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Original Research Report

Risk Factors for New-Onset Depression After First-Time Traumatic Brain Injury

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Background: *Major depression after traumatic brain injury (TBI) has devastating consequences as it increases the risk of suicide, impairs overall quality of life, and affects interpersonal, occupational, and social functioning. Although the literature has reported factors associated with depression after TBI, very few studies have examined the prevalence and correlates focused on the development of new-onset depression (NOD) after first-time TBI. Our study aimed to identify TBI- and non–TBI-related factors associated with the development of NOD in the first year after TBI.* **Methods:** *A total of 103 subjects with first-time TBI were seen within 12 months postinjury and evaluated for the development of NOD at 3, 6, and 12 months.* **Results:** *Frontal lobe functioning, frontal lesions, and pre-TBI/early post-TBI social impairment were not found to be predictors of development of NOD within the first year after injury. Decreased post-TBI social functioning as perceived by the subject at 3, 6, and 12 months was found to be associated with NOD at each of these time points, respectively.* **Conclusion:** *The study findings highlight the importance of psychotherapeutic interventions to address the individuals' overall perception of their social impairment in the early-TBI period. This may help decrease the progression of major depression within the first year after injury.*

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Key words: Traumatic brain injury; Neuropsychiatry; Depression.

INTRODUCTION

Depression is the most common psychiatric complication of traumatic brain injury (TBI), with prevalence rates of 30–40%.[1–6] Major depression after TBI can have severe consequences for rehabilitation outcomes and can significantly affect interpersonal, occupational, and social functioning. It can impair activities of daily living and overall quality of life and can increase the risk for suicide.[7–10] The etiology of post-TBI depression is often difficult to determine because it may be driven both by psychosocial and biological

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factors. Psychosocial factors may include loss of function in multiple domains of everyday life, causing demoralization, which subsequently predisposes one to depression.[8] Biological factors may include location and severity of the brain injury. Studies using resting state neuroimaging have implicated disruption of frontal brain networks as a potential contributor to the development of major depression,[11] and these same regions have been an area of interest in studies of TBI-associated depression.[1,2,12]

Although the pathophysiology of post-TBI depression is not exactly known, it likely involves an interplay of factors before, during, and after TBI. Though the literature has focused on the role of pre-TBI depressive disorders in the development of post-TBI depression, risk factors for the development of new-onset depression (NOD) after TBI have received little attention. The authors define the development of NOD as major depressive disorder defined by the Diagnostic Statistical Manual-IV (DSM-IV)[13] developing for the first time after TBI in those with no previous history of depressive disorder. Understanding and managing risk factors in the early post-TBI period, that is, within the first 3 months, can help prevent the development of this debilitating syndrome and ameliorate its severity.

To date, several studies have examined the prevalence, risk factors, and treatment of post-TBI depression[2,4,14]; however, many of these studies have included cohorts both with pre- and post-TBI depression. In these studies, psychosocial factors associated with depressive symptoms after TBI include (1) less than high school education; (2) poor pre-injury work record; (3) alcohol abuse; (4) impaired pre- and post-injury social functioning as defined by decreased educational, vocational, and interpersonal performance; and (5) decreased activities of daily living.[15–23] Biological factors include left dorsolateral and ventromedial prefrontal cortical lesions, intellectual impairment, comorbid anxiety, aggressive behavior, and prolonged syndromal major depression in the pre-TBI period.[2,5,24]

Attempts at a better understanding of pre-injury risk factors for the development of psychiatric morbidity post-TBI have been hampered by small sample size, heterogeneity of subjects, selection biases, retrospective designs, and lack of diagnostic validity of psychiatric measures, as only few studies have used structured instruments such as the Structured Clinical Interview Diagnostic assessment.[16,25] A study conducted by Diaz et al.[16] was one of the first to show that there is a significant association between major depressive disorder, personality changes, and health-related quality of life following TBI; however, this sample only included subjects with severe TBI. A study conducted by Jorge et al.[2] found that those with major depression after TBI were more likely to have a (1) pre-injury history of depression and anxiety, (2) decreased social functioning at 6 and 12 months post-injury, and (3) were found to have significantly reduced left prefrontal gray matter volumes. This cohort, however, did not sample those with only NOD after TBI and included individuals with pre-TBI depression.

Few studies have examined the pre-injury risk factors associated with post-TBI NOD in those with no prior history of depression. These studies, however, have focused on the longitudinal course and temporal relationship of depression 1 year or more after TBI rather than immediate risk factors for NOD within 1 year post-injury. Gould et al.[27] found that rates of new psychiatric disorders, including depression, increased over the first year for those individuals with no prior history, and that age and sex did not predict who would be affected. Pagaluyan et al.[26] revealed a strong relationship between depression and perceived psychosocial functioning, but that over time, injury-related changes were not associated with depression. Hart et al.[28] reported that greater cognitive and physical disability, as well as substance use, was associated with worsening depression in the progression from year 1 to year 2. A study conducted by Wee et al.[29] focused on the role of hyperlipidemia and NOD. The study found that subjects with TBI and hyperlipidemia had a 1.72-fold increase in rates of NOD after TBI longitudinally compared to those without hyperlipidemia.[29]

The objective of the current analysis was to determine TBI- and non–TBI-related factors associated with the development of NOD in the first year after TBI. We hypothesize that (1) impaired frontal lobe functioning, as assessed by tests of executive functioning on neuropsychological testing, and the presence of frontal lesions on computerized tomography (CT) are risk factors for development of NOD within the first year after TBI; (2) impaired psychosocial status as determined by the absence of social ties

and impaired social functioning in the pre-TBI and early-TBI period (within the first 3 months of TBI) is a risk factor for development of NOD within the first year after TBI. The present study is a secondary analysis of the larger Rao et al.[30] study, which was designed to determine biopsychosocial correlates of major depression after TBI that included those with a pre-TBI history of depressive disorders and all severities of TBI.

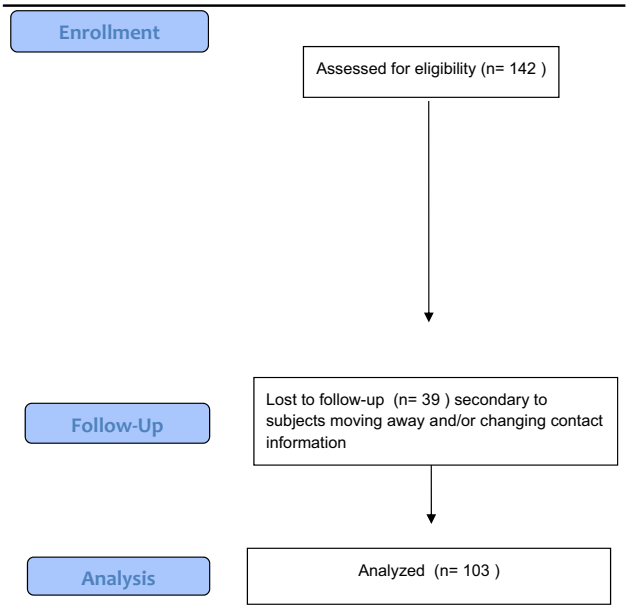
METHODS

Participants and Procedures

A total of 142 participants with first-time TBI were recruited from the trauma units of the Johns Hopkins Hospital and the Brain Injury (rehabilitation) Unit of Kernan Hospital at the University of Maryland. Thirty-nine participants were lost to follow-up, and 103 participants were assessed at 3, 6, and 12 months after TBI (Figure). For the purposes of the study, TBI was defined as having *at least one of the following*: (1) clear history of loss of consciousness (LOC), (2) Glasgow Coma Score 15 or less, or (3) evidence of trauma (contusion or hemorrhage) on CT scans done as part of clinical workup. Other inclusion criteria included (1) ability to provide consent personally, (2) ≥18 years of age, and (3) admission to the hospital for evaluation of TBI. Exclusion criteria included (1) prior TBI, (2) an open-head injury (e.g., displaced skull fracture or a gunshot wound), or (3) a history of any other type of brain illness (e.g., stroke, seizure, and encephalitis). As the current analysis is secondary and part of a larger study on biopsychosocial correlates of major depression after TBI, the authors chose to have a fairly homogenous sample of subjects with only closed head injury. The study was approved by the Institutional Review Board of both universities.

All subjects received 3–4 evaluations within the first year of TBI. The first evaluation focused on lifetime history of psychiatric problems and pre-TBI psychosocial functioning for participants who were able to provide written informed consent within the first 2 weeks of trauma. The second, third, and fourth evaluations of these subjects were performed at 3, 6, and 12 months post-TBI respectively, and focused on psychiatric problems and psychosocial functioning after TBI.

FIGURE 1. Flow Diagram of Recruitment and Follow-up.



TBI Severity

The severity of TBI was determined by the Glasgow Coma Scale (GCS), a scale that is administered by emergency medical technicians, trauma staff, or emergency department personnel in their initial evaluation. It has a range of 3–15; GCS scores of 3–8 are considered severe TBI, 9–12 moderate TBI, and 13–15 mild TBI.[31] All those determined to have mild TBI per GCS, also met criteria for mild TBI of the American Congress of Rehabilitation.[32] When GCS was not available, the duration of LOC was used: An LOC of 0–29 minutes was considered mild TBI, an LOC of 30 minutes to 24 hours was considered moderate TBI, and an LOC of >24 hours was considered severe TBI. Post-traumatic amnesia was not assessed.

MEASURES

Psychiatric Assessment

At each time point, participants underwent a comprehensive psychiatric evaluation by a neuropsychiatrist (V.R.). Axis 1 psychiatric diagnosis of major depressive disorder was determined using the Structured Clinical Interview for DSM-IV Axis 1 disorders (SCID-I)—Clinician Version.[33] If depression

was identified, level of severity was determined using the Hamilton Depression Scale (HAM-D). Pre-injury variables were determined based on the subject's recall of pre-injury status during psychiatric evaluation.

Psychosocial Functioning

Participants' pre- and post-TBI psychosocial functioning was assessed using the Social Functioning Examination (SFE) and Social Ties Checklist (STC). Both these scales have been used in prior TBI studies and have been shown to demonstrate reliability and validity in people with brain injury.[4,34,35] The SFE is a scale that assesses the participants' perception of their social status, whereas the STC assesses the presence or absence of social connections. Specifically, the SFE assesses participants' satisfaction with their (1) spousal or next closest relationship, (2) relationship with children, (3) family responsibilities, (4) work, (5) social activities, (6) financial security, (7) their home environment, (8) ability to use or access medical services, and (9) family's ability to cope with chronic illness. Scores on the SFE range from 0 (greatest satisfaction) to 1 (least satisfaction). STC assesses the presence or absence of social connections, specifically (1) living arrangements; (2) eating main meals by themselves vs with others; (3) ownership of pets; (4) involvement in any social agency or formal organizations (such as churches or social clubs); and (5) socialization with peers and family members. Higher scores indicate more impairment (i.e., fewer social connections).

Cognitive Testing

Neuropsychological tests were administered to all study participants within 3 months of TBI. The battery consisted of Mini-Mental State Examination (MMSE); National Adult Reading Test; Verbal Fluency Test, both letter (letters "s" and "p") and category fluency (animals and supermarket items); Hopkins Verbal Learning Test—Revised; Brief Visuospatial Memory Test—Revised; Trail Making Test; Stroop Color and Word Test; Brief Test of Attention; and the Wisconsin Card Sorting Test.[36–43] The aforementioned neurocognitive battery included a selection of frontal and non-frontal assessments to test the hypothesis that impaired frontal functioning is associated with the development of TBI depression.

Neuroimaging

All participants had CT brain scans done as part of routine clinical care. CT results were categorized based on the presence or absence of lesions (contusions, hemorrhages) in distinct brain regions (i.e., right, left, bilateral frontal, temporal, parietal, occipital, and subcortical).

Data Analysis

Descriptive statistics were performed on all participants. Significant differences (two-tailed) between depressed and non-depressed subgroups on individual variables were compared using Fisher exact test for categorical variables and Wilcoxon rank sum test or Student t test for continuous variables. Regression analysis was done to determine predictors of NOD at 3, 6, and 12 months post-TBI. Analyses were controlled for age and TBI severity. The criterion for statistical significance was set at $p < 0.05$.

RESULTS

Sample Demographics

Table 1 provides the demographic description of the sample. The average age in years was 42.6, and the average education level was 12.9 years. Male sex accounted for 62% of the sample, and 73.4 % were diagnosed with any psychiatric illness before TBI. Motor vehicle accident (57.6%) was the most common cause of TBI followed by assaults (21.2%) and falls (20.2%). Most subjects (61%) had mild TBI; the rest had moderate and severe TBI.

Rates of Any Type of Depressive Disorder and Rate of NOD Within the First Year After TBI

Rates of any depression were divided into 2 groups. The first group included those who were diagnosed with any depression (both pre- and post-TBI diagnosis of depression). The second group included those who were diagnosed with major depression for the first time (i.e., new-onset) that developed at any point from the time of injury to within the first year after injury. "Any depression" includes a diagnosis of depressive disorder not otherwise specified, major depressive disorder, or major depression owing to general medical condition. The prevalence of any depression within the first year

TABLE 1. Demographic Characteristics at Baseline ($n = 103$)

	N	Mean or *n*	SD or %
Demographic variables			
Age in years	103	42.6	18.0
Education level in years	103	12.9	2.9
Male sex	103	64	62.1%
Full- or part-time employed before TBI	103	77	74.8%
Married or presence of partner before TBI	103	56	54.4%
Annual income >$20K	103	58	56.3%
White race	103	53	51.5%
Clinical variables			
SFE total score	99	0.22	0.15
STC total score	99	3.36	1.77
HAM-D total score	95	2.26	4.22
Family history of mood disorder	102	43	42.2%
Family history of non-mood psychiatric disorder	102	28	27.4%
Any depression before TBI	103	18	17.5%
Any axis-I psychiatric diagnosis before TBI	103	76	73.4%
Type of injury	99		
MVA		57	57.6%
Fall		20	20.2%
Assault		21	21.2%
Other		1	1.0%
Severity	100		
Mild		61	61%
Moderate and severe		39	39%

HAM-D = Hamilton Depression Scale; MVA = motor vehicle accident; SFE = Social Functioning Examination; STC = Social Ties Checklist; TBI = traumatic brain injury.

post-TBI was 52.4%, and the incidence of new-onset major depression (NOD) any time within the first year of TBI was 15.3%. Table 2 summarizes the rates of NOD at 3, 6, and 12 months post-TBI.

Comparison on Demographic and Clinical Variables Between Those With NOD at Any Time Within the First Year of TBI and Those Without

There were no statistically significant differences in any of the demographic variables (age, sex, living situation, pre-TBI employment, and pre-TBI marital status) when comparing NOD to non-NOD groups (Table 3). When comparing the NOD vs non-NOD groups, there was a statistically significant difference in social functioning ($p = 0.007$) (i.e., decreased social functioning in the NOD group) at 3 months after TBI. There were no statistically significant differences between clinical variables (TBI severity, mode of injury, and pre-TBI psychiatric diagnosis) between those with NOD and those without (Table 3).

TABLE 2. Rates of NOD Due to MDGMC at 3, 6, and 12 mo (N = 98)

NOD	NOD at 3 mo post-TBI	NOD at 6 mo post-TBI	NOD at 12 mo post-TBI	Any NOD post-TBI*
No	87 (88.8%)	92 (93.9%)	94 (95.9%)	83 (84.7%)
Yes	11 (11.2%)	6 (6.1%)	4 (4.1%)	15 (15.3%)

NOD = new-onset depression; TBI = traumatic brain injury.

* At any time within the first year after TBI.

Association Between Frontal Lesions and Executive Impairments and NOD

There was no statistically significant association between the presence of either frontal or frontotemporal lesions and executive function tests at the time of TBI with the development of NOD within the first year of TBI (Tables 4 and 5).

SFE and NOD

Pre-TBI SFE was not associated with NOD at 3, 6, and 12 months post-TBI. Given that low social

TABLE 3. Comparison of New-Onset Depression (NOD) and Non-NOD on Demographics and Clinical Variables*

Variables	Non-NOD	NOD	Exact (*p*)†
Male sex	55 (66.3%)	7 (46.7%)	0.159
Living with others	67 (82.7%)	14 (93.3%)	0.453
Full- or part-time employed before TBI	61 (73.5%)	11 (73.3%)	1.000
Married or presence of partner before TBI	45 (54.2%)	10 (66.7%)	0.412
Cause of injury			1.000
MVA	45 (57%)	9 (60%)	
Fall	16 (20.3%)	3 (20%)	
Assault	17 (21.5%)	3 (20%)	
Other	1 (1.3%)	0 (0%)	
Severity			0.398
Mild	52 (65%)	8 (53.3%)	
Moderate and severe	28 (35%)	7 (46.7%)	
Any axis-I psychiatric (V1)	23 (76.7%)	8 (88.9%)	0.653
Frontotemporal lesions	34 (41.5%)	7 (46.7%)	0.780

Variables	Non-NOD	NOD	*t*	df	*p* Value
Age	41.9 (18.0)	49.5 (18.55)	−1.51	96	0.135
Social functioning (3 mo after TBI)	0.26 (0.13)	0.36 (0.18)	−2.73	92	0.007
Social ties (3 mo after TBI)	3.8 (1.75)	4.07 (1.54)	−0.54	92	0.587
GMHR (V1)	3.12 (0.91)	2.97 (0.52)	1.05	94	0.294
Psychiatric Dx number (V1)	1.29 (1.04)	1.73 (0.88)	−1.55	96	0.124

GMHR = General Medical Health Rating; TBI = traumatic brain injury; V1 = 3 mo of post-TBI.

* At any time within the first year after TBI.

† Fisher exact test.

functioning based on the SFE at 3 months was the only variable that was statistically significant when comparing NOD vs non-NOD (Table 3), regression analyses were completed to determine whether SFE at 3 months could predict NOD at 6 and 12 months (Table 6). SFE at 3 months was associated with NOD at 3 months and remained statistically significant after controlling for age, sex, and TBI severity (Table 7). SFE at 3 months was not significantly correlated with NOD at 6 and 12 months. SFE at 6 months was associated with NOD at 6 months and remained statistically significant after adjusting for age, sex, and TBI severity. SFE at 12 months was associated with NOD at 12 months, but lost statistical significance after controlling for age, sex, and TBI severity (Table 8).

DISCUSSION

This study is the first, to our knowledge, to examine pre- and post-TBI risk factors associated with the

TABLE 4. The Association Between Frontal Lesions and New-Onset Depression (NOD)

Variables	B	SE	*P* Value	95% CI	OR
Any NOD in the first year of TBI					
Frontal temporal lesions	0.21	0.56	0.708	−0.89–1.32	1.24
Frontal lesions	0.09	0.57	0.872	−1.03–1.22	1.10

OR = odds ratio; SE = standard error; TBI = traumatic brain injury.

TABLE 5. Neuropsychological Cognitive Variables at 3 mo Predicting any MDGMC in Post-TBI (6 and 12 mo)

Variables	B	SE	*p* Value	95% CI	Exp (B)
NOD at 6 mo of post-TBI					
BTA highest score	−0.08	0.17	0.645	−0.4–0.25	0.93
BVMT delayed recall	−0.33	0.21	0.119	−0.74–0.08	0.72
BVMT total recall	−0.13	0.08	0.12	−0.3–0.03	0.88
Design fluency total	−0.07	0.07	0.329	−0.22–0.07	0.93
*Dominant hand errors	–	–	–	–	–
Dominant hand time	−0.03	0.02	0.104	−0.07–0.01	0.97
*Nondominant hand errors	–	–	–	–	–
Nondominant hand time	−0.03	0.02	0.10	−0.06–0.01	0.97
HVLT total recall	−0.05	0.06	0.432	−0.18–0.08	0.95
MMSE	−0.13	0.12	0.279	−0.35–0.1	0.88
Stroop color world	−0.01	0.04	0.769	−0.08–0.06	0.99
Trails A	0.01	0.01	0.264	−0.01–0.03	1.01
Trails B	0.004	0.003	0.244	0–0.01	1.001
Fluency sum letters	0.03	0.05	0.547	−0.07–0.13	1.03
WCST correct	0.11	0.12	0.363	−0.13–0.35	1.12
WCST perseverative errors	−0.16	0.24	0.50	−0.62–0.3	0.85
NOD at 12 months of post-TBI					
BTA highest score	−0.35	0.21	0.092	−0.76–0.06	0.70
BVMT delayed recall	−0.17	0.21	0.407	−0.58–0.24	0.84
BVMT total recall	−0.04	0.08	0.597	−0.2–0.12	0.96
Design fluency total	−0.05	0.07	0.486	−0.18–0.09	0.95
Dominant hand errors	0.11	0.18	0.539	−0.24–0.46	1.12
Dominant hand time	−0.03	0.02	0.054	−0.07–0	0.97
Nondominant hand errors	−0.01	0.39	0.975	−0.78–0.76	0.99
Nondominant hand time	−0.02	0.01	0.187	−0.04–0.01	0.98
HVLT total recall	0.01	0.08	0.93	−0.15–0.16	1.01
MMSE	−0.13	0.15	0.396	−0.43–0.17	0.88
Stroop color world	0.04	0.04	0.333	−0.04–0.12	1.04
Trails A	0	0.02	0.99	−0.03–0.03	1
Trails B	0.004	0.003	0.846	−0.01–0.01	1.004
Fluency sum letters	−0.01	0.05	0.915	−0.11–0.1	0.99
WCST correct	0.02	0.07	0.77	−0.12–0.16	1.02
WCST perseverative errors	−0.05	0.12	0.658	−0.28–0.18	0.95

BTA = Brief Test of Attention; BVMT = Brief Visuospatial Memory Test; HVLT = Hopkins Verbal Learning Test; MDGMC = major depression due to general medical condition (TBI); MMSE = Mini-Mental State Examination; SE = standard error; TBI = traumatic brain injury; WCST = Wisconsin Card Sorting Test.

* The dependent variable is any MDGMC (NOD, yes/no) in post-TBI (6 and 12 mo). Univariate logistic regression was used in all models.Model not converged (NOD are not enough number at model with dominant hand errors and nondominant hand errors).

TABLE 6. The Association Between Social Function Examination (SFE) at 3 mo and NOD at 6 and 12 mo

Variables	B	SE	*p* Value	95% CI	OR
NOD at 6 mo					
SFE at 3 mo	5.31	3.14	0.091	−0.84–11.46	201.77
NOD at 12 mo					
SFE at 3 mo	6.18	3.52	0.079	−0.72–13.07	482.68

OR = odds ratio; SE = standard error.

development of NOD within the first year after TBI. The first major finding of this analysis was that frontal lesions and frontal functioning based on tests of executive function were not associated with the development of NOD after TBI. There are studies in the literature that have reported an association between the presence of TBI depression and frontal lesions/executive dysfunction[2] that is inconsistent with our findings. This may be due to the fact that frontal lesions in our study were detected using CT scans only,

TABLE 7. Social Function Examination (SFE) and Related Covariates Predicting New-Onset Depression (NOD)

Variables	B	SE	*p* Value	95% CI	OR
NOD at 3 mo					
SFE at 3 mo	7.95	2.56	0.002	2.94–12.97	2849.02
SFE at 3 mo	10.94	3.48	0.002	4.13–17.75	56281.7
Age	0.06	0.03	0.019	0.01–0.11	1.06
Male	−0.14	0.78	0.855	−1.67–1.39	0.87
Severity TBI	0.41	0.76	0.595	−1.09–1.90	1.50

OR = odds ratio; SE = standard error; TBI = traumatic brain injury.

and more sophisticated neuroimaging modalities were not used. Furthermore, only 4 neuropsychological tests were used to detect frontal impairment. Other tests of frontal functioning, such as the Frontal Behavior Rating Scale[44] or The Behavior Rating Inventory Rating of Executive Function (BRIEF),[45] were not used, and these or other measures may have captured other elements of executive dysfunction.

Our second major finding was that poor social functioning at 3 months did not predict NOD at 6 and 12 months. Prior studies[2–5,15,16] have reported an association between psychosocial impairment in the early-TBI period and development of depression in the chronic TBI period. These previous studies, however, included those with pre-injury depression. It is possible that because of the chronicity of the illness, people with pre-TBI depression may have more severe psychosocial impairment after TBI, and thus may be more likely to have triggers for relapse of depression in the chronic TBI period. A second explanation for the lack of predictive power of psychosocial functioning is that our study focused only on major depression in the first year after TBI, but previous studies have included a heterogeneous group of depressive disorders such as major depression, minor depression, persistent depressive syndrome, and unspecified depressive disorder. It is possible that early psychosocial impairment may be a risk factor for only certain subtypes of depressive disorders at a given time. Some of our participants also went on to receive treatment for depressive symptoms. This may also account for the lack of association between psychosocial impairment at 3 months and NOD at 6 and 12 months. Finally, although we analyzed psychosocial impairment as a broad measure, other studies have noted specific aspects of psychosocial functioning linked to depression. Gomez-Hernandez et al.[15] discussed the effect of social functioning in the early post-TBI period and the development of depression. The study reported that job satisfaction and job loss in the acute TBI period play a critical role in the development of depression in the chronic (after 1 year) post-TBI period.[15] It is thus possible that specific psychosocial factors may have a greater effect in predicting depression.

TABLE 8. The Association Between Social Function Examination (SFE) and New-Onset Depression (NOD) at the Same Visit

Variables	B	SE	*p* Value	95% CI	OR
NOD at 3 mo					
SFE at 3 mo (unadjusted)	7.95	2.56	0.002	2.94–12.97	2849.02
SFE at 3 mo (adjusted)*	10.94	3.48	0.002	4.13–17.75	56281.7
NOD at 6 mo					
SFE at 6 mo (unadjusted)	7.01	3.27	0.032	0.6–13.41	1104.02
SFE at 6 mo (adjusted)*	9.13	4.31	0.034	0.68–17.57	9202.83
NOD at 12 mo					
SFE at 12 mo (unadjusted)	7.69	3.47	0.027	0.89–14.49	2188.98
SFE at 12 mo (adjusted)*	10.02	5.69	0.078	−1.13–21.18	22552.25

* Adjusted model: adjusted age, male, and severity TBI. OR = odds ratio; SE = standard error; TBI = traumatic brain injury.

The third major finding of the study is the presence of a bidirectional relationship between NOD and post-TBI psychosocial functioning. Although a bidirectional relationship between post-TBI depression and psychosocial functioning has been well established,[15–18] we only found an association between participants' perception of social functioning and NOD; there was no association between NOD and participants' existing social network (as assessed by the STC) at 3, 6, or 12 months. This has strong clinical implications, as this provides a rationale for interventions such as cognitive-behavioral therapy, interpersonal therapy, and other psychotherapeutic treatments that target change of the individual's perception to something that is more realistic. This finding is consistent with those from the Pagulayan et al.[26] study. This model of perceived impairment and the utility of early intervention is also similar to what has been suggested in studies examining stress and coping in patients with other types of brain injury, in which poor coping has been associated with elevated levels of perceived distress.[26,46]

It is important to note the limitations of our study. First, our study sample included only hospitalized individuals with documented LOC. Subjects with only a history of altered mental status and those not admitted to trauma units were excluded. Because of such fairly strict criteria, a number of people with mild TBI may have been omitted from the sample. These strict inclusion and exclusion criteria limit the generalizability of our findings to other TBI populations. Second, subjects with only first-time TBI were included. This is important to consider, as it has previously been suggested that repeated TBI increases the risk for subsequent neuropsychiatric symptoms, including symptoms of depression and anxiety.[47,48] Third, there were 39 subjects that were lost to follow-up, and as a result, only 103 subjects were followed for analysis. This may explain the lack of predictive power for some of the findings. Fourth, both pre- and post-TBI historical information was obtained from subjects as well as family members, a condition that introduces a possible recall bias because subjects may not have been able to recall the presence or absence of psychiatric or other clinical information pre-injury.

Despite these limitations, the main strength of this study is that it is the first to look at risk factors and correlates of NOD after first-time TBI in the first year after injury. Future studies using sophisticate neuroimaging techniques to assess regions of brain dysfunction and well validated instruments recommended by the Common Data Elements in TBI initiative to capture psychosocial functioning are indicated as they can shed more light on risk factors associated with the development of NOD. Understanding determinants and correlates of NOD can help us better understand the pathophysiology of TBI and its most common neuropsychiatric sequela.

CONCLUSION

Frontal lobe functioning, frontal lesions, and pre-TBI/early post-TBI social impairment were not found to be predictors of development of NOD. Decreased perceived post-TBI social functioning at 3, 6, and 12 months was found to be associated with NOD at these points, underscoring the importance of continued psychotherapeutic interventions in those who have developed depression in the early post-TBI period. Further treatment studies examining outcomes of psychosocial interventions in the early-TBI period in the prevention of TBI depression and additional studies analyzing samples generalizable to the TBI population may be indicated.

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