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

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Abstract

Background—Major depression after traumatic brain injury (TBI) has devastating consequences as it increases the risk of suicide, impairs overall quality of life, and impacts interpersonal, occupational, and social functioning. While 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—103 subjects with first-time TBI were seen within twelve months post-injury 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 individual's 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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Keywords

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 impact interpersonal, occupational, and social functioning. It can impair activities of daily living and overall quality of life, and can increase the risk for suicide⁷⁻¹⁰. The etiology of post-TBI depression is often difficult to determine because it may be driven both by psychosocial and biological factors. Psychosocial factors may include loss of function in multiple domains of everyday life, causing demoralization that subsequently predisposes one to depression⁸. 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 depression¹¹, and these same regions have been an area of interest in studies of TBI depression^{1,2,12}.

While 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 new-onset depression (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, i.e. within the first three 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 3) decreased activities of daily living¹⁵⁻²³. Biological factors include left dorsolateral and ventromedial pre-frontal 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., 2004 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 TBI¹⁶. A study conducted by Jorge et al., 2004 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 volumes². 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 one year or more after TBI rather than immediate risk factors for NOD within one year post-injury. Gould et al 2011²⁶ 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 2008 revealed a strong relationship between depression and perceived psychosocial functioning, but that over time injury related changes were not associated with depression²⁷. Hart et al 2012 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 2²⁸. A study conducted by Wee et al. 2016 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 new-onset depression after TBI longitudinally compared to those without hyperlipidemia²⁹.

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; and 2) impaired psychosocial status as determined by 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., 2009 study³⁰, which was designed to determine biopsychosocial correlates of major depression after TBI which 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. 103 participants were assessed at 3, 6, and 12 months after TBI. Please see Figure 1. For the purposes of the study, TBI was defined as having *at least one of the following*: (a) clear history of loss of consciousness; (b) Glasgow Coma Score 15 or less; or (c) evidence of trauma (contusion or hemorrhage) on computerized tomography (CT) scans done as part of clinical workup. Other inclusion criteria included: (a) ability to provide consent personally; (b) 18 years of age; and (c) admission to the hospital for evaluation of traumatic brain injury. Exclusion criteria

included (a) prior TBI; (b) an open-head injury (e.g., displaced skull fracture or a gunshot wound); or (c) a history of any other type of brain illness (e.g. stroke, seizure, 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 three to four 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 two weeks of trauma. The second, third, and fourth evaluations of these subjects were performed at three, six, and twelve months post-TBI respectively, and focused on psychiatric problems and psychosocial functioning after TBI.

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 room 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 TBI³¹. All those determined to have mild TBI per GCS, also met criteria for mild TBI of the American Congress of Rehabilitation³². When GCS was not available, the duration of loss of consciousness (LOC) was used: A loss of consciousness of 0-29 minutes was considered mild TBI, a loss of consciousness of 30 minutes to 24 hours was considered moderate TBI, and a loss of consciousness of >24 hours was considered severe TBI. Posttraumatic amnesia was not assessed.

Measures

Psychiatric Assessment—At each time point, participants underwent a comprehensive psychiatric evaluation by a neuropsychiatrist (VR). Axis 1 psychiatric diagnosis of major depressive disorder was determined using the Structured Clinical Interview for DSM-IV Axis 1 disorders (SCID-I) -Clinician Version³³. 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 Exam (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, while 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 versus 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 three 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 Test³⁶⁻⁴³. The above 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 computerized tomography (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, 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's exact test for categorical variables and Wilcoxon rank sum test or Student's 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 gender accounted for 62% of the sample, and 73.4 % were diagnosed with any psychiatric illness prior to 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 two 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 injury within the first year after injury. “Any depression” includes a diagnosis of depressive disorder not otherwise specified, major depressive disorder, or major depression due to general medical condition. The prevalence of any depression within the first year post-TBI was 52.4%, and the incidence of new onset major depression (NOD) anytime 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, gender, living situation, pre-TBI employment, and pre-TBI marital status) when comparing NOD to non-NOD groups (Table 3). When comparing the NOD versus 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).

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).

Social functioning exam (SFE) and NOD

Pre-TBI SFE was not associated with NOD at 3, 6, and 12 months post-TBI. Given that low social functioning based on the SFE at 3 months was the only variable that was statistically significant when comparing NOD versus non-NOD (Table 3), regression analyses were completed to determine if 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, gender, 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, gender, and TBI severity. SFE at 12 months was associated with NOD at 12 months, but lost statistical significance after controlling for age, gender, 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 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 dysfunction² which is inconsistent with our findings. This may be due to the fact that frontal lesions in our study were detected using CT scans only, and more sophisticated neuroimaging modalities were not used. Furthermore, only four neuropsychological tests were used to detect frontal impairment. Other tests of frontal functioning, such as the Frontal Behavior Rating Scale⁴⁴ 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 new-onset depression 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, while we analyzed psychosocial impairment as a broad measure, other studies have noted specific aspects of psychosocial functioning linked to depression. Gomez-Hernandez et al., 1997 discussed the impact 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 one year) post-TBI period¹⁵. It is thus possible that specific psychosocial factors may have a greater impact in predicting depression.

The third major finding of the study is the presence of a bidirectional relationship between NOD and post-TBI psychosocial functioning. While a bidirectional relationship between post-TBI depression and psychosocial functioning has been well-established¹⁵⁻¹⁸, 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 targeted at changing the individual's perception to something that is more realistic. This finding is consistent with those from the Pagulayan et al 2008 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 loss of consciousness. Subjects with only a history of altered mental status and those not admitted to trauma units were excluded. As a result 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 sophisticated 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 new-onset depression. 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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Figure 1. Flow Diagram of Recruitment and Follow Up

Table 1
Demographic characteristics at baseline (n=103)

Demographic Variables	N	Mean or n	SD or %
Age in years	103	42.6	18.0
Education level in years	103	12.9	2.9
Male gender	103	64	62.1%
Full- or part-time employed prior to TBI	103	77	74.8%
Married or presence of partner prior to TBI	103	56	54.4%
Annual income>\$20K	103	58	56.3%
Caucasian race	103	53	51.5%
Clinical Variables	N	Mean or n	SD or %
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 prior to TBI	103	18	17.5%
Any axis-I psychiatric diagnosis prior to 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 & Severe		39	39%

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

Table 2
Rates of NOD due to MDGMC at 3, 6 and 12 months (N=98)

NOD	NOD at 3m post-TBI	NOD at 6ms post-TBI	NOD at 12ms 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%)

*
 at any time within the first year after TBI

Table 3
Comparison of New Onset Depression (NOD) and non-NOD on demographics, clinical variables*

Variables	non-NOD	NOD	Exact(P)**
Male Gender	55(66.3%)	7(46.7%)	0.159
Living with others	67(82.7%)	14(93.3%)	0.453
Full- or part-time employed prior to TBI	61(73.5%)	11(73.3%)	1.000
Married or presence of partner prior to 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 & 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 months after TBI	0.26(0.13)	0.36(0.18)	-2.73	92	0.007
Social Ties (- 3 months 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

V1: 3 months of post-TBI

* at any time within the first year after TBI

** Fisher's exact test

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Table 4
The association between Frontal lesions and New Onset Depression (NOD)

Variables	B	SE	P-value	95% C.I.	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

Table 5
Neuropsychological cognitive variables at 3 months predicting any MDGMC in post-TBI (6 months and 12 months)

Variables	B	SE	P-value	95% C.I.	Exp(B)
NOD at 6 months 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
* Non-Dominant Hand Errors	-	-	-	-	-
Non-Dominant 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
Trail A	0.01	0.01	0.264	-0.01, 0.03	1.01
Trail 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
Non-Dominant Hand Errors	-0.01	0.39	0.975	-0.78, 0.76	0.99
Non-Dominant 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

Variables	B	SE	P-value	95% C.I.	Exp(B)
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

MDGMC= Major depression due to general medical condition (TBD); BTA= Brief Test of Attention; BVMT= Brief Visuo-Spatial Memory Test; HVLT= Hopkins Verbal Learning Test; MMSE = Mini Mental State Examination; WCST= Wisconsin Card Sorting Test

* The dependent variable is any MDGMC (NOD, Yes/No) in post-TBI (6months and 12months). Univariate Logistic regression was used in all models.

* Model not converged (NOD are not enough number at model with Dominant Hand Errors and Non-Dominant Hand Errors)

Table 6
The association between Social Function Exam (SFE) at 3 months and NOD at 6 and 12 months

Variables	B	SE	P-value	95% C.I.	OR
NOD at 6 months					
SFE at 3 months	5.31	3.14	0.091	-0.84, 11.46	201.77
NOD at 12 months					
SFE at 3 months	6.18	3.52	0.079	-0.72, 13.07	482.68

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Table 7
Social Function Exam (SFE) and related covariates predicting New Onset Depression (NOD)

Variables	B	SE	P-value	95% C.I.	OR
NOD at 3 months					
SFE at 3 months	7.95	2.56	0.002	2.94, 12.97	2849.02
SFE at 3 months					
Age	10.94	3.48	0.002	4.13, 17.75	56281.7
Male	0.06	0.03	0.019	0.01, 0.11	1.06
Severity TBI	-0.14	0.78	0.855	-1.67, 1.39	0.87
	0.41	0.76	0.595	-1.09, 1.90	1.50

Table 8
The association between Social Function Exam (SFE) and New Onset Depression (NOD) at the same visit

Variables	B	SE	P-value	95% C.I.	OR
NOD at 3 months					
SFE at 3 months(Unadjusted)	7.95	2.56	0.002	2.94, 12.97	2849.02
SFE at 3 months(Adjusted)	10.94	3.48	0.002	4.13, 17.75	56281.7
NOD at 6 months					
SFE at 6 months(Unadjusted)	7.01	3.27	0.032	0.6, 13.41	1104.02
SFE at 6 months(Adjusted)	9.13	4.31	0.034	0.68, 17.57	9202.83
NOD at 12 months					
SFE at 12 months(Unadjusted)	7.69	3.47	0.027	0.89, 14.49	2188.98
SFE at 12 months(Adjusted)	10.02	5.69	0.078	-1.13, 21.18	22552.25

* Adjusted model: adjusted Age, Male and Severity TBI.