The Long-Term Psychiatric Sequelae of Severe Injury:
A 6-Year Follow-Up Study

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ABSTRACT

Objective: The impact of mental health on disease burden associated with injury represents a major public health issue, yet almost no information is available on the associated long-term mental health outcomes. The primary aim of this study was to assess the psychiatric outcomes 6 years after a severe injury and their subsequent impact on long-term disability. The secondary aim was to investigate the relationship between a mild traumatic brain injury (mTBI) and long-term psychiatric disorder and its impact on disability.

Methods: From April 2004 to February 2006, randomly selected injury patients admitted to 4 hospitals across Australia were assessed during hospitalization and at 72 months after trauma (N = 592). Injury characteristics, the presence of an mTBI (*ICD-9* criteria), and previous psychiatric history were assessed during hospitalization. Structured clinical interviews for psychiatric disorders (*DSM-IV* and *DSM-5*) and a self-report measure of disability (WHODAS II) were administered at 72 months.

Results: At 72 months after a severe injury, 28% of patients met criteria for at least 1 psychiatric disorder, with 45% of those presenting with comorbid diagnoses. The most prevalent psychiatric disorder was a major depressive episode (11%) followed by substance use disorder (9%), agoraphobia (9%), posttraumatic stress disorder (6%), and generalized anxiety disorder (6%). The presence of any psychiatric disorder was found to increase the risk for disability ($P < .001$, odds ratio = 6.04). An mTBI was found to increase the risk for having some anxiety disorders but not to increase disability by itself.

Conclusions: The long-term psychiatric consequences of severe injury are substantial and represent a significant contributor to long-term disability. This study points to an important intersection between injury and psychiatric disorder as a leading contributor to disease burden and suggests this growing burden will impose new challenges on health systems.

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Injury is a growing contributor to the global burden of disease.[1] The 2010 report of the Global Burden of Disease[2] highlights that injury accounted for 75.5 million disability-adjusted life-years (up from 56.7 million in 1990). While most injury research has focused on physical consequences, more recently the psychiatric impact of injury has been recognized. In one of the most comprehensive studies to date,[3] our research group found that 24% of those hospitalized for injury developed at least 1 new psychiatric disorder in the first 12 months postinjury. Importantly, there is evidence that psychiatric disorders are a powerful contributor to injury-related disability.[4,5] The impact of mental health on disease burden associated with injury therefore represents a major public health issue.

Most research into psychiatric outcomes after injury has focused on posttraumatic stress disorder (PTSD) and major depressive disorder (MDD). After experiencing a severe injury, PTSD prevalence rates range from 10%–28%, and MDD rates range from 7%–29%.[3,6,7] Patients in the current injury sample were previously subjected to a comprehensive analysis of psychopathology at 12 months after their trauma.[3] In addition to elevated depression and PTSD rates, other anxiety disorders and substance use disorders were also higher than comparable community samples.

While the research examining psychiatric disorders after injury is well developed in the short term, there is limited research examining long-term psychiatric outcomes. Studies into the long-term (ie, greater than 5 years) psychiatric sequelae of injury are critical if progress is to be made in determining the health burden and needs of injury survivors. In the only study to date to examine long-term psychiatric outcomes, Mayou et al[8] found that 8% of injury patients met criteria for PTSD, and 28% were classified as probable for a specific phobia (ie, travel) at 5 years postinjury. However, no other psychiatric disorders were examined. While other studies have examined long-term mental health outcomes after specific injuries such as spinal cord injury[9] or traumatic brain injury,[10] the degree to which the findings generalize to the majority of patients admitted to trauma services is unknown. Hence, there is an urgent need to establish estimates of long-term outcome associated with serious injury.

Research investigating the role of psychological factors on disability after injury has grown recently. Zatzick and colleagues[7] found that in a US injury sample, both depression and PTSD were associated with lower functional outcomes at 12 months postinjury. In our own research, we found that psychiatric symptoms 1 week after a severe injury and at 12 months after injury were the greatest predictors of disability 12 months

Clinical Points

- Psychiatric disorders are highly prevalent in the first 12 months after severe injury, but their long-term prevalence (greater than 5 years) has not been previously investigated.
- Mild traumatic brain injury can be associated with an additional risk for developing anxiety and fear-based disorders beyond the risks incurred by severe injury, and this risk is enduring.
- Analysis 6 years postinjury shows that if patients' recovery is delayed following severe injury and their level of disability is high, it is essential that a comprehensive mental health assessment be completed.

after injury.[4] The important role played by psychiatric symptoms in predicting disability has also been established in a predominantly minor-injury motor vehicle accident sample.[11] However, no studies to date have examined the impact of psychiatric disorder on long-term injury disability outcomes in a prospective study.

Recent evidence has emerged highlighting the important role played by mild traumatic brain injury (mTBI) as a risk factor for negative psychiatric outcomes. For example, it has been found that at 12 months postinjury, injuries that include an mTBI are associated with higher levels of psychopathology than injuries without an mTBI.[3] This is consistent with other research that has established a link between mTBI and an increased risk for psychiatric disorders.[12–14] The long-term outcomes of mTBI, however, are unclear, as the majority of studies have been limited to 6–12 months, are cross-sectional in design, or have a small sample. Additionally, few studies comprehensively investigate a range of psychiatric disorders in mTBI samples.[3,15]That mTBI can cause longer-term impairments is of great importance, given the perception that the injury is transient in nature.[16] Therefore, it is imperative to disentangle the role of mTBI from other potential risk factors for a psychiatric disorder following injury.

This current study reports the long-term follow-up of the Australian Injury Vulnerability Study, a large longitudinal multisite study of injury patients. The aim of the 6-year wave of data collection was to investigate (1) the 1-month point prevalence and incidence of Axis I psychiatric disorders using structured clinical interviews; (2) the association of psychiatric disorder with disability; and (3) the relationship between mTBI and long-term psychiatric outcomes and its impact on disability.

METHODS

Participants

A detailed description of the original sample has been provided previously.[3] In brief, admissions across 4 level I trauma centers in Australia were recruited to the study from April 2004 to February 2006 provided the patient was aged between 16 and 70 years, was proficient in English, and had experienced an injury that required hospitalization for greater than 24 hours. A level I trauma center provides the full spectrum of care (comprehensive service) to critically injured patients 24 hours a day. We excluded patients older than 70 years to minimize the potential bias of age-related cognitive decline on changes in psychopathology across the 6 years of the study. Patients also were excluded from the study if they were suicidal or psychotic, had a serious spinal cord injury, or had a moderate to severe traumatic brain injury. Patients were included if they had a mild traumatic brain injury defined according to *ICD-9*, which requires a documented blow to the head, loss of consciousness for less than 30 minutes, and no focal neurologic deficit or intracranial complication.[17] Patients were selected for the study using an automated random selection procedure with stratification by length of stay.[18]

Baseline data were collected prior to discharge, and follow-up assessments were conducted 3, 12, 24, and 72 months after discharge. Three- and 12-month prevalence rates are reported elsewhere.[3] Of the original sample completing baseline assessments (N = 1,084), 592 (55%) completed the 72-month assessment. Those who completed the 72-month assessment did not differ from noncompleters in gender, length of hospital admission, injury severity, past psychiatric history, or mTBI status. Completers of the 72-month assessment were slightly older than noncompleters (mean age = 39.5 vs 36.0 years, $P < .001$).

Demographic information for participants who completed the 72-month assessment is provided in Table 1. Those with an mTBI did not differ from those without an mTBI on length of hospital admission, gender, or past psychiatric history. Those with an mTBI were slightly younger (mean = 38.0 vs 40.6 years of age, $P = .02$), had higher Injury Severity Score (ISS) scores (mean = 13.9 vs 9.0, $P < .001$), spent more days in the intensive care unit (mean = 1.6 vs 0.5, $P < .001$), and were more likely to be single (52.7% vs 42.6%, $P = .037$).

Measures

Prevalence and incidence of psychiatric disorders. The Mini-International Neuropsychiatric Interview (MINI version 5.5)[19] was administered twice. It was administered just after the injury event to assess for psychiatric disorder prior to index injury (ie, a retrospective measure). It was also administered at 72 months postinjury to assess 72-month diagnosis (1-month point prevalence) of major depressive episode (MDE), PTSD (prior to injury), generalized anxiety disorder (GAD), social phobia, panic disorder, agoraphobia, obsessive-compulsive disorder (OCD), and a substance use disorder. The MINI is based on the *DSM-IV* and the *ICD-10* classifications of mental illness and has good reliability for all included diagnoses.[19]

One-month PTSD prevalence at the 72-month assessment point was assessed using the Clinician-Administered PTSD Scale (CAPS).[20] In this study, PTSD symptoms were anchored to the index injury event. PTSD was also assessed applying *DSM-5* criteria with adapted questions written by the original authors or the CAPS. The results tables include both *DSM-IV* and *DSM-5* data, while in the text unless explicitly stated otherwise, we are referring to *DSM-5* PTSD.

Table 1. Demographic Information for the Sample of Severe Injury Patients Who Were Followed Up at 72 Months Postinjury (N = 592)

Variable	Value
Age, mean (SD), y	39.5 (13.5)
Male, %	71.5
Relationship status at time of injury, %	
Married or living together	52.7
Single	47.3
Mechanism of injury, %	
Motor vehicle accident	66.6
Fall	16.2
Assault	6.1
Work	4.7
Other	6.4
Injury characteristics	
Injury Severity Score, mean (SD)	11.1 (7.7)
Length of stay, mean (SD), d	12.9 (14.4)
Discharge to rehabilitation facility, %	21.3
Intensive care unit stay, mean (SD), d	1.0 (3.6)
Psychiatric history, %	60.2

Disability. Disability at 72 months was measured using the World Health Organization Disability Assessment Schedule II (WHODAS II).[21] Using a 12-item 5-point Likert scale, the WHODAS II measures 6 domains of activity limitations: understanding and communication, getting around, self-care, getting along with others, household and work activities, and participation in society. The WHODAS II was dichotomized into disability (≥ 10) and no (or lesser) disability (< 10). Normative data for the Australian population found 10% of respondents scored 10 or above, and the same recoding rules have been used previously.[22]

Pain. Average pain severity was measured using a Visual Analog Scale (VAS).[23]

Health service use. Number of visits to a psychiatrist, psychologist, and other mental health specialist over the preceding 24 months was recorded by self-report.

Hospital records. Information regarding the injury (eg, injury severity, Glasgow Coma Scale,[24] presence of a loss of consciousness, length of posttraumatic amnesia, mechanism of injury) was obtained from the hospital files. Injury severity was assessed using the ISS.[25]

Procedure

Informed consent was received from all participants. The study received ethics approval from each hospital. Patients were assessed prior to discharge (on average 7.2 days after their injury) in a face-to-face interview. Here the MINI was administered by trained researchers to assess lifetime psychiatric disorder. A self-report questionnaire was also given to participants that included the VAS.

Patients were reassessed at 72 months. Self-report questionnaires that included the WHODAS II and VAS were mailed to participants and returned in a replied paid envelope. The CAPS and MINI were administered by telephone interview, a reliable way of conducting the assessment.[26] Five percent of interviews were randomly selected and reassessed by a blinded, independent assessor. Diagnostic consistency for the MINI across all diagnoses was as follows: Lifetime = 1.00, 72 months = 1.00. The diagnostic consistency for the CAPS at 72 months was 1.00.

Data Analysis

The injury sample 1-month prevalence rate at 72 months was defined as the rate of disorder at 72 months. The injury sample 1-month incidence rate at 72 months was computed by excluding patients who had a history of the same psychiatric disorder at any time prior to the index injury.

Fisher exact tests were used to compare prevalence rates of psychiatric disorders at 72 months with Australian community norms. To investigate the association of psychiatric disorder with disability, a group of logistic regressions was conducted. Control variables were entered into block 1 (age at admission, VAS at baseline, motor vehicle accident [yes/no], psychiatric history [yes/no], mTBI [yes/no], and ISS) and psychiatric disorders were entered in block 2 to predict levels of disability at 72 months.

Fisher exact tests were used to compare prevalence and incidence rates of psychiatric disorders at 72 months between those with and without an mTBI. To further explore the risk that an mTBI infers in developing a psychiatric disorder, a set of logistic regressions was conducted. Control variables were entered into block 1 (age at admission, VAS at baseline, motor vehicle accident [yes/no], psychiatric history [yes/no], and ISS), and in block 2 mTBI was entered to predict the presence of a psychiatric disorder. Another set of logistic regressions was conducted to investigate how mTBI uniquely impacted disability. Here, the same control variables were entered in block 1. In block 2, mTBI with various psychiatric disorders (yes/no) were entered. Adjusted odds ratios with 95% confidence intervals were calculated for each logistic regression.

Prior to this study, only the Australian national 12-month prevalence rates were available from the 2007 National Survey of Mental Health and Well-being.[27] To permit a comparison in this study, we calculated the Australian national point prevalence rates using the data from this survey. We were provided with access to the raw data, which included whether participants reported symptoms in the last 30 days. This information was used to generate the Australian national point prevalence rates (see Table 2) using the same statistical procedures as described by Slade et al.[27]

RESULTS

At 72 months after injury, the 1-month point prevalence rate for any psychiatric disorder was 28% and the 1-month incidence for any psychiatric disorder was 19.4%. Table 2 shows the injury sample prevalence and incidence rates for each disorder and the Australian community point prevalence rates. For comparison purposes, the 12-month disorder rates from Bryant et al[3] have also been included. Prevalence rates at 72 months for all psychiatric disorders in the injury sample were significantly higher than those of the general Australian community. There was evidence that these disorders were persistent. For example, 56% (20 of 36)

Table 2. Australian Community (N = 8,841) 1-Month Point Prevalence and Injury Sample (n=592) 1-Month Incidence and Prevalence Rates 72 Months After Injury (all values shown as %)

Disorder	Australian 1-Month Point Prevalence[a]	12-Month Prevalence[b]	Injury Sample 72-Month Prevalence Total	mTBI	No mTBI	72-Month Incidence Total	mTBI	No mTBI
Posttraumatic stress disorder (*DSM-5*)	NA	NA	6.1**	8.4[c]	4.4	4.7	8.0[c]	4.2
Posttraumatic stress disorder (*DSM-IV*)	2.5	9.7	7.4**	10.4[d]	4.7	6.2	10.5[d]	4.5
Social phobia	2.4	6.7	4.1*	6.8[d]	2.1	3.0	5.0[c]	1.6
Panic disorder	0.6	5.9	2.0**	3.6[c]	0.9	1.3	2.2[e]	0.3
Agoraphobia	0.6	9.7	9.0**	9.6[d]	8.5	5.6	9.3[d]	7.6
Obsessive-compulsive disorder	2.1	3.5	4.7**	8.4[d]	2.1	4.3	7.1[d]	2.2
Generalized anxiety disorder	0.9	11.1	6.1*	6.4[d]	5.9	2.8	4.7[d]	4.9
Major depressive episode	2.0	16.3	11.0**	10.8[d]	11.1	3.9	6.1[d]	7.5
Substance use disorder	2.0	9.9	9.3**	9.2[d]	9.4	3.8	5.7[d]	3.2
Any psychiatric disorder	9.3	31.0	27.7**	29.9[d]	26.1	19.4	23.7[d]	14.7

[a]Rates calculated using data and formula from Slade et al.[27]
[b]Rates originally presented in Bryant et al.[3]
[c]$P < .05$ compared with no mTBI. [d]$P < .01$ compared with no mTBI. [e]$P = .09$ compared with no mTBI.
*$P < .05$. **$P < .001$ sample prevalence rate compared with the Australian Point Prevalence.
Abbreviations: *DSM-5* = *Diagnostic and Statistical Manual for Mental Disorders*, Fifth Edition; *DSM-IV* = *Diagnostic and Statistical Manual for Mental Disorders*, Fourth Edition; mTBI = mild traumatic brain injury; NA = not applicable.

Table 3. Adjusted Odds Ratio for Reporting High Disability at 72 Months Postinjury for Each Psychiatric Disorder[a]

Diagnosis	Est	SE	*P*[b]	OR	95% CI Low	95% CI High
PTSD (*DSM-5*)	2.56	0.58	**<.001**	12.96	4.18	40.19
PTSD (*DSM-IV*)	2.01	0.47	**<.001**	7.47	2.97	18.78
Social phobia	1.59	0.56	**.005**	4.89	1.63	14.64
Panic disorder[c]						
Agoraphobia	1.32	0.37	**<.001**	3.76	1.82	7.77
Obsessive-compulsive disorder	0.82	0.45	.066	2.27	0.95	5.45
Generalized anxiety disorder	1.51	0.46	**.001**	4.51	1.85	11.00
Major depressive episode	2.71	0.41	**<.001**	14.97	6.71	33.38
Substance use disorder	1.31	0.37	**<.001**	3.71	1.81	7.58
Any psychiatric disorder	1.81	0.26	**<.001**	6.09	3.70	10.04

[a]Control variables: age, pain severity at baseline, psychiatric history (0/1), type of trauma (motor vehicle accident 0/1), Injury Severity Score, and mild traumatic brain injury status (0/1).
[b]Boldface values indicate statistical significance.
[c]Every person who met panic disorder criteria at 72 months also met disability threshold precluding odds ratio analyses.
Abbreviations: *DSM-5* = *Diagnostic and Statistical Manual for Mental Disorders*, Fifth Edition; *DSM-IV* = *Diagnostic and Statistical Manual for Mental Disorders*, Fourth Edition; OR = odds ratio; PTSD = posttraumatic stress disorder.

Table 4. Adjusted Odds Ratio for Developing a Psychiatric Disorder Among Patients Who Had mTBI Compared With non-mTBI Patients[a]

Disorder	Est	SE	*P*[b]	OR	95% CI Low	95% CI High
PTSD (*DSM-5*)	0.65	0.39	.096	1.92	0.89	4.14
PTSD (*DSM-IV*)	0.84	0.38	**.025**	2.32	1.11	4.84
Social phobia	1.42	0.54	**.009**	4.12	1.42	11.93
Panic disorder	2.35	1.10	**.033**	10.44	1.21	90.43
Agoraphobia	−0.22	0.34	.523	0.81	0.42	1.56
Obsessive-compulsive disorder	1.32	0.47	**.005**	3.74	1.49	9.39
Generalized anxiety disorder	−0.12	0.39	.753	0.88	0.41	1.90
Major depressive episode	−0.16	0.30	.598	0.85	0.47	1.54
Substance use disorder	−0.35	0.34	.313	0.71	0.36	1.39
Any psychiatric disorder	−0.04	0.22	.841	0.96	0.63	1.46

[a]Control variables: age, pain severity at baseline, psychiatric history (0/1), type of trauma (motor vehicle accident 0/1), and Injury Severity Score.
[b]Boldface values indicate statistical significance.
Abbreviations: *DSM-5* = *Diagnostic and Statistical Manual for Mental Disorders*, Fifth Edition; *DSM-IV-TR* = *Diagnostic and Statistical Manual for Mental Disorders*, Fourth Edition; mTBI = mild traumatic brain injury; OR = odds ratio; PTSD = posttraumatic stress disorder.

of those who had PTSD at 72 months were also diagnosed with PTSD in the first 12 months after their injury. Similarly 62% (40 of 65) of those who had MDE at 72 months were also diagnosed with MDE in the first 12 months after their injury.

The psychiatric presentations were highly complex as indicated by the high level of comorbidity. Of those diagnosed with a psychiatric disorder at 72 months (n = 163, [mTBI = 75, no mTBI = 88]), 45% (n = 74) met criteria for more than 1 psychiatric disorder (range, 1–7; mean = 1.9; SD = 1.3). Although PTSD is often the focus of posttrauma research, it was notable that 78% of all patients with psychiatric diagnoses at 72 months did not have a diagnosis of PTSD. Only 7% of PTSD cases occurred with no comorbid disorders. Major depression (65%), anxiety disorders (73%), and substance use disorders (86%) occurred more often without PTSD than with PTSD. The proportion of comorbidity among those diagnosed with a psychiatric disorder in the mTBI group was 55% (n = 41) and in the no mTBI group it was 38% (n = 33).

At 72 months postinjury, high levels of disability were reported with 31% of the total sample scoring above threshold relative to 10% in the Australian community.[22] Table 3 reports the risk for reporting high disability associated with each psychiatric disorder. Each psychiatric disorder, except for OCD, significantly contributed to disability risk. Panic disorder was particularly associated with high levels of disability, with every case of panic reaching disability threshold. MDE and PTSD were also associated with high likelihood of disability—participants with these disorders were 13–15 times more likely to report high disability than those without. Despite the high levels of psychopathology

Table 5. Adjusted Odds Ratio for Reporting High Disability for Mild Traumatic Brain Injury and Comorbid Psychiatric Disorders at 72 Months[a]

					95% CI	
Diagnosis	Est	SE	*P*	OR	Low	High
Mild traumatic brain injury (mTBI)	0.18	0.23	.417	1.20	0.77	1.87
mTBI and PTSD (*DSM-5*)	2.19	0.73	**.003**	8.96	2.13	37.26
mTBI and PTSD (*DSM-IV*)	1.66	0.58	**.004**	5.26	1.70	16.22
mTBI and MDE	3.40	0.83	**<.001**	30.03	5.89	153.10
mTBI and any anxiety disorder	1.62	0.41	**<.001**	5.07	2.26	11.42
mTBI and substance use disorder	1.64	0.62	**.008**	5.16	1.52	17.50
mTBI and any disorder	1.99	0.40	**<.001**	7.30	3.36	15.86

[a]Control variables: age, pain severity at baseline, psychiatric history (0/1), type of trauma (motor vehicle accident 0/1), and Injury Severity Score.
[b]Boldface values indicate statistical significance.
Abbreviations: *DSM-5* = *Diagnostic and Statistical Manual for Mental Disorders*, Fifth Edition; *DSM-IV*= *Diagnostic and Statistical Manual for Mental Disorders*, Fourth Edition; MDE = major depressive episode; OR = odds ratio; PTSD = posttraumatic stress disorder.

and its associated disability, the majority of people had not sought mental health care. Of those meeting criteria for a psychiatric disorder at 72 months, only 37% reported seeing a psychiatrist, psychologist, or mental health specialist over the previous 2 years.

Comparisons of the injury sample psychiatric disorder incidence and prevalence rates at 72 months for those with and those without mTBI are provided in Table 2. Table 4 shows the adjusted odds ratio for developing a new postinjury psychiatric disorder based on the presence or absence of mTBI. Most, but not all, anxiety disorders were at significantly increased risk of occurrence when mTBI was present. The risks of developing social phobia or OCD were increased 4-fold in people experiencing mTBI, while the odds of developing a panic disorder were increased 10-fold. Although only trending toward significance ($P = .09$), the risk of PTSD (*DSM-5*) almost doubled with the presence of mTBI (interestingly, this risk was significant when scored using *DSM-IV* algorithm).

Table 5 presents the risk for reporting high disability associated with an mTBI. While mTBI on its own did not increase the risk of high levels of disability, when it was comorbid with any psychiatric disorder it significantly increased the risk for disability. This increased risk was consistently 5 to 7 times more likely for all disorders and up to 9 times when comorbid with PTSD. Comorbid depression and mTBI was the largest, with the risk of disability increasing by 30 times if mTBI was comorbid with depression. Overall, these results indicate that the risk for disability is driven by the presence of a psychiatric disorder and not an mTBI.

DISCUSSION

The Long-Term Risk of Psychiatric Disorders After Injury

At 6 years postinjury, 28% of patients met criteria for at least 1 psychiatric disorder in the preceding month, and 19% of patients had a psychiatric disorder they had never experienced prior to the injury. This rate of psychiatric disorders was 3 times higher than in the Australian general population where the 1-month national prevalence of a similar range of psychiatric disorders is 9%. The most common disorders among the injury patients were MDE (11%), agoraphobia without panic (9%), PTSD (6%), and GAD (6%). These rates are similar to those found at 12 months postinjury.[3] The rate of long-term PTSD was similar to that found previously in a sample of injury patients.[8] A novel finding was that marginally more than half of people with PTSD or MDE at the 72-month point were also diagnosed with the same disorder in the first 12 months after their injury. These findings support concerns about the chronicity of psychiatric disorder after injury in a significant proportion of people and underscores previous reports of a subsection of trauma-exposed people who suffer chronic trajectories of psychopathology.[28,29]

The Risk of Disability

Six years after injury, one-third of participants in this study reported high levels of disability. Importantly, much of this disability was associated with psychiatric disorder, with panic disorder, PTSD, and MDE particularly detrimental. These findings replicate past findings that psychiatric disorder is associated with disability in the first 12 months postinjury[4,7] and extends past research by showing that disability associated with psychiatric disorder persists for many years postinjury. The high prevalence of psychiatric disorder, its associated high disability, and the failure of those with psychiatric disorder to access mental health care completes a disturbing picture.

The Risk of Psychiatric Disorder Incurred by mTBI

The presence of mTBI was associated with an additional risk for developing PTSD, panic disorder, OCD, and social phobia beyond the already elevated risks incurred by suffering a serious injury. We did not find a comparable increase in risk for MDE, GAD, agoraphobia without panic, or substance use disorder. These findings are consistent with our results at 12 months postinjury, when the odds for developing a fear-based psychiatric disorder were significantly higher in the presence of mTBI relative to no TBI.[3] Thus, not only is the risk for developing an anxiety disorder elevated in the presence of mTBI, but also it is an enduring risk.

Several explanations are proposed to explain why the risk of anxiety disorders is elevated in the presence of mTBI, with research beginning to establish a link between fear responses and mTBI. Each of the disorders with elevated risk following mTBI have been conceptualized as fear circuitry disorders, which are characterized by common dysfunctions in neural networks involving the amygdala, medial prefrontal cortex, and hippocampus.[30] It is suggested that these networks are compromised following mTBI, thereby impairing the person's capacity to engage in extinction learning and

implement emotion regulation.[31] Consistent with this proposal, animal models have shown that mTBI predisposes the brain toward heightened fear learning during stressful postinjury events.[32] Similarly, human studies have found a reduction in white matter regional volume in the cingulate cortex 12 months after mTBI,[33] suggesting structural changes in the neurologic regions associated with fear circuity. It has also been noted that in mTBI, the hypothalamus is disproportionately affected due to secondary injuries, such as hypoxia and ischemia,[34] which may further compound stress reactions following injury.

The current finding that susceptibility of fear-based disorders to the effects of mTBI is ongoing at 6 years postinjury suggests that the mTBI may be important not only in the development of these disorders in the short term but also in the existence of these disorders in the long term. This susceptibility may occur due to the apparent failure of the fear response to extinguish and the difficulty in managing the ongoing stresses that occur in the postinjury phase.

Furthermore, while rates of psychopathology were higher in the mTBI group, mTBI was associated with increased disability only when it was comorbid with a psychiatric disorder. This finding is consistent with previous research[3,12,35] but extends it to the long term. The finding that mTBI did not account for high levels of disability until comorbid psychiatric disorders were considered suggests neurologic factors associated with an mTBI are insufficient to explain impairment. These findings also suggest that research investigating the long-term outcomes of mTBI needs to comprehensively account for comorbid psychiatric disorders.

Limitations

This study is the first to assess long-term psychiatric and functional sequelae in patients with serious injury across a variety of mechanisms of injury and psychiatric disorders using a large prospective, multisite sample over a 6-year period. The results, however, need to be considered alongside a number of limitations. First, the 6-year follow-up rate was only moderate at 55% of baseline, and attrition may have impacted the measured outcomes. Mitigating this is the finding that there were few differences between the sample retained and those lost to follow-up on a comprehensive range of demographic characteristics including psychiatric history prior to injury and presence of an mTBI. Second, while the MINI is a well-validated structured clinical interview, it is important to acknowledge that it does not screen all symptoms in all disorders, which may have an impact on prevalence rates of disorders reported. Clinical collaboration studies do, however, report high concordance rates, especially in anxiety and depressive disorders.[19]

CONCLUSION

The 2010 iteration of the Global Burden of Disease statistics[2] points to the growing impact of injury. It also highlights the mounting burden of mental illness, which increased by 38% from 1990 to 2010. The findings from our study point to an important intersection between these 2 causes of disease burden (injury and psychiatric disorder) and suggest this growing burden will impose new challenges on health systems. Improved understanding of this intersection is the first step toward prevention and management of disability associated with serious injury.

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