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Predictors of New-Onset Depression after Mild Traumatic Brain Injury

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Abstract

Mild traumatic brain injury (mTBI) is the most common form of TBI. Most people recover after mTBI but a small percentage continues to have persistent problems, predominantly depression. There is however minimal literature on the risk factors associated with mTBI depression. In a sample of 43 mTBI patients, followed longitudinally for one year the prevalence of new-onset depression was found to be 18%. Older age and presence of frontal subdural hemorrhage were the only two significant findings noted in the depressed group compared to the non-depressed group. Identifying risk factors for mTBI depression can aid in early diagnosis and treatment.

Introduction

Traumatic brain injury (TBI) is a growing public health problem with an annual incidence of at least 1.4 million[1] of which 75% is Mild TBI (mTBI). While 80-90% of individuals with mTBI usually make a good recovery[2], 10-20% continue to have psychosocial problems, predominantly mood disorder[3-6]. Depression is quite common after mTBI with a prevalence of 15.3%[7] and is a risk factor for poor recovery[8-9]. Remarkably enough, mTBI subjects have *higher* rates of depression, postconcussive syndrome and poor global outcome than those with more severe TBI[10]. There are only few studies of clinical correlates of MTBI and depression. Levin et. al.[11] report that risk factors for developing major depression in mTBI within 3 months of injury include older age and abnormal computerized tomography (CT) scans, with an odds ratio of 7.8 for the latter. To our knowledge, no other studies have looked at pre-injury and injury factors associated with the development of depression after mTBI. This is an important area of study, as identifying people at risk to develop depression soon after the injury can help initiate treatment early on. We present here the preliminary results from an ongoing 1-year longitudinal study examining risk factors for depression after

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TBI. The current analysis focuses only on risk factors associated with the development of new-onset depression after mTBI.

Participants & Procedures

mTBI patients were recruited from the trauma unit of the Johns Hopkins Hospital and the Brain Injury unit of Kernan Hospital, University of Maryland. The study was approved and overseen by the Johns Hopkins Institutional Review Boards and the Kernan Hospital Medical Executive Committee. All participants gave written informed consent. All participants received two study evaluations within the first three months of the TBI. If participants were able to provide written informed consent within the first two weeks of trauma, the first evaluation (V0), was done within the first two weeks of TBI (assessing pre-TBI functioning) and the second evaluation (V1) was done around the third month of TBI to assess psychiatric problems and psychosocial functioning soon after TBI. However, for subjects who were unable to give consent within the first two weeks of trauma or unable to be contacted both the pre-TBI (V0) and post-TBI (V1) status were assessed at the time they were contacted and able to provide informed consent, either in the second or third month post-trauma. Follow-up visits were done at 6 and 12 months post-trauma.

Inclusion criteria included—(a) first time closed head injury; (b) clear history of altered mental status or Glasgow Coma Scale (GCS) less than 15 soon after injury as assessed by the trauma staff or emergency room personnel; (c) admission to the in-patient trauma units for assessment of brain injury; (d) ability to provide consent; and (e) ≥18 years of age.

Exclusion criteria included—(a) prior TBI; (b) an open-head injury (e.g. a displaced skull fracture or a gun shot wound); or (c) history of any other type of brain illness (e.g. stroke, seizure, encephalitis).

As the focus of the analysis, is to examine risk factors for new-onset depresion after mTBI, only patients with duration of loss of consciousness less than 30 minutes and no past psychiatric history of mood disorder were included. The results presented here are preliminary and part of an ongoing study on risk factors for depression after TBI of all severities.

Measures

Psychiatric Diagnosis—All participants were interviewed with the Structured Clinical Interview for DSM-IV Axis 1 disorders (SCID-IV). The SCID was administered by a neuropsychiatrist (VR) at each visit. Patients were diagnosed to have ‘Depression’ if they met the criteria for Mood disorder secondary to General Medical Condition (TBI), Major Depressive-like episode or Other Depressive-symptoms.

Clinical Variables—Demographic information was collected via interviews and review of medical records. Psychosocial functioning was also established by a semi-structured interview using the Social Functioning Examination (SFE) scale and the Social Ties Check List (STC). Scores range from 0.00 to 1.00, with higher values indicating poorer levels of satisfaction. The Family Health Screen (FHS) was used to collect lifetime psychiatric history of family members. Medical comorbidity was assessed using the General Medical Health Rating scale, a 4-item Likert scale with 4 indicating ‘Excellent health’ and 1 indicating ‘Poor health’. In addition, the presence of non-head injuries was captured as presence or absence of body injuries.

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Lesion Location—Assessment of lesion location was obtained via CT scans conducted as part of the clinical work up. The CT scans were done soon after injury. For the purpose of this analysis, results were characterized as presence/absence of contusion, intracerebral bleed, subarachnoid hemorrhage, epidural bleed, and subdural bleed in different brain regions grouped as frontal, temporal, parietal, occipital subcortical and/or cerebellar sites.

Cognitive Tests—included Mini Mental State Examination (MMSE); National Adult Reading Test; Verbal fluency (letter 's' and 'p') and category (animals & supermarket); 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.

Statistical methods

Results were analyzed used a nested case-control design. Cases were patients who were diagnosed with 'Mood Disorder Due to General Medical Condition (TBI), Major Depressive-like episode or Other Depressive-symptoms at any time over the follow-up (n=8) while controls had no depression diagnosis at any time (n=35). None of the cases had a pre-TBI lifetime history of major depression, minor depression or any other depressive disorder. As there was little difference in results from parametric vs. non-parametric tests, parametric tests were chosen. To compare dichotomous diagnostic groups, unpaired t-tests were used for continuous variables and Fisher's Exact test for dichotomous variables. The significance level was set *a priori* at $p<0.05$. After identifying group differences, logistic regression was used to examine the odds ratio of having a major depression diagnosis for variables that were statistically significant ($p=0.05$).

Results

43 participants who completed at least 1 follow-up examination during the 1-year follow-up, period were included in the present analysis. The mean age of the sample was 44.5 (SD=17.5) and mean education level 12.9 years (SD=2.9). Fifty three percent were males and 57% non-Caucasians. The majority (93%) lived with family/friends, was either married or had a partner (74%) and had a full time/part-time job (72%). Fifty eight percent had an annual income of 20K or greater. Motor vehicle accidents were the most common cause (45%) of TBI and falls and assaults each accounted for 25%.

Incidence and persistence of post-TBI depression

Eight of the 43 participants (18.6%) met the diagnostic criterion for Mood disorder due to General Medical Condition (mTBI) during the first year of trauma. Of these, 6 (75%) met the diagnostic criterion for Mood disorder due to General Medical Condition, Major Depressive-like Episode and two (25%) met criteria for Mood disorder due to General Medical Condition, Other Depressive Symptoms. Of the 8 participants who had depression, 7 were diagnosed at the first follow up visit (V1, ie. 2-3 months after trauma) and 1 was diagnosed for the first time at the 12 month visit (V12). Of the seven, 3 were still depressed at the 12 month visit (V12), two were lost to follow up, one had resolution of depression by the end of 12 months and the other had not yet completed 1 year.

Comparison of Depressed to Non-Depressed MTBI Participants (Table)

The total sample was divided into 2 groups: Those diagnosed with Mood disorder due to General Medical Condition (Depressed) at any time over the follow-up and those without (Non-Depressed). On comparison of the two groups the only significant differences were the greater age and presence of frontal sub-dural hemorrhage in the depressed group. Lesion laterality could not be analysed secondary to the small numbers.

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The two groups also did not differ on the cognitive tests at any of the follow-up periods. There were no differences in demographic or clinical variables between subjects with minor depression (N= 2) and major depression (N=6).

Discussion

Incident depression was found in 18% of patients up to a year after mTBI. This rate is consistent with Rappaport et al[7] who found a prevalence of 15% in the first three months post-mTBI. On analysis of demographic variables, most pre-injury clinical factors did not differ between depressed and nondepressed participants. The only significant differences were increased age and the presence of frontal subdural lesions in the depressed group. These findings are similar to the study by Levin et al[11] who found increased age and presence of an abnormal CT scan done soon after mTBI to predict the development of depression within the first three months post-TBI.

The relationship between advanced age and the development of depression after mTBI is controversial. While our findings support the findings of Levin et al[11]; Rappaport et al[12] have found that older mTBI patients are not at increased risk of developing depression in the immediate trauma period. Our study had longer duration of follow-up (1 year) and included participants with minor as well as major depression; which may be an equally important contributor to morbidity[13].

Jorge et al[14,15] report in two studies that major depression post-TBI is associated with left frontal abnormality. Our finding of the positive association between mTBI depression and frontal subdural hemorrhages supports this association of lesion location with post-TBI depression and extends the results specifically to MTBI.

Strengths of the study include longitudinal design and use of well-validated psychiatric diagnostic and clinical measures. Limitations include the small sample size which may have limited identifying other correlates of mTBI depression and the absence of more sensitive neuroimaging scans. It is also possible that some patients may have had pre-existing microvascular ischemic lesions and executive functioning deficits that may have been misdiagnosed as minor depression. Another limitation is that, assessment of pre-TBI status (V0) was done in the first two weeks of trauma in only those who could be contacted and/or provide informed consent within the first two weeks of trauma. The rest had their pre-TBI status assessment at 2-3 months post trauma, which could be subject to recall bias.

Conclusion

As mTBI is a growing public health concern and depression after mTBI a common cause of morbidity, it is important to identify predictors so that treatment interventions can be instituted early on. The results of this study, though preliminary, suggest that there are at least two robust factors (age and frontal subdural lesions) of several possible predictive factors that are associated with mTBI depression. Emergency room physicians and trauma clinicians can use these results to identify high risk mTBI patients and make appropriate referrals.

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Comparison of Depressed to non-Depressed on Demographic, Pre-TBI Clinical variables & Injury Related Factors.

Demographic Variables	**Non-Depressed Mean (SD)**	**Depressed Mean (SD)**	**P-value**	**Logistic Regression**	
				Odds Ratio (CI)	**p-value**
Age Mean (SD)	**41.89 (16.9)**	**56.13 (16.2)**	**0.037**	1.047 (1.00-1.09)	**0.051**
*Female Gender: Percentage (N)	40% (14)	75% (6)	0.118		
Education yrs Mean (SD)	12.7 (2.9)	13.5 (2.6)	0.525		
Race Caucasian: Percentage (N)	41% (14)	50% (4)	0.706		
Living with others: Percentage (N)	91% (30)	100% (8)	1.000		
Married/Partner: Percentage (N)	71% (25)	88% (7)	0.656		
Working: Percentage (N)	77% (27)	50% (4)	0.189		
Cause of Injury MVA : Percentage (N)	43% (15)	63%(5)	0.699		
Abnormal CT: Percentage (N)	34% (12)	50% (4)	0.443		
Frontal subdural hematoma Percentage (N)	**3% (1)**	**37.5% (3)**	**0.016**	**20.4 (1.76-236.43)**	**0.016**
Any intracranial frontal lesions	**28.6 % (10)**	**37.5% (3)**	**0.680**		
Any intracranial temporal lesions	**8.6% (3)**	**25 % (2)**	**0.228**		
Any intracranial parietal lesions	**8.6% (3)**	**12.5% (1)**	**1.000**		
Any intracranial occipital lesions	**0 % (0)**	**12.5% (1)**	**0.186**		
Social functioning Exam Pre-TBI: Mean (SD)	0.22 (.13)	0.21 (.10)	0.900		
Social ties Checklist Pre-TBI: Mean (SD)	0.36 (.19)	0.3 (.18)	0.437		
Pre-Injury alcohol and/or drug abuse/dependence: Percentage (N)	68.6% (24)	37.5% (3)	0.125		
Presence of Body Injury post-TBI: Percentage (N)	53% (18)	88% (7)	0.114		

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Demographic Variables	Non-Depressed Mean (SD)	Depressed Mean (SD)	P-value	Logistic Regression	
				Odds Ratio (CI)	p-value
Brain Surgery: Percentage (N)	97% (34)	100% (8)	1.000		
Medical Comorbidity Pre-TBI Good/Excellent health: Percentage (N)	83% (29)	88% (7)	0.780		
Family history of Mood d/o: Percentage (N)	56% (19)	50% (4)	1.000		
Brief Test of Attention*	6.3 (3.2)	4.8 (4.4)	0.25		
Hopkins Verbal Learning Test: Sum of learning trials*	22.9 (7.3)	20.3 (7.3)	0.37		
Hopkins Verbal Learning Test: Delayed Recall*	7.3 (3.1)	7.1 (3.3)	0.88		
Brief Visual Memory Test: Sum of learning trials*	21.0 (7.3)	18.8 (7.9)	0.51		
Brief Visual Memory Test: Delayed Recall*	7.5 (2.7)	7.5 (3.2)	0.98		
Trail Making Test, part A time	47.9 (37.6)	49.3 (32.3)	0.93		
Trail Making Test, part B time*	127.6 (116.7)	187.1 (159.7)	0.24		
Sum of Letter Fluency*	23.1 (9.4)	19.9 (16.8)	0.48		
Sum of Category Fluency*	40.2 (12.2)	37.6 (10.7)	0.61		
Stroop Color Word Trial T-score*	32 (13.3)	31.5 (18.2)	0.93		
Mini Mental State Exam *	27.8 (2.8)	26.4 (3.7)	0.21		
Mini Mental State Exam at 6 months	28.7 (2.1)	28.5 (.71)	0.89		
Mini Mental State Exam at 12 months	28 (3.1)	27 (3.4)	0.55		

*Cognitive test results at the first follow-up visit (i.e. 2-3 months after injury)

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