Pathological Laughter and Crying and Psychiatric Comorbidity After Traumatic Brain Injury

Durga Roy, M.D., Una McCann, M.D., Dingfen Han, Ph.D., Vani Rao, M.D.

There are limited data regarding the incidence of pathological laughter and crying (PLC) after traumatic brain injury (TBI). This study aimed to identify the occurrence of PLC in the first year after TBI and to determine whether there is a relationship between PLC and other clinical features or demographics. Subjects who sustained a first-time TBI were recruited from acute trauma units and were assessed at 3, 6, and 12 months after TBI. Rates of PLC at 3, 6, and 12 months after TBI were 21.4%, 17.5%, and 15.5%, respectively. Patients with PLC had higher percentages of psychiatric diagnoses, including personality changes, depressive disorders, and mood disorders secondary to a general medical condition, as well as higher rates of posttraumatic stress disorder. Univariate logistic and linear regression analyses indicated a significant association between PLC and scores on the Clinical Anxiety Scale 3 months after TBI and on the Hamilton Depression Rating Scale 12 months after TBI. Individuals who have PLC during the first year after TBI are more likely to have any psychiatric diagnosis as well as higher rates of mood and anxiety symptoms. In addition, PLC in the early TBI period may serve as a predictor of depression and anxiety symptoms at 12 months after TBI.

J Neuropsychiatry Clin Neurosci 2015; 27:299–303; doi: 10.1176/appi.neuropsych.15030045

Traumatic brain injury (TBI) can trigger a myriad of neuropsychiatric sequelae, including the onset of mood, anxiety, psychotic, cognitive, and substance use disorders. In addition to formal psychiatric disorders, many patients also experience changes in personality and behavioral or emotional dysregulation. The presence of emotional dysregulation is a significant clinical burden and can complicate medical and psychiatric treatments. One particular cluster of symptoms that can develop after TBI as part of an emotional dysregulation syndrome is that of pathological laughter and crying (PLC). PLC has been defined as irrepressible episodes of laughing or crying that are triggered by a stimulus that would not cause such an emotional response under normal circumstances.[1] PLC has also historically been called "emotional incontinence" and "pseudobulbar affect," and clinicians have suggested that a patient's subjective experience of distress is required for treatment to be indicated.[2,3] Studies of PLC are lacking, but the prevalence of PLC during the first year after TBI is estimated to be between 5% and 11%.[4] Although mechanisms of PLC are poorly understood, dysregulation of prefrontal limbic circuits has been hypothesized, in addition to release of cortical inhibition of upper brainstem centers involved in the integration of motor activation patterns.[1]

There is a paucity of research focusing on PLC after TBI. Zeilig et al.[5] reported the development of PLC in 16 of 301 patients with severe TBI admitted to a rehabilitation unit. In the same population, PLC was associated with greater severity of brain injury. Tateno et al.[1] examined the prevalence of PLC using the Pathological Laughter and Crying Scale[6] in 92 consecutive patients with all severities of TBI at 3, 6, and 12 months after injury. In this population, rates of PLC were 10.9% during the first year after TBI.

The relationship between PLC and mood disorders has not yet been clearly delineated, and indeed, results have been conflicting. Whereas some studies have shown that PLC is associated with major depression,[7–9] other studies have shown no correlation.[10–12] Importantly, subjects with PLC in these studies were primarily individuals who experienced symptoms after a stroke. The study by Tateno et al.[1] was the first, and thus far the only, study to demonstrate a correlation between PLC in patients with TBI and the presence of an anxiety disorder during the first year after TBI.[1] No subsequent studies have examined TBI-related PLC and its association with anxiety or mood disorders. Our study aimed to evaluate the rate of PLC during the first year after a closed head TBI and to determine whether there is a relationship between TBI-related PLC and particular demographics or psychiatric disorders. This research project is part of a larger study to determine the prevalence of and risk factors for the development of psychiatric disorders after TBI.

METHODS

Participants and Procedures

A total of 103 subjects with first-time closed head injuries were recruited from the acute trauma unit of the Johns

TABLE 1. Sample Demographics (N=103)[a]

Variable	Value
Age in years, mean (SD)	42.6 (18.0)
Educational level in years, mean (SD)	12.9 (2.9)
Gender	
Male	64 (62.1)
Female	39 (37.9)
Employment status before TBI	
Not working	26 (25.2)
Employed full time or part time	77 (74.8)
Marital status before TBI	
Alone/no partner	47 (45.6)
Married/partner	56 (54.4)
Annual income >$20,000	
<$20,000	45 (43.7)
≥$20,000	58 (56.3)
Race	
Non-Caucasian	50 (48.5)
Caucasian	53 (51.5)
TBI cause	
Motor vehicle accident	57 (55.3)
Assault	21 (19.4)
Fall	20 (20.4)
Other	1 (0.1)
Missing	4 (3.9)
TBI severity	
Mild	59 (57.3)
Moderate and severe	41 (39.8)
Missing	3 (2.9)

[a] Data are presented as N (%), unless otherwise indicated. TBI, traumatic brain injury.

Hopkins Hospital and the Brain Injury (rehabilitation) Unit of Kernan Hospital at the University of Maryland. Subjects were assessed 3, 6, and 12 months after TBI. For the purposes of this study, TBI was defined as a physical trauma to the head secondary to an external force and was associated with at least one of the following: 1) clear history of loss of consciousness, 2) Glasgow Coma Scale score <15, and/or 3) evidence of trauma (contusion or hemorrhage) on CT scans done as part of the clinical workup. These patients should have been admitted to the trauma unit either at Johns Hopkins Hospital or Kernan Hospital at the University of Maryland. Severity of TBI was assessed using two criteria: the Glasgow Coma Scale score and the duration of loss of consciousness. A loss of consciousness of <30 minutes was considered mild TBI, a loss of consciousness of 30 minutes to 24 hours was considered moderate TBI, and a loss of consciousness of >24 hours was considered severe TBI. Posttraumatic amnesia was not assessed. TBI was considered mild if the patient's Glasgow Coma Scale score was 13–14 and loss of consciousness was <30 minutes. In patients in whom the Glasgow Coma Scale score was not available, the loss-of-consciousness criteria were used.

Other inclusion criteria included the ability to provide consent personally, age of at least 18 years, and admission to the hospital for evaluation of head trauma. Exclusion criteria included a previous TBI, an open head injury (e.g., a displaced skull fracture or a gunshot wound), or a history of any other type of brain illness (e.g., stroke, seizure, Parkinson's disease, or encephalitis).

TABLE 2. Rates of Pathological Laughter or Crying and Overall Rates of PLC[a]

Variable	3 Months	6 Months	12 Months
Pathological crying			
No	77 (74.7)	59 (57.3)	56 (54.4)
Yes	21 (20.4)	14 (13.6)	14 (13.6)
Missing	5 (4.9)	30 (29.1)	33 (32.0)
Pathological laughter			
No	97 (94.2)	68 (66.0)	67 (65.1)
Yes	1 (0.97)	5 (4.9)	3 (2.9)
Missing	5 (4.9)	30 (29.1)	33 (32.0)
Overall rates of PLC			
No	76 (73.8)	55 (53.4)	54 (52.4)
Yes	22 (21.4)	18 (17.5)	16 (15.5)
Missing	5 (4.9)	30 (29.1)	33 (32.0)

[a] Data are presented as N (%), unless otherwise indicated. PLC, pathological laughter and crying.

Psychiatric Evaluations

At each time point, subjects underwent a comprehensive psychiatric evaluation that was conducted by a neuropsychiatrist (V.R.). Axis I psychiatric diagnoses were determined using the Structured Clinical Interview for DSM-IV Axis I Disorders–Clinician Version (SCID-CV). When the presence of depression was identified, the level of severity was assessed using the Hamilton Depression Rating Scale. When an anxiety disorder was identified, its severity was assessed using the Clinical Anxiety Scale. The diagnosis of PLC was made based on the following criteria, as defined by Tateno et al.[1] First, there was an occurrence of frequent episodes of sudden, uncontrollable emotional expression. Second, emotional responses were elicited by either nonspecific stimuli or, when elicited by appropriate stimuli, the intensity of the emotional response was out of proportion to the intensity of the stimulus. Third, episodes did not have a clear association with the prevailing mood state. PLC severity was assessed using the Pathological Laughter and Crying Scale, as described by Robinson et al.[6]

Data Analyses

Descriptive statistics were calculated for all participants. Significant differences (two-tailed) on individual variables were compared between the subgroups with and without PLC using Fisher's exact test for categorical variables and the Wilcoxon rank sum test or the Student's t test for continuous variables. The criterion for statistical significance was set at $p<0.05$.

Logistic or linear regressions were used to determine whether PLC during the first 3 months of TBI was predictive of psychiatric morbidity 12 months after TBI. In these analyses, PLC at the 3-month time point was used as the independent variable, and psychiatric disorders and symptoms at the 12-month time point were considered dependent

variables. Analyses were controlled for age and severity of TBI. Significance levels were set at $p<0.05$.

RESULTS

Demographic data of the entire sample revealed that participants had a mean age of 42.6 years, an average education of 12.9 years, were mostly employed full time before TBI, and were more likely to be men. The most common severity of TBI was mild, with motor vehicle accidents being the most common cause (Table 1). Prevalence rates of PLC at the 3-, 6-, and 12-month post-TBI time points were 21.4%, 17.5%, and 15.5%, respectively. Prevalence rates of pathological crying at the same time points were 20.4%, 13.6%, and 13.6%, respectively, whereas prevalence rates of pathological laughter were 0.97%, 4.9%, and 2.9%, respectively (Table 2). Patients with mild TBI were noted to have the highest rates of PLC (66.3%) at any time during 1 year after TBI. The results summarizing TBI severity and rates of PLC any time at 1 year after the TBI are shown in Table 3.

Compared with patients without PLC, patients with PLC during the year after TBI had higher percentages of the following: 1) any psychiatric diagnosis (97.1% versus 80.9%, p=0.03); 2) any type of depressive disorder, such as major depression, recurrent depressive disorder not otherwise specified, or major or minor depression attributable to TBI (76.5% versus 40.6%, p=0.001); 3) mood disorder due to general medical condition (i.e., the TBI) at any time in the first year of trauma (50% versus 20.3%, p=0.001); 4) TBI-related personality change, as defined by the presence of aggression, impulsivity, or disinhibition after TBI (29.4% versus 8.7%, p=0.01); and 5) posttraumatic stress disorder (23.5% versus 1.5%, p=0.001). In regard to severity of depression and anxiety, Hamilton Depression Rating Scale scores were higher in patients with PLC at 3 months (9.72 versus 5.59, $p<0.001$) and at 12 months (8.64 versus 3.61, $p<0.001$). Clinical Anxiety Scale scores were also higher at 3 months (6.48 versus 3.07, $p<0.001$) and at 12 months (6.47 versus 2.20, $p<0.001$) (Table 4).

Logistic regression aimed at determining whether the presence of PLC at 3 months predicted psychiatric illness at 12 months revealed only one significant association. In particular, the presence of TBI-related PLC at 12 months was significantly associated with "any psychiatric disorder" at 12 months (β=1.60, SE=0.57, z=2.60, p=0.01), as summarized in Table 5. Similarly, linear regressions to determine the potential predictive relationship between TBI-related PLC at 3 months and severity of psychiatric symptoms at 12 months indicated that PLC at 3 months was associated with increased Clinical Anxiety Scale scores and Hamilton Depression Rating Scale scores at 12 months (β=3.82, SE=1.45, z=2.63, p=0.01; and β=5.30, SE=2.12, z=2.5, p=0.02, respectively; Table 6).

TABLE 3. Rates of Pathological Laughter or Crying at Any Time During 1 Year Across TBI Severity Groups[a]

TBI Severity	Rates of PLC
Mild (GCS score 13–15)	59 (66.3)
Moderate (GCS score 9–12)	13 (14.6)
Severe (GCS score <8)	17 (19.1)
Total	89 (100)

[a] Data are presented as N (%), unless otherwise indicated. GCS, Glasgow Coma Scale; PLC, pathological laughter and crying; TBI, traumatic brain injury.

DISCUSSION

Findings from this study confirm and extend findings from the single previous study in the literature evaluating the prevalence and clinical correlates of TBI-related PLC[1] as well as some studies of PLC related to other neurological conditions, such as stroke.[5] In particular, TBI-related PLC was found to be associated with increased rates of psychiatric disorders overall and mood and anxiety symptoms in particular. PLC was also found to be associated with TBI-related changes in personality. Notably, the prevalence of TBI-related PLC in this study was nearly double that reported by Tateno et al.[1] It is difficult to account for the

TABLE 4. Demographic and Psychiatric Morbidity Variables[a]

Variable	No PLC (N=69)	Any PLC (N=34)	p
Age in years[b]	69, 40.7 (18.8)	34, 46.3 (15.9)	0.06
Education[b]	69, 12.7 (2.6)	34, 13.4 (3.4)	0.29
Male gender	44 (63.8)	20 (58.8)	0.67
Race (non-Caucasian)	36 (52.2)	14 (41.2)	0.31
Living with others	53 (79.1)	32 (94.1)	0.08
Married/partner	33 (47.8)	23 (67.7)	0.06
Any depression	28 (40.6)	26 (76.5)	0.001
Any mood disorder due to general medical condition	14 (20.3)	17 (50)	0.003
Any psychiatric disorder postinjury	55 (80.9)	33 (97.1)	0.03
Any personality change	6 (8.7)	10 (29.4)	0.01
Any apathy	7 (10.1)	2 (5.9)	0.71
Any postinjury anxiety	14 (73.7)	18 (85.7)	0.44
Any substance dependence	15 (71.4)	6 (50)	0.27
Any ethanol dependence	26 (83.9)	8 (57.1)	0.07
Any posttraumatic stress disorder	1 (1.5)	8 (23.5)	0.001
Any ethanol and substance abuse	28 (84.9)	10 (62.5)	0.14
Any postconcussion syndrome symptoms	7 (77.8)	17 (94.4)	0.25
Hamilton Depression Rating Scale score			
3 months	6.1 (5.59)	14.6 (9.72)	<0.001
12 months	3.03 (3.61)	11.5 (8.64)	<0.001
Clinical Anxiety Scale score			
3 months	1.95 (3.07)	7.3 (6.48)	<0.001
12 months	1.1 (2.20)	6.5 (6.47)	<0.001

[a] Fisher's exact test was used for all categorical variables, and the Wilcoxon rank sum test was used for continuous variables. Data are presented as N (%), unless otherwise indicated.
[b] Data are presented as the number of patients, along with the mean (SD).

TABLE 5. Univariate Logistic Regression[a]

Dependent Variable at 12 Months	β	SE	z	p	95% CI Lower	95% CI Upper
Psychiatric disorder	1.60	0.57	2.84	0.01	0.50	2.71
Mood disorder due to GMC	−0.50	0.94	−0.53	0.60	−2.33	1.34
Any depression	−0.42	1.05	−0.4	0.69	−2.48	1.63
Posttraumatic stress disorder	−0.21	1.35	−0.16	0.87	−2.86	2.43
Personality change	0.03	0.98	0.03	0.98	−1.90	1.96

[a] The independent variable is any PLC at 3 months adjusted for age and severity of TBI. GMC, general medical condition.

magnitude of this difference, but it is possible that our subject population included individuals with affective lability secondary to personality changes after TBI (although Tateno et al.[1] did not explicitly exclude such subjects). The possibility that emotional lability in some subjects might have been related to personality changes is supported by our finding that subjects with TBI-related PLC had higher rates of personality change than patients with TBI without PLC.

The observation that subjects with TBI-related PLC had higher rates of mood and anxiety symptoms suggests that the two have overlapping neurological substrates. Alternatively, the presence of PLC could be one of many factors that, in combination, increase the likelihood for mood and anxiety disorders. Indeed, the observation that PLC in the acute period is associated with higher Hamilton Depression Rating Scale scores and Clinical Anxiety Scale scores at 12 months could be viewed as supportive for either of these possibilities. Additional research is required to determine whether early-onset PLC can serve as a predictor for the subsequent development of affective pathology. Similarly, it remains to be determined whether treatment of PLC early after TBI can prevent or attenuate subsequent mood and affective disorders. Treatment with medications with known efficacy for mood and anxiety disorders, such as selective serotonin reuptake inhibitors in patients with TBI-related PLC, may hold promise.

It is important to highlight limitations of our research. For example, our study sample included only those with a first-time 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. Because of these fairly strict criteria, several persons with mild TBI may have been omitted from the sample. These strict inclusion and exclusion criteria limit the ability to generalize these findings to other TBI populations. Importantly, it was previously suggested that repeated TBI increases the risk for subsequent neuropsychiatric symptoms, including symptoms of depression and anxiety.[13,14] In addition, if psychiatric symptoms were identified on the psychiatric evaluations at 1 month, subjects were referred to the Johns Hopkins Brain Injury Clinic, and some were initially prescribed psychotropic medications. This may have confounded results of Hamilton Depression Rating Scale scores and Clinical Anxiety Scale scores in subsequent follow-up visits. Finally, systematic analysis of brain imaging data was also not performed; as such, we were unable to associate the relationship between the neuroanatomy of a TBI lesion and that of PLC (or subsequent psychiatric symptoms). PLC in this study was found to be associated with the presence of mood (and anxiety) disorders. It is well established that damage to the circuitry involving regions of the prefrontal cortex, amygdala, hippocampus, basal ganglia, and thalamus is associated with mood disorders after TBI,[15] suggesting that similar circuitry is involved in post-TBI PLC. Future neuroimaging studies are needed to confirm this hypothesis.

In summary, subjects with TBI-related PLC within 1 year after TBI have higher rates of psychiatric morbidity and more severe depressive and anxiety symptoms. Early PLC was also found to be predictive of subsequent mood and anxiety symptoms. Future studies are needed to determine whether the neuroanatomy of TBI-related PLC overlaps that of TBI-related mood and anxiety disorders and whether early treatment of TBI-related PLC can prevent or attenuate subsequent psychiatric morbidity.

TABLE 6. Univariate Linear Regression of CAS and HAM-D Scores at 12 Months[a]

Dependent Variable at 12 Months	β	SE	z	p	95% CI Lower	95% CI Upper
CAS score	3.82	1.45	2.63	0.01	0.91	6.72
HAM-D score	5.30	2.12	2.5	0.02	1.06	9.53

[a] The independent variable is any PLC at 3 months adjusted for age and severity of TBI. CAS, Clinical Anxiety Scale; HAM-D, Hamilton Depression Rating Scale.

AUTHOR AND ARTICLE INFORMATION

From the Dept. of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD.

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

This paper was presented as a poster at the American Neuropsychiatric Association Annual Meeting, Seattle, WA, Feb. 15–18, 2014.

This research study was conducted at the Johns Hopkins Hospital and the Brain Injury (rehabilitation) Unit of Kernan Hospital at the University of Maryland.

This study was supported by NIMH grant K23 MH 066894. This literature review was supported in part by Department of Defense grant W81XWH-13-1-0469.

The authors report no competing interests.

Received March 2, 2015; revision received April 30, 2015; accepted May 6, 2015; published online August 10, 2015.

REFERENCES

1. Tateno A, Jorge RE, Robinson RG: Pathological laughing and crying following traumatic brain injury. J Neuropsychiatry Clin Neurosci 2004; 16:426–434
2. Arciniegas DB, Wortzel HS: Emotional and behavioral dyscontrol after traumatic brain injury. Psychiatr Clin North Am 2014; 37: 31–53

3. Wortzel HS, Oster TJ, Anderson CA, et al: Pathological laughing and crying : epidemiology, pathophysiology and treatment. CNS Drugs 2008; 22:531–545
4. Parvizi J, Coburn KL, Shillcutt SD, et al: Neuroanatomy of pathological laughing and crying: a report of the American Neuropsychiatric Association Committee on Research. J Neuropsychiatry Clin Neurosci 2009; 21:75–87
5. Zeilig G, Drubach DA, Katz-Zeilig M, et al: Pathological laughter and crying in patients with closed traumatic brain injury. Brain Inj 1996; 10:591–597
6. Robinson RG, Parikh RM, Lipsey JR, et al: Pathological laughing and crying following stroke: validation of a measurement scale and a double-blind treatment study. Am J Psychiatry 1993; 150: 286–293
7. Starkstein SE, Migliorelli R, Tesón A, et al: Prevalence and clinical correlates of pathological affective display in Alzheimer's disease. J Neurol Neurosurg Psychiatry 1995; 59:55–60
8. House A, Dennis M, Molyneux A, et al: Emotionalism after stroke. BMJ 1989; 298:991–994
9. Calvert T, Knapp P, House A: Psychological associations with emotionalism after stroke. J Neurol Neurosurg Psychiatry 1998; 65:928–929
10. McCullagh S, Moore M, Gawel M, et al: Pathological laughing and crying in amyotrophic lateral sclerosis: an association with prefrontal cognitive dysfunction. J Neurol Sci 1999; 169:43–48
11. Kim JS, Choi-Kwon S: Poststroke depression and emotional incontinence: correlation with lesion location. Neurology 2000; 54: 1805–1810
12. Morris PL, Robinson RG, Raphael B: Emotional lability after stroke. Aust N Z J Psychiatry 1993; 27:601–605
13. Bryan CJ, Clemans TA: Repetitive traumatic brain injury, psychological symptoms, and suicide risk in a clinical sample of deployed military personnel. JAMA Psychiatry 2013; 70:686–691
14. Corrigan JD, Bogner J, Mellick D, et al: Prior history of traumatic brain injury among persons in the Traumatic Brain Injury Model Systems National Database. Arch Phys Med Rehabil 2013; 94:1940–1950
15. Jorge RE, Starkstein SE: Pathophysiologic aspects of major depression following traumatic brain injury. J Head Trauma Rehabil 2005; 20:475–487