Psychiatric Illness After Mild Traumatic Brain Injury in Children

Teresa L. Massagli, MD, Jesse R. Fann, MD, MPH, Bart E. Burington, MS, Kenneth M. Jaffe, MD, Wayne J. Katon, MD, Robert S. Thompson, MD

ABSTRACT. Massagli TL, Fann JR, Burington BE, Jaffe KM, Katon WJ, Thompson RS. Psychiatric illness after mild traumatic brain injury in children. Arch Phys Med Rehabil 2004;85:1428-34.

Objective: To determine the incidence of psychiatric illness 3 years after mild traumatic brain injury (TBI) in children.

Design: Prospective cohort study with 3-year follow-up.

Setting: Emergency department, hospital, and outpatient clinics in a large health maintenance organization.

Participants: Children, 14 years old or less (n=490), who sustained a mild TBI in 1993. Three TBI unexposed subjects per TBI exposed patient were matched by sex, age, and enrollment at the time of injury (n=1470).

Interventions: Not applicable.

Main Outcome Measures: Computerized records were examined to identify psychiatric diagnoses, psychiatric medication prescription, and utilization of psychiatric services for the year before TBI and 3 years after. Adjusted relative risks for incidence of psychiatric illness were estimated for those with and without a premorbid psychiatric disorder.

Results: The cumulative incidence estimates for any psychiatric illness in the 3 years after mild TBI were 30% in children exposed to mild TBI and 20% in unexposed children ($P=.0001$). Cumulative incidence estimates were particularly high in both TBI exposed (55%) and unexposed children (63%) who had psychiatric illness in the year before the index TBI (psychiatric history). The exposed and unexposed children with psychiatric history did not have significantly different estimates of incidence during follow-up for any of the studied indicators of psychiatric illness. In those with no psychiatric history, 26% of exposed and 16% of unexposed children ($P<.0001$) had evidence of a psychiatric illness in the 3 years after mild TBI. For those with no psychiatric history, the adjusted relative risk estimate of any psychiatric illness in TBI exposed versus unexposed children, in the first year after TBI, was 2.03 (95% confidence interval [CI], 1.4–2.9). Children with mild TBI but no psychiatric history were at higher risk for hyperactivity (diagnosis of hyperkinetic syndrome of childhood or prescription of psychostimulants) in the first year after injury (incidence, 3%; first year relative risk, 7.59; 95% CI, 2.7–21.6).

Conclusions: In the 3 years after mild TBI, children with no evidence of prior-year psychiatric history were at significantly increased risk for psychiatric illness, particularly hyperactivity in the first year after injury. Prior-year psychiatric history conferred a significant independent risk for subsequent psychiatric illness. There was no evidence for an additional increase in risk in the 3-year follow-up that is attributable to mild TBI in children with prior psychiatric history.

Key Words: Brain injuries; Psychiatry; Rehabilitation.

MILD TRAUMATIC BRAIN INJURIES (TBI) are common in children and adolescents. One population-based study[1] from 1981 estimated the incidence of TBI resulting in hospitalization or death of children less than 15 years old at 185 per 100,000 per year. The majority (86%) of those who survived had mild TBI.[1] However, hospitalization of children with mild TBI has decreased dramatically in recent years.[2] In 1995, the incidence of TBI resulting in hospitalization of children 4 years old and younger and 5 to 14 years old was estimated to be 75 to 105 per 100,000 per year; most were the result of moderate and severe injuries. The number of children who sustain mild TBI but who do not require hospitalization is unknown, but among the 1 million adults and children with TBI-related emergency department visits each year, about 80% are not admitted to hospitals.[2] Children with mild TBI may also be evaluated and treated in primary care settings.

Psychiatric illness may contribute to disability after TBI. Studies[3-5] in both children and adults with TBI have shown that patients with postinjury psychiatric illness have greater disability than do those with a similar severity of brain injury but without psychiatric illness. It is important to identify treatable comorbidities to improve functional outcome after TBI. In adults with mild TBI, treatment of depression resulted in improvement on neuropsychologic measures such as psychomotor speed, recent verbal memory, cognitive efficiency, and mental flexibility, as well as in postconcussive symptoms.[6]

Although cognitive, behavioral, and psychiatric sequelae have been commonly reported after severe TBI in children,[3,7-11] it remains controversial whether mild TBI is associated with significant behavioral and psychiatric morbidity in children. Several prospective[12,13] and retrospective[9,14] studies have found no clinically significant cognitive or academic deficits after mild TBI in children. However, mixed results have been found for behavioral and psychiatric illness after mild TBI.[15]

Hyperactivity, phobias, rage attacks, depression, aggressive and antisocial behavior, anxiety disorders, oppositional defiant disorder (ODD), and impaired adaptive functioning are among the disorders reported in 20% to 70% of children after mild TBI.[16-25] Other researchers have found no evidence for behavior change[26] or problems with adaptive functioning after mild TBI,[27] or no difference in frequency of psychiatric diagnoses when children with mild TBI are compared with those with orthopedic injuries.[28] While Max et al observed new psychiatric symptoms after mild TBI only in those with a psychiatric history,[22] Bloom et al found that novel psychiatric disorders occurred in 40% of a small sample of children with mild TBI,

From the Departments of Rehabilitation Medicine (Massagli, Fann, Jaffe), Pediatrics (Massagli, Jaffe), Psychiatry and Behavioral Sciences (Fann, Katon), and Biostatistics (Burington), University of Washington, Seattle, WA; and the Center for Health Studies, Group Health Cooperative of Puget Sound, Seattle, WA (Thompson).

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Correspondence to Teresa L. Massagli, MD, PO Box 5371, Mail Stop 6G3, Children's Hospital and Regional Medical Center, Seattle, WA 98105, e-mail: *massagli@u.washington.edu.* Reprints are not available from the author.

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independent of their psychiatric history.[18] It is difficult to generalize findings from these studies because of a lack of comparison groups,[19,22] failure to control for preinjury psychiatric illness,[16] reliance on delayed determination (often 1–2y after TBI) of prior behavioral disorders or psychiatric illness,[17-21,28] small sample size,[17,18,22,24,27] sample bias because of reliance on hospital admission[17-20,22-24,26,27] or clinic referral[25] for case ascertainment, differences in definition of mild TBI, and the wide range of outcome measures selected for investigation.

Many studies have suggested that some children with mild TBI develop new psychiatric problems; however, to estimate the incidence of such outcomes, it would be necessary to conduct population-based studies using patients identified from primary referral sources, not from specialty clinics or patients seeking treatment. This is particularly important given the decline in the number of children hospitalized for mild TBI during the 1980s and 1990s.[2] Children who are hospitalized may constitute a more severely injured group and may not be representative of all children with mild TBI.

In the only other population-based study of a large cohort, 114 of 13,000 British children were identified as having a mild TBI that required ambulatory care or overnight hospitalization.[14] At follow-up 1 to 5 years after injury, those children differed from uninjured children only on teacher ratings of hyperactivity, and the magnitude of their increased hyperactivity was small. This study was limited to children injured when they were between the ages of 5 to 10 years. Behavior problems were assessed by parent and teacher standardized questionnaires, but there were no outcomes reported from medical providers. Outcome assessments were done only when the child became 10 years old; consequently, some children were assessed 1 year after TBI and some as many as 5 years after injury.

Our purpose in this study was to examine a large cohort of children under 15 years old to determine the incidence and risk of psychiatric illness as identified by medical practitioners in each of the first 3 years after mild TBI. The cohort was selected from outpatient, emergency department, and inpatient records at a large health maintenance organization (HMO).

METHODS

This was a prospective cohort study using computerized records of patients in a large staff model HMO, Group Health Cooperative of Puget Sound (GHC). This HMO serves approximately 450,000 members in 6 counties in the Puget Sound area of Washington State. The health plan members are generally representative of the region's population in terms of sex, age, race, and marital status.[29] The study data included information on all inpatient and outpatient visits and diagnoses, all prescriptions provided from GHC pharmacies, and demographic information. Diagnoses in 1992 were recorded on 95% of all visit records.[29] Only about 7% of plan members have dual insurance coverage, so determination of use of medical services in this study is nearly complete. GHC has a low rate of member disenrollment (13.1% for 1992–1993), making it possible to maintain a stable study base. The institutional review boards of GHC and the University of Washington approved this study.

Participants

Subjects were children less than 15 years old and were diagnosed with mild TBI in an emergency department, hospital, or outpatient clinic in 1993. TBI was defined by the diagnostic categories used by the US Centers for Disease Control and Prevention (CDC) in their surveillance studies.[30] These include the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) codes: 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 hemorrhage (850.0–854.1).[31] Subjects were categorized with mild TBI according to CDC criteria: ICD-9-CM codes indicated brief (<1h) or no loss of consciousness and no traumatic intracranial lesions.[32] If a child had more than 1 diagnosis of TBI in 1993, the first diagnosis was considered the incident TBI and the reference date was assigned to this incident.

Three subjects without TBI (controls) per TBI subject were selected at random from GHC enrollment files and were frequency matched to TBI subjects by sex, age (in groups of 5y [0–4y, 5–9y, 10–14y]), and enrollment at the time of the case's reference date.

Both TBI subjects and controls had to have been enrolled in GHC on the reference date, had to have been continuously enrolled in GHC for the year before the reference date, and not have had an ICD-9-CM diagnosis of TBI in the year before the reference date.

Indicators of Psychiatric Illness

The computerized records of all study subjects were examined to establish psychiatric illness over 6-month periods in the 1 year before the reference date and in the 3 subsequent years. Psychiatric illness was determined by psychiatric diagnosis, or by the filling of a prescription for a psychiatric medication, or by using psychiatric services. A designation of "any psychiatric illness" was defined as positive status according to any of these 3 methods. Subjects with "psychiatric history" were defined as those positive for any psychiatric illness in the year before the reference date.

ICD-9-CM codes made by any GHC provider were used to identify psychiatric diagnoses.[31] These diagnoses were categorized as: acute reaction to stress or adjustment reaction (308, 309); alcohol or drug intoxication, withdrawal, or dependence (291.0–292.9, 303.0, 303.9, 304, 305); anxiety (300.0, 300.2, 300.3, 799.2); depression (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–.9, 293.0–294.9); organic nonpsychotic mental disorders (310, 780.09); schizophrenia, hallucinations, or paranoia (295, 297.0–299.9, 780.1); somatoform disorders (300.1, 300.6–.9, 306, 307.8, 307.89); or other psychiatric disorders (307, 316, V40.2–.9, V62.81, V62.89, V65.9). When the study sample for the larger study of adults and children was identified, several psychiatric diagnoses occurred rarely, or only in non-TBI subjects and they were excluded. The diagnoses included conduct disorders (312); developmental disorder (315, 317, 318.0–.2, 319, V40.0); disturbances of emotion-childhood (313); impulse control problems (301.3, 312, 312.3); manic and manic depressive disorders (296, 296.4–.8); personality disorders (301); parent-child counseling (V61.20); and sleep disorder (780.5).

Subjects were considered to have had a psychiatric prescription filled if computerized GHC pharmacy data indicated a prescription from any provider for medications in the following classes: antidepressants, antipsychotics, anxiolytics, lithium, or psychostimulants. Because some medications are prescribed for other than psychiatric diagnoses, antidepressants and anxiolytics were considered to be for a psychiatric indication only if the prescription was filled within 60 days of a diagnosis of depression or anxiety, respectively. Surveys from 1985 and 1986 indicated that more than 90% of medications prescribed

Table 1: Mild TBI Versus No TBI Relative Risk Estimates (95% Confidence Intervals) for Psychiatric Illness in the 3 Years After TBI

Psychiatric Indicator	0–12 Months	12–24 Months	24–36 Months
Hyperactivity			
No prior year psychiatric illness (P=.002)*	7.59 (2.7–21.6)¶	1.32 (0.6–3.1)	1.00 (0.4–2.6)
Prior year psychiatric illness (P=.19)*	0.50 (0.2–1.0)	0.92 (0.3–2.8)	–‖
Other or unspecified			
No prior year psychiatric illness (P=.003)*	2.65 (1.5–4.8)¶	0.59 (0.2–1.5)	1.88 (1.0–3.6)
Prior year psychiatric illness (P=.96)*	0.95 (0.4–2.4)	1.21 (0.3–4.2)	0.73 (0.2–2.7)
Psychiatric diagnosis†			
No prior year psychiatric illness (P<.001)‡	2.79 (1.8–4.3)¶	1.23 (0.7–2.1)	1.62 (1.0–2.7)
Prior year psychiatric illness (P=.96)‡	0.93 (0.5–1.7)	1.19 (0.5–3.1)	0.78 (0.2–2.9)
Psychiatric prescription			
No prior year psychiatric illness (P=.37)*	2.47 (0.6–10.8)	0.54 (0.1–4.1)	3.27 (0.5–22.6)
Prior year psychiatric illness (P=.10)*	0.25 (0.1–1.2)	0.27 (0.0–2.1)	–‖
Psychiatric utilization			
No prior year psychiatric illness (P=.31)*	1.08 (0.6–1.9)	1.60 (0.9–2.7)	1.36 (0.6–2.9)
Prior year psychiatric illness (P=.75)*	1.20 (0.7–2.1)	0.50 (0.1–2.3)	0.94 (0.3–3.2)
Any psychiatric illness			
No prior year psychiatric illness (P<.001)‡	2.03 (1.4–2.9)¶	1.41 (0.9–2.2)	1.50 (0.9–2.7)
Prior year psychiatric illness (P=.74)‡	0.93 (0.6–1.5)	0.55 (0.1–2.0)	0.62 (0.1–3.2)

NOTE. Refer to P values in first column for test of overall 3-year effect of TBI.
*Adjusted for age, gender, comorbid injuries, and log of costs for prior year.
†Psychiatric diagnosis: affective disorder, adjustment reaction, somatoform-disorder, psychotic disorder, organic nonpsychotic disorder, substance abuse, hyperactivity, and other.
‡Adjusted for age, gender, index month, comorbid injuries, and log of costs for prior year.
‖The relative risk estimate is held constant in years 2 and 3. There are no new events in year 3 among TBI subjects with a prior illness.
¶Significantly different from 1, at level .05.

at GHC were filled in GHC pharmacies because of prescription insurance coverage in the GHC plan.[29]

Use of psychiatric services was determined based on computerized records of inpatient psychiatric hospitalization, outpatient mental health clinic visits, and alcohol or drug treatment inpatient or outpatient visits. Out-of-plan use of mental health services is rare because of the comprehensive mental health services and small copayments available to patients in GHC.

Data Analysis

Eight categories of psychiatric illness were used for analysis. Affective disorders included depressive disorders, anxiety disorders, and prescription of antidepressants, lithium, or anxiolytics. Adjustment reaction included acute reaction to stress, adjustment disorder, malaise, or fatigue. Psychotic disorders included schizophrenia, hallucinations, paranoia, organic psychotic disorders, and prescription of antipsychotics. Hyperactivity included hyperkinetic syndrome of childhood and prescription of psychostimulants. Substance abuse included alcohol or drug abuse or dependence. Somatoform disorder, organic nonpsychotic mental disorder, and other or unspecified mental disorders were the other 3 categories.

Cumulative incidence rates and predicted numbers of events (n=predicted positive for psychiatric indicator) were computed using Kaplan-Meier estimates to account for censoring. Because of disenrollment, rates computed using raw outcome counts would underestimate the true incidence. Adjusted relative risk ratios were computed using complementary log-log generalized linear models for fixed-interval, interval-censored data.[33] Age was categorized in 5-year intervals and the reference date was categorized as the month of injury. The log of costs in the previous year and comorbid injuries coded in the 6 months before and after TBI were used as proxies for medical comorbidity. Relative risks were adjusted for age, gender, index month, comorbid injuries, and log of costs for the previous year. Adjusted estimates for the subgroups with and without prior psychiatric history were computed separately. P values for the tests for overall effect of TBI within these subgroups (table 1) were not adjusted for multiple comparisons. Although the 4 P values that were significant at level .05 remained significant after a Bonferroni adjustment for the 12 tests, we considered the outcomes and subgroups to represent different scientific questions. In addition, because "any psychiatric illness" is a conglomerate and the specific diagnoses, the psychiatric diagnosis indicator, and the psychiatric prescription indicator were positively correlated by construction, the 12 P values represented less than 12 independent tests. The pointwise confidence intervals (CIs) and indicators of nominal level .05 significance for the relative risk estimates over time are given for reference and should be considered subordinate to their respective tests for overall effect. Analyses were performed using SPLUS, version 6.1,[a] and Stata, version 7.[b]

RESULTS

In 1993, 490 GHC members under 15 years old, who had been enrolled at least 1 year and who did not have a diagnosis of TBI in the previous year, were diagnosed with mild TBI. Eleven additional children had either a moderately severe or a severe TBI and were not included in this study. Most mild TBI subjects (96%) were diagnosed in the emergency department (n=279) or in an outpatient setting (n=191); only 4% were diagnosed in the hospital (n=20).

The ages and gender of all study subjects are shown in table 2. The number of boys and girls in the youngest age group was nearly equal (65 and 64, respectively), but boys outnumbered girls in the 2 older groups and comprised 62% of the TBI subjects. All participants were similar with regard to insurance type, with 99% being plan members and 1% having Medicaid. TBI events were relatively evenly distributed by month. Twenty-six (5.3%) mild TBI subjects and 32 (2.2%) controls (P=.004) were predicted to have a subsequent TBI diagnostic code

Table 2: Characteristics of Study Subjects

Age (y)	Exposure Status	Male n	Male %	Female n	Female %	Total n
0–4	Mild TBI	65	50	64	50	129
	No TBI	195	50	192	50	387
5–9	Mild TBI	106	66	55	34	161
	No TBI	318	66	165	34	483
10–14	Mild TBI	134	67	66	33	200
	No TBI	402	67	198	33	600
Total	Mild TBI	305	62	185	38	490
	No TBI	915	62	555	38	1470
						1960
Grand total		1220	62	740	38	

during the follow-up period. The frequency of dropouts was 21% for both TBI subjects and controls at the end of the 3-year follow-up.

Table 3 shows the Kaplan-Meier estimated cumulative incidence of psychiatric illness by category, psychiatric diagnosis, psychiatric medication prescription, psychiatric utilization, and any psychiatric illness indicator for those with and without TBI exposure. The estimates for cumulative incidence and numbers of positive indicators (n), which were adjusted for censoring, were slightly larger than the raw counts and percentages (not shown). One TBI subject disenrolled in the first 6-month follow-up interval, reducing the denominator to 489 subjects in the 0- to 12-month time frame. Over the 3 years, an estimated 30% of TBI subjects and 20% of controls ($P=.0001$) had evidence of a psychiatric illness (psychiatric diagnosis, prescription, or utilization). The highest incidence occurred in the first year. For mild TBI subjects, the most frequently occurring disorders over the 3 years were: other or unspecified mental disorder (13%), hyperactivity (10%), and adjustment reaction (6%). Psychiatric prescriptions were uncommon, except for controls with a psychiatric history (15%) (table 4); only 2% of TBI subjects and 1% of controls with no psychiatric history, and 5% of TBI subjects with a psychiatric history had psychiatric prescriptions during the 3-year follow-up. Psychiatric utilization was highest for those with a previous psychiatric history: 41% of TBI subjects and 42% of controls versus 13% of TBI subjects and 8% of controls with no prior history.

Psychiatric history was a strong predictor of psychiatric illness during follow-up, regardless of TBI exposure. The adjusted relative risk for psychiatric illness in the 3-year follow-up period for subjects with psychiatric history versus subjects without was estimated at 6.21 (95% CI, 4.6–8.4; $P<.0001$) for controls and 2.74 (95% CI, 1.8–4.2; $P<.0001$) for those with mild TBI. Psychiatric history significantly modified the effect of mild TBI on subsequent psychiatric illness ($P=.002$). Evidence of any psychiatric illness during the 3-year follow-up was estimated to occur in 26% of mild TBI subjects and 16% of controls ($P<.0001$) with no psychiatric history. Psychiatric illness was estimated to occur in 55% of mild TBI subjects and in 63% of controls ($P=.63$) who had a prior psychiatric history. Among subjects with a prior psychiatric diagnosis, novel psychiatric diagnoses were estimated to occur with similar frequency in the mild TBI subjects (29%) and in controls (33%) ($P=.74$).

The adjusted relative risk estimates in table 5 show an increasing risk of a psychiatric illness with increasing age during the 3 years of follow-up, for children both with ($P=.004$) and without a psychiatric history ($P<.0001$). For those with no psychiatric history, boys and girls had a similar estimated risk of psychiatric illness after TBI ($P=.85$). However, among those with a prior psychiatric history, boys had an

Table 3: Incidence of Psychiatric Illness Indicators by Year During 3-Year Follow-Up in Subjects With Mild TBI and Those With No TBI*

Psychiatric Indicator	Exposure Category	0–12 Months n/N	0–12 Months (%)	12–24 Months n/N	12–24 Months (%)	24–36 Months n/N	24–36 Months (%)	Predicted 3y n/N	Predicted 3y (%)
Affective disorder	Mild TBI	3/489	(1)	4/441	(1)	5/394	(1)	14/489	(3)
	No TBI	15/1470	(1)	9/1313	(1)	14/1188	(1)	43/1470	(3)
Adjustment reaction	Mild TBI	10/489	(2)	8/435	(2)	10/387	(3)	32/489	(6)
	No TBI	14/1470	(1)	15/1315	(1)	17/1181	(1)	53/1470	(4)
Somatoform disorder	Mild TBI	1/489	(0)	0/444	(0)	0/400	(0)	3/489	(1)
	No TBI	1/1470	(0)	3/1326	(0)	4/1204	(0)	9/1470	(1)
Psychotic disorder	Mild TBI	0/489	(0)	3/444	(1)	3/398	(1)	7/489	(1)
	No TBI	1/1470	(0)	3/1326	(0)	2/1204	(0)	7/1470	(0)
Organic nonpsychotic	Mild TBI	4/489	(1)	0/440	(0)	0/396	(0)	6/489	(1)
	No TBI	0/1470	(0)	0/1327	(0)	0/1207	(0)	0/1470	(0)
Substance abuse	Mild TBI	1/489	(0)	2/444	(0)	5/399	(1)	9/489	(2)
	No TBI	4/1470	(0)	10/1324	(1)	11/1196	(1)	29/1470	(2)
Hyperactivity	Mild TBI	24/489	(5)	13/421	(3)	6/367	(2)	47/489	(10)
	No TBI	44/1470	(3)	24/1286	(2)	21/1149	(2)	97/1470	(7)
Other	Mild TBI	29/489	(6)	9/417	(2)	19/370	(5)	62/489	(13)
	No TBI	41/1470	(3)	33/1290	(3)	32/1141	(3)	117/1470	(8)
Psychiatric diagnosis	Mild TBI	62/489	(13)	28/389	(7)	27/327	(8)	124/489	(25)
	No TBI	92/1470	(6)	67/1245	(5)	56/1068	(5)	234/1470	(16)
Psychiatric medication	Mild TBI	5/489	(1)	2/439	(0)	2/394	(1)	10/489	(2)
	No TBI	18/1470	(1)	7/1310	(1)	6/1186	(1)	34/1470	(2)
Psychiatric utilization	Mild TBI	38/489	(8)	24/410	(6)	14/348	(4)	81/489	(17)
	No TBI	81/1470	(5)	47/1248	(4)	30/1091	(3)	170/1470	(12)
Any psychiatric illness	Mild TBI	84/489	(17)	34/368	(9)	20/303	(7)	146/489	(30)
	No TBI	147/1470	(10)	80/1190	(7)	46/1006	(5)	293/1470	(20)

*Predicted cumulative incidence, adjusted for censoring.

Table 4: Incidence of Psychiatric Illness Indicators by Prior Psychiatric History* in Subjects With Mild TBI and Those With No TBI†

Psychiatric Indicator	Exposure Category	Psychiatric History	0–12 Months		12–24 Months		24–36 Months		3-Year Totals	
			n/N	(%)	n/N	(%)	n/N	(%)	n/N	(%)
Hyperactivity	Mild TBI	No	14/421	(3)	8/369	(2)	6/324	(2)	31/421	(7)
	No TBI	No	5/1334	(0)	18/1200	(1)	17/1076	(2)	46/1334	(3)
	Mild TBI	Yes	10/68	(15)	5/52	(10)	0/43	(0)	16/68	(23)
	No TBI	Yes	39/136	(29)	6/86	(7)	4/73	(6)	51/136	(38)
Other or unspecified disorder	Mild TBI	No	23/421	(5)	5/362	(1)	15/324	(5)	47/421	(11)
	No TBI	No	27/1334	(2)	26/1180	(2)	24/1046	(2)	86/1334	(6)
	Mild TBI	Yes	6/68	(9)	4/55	(7)	3/46	(7)	15/68	(21)
	No TBI	Yes	13/136	(10)	7/110	(7)	8/95	(9)	31/136	(23)
Psychiatric diagnosis	Mild TBI	No	43/421	(10)	20/344	(6)	24/293	(8)	94/421	(22)
	No TBI	No	47/1334	(4)	54/1163	(5)	48/1006	(5)	165/1334	(12)
	Mild TBI	Yes	18/68	(27)	7/45	(16)	3/34	(9)	30/68	(44)
	No TBI	Yes	44/136	(33)	13/82	(16)	8/62	(13)	69/136	(51)
Psychiatric medication	Mild TBI	No	3/421	(1)	0/380	(0)	2/342	(1)	7/421	(2)
	No TBI	No	5/1334	(0)	5/1200	(0)	2/1087	(0)	13/1334	(1)
	Mild TBI	Yes	2/68	(3)	0/59	(0)	0/52	(0)	3/68	(5)
	No TBI	Yes	13/136	(10)	2/110	(2)	4/99	(4)	20/136	(15)
Psychiatric utilization	Mild TBI	No	17/421	(4)	22/367	(6)	10/313	(3)	54/421	(13)
	No TBI	No	43/1334	(3)	39/1162	(3)	22/1022	(2)	113/1334	(8)
	Mild TBI	Yes	20/68	(30)	2/43	(5)	4/35	(11)	28/68	(41)
	No TBI	Yes	37/136	(27)	8/86	(9)	8/69	(12)	57/136	(42)
Any psychiatric illness	Mild TBI	No	52/421	(12)	31/335	(9)	18/277	(7)	108/421	(26)
	No TBI	No	79/1334	(6)	71/1132	(6)	41/963	(4)	207/1334	(16)
	Mild TBI	Yes	32/68	(47)	3/33	(9)	2/26	(8)	38/68	(55)
	No TBI	Yes	68/136	(50)	9/58	(16)	5/43	(12)	86/136	(63)

*Psychiatric history is defined as any psychiatric illness in the year prior to the reference date.
†Predicted cumulative incidence, adjusted for censoring.

estimated 70% higher risk of psychiatric illness in the 3-year follow-up period.

Adjusted relative risk estimates stratified by prior psychiatric illness for hyperactivity, other or unspecified mental disorder, psychiatric diagnosis, psychiatric prescription, psychiatric utilization, and any psychiatric illness indicator for each follow-up year are presented in table 1. Among those with a psychiatric history, TBI subjects and controls had a similar estimated risk of any indicator of psychiatric illness in the follow-up period ($P=.74$). Subjects with mild TBI but no prior psychiatric history were at higher estimated risk for a new psychiatric diagnosis or any psychiatric illness only in the first year after injury. Within the specific psychiatric illness categories, only "hyperactivity" (hyperkinetic syndrome of childhood or prescription of psychostimulants) and "other or unspecified mental disorder" were estimated to occur at a significantly higher rate after mild TBI. These 2 categories were probably the main contributors to the significantly increased psychiatric diagnosis and any psychiatric illness indicators in the first year after TBI. Among those with no psychiatric history, the relative risk for hyperactivity in the first year of follow-up was estimated at 7.59 (95% CI, 2.7–21.6). In this group, subjects with hyperactivity were more likely to be boys (relative risk = 2.82; 95% CI, 1.5–5.4; $P=.002$), and in the 5- to 9-year age group. The relative risk estimate for ages 5 to 9 versus 0 to 4 was 3.55 (95% CI, 1.6–8.1) and for ages 10 to 14 versus 0 to 4 it was 2.36 (95% CI, 1.0–5.5; $P=.008$ for the overall effect of age). Nearly all of the TBI exposed and unexposed subjects who were categorized with "hyperactivity" by the ICD-9-CM codes for hyperkinetic syndrome of childhood (vs prescription of psychostimulants) had the ICD-9-CM code 314.0 (attention deficit disorder [ADD]).

DISCUSSION

This study is the largest prospective cohort study of children with mild TBI drawing from patients largely representative of the local population. We stratified analyses by prior psychiatric illnesses, controlled for medical comorbidity, used a standard definition of mild TBI for case ascertainment, had a long follow-up period, and included a broad age range of children. We found that psychiatric illnesses are common in the first 3 years after mild TBI, occurring in 26% of those with no prior

Table 5: Relative Risk Ratios for Psychiatric Illness by Age and Gender in the 3 Years After Mild TBI*

Comparison	No Prior Psychiatric History (280 events in 1755 subjects)		Prior Psychiatric History (118 events in 204 subjects)	
	Relative Risk (95% CI)	*P* Value	Relative Risk (95% CI)	*P* Value
Boys vs girls	1.02 (0.8–1.3)	.852	1.70 (1.1–2.6)	.018
Ages 5–9 vs 0–4y	1.41 (1.0–2.1)		1.71 (0.8–3.7)	
Ages 10–14 vs 0–4y	2.31 (1.7–3.2)	<.0001	2.84 (1.4–5.6)	.004

*Adjusted for TBI exposure, index month, comorbid injuries, and log of costs for prior year.

psychiatric history. Incidence was highest in the first year. The relative risk of hyperactivity (primarily ADD) in subjects with no prior psychiatric history is particularly high in the first year after injury. Still, its incidence was low, occurring in only 3% of those subjects. Boys and children 5 to 9 years old and 10 to 14 years old had the highest relative risks for hyperactivity. It is important to identify psychiatric illness occurring after TBI, because treatment may reduce morbidity.[6]

The only other population-based study is that of the Bijur group,[14] which identified 114 children with mild TBI from a cohort of 13,000 British children. That study group included only children between ages 5 to 10 years, and follow-up was done only when each child turned 10 years old, that is, at a variable time after TBI. Among measures of cognition, academic achievement, and behavior, only teacher ratings of hyperactivity were found to distinguish children with TBI from uninjured controls. Given the small magnitude of the effect and the overall negative findings, Bijur downplayed the findings. It is possible that the inconsistent timing of follow-up and the smaller sample size obscured any early problems.

This study and that of Bijur do not support the high frequency of psychiatric and behavioral symptoms reported in some smaller studies that relied on hospitalized or referred patients for case ascertainment. Our study and that of Bijur focused on TBI subjects who were managed via ambulatory care, so injuries may have been milder than those reported in other studies. The relative mildness of our patients' injuries might also explain why, in contrast to studies by others,[8,22] we did not find that mild TBI in those with prior psychiatric illness was a predictor of psychiatric illness after TBI. Psychiatric illness seems to be a greater risk factor than mild TBI in determining whether there will be a subsequent psychiatric illness.[34] When evaluating a patient with mild TBI who presents with a psychiatric diagnosis, it is important to seek a premorbid history of psychiatric disorder before attributing such symptoms to the TBI. However, we did find that novel psychiatric illnesses occurred in those with prior disorders.

It seems plausible that there are multiple determinants of psychiatric problems after TBI.[24] A psychiatric problem present before TBI could place the patient at risk for TBI.[35] The TBI could worsen a preexisting psychiatric problem.[7,8,22] The new psychiatric disorder could be the result of the brain injury[14] and could be secondary to other problems, such as changes in appearance, memory, family functioning after injury,[4,7,22,25,36] postinjury stress,[23] or socioeconomic status.[11] This may be especially true for late arising problems. Max et al[37] suggested that the etiology may even differ for different disorders: for postinjury attention-deficit hyperactivity disorder (ADHD), they found risks of severity of injury and preinjury ADHD. For postinjury ODD, the risks appeared to be preinjury family functioning, preinjury ODD, and socioeconomic status, but not injury severity. In our study, the significant increase in the incidence of hyperactivity was found only in those with no prior psychiatric illness and was significant only in the first year after injury, suggesting a cause and effect relationship. Although the incidence declined over time, the prevalence increased, indicating a persistence of the disorder.

There are several limitations to this study. Assignment of diagnoses relied on primarily nonpsychiatric practitioners. This may have resulted in underidentification of psychiatric problems after TBI in those with no prior history, whereas those with a history may have had ongoing psychiatric diagnoses, medications, or mental health services that would make psychiatric concerns more likely to be identified. This would bias TBI effect estimates toward the null. Some psychiatric diagnoses were not included in the data because of their low incidence, as noted on initial screening of the database. Another limitation is that by relying on ICD-9-CM coded psychiatric diagnoses, psychiatric medication prescriptions, and psychiatric utilization, we may have underestimated the incidence and risk of behavioral problems that occur after mild TBI. However, the problem had to reach the threshold for identification by a medical provider to be included in the study. Another potential limitation is that psychiatric illness may have existed but was undiagnosed before the TBI. The TBI itself may have led to more medical attention and the subsequent diagnosis of what had been a preexisting condition. We also cannot rule out the effects that family disruption, cognitive changes, somatic complaints, unidentified substance abuse, or postinjury stress might have had on the development of psychiatric illness after TBI, although we do believe that the timing of hyperactivity disorders suggests a direct relationship with the mild TBI. Another potential limitation is that subjects may have had a subsequent TBI during the follow-up period. Although subjects with mild TBI had more subsequent TBI codes than controls, we were unable to determine which of these represent a new TBI exposure. We did, however, examine the effect of subsequent TBI codes and found that it had a negligible effect on the relative risk for subsequent psychiatric illness in patients without prior illness. We chose to report estimates unadjusted for subsequent TBI because these events are not baseline confounders and, for consideration of the exposed and unexposed cohorts, may be considered part of the composite risk for psychiatric illness that is associated with an initial TBI.

CONCLUSIONS

Psychiatric illnesses occur fairly frequently among children with mild TBI. There is a significantly increased risk for psychiatric illness, particularly hyperactivity, in the first year after injury in children with no prior psychiatric history. Identification and treatment of hyperactivity may result in reduced morbidity after mild TBI. Prior psychiatric illness confers a significant independent risk for subsequent psychiatric illness. It is important to inquire about prior psychiatric history before attributing psychiatric symptoms to the mild TBI. However, novel psychiatric disorders do occur after mild TBI in children with a prior psychiatric history.

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