

The Clinical Significance of Major Depression Following Mild Traumatic Brain Injury

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Objective: The authors assessed the association of major depression with behavioral outcome following mild traumatic brain injury. Method: Consecutive patients with mild traumatic brain injury (N = 170) were assessed for major depression. Those with major depression were compared with those without on self-report measures of psychosocial dysfunction, psychological distress, and postconcussive symptoms in addition to examiner-rated neurobehavioral disturbance. Results: Major depression was seen in 15.3% (N = 26) of the subjects after traumatic brain injury, and these individuals showed subjective and objective evidence of poorer outcome. Conclusions: Major depression is associated with poor outcome across multiple domains. This study highlights the need for the early diagnosis and prompt treatment of major depression following mild traumatic brain injury.

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Major depression following traumatic brain injury is relatively common, with a point prevalence of 14%–29%.^{1–3} Major depression may be particularly common following mild traumatic brain injury. Alexander⁴ found that subjects with mild traumatic brain injury had higher rates of major depression, postconcussive symptoms, and poor global outcome than those with severe traumatic brain injury. However, the relationship between the relevant variables was not explored. While studies thus far have demonstrated an association between major depression and poor psychosocial functioning following traumatic brain injury,^{1,2,5–11} most studies have not focused on patients with mild traumatic brain injury. Traumatic brain injury sample selection in these studies has either been heterogeneous,^{1,2,5,6,11} moderate to severe,^{7,8,10} or unclear.⁹ Furthermore, three of the studies had small numbers of subjects,^{1,2,5} and four did not use diagnostic interviews for assessment of depression.^{6–8,10}

Levin et al.,¹² in a group of subjects with mild and moderate traumatic brain injury, found that the presence of major depression was associated with poor global and psychosocial functioning. However, the study group size was small (N = 69), subjects with premorbid major depression

were not excluded from the analysis of the relationship between depression and functioning, and postconcussive symptoms were not assessed.

In community samples, major depression uncomplicated by head injury has been associated with significant levels of disability.¹³ Given that mild traumatic brain injury is associated with poor outcome in 15%–20%,^{4,14} the question of to what extent this is associated with major depression deserves further study.

The purpose of the present study is to assess the association between major depression and a number of outcome measures following mild traumatic brain injury, namely global outcome, level of psychosocial functioning,

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degree of psychological distress and neurobehavioral disturbance, and severity of postconcussive symptoms. We hypothesized that major depression would be associated with adverse outcome in these domains.

METHOD

Patient Selection

A consecutive group of patients attending a traumatic brain injury clinic for their first follow-up appointment after injury was assessed for the presence of major depression. The clinic is part of a large general hospital that serves as a tertiary referral center for trauma patients who are referred to the clinic from the emergency department, trauma wards, community hospitals, and by local physicians. All our subjects sustained a nonpenetrating mild traumatic brain injury, as defined by the American Congress of Rehabilitation Medicine: loss or alteration of consciousness at the time of injury for 30 minutes or less, an initial Glasgow Coma Score of 13–15, and posttraumatic amnesia of less than 24 hours.¹⁵ Exclusion criteria were a premorbid history of focal brain disease (e.g., stroke, tumor), serious acute medical illness (heart or renal failure, malignancy), or previous history of dementia, schizophrenia, bipolar disorder, or major depression. Subjects provided informed consent.

Two hundred eleven patients were seen at the clinic. Forty-one patients with a preexisting mood disorder (bipolar disorder or major depressive disorder) were excluded. No subjects were excluded on the basis of the other criteria.

Data Collection

Demographic and head injury data were collected from a clinician's review of the chart and discussion with the patient (and informant, where available). Demographic information included age, gender, marital status, living situation, employment, educational history, medical history (presence of illnesses unrelated to injury), and the presence or absence of a prior diagnosis of psychiatric disorder (major depressive disorder, bipolar disorder, schizophrenia, anxiety disorder, or dementia). The use of alcohol and illicit substances were codified as "significant" on the basis of interview and clinician's judgment. Family psychiatric history was attained by inquiring about formal psychiatric contact or diagnosis in first- or second-degree biological relatives. Injury data, namely the mechanism of accident,

duration of loss of consciousness, Glasgow Coma Scale score in the emergency room, duration of posttraumatic amnesia,¹⁶ other musculoskeletal injuries (coded as none, soft tissue only, or fractures), and results of the brain CT scans (coded as focal intracranial abnormality, atrophy, or normal), were also recorded.

All subjects (N = 170) were assessed by a psychiatrist (who was unaware of the results of the self-report outcome measures) for the presence of a major depressive episode using the depression module of the Structured Clinical Interview for DSM-IV axis I disorders (SCID).¹⁷ DSM criteria are considered reliable and valid in traumatic brain injury samples.^{18,19}

Outcome Measures

Psychosocial outcome was recorded by using the Rivermead Head Injury Follow-Up Questionnaire,²⁰ which gives a more detailed description of psychosocial functioning. This 4-point self-report scale addresses 10 aspects of a patient's functioning—such as relationships, work, domestic activities, and the ability to hold a conversation—following traumatic brain injury.

Psychological distress and symptoms of postconcussive disorder were noted with the General Health Questionnaire²¹ and the Rivermead Post Concussion Symptoms Questionnaire,²² respectively. The 28-item General Health Questionnaire, a self-report questionnaire used previously in a neurological setting^{23–25} and in traumatic brain injury research,^{26,27} contains four subscales of seven questions each pertaining to somatic distress, social dysfunction, anxiety, and depression. Each question has four possible responses, which were rated binomially (i.e., 0-0-1-1) in accordance with the scale's guidelines. The Rivermead Post Concussion Disorder Questionnaire measures on a 4-point scale the severity of 18 physical symptoms (e.g., headache, dizziness) commonly seen following traumatic brain injury.

Objective measures of outcome were administered by a clinician who was blind to the results of the self-report questionnaires but not to the results of the SCID. These measures included the Glasgow Outcome Scale²⁸ and the Neurobehavioral Rating Scale—Revised.²⁹ The Glasgow Outcome Scale is a widely used clinician-rated instrument developed specifically for patients with traumatic brain injury to assess global functioning. It is rated on a 5-point scale (5 = "good recovery"; 4 = "moderate disability"; 3 = "severe disability"; 2 = "vegetative"; 1 = "dead"). The Neurobehavioral Rating Scale—Revised is a multidimen-

sional clinician-based assessment instrument designed to measure neurobehavioral disturbances following traumatic brain injury. The Neurobehavioral Rating Scale—Revised is not a symptom checklist; it is administered by a brief structured interview that includes questions and observations about behavioral and emotional sequelae common to traumatic brain injury and incorporates performance on cognitive tasks (e.g., orientation, four-item object recall, verbal problem solving). The Neurobehavioral Rating Scale—Revised has been shown to be reliable and valid for quantifying behavioral disturbances and cognitive impairments in individuals with traumatic brain injury.^{29–31} For purposes of analysis, and to avoid overlap of scores with the presence of SCID-defined major depression, we removed the “depression” item from the total score. As a further objective index of outcome, we inquired whether or not the subjects had returned to work after their injury.

Statistics

Patients with and without major depression were compared by using the chi-square statistic (or Fisher’s exact test, where appropriate) for categorical demographic and injury variables as well as the Glasgow Outcome Scale and “return to work” variable. Age, time postinjury, and the continuous outcome variables were compared between groups by using analysis of variance. A Bonferroni correction was applied to correct for multiple comparisons: with 10 outcome variables, the critical *p* value is 0.005 (i.e., 0.05/10). The potentially confounding effects of demographic mismatch between groups with and without major depression were controlled for by using analysis of covariance.

RESULTS

Subjects were on average 44.2 years of age (*SD* = 20.1, range = 15–91) and were seen at a mean of 48.4 days (*SD* = 33.6, range = 1–227) after their injury. With regard to past psychiatric problems, 16 subjects had significant substance misuse, 13 had alcohol misuse, and four had anxiety disorder.

Eighteen subjects (10.6%) were too ill to complete the self-report outcome measures. They were more likely to be older ($F = 13.02$, *df* = 1, 168, $p < 0.0001$) and to have medical illnesses ($\chi^2 = 5.12$, *df* = 1, $p < 0.05$), but there were no significant differences in the prevalence of major depression or other demographic or injury variables between the groups.

According to the SCID, 26 (15.3%) of 170 patients met criteria for major depression.

Subjects with major depression were more likely to have sustained their accident as a result of a motor vehicle-related accident than those without major depression, but there were no other significant differences in demographic or injury variables between the groups (Table 1).

Subjects with major depression reported higher levels of psychosocial dysfunction (Rivermead Head Injury Follow-Up Questionnaire), psychological distress (General Health Questionnaire), and symptoms of postconcussive disorder (Rivermead Post Concussion Symptoms Questionnaire) than those without (Table 2). These relationships remained significant at the $p < 0.0001$ level even after mechanism of injury was controlled. Subjects with major depression reported higher levels of postconcussive symptoms, even excluding postconcussive symptoms that overlap with those of major depression (i.e., depressed mood, insomnia, fatigue, irritability, frustration, restlessness, and concentration difficulties).

In terms of three objective outcome measures, subjects with major depression had significantly higher scores (more neurobehavioral disturbance) on the Neurobehavioral Rating Scale—Revised (total score minus depression item) (Table 2), a finding that remained significant after we controlled for mechanism of injury. Subjects with major depression also showed poorer outcome on the Glasgow Outcome Scale than those without major depression (19.2% versus 36.8% with good outcome), although this was not statistically significant (Table 2). There were no differences in numbers of people who had returned to work.

DISCUSSION

This study demonstrated that, in a sample confined to mild traumatic brain injury, major depression in the acute period following injury is associated with greater psychosocial dysfunction, more psychological distress, increased postconcussive symptoms, and more neurobehavioral dysfunction. As the aim of this study was to address the relationship between major depression and behavioral outcome following traumatic brain injury, the study had a built-in control group (i.e., major depression versus no major depression), thereby obviating a need for orthopedic or healthy comparison subjects.

The prevalence in this study of major depression was 15%, which is consistent with other studies that have examined point prevalence of DSM-defined major depres-

sion,¹⁻³ but lower than the pooled prevalence estimate of >40% in a recent review.³² Strict comparisons, however, are difficult, since many of the previous studies of depression in traumatic brain injury have relied on self-report depression rating scales and have incorporated subjects with traumatic brain injury of heterogeneous severity and at various time points postinjury.^{32,33}

The finding of an association between major depression and poor psychosocial functioning following mild traumatic brain injury is consistent with findings in other studies of traumatic brain injury of more severe or heterogeneous severity.^{1,2,5-11} While Fann et al.⁵ noted an association between major depression and postconcussive symptoms, our data are particularly robust because we controlled for overlap in symptoms between the two disorders. Furthermore, in the study by Fann et al., the sample selection was heterogeneous.

Our study found a relationship that approached significance between major depression and global outcome according to the Glasgow Outcome Scale. While three

studies^{7,8,12} have previously found that depressive symptoms were associated with poor functioning on the Glasgow Outcome Scale, two of the studies concerned moderate to severe traumatic brain injury and relied on self-report of depressive symptoms,^{7,8} while the third study (in subjects with mild to moderate traumatic brain injury and general trauma) used the more sensitive extended version of the Glasgow Outcome Scale and did not exclude patients with a prior history of depression.¹² The Glasgow Outcome Scale, with its narrow range of potential scores, does not appear to be a particularly sensitive measure of outcome following mild traumatic brain injury.³⁴ Similarly, the "return to work" variable may be a premature, and therefore insensitive, way of judging outcome given the acute nature of our sample, seen on average 1½ months after injury.

The strength of this study is the combination of patient recruitment limited to those with mild traumatic brain injury and no premorbid history of mood disorder, direct structured interview of all subjects by a psychiatrist to as-

TABLE 1. Demographic and Injury Characteristics for Subjects With or Without Onset of Major Depression Following Mild Traumatic Brain Injury

Characteristic	Patients With Mild Traumatic Brain Injury (N = 170)			
	Depression Onset After Injury (N = 26)		No Depression Onset After Injury (N = 144)	
	Mean	SD	Mean	SD
Age (years)	41.3	17.8	44.8	20.5
Time postinjury (days)	57.0	36.5	46.8	33.0
	N	%	N	%
Male	13	50.0	98	68.1
Unattached marital status (single, divorced, or widowed)	12	46.2	72	50.0
Education beyond high school	14	53.8	66	45.8
Employed at the time of injury	19	73.1	96	66.7
Mechanism related to motor vehicle accident ^a	17	65.4	64	44.4
Other injuries				
None	4	15.4	32	22.2
Soft tissue only	13	50.0	75	52.1
Fractures	9	34.6	37	25.7
CT scan ^b				
Normal	15	75.0	79	70.5
Atrophy	1	5.0	10	8.9
Focal abnormality	4	20.0	23	20.5
Litigation ^c	1	3.9	4	2.8
Prior traumatic brain injury	6	23.1	33	22.9
Family psychiatric history	8	30.8	40	27.8
Medical problems unrelated to traumatic brain injury	11	42.3	69	47.9
History of significant alcohol misuse ^c	3	11.5	10	6.9
History of significant substance misuse ^c	3	11.5	13	9.0

^aSignificant difference between groups ($\chi^2 = 3.87$, $df = 1$, $p < 0.05$).
^bPercentages based on 20 subjects with and 112 without major depression.
^cBecause of small group size, Fisher's exact test was used to compare groups; all differences were nonsignificant.

sess major depression, and the use of a broad array of subjective and objective outcome measures. Given the relative insensitivity of the Glasgow Outcome Scale in mild traumatic brain injury, the addition of three other self-reported outcome measures that capture a spectrum of symptoms, as well as the more comprehensive and objective Neurobehavioral Rating Scale—Revised, enhanced our ability to determine how patients fare in the acute period following injury.

The pathogenesis of persisting symptom complaints following mild traumatic brain injury is unclear. Psychosocial factors such as psychiatric history, substance abuse, financial incentives, misattribution of symptoms, and expectancies have been posited as important.^{35–37} It is also possible that major depression might lead to symptom amplification. As such, any explanation is likely to be complex. We have, however, shown that litigation does not differ between those with and without major depression and similarly have excluded premorbid mood disorder, having set this as an exclusion factor in patient selection. Finally, while symptom amplification is likely to affect self-report response of subjects, the use of a structured interview such as the Neurobehavioral Rating Scale—Revised adds weight to our objective impressions that subjects with major depression do more poorly.

There are several potential sources of bias in this re-

search. First is the fact that approximately 11% of the sample did not complete all outcome measures. However, 167 of 170 subjects (98%) were rated on the more objective Neurobehavioral Rating Scale—Revised, and the principal finding of more psychosocial (or more specifically, neurobehavioral) difficulties among those with major depression was corroborated. The use of direct and observer-rated measures of functioning may be ways of addressing this concern in future studies. Referral bias is a potential confound in any clinical study of outcome following traumatic brain injury. Given the sources of referral in this study, it is possible that patients seen were more symptomatic. However, this does not affect the central aim of the study, which was to study the functioning of patients with and without major depression following traumatic brain injury, rather than to study predictors of posttraumatic major depression. The third potential source of bias is the fact that a single rater completed the SCID, the Neurobehavioral Rating Scale—Revised, and the Glasgow Outcome Scale. However, the highly structured nature of these scales is likely to mitigate any built-in bias in this regard.

It is important to note that the association between major depression and poor functioning is not necessarily a causal one. Although this study was cross-sectional in nature, focusing on the acute period following injury, further longitudinal studies are underway in order to elucidate bet-

TABLE 2. Outcome for Subjects With or Without Onset of Major Depression Following Mild Traumatic Brain Injury

Variable	Patients With Mild Traumatic Brain Injury (N = 152)				Analysis		
	Depression Onset After Injury (N = 22)		No Depression Onset After Injury (N = 130)				
	Mean	SD	Mean	SD	F	df	p
	N	%	N	%	χ ²	df	p
General Health Questionnaire							
Total	20.23	6.6	9.57	7.7	36.88	1, 151	<0.0001
Somatic	5.73	1.8	2.97	2.4	27.31	1, 151	<0.0001
Social	5.73	2.0	3.21	2.6	19.27	1, 151	<0.0001
Anxiety	5.50	2.3	2.61	2.6	24.18	1, 151	<0.0001
Depression	3.27	2.2	0.78	1.5	44.76	1, 151	<0.0001
Rivermead Head Injury Follow-Up Questionnaire	27.50	11.8	15.17	12.4	18.83	1, 151	<0.0001
Rivermead Post Concussion Disorder Questionnaire	43.41	17.2	19.89	17.3	34.88	1, 151	<0.0001
Neurobehavioral Rating Scale ^a	38.46	5.3	31.57	3.8	64.31	1, 166	<0.0001
	N	%	N	%	χ ²	df	p
Glasgow Outcome Scale of 5 (good outcome) ^b	5	19.2	53	36.8	3.03	1	0.09
Returned to work ^b	7	26.9	42	29.2	0.05	1	0.82

^aNeurobehavioral Rating Scale—Revised total score = total score minus depression item subscore. Subjects with major depression, N = 26; subjects without major depression, N = 141.

^bPercentages based on 26 subjects with and 144 without major depression.

ter the nature of the relationship between major depression and dysfunction following mild traumatic brain injury.

What emerges from the data is the strong association between clinical major depression following traumatic brain injury and poor behavioral outcome. Of considerable clinical relevance for health care workers in the field, major depression is treatable in patients with traumatic brain injury.^{38,39} Our data suggest that targeting major depression may improve outcome in the domains of global and psychosocial function, psychological distress, postconcussive symptoms, and neurobehavioral difficulties. Thus, there is potential that the early identification and treatment of major

depression may directly improve outcome and quality of life for these patients.

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