Natural History of Depression in Traumatic Brain Injury

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ABSTRACT. Dikmen SS, Bombardier CH, Machamer JE, Fann JR, Temkin NR. Natural history of depression in traumatic brain injury. Arch Phys Med Rehabil 2004;85:1457-64.

Objective: To examine prospectively the rates, risk factors, and phenomenology of depression over 3 to 5 years after traumatic brain injury (TBI).

Design: Inception cohort longitudinal study.

Setting: Level I trauma center.

Participants: Consecutive admissions of 283 adults with moderate to severe TBI.

Interventions: Not applicable.

Main Outcome Measure: Center for Epidemiologic Studies Depression (CES-D) Scale.

Results: The rates of moderate to severe depression ranged from 31% at 1 month to 17% at 3 to 5 years. With 1 exception, the relation between brain injury severity and depression was negligible. Less than high school education, preinjury unstable work history, and alcohol abuse predicted depression after injury. Examination of CES-D factors indicate that, in addition to somatic symptoms, both depressed affect and lack of positive affect contribute to elevated CES-D scores.

Conclusions: High rates of depressive symptoms cannot be dismissed on grounds that somatic symptoms related to brain injury are mistaken for depression. Depressed affect and lack of positive affect are also elevated in persons with TBI. Preinjury psychosocial factors are predictive of depression and knowing them should facilitate efforts to detect, prevent, and treat depression after TBI.

Key Words: Brain injuries; Depression; Risk factors; Rehabilitation.

DEPRESSION CAN SIGNIFICANTLY add to the suffering and functional impairment of persons who sustain traumatic brain injuries (TBI).[1] However, rates, risk factors, and phenomenology of depression after TBI may not follow patterns found in community or other medical populations.

Rate estimates for depression after TBI have ranged from 14% to 42% within the first year[2-6] and from 11% to 61% at various time points up to 50 years after injury.[7-13] The wide range of rate estimates likely stems from estimates made at differing times postinjury as well as differences in patient populations and depression ascertainment methods. Many studies have drawn from small samples and tertiary referral populations, thus limiting generalizability of the findings.

Although some studies[5,14,15] have reported a higher rate of depression among person's with more severe TBI, the findings of various other studies[6-8,16,17] have been inconsistent with respect to the relations between TBI severity indicators, such as duration of loss of consciousness and posttraumatic amnesia (PTA), and the incidence and severity of depression. Studies[2,3,5,6,18] examining demographic and preinjury risk factors have suggested poor social functioning, unstable work status, lower education, younger age, and past psychiatric history as risk factors for subsequent depression. However, these and other risk factor data have not been consistently replicated in the literature.[1]

Some investigators have suggested that the phenomenology of depressive symptoms that arise after TBI differs from that which arises de novo or secondary to other medical conditions, and that these symptoms may also vary according to the time postinjury.[19,20] Although the most prevalent depression-related symptoms include fatigue and concentration difficulties, more severe depression and presence of anxiety and vegetative or somatic symptoms seem more common in early-onset depression than in later-onset depression.[19,20] Few studies have longitudinally examined depression phenomenology beyond 1 year after TBI.[21,22] These studies indicate only a general attenuation of depression symptoms after 1 year.

A better understanding of the magnitude and unique presentation of post-TBI depression may assist clinicians in communicating with patients about their symptoms and recognizing and treating depression and associated behaviors in this population. The goal of the present study was to examine prospectively the rates, risk factors, and phenomenology of depressive symptoms over a 3- to 5-year period in persons with moderate to severe TBI.

METHODS

Participants

The subjects for this study were adult patients with TBI involving intracranial abnormalities consecutively admitted to a level I trauma center. The subjects were enrolled between 1991 and 1995 in the Valproate Prophylaxis Study.[23] This was a randomized, placebo-controlled and double-blinded investigation of the efficacy of valproate sodium in preventing posttraumatic seizures and its neuropsychologic side effects. The selection criteria principally required computed tomography (CT) evidence or intracranial abnormality, including cortical contusion, intracerebral, subdural, or epidural hematoma, depressed skull fracture, or penetrating brain injury. Subjects were further required to be at least 14 years old when injured and have no history of preinjury seizures or other significant brain injury or neurologic condition. The subjects included in the present study can be described as those hospitalized with severity of brain injury ranging from complicated mild (ie,

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Glasgow Coma Scale [GCS] score, 13–15 with CT abnormalities) to severe (GCS score, 3–12). Approximately one third of hospitalized cases in our series with a GCS score of 13 to 15 had CT abnormalities; for those with more severe injuries, over 90% had CT abnormalities. We believe the cases of this study are representative of cases with complicated mild to severe brain injuries.

Subjects who were available for neurobehavioral testing and able to take the tests validly (cognitive status did not preclude valid testing) were evaluated at 1 month (n=213), 6 months (n=249), 12 months (n=193), and 3 to 5 years postinjury (n=175). Tested subjects were oriented times 3, were able to participate at least 1 hour in the testing session, and could show that they comprehended the questions and were able to give reliable responses to the examiner. This study was approved by the University of Washington Institutional Review Board.

Findings on the impact of valproate on posttraumatic seizures and neuropsychologic functioning show that valproate does not prevent late posttraumatic seizures and does not have negative or positive effects on neuropsychologic functioning.[23,24]

Measures

Depressive symptoms were evaluated by the Center for Epidemiologic Studies Depression (CES-D) Scale.[25] This is a well-validated measure that consists of 20 symptoms that are rated by frequency of occurrence in the last week, with 0 being less than 1 day a week, 1 representing 1 to 2 days a week, 2 denoting 3 to 4 days a week, and 3 representing 5 to 7 days a week. Total scores range from 0 to 60. Several components of the CES-D were derived for analysis, including the total score and 3 cutoff scores representing different levels of depression severity, with 16 indicating mild or clinically significant depressive symptoms,[26,27] 21 indicating moderate depression,[28-30] and 27 indicating severe or probable major depression.[31-33] Further, we calculated the 4 factor scores[25,34]: depressed affect, somatic activity, interpersonal problems, and positive affect. Individual item frequencies endorsed 3 or more days a week also were reported. Positive affect items were reverse scored (ie, 3 minus the score for the frequency actually endorsed) both for obtaining the total score and the positive affect factor score, so high values indicate more depressive symptoms.

Demographic information, brain injury severity, other system injury severity, and the subject's preinjury psychosocial history were evaluated in relation to depression. Demographic data included age, education, and gender.

Brain injury severity was evaluated by using the GCS,[35] time to follow commands (TFC), and PTA.[36] The GCS measures depth of coma[35] as assessed in the emergency department. TFC is used as a measure of coma length and is operationally defined as the time to achieve a consistent score of 6 on the motor component of the GCS. Subjects were asked retrospectively about PTA duration during the 1-month postinjury testing session.[36] Those too impaired to be tested at 1 month were considered to be still in PTA. Other system injuries were evaluated with a modified Injury Severity Score (ISS).[37] The score used was the sum of the squares of the highest Abbreviated Injury Scale scores assigned to the 3 most severely injured body areas, excluding the head.

Preinjury psychosocial history variables included patient-reported living situation, work stability, psychiatric history, and alcohol abuse. Living situation preinjury was divided into 2 groups based on with whom subjects were living as a proxy for level of support. Supportive living situations were those in which the subject lived with parents, other family members, guardian, spouse, or significant other. Nonsupportive living situations included living alone, with roommates, group home, congregate care facilities, hospital, nursing home, or other institutions. Work stability was examined for those whose major preinjury activity was work as opposed to school, homemaking, or retirement. Stable workers were defined as those who were working half time or more in the same job in the immediate 6 months before injury. Unstable workers were either unemployed at the time of the injury, employed for less than half time, or at the same job for less than 6 months. Subjects were divided into those with or without a preexisting psychiatric history. Subjects considered to have a prior psychiatric history had 1 or more of the following: outpatient help from a psychiatrist, psychologist, social worker, or counselor; hospitalization for emotional or psychiatric reasons; or medication for emotional problems. Psychiatric history was evaluated for the year before the injury and for anytime preinjury. Preinjury alcohol abuse was determined by using the Short Michigan Alcoholism Screening Test[38] (SMAST). The SMAST is a 13-item questionnaire that examines the negative consequences of drinking, prior treatment, and dependence symptoms. Preinjury SMAST scores formed 2 groups, those with little or no alcohol problems (SMAST score, $\leq$2) and those with scores indicative of significant alcohol problems (SMAST score, $\geq$3). The SMAST was evaluated for the year before the injury and for anytime preinjury.

Data Analysis

The data were analyzed to answer the following questions: (1) What is the degree of depressive symptoms found in a prospectively studied sample of subjects with TBI at 1 month, 6 months, 12 months, and 3 to 5 years postinjury? and (2) Does severity of depressive symptoms vary as a function of demographics, head injury, and other system injury severity, and/or preinjury characteristics?

The depression data was summarized descriptively in tabular and graphic form across the 4 time periods by examining total scores, cutoffs for depression, and item responses within each factor scale. Factor scale means are presented graphically and at 1 month and 3 to 5 years postinjury; differences among the 4 factor scores were analyzed by paired *t* tests. These times were chosen to consider the pattern of factors early and late after the injury and to reduce multiple comparisons. Mann-Whitney and Kruskal-Wallis analyses were used to determine the relationship between depressive symptoms at 1 month and 12 months postinjury and demographic, head injury, and other system injury severity and preinjury characteristics. These times were chosen to give an indication of factors related to depressive symptoms at an early and later time frame. These analyses were run at only 2 time periods to reduce multiple comparisons. However, the pattern of the findings was similar at the other time points. To evaluate the longitudinal trend in depressive symptoms, a linear contrast was calculated for each subject with CES-D scores at all 4 times, and the slope was compared with zero (ie, no trend).[39] This method was chosen over repeated-measures analysis of variance (ANOVA) because the ANOVA assumptions are not met by these data and the contrast targets the question of particular interest, that is, whether depressive symptoms increase or decrease with time.

RESULTS

Table 1 provides subjects' demographic and preinjury condition information, and table 2 provides information about their brain injury and other system injury severity. The tables give the information for the 283 cases who were tested at least once over the follow-up period. Most of the subjects were young (mean age $\pm$ standard deviation, 35.5$\pm$14.6y), white (85%),

Table 1: Demographics and Preinjury Conditions

N*	283
Mean age ± SD (range)	35.5±14.6 (14–89)
Mean education ± SD	12.5±2.4
Men (%)	81
White (%)	85
Unemployed (%)	15
Unstable worker preinjury (%)	40
Nonsupportive living situation preinjury (%)	43
Psychiatric treatment anytime preinjury (%)	33
Psychiatric treatment in year preinjury (%)	11
SMAST ≥3 anytime preinjury (%)	41
SMAST ≥3 in year preinjury (%)	23

Abbreviation: SD, standard deviation.
*Subjects tested at least once over the follow-up period.

men (81%), and had a high school education (mean education, 12.5±2.4y). Of note is the sizable percentage of the cases with problematic preinjury history, including drinking, unemployment, and treatment for emotional problems. These finding are consistent with what is reported in the literature, rather than representing a biased sample.[1,40,41] A broad spectrum of brain injury severity is represented in the group (see table 2). The severity ranges from complicated mild or moderate head injury as defined by Williams et al[42] (GCS score, 13–15 with CT abnormality, a minimum criteria for inclusion in the study) to severe head injury as reflected in GCS scores, TFC, and PTA. Some subjects did not take the CES-D at 1 month because they were too impaired to validly take the measure. Their demographics were similar to the entire group, but, as expected, those not taking the CES-D at 1 month were somewhat more severely injured.

Table 3 shows the endorsement rates for individual CES-D items at 4 time points after injury, the median total score, and the percentage of subjects whose total score falls above 3 cutoff values representing depressive symptom severity. The items are grouped according to 4 factors frequently identified in the literature to represent the content of the CES-D.[25,34,43,44] The table indicates the percentage who endorse the item 3 or more days a week, a frequency that is a good indicator of clinically significant depression. This cutoff is consistent with the symptom level used for maximum sensitivity and specificity of major depression diagnosis on the Patient Health Questionnaire,[45] a widely used self-report measure based on *Diagnostic and Statistical Manual of Mental Disorders, 4th edition*[46] (DSM-IV) diagnostic criteria. For positive affect items (reverse scored), it indicates those endorsing the positive item 4 or fewer days, that is, those who do not have the positive feeling 3 or more days a week.

At 1 month postinjury, almost half of the subjects scored 16 or more, the cutoff usually used to indicate at least mild, clinically significant depression. Fifteen percent scored above 27, a cutoff some use for probable major depression in medically ill populations.[31] Median scores decreased at least somewhat over the first year but remained unchanged between 1 and 3 to 5 years postinjury.

Table 4 shows median CES-D totals at 1 and 12 months postinjury for subgroups based on demographic factors. At 1 month, there was no relationship seen between CES-D and age, education, or gender. By 12 months, men and those with less education had significantly higher CES-D scores. Table 5 shows the corresponding values for subgroups defined by brain injury severity. At 1 month, the more severely injured according to TFC indicated significantly less depression; at 1 year, the direction was reversed, although the differences were not significant.

Table 6 shows median CES-D scores by preinjury characteristics. Subjects with an unstable preinjury work history were more depressed both at 1 and especially at 12 months after injury. Subjects with prior alcohol problems were more depressed at 1 year, especially when the time frame for problems was the year before injury. No relation between alcohol problems and depression was found at 1 month after TBI. Interestingly, subjects with a prior psychiatric history did not differ on depression after TBI from those who had no psychiatric history.

Figure 1 displays the mean item score for each CES-D factor. At 1 month, items on the somatic and (absence of) positive affect factor were endorsed most strongly while interpersonal items were endorsed the least. The differences among all pairs of factors except the positive affect and somatic were significant ($P<.001$) at both 1 month and 3 to 5 years. The figure displays a trend toward lower scores over time on the somatic, positive affect, and depressed affect factors, whereas endorsement of interpersonal items tended to increase with time from 1 to 6 months. Longitudinal analysis based on subjects with CES-D total scores at all 4 time points indicated a decreasing trend of overall endorsement, which was highly significant ($P<.004$), with 65% of subjects showing a decreasing trend and 35% showing an increasing trend.

Table 2: Head Injury and Other System Injury Severity

N	283
Etiology (%)	
Motor-vehicle related	52
Falls	18
Assault	24
Other	6
Mean GCS score ± SD	12.4±3.2
3–8 (%)	15
9–12 (%)	21
13–15 (%)	64
PTA (%)	
<24h	11
1–6d	27
7–13d	25
14–20d	8
≥21d	29
TFC (%)	
≤24h	62
25h to 6d	18
7–13d	8
14–28d	7
≥29d	5
ISS (excluding head injury) (%)	
0	31
1–8	44
≥9	25
CT findings* (%)	
Cortical contusion	76
Depressed skull fracture	16
Subdural hematoma	35
Epidural hematoma	23
Intracerebral hematoma	8
Penetrating head injury	5
Early seizures	6

*Percentages exceed 100% because subject could have more than 1 CT finding.

Table 3: CES-D Items and Scores by Time Postinjury

	1 Month	6 Months	1 Year	3–5 Years
n	218	251	193	175
Depressed affect*				
3. I felt that I could not shake off the blues even with the help of family or friends	18	20	12	10
6. I felt depressed	26	23	20	18
9. I thought my life had been a failure	5	9	8	9
10. I felt fearful	18	10	11	7
14. I felt lonely	21	23	19	21
17. I had crying spells	7	5	9	3
18. I felt sad	19	20	16	14
Somatic activity*				
1. I was bothered by things that usually don't bother me	24	16	12	8
2. I did not feel like eating; my appetite was poor	22	12	16	11
5. I had trouble keeping my mind on what I was doing	29	24	24	18
7. I felt that everything I did was an effort	42	31	25	24
11. My sleep was restless	44	24	23	26
13. I talked less than usual	32	25	21	15
20. I could not get "going"	24	19	18	22
Interpersonal problems*				
15. People were unfriendly	4	6	8	9
19. I felt that people dislike me	4	7	9	7
Positive affect†				
4. I felt that I was as good as other people	50	43	35	35
8. I felt hopeful about the future	58	48	44	47
12. I was happy	62	53	48	50
16. I enjoyed life	51	45	36	41
Total score				
Median	14	12	9	9
% ≥16	46	35	28	30
% ≥21	31	22	19	17
% ≥27	15	12	12	10

*Percentage of subjects who endorsed item for ≥3 d/wk by factor.
†Percentage of subjects who endorsed item for ≤4d/wk.

DISCUSSION

This study documents high rates of depressive symptoms up to 5 years after injury in a large consecutive series of persons who had been hospitalized for TBI. The prevalence of moderate to severe depression, as judged by a CES-D score of 21 or more, ranged from 10% to 31% across 4 time points. At 1 month after injury, nearly half (46%) of the sample endorsed a level of depression (CES-D score, ≥16) that has been considered clinically significant in epidemiologic studies,[26,47] and 30% endorsed symptom severity above this threshold 3 to 5 years postinjury.

The present study showed a trend toward less severe symptoms as time since injury increased. For comparison, 17% to 21% of white men between the ages of 25 and 44 years from a general population survey scored at or above 16 on the CES-D.[26] The present results are consistent with other studies that have shown a history of TBI is a significant risk factor for depressive disorders up to 50 years after injury.[5,8,10]

Table 4: CES-D Scores at 1 and 12 Months Postinjury by Demographic Factors

	1 Month			12 Months		
	n	Median	*P*	n	Median	*P*
Age (y)			.210			.228
≤30	98	12.5		88	8.5	
31–50	85	16		75	10.0	
>50	30	15.5		30	6.0	
Education			.664			.003
<High school	47	16		49	11.0	
High school	134	13		114	9.0	
College	32	15		30	3.0	
Gender			.980			.004
Men	172	14		155	10.0	
Women	41	15		38	5.0	

Table 5: CES-D Scores at 1 and 12 Months Postinjury by Severity Factors

	1 Month			12 Months		
	n	Median	*P*	n	Median	*P*
TFC			.007			.715
<24h	154	16.0		117	8.0	
1–6d	33	12.0		36	9.5	
≥7d	25	8.0		40	10.5	
PTA			.712			.539
≤24h	28	15.5		19	10.0	
1–6d	69	13.0		52	7.0	
≥7d	111	14.0		117	9.0	
ISS			.222			.697
0	69	15.0		59	8.0	
1–8	84	16.0		82	8.0	
≥9	50	12.0		45	11.0	

Table 6: CES-D Scores at 1 and 12 Months Postinjury by Preinjury Characteristics

	1 Month			12 Months		
	n	Median	*P*	n	Median	*P*
Preexisting psych* anytime preinjury			.387			.726
No	147	14.0		126	9	
Yes	65	15.0		67	8	
Preexisting psych* in year preinjury			.503			.663
No	194	14.0		170	9	
Yes	18	17.0		23	9	
Preexisting SMAST anytime preinjury			.756			.054
<3	126	15.5		104	7	
≥3	79	14.0		70	10	
Preexisting SMAST in year preinjury			.497			.004
<3	163	14.0		133	7	
≥3	42	15.0		41	11	
Preinjury stability of work			.032			.000
Unstable	71	16.0		63	13	
Stable	107	13.0		97	7	
Preinjury living situation†			.881			.418
Supportive	120	14.0		111	8	
Nonsupportive	92	14.5		82	10	

*Preexisting psych: yes to outpatient help and/or hospitalization and/or medication.
†Supportive: lived with parents or spouse; nonsupportive: all other living situations.

The validity of standard depression assessment after TBI has been criticized on the grounds that potentially significant overlap exists between the symptoms of depression and symptoms that might be otherwise attributed more parsimoniously to brain injury.[1] Mean item scores on the 4 CES-D factors (see fig 1) and the pattern of responses on individual items (see table 3), particularly at 1 month, lend some credence to this concern. Inspection of the mean item scores within each factor reveals a relatively high endorsement of items on the somatic factor at 1 month after TBI. The acute somatic and cognitive effects of TBI, such as inattention, sleep disturbance, anergia, and amotivational states, may contribute disproportionately to depressive symptoms observed within the first month postinjury. On the other hand, mean item endorsement on the (absence of) positive affect factor was almost as high as on the somatic factor, followed by depressed affect and interpersonal problems factor mean item scores at 1 month (fig 1, table 3). However, in healthy populations and in those suffering from cancer and multiple sclerosis, others have found that the level of endorsement on different factors does vary.[43,48] Our TBI sample showed about the same level of endorsement as other studies on (absence of) positive affect and on interpersonal problems. However, in the other populations, the somatic and, especially, the depressed affect scores were considerably lower, suggesting that, in addition to the somatic symptoms, depressed affect was clearly elevated in patients with TBI.

Taken together, the factor data suggest that early depressive symptomatology is not comprised entirely of brain injury–related somatic and cognitive symptoms; rather, depressed affect, the lack of positive affect, and interpersonal problems also contribute. Nevertheless, the clinician or researcher seeking to make a diagnosis of major depression within the first month after TBI is cautioned about the disproportionate role that potentially transient somatic and cognitive symptoms may have, especially when using symptom severity measures such as the CES-D. It is less clear what influence these early brain injury–related symptoms may have on diagnostic assessments using the DSM-IV[46] to assess major depressive disorder in which essential features, such as depressed mood or anhedonia, must be present and persistent to make the diagnosis. More studies are needed that examine the reliability and validity of other self-report measures and standardized clinical diagnostic assessments within the first 1 to 3 months after TBI. Until then, clinicians and researchers will have to weigh the likely costs and benefits of underdiagnosis versus overdiagnosis, especially within this early time frame.

These data do not support a simple dose-response relation between TBI severity and severity of depressive symptoms. TFC was the only severity indicator that predicted depression severity, and this relationship did not even persist until 12 months. In fact, greater depressive symptoms were significantly associated with less severe TBI. The literature on the relation between TBI injury severity and subsequent depressive disorders is equivocal, with some studies finding positive, inverse, or no relation between injury severity and depression.[49] The relation between severity of brain injury and depression, however, may be quite complex and may be mediated by other factors, such as injury-related disabilities and awareness of impairments. Greater depression in persons with milder injuries at 1 month after injury perhaps supports such an interpretation. Conversely, depressive symptoms such as poor concentration or anergia may contribute directly to poor neuropsychologic functioning. Treatment studies of depression could potentially elucidate this issue.

The present study suggests that educational, vocational, and psychologic factors do predict depressive symptom severity, especially at 1 year after injury. Several preinjury factors, such as less education and unstable work history, were associated with higher median CES-D scores at 1 year. Deb et al[5] also reported that less education was associated with a higher rate of major depression after TBI. Gomez-Hernandez et al[50] found that preinjury job dissatisfaction and fear of job loss was associated with depression only at 1 month after TBI. They also reported that fear of job loss after TBI was associated with depression at 6, 9, and 12 months. These findings parallel the general epidemiologic literature on psychiatric disorders, which shows that less education and job loss increase the risk of developing major depression.[51]

Preinjury alcohol-related problems, particularly within the year before injury, also predicted depression symptom severity

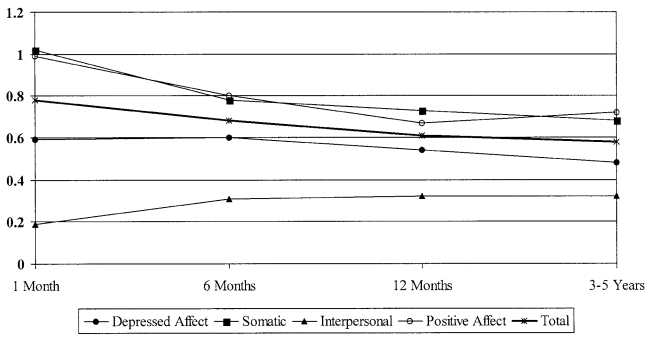

Fig 1. Mean item scores by CES-D factor at 4 time points.

at 1 year after injury. Although we do not know of other prospective studies of TBI survivors that have found this relationship, a retrospective study of veterans with documented TBI reported a significant cross-sectional association between alcohol abuse and major depression.[10] Certainly, alcoholism and major depression are common comorbid conditions in psychiatric and substance abusing populations,[52] and remission of depressive symptoms is associated with higher rates of remission from alcohol problems in persons with both disorders.[53] It is becoming increasingly clear that problems such as substance abuse and depression after TBI should not be studied or treated in isolation.

It is notable that we did not find higher median depressive symptom severity among those who reported a history of inpatient, outpatient, or pharmacologic treatment for psychiatric problems before TBI. Because these indicators of previous mental health problems are confounded by help-seeking behavior, we remain uncertain whether prior mental health problems are predictive of depressive symptoms after TBI. Furthermore, subjects were not asked what mental health problems led them to seek help. The nature of the problems for which they sought help, for example, anger management or marital conflict, might not necessarily predict postinjury depression.

These data suggest a vicious cycle involving depression and the exacerbation of preinjury vocational and psychosocial problems after TBI. People with less education, substance abuse problems, and trouble maintaining steady work are likely to have been functioning at a marginal level before TBI. Their increased risk for depression may derive, in part, from having fewer personal, financial, or social resources with which to cope with TBI-related disability and perhaps more difficulty resuming work or other meaningful activities. These interrelationships highlight the need for research and clinical interventions that are multidisciplinary and target biologic, social, and vocational risk factors to promote better overall outcomes. These data also reinforce the idea that there may be merit in early identification of persons at risk for poor psychosocial outcomes.[54]

Somewhat surprisingly, men had significantly higher median CES-D scores than women at 1 year after TBI. This finding is in contrast to the more general literature on gender and depression[51] and some studies on depression and TBI.[55] One other study[56] has reported higher rates of depression among male survivors of TBI. Because of the unexpected nature of this finding, gender differences on the CES-D were examined at all time points including 1 and 6 months, and 3 to 5 years after injury. The difference was significant only at 1 year. Given this finding, we have no good explanation for the significant gender effect at 12 months and suspect that it may represent a chance finding.

Before concluding, several limitations of the present study must be acknowledged. The study was conducted at a single site, and, consistent with the epidemiology of TBI and the population in the area, included relatively few women or racial/ethnic minorities. Therefore, one must be careful in generalizing to other regions, to women, or to people who are not white. On the other hand, the data reported here represent a large sample of unselected cases with moderate (or complicated mild) to severe TBI. As such, this sample avoids the biases present in other studies in which participants were drawn from outpatient tertiary care clinics or other referral populations that tend to overestimate the magnitude of the problems.

Even though the CES-D is a widely used measure of depressive symptomatology, it is not a diagnostic measure of major depressive disorder. In neurologic rehabilitation populations, the CES-D is likely to have fairly good sensitivity but limited specificity for major depressive disorder[57]; therefore, the results of the present study cannot definitively estimate rates of major depression. Nonetheless, using a highly conservative CES-D cutoff of 27 as an indicator of severe depression, we obtained rates of 15% at 1 month, 12% at 6 months and 1 year, and 10% at 3 to 5 years. This cutoff has been used to validly predict major depression in other medical populations.[31] Future studies should test instrument validity using diagnostic measures and should examine injury-related and psychosocial predictors of major depressive disorder.

We lack data on antidepressant medication or other drug usage or psychotherapy at the time of the follow-up evaluations. Moreover, two thirds of the subjects were administered valproic acid for up to 6 months after injury as part of a seizure prophylaxis trial. The potential effect that valproic acid and other treatments may have had on emotional functioning is uncertain and beyond the scope of this article. Assuming that at least some subjects received beneficial treatment for depressive symptoms, these data probably underestimate the magnitude of depressive symptoms after TBI.

It should be acknowledged that the present study was not designed to evaluate rates of depression across the whole spectrum of brain injury severity. In fact, subjects were enrolled only if they were hospitalized primarily with CT evidence of intracranial pathology or depressed skull fracture. Prospective studies are needed that examine rates of depression in unselected cases from the entire range of brain injury severity. Studies are also needed that examine the psychologic influence of more specific parameters of injury severity and type, such as lesion location, disruption of functional neuronal circuits (eg, frontal lobe-basal ganglia),[58] neurotransmitter systems (eg, serotonergic functioning),[59] neuropsychologic impairment,[60] and postinjury psychosocial risk factors.

CONCLUSIONS

There is increasing recognition that depression is a common and potentially disabling secondary complication of TBI. This study adds to the growing literature on this topic by prospectively documenting high rates and varying phenomenology of depressive symptoms in unselected cases of TBI up to 5 years after injury. This study also highlights the importance of psychosocial factors as predictors of those who will report significant depression up to 1 year after injury. Rehabilitation and mental health professionals must improve how we recognize, provide secondary prevention for, and treat people who are at risk for poorer outcomes and increased disability due to depression after TBI.

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