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

Durga Roy, M.D., Sandeep Vaishnavi, M.D., Ph.D., Dingfen Han, Ph.D., Vani Rao, M.D.

Few studies have examined clinical correlates of aggression after first-time traumatic brain injury (TBI) within the first year after injury. The authors aimed to identify the rates of aggression at 6 and 12 months post-TBI and establish clinical and demographic correlates. A total of 103 subjects with first-time TBI were seen within 12 months postinjury 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.

J Neuropsychiatry Clin Neurosci 2017; 29:334–342; doi: 10.1176/appi.neuropsych.16050088

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 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 premorbid psychosocial functioning, and substance abuse.[4–6] The largest study to date on post-TBI aggression, conducted by Sabaz et al.,[7] reported on 507 subjects with severe TBI and found the prevalence of aggression within 6 months postinjury 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 workforce 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.[1] 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. Dyer et al.[8] found that verbal aggression was most prevalent (35%−38%) in a cohort of 24 patients with TBI, and physical aggression was seen only in extreme cases. A recent study by James et al.[9] showed that premorbid history of aggression predicted verbal but not physical aggression.

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 present 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 hypothesized that the development of psychiatric illness within the early TBI period (first 3 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 3 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.,[10] which examined aggression in the first 3 months of TBI, characterizing its severity and correlates with psychiatric diagnoses in adults with first-time TBI. 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 et al.[10] study, which was designed to determine biopsychosocial correlates of major depression after TBI. The 3-month prevalence data from Rao et al.[10] are 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 University of Maryland. Thirty-nine participants were lost to follow-up. A total of 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: 1) clear history of loss of consciousness; 2) Glasgow Coma Score of 15 or less; and 3) evidence of trauma (contusion or hemorrhage) on computerized tomography (CT) scans done as part of clinical work-up. 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); and 3) a history of any other type of brain illness (e.g., stroke, seizure, encephalitis). Because 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 boards of both universities.

All participants received either three or four study evaluations within the first year of TBI. Evaluations were completed only for participants who were able to provide 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 3 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 2 weeks of trauma. The second evaluation for these participants was done approximately 3 months post-TBI to assess psychiatric problems and psychosocial functioning after TBI. However, for participants who were unable to give consent within the first 2 weeks post-TBI, both the pre- and post-TBI status were assessed at the time they were able to provide informed consent, within the 3 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- 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 three 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. Because 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.

Psychiatric diagnoses. Axis 1 psychiatric diagnosis was determined using the Structured Clinical Interview for DSM-IV Axis 1 Disorders—Clinician Version (SCID-IV).[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 psychiatric history. 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 department 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 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.[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 a 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; 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;

TABLE 1. Comparison of Subjects Who Participated Versus Those Lost to Follow-Up

Variable	At Least One Follow-Up		
	No (N=39)	Yes[a] (N=103)	Exact p[b]
Type of injury			0.171
Motor vehicle accident	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 and 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%)	
General medical health rating 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%)	

[a] Data were available for at least one follow-up.
[b] Analysis was conducted using Fisher's exact test.

TABLE 2. Comparison of Demographic and Clinical Variables on Total Completers Versus Partial Completers

Variable	Follow-Up at 3, 6, and 12 Months		
	No (N=47)	Yes (N=56)	Exact p
Type of injury			0.737
Motor vehicle accident	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 and 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%)	
General medical health rating 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%)	

[a] The total completers completed follow-up at all three time points (i.e., at 3, 6, and 12 months); the partial completers did not complete the follow-up (i.e., missed follow-up at 3, 6, or 12 months).

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 "nonfrontal" tests that were put together for the larger study to test the hypothesis of whether 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.

Neuroimaging

All participants had 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 toward significance were included as independent variables in the univariate logistic regression analyses. Significance levels were set at $p<0.05$. Given that a multiple pairwise 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 pairwise tests are performed on a single set of data.

RESULTS

Sample Demographic Variables

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. Pre-TBI status was assessed either at 2 weeks or at 3 months for 99.0% of participants; 97.1% completed follow-up at 3 months;

70.9% completed follow-up at 6 months; and 70% completed follow-up at 12 months. Additionally, 0.97% came for no follow-up; 17.5% came for one follow-up; 27.2% came for two follow-ups; and 54.4% came for three 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 three times) and 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 and those who completed fewer follow-ups (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%).

TABLE 3. Sample Demographic and Clinical Variables[a]

Demographic Variables	Total N	Mean or N	SD or %
Age (years), mean (SD)	103	42.6	18.0
Education level (years), mean (SD)	103	12.9	2.9
Male gender, N (%)	103	64	62.1%
Married or presence of partner prior to TBI, N (%)	103	56	54.4%
Annual income >$20K, N (%)	103	58	56.3%
Caucasian, N (%)	103	53	51.5%
Clinical variables	**Total N**	**Mean or N**	**SD or %**
Family history of nonmood psychiatric disorder, N (%)	102[b]	28	27.4%
Any depression prior to TBI, N (%)	103	18	17.5%
Any axis I psychiatric diagnosis prior to TBI, N (%)	103	76	73.4%
Type of injury	99[c]		
Motor vehicle accident, N (%)		57	57.6%
Fall, N (%)		20	20.2%
Assault, N (%)		21	21.2%
Other, N (%)		1	1.0%
Severity	100[d]		
Mild, N (%)		61	61%
Moderate and severe, N (%)		39	39%
SFE pre-TBI score, mean (SD)	99[c]	0.22	0.15
STC pre-TBI score, mean (SD)	99[c]	3.36	1.77
HAM-D pre-TBI score, mean (SD)	95[e]	2.26	4.22

[a] HAM-D=Hamilton Depression Rating Scale; SFE=Social Functioning Examination; STC=Social Ties Checklist.
[b] Data were missing for one subject.
[c] Data were missing for four subjects.
[d] Data were missing for three subjects.
[e] Data were missing for eight subjects.

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 fewer 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) at 3 months postinjury 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

TABLE 4. Prevalence of Subtypes of Aggression

	3 Months		6 Months[a]		12 Months[a]	
Variable	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%)

[a] Aggression (yes/no) at 6 months and 12 months is counted for any participant with verbal aggression, physical aggression against self, aggression against objects, or aggression against others at 6 months and 12 months, respectively.

TABLE 5. Comparison of Participants With and Without Aggression on Demographic and Injury Variables at 6 and 12 Months[a]

	6 Months				12 Months			
Variable	No Aggression (N=43)	Aggression (N=30)	df	t(p)	No Aggression (N=44)	Aggression (N=27)	df	t(p)
Demographic variables								
Age[b]	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[b]	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	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/living partner	23 (53.5%)	16 (53.3%)		1.00	22 (50%)	18 (66.7%)		0.22
Working part-time/full-time	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[b]	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: motor vehicle accident	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 history pre-TBI	29 (67.4%)	23 (76.7%)		0.44	30 (68.2%)	18 (66.7%)		1.00
Any psychiatric history 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 abuse/dependence pre-TBI	18 (42.9%)	15 (53.6%)		0.47	16 (38.1%)	12 (46.1%)		0.61
Alcohol abuse/dependence post-TBI	12 (70.6%)	10 (71.4%)		1.00	13 (72.2%)	9 (75.0%)		1.00
Substance abuse/dependence pre-TBI	18 (43.9%)	16 (53.3%)		0.48	21 (48.8%)	9 (34.6%)		0.32
Substance abuse/dependence post-TBI	7 (58.3%)	9 (69.2%)		0.69	10 (66.7%)	4 (50.0%)		0.66
Adult behavior pre-TBI[c]	0	0		—	1 (2.9%)	0		1.00
Adult behavior post-TBI[c]	0	1 (3.6%)		0.41	1 (2.6%)	0		1.00
Social functioning pre-TBI[b]	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 post-TBI[b]	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[b]	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[b]	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 and instrumental activities of daily living pre-TBI[b]	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 and instrumental activities of daily living post-TBI[b]	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 major depression due to general medical condition	5 (11.9%)	5 (18.5%)		0.497	4 (9.8%)	8 (30.8%)		0.048

continued

TABLE 5, *continued*

Variable	6 Months				12 Months			
	No Aggression (N=43)	Aggression (N=30)	df	t(p)	No Aggression (N=44)	Aggression (N=27)	df	t(p)
Major depression due to general medical condition at 3 months	3 (7.1%)	4 (14.8%)		0.42	2 (4.9%)	6 (23.1%)		0.048
Major depression due to general medical condition at 6 months	2 (4.8%)	4 (14.8%)		0.201	—	—		—
Major depression due to general medical condition at 12 months	—	—		—	1 (2.4%)	1 (3.7%)		1.00

[a] Analysis was conducted using Fisher's exact test except where indicated otherwise; variables at baseline were used for analysis pre-TBI; variables at 3 months were used for analysis post-TBI.
[b] Analysis was conducted using t tests.
[c] Includes legal problems (arrests, incarcerations).

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.[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 whether 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

To further understand the risk of developing aggression throughout the course of the first year after TBI and to determine whether there was any one particular time point at which individuals were placed most at risk, we fit a generalized estimating equation (GEE) with a population-average logistic regression model. The analysis revealed that there were no significant changes in odds ratio at 6 months and 12 months compared with 3 months after TBI, both unadjusted and adjusted for age, education, gender, 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 during 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-month period post-TBI.

The second interesting finding from this study is that the presence of new-onset depression after TBI at 3 months (but

TABLE 6. Neuropsychological Cognitive Variables at 3 Months Predicting any Aggression in Post-TBI (6 Months and 12 Months)[a]

Variables	B	SE	p	95% CI	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 and Word	0.03	0.02	0.163	−0.01, 0.07	1.03
Trail-Making Test, Part A	−0.01	0.01	0.494	−0.02, 0.01	0.99
Trail-Making Test, Part 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
Stroop Color and Word	0.00	0.02	0.901	−0.04, 0.04	1.00
Trail-Making Test, Part A	−0.01	0.01	0.281	−0.03, 0.01	0.99
Trail-Making Test, Part 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

[a] The dependent variable is any aggression (yes/no) in post-TBI (6 and 12 months); logistic regression was used in all models. Abbreviations: 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.

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 3 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 3 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 first year after TBI.

TABLE 7. Demographic and Clinical Variables Associated with Aggression at 6 and 12 Months

Variable	B	SE	p	95% CI	Exp(B)
Any aggression in post-TBI at 6 months[a]					
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[a]					
Major depression due to general medical condition at 3 months	1.77	0.86	0.040	0.08, 3.46	5.85
Social Functioning Examination 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

[a] Any aggression denotes any verbal or physical aggression.

While this study showed no significant association between cognitive deficits, substance abuse, and frontal lobe injuries as has been reported in prior studies,[1,4,5] it was consistent with those studies in showing that depression and post-TBI social

TABLE 8. Aggression at 3 Months Postinjury as a Predictor of Later Aggression at 6 or 12 Months

Variables	B	SE	p	95% CI	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

TABLE 9. Longitudinal Analysis of Aggression in the First Year After TBI[a]

	Model Parameter Estimates		
Any Aggression	Odds Ratio	95% CI	p
Model 1[b]			
6 months	1.43	0.86, 2.39	0.171
12 months	1.21	0.72, 2.04	0.476
Model 2[c]			
6 months	1.45	0.86, 2.45	0.165
12 months	1.24	0.72, 2.11	0.438
Model 3[d]			
6 months	1.60	0.88, 2.90	0.122
12 months	1.62	0.88, 2.96	0.120

[a] Analysis was conducted using generalized estimating equation with population-average model.
[b] Model was unadjusted.
[c] Model was for adjusted age, education, and male gender.
[d] Model 3 was for adjusted age, education, male gender, body injury present, and major depression due to general medical condition at 3 months.

functioning are associated with aggression. The finding 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.,[1] Rapoport et al.,[6] and Dyer et al.[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.[5] 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. 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 that 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.,[30] out of a sample of 34 subjects, there were more commonly observed episodes of verbal aggression compared with physical aggression. In contrast, the above-referenced study by Sabaz et al.[7] 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 TBI (and only those with closed- head injury), clear history of loss of consciousness, and hospitalized individuals. Subjects with only a history of altered mental status and those not admitted to the 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 at approximately 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 those at approximately 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 may be responsible for aggression, including TBI severity, general medical comorbidities, or environmental triggers. These are all confounders that might have been

addressed with a control comparator arm. There was also notable loss to follow-up at 6 and 12 months compared with the 3-month time points, which affected the sample size for data collection toward the end of the study.

CONCLUSIONS

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 demonstrate that early aggression after TBI is correlated to aggression later during 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 the 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.

AUTHOR AND ARTICLE INFORMATION

From the Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore (DR, DH, VR); the Neuropsychiatric Clinic at Carolina Partners, Durham, N.C. (SV); the Department of Community and Family Medicine, Duke University School of Medicine, Durham, N.C. (SV); and the Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, N.C. (SV).

Send correspondence to Dr. Roy; e-mail: droy4@jhmi.edu

Previously presented in part as an abstract at the Annual Meeting of the American Neuropsychiatric Association, San Diego, March 16–19, 2016.

Supported by NIMH grant K23 MH 066894 to Dr. Rao and in part by Department of Defense grant W81XWH-13-1-0469 to Dr. Rao.

The authors report no financial relationships with commercial interests.

The views discussed in this study are solely those of the authors.

Received May 5, 2016; revisions received Sept. 29, 2016, and March 23, 2017; accepted March 24, 2017; published online May 30, 2017.

REFERENCES

1. Tateno A, Jorge RE, Robinson RG: Clinical correlates of aggressive behavior after traumatic brain injury. J Neuropsychiatry Clin Neurosci 2003; 15:155–160
2. Arciniegas DB, Wortzel HS: Emotional and behavioral dyscontrol after traumatic brain injury. Psychiatr Clin North Am 2014; 37: 31–53
3. Alderman N: Contemporary approaches to the management of irritability and aggression following traumatic brain injury. Neuropsychol Rehabil 2003; 13:211–240
4. Baguley IJ, Cooper J, Felmingham K: Aggressive behavior following traumatic brain injury: how common is common? J Head Trauma Rehabil 2006; 21:45–56
5. Greve KW, Sherwin E, Stanford MS, et al: Personality and neurocognitive correlates of impulsive aggression in long-term survivors of severe traumatic brain injury. Brain Inj 2001; 15:255–262
6. Rapoport M, McCauley S, Levin H, et al: The role of injury severity in neurobehavioral outcome 3 months after traumatic brain injury. Neuropsychiatry Neuropsychol Behav Neurol 2002; 15:123–132
7. Sabaz M, Simpson GK, Walker AJ, et al: Prevalence, comorbidities, and correlates of challenging behavior among community-dwelling adults with severe traumatic brain injury: a multicenter study. J Head Trauma Rehabil 2014; 29:E19–E30
8. Dyer KF, Bell R, McCann J, et al: Aggression after traumatic brain injury: analyzing socially desirable responses and the nature of aggressive traits. Brain Inj 2006; 20:1163–1173
9. James AI, Young AW: Clinical correlates of verbal aggression, physical aggression and inappropriate sexual behaviour after brain injury. Brain Inj 2013; 27:1162–1172
10. Rao V, Rosenberg P, Bertrand M, et al: Aggression after traumatic brain injury: prevalence and correlates. J Neuropsychiatry Clin Neurosci 2009; 21:420–429
11. Yudofsky SC, Silver JM, Jackson W, et al: The Overt Aggression Scale for the objective rating of verbal and physical aggression. Am J Psychiatry 1986; 143:35–39
12. Silver JM, Yudofsky SC: The Overt Aggression Scale: overview and guiding principles. J Neuropsychiatry Clin Neurosci 1991; 3:S22–S29
13. McNiel DE, Binder RL: Clinical assessment of the risk of violence among psychiatric inpatients. Am J Psychiatry 1991; 148:1317–1321
14. Kafantaris V, Lee DO, Magee H, et al: Assessment of children with the overt aggression scale. J Neuropsychiatry Clin Neurosci 1996; 8:186–193
15. First MB, Spitzer RL, Gibbon M, et al: Structured Clinical Interview for DSM-IV–Clinical Version (SCID-CV) (User's Guide and Interview). Washington, DC, American Psychiatric Publishing, 1997
16. Teasdale G, Jennett B: Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2:81–84
17. Kay T, Harrington DE, Adams R, et al: Definition of mild traumatic brain injury. J Head Trauma Rehabil 1993; 8:86–87
18. Starr LB, Robinson RG, Price TR: Reliability, validity, and clinical utility of the social functioning exam in the assessment of stroke patients. Exp Aging Res 1983; 9:101–106
19. Jorge RE, Robinson RG, Arndt SV, et al: Comparison between acute- and delayed-onset depression following traumatic brain injury. J Neuropsychiatry Clin Neurosci 1993; 5:43–49
20. Jorge RE, Robinson RG, Moser D, et al: Major depression following traumatic brain injury. Arch Gen Psychiatry 2004; 61:42–50
21. Folstein MF, Folstein SE, McHugh PR: "Mini-Mental State": A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12:189–198
22. Nelson HE: National Adult Reading Test (NART): Test Manual. Windsor, United Kingdom, NFER Nelson, 1982
23. Brandt, J., Benedict, RHB: Hopkins Verbal Learning Test-Revised (HVLT-R): Professional. Lutz, Fla, Psychological Assessment Resources, Inc; 2001
24. Benedict RHB: Brief Visuospatial Memory Test-Revised (BVMT-R): Professional Manual. Odessa, Fla, Psychological Assessment Resources, Inc, 1997
25. Wolfson D: The Halstead-Reitan Neuropsychological Test Battery-Therapy and Clinical Interpretation. Tucson, Ariz, Neuropsychological Press, 1985
26. Golden JC: Stroop Color and Word Test. Chicago, Stoelting Co, 1978
27. Schretlen D: Brief Test of Attention (BTA): Professional Manual. Odessa, Fla, Psychological Assessment Resources, Inc, 1996
28. Grant DA, Berg EA: A behavioral analysis of degree of reinforcement and ease of shifting to new responses in a Weigl-type card-sorting problem. J Exp Psychol 1948; 38:404–411
29. Stéfan A, Mathé JF: What are the disruptive symptoms of behavioral disorders after traumatic brain injury? A systematic review leading to recommendations for good practices. Ann Phys Rehabil Med 2016; 59:5–17
30. Giles GM, Mohr JD: Overview and inter-rater reliability of an incident-based rating scale for aggressive behaviour following traumatic brain injury: The Overt Aggression Scale—Modified for Neurorehabilitation—Extended (OAS-MNR-E). Brain Inj 2007; 21: 505–511