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Correlates and Prevalence of Aggression at Six Months and One Year After First-Time Traumatic Brain Injury

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Abstract

Few studies have examined clinical correlates of aggression after first-time traumatic brain injury (TBI) within the first year after injury. Our study aimed to identify the rates of aggression at 6 and 12 months post-TBI and establish clinical and demographic correlates. 103 subjects with first-time TBI were seen within twelve months post-injury and evaluated for aggression. Post-TBI social functioning and new-onset depression (within 3 months of the TBI)may serve as particularly important predictors for aggression within the first year of TBI, as these factors may afford intervention and subsequent decreased risk of aggression.

Keywords

Traumatic Brain Injury; Mood Disorders; Aggression

Introduction

While aggression is one of the most common neuropsychiatric sequelae after traumatic brain injury (TBI), its relationship to psychiatric morbidity has not been well studied. Post-TBI aggression has an overall prevalence range from 11% to 34% {1}. It results in delayed rehabilitation, and significantly contributes to patient and caregiver burden {1, 2}.The definition of post-TBI aggression has been in flux and has been described with a wide range of phenomenology. In the TBI literature, the term has been used to refer to symptoms of disinhibition, anger, and irritability within the syndromes of behavioral and emotional

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dyscontrol {2}. In this study, we utilize the above description and further define post-TBI aggression as verbal outbursts or physical violence to objects, self, or others {2,3}.

Previous studies have associated post-TBI aggression with frontal lobe lesions, the presence of psychiatric syndromes, poor pre-morbid psychosocial functioning, and substance abuse {4-6}. The largest study to date on post-TBI aggression, published by Sabaz et al. 2014, reported on 507 subjects with severe TBI and found the prevalence of aggression within 6 months post-injury to be 31.7%. This study examined aggression as one of three challenging behaviors after severe TBI and found that these behaviors were correlated with longer duration of posttraumatic amnesia, increasing functional disability, greater restrictions in work force participation, increased support needs, and greater degrees of psychiatric disturbance. Verbal aggression was found to be more prevalent than physical aggression {7}. A study conducted by Tateno et al 2003 examined aggression within 6 months of TBI and found prevalence rates of 33.7% and that aggressive behavior was associated with depression, frontal lobe lesions, and substance abuse {1}. Dyer et al. 2006 found that verbal aggression was most prevalent (35-38%) in a cohort of twenty four patients with TBI, and physical aggression was seen only in extreme cases {8}. A recent study by James et al. 2014 highlighted that pre-morbid history of aggression predicted verbal but not physical aggression {9}.

While there have been studies that have examined correlates of post TBI aggression, as noted above, few focus solely on aggression as a post-TBI outcome, and even fewer focus on aggression only within the first year after TBI, in persons with first time TBI. Determining what clinical and demographic factors predispose persons to post-TBI aggression has the potential to identify predictors of aggression soon after injury and can provide information about early intervention. The aim of the current study was to examine the prevalence and clinical correlates of post-TBI aggression at both 6 and 12 months after injury in patients with first-time TBI. We hypothesize that the development of psychiatric illness within the early TBI period (first three months of injury) predicts the development of aggression at 6 and 12 months, and that the presence of aggression in the early TBI period (first three months after injury) will predict aggressive behavior at 6 and 12 months. This study is a continuation of a previously published study by Rao et al. 2009 {10} that examined aggression in the first three months of TBI, characterizing its severity and correlates with psychiatric diagnoses in adults with first-time traumatic brain injury. In that study, post-TBI aggression was associated with new-onset major depression, poorer social functioning, and increased dependency on activities of daily living, but not with a history of substance abuse or adult/childhood behavioral problems {10}. The present study is a secondary analysis of the larger Rao 2009 study, which was designed to determine biopsychosocial correlates of major depression after TBI. The 3 month prevalence data from Rao et al. 2009 is included in our current study to enhance longitudinal analysis.

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

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University of Maryland. Thirty nine participants were lost to follow up. 103 participants were assessed 3, 6, and 12 months after TBI. 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; and/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, we 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 participants received either three or four study evaluations within the first year of TBI. Evaluations were completed only on participants able to give informed consent; we evaluated the ability of participants to give informed consent based on their treating physicians' opinions and based on the abilities of the participants to accurately summarize the study and their roles in it. All participants received two study evaluations within three months of the TBI. The first evaluation was done to assess lifetime history of psychiatric problems and pre-TBI psychosocial functioning in those participants who were able to provide written informed consent within the first two weeks of trauma. The second evaluation for these participants was done approximately three months post-TBI to assess psychiatric problems and psychosocial functioning after TBI. However, for participants who were unable to give consent within the first two weeks post-TBI, both the pre-TBI and post-TBI status were assessed at the time they were able to provide informed consent, within the three months post-TBI. The other two evaluations were done at 6 and 12 months after injury. Information from a collateral informant was collected whenever possible on both the pre-TBI and post-TBI status on all psychosocial measures.

Measures

Aggression

The Overt Aggression Scale (OAS) {11-14} was used to assess verbal and physical aggressive behavior. The OAS was measured at 3 time points: at 3 months, 6 months and 12 months post-TBI, and was administered by a neuropsychiatrist, one of the authors (VR).

The OAS has two sections. The first section assesses four types of aggressive behavior: (1) verbal aggression, (2) physical aggression against objects, (3) physical aggression against self, and (4) physical aggression against others. The second section rates interventions provided by staff at the time of the incident. As the focus of the study was to assess rates and correlates of aggression after TBI, only the first section of the scale was administered at all the visits; more specifically presence or absence of aggression. The severity of aggression or interventions administered was not evaluated. Pre-TBI OAS was not assessed.

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Psychiatric Diagnoses

Axis 1 psychiatric diagnosis was determined using the Structured Clinical Interview for DSM-IV Axis 1 Disorders (SCID-IV) - Clinician Version {15}. SCID-IV was done within 2 weeks of TBI for those who came for assessment of pre-TBI psychiatric history. For those who did not, SCID-IV was done approximately at 3 months to assess pre-TBI and post TBI psych history. The psychiatric diagnoses obtained from the SCID evaluations are listed in Table 5. The SCID-IV does not incorporate diagnoses such as impulse control disorder and intermittent explosive disorder. As such, diagnoses such as these were not included in the study.

Severity of TBI

The severity of TBI was determined by the Glasgow Coma Scale (GCS), the most widely used instrument for quantifying TBI severity. The GCS is administered by the trauma staff or the emergency room personnel in their initial evaluation, and has a range of 3-15. GCS scores of 3-8 are considered severe TBI, 9-12 moderate TBI, and 13-15 mild TBI {16}. All those determined to have mild TBI, as defined by the GCS, also met the mild TBI criteria of the American Congress of Rehabilitation{17}.

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 {18-20}. Scores on the SFE and STC range from 0 (greatest satisfaction) to 1 (least satisfaction). The SFE is a scale that assesses participants' satisfaction and perception of their social network such as relationship with spouse/partner, relationship with children, family responsibilities, work, financial security and ability of family to cope with chronic illness.

The STC assesses presence or absence of stable social network such as close relationships, engagement in social activities, ownership of pets and connections with social agencies.

Cognitive Testing

Neuropsychological tests were administered to all study participants at approximately 3 months post-TBI. The battery consisted of the Mini Mental State Examination (MMSE), National Adult Reading Test; Verbal fluency, which included lexical fluency 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{21-28}. The above neurocognitive battery includes a selection of ‘frontal’ and ‘non-frontal’ tests that were put together for the larger study to test the hypothesis if impaired frontal functioning is associated with the development of TBI depression. These tests were chosen for the ease of use and availability of the instruments.

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Neuroimaging

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

Data Analysis

Participants were categorized as having “aggression” if they endorsed any of the subtype anchor questions on the OAS. Severity of aggression was not assessed. Descriptive statistics were calculated for all participants and for subgroups stratified by post-TBI aggression status. The significance of group differences (two-tailed) on individual variables were compared using Pearson's chi-square and Fisher's exact test for categorical variables and Students' t-test for continuous variables. A value set a priori at $p<0.05$ was considered statistically significant. To assess the strength of the relationship between aggression and the demographic and clinical factors, we conducted either a t-test or Fisher's exact test with presence/absence of aggression as the dependent variable. On comparison of the two groups, those variables that were statistically significant and those that trended towards significance were included as independent variables in the univariate logistic regression analyses. Significance levels were set at $p<0.05$. Given that a multiple pair-wise test was not used, the Bonferroni correction could not be applied, as it is used to reduce the chances of obtaining false-positive results (type I errors) when multiple pair wise tests are performed on a single set of data.

Results

Sample Demographics

A total of 142 subjects were enrolled in the study. Thirty nine subjects signed the informed consent form, but did not attend even one follow-up evaluation and were therefore excluded from the analysis. One hundred and three subjects had at least one follow-up and were included in the analysis.99.0% of participants had pre-TBI status assessed either at 2 weeks or 3 months, 97.1% completed follow up at 3 months, 70.9% completed follow up at 6 months, and 70% completed follow up at 12 months. 0.97% came for no follow up, 17.5% came for one follow up, 27.2% came for 2 follow ups and 54.4% came for 3 follow ups. There was no difference in demographic variables between those participants who completed the study and those lost to follow-up (Table 1). Table 2 reports a comparison of variables between follow-up at 3 months, 6 months, and 12 months (participants who came for follow up for a total of 3 times) versus those who came in less than that. There was no difference in demographic variables between those who completed follow ups at 3, 6 and 12 months versus those who completed less (Table 2). Table 3 provides the demographic and clinical 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 62.1% 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%). Mild TBI (GCS score of 13-15) was the most common severity of TBI (61%) followed by moderate and severe TBI (39%).

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Rates of Aggression

Table 4 provides a summary of the rates of overall aggression and aggression subtypes at 3, 6, and 12 months. The rate of aggression at 3 months was found to be 34.3%. Rates of aggression at 6 and 12 months were found to be 41.1% and 38.0% respectively. Verbal aggression was the most prevalent subtype of reported aggression in the post-TBI period, and the prevalence of verbal aggression was 41.1% and 38.0% at 6 and 12 months respectively.

Comparison of participants with and without aggression on demographic and clinical variables at 6 and 12 months

Table 5 summarizes a comparison of participants with and without aggression on demographic and clinical variables. Those with aggression at 6 months had less total years of education (12.2) than those with no aggression at 6 months (13.6), p=0.04. Male gender was associated with aggression at 12 months (p=0.04), but not 6 months. There was no statistically significant association between the presence of CT head lesions (frontal, temporal, parietal or occipital) and aggression at 6 and 12 months. Decreased social functioning at 3 months after TBI and new-onset depression (potentially due to TBI) 3 months post-injury was associated with aggression at 12 months. Body injury (injury below the neck)was associated with aggression at 6 months (p=0.012), but not at 12 months (p=0.80). There were no statistically significant differences in any other clinical variables. There was no significant difference between the two groups on cognitive tests (Table 6). Comparison of participants with and without aggression on demographic and clinical variables analyzed at 3 months can be found in the previously published study by Rao et al 2009 {10} and are not part of the analysis for this study.

Demographic and Clinical Variables Associated with Aggression at 6 and 12 Months

Based on the results of comparing those with and without aggression in the first year of TBI, we conducted regression analysis to determine clinical and demographic variables associated with aggression at 6 and 12 months. On univariate regression analysis (Table 7) low education and body injury were associated with aggression at 6 months. Aggression at 12 months was associated with male gender, new onset major depression due to general medical condition (TBI) at 3 months and poor social functioning at 3 months.

Aggression at 3 months as predictor for aggression at 6 and 12 months

A logistic regression analysis was performed to determine if aggression in the early TBI period predicted aggression later within the first year after TBI. Results revealed that aggression at 3 months was a strong predictor for aggression at 6 and 12 months (Table 8).

Longitudinal analysis of aggression in the first year after TBI

In order to further understand the risk of developing aggression throughout the course of the first year after TBI and to determine if there was any one particular time point at which individuals were placed most at risk, we fit a generalized estimating equation (GEE) with population-average logistic regression model. The analysis revealed that there was no significant changes in odds ratio at 6 months and 12 months as compared to 3 months after

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TBI, with or without adjusted for age, education, gender, and body injury present and new onset major depression due to general medical condition (TBI) at 3 months (Table 9).

Discussion

The first major finding of this study was that the presence of aggression at 3 months predicted aggression at 6 and 12 months. The implication of this is that critical assessment of aggression via evaluation of psychosocial and psychiatric disease burden in the early TBI period can allow for early interventions to potentially prevent progression of aggressive behavior later on in the first year after TBI. Verbal aggression was found to be the most prominent subtype of aggression at 6 months, and prevalence of physical aggression was negligible. Male gender, body injury, lower education, and decreased post-TBI social functioning in the early TBI period were all associated with aggression in the 6 to 12 months post-TBI period.

The second interesting finding from this study is that the presence of new-onset depression after TBI at 3 months (but not premorbid major depression) was associated with the development of aggression at 12 months. Given that aggression at 3 months was associated with aggression at 6 and 12 months, and that development of depression 3 months after TBI was associated with aggression at 12 months it might be possible that the aggression is a manifestation of a depressive syndrome. It may be that depressive symptoms with brain damage place individuals at higher risk for affective dyscontrol and subsequently verbal aggression in the late TBI period. The association between early new-onset TBI depression and chronic aggression in persons with first time TBI highlights the role of brain injury in the development of aggression and underscores the importance of early intervention to minimize or prevent aggression. While several studies have shown depression to be associated with aggressive behaviors {1, 27-29}, ours is the first to our knowledge to show that the presence of ***new*** onset depression 3 months after TBI predicts aggression at 12 months. These findings suggest that identification and treatment of depression within the first three months of TBI may reduce the burden of disease that ensues from aggression within the first year post-injury. This may emphasize the need for rigorous screening for new-onset depressive symptoms immediately after injury to significantly reduce the risk of aggression later on. No other new onset psychiatric illness was associated with aggression, stressing the importance of studying the ramifications of depression in the early TBI period and its implications.

The third finding from this study is that the presence of poor social functioning within the first three months of TBI is associated with aggression at 12 months after TBI. This was determined based on low SFE scores, indicating that an individual's satisfaction and perception of social networks in the acute TBI phase may predict aggression in the chronic TBI phase. These findings emphasize that early psychosocial interventions are critical in the early post-TBI period, as this alone may reduce the imminent risk of aggression in the in the first year after TBI.

While this present study showed no significant association between cognitive deficits, substance abuse, and frontal lobe injuries as reported in prior studies {1,4,5}, it was

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consistent with those studies in showing that depression and post- TBI social functioning are associated with aggression. The findings that no association of aggression exists between cognitive deficits, frontal lobe injuries, and substance abuse is likely due to the fact that the present study found negligible rates of physical aggression and predominantly found high rates of verbal aggression. Prior studies including those by Tateno et al. 2003, Rapoport et al. 2002, and Dyer et al. 2006 {1,6,8} had higher rates of physical aggression, and aggression overall was associated with cognitive deficits, frontal lobe injuries, and substance abuse in these studies. These studies had higher severity of TBI in the cohorts sampled with more heterogeneous samples (spinal cord injuries, and wider range of TBI severity). In addition, it has been shown in a study by Greve et al. 2001 that impulsive aggression after TBI has been associated with male gender, antisocial personality, and younger age, which seem to have been present in this study as well {5}. Several studies on TBI aggression have demonstrated that physical aggression is the most common subtype {27,28}. However, these cohorts were followed after the first year after TBI.

In the present study, it is unclear why aggression at 6 months was associated with lower total years in education. It is possible that this may be due to lower education as a risk factor for poor health, and lower self-confidence, which might result in poor coping skills. This might also be a reflection of fluctuations in the sample in terms of education level of participants who completed the assessments at each time point. In the 6 months following TBI, these factors may add to the intensity of emotions felt and in conjunction with poor coping skills, lead to more aggressive tendencies. Those with body injury were found to be more aggressive at 6 months, yet at 12 months, there was no association. Body injury may be an arbitrator of aggression in this population, and it is possible these individuals recovered from their body injuries at 12 months.

There are several limitations to this study. First, as this analysis focused on the presence or absence of aggression, severity of aggression was not assessed. As such, it was not determined what degree of aggression was considered pathological and what was considered normal. This has implications when determining psychiatric predictors of aggressive behaviors and can affect determination of prognosis. Second, it is important to note that mild TBI was the most prevalent severity subtype in this study. While this is representative of real world populations, the finding that verbal aggression was most prominent in the study sample cannot be generalized to the entire population of TBI aggression. Third, comparisons of verbal and physical aggression prevalence in the literature vary, though most studies have found verbal aggression to be more prevalent than the physical subtype in TBI populations. In one study conducted by Giles et al. 2007, out of a sample of 34 subjects, there were more commonly observed episodes of verbal aggression as compared to physical aggression. In contrast, the above referenced study by Sabaz et al 2014 found that both verbal and physical aggression increased with growing severity. This points to the importance of using homogenous samples such that severity groups do not become conflated.

Fourth, the study sample included only those with first-time traumatic brain injury (and only those with closed head injury), clear history of loss of consciousness, and hospitalized individuals. Subjects with only history of altered mental status and those not admitted to the

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trauma units were excluded. These strict criteria may have thus omitted a number of persons with mild TBI and limited the ability to generalize these findings to other TBI populations.

Fifth, pre-TBI psychiatric history was obtained either within 2 weeks after TBI for those who could provide informed consent and participate in the evaluation or approximately at 3 months after TBI, for those who could not. We also do not have data on the percentages of participants seen within 2 weeks versus approximately at 3 months to do any comparisons. This can cause significant concern for recall bias and can possibly explain the high rates of major mental illness pre-TBI. Sixth, the study did not demonstrate that TBI was the cause of aggression directly. The lack of control groups with exposure to non-TBI bodily injuries or no injury is a limitation. Such issues did not allow for systematic assessment of mediators and interactions. In addition to body injury, factors other than the presence of TBI itself that may be responsible for aggression, including TBI severity, general medical comorbidities, or environmental triggers. These are all confounders that may have been addressed with a control comparator arm. There was also notable loss to follow up at 6 and 12 months compared to the 3 month time points, which impacted the sample size for data collection towards the end of the study.

Conclusion

Few studies have examined the impact of correlates in the early TBI period. This study is the first to our knowledge to assess clinical and demographic variables at 3 months post-TBI and aggression at 6 and 12 months post TBI. Our findings highlight that early aggression after TBI is correlated to aggression later on within the first year after TBI, and that new-onset depression and in the early TBI period is associated with aggression in the chronic TBI period. Decreased psychosocial functioning is another malleable factor associated with aggression in this study. Early intervention for the screening and treatment of depression and immediate psychosocial interventions may reduce burden of disease. Future studies should focus on effective early screening for new-onset depression after TBI and early psychosocial interventions to improve psychosocial functioning.

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Table 1
Comparison of subjects who participated versus those lost to follow up

Variables	At least one follow-up		Exact P**
	No (N=39)	Yes* (N=103)	
Type of injury			0.171
MVA	11(36.7%)	57(57.6%)	
Fall	9(30%)	20(20.2%)	
Assault	10(33.3%)	21(21.2%)	
Other	0	1(1.01%)	
Severity			0.069
Mild	30(78.9%)	61(61%)	
Moderate & Severe	8(21.1%)	39(39%)	
Any axis-I psychiatric diagnosis prior to TBI			
No	13(33.3%)	27(26.2%)	0.41
Yes	26(66.7%)	76(73.4%)	
Any depression prior to TBI			
No	33(84.6%)	85(82.5%)	1.00
Yes	6(15.4%)	18(17.5%)	
Substance dependence or abuse prior to TBI			
No	22(57.9%)	52(51.5%)	0.569
Yes	16(42.1%)	49(48.5%)	
GMHR prior to TBI			0.60
1	0	1(0.98%)	
2	3(12%)	6(5.9%)	
3	2(8%)	7(6.9%)	
4	20(80%)	88(86.3%)	

*At least one follow-up

**Fisher's exact test

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Table 2

Comparison of Demographic and Clinical Variables on Total Completers* vs Partial Completers**

Variables	Follow-up at 3, 6 and 12 months		Exact P
	No (N=47)	Yes (N=56)	
Type of injury			0.737
MVA	25(55.6%)	32(59.3%)	
Fall	11(24.4%)	9(16.7%)	
Assault	9(20.0%)	12(22.2%)	
Other	0	1(1.85%)	
Severity			0.413
Mild	31(66.0%)	30(56.6%)	
Moderate & Severe	16(34.0%)	23(43.4%)	
Any axis-I psychiatric diagnosis prior to TBI			
No	10(21.3%)	17(30.4%)	0.370
Yes	37(78.7%)	39(69.4%)	
Any depression prior to TBI			
No	41(87.2%)	44(78.6%)	0.304
Yes	6(12.8%)	12(21.4%)	
Substance dependence or abuse prior to TBI			
No	23(48.9%)	29(53.7%)	0.692
Yes	24(51.6%)	25(46.3%)	
GMHR prior to TBI			0.515
1	1(2.2%)	0	
2	4(8.7%)	2(3.6%)	
3	3(6.5%)	4(7.1%)	
4	38(82.6%)	50(89.3%)	

*completed follow-up at all three time points: 3, 6 and 12 months

**did not complete follow up (i.e. missed follow up at either 3, 6 or 12 months)

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Table 3
Sample Demographics and Clinical Variables

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%
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 %**
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 pre-TBI score	99	0.22	0.15
STC pre-TBI score	99	3.36	1.77
HAM-D pre-TBI score	95	2.26	4.22

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

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Table 4

Prevalence of subtypes of aggression

Variable	3 months		6 months		12 months	
	No Aggression	Aggression	No Aggression	Aggression	No Aggression	Aggression
Verbal Aggression	65(65.7%)	34(34.3%)	43(58.9%)	30(41.1%)	44(62.0%)	27(38%)
Physical Aggression against self	97(99.0%)	1(1.02%)	69(94.5%)	4(5.5%)	69(97.2%)	2(2.8%)
Aggression against objects	98(99.0%)	1(1.01%)	67(91.8%)	6(8.2%)	66(93%)	5(7%)
Aggression against others	98(100%)	0	70(97.2%)	2(2.8%)	70(98.6%)	1(1.4%)
Any Aggression	65(65.7%)	34(34.3%)	43(58.9%)	30(41.1%)	44(62.0%)	27(38%)

*Aggression (Yes/No) in 6 months and 12 months are counted from either one who have Verbal Aggression, Physical Aggression against self, Aggression against objects or Aggression against others at 6 months and 12 months, respectively

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Table 5

Comparison of those with and without aggression on demographic and injury variables at 6 and 12 months

Variables	6 months				12 months			
	No Aggression (N=43)	Aggression (N=30)	df	t(P)	No Aggression (N=44)	Aggression (N=27)	df	t(P)
Demographic Variables								
Age *	44.9(2.88)	41.4(3.37)	71	0.8(0.43)	45.6(3.16)	43.2(3.39)	69	0.51(0.61)
Education *	13.6(0.45)	12.2(0.5)	71	2.1(0.04)	12.8(0.36)	13.7(0.72)	69	-1.12(0.24)
Male gender	24(55.8%)	21(70%)		0.328	32(72.7%)	13(48.2%)		0.045
Caucasian race	23(53.5%)	18(60%)		0.64	21(47.7%)	16(59.3%)		0.46
Living with others	36(83.7%)	24(82.8%)		1.00	36(81.8%)	25(96.2%)		0.14
Married/Partner	23(53.5%)	16(53.3%)		1.00	22(50%)	18(66.7%)		0.22
Working PT/FT	33(76.7%)	22(73.3%)		0.79	33(75%)	18(66.7%)		0.59
Religion	34(81%)	27(90%)		0.34	37(86.1%)	23(85.2%)		1.00
Clinical Variables								
GCS *	11.8(0.6)	12(0.8)	60	-0.11(0.91)	11.7(0.6)	12.1(0.9)	58	-0.43(0.67)
Type of injury: MVA	26(61.9%)	16(57.1%)		0.80	22(51.2%)	17(65.4%)		0.32
Body injury present	23(54.5%)	24(82.8%)		0.012	28(65.1%)	19(70.4%)		0.80
CT Head	5(100%)	0		-	4(100%)	2(66.7%)		0.43
Frontal Cortex Lesion	20(46.5%)	7(24.1%)		0.08	18(41.9%)	12(44.4%)		1.00
Temporal Cortex Lesion	8(18.6%)	6(20.7%)		1.00	6(14.0%)	7(26.9%)		0.21
Parietal Cortex Lesion	7(16.3%)	3(10.3%)		0.73	7(16.3%)	2(7.7%)		0.47
Occipital Cortex Lesion	2(4.7%)	3(10.3%)		0.39	4(9.3%)	2(7.7%)		1.00
Brain Surgery	4(9.3%)	3(10.3%)		1.00	2(4.7%)	5(19.2%)		0.09
Any psychiatric pre-TBI	29(67.4%)	23(76.7%)		0.44	30(68.2%)	18(66.7%)		1.00
Any psychiatric post-TBI	35(81.4%)	24(80.0%)		1.00	34(77.3%)	25(92.6%)		0.12
Major Depression pre-TBI	7(63.6%)	2(22.2%)		0.09	4(44.4%)	4(50.0%)		1.00
Major Depression post-TBI	2(33.3%)	0		0.46	0	1(33.3%)		0.33
Anxiety Disorder pre-TBI	2(4.7%)	2(6.7%)		1.00	1(2.3%)	2(7.4%)		0.55
Anxiety Disorder post-TBI	6(54.5%)	10(90.9%)		0.15	8(61.5%)	8(88.9%)		0.33
Alcohol pre-TBI abuse/dependence pre-TBI	18(42.9%)	15(53.6%)		0.47	16(38.1%)	12(46.1%)		0.61

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Variables	6 months				12 months			
	No Aggression (N=43)	Aggression (N=30)	df	t(P)	No Aggression (N=44)	Aggression (N=27)	df	t(P)
Alcohol post-TBI abuse/dependence post-TBI	12(70.6%)	10(71.4%)		1.00	13(72.2%)	9(75.0%)		1.00
Substance pre-TBI abuse/dependence pre-TBI	18(43.9%)	16(53.3%)		0.48	21(48.8%)	9(34.6%)		0.32
Substance post-TBI abuse/dependence post-TBI	7(58.3%)	9(69.2%)		0.69	10(66.7%)	4(50.0%)		0.66
Adult Behavior ** pre-TBI	0	0		-	1(2.9%)	0		1.00
Adult Behavior ** post-TBI	0	1(3.6%)		0.41	1(2.6%)	0		1.00
Social Functioning pre-TBI TBI *	0.21(0.02)	0.24(0.03)	70	-0.81(0.42)	0.19(0.02)	0.22(0.03)	67	-0.78(0.44)
Social Functioning pre-TBI TBI *	0.25(0.02)	0.3(0.03)	67	-1.4(0.17)	0.23(0.02)	0.31(0.03)	66	-2.46(0.02)
Social Ties pre-TBI *	2.98(0.22)	3.41(0.38)	69	-1.1(0.29)	2.91(0.19)	3.2(0.37)	66	-0.77(0.44)
Social Ties post-TBI *	3.58(0.23)	3.61(0.32)	67	-0.1(0.95)	3.58(0.25)	3.56(0.29)	66	0.07(0.94)
Personal & Instrumental activities of daily living pre-TBI *	0.81(0.41)	0.47(0.2)	69	0.66(0.51)	1.07(0.42)	0.42(0.19)	66	1.18(0.24)
Personal & Instrumental activities of daily living post-TBI *	4.66(0.81)	5.21(1.07)	67	-0.42(0.67)	4.24(0.78)	6.04(1.01)	66	-1.42(0.16)
Any MDGMC	5(11.9%)	5(18.5%)		0.497	4(9.8%)	8(30.8%)		0.048
MDGMC at 3 months	3(7.1%)	4(14.8%)		0.42	2(4.9%)	6(23.1%)		0.048
MDGMC at 6 months	2(4.8%)	4(14.8%)		0.201	-	-		-
MDGMC at 12 months	-	-		-	1(2.4%)	1(3.7%)		1.00

* t-test; All others are Fisher's exact test

** includes legal problems (arrests, incarcerations)

All Pre- used variables in baseline; All Post- used variables in 3months

MDGMC= Major depression due to general medical condition (TBI)

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Table 6

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

Variables	B	SE	P-value	95% C.I.	Exp(B)
Any aggression in post-TBI at 6 months					
BTA Highest Score	-0.13	0.11	0.248	-0.35, 0.09	0.88
BVMT Delayed Recall	-0.07	0.09	0.458	-0.25, 0.11	0.93
BVMT Total Recall	-0.03	0.04	0.468	-0.1, 0.04	0.97
Design Fluency Total	-0.04	0.03	0.267	-0.1, 0.03	0.96
Dominant Hand Errors	-0.06	0.15	0.668	-0.35, 0.23	0.94
Dominant Hand Time	0.00	0.00	0.541	-0.01, 0	1.00
Non-Dominant Hand Errors	0.44	0.69	0.522	-0.91, 1.8	1.56
Non-Dominant Hand Time	0.00	0.01	0.866	-0.02, 0.01	1.00
HVLT Total Recall	0.02	0.04	0.566	-0.05, 0.1	1.02
MMSE	-0.02	0.08	0.755	-0.17, 0.13	0.98
Stroop Color World	0.03	0.02	0.163	-0.01, 0.07	1.03
Trails A	-0.01	0.01	0.494	-0.02, 0.01	0.99
Trails B	0.00	0.00	0.338	-0.01, 0	1.00
Fluency Sum Letters	0.03	0.03	0.385	-0.03, 0.08	1.03
WCST Correct	-0.03	0.03	0.245	-0.09, 0.02	0.97
WCST Perseverative Errors	-0.02	0.03	0.587	-0.08, 0.04	0.98
Any aggression in post-TBI at 12 months					
BTA Highest Score	-0.06	0.11	0.571	-0.27, 0.15	0.94
BVMT Delayed Recall	-0.06	0.09	0.479	-0.24, 0.11	0.94
BVMT Total Recall	-0.04	0.04	0.316	-0.1, 0.03	0.97
Design Fluency Total	0.00	0.04	0.972	-0.07, 0.07	1.00
Dominant Hand Errors	-0.02	0.14	0.897	-0.3, 0.26	0.98
Dominant Hand Time	0.00	0.00	0.483	-0.01, 0.01	1.00
Non-Dominant Hand Errors	-0.39	0.79	0.622	-1.93, 1.15	0.68
Non-Dominant Hand Time	-0.01	0.01	0.248	-0.03, 0.01	0.99
HVLT Total Recall	0.01	0.04	0.884	-0.07, 0.08	1.01
MMSE	-0.02	0.08	0.775	-0.19, 0.14	0.98

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Variables	B	SE	P-value	95% C.I.	Exp(B)
Stroop Color World	0.00	0.02	0.901	-0.04, 0.04	1.00
Trails A	-0.01	0.01	0.281	-0.03, 0.01	0.99
Trails B	0.00	0.00	0.738	0, 0.01	1.00
Fluency Sum Letters	0.03	0.03	0.387	-0.03, 0.08	1.03
WCST Correct	-0.02	0.03	0.448	-0.08, 0.04	0.98
WCST Perseverative Errors	0.01	0.03	0.803	-0.05, 0.07	1.01

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 aggression (Yes/No) in post-TBI (6months and 12months). Logistic regression was used in all models.

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Table 7

Demographic and Clinical Variables Associated with Aggression at 6 and 12 Months

Variables	B	SE	P-value	95% C.I.	Exp(B)
Any * aggression in post-TBI at 6 months					
Education	-0.19	0.09	0.048	-0.37, -0.002	0.83
Body Injury present	1.43	0.58	0.014	0.29, 2.56	4.17
Any * aggression in post-TBI at 12 months					
MDGMC at 3 months	1.77	0.86	0.040	0.08, 3.46	5.85
SFE at 3 months	4.77	2.09	0.022	0.68, 8.85	117.49
Male gender	-1.05	0.51	0.040	-2.05, -0.05	0.35

MDGMC= Major depression due to general medical condition (TBI)

* Any aggression denotes any verbal or physical aggression

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Table 8

Aggression at 3 months post-injury as a predictor of later aggression at 6 or 12 months

Variables	B	SE	P-value	95% C.I.	Exp(B)
Any aggression in post-TBI at 6 months					
Any aggression at 3 months	1.52	0.54	0.005	0.46, 2.58	4.57
Any aggression in post-TBI at 12 months					
Any aggression at 3 months	1.89	0.56	0.001	0.78, 2.99	6.6

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Table 9
Longitudinal analysis of aggression in the first year after TBI

Any aggression	Model parameter estimates		
	OR	95%CI	P-value
Model-1			
6mo	1.43	0.86, 2.39	0.171
12mo	1.21	0.72, 2.04	0.476
Model-2			
6mo	1.45	0.86, 2.45	0.165
12mo	1.24	0.72, 2.11	0.438
Model-3			
6mo	1.60	0.88, 2.90	0.122
12mo	1.62	0.88, 2.96	0.120

Note: Generalized estimating equation (GEE) with population-average model: Model-1: Unadjusted; Model-2: adjusted age, education and male gender; Model-3: adjusted age, education, male gender, body injury present and MDGMC at 3 months.