The association between head injuries and psychiatric disorders: findings from the New Haven NIMH Epidemiologic Catchment Area Study

JONATHAN M. SILVER††, RACHEL KRAMER§#, STEVEN GREENWALD§# and MYRNA WEISSMAN§#

† New York University School of Medicine, NY, USA
‡ Lenox Hill Hospital, NY, USA
§ Columbia University, College of Physicians and Surgeons, NY, USA
# New York State Psychiatric Institute, NY, USA

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Primary objective: To determine the association of report of any history of head injury with loss of consciousness or confusion and a lifetime diagnosis of psychiatric disorder in a general population.

Research design: A probability sample of adults from the New Haven portion of the NIMH Epidemiologic Catchment Area programme were administered standardized and validated structured interviews. The main outcome measures were lifetime prevalence of psychiatric disorders and suicide attempt in individuals with and without a history of traumatic brain injury.

Main outcomes and results: Among 5034 individuals interviewed, 361 admitted to a history of severe brain trauma with loss of consciousness or confusion (weighted rate of 8.5/100). When controlling for sociodemographic factors, quality of life indicators and alcohol use, risk was increased for major depression, dysthymia, panic disorder, OCD, phobic disorder and drug abuse/dependence. In addition, lifetime risk of suicide attempt was greater in those who had suffered head injury.

Conclusion: Individuals with a history of traumatic brain injury have significantly higher occurrence for psychiatric disorders and suicide attempts in comparison with those without head injury and have a poorer quality of life. Future studies should examine the nature of this relationship, focusing on the severity of the brain injury and the temporal contiguity of the brain injury and psychiatric disorder.

Introduction

Each year in the US, more than two million people sustain a traumatic brain injury (TBI); 300 000 of these persons require hospitalization [1]. A conservative estimate of the annual incidence of TBI (including brain trauma and transient and persistent post-concussion syndromes) is 200 per 100 000 per year [1]. Estimates of the prevalence of TBI ranges from 2.5–6.5 million individuals [2]. Disorders arising from traumatic injuries to the brain are more common than any other neurological
disease, with the exception of headache [3]. The total economic cost of brain injury is staggering: an estimated $37.8 billion a year for the US alone to treat 328,000 victims of brain injury [4]. The average lifetime cost of treatment per person ranges from $77,000 to $93,000 dollars for minor, moderate, and severe brain injury. Because the victims of TBI most commonly are young adults, they may require prolonged rehabilitation. In this population, psychosocial and psychological deficits are commonly the major source of disability to the victims and of stress to their families.

While treatment and rehabilitation of TBI is usually focused on the cognitive difficulties, the emotional and behavioural problems, including co-morbid psychiatric disorders, significantly impair quality of life after injury [5–10]. Specifically, recent studies that utilize standard psychiatric diagnostic criteria have found that several psychiatric disorders are common in individuals with TBI [6–9]. In a group of patients referred to a brain injury rehabilitation centre, Fann et al. [6] found that 26% had current major depression, 14% had current dysthymia, 24% had current generalized anxiety disorder, and 8% had current substance abuse. There was a 12% occurrence of pre-TBI depression. Deb et al. [7] performed a psychiatric evaluation of 196 individuals who were hospitalized after TBI. They found that a psychiatric disorder was found in 21.7% vs. 16.4% of a control population hospitalized for other reasons. When compared to the control group, the individuals with TBI had a higher rate of depression (13.9% vs. 2.1%) and panic disorder (9.0% vs. 0.8%). Factors associated with these psychiatric disorders included a history of psychiatric illness, pre-injury alcohol use, unfavourable outcome, lower Mini Mental Status Examination scores, and fewer years of education. Hibbard et al. [8] administered a structured psychiatric interview to 100 individuals with TBI. Major depression (61%), substance use disorder (28%), and post-traumatic stress disorder (19%) were the most common psychiatric diagnoses elicited. Jorge et al. [9] found that 26% of individuals had major depression 1 month after injury and 11% had co-morbid generalized anxiety disorder. Other psychiatric disorders, such as schizophrenia, phobias and obsessive-compulsive disorder, have also been reported to be associated with TBI, often in the form of case reports [10].

These studies are limited, however, in that they depend upon the patient being first identified as an individual with brain injury, either in a brain injury treatment programme or admitted to the hospital after TBI. Patients who view their problem as mainly psychiatric are not treated in the brain injury rehabilitation system. Those individuals who are treated for psychiatric disorders in traditional mental health settings, or who are in the community and receiving no treatment, are not included.

In an effort to overcome this referral bias, the authors have examined the relationship between head injury and psychiatric diagnoses in the general population using the data from the New Haven site of the Epidemiologic Catchment Area Study, since that was the only site that the question about head injury was asked [11]. It was hypothesized that psychiatric disorders would be more common in patients with TBI. A higher rate of psychiatric disorders could be due to the effects of TBI on brain functioning, the psychological effects of the accident (i.e. PTSD), or the effects of disabilities resulting from the TBI. In addition to psychiatric disorder, a set of quality of life variables were also evaluated, including physical health, emotional health, or being on welfare or disability. This analysis could help evaluate one’s understanding of the prevalence of psychiatric problems in those with TBI and the need for mental health services and treatment.
Methods

Setting
The sample included participants from the Epidemiologic Catchment Area (ECA) Study, an epidemiologic study of rates and risks for psychiatric disorders based on a probability sample of five communities in the US (New Haven, CT; St. Louis, MO; Baltimore, MD; Durham, NC; and Los Angeles, CA). Only the New Haven data are presented here.

Sample
This sample was drawn from 13 towns in the New Haven, CT standard metropolitan statistical area; 5034 persons were interviewed, including an oversampling of 2500 persons 65 years of age and older.

Measurements
Each site administered the NIMH Diagnostic Interview Schedule (DIS), a highly structured interview designed to be used by lay interviewers in epidemiologic studies, which generated DSM-III definitions of psychiatric disorders [12, 13]. There was an additional set of administered questions unique to each site. A description of this study and the methodology has been presented in detail elsewhere [11].

Outcome measures include comorbidity with other psychiatric disorders based on (lifetime) DSM-III criteria derived from the Diagnostic Interview Schedule, subjective assessments of physical and emotional health, and economic and work functioning. The measures were selected based on their previous use in studies of chronic conditions [14].

This analysis only presents results from the New Haven site, as it was unique in collecting information on the history of a TBI. Weights were assigned to each respondent to compensate for the determination of population prevalence rates.

Analytic variables

Traumatic brain injury
Individuals with TBI were identified as those responding ‘yes’ to the question, ‘Have you ever had a severe head injury that was associated with a loss of consciousness or confusion?’ There was no information regarding the date of occurrence of the injury or the temporal relationship to the occurrence of psychiatric disorder.

Psychiatric disorder
The presence and number of psychiatric disorders was determined by the DSM-III based lifetime diagnoses generated from the DIS: major depression, dysthymia, bipolar disorder, panic disorder, obsessive-compulsive disorder, phobic disorder, alcohol or drug abuse/dependence, and schizophrenia. History of suicide attempt was also reported.
Sociodemographic factors
The sociodemographic variables used in this analysis included gender, age, race/ethnicity (White, Black, Hispanic, or other), socioeconomic status (SES) (lower, middle, and upper) as represented by a composite score for education, income, and occupation, and marital status (married, widowed, separated/divorced or never married).

Quality of life
Indicators of poor current quality of life included poor physical health, poor emotional health, memory problems, being on welfare or disability, time with friends or relatives, time on hobbies, and time on social activities.

Data analysis
Cross-tabulations between a history of TBI and lifetime history of each psychiatric disorder and the quality of life indicators, were performed. Analyses took into account the sample weights, so that the sample was representative of the target population from which it was selected. Weights were assigned to each subject to compensate for the oversampling of the elderly. Chi-squares were calculated for all cross-tabulations to determine the statistical significance of the associations.

Logistic regression was conducted, with psychiatric disorder as the dependent outcome variable and TBI as the independent variable to take into account potentially confounding factors. Adjusted prevalence odds ratios (ORs) with 95% confidence intervals (CIs) were generated for the association between TBI and each psychiatric diagnosis, taking into account the sociodemographic variables and quality of life indicators to adjust for confounding. The ORs indicate the strength of the association between the diagnostic groups and the outcome variables. The statistical significance of the adjusted ORs can be judged from the CIs and whether the interval excludes 1.0. Odds ratios with CIs greater than or equal to 1.0 represent statistically significant increases in risk for adverse outcomes.

Because of the common occurrence of alcohol intoxication in individuals who sustain injury in motor vehicle accidents, the effect of comorbidity with alcohol abuse was also evaluated, running an additional set of models controlling for alcohol abuse. The association was also assessed by examining the number of psychiatric disorders among those with and without a history of TBI.

Results

Demographic characteristics
The demographic characteristics of the sample, stratified by history of TBI, are found in table 1. Of the entire group interviewed, 7.2% experienced a TBI. When this is adjusted for the weighted sample, the rate of TBI is 8.5%. This group was predominately male (61.9%) and demonstrated a difference in distribution of age, socioeconomic status, and marital status when compared to the group without brain injury. No difference was found in the distribution of ethnicity.
Quality of life

The sample with TBI had significantly poorer physical health, emotional health, and memory problems, and was more frequently receiving disability than the non-head injured group (table 2). No difference was demonstrated on leisure time activities (time with friends or relatives, time on hobbies, and time on social activities).

Table 1. Demographic characteristics of those with and without a history of TBI from the New Haven Epidemiologic Catchment Area Study (n = 5034)

<table>
<thead>
<tr>
<th></th>
<th>Head injury (n = 361)</th>
<th>No head injury (n = 4673)</th>
<th>( \chi^2 )</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Males (n = 2062)</td>
<td>61.9</td>
<td>44.8</td>
<td>44.6</td>
<td>0.000</td>
</tr>
<tr>
<td>Females (n = 2972)</td>
<td>38.0</td>
<td>55.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–25 (n = 498)</td>
<td>23.1</td>
<td>17.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26–44 (n = 1159)</td>
<td>41.9</td>
<td>35.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45–64 (n = 790)</td>
<td>25.1</td>
<td>30.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65+ (n = 2587)</td>
<td>9.9</td>
<td>16.7</td>
<td>43.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Ethnic group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (n = 4337)</td>
<td>88.5</td>
<td>86.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black (n = 420)</td>
<td>9.1</td>
<td>10.1</td>
<td></td>
<td></td>
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<tr>
<td>Hispanic (n = 67)</td>
<td>2.0</td>
<td>1.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (n = 72)</td>
<td>0.4</td>
<td>1.5</td>
<td>4.8</td>
<td>0.311</td>
</tr>
<tr>
<td>SES</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower (n = 1032)</td>
<td>8.8</td>
<td>10.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower middle (n = 1647)</td>
<td>26.0</td>
<td>28.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper middle (n = 1531)</td>
<td>40.7</td>
<td>38.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper (n = 801)</td>
<td>24.5</td>
<td>22.2</td>
<td>8.8</td>
<td>0.033</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married (n = 2492)</td>
<td>52.2</td>
<td>60.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Widowed (n = 1231)</td>
<td>5.4</td>
<td>8.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Separated/divorced (n = 527)</td>
<td>12.7</td>
<td>9.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never married (n = 792)</td>
<td>29.7</td>
<td>21.8</td>
<td>40.2</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Table 2. Quality of life in persons by head injury status from the New Haven Epidemiologic Catchment Area Study (n = 5034)

<table>
<thead>
<tr>
<th></th>
<th>Head injury (( % ) (n = 361)</th>
<th>No head injury (( % ) (n = 4673)</th>
<th>( \chi^2 )</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair or poor physical health</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(current, n = 1252)</td>
<td>21.3</td>
<td>15.5</td>
<td>25.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Fair or poor emotional health</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(current, n = 926)</td>
<td>22.1</td>
<td>13.3</td>
<td>32.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>Memory problems</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(current, n = 901)</td>
<td>14.1</td>
<td>12.2</td>
<td>5.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Welfare or disability</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(current, n = 422)</td>
<td>12.7</td>
<td>7.3</td>
<td>15.6</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Adjusted by age, sex, SES, and marital status.
Psychiatric diagnoses

All psychiatric diagnoses, except bipolar disorder and schizophrenia, were more prevalent in the group with head injury compared to those with no history of a head injury (table 3). The odds ratio for each diagnosis, except bipolar disorder, showed increased risk, after adjusting for age, sex, race, SES, and quality of life (table 4).

Because TBI commonly occurs in the presence of alcohol use (which itself is associated with psychiatric disorders), the occurrence of psychiatric diagnoses was analysed controlling for this factor. The occurrence of schizophrenia was of borderline significance (odds ratio 1.7, CI 0.9–3.0) after controlling for the presence of alcohol abuse (table 4).

Those with a TBI were significantly more likely to have had a lifetime history of a suicide attempt (8.1% vs. 1.9%, \( \chi^2 = 40.9, p = 0.0001 \)). The risk for a history of suicide attempt remained significant after adjusting for demographics, quality of life variables, and alcohol abuse (table 4), and remained significant after controlling for the presence of any comorbid psychiatric disorder (odds ratio 2.39 with a 95% CI 1.32–4.31).
Examining the association between brain injury and the number of psychiatric diagnoses, it was found that those with a history of TBI also had a significantly greater number of psychiatric diagnoses compared to those with no history of injury, after controlling for sociodemographic factors and quality of life ($\beta = 0.363, p = 0.0001$). Almost 43% of those with a TBI had at least one psychiatric diagnosis, while only 20% of those without a history of brain injury had at least one psychiatric diagnosis.

**Comment**

The findings from this study suggest that a history of TBI is associated with an increased likelihood of having a psychiatric disorder. Individuals with TBI had a higher proportion of depression, dysthymia, OCD, phobias, panic disorder, alcohol or substance abuse/dependence, bipolar disorder, and schizophrenia compared to those without TBI. Indicators of quality of life (poorer physical or emotional health, more likely to be on welfare) were also higher for those with TBI compared to those without TBI. After adjusting for the potentially confounding effects of demographic factors, quality of life and alcohol abuse, TBI remained significantly associated with all psychiatric disorders except for bipolar disorder, while the occurrence of schizophrenia was of borderline significance. Finally, in this community probability sample, the occurrence of TBI with loss of consciousness (8.5%) was significantly greater than previously reported. This would translate into $\sim 21$ million individuals in the US who have sustained TBI with loss of consciousness (LOC).

The findings are dependent upon recall bias. The presence of brain injury was by self-report. However, these results are consistent with other studies that have relied on patient samples that have been obtained from TBI populations. These findings are unique because they are from a community sample and are not affected by referral bias found in other studies that examine this topic. Previous reports in the literature have documented that the presence of psychiatric disorders are frequent subsequent to TBI. Major depression was found in 11.1% of those with brain injury in this study. In a group of 66 patients admitted to the hospital with the diagnosis of brain injury, 42% developed major depression during the first year after injury [15, 16]. Deb et al. [7] found that 13.9% developed depression.

In the current study, bipolar disorder occurred in 1.6% of those with brain injury. However, the odds ratio was no longer significant when sociodemographic factors and quality of life was controlled. Manic episodes and bipolar disorders have also been reported to occur after TBI [17], although the occurrence is less frequent than that of depression after brain injury.

Panic disorder (3.2%) and phobic disorder (11.2%) were more common in this study among individuals with a history of head injury. Jorge et al. [9] found that 11% of 66 patients (the same group as above) with TBI developed generalized anxiety disorder in addition to major depression. Fann et al. [6] evaluated 50 outpatients with TBI; 24% had generalized anxiety disorder. Deb et al. [7] found that 9.0% of 196 individuals who were hospitalized with TBI had panic disorder.

The rate of schizophrenia in the group of individuals with a history of TBI was 3.4%. However, after controlling for alcohol abuse and dependence, the risk for the occurrence of schizophrenia was of borderline significance. This figure is consistent with the findings of Violon and DeMol [18], who found that of 530 head injury patients, 3.4% developed psychosis 1–10 years after the injury (although there was
Wilcox and Nasrallah [19] found that a group of patients diagnosed with schizophrenia had a history of brain injury with loss of consciousness before the age of 10 significantly more frequently than did patients who were diagnosed with mania or depression or patients who were hospitalized for surgery. Achte et al. [20] reported on a sample of 2907 war veterans in Finland who sustained brain injury. They found that 26% of these veterans had psychotic disorders. In a detailed evaluation of 100 of these veterans, the authors found that 14% had paranoid schizophrenia.

Those with brain injury reported a higher frequency of suicide attempts than those individuals without TBI (8.1% vs. 1.9%). This remained significant even after adjusting for sociodemographic factors, quality of life variables, and the presence of any co-existing psychiatric disorder. Other studies consistently report increased risk of suicide subsequent to TBI [21, 22]. Mann et al. [23] found an increased occurrence of TBI in individuals who have made suicide attempts.

This study found that 8.5% of individuals suffered a TBI. While previous estimates of the prevalence of TBI have ranged from 2.5–6.5 million, these figures have depended upon information about hospitalized patients and those who die prior to hospitalization [2]. This estimate is 3–5 fold greater and translates to ~21 million people in the US. This study offers an unique opportunity to look at these relationships in a population-based sample. This has implications for the cost and provision of healthcare. Those with brain injury had a poorer quality of life as measured by several variables: physical health, emotional health, memory problems, and receiving welfare or on disability. Considering the significant cost of care and the loss of productivity and increased resources necessary to care for these individuals (based on quality of life measures), TBI is a striking public health problem.

While these data are based on a large community probability sample, using structured standardized diagnostic instruments and criteria, there are several limitations to this study. This data is retrospective, and, since no information is available as to whether the psychiatric disorder preceded the injury or occurred at a later time, causality cannot be determined from this study. This study cannot differentiate the effect of biologic changes from head injury as opposed to the effect of poorer physical and emotional health. In a prospective study of the psychiatric disorders that occur after brain injury in children, many developed new psychiatric disorders after the injury [24]. However, at certain times after the injury, psychosocial variables, such as family stress, predicted the occurrence of these.

Because there was no information in this survey regarding when the TBI occurred, there was no way to determine if psychiatric disorders occurred before or after the occurrence of brain injury. However, several studies suggest that individuals who experience TBI have a higher than expected rate of pre-injury psychiatric disorders. Prior histories of psychiatric disorders in individuals with TBI have varied between 17% [15] and 44% [25], and pre-TBI substance use figures have ranged from 22–30% [15, 25]. Fann et al. [6] found that 50% of individuals who had suffered TBI reported a history of psychiatric problems prior to the injury. The Research and Training Centre for the Community Integration of Individuals with TBI at Mt Sinai Medical Center in New York found that, in a group of 100 individuals with TBI, 51% had pre-TBI psychiatric disorders, most commonly major depression or substance use disorders, that occurred at rates of over twice that reported in community samples [8]. An Axis I disorder was found subsequent to
TBI in 80% of this group; the most common diagnoses were major depression (61%), substance use (28%), and PTSD (19%).

The severity of these brain injuries cannot be determined from the information provided in the survey. The question on the survey was ‘Have you ever had a severe head injury that was associated with a loss of consciousness or confusion?’ There are no detailed questions regarding duration of loss of consciousness, amnesia, or treatment. There was no way to determine the criteria used by those individuals to acknowledge the presence of a brain injury. There was no historical confirmation regarding the presence or extent of the TBI (such as medical records). Thus, the authors relied on the individual to be a reliable reporter of their brain injury history. Future psychiatric epidemiologic studies should request further details about brain injury and cross-validation of its occurrence.

It is unlikely that only ‘severe’ injuries were included if the currently accepted definition of ‘severe’ is used, i.e. loss of consciousness for greater than 1 week, and Glasgow Coma Score of less than 10 [26]. Thus, a range of injury severity was included. However, the wording of the question may have excluded many individuals with mild brain injuries (i.e. brief loss of consciousness or brief alteration in mental state). While 85% of TBIs are classified as mild, it is not clear whether the lifetime rates of psychiatric disorders and quality of life measures would be affected.

This frequent co-morbidity of TBI and psychiatric diagnoses has clinical implications. Pharmacotherapy of behavioural and emotional sequelae of individuals with TBI requires modification [26]. In addition, patients who have psychiatric disorders and brain injury may require additional cognitive and psychotherapeutic interventions not usually available to patients who only have psychiatric diagnoses. This association highlights the need for clinicians and investigators to carefully assess individuals for a past history of TBI.

The economic cost of TBI is greater than that previously realized. While the direct care costs have been calculated, the additional economic burden in terms of treatment of psychiatric disorders, and financial supplementation in terms of welfare and disability are great. According to this study, there has been significant underestimation of the prevalence and cost of TBI. Further study and resources are necessary to ascertain those individuals who have sustained TBI and the treatment interventions that they require.

It is apparent that most of these individuals never come to the attention of psychiatrists, and may only be seen by primary care providers. Individuals with ‘hidden’ TBI, who have sustained TBI but have not connected their current problems with the injury, experience emotional distress from the injury [27]. Physicians need to appreciate the occurrence of ‘hidden TBI’, where the patient does not associate the connection between their current problems and a previous TBI. Without doing so, appropriate treatment of brain injury related symptoms, such as problems with memory, attention, fatigue, processing multiple stimuli, and impulse control cannot be prescribed.

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References


