumatic stress disorder (PTSD) may also mediate chronic pain symptoms.

Objectives To determine the prevalence of chronic pain as an underdiagnosed consequence of TBI and to review the interaction between chronic pain and severity of TBI as well as the characteristics of pain after TBI among civilians and combatants.

Evidence Acquisition The Ovid/MEDLINE database was searched for articles published between 1951 and February 2008 using any combination of the terms *brain injury, pain, headache, blast injury, and combat (combat disorders, war, military medicine, wounds and injuries, military personnel, veterans)*. The PubMed and MD Consult databases were searched in a similar fashion. The Cochrane Collaboration, National Institutes of Health Clinical Trials Database, Meta-Register of Current Controlled Trials, and CRISP databases were searched using the keyword *brain injury*. All articles in peer-reviewed journals reporting original data on pain syndromes in adult patients with TBI with regard to pain prevalence, pain category, risk factors, pathogenesis, and clinical course were selected, and manual searches were performed of their reference lists. The data were pooled and prevalence rates calculated.

Evidence Synthesis Twenty-three studies (15 cross-sectional, 5 prospective, and 3 retrospective) including 4206 patients were identified. Twelve studies assessed headache pain in 1670 patients. Of these, 966 complained of chronic headache, yielding a prevalence of 57.8% (95% confidence interval [CI], 55.5%-60.2%). Among civilians, the prevalence of chronic pain was greater in patients with mild TBI (75.3% [95% CI, 72.7%-77.9%]) compared with moderate or severe TBI (32.1% [95% CI, 29.3%-34.9%]). Twenty studies including 3289 civilian patients with TBI yielded a chronic pain prevalence of 51.5% (95% CI, 49.8%-53.2%). Three studies assessed TBI among 917 veterans and yielded a pain prevalence of 43.1% (95% CI, 39.9%-46.3%). PTSD may mediate chronic pain, but brain injury appears to have an independent correlation with chronic pain.

Conclusions Chronic pain is a common complication of TBI. It is independent of psychological disorders such as PTSD and depression and is common even among patients with apparently minor injuries to the brain.

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suggestive of TBI.⁵⁻⁸ The Defense and Veterans Brain Injury Center estimates that 10% to 20% of all soldiers returning from duty in Iraq and Afghanistan have sustained some type of TBI.⁹ As of 2008, at least 25 000 soldiers have been diagnosed with TBI, with a projected cost of \$14 billion for their care over the next 20 years.⁹

The association of TBI and chronic pain was described as early as 1915 in troops returning from World War I with “shell shock.”¹⁰ Other studies have supported the association between TBI and chronic pain syndromes, the most common of which is headache. One study of Operation Iraqi Freedom/Operation Enduring Freedom veterans experiencing

postconcussive syndrome found that posttraumatic stress disorder (PTSD) accounted for all symptoms except pain, suggesting that pain is physiologically linked to brain injury.³

Given the morbidity associated with chronic pain, the strategies available for its early treatment, and the financial burden it imposes on patients and society, this review was undertaken to (1) determine the prevalence of chronic pain syndromes such as headache among patients with TBI; (2) discuss other potential pain syndromes in these patients; (3) describe the relationship between pain and severity of brain injury; (4) investigate the effect of civilian vs combat veteran status on chronic

pain after TBI; and (5) examine the role of psychiatric comorbid disorders such as depression, PTSD, and/or substance disorders in posttraumatic pain.

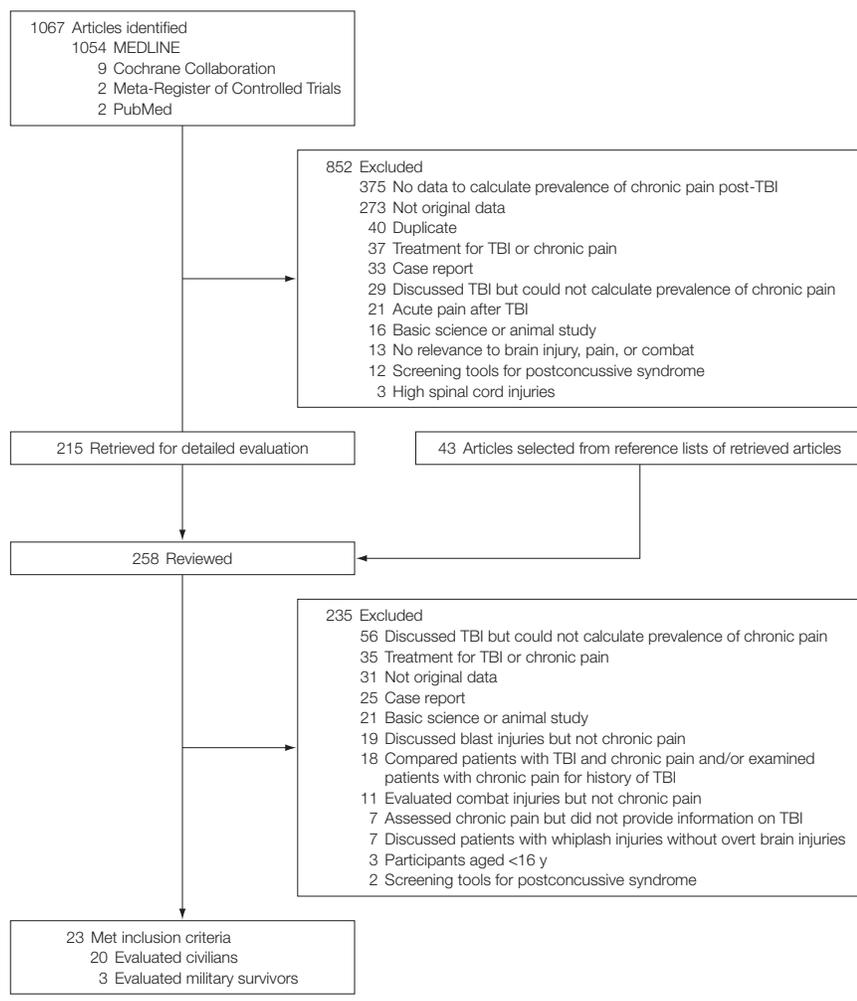
EVIDENCE ACQUISITION

Studies were identified that could provide information on the prevalence of pain among adult patients with TBI. The Ovid/MEDLINE database was searched for articles published between 1951 and February 2008 using any combination of the terms *brain injury*, *pain*, *headache*, *blast injury*, and *combat (combat disorders, war, military medicine, wounds and injuries, military personnel, and veterans)*. The PubMed and MD Consult databases were searched in a similar fashion for additional articles. The Cochrane Collaboration, National Institutes of Health Clinical Trials Database, Meta-Register of Current Controlled Trials, and CRISP databases were searched using the keyword *brain injury*.

All selected articles were published in peer-reviewed journals and contained original data on pain syndromes after TBI with respect to prevalence, pain category, risk factors, pathogenesis, and clinical course. Manual searches were performed of the reference lists of selected articles, and the authors of 2 selected studies were contacted for additional citations. The search was not limited by language or publication status. No randomized controlled studies were found in the search (all patients were recruited into studies after the brain injury had occurred). Case reports and review articles were cited only if no other data were available (FIGURE).

The initial search yielded 1067 articles, and 43 others were selected from the reference lists of retrieved articles. Of these 1110 articles, 1087 were excluded because they did not fulfill the primary inclusion criteria; ie, the prevalence of chronic pain in their TBI populations could not be calculated. Three studies that met all other criteria were excluded because they focused on individuals younger than 16 years. Two abstracts of unpublished data were also

Figure. Selection of Articles for Inclusion in Review



TBI indicates traumatic brain injury.

included. The 3 experts contacted for this study were not aware of any negative studies that had not been published.

The data from the final 23 studies were pooled by adding results across studies. Since the studies were cross-sectional (15), prospective observational (5), or retrospective (3), none were given additional weighting. The data from the studies evaluating headache were pooled to determine the overall prevalence of headache among patients with TBI. Subsequently, the studies having groups of patients with mild TBI were compared with the studies having groups of patients with severe TBI to assess respective prevalences of chronic pain. Mild TBI was defined according to American College of Rehabilitation Medicine criteria (BOX 1).² Studies in which the investigators defined the patients as having mild TBI or severe TBI were also included. The studies were then compared with respect to chronic pain between groups of civilians and military survivors.

P values were derived by significance testing of 2 population-proportions using a 2-proportion *z* test with unequal variances. The results of each individual study were compared with those of the studies combined. The prevalence rates of pain were calculated with 95% confidence intervals (CIs) in each single study and in the pooled data. Analyses were performed using SAS version 9.1 (SAS Institute Inc, Cary, NC); *P* < .05 was considered statistically significant.

EVIDENCE SYNTHESIS

Traumatic brain injury can have detrimental consequences (BOX 2).¹¹⁻¹³ TABLE 1¹⁴⁻³⁴ and TABLE 2^{3,35,36} provide a summary of the articles selected for review. Twenty-three studies including 4206 patients reported on the prevalence of chronic pain after TBI.

Headache

Twelve studies^{14,19,23-25,27,29-34} reported on headache prevalence after TBI. Of the 1670 patients included in these stud-

ies, 966 reported experiencing chronic headache, yielding a prevalence of 57.8% (95% CI, 55.5%-60.2%). Selected studies suggest that headache is a common physical manifestation of TBI^{14,19,23-25,27,29-34} and that patients with preexisting headache syndromes often experience worsening of their prior symptoms.^{23,25}

De Benedettis and De Santis¹⁹ retrospectively studied 130 consecutive patients with TBI admitted to a university hospital in Milan, Italy. Patients with preexisting headache or who had required neurosurgery were excluded. Pain prevalence was not stratified by injury severity, but descriptive information about TBI severity was provided. After the initial injury, 26% had no change in mental status, 35% had "brief" LOC, 25% were in a superficial coma, 9% were in a coma of intermediate severity, and 5% were in a deep coma. Computed tomography (CT) scans were performed in 65%, with normal results. Sixteen percent of the patients were reevaluated between 6 and 12 months after the injury, 47% were reassessed at 2 years, and 37% had a longer follow-up period that was variable in duration. Posttraumatic headache was reported by 44% of patients after 6 months. Posttraumatic headache began at the time of injury in 30% of patients, between 15 days and 1 month in 21%, between 1 and 3 months in 18%, and after 3 months in 32%. Eleven percent still had headache at 6 months, 54% at 1 year, and 30% after 2 years. The majority of patients (52%) complained of headache of moderate intensity (3-7 on a visual analog scale). Fifty-six percent experienced headache between 4 and 15 times per month. The majority of headaches (51%) occurred in the occipital region. However, among these patients with TBI, no significant relationship was found between the location of the head trauma and the location of pain.

Jensen and Nielsen,²³ assessing patients 9 to 12 months after injury, interviewed 168 of 233 patients with suspected cerebral concussion who were admitted over a 1-year period to a county

Box 1. Acute Symptoms of Mild Brain Injury: Definition of Mild Traumatic Brain Injury According to the American Congress of Rehabilitation Medicine²

1. Any period of loss of consciousness;
2. Any loss of memory for events immediately before or after the accident;
3. Any alteration in mental state at the time of the accident (eg, feeling dazed, disoriented, or confused); and
4. Focal neurological deficit(s) that may or may not be transient; but where the severity of the injury does not exceed the following:

Posttraumatic amnesia not greater than 24 h

After 30 min, an initial Glasgow Coma Scale score of 13-15

Loss of consciousness of approximately 30 min or less

hospital in Denmark. Although 49% of these patients had been hospitalized for a mean duration of 4.3 days, all participants were classified as having sustained mild TBI. Jensen and Nielsen excluded patients with LOC longer than 24 hours, cerebral contusion, or intracerebral hemorrhage. Of the included patients, 29% reported no LOC, 44% had LOC less than 15 minutes, and 39.9% had preexisting headache. After the trauma, 64.3% of patients had headaches, with 34.3% experiencing worsening of their preexisting headache. Four patients (2.4%) reported that their baseline headaches had decreased after the trauma. This is the only selected study that comments on resolution of headache after trauma.

Rimel et al³⁰ studied 538 patients with mild TBI (defined in that study as LOC shorter than 20 minutes, Glasgow Coma Scale [GCS] score of 13 to 15, and hospital length of stay shorter than 48 hours) and conducted interviews

Box 2. Clinical Characteristics of Traumatic Brain Injury (TBI)**Mild TBI Can Lead to Deficits in**

Cognition

Attention

Memory

Calculation

Judgment

Insight

Reasoning

Sensory processing

Sight

Hearing

Touch

Communication

Language expression

Understanding

Social function

Compassion

Interpersonal social awareness

Mental health

Depression

Anxiety

Personality changes

Aggression/irritability

Social inappropriateness

Sleep disturbance

Vertigo/dizziness

Moderate to Severe TBI Can Have Additional Consequences

Abnormal states of consciousness

Deficits in speech and swallowing

Cranial neuropathies

Paresis/paralysis

Complications of prolonged bed rest

Seizure disorders

Movement disorders

All patients can exhibit signs and symptoms of trauma in addition to these symptoms.¹¹⁻¹³

jured in motor vehicle crashes, and 43% had positive blood alcohol levels. Four hundred twenty-four were followed up at 3 months postinjury; of these, 79% had persistent headaches. Of the patients employed at the time of the injury, only 66% remained employed at 3 months.

Uomoto and Esselman³³ evaluated 104 patients seen in an outpatient TBI rehabilitation program. Of these, 63.5% were male, 36.5% were female, and the average time postinjury was 26 months. Patients with mild TBI had LOC shorter than 1 hour and GCS scores of 13 to 15, while those with moderate to severe TBI had LOC longer than 1 hour and GCS scores of 12 or less. Of patients with mild TBI, 89% reported headache, compared with 18% of those with severe TBI ($P < .001$), but similar rates were found for chronic neck/shoulder, back, and other pain symptoms. The group with mild TBI also had a higher frequency of concomitant pain syndromes.

Other Potential Pain Syndromes

Some of the most mystifying pain conditions were first observed during times of war.³⁷ For example, complex regional pain syndrome (CRPS), formerly known as reflex sympathetic dystrophy, was first described after the American Civil War. In 1992, Gellman et al²¹ addressed the issue of CRPS in patients with TBI. In that study, 100 patients admitted consecutively to an inpatient rehabilitation unit with GCS scores less than 8 were evaluated for signs of CRPS. On average, the patients were 4 months post-TBI. During their hospitalizations, 13 patients developed clinical signs and symptoms of CRPS such as pain with withdrawal response, vasomotor and temperature changes, discoloration, and palmar fibrosis; these patients underwent formal testing. Of these 13 patients, 12 had bone scan results consistent with CRPS in the upper extremity. These patients also had a combined total of 8 peripheral nerve injuries, 4 fractures, 2 joints with periarticular heterotopic ossification, 1

shoulder dislocation, and 1 rotator cuff tear. Gellman et al found a 12% incidence of CRPS post-TBI, as compared with the 12.5% to 25% incidence of CRPS reported after stroke.³⁷

Garland et al²⁰ retrospectively reviewed the records of 496 adults with severe TBI admitted to a head trauma service over a 4-year period and, after excluding patients with traumatized joints, found that 100 joints in 57 patients (11%) had painful heterotopic ossification with decreased range of motion in the adjacent joint. Workup for heterotopic ossification was initiated when examiners elicited painful resistance to movement at a joint.

In terms of peripheral neuropathic pain, in a study of 132 inpatients with TBI,¹⁸ 15 were found to have flaccidity for longer than 1 month, areflexia for longer than 1 month, and abnormal motor patterns. These patients underwent nerve conduction studies and electromyography, and 13 of 132 (10%) were diagnosed with peripheral neuropathies. The mean time elapsed between the trauma and diagnosis was 51 days (range, 14-170). Of the 13 patients, 3 had preventable pressure palsies and 4 had developed signs and symptoms of CRPS.¹⁸ This study might not have captured several pain syndromes that can afflict patients. For example, central/deafferentation pain (eg, phantom limb pain) has been cited after TBI.³⁸

Neuromuscular spasticity is often seen in patients with severe TBI. It is theorized to directly cause pain as well as to indirectly lead to painful conditions such as subluxation, tendinitis, and capsulitis.³⁹ However, the presence of pain due to spasticity, as well as the ability of pain to exacerbate pre-existing spasticity, has not been well studied,³⁹ and this literature search did not reveal any studies delineating the prevalence of pain in the population of patients with TBI who experience spasticity.

Severity of Brain Injury

Ten studies^{14-16,23,24,27,30,32-34} reported the prevalence of pain in patients with mild

with 79%. The 538 patients constituted all of the mild TBIs seen at a university hospital over a 20-month period. Of these patients, 66% were male. Almost half of the patients had been in-

Table 1. Pain Prevalence in Adult Patients With Traumatic Brain Injury (TBI)^a

Study	Study Design	Total Patients	Time After Event	Severity	Pain Prevalence
Alfano et al, ¹⁴ 2000	Cross-sectional	8	>3 mo	Reported as mild TBI	88% (95% CI, 64.5%-100%) with chronic headache interfering with activities; 75% with pain elsewhere
Alfano, ¹⁵ 2006	Cross-sectional	53	12.9 (SD, 11.3) mo	LOC <30 min and posttraumatic amnesia <24 h	91.0% (95% CI, 82.6%-98.4%) with chronic pain (5.7% mild; 73.6% moderate; 32.1% severe)
Beetar et al, ¹⁶ 1996	Retrospective	202	1 mo to >60 mo	127 had LOC <30 min and posttraumatic amnesia <24 h; 75 reported as having severe TBI	70% (95% CI, 62.1%-78.0%) with mild TBI; 40% (95% CI, 28.9%-51.0%) with severe TBI 51.3% with pain at 1-12 mo; 37.8% with pain at 13-59 mo; 10.9% with pain at ≥60 mo
Bryant et al, ¹⁷ 1999	Cross-sectional	96	6.27 (SD, 1.27) mo	Mean GCS score, 8.0 (SD <3.8); mean duration of posttraumatic amnesia, 37 (SD, 31) d	62% (95% CI, 52.8%-72.1%) with pain; 9% with <1 pain episode/wk; 24% with daily pain; 7% with constant pain
Cosgrove et al, ¹⁸ 1989	Cross-sectional	132	NR	Rancho Los Amigos Scale score III to VIII	13 (10%) with peripheral neuropathy; 3 radial, 2 peroneal, 1 femoral, 2 lumbosacral plexopathies, and 8 brachial plexopathies; mean time to diagnosis of peripheral neuropathy, 51 (14-170) d
De Benedettis and De Santis, ¹⁹ 1983	Retrospective	130 ^b	Not reported	35 with LOC <24 h	44% (95% CI, 35.3%-52.4%) with headache; 30% with onset of headache after trauma; 21% at 15-30 d; 18% at 1-3 mo; 32% after 3 mo; 54% with headache at 1 y; 30% at 2 y
Garland et al, ²⁰ 1980	Cross-sectional	496	NR	Reported as having severe TBI	11% (95% CI, 8.2%-13.7%) with painful heterotopic ossification that decreased range of motion
Gellman et al, ²¹ 1992	Cross-sectional	100	Mean, 4 mo	GCS score <8	12% (95% CI, 5.6%-18.3%) with complex regional pain syndrome in upper extremity
Hoffman et al, ²² 2007	Prospective longitudinal	202 ^c	1 y	Inpatients reported as having severe TBI with mean GCS score 9.2 (SD, 3.1)	72.6% (95% CI, 65.3-79.8) with chronic pain; mean SF-36 score, 66.7 (SD, 28.4) (mean, 78.3 if violent injury; 51.0 if nonviolent injury); 55% with pain interfering with activities
Jensen and Nielsen, ²³ 1990	Cross-sectional	168	9-12 mo	LOC <24 h	39.9% with preexisting headache; 64.3% (95% CI, 57.0%-71.5%) with posttraumatic headache
Lahz and Bryant, ²⁴ 1996	Cross-sectional	132	Mild TBI: 10.5 (SD, 33.1) mo Severe TBI: 12.6 (SD, 33.7) mo	40.1% with LOC <1 h and GCS score 13-15; 59.8% with GCS score ≤12	Mild TBI: 58% (95% CI, 45.2%-71.7%) with chronic pain; 47% with headache; 28% with neck/shoulder pain; 19% with low back pain Severe TBI: 52% (95% CI, 40.9%-62.9%) with chronic pain; 34% with headache; 24% with neck/shoulder pain; 16% with low back pain
Landy, ²⁵ 1998	Prospective longitudinal	135	3 mo-7 y	Posttraumatic amnesia <2 h	63.7% (95% CI, 55.6%-71.2%) with headache
Leung et al, ²⁶ 2007	Prospective longitudinal	87	45 (SD, 24) d	Inpatients with mean posttraumatic amnesia duration of 54 (SD, 46) d	65% (95% CI, 53.9%-75.7%) with shoulder pain (35.4% bilaterally)
Mooney et al, ²⁷ 2005	Cross-sectional	67	>3 mo	Reported as having mild TBI	72% (95% CI, 61.1%-82.7%) with headache; 64% with pain elsewhere 9% with mild TBI + pain; 49% with mild TBI + pain + psychiatric diagnosis; 34% with history of psychological trauma; 57% of those with childhood abuse or sexual trauma and with correlation between pain and postconcussive symptoms (<i>P</i> < .001)
Olver et al, ²⁸ 1996	Prospective longitudinal	254 ^d	2 y/5 y	NR	31% (95% CI, 25.4%-36.8%) with headache at 2 y; 42% with headache at 5 y
Ouellet et al, ²⁹ 2006	Cross-sectional	452	Mean, 7.85 y	16.8% with GCS score 13-15, LOC <30 min, and negative imaging results; 83.2% reported as having severe TBI	59% (95% CI, 54.5%-63.6%) with pain

(continued)

Table 1. Pain Prevalence In Adult Patients With Traumatic Brain Injury (TBI)^a (cont)

Study	Study Design	Total Patients	Time After Event	Severity	Pain Prevalence
Rimel et al, ³⁰ 1981	Cross-sectional	424	3 mo	LOC <20 min and GCS score 13-15	79% (95% CI, 74.8%-82.7%) with headache
Schaller, ³¹ 1939	Cross-sectional	100	NR	Reported as severe TBI	77% (95% CI, 68.7%-85.2%) with headache
Smith-Seemiller et al, ³² 2003	Cross-sectional	27	12.3 (SD, 15.5) mo	Reported as having mild TBI	93.0% (95% CI, 82.7%-100%) with chronic pain; 81% with headache; 41% with pain elsewhere
Uomoto and Esselman, ³³ 1993	Retrospective	104	Mild TBI: 24.2 (SD, 30.6) mo Severe TBI: 28.0 (SD, 37.0) mo	Mild TBI: n = 55 with LOC <1 h or GCS score 13-15 Severe TBI: n = 49 with GCS score <12	60.6% (95% CI, 51.1%-70.0%) with chronic pain; 94.5% (95% CI, 88.5%-100%) with mild TBI and chronic pain; 89% with mild TBI and headache; 22% (95% CI, 10.7%-34.1%) with severe TBI and chronic pain; 18% with severe TBI and headache; 13% with mild TBI with 4 sites of pain vs 0% with severe TBI; 47% with TBI with headache and concurrent shoulder pain; 44% with headache and concurrent low back pain
Yamaguchi, ³⁴ 1992	Cross-sectional	121	NR	52.9% with mild TBI; 47.1% with severe TBI	71.8% (95% CI, 60.9%-82.9%) with mild TBI and severe headache; 33.3% (95% CI, 21.0%-45.6%) with severe TBI and severe headache

Abbreviations: CI, confidence interval; GCS, Glasgow Coma Scale; LOC, loss of consciousness; NR, not reported; SF-36, 36-Item Short-Form Health Survey.

^aData from 12 studies^{14,19,23-25,27,29-34} assessing headache were pooled and showed that 966 of 1670 patients experienced chronic headache, yielding a prevalence of 57.8% (95% CI, 55.5%-60.2%). For the purposes of this review, mild TBI was defined according to American College of Rehabilitation Medicine criteria. Studies in which the investigators defined the patients as having mild or severe TBI were also included. Civilian data from 10 studies^{14-16,23,24,27,30,32-34} on mild TBI were pooled, as were data from 9 studies^{16-18,20,22,24,33,34} on severe TBI.

Among civilians, the prevalence of chronic pain was greater in patients with mild TBI (75.3% [95% CI, 72.7%-77.9%]) compared with severe TBI (32.1% [95% CI, 29.3%-34.9%]).

^bFollow-up data available for 16% at 1 year, for 47% at 2 years, and for 35% beyond 2 years.

^cFollow-up data available for 146.

^dFollow-up data available for 103.

TBI. Of the 1046 patients included in these studies, 788 reported pain, producing a prevalence rate of 75.3% (95% CI, 72.7%-77.9%). Nine studies^{16-18,20-22,24,33,34} furnished data on the prevalence of pain in patients with severe TBI. Of the 1063 patients included in these studies, 341 reported chronic pain, producing a prevalence rate of 32.1% (95% CI, 29.3%-34.9%).

Although this review confirmed the clinical perception that patients with mild TBI have a higher prevalence of chronic pain syndromes than those with moderate to severe TBI ($P < .001$), it remains unclear why this should be so. Part of the problem may be that patients with more severe TBI may have difficulty reporting or processing their symptoms because of memory disturbances, language deficits, and executive dysfunction.⁴⁰

Combat Veterans

Given that TBI is the hallmark injury of the current conflicts in Iraq and Afghanistan,⁹ the high prevalence of chronic pain after TBI is of particular significance. Our literature search produced 3 studies^{3,35,36} including a total

of 917 combat veterans with data regarding the prevalence of pain among patients with combat-associated brain injuries. Of these 917 patients, 395 complained of pain, yielding an estimated prevalence rate of 43.1% (95% CI, 39.9%-46.3%). These 3 studies^{3,35,36} described 329 of the 917 combat veterans as having headache, producing a prevalence rate of 35.9% (95% CI, 32.8%-39.0%). Twenty studies¹⁴⁻³⁴ including a total of 3289 civilian patients with TBI yielded a chronic pain prevalence of 51.5%.

Hoge et al³ performed a large cross-sectional study of 2525 US Army Infantry soldiers with combat exposure in Iraq or Afghanistan. Of these, 95.5% were men and 55.5% were younger than 30 years. Of those soldiers who had attended study recruitment meetings, 59% completed the study. The lack of availability for soldiers to complete the questionnaires was attributed to normal transfers and training, although it is possible that soldiers with more serious illnesses and injuries did not have the opportunity to participate. Although the study used a convenience sample, it appears to be representative

of Operation Iraqi Freedom/Operation Enduring Freedom veterans. The soldiers were questioned at 3 to 4 months after their return to the United States to provide an appropriate amount of time to assess for postconcussive symptoms while minimizing recall bias. Of the soldiers completing the study, 4.9% experienced LOC shorter than 30 minutes, and 10.3% had alterations in mental status without LOC. Criteria for PTSD were met by 43.9% of soldiers with LOC and 27.3% of those with altered mental status without LOC; PTSD also was diagnosed in 16.2% of the soldiers with injuries other than TBI and in 9.1% of uninjured soldiers. Controlling for other factors, LOC and combat intensity remained significantly associated with PTSD (odds ratio for LOC, 2.98 [95% CI, 1.70-5.24]; for highest vs lowest quartiles of combat intensity, 11.58 [95% CI, 2.99-44.82]), and LOC was independently associated with the diagnosis of major depression (odds ratio, 3.67 [95% CI, 1.65-8.16]). After adjusting for PTSD and depression, TBI was no longer correlated with any physical health symptoms except for headache pain.

Table 2. Pain Prevalence In Military Survivors With Traumatic Brain Injury (TBI)^a

Study	Study Design	Total Patients	Time After Event	Severity of Injury	Pain Prevalence
Hoge et al, ³ 2008	Cross-sectional	375	>3-4 mo	Reported as mild TBI based on LOC and altered mental status	At least 40% (95% CI, 35.0%-45.0%) with 1 pain complaint; 22% (95% CI, 18.2%-26.6%) with headache
Walker et al, ³⁵ 2005	Prospective longitudinal	109	On return from deployment, 6 mo, and 1 y	Reported as severe TBI	38% (95% CI, 28.5%-46.7%) with headache (53.7% at 6 mo; 51.2% at 1 y)
Warden et al, ³⁶ 2005	Cross-sectional	433	On return from deployment	74% with LOC \leq 1 h; 43% with posttraumatic amnesia <24 h	47% (95% CI, 42.4%-51.8%) with headache

Abbreviations: CI, confidence interval; GCS, Glasgow Coma Scale; LOC, loss of consciousness.

^aTwenty studies^{14-25,27-34} including a total of 3289 patients with TBI yielded a chronic pain prevalence of 51.5%. Three studies^{3,35,36} assessed TBI among 917 veterans and yielded a pain prevalence of 43.1% (95% CI, 39.9%-46.3%). Military survivors were less likely than civilians to report chronic pain.

Walker et al³⁵ evaluated 109 patients with severe TBI seen consecutively at 1 of 4 rehabilitation Veterans Affairs medical centers. These patients were seen for acute rehabilitation and reevaluated at 6 and 12 months. Of the 109 patients, 38% had acute postconcussive headache, with 48.8% experiencing this in the frontal area; 75.6% had daily headache. No relationship was found between the presence of headache and demographic, injury severity, or emotional variables. Improvement at 6 months was associated with less anxiety and depression. Of the patients who had headache at 6 months, 95.5% continued to have headache at 12 months. At the times of follow-up, the severity of posttraumatic headache had decreased.

Contrary to expectations, the prevalence rate of pain after TBI appears to be higher in civilians than in combat veterans. This could be due to a variety of reasons. Military survivors may be less likely to report pain because of factors such as peer pressure or fear of being medically evaluated and perhaps separated from fellow soldiers. Conversely, civilians may be more likely to overreport their pain, potentially for secondary gain. Or, since convenience samples were used, civilians with unresolved pain may be recruited more frequently into these studies. The characteristics of the samples may differ as well.

Military personnel may be healthier than their civilian cohorts. Previous studies have suggested that pain in soldiers is primarily due to the increased

level of physical activity experienced during military training.⁴¹

Of the 3 studies of combat veterans,^{3,35,36} 2 were performed immediately after the soldiers returned from deployment.^{35,36} It could be argued that this was too early for chronic posttraumatic headache to develop. However, in a retrospective study of 70 civilian outpatients experiencing posttraumatic headache, 35% developed the headache within an hour of the initial trauma, 14% within 24 hours, and 27% within 7 days. Of the 70 outpatients, 56% described chronic daily headache with symptoms for at least 21 of the 30 days recorded. Most patients reported that the pain was of at least moderate intensity and often interfered with work-related and other functional activities.⁴²

Finally, given the importance that the Departments of Defense and Veterans Affairs have placed on TBI screening among returning soldiers as well as the overlap in criteria between TBI and PTSD among other psychiatric disorders, the number of true TBIs in the military sample may be overestimated. This in turn may dilute the sample and cause an underestimation of the true prevalence of pain in that population.

Military survivors with brain injuries may have a variety of pain syndromes. In the survey by Hoge et al,³ in those soldiers who reported having sustained TBI during deployment (as compared with soldiers having other injuries), 32.2% had headache ($P < .001$), 14.0% had chest pain ($P < .001$), and

8.3% had pain or problems during sexual intercourse ($P = .04$). Although the difference between groups was not statistically significant, individuals with TBI also reported stomach pain (11.7%), back pain (33.1%), and arm, leg, or joint pain (37.2%).

It is possible that individuals having TBI due to violent trauma, such as assaults, have increased pain compared with those having TBI due to unintentional trauma, such as sports injuries or falls.⁴³ This review could not distinguish civilians who had sustained TBI through random violence from the rest of the sample. Although patients who had sustained violent injuries were not excluded from any of the studies reviewed, none of the studies created subgroups based on mechanism of injury.

Psychiatric Disorders

The relationship between pain and mood disorders such as depression is complex. Hoffman et al²² evaluated 146 of 202 consecutive patients during inpatient rehabilitation and at 1 year postinjury. These patients had severe TBI, defined as a GCS score of 12 or less. Of the 146 patients, 76% were male and 24% were female; 78.1% were white and 21.9% were of other race/ethnicity; and 48.6% were injured in motor vehicle crashes and 11.6% through violence. Of the evaluated patients, 72.6% had pain 1 year out from their injuries, and 55% reported interference with activities of daily living. The mean bodily pain score on the 36-Item Short-Form Health Survey was 66.7 on a scale of 100. Higher

pain scores at 1 year postinjury were associated with depression during inpatient rehabilitation, female sex, and race/ethnicity other than white. Pain was associated with community participation, but, when depression was factored in, the pain variable lost significance. This study underscores the relationship between pain and mood disorders.

Bryant et al¹⁷ examined 96 of 161 patients admitted for severe TBI to a tertiary-care TBI unit to determine whether there was a relationship between pain and PTSD measures. In that study, 22 patients were excluded because of cognitive dysfunction causing them to be unable to understand or respond to the interviewer. The final population was evaluated between 5 and 7 months posttrauma. Chronic pain was defined as pain at least once a week of greater than 6 months' duration. The McGill Pain Questionnaire and a 10-point scale were used to assess pain complaints. Of the included patients, 62% reported chronic pain, 24% reported daily pain, and 7% reported constant pain. Bryant et al found that higher pain severity was associated with increased severity of PTSD, depression, poor satisfaction with life, and avoidant coping style. After controlling for the effects of PTSD, the only factor that still correlated with pain severity was avoidant coping style.

Other studies have supported the relationship between chronic pain syndromes and PTSD.⁴⁴⁻⁴⁷ Trauma patients with multiple symptoms of PTSD generally report higher levels of pain and affective disturbances than those who do not have many symptoms of PTSD.⁴⁸

The relationship between brain injury and PTSD has been debated since 1939, when Schaller³¹ surmised that the rate of pain in posttrauma psychoneurotic states would be greater than that in patients with TBI. In the cohort of 100 patients with TBI in that study, 77% had persistent headache, which was similar to the rate of headache (97%) in patients with "posttraumatic psychoneurosis or hysteria."

PTSD may be associated with increased pain severity for many reasons. Pain perception can be heightened by increased anxiety, and the ability to cope with pain in PTSD may be impeded by catastrophic interpretations of pain. In addition, patients may not have the concentration required, due to intrusive thoughts, to use cognitive strategies to reduce pain. Alternatively, they may display an attentional bias to negative events. Finally, the concordance between PTSD and somatoform pain disorder is high.¹⁷

Although several studies attest that substance abuse may be a causative factor in the occurrence,⁴⁹ severity,⁵⁰ and prognosis⁵⁰ of TBI, no studies have examined the relationship between substance abuse and pain after TBI. It is possible, however, that patients may use illicit substances to self-medicate for pain.

COMMENT

This review is limited by several factors. First, all of the studies were cross-sectional, observational, or retrospective. Second, the civilian study populations demonstrated heterogeneity in terms of comorbid psychiatric disorders, cause of injury, and time elapsed since injury, as well as in the recruitment procedures. Patients were recruited from rehabilitation units and clinics but not from skilled nursing facilities, where the most severely injured patients might reside. All of the studies used convenience samples rather than random samples. Third, all of the information gathered relied on patient report. It is possible that patients with TBI who had more cognitive dysfunction were unable to comprehend or accurately respond to questions about their pain. Fourth, the definition of TBI varied across studies, as did the definitions and measures of chronic pain. Fifth, most studies did not provide information key to subgroup analyses.

Further research in brain injury would benefit from standardized criteria for measurement of severity of TBI. Data analysis would be enhanced by re-

porting of symptoms based on severity, mechanism, and duration of injury, as well as on comorbid psychiatric disorders.

Chronic pain is a common complication of TBI and contributes to morbidity and potentially poor recovery after brain injury. Patients who appear clinically to have less severe brain injuries may in fact develop more pain symptoms. Patients who have sustained TBIs in combat have a higher rate of chronic pain than the general population. However, they appear to have lower rates of pain than civilians with TBI. Patients with TBI would benefit from early screening and treatment for pain syndromes to decrease the morbidity that untreated chronic pain additionally imposes on them and on society. In addition, clinicians treating patients who have any history of mild head injuries should consider inquiring further about coexisting symptoms. These may affect how the patients comprehend and follow treatment recommendations.

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