Psychiatric illness and subsequent traumatic brain injury: a case control study

J R Fann, A Leonetti, K Jaffe, W J Katon, P Cummings, R S Thompson

Objective: To determine whether psychiatric illness is a risk factor for subsequent traumatic brain injury (TBI).

Methods: Case control study in a large staff model health maintenance organisation in western Washington State. Patients with TBI, determined by International classification of diseases, 9th revision, clinical modification (ICD-9-CM) diagnoses, were 1440 health plan members who had TBI diagnosed in 1993 and who had been enrolled in the previous year, during which no TBI was ascertained. Three health plan members were randomly selected as control subjects, matched by age, sex, and reference date. Psychiatric illness in the year before the TBI reference date was determined by using computerised records of ICD-9-CM diagnoses, psychiatric medication prescriptions, and utilisation of a psychiatric service.

Results: For those with a psychiatric diagnosis in the year before the reference date, the adjusted relative risk for TBI was 1.7 (95% confidence interval (CI) 1.4 to 2.0) compared with those without a psychiatric diagnosis. Patients who had filled a psychiatric medication prescription had an adjusted relative risk for TBI of 1.6 (95% CI 1.2 to 2.1) compared with those who had not filled a psychiatric medication prescription. Patients who had utilised psychiatric services had an adjusted relative risk for TBI of 1.3 (95% CI 1.0 to 1.6) compared with those who had not utilised psychiatric services. The adjusted relative risk for TBI for patients with psychiatric illness determined by any of the three psychiatric indicators was 1.6 (95% CI 1.4 to 1.9) compared with those without any psychiatric indicator.

Conclusion: Psychiatric illness appears to be associated with an increased risk for TBI.

METHODS

The study was conducted using computerised records from the Group Health Cooperative of Puget Sound (GHC), a large staff model health maintenance organisation located in western Washington State. GHC serves approximately 450,000 members, who are generally representative of the area’s population in terms of age, sex, race, and marital status. Patients received medical care from one of GHC’s facilities located in six counties in the Puget Sound area of western Washington State. Data on health plan members were derived from GHC’s computerised databases, which included information on all inpatient and outpatient visits and diagnoses, all prescriptions dispensed from GHC pharmacies, age, sex, and insurance type (Medicare, Medicaid, GHC individual or family plan, GHC group plan, or other plan). Each GHC member has a unique number that makes linkage of all utilisations possible. This number is permanent and stays with the person if he or she disenrols or re-enrolls. GHC tracks enrolment closely and has a low rate of member disenrolment (13.1% for 1992 through 1993), which made it possible for us to maintain a stable study base. Diagnoses in 1992 were recorded on 95% of all visits, while diagnoses in 1993 were recorded on 97% of all visits.

Abbreviations: ACG, Johns Hopkins Ambulatory Care Group; CDC, Centers for Disease Control and Prevention; CI, confidence interval; GHC, Group Health Cooperative of Puget Sound; ICD-9-CM, International classification of diseases, 9th revision, clinical modification; TBI, traumatic brain injury.
Patients with TBI
Cases were diagnoses of TBI made in the emergency room, hospital, or an outpatient clinic in 1993. The following diagnostic categories and International classification of diseases, 9th revision, clinical modification (ICD-9-CM) codes were used to identify TBI: fracture of the vault or base of the skull (800.0–801.9); other, unqualified, and multiple fractures of the skull (803.0–804.9); and intracranial injury, including concussion, contusion, laceration, and haemorrhage (850.0–854.1). These diagnostic categories for TBI were used by the Centers for Disease Control and Prevention (CDC) in their TBI surveillance studies. If a person had more than one visit with a TBI diagnosis in 1993, the first diagnosis was considered the incident TBI. The reference date for cases was the date of this incident TBI diagnosis. Patients were required to have been continuously enrolled at GHC for the year before their TBI diagnosis to ensure that records were available to assess indicators of psychiatric illness. Cases were taken from six counties in the Puget Sound area that provided complete health services utilisation data. To maximise the likelihood of ascertaining incident TBI cases, patients who had an ICD-9-CM diagnosis of TBI in the year before their reference date were excluded from the case group.

Severity of TBI was dichotomised into mild TBI and moderate to severe TBI using the CDC categorisation criteria. Cases were considered to be mild if ICD-9-CM codes indicated brief (< 1 hour) or no loss of consciousness and no traumatic intracranial lesions were documented. Cases were considered to be moderate or severe if ICD-9-CM code indicated prolonged loss of consciousness or a documented traumatic intracranial or brain lesion. Patients whose TBI severity was undetermined were excluded from the study.

Non-TBI control subjects
Three control subjects per patient were selected at random from GHC enrolment files and were frequency matched to patients by sex, age in groups of five years (0–4 years, 5–9 years, 10–14 years, and so on, to ≥ 95 years), and enrolment at the time of the case patient’s reference date. Similar to the patients, control subjects had to be GHC members on their assigned reference date, had to be GHC members continuously during the year before their reference date, and could not have had a TBI diagnosis during that year.

Psychiatric illness indicators
Psychiatric illness in the year before the reference date was ascertained by three separate methods: presence of a psychiatric diagnosis, filling of a prescription for a psychiatric medication, or utilisation of psychiatric services. Presence of a psychiatric diagnosis was determined by using ICD-9-CM codes recorded in the year before the reference date and was categorised as follows: acute reaction to stress or adjustment reaction (308, 309); alcohol or drug intoxication, withdrawal, or dependence (291.0–291.2, 293.0, 293.3, 293.4, 293.8, 294.9, 296.2, 296.3, 296.82, 296.9, 300.4, 311); hyperkinetic syndrome of childhood (314); malaise or fatigue (300.5, 780.7); organic psychotic mental disorders (290.0–290.9, 293.0–293.9); organic non-psychotic mental disorders (310, 780.09); schizophrenia, hallucinations, or paranoia (295, 297.0–299.9, 790.1); somatoform disorders (300.1, 300.6–300.9, 306, 307.8, 307.89); or other psychiatric disorders (307, 316, V40.2–40.9, V62.81, V62.89, V65.9).

Subjects were considered to have filled a psychiatric medication prescription if automated GHC pharmacy data indicated that a prescription for a psychiatric medication in any of the following classes was filled in the year before the reference date: antidepressants, antipsychotics, anxiolytics, lithium, or psychostimulants. Surveys in 1985 and 1986 showed that over 90% of all medications prescribed at GHC were filled in GHC pharmacies and a study found that 97.6% of those treated with antidepressant medications in 1991–92 filled their prescriptions at GHC pharmacies. Because antidepressants are commonly used for other indications, they were considered to be for a psychiatric indication only if the prescription was filled within 60 days of a depression diagnosis. Anxiolytics were considered to be for a psychiatric indication if the prescription was filled within 60 days of an anxiety diagnosis. Psychostimulants were excluded if there was a diagnosis of narcolepsy within a year before the reference date.

Utilisation of psychiatric services was ascertained based on computerised records of inpatient psychiatric hospitalisations, outpatient mental health clinic visits, and alcohol or drug treatment inpatient stays or outpatient visits in the year before the reference date. Out of plan mental health services use is rare due to comprehensive mental health services with small service payment responsibilities by patients within GHC.

An overall summary determination of psychiatric illness was made based on the presence of any psychiatric diagnosis, psychiatric medication prescription, or psychiatric utilisation during the year before the reference date.

Medical comorbidity
Medical comorbidity was determined using the Johns Hopkins Ambulatory Care Group (ACG) case mix system (version 4.1), which is a measure of relative health status designed to be indicative of expected resource consumption. ACGs use age, sex, and ICD-9-CM diagnoses assigned during patient-health care provider encounters over a period of time (such as a year) to assign a person to one of 106 mutually exclusive categories. The ACG system has been found to be useful in predicting both concurrent and subsequent ambulatory care use and costs, as well as subsequent morbidity, and has been used extensively to control for medical comorbidity. In this study, ICD-9-CM codes for psychiatric diagnoses were excluded from the ACG category determination to arrive at ACG categories derived solely from medical diagnoses.

Analysis
Odds ratios using unconditional logistic regression were used to approximate relative risks of TBI in those with indicators of psychiatric illness relative to those without. The matching variables were included in all models: age was categorised in five year intervals and reference date was categorised as the month of injury. Insurance type, used as a proxy measure of socioeconomic status, and medical comorbidity were examined as potential confounders. Possible effect modification of the association between psychiatric illness and TBI by age and sex was assessed. Possible interaction between ICD-9-CM psychiatric diagnosis and psychiatric medication prescription was analysed.

RESULTS
In 1993, 2250 GHC members had a diagnosis of TBI. Among these, 1641 were enrolled in GHC for at least one year before their index TBI, 1541 were enrolled in the six county study region, and 1445 did not have a TBI in the year before their incident TBI. TBI severity was determined in 1440 patients. These constitute the TBI case group.

Among case patients, 1366 (94.9%) had a diagnosis of intracranial injuries (concussion, contusion, laceration, or haemorrhage); 37 (2.6%) had a diagnosis of fracture of the vault or base of the skull; and 37 (2.6%) had a diagnosis of other, unqualified, and multiple skull fractures. Most cases were classified as mild TBI (n = 1293, 89.8%). Most cases of TBI were diagnosed in an outpatient setting (n = 691, 48.0%) or in the emergency room (n = 582, 40.4%), and 167 (11.6%) were diagnosed in the hospital. The overall annual incidence rate of TBI was 475.2 per 100 000 person years, using a...
population denominator of 303,001 person years (those enrolled at GHC for at least one year at mid-year 1993).

Almost half of the patients with TBI were 19 years and younger, with 294 (20.4%) less than 9 years and 411 (28.3%) 10–19 years; 115 (8.0%) were 20–29 years, 282 (19.6%) were 30–49 years, 152 (10.6%) were 50–69 years, and 186 (12.9%) were 70 years or older. Among the patients with TBI, 769 (53.4%) were male. Case patients and control subjects were similar with regard to insurance type, with about 80% group dependents or subscribers. TBI events were distributed fairly evenly by month, although there was a slightly lower proportion of cases in the winter months. In the year before the reference date, case patients had a mean (SD) of 7.5 (9.7) outpatient visits compared with 5.3 (7.0) visits by control subjects (p < 0.001); these included primary care visits, specialty care visits, hospital outpatient visits, and outpatient mental health services.

As table 1 shows, the relative risks for TBI were generally 1.3– to 4-fold higher for those with preceding psychiatric condition indicators, whether assessed by diagnosis codes, medication prescriptions, or utilisation profiles. Exceptions to this general pattern were seen for hyperkinetic disorder and use of psychostimulants. Among case patients, 24.2% had some indication of a psychiatric illness before TBI compared with 14.3% of control subjects. With an attributable risk of 37.5% for any psychiatric illness indicator, the proportion of TBI cases that might be attributable to psychiatric illness was 9.1%.

A more detailed examination of the subcategories in table 1 shows that all diagnostic categories were associated with an increased adjusted relative risk of TBI except for hyperkinetic disorder of childhood. Those who had a diagnosis of organic non-psychotic disorders had the highest risk of TBI compared with those without such a diagnosis. Those diagnosed with organic psychotic disorders and somatoform disorders also had relative risks of TBI > 2. Groups with a diagnosis of acute reaction to stress or adjustment reaction, alcohol or drug intoxication, withdrawal, or dependence, malaise or fatigue also had significantly greater risks of TBI than those without these diagnoses. Most psychiatric diagnoses were made by non-mental health professionals, with 50% made by family practice physicians.

Three of the five psychiatric medication types were found to be significantly associated with an increased risk of TBI. Compared with those who had not filled a prescription, those who had filled a prescription for anxiolytics and antipsychotics were approximately two and a half times as likely to have a TBI. The relative risk of TBI for those who had filled a prescription for antidepressants was 1.5 (95% confidence interval (CI) 1.1 to 2.2).

ACGs, indicators of medical comorbidity, were found to confound the relation between psychiatric illness and subsequent TBI, decreasing the relative risk estimate for TBI for all indicators of psychiatric illness. Insurance type was neither a risk factor for TBI nor a confounder of the psychiatric illness-TBI relation for all measures of psychiatric illness.

The relation between psychiatric illness and TBI was significantly modified by age only in the category of any psychiatric ICD-9-CM diagnosis (p = 0.03 for test of heterogeneity). For patients with any psychiatric diagnosis versus those who did not have a diagnosis, those in the age group 25–64 years had the highest relative risk of TBI (relative risk 2.2, 95% CI 1.7 to 2.9) followed by those in age group ≥ 65 years (relative risk 1.7, 95% CI 1.2 to 2.4) and those in age group 0–24 years (relative risk 1.3, 95% CI 0.9 to 1.7). The relation between psychiatric illness and TBI was not significantly modified by sex or insurance type for any indicator of psychiatric illness.

### Table 1

<table>
<thead>
<tr>
<th>Psychiatric Illness Indicator</th>
<th>Cases (n=1440)</th>
<th>Controls (n=4320)</th>
<th>Adjusted Relative Risk*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric ICD-9-CM diagnosis</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Acute reaction to stress or adjustment reaction</td>
<td>48 (3.3)</td>
<td>62 (1.4)</td>
<td>1.9</td>
<td>1.3 to 2.9</td>
</tr>
<tr>
<td>Alcohol or drug intoxication, withdrawal, or dependence</td>
<td>34 (2.4)</td>
<td>51 (1.2)</td>
<td>1.6</td>
<td>1.0 to 2.6†</td>
</tr>
<tr>
<td>Anxiety</td>
<td>26 (1.8)</td>
<td>38 (0.9)</td>
<td>1.5</td>
<td>0.9 to 2.6</td>
</tr>
<tr>
<td>Depression</td>
<td>54 (3.8)</td>
<td>87 (2.0)</td>
<td>1.4</td>
<td>1.0 to 2.0</td>
</tr>
<tr>
<td>Hyperkinetic disorder</td>
<td>14 (1.0)</td>
<td>48 (1.1)</td>
<td>0.7</td>
<td>0.4 to 1.3</td>
</tr>
<tr>
<td>Malaise or fatigue</td>
<td>44 (3.1)</td>
<td>64 (1.5)</td>
<td>1.3</td>
<td>1.1 to 2.6</td>
</tr>
<tr>
<td>Organic non-psychotic disorders</td>
<td>10 (0.7)</td>
<td>6 (0.1)</td>
<td>4.4</td>
<td>1.5 to 12.5</td>
</tr>
<tr>
<td>Organic psychotic disorders</td>
<td>15 (1.0)</td>
<td>11 (0.3)</td>
<td>3.7</td>
<td>1.6 to 8.7</td>
</tr>
<tr>
<td>Schizophrenia, hallucination, or paranoia</td>
<td>17 (1.2)</td>
<td>26 (0.6)</td>
<td>1.9</td>
<td>1.0 to 3.7</td>
</tr>
<tr>
<td>Somatoform disorders</td>
<td>19 (1.3)</td>
<td>14 (0.3)</td>
<td>2.8</td>
<td>1.3 to 5.8</td>
</tr>
<tr>
<td>Other</td>
<td>70 (5.0)</td>
<td>124 (2.9)</td>
<td>1.3</td>
<td>1.0 to 1.9</td>
</tr>
</tbody>
</table>

*Relative risk adjusted for age, sex, reference date, and Ambulatory Care Group. Reference group is made up of those without each specific indicator.
†Lower limit rounded down to 1.0.
‡Determined by psychiatric ICD-9-CM (International Classification of Diseases, 9th revision, clinical modification), diagnosis, psychiatric medication prescription, or psychiatric service utilisation. CI, confidence interval.
There was no significant interaction between the following: alcohol or drug intoxication, withdrawal, or dependence diagnosis and any other psychiatric diagnosis; anxiety diagnosis and depression diagnosis; depression diagnosis and antidepresant prescription; anxiety diagnosis and anxiolytic prescription; and schizophrenia, hallucination, or paranoia diagnosis and antipsychotic prescription.

DISCUSSION

The main finding of our study was that patients with any indicator of psychiatric illness experienced an increased risk of subsequent TBI (relative risk 1.6) compared with those who had no indicator of psychiatric illness. This increase was seen with three different indicators of psychiatric illness: ICD-9-CM diagnoses, psychiatric medication prescription, and psychiatric service utilisation. A significantly greater relative risk for TBI was found for patients who had a previous diagnosis of acute reaction to stress or adjustment reaction; alcohol or drug intoxication, withdrawal, or dependence; malaise or fatigue; organic non-psychotic disorders; organic psychotic disorders; and somatoform disorders compared with those without the specific diagnoses. The presence or absence of alcohol or drug related conditions did not modify the associations between the other psychiatric conditions and subsequent risk for TBI. Previous medication prescription categories of anxiolytics, antidepressants, and antipsychotics were also associated with increased TBI risk.

A few studies have examined the relationship between emotional, behavioural, and cognitive problems and TBI in selected populations. While Brown et al. found that children with mild head injuries had significantly more premorbid behavioural problems than children with severe head injuries or orthopaedic injuries, Pelco et al. did not find a higher rate of premorbid emotional and behavioural problems in hospitalised children with mild head injuries compared with children in the general community. The small number of people with hyperkinetic disorder and the presence of comprehensive paediatric care at GHC may explain the lack of a significant association between hyperkinetic disorder and TBI in our study. Dicker found that adults who sustained a mild head injury were more likely to have a learning disability before the injury than population controls. Similarly, Engberg et al. found the relative risk for concussion in the presence of pre-existing cognitive dysfunction among men ages 16 to 24 to be 1.6 (95% CI 1.3 to 1.9) compared with men without cognitive dysfunction.

Previous studies have examined possible associations between psychiatric factors and accidents. Alcohol use has a dose-response relation with an increased risk of injury. Children with high accident liability are more likely to have had evidence of personal and social maladjustment, psychosomatic ailments, and referrals to counsellors or psychiatrists before their accidents. Motor vehicle accidents are a major cause of TBI and it has been estimated that 90% of such accidents are caused by driver error. Studies have suggested that people with psychiatric problems have 1.5 to 2.5 times the risk of a motor vehicle accident compared with other drivers. Transient factors, such as stressful life events, anxiety, depression, functional somatic complaints, alcohol use, and fatigue, may interact with stable traits, such as cognitive impairment, impulsivity, antisocial attitudes, neuromticism, and external locus of control, in causing collisions.

The associations found between psychiatric illness and TBI are likely due to complex causal pathways that differ in the various psychiatric indicators. Alcohol, as well as other substances, places a person at a higher risk for TBI through its effects on cognition, coordination, and judgement. Our study found only a minimally significant association between alcohol and drug use disorders and TBI, perhaps in part because of the relatively low numbers of these disorders in the GHC population and the presence of comprehensive substance abuse treatment programs at GHC. People with organic mental disorders were found to be at increased risk for TBI and include those with dementia, delirium, and frontal lobe syndrome. Demented and delirious people have impaired cognitive and physical functioning, making them more prone to accidents and self injury. Driving, for example, is a complex skill in which various cognitive processes such as perception, attention, reaction time, and motor control are involved. Cognitive deficits, agitation, impulsivity, and impaired insight and judgement associated with organic mental disorders may lead to risk taking or carelessness, which can lead to injury. Patients with psychotic symptoms, such as hallucinations or delusions, may also have similar impairments, which may lead to situations conducive to TBI.

We also found that acute reaction to stress or adjustment reaction, malaise or fatigue, and somatoform disorders may lead to increased risk of TBI. These diagnoses may be proxies for general psychiatric distress, including depression and anxiety, that are modifiable risk factors for TBI. These non-specific conditions are common presentations of psychological distress in the medical setting. Those with somatoform disorders and chronic fatigue have been found to have a high burden of comorbid psychiatric illness, such as depression and anxiety. People with depression suffer from decreased attention and concentration and slowed reaction times, which may result in motor vehicle collisions, falls, and recreation related injuries that may lead to TBI. Because depressed patients are at increased risk of attempting suicide, it is possible that some of the TBI in this study were self inflicted. Depression is also associated with impaired overall health related functioning, which may result in decreased self care and increased risk of accidents. Anxiety disorders are characterised by distractibility, autonomic hyperactivity, motor tension, shakiness, and fatigue, all of which may contribute to events that cause injury.

Our results show that use of antidepressants, anxiolytics, and antipsychotics confers significantly increased relative risks for TBI. Studies have reported that use of psychoactive medications such as cyclic antidepressants and benzodiazepines increase the risk of injurious motor vehicle collisions and falls. These and other psychiatric medications may cause cognitive and motor impairment, sedation, dizziness, and agitation, especially in the elderly. Psychostimulants may increase alertness in some patients, perhaps explaining our finding of a trend towards decreased risk of TBI. Although it is known from automated data that a prescription was filled, it is unknown how much of the medication was taken. Another consideration is whether an increased relative risk for TBI associated with prescription medication is related to underlying psychiatric illness for which the medication was prescribed or to the pharmacological effects of the medications.

Psychiatric diagnosis, prescriptions filled, and utilisations were all recorded before the TBI diagnosis. Therefore, possible bias due to differential recall between case patients and control subjects was eliminated. Because of the completeness and uniformity of the database, the determination of psychiatric illness was not subject to the limitations of incomplete recall or information bias. Because health care providers at GHC are not influenced by the risk that making a psychiatric diagnosis may not receive full reimbursement, as may be the case in fee for service settings, there was not likely to be reporting bias of psychiatric diagnoses due to reimbursement rates.

Limitations of this study include the paucity of information on TBI history beyond one year before the incident TBI in 1993, as well as possible lack of precision in outcome and exposure measurement. Because those of low socioeconomic status have been shown to have higher rates of TBI, there may be residual confounding by socioeconomic status that
was not controlled for in the analyses. However, insurance type, which was used as a proxy measure for socioeconomic status, was not shown to be a confounding factor for both psychiatric illness and subsequent TBI. Those with prior TBI would be more likely to have a psychiatric illness, as well as a subsequent TBI, and thus our relative risks may be spuriously increased. The method used to determine psychiatric illness may have been subject to misclassification. Psychiatric diagnoses assigned by non-medical health practitioners may be less sensitive and specific than diagnoses made by mental health practitioners. Subjects could have been incorrectly assigned to diagnostic categories or may not have received a diagnosis when a psychiatric illness was present. However, this potential non-differential misclassification would likely bias effect estimates towards the null.

People with psychiatric distress often present with many unexplained medical complaints and are high utilizers of medical care. Because those with psychiatric distress visit the doctor more frequently, it is more likely that a mild TBI in these patients would be recognised and recorded, while a person without psychiatric distress may not present to a GHC clinic and a TBI would not be recognised. Several studies have suggested that psychiatric patients or people with previous psychosocial problems such as depression, alcohol abuse, stressful life events, and social difficulties before their TBI may complain of a greater number of or more persistent postconcussive symptoms. These patients may have more frequent medical utilisation and a higher likelihood of having a diagnosis of TBI.

Despite these limitations, our results showed a significant association between pre-existing psychiatric illness and subsequent TBI. Given the impact of TBI on morbidity, mortality, and health care costs, the identification of psychiatric illness as a potentially modifiable risk factor for TBI is important for the prevention of TBI and its sequelae. Increased efforts should be made to educate medical practitioners, patients, and families about the increased risk of TBI in psychiatric populations. Discussions may address ways of decreasing behaviours that can increase the risk of TBI and increasing preventive measures, such as the use of seat belts and bicycle helmets. A better understanding of the relation between specific psychiatric factors and TBI is needed. Also, studies that differentiate the physiological effects of psychiatric medications from the underlying illness that the medications treat should be undertaken.

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