Published in final edited form as:

Int J Dev Neurosci. 2012 May ; 30(3): 239–245. doi:10.1016/j.ijdevneu.2011.12.005.

Depression in Children and Adolescents in the First Six Months After Traumatic Brain Injury

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Abstract

The objective was to assess the nature, rate, predictive factors, and neuroimaging correlates of novel (new-onset) depressive disorders, both definite and subclinical, after traumatic brain injury (TBI). Children with TBI from consecutive admissions were enrolled and studied with psychiatric interviews soon after injury (baseline), and again 6 months post-injury. Novel definite/subclinical

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depressive disorders at 6-month follow up occurred in 11% (n=15) of the children and subsets of children with non-anxious depression (n=9) and anxious depression (n=6) were identified. Novel definite/subclinical depressive disorder was significantly associated with older age at the time of injury, family history of anxiety disorder, left inferior frontal gyrus (IFG) lesions, and right frontal white matter lesions. Non-anxious depressions were associated with older age at injury, left IFG and left temporal pole lesions. Anxious depressions were associated with family history of anxiety disorder, Personality Change due to TBI, right frontal white matter lesions, and left parietal lesions. These findings, which are similar to those reported after adult TBI, identify both similarities and differences in non-anxious and anxious depression following childhood TBI with respect to lesion laterality, genetic factors (in the form of family psychiatric history of anxiety disorder), age at injury, and more generalized affective dysregulation.

Keywords

Depression; Anxiety; Traumatic Brain Injury; Children; Adolescents; Frontal Lobe

1. Introduction

Pediatric traumatic brain injury (TBI) is a major public health problem (Langlois et al., 2005). Preinjury psychiatric disorders are very common in children who sustain TBI, with occurrence ranging from 33-50% in prospectively studied samples (Brown et al., 1981; Max et al., 1997b). Psychiatric disorders with their onset after TBI are common and varied (Brown et al., 1981; Max et al., 1997a). Depression in children and adolescents in the non-TBI general population is an important problem and increases with age, such that the prevalence rate in children is up to 2.5% and for adolescents is up to 8.3% (Birmaher et al., 1996). Part of the morbidity of pediatric TBI is new-onset depressive symptomatology, although this topic has previously received minimal systematic study. A retrospective psychiatric interview study of severe TBI found that ongoing postinjury-onset depressive disorder occurred in 25% of children with severe TBI and that 1/3 of the children had a depressive disorder at some point after the injury (Max et al., 1998b). A prospective study found that TBI increased the risk of depressive symptoms, recorded from child self-report and parent questionnaires, especially among more socially disadvantaged children, and that depressive symptoms were not strongly related to post-injury neurocognitive scores (Kirkwood et al., 2000). A prospective psychiatric interview study suggested a link between preinjury depressive disorder, family history of major depression and preinjury anxiety disorder in cases of postinjury depressive disorder (Max, 2011). There have been no published studies systematically examining lesions in relation to new-onset depressive symptomatology in pediatric TBI.

In adults with TBI, new-onset depression has been studied more extensively. Prevalence rates of new-onset psychiatric disorders in adults post TBI range from 18-50% with the most common being depressive and anxiety disorders, which have a high rate of comorbidity (Holsinger et al., 2002; Jorge et al., 2004; Bryant et al., 2010). Personal history of mood and anxiety disorders are associated with postinjury major depression (Jorge et al., 1993a; Jorge et al., 2004). Studies in adult TBI suggest that new-onset depression may be associated with left hemisphere lesions, especially lesions in the left lateral frontal cortex. The investigators found depression post TBI associated with decreased left frontal gray matter volumes, specifically in the left inferior, middle and superior frontal gyri (Jorge et al., 2004), and lesions in the left dorsolateral frontal cortex and left basal ganglia (Jorge et al., 1993b). Furthermore, the investigators found that anxious depressions (depressive disorder comorbid with an anxiety disorder) were associated with right-sided lesions (Jorge et al., 1993b).

Our goal was to study the demographic, psychosocial, and lesion predictors as well as the occurrence and phenomenology of new-onset depressive symptomatology in children after TBI. Based on the above review we hypothesized that new-onset depression symptomatology post TBI would be positively associated with 1) demographic, 2) psychiatric, and 3) injury variables as follows: 1) older age of injury; 2) family history of depressive disorder, family history of anxiety disorder, preinjury anxiety, other symptoms of affective dysregulation i.e., Personality Change due to TBI; and 3) lesion location and lesion laterality (for the combined group of non-anxious and anxious depression we predicted lesions of left and right frontal lobe; for those with non-anxious depression we predicted lesions of the left frontal lobe; and for those with anxious depression we predicted right frontal lesion location).

2. Materials and Methods

Participants in this study were 177 children aged 5-14 years who had a TBI from 1998-2003. The children were recruited from consecutive admissions to 5 medical centers (3 in Texas, 1 in San Diego, and 1 in Toronto). Children with mild to severe TBI were enrolled from all centers except San Diego where only those with “complicated mild” TBI (i.e., with neuroimaging abnormalities) to severe TBI patients were recruited. Exclusion criteria included pre-existing schizophrenia or autistic disorder, mental retardation, and injury due to child abuse or penetrating missile injury. In San Diego only, children with pre-existing attention-deficit/hyperactivity disorder were excluded. Data regarding the number of children who were approached, the proportion who were eligible for recruitment, and participation rate among those eligible is missing, due in part to the fact that children were not required to answer eligibility questions prior to deciding whether to participate in the study. Consistent with the requirements of the Institutional Review Boards, all legal guardians signed informed consent and all children signed an assent form to participate. Demographic, pre-injury psychosocial variables and injury indices for participants are shown in Table 1.

2.1 Psychiatric Diagnoses

DSM-IV-TR psychiatric diagnoses (American Psychiatric Association, 2000) were based on data using the Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997) and the Neuropsychiatric Rating Schedule (NPRS) (Max et al., 1998a). The K-SADS-PL and NPRS were administered at baseline (after resolution of post-traumatic amnesia documented by administration of the Children’s Orientation and Amnesia Scale) (Ewing-Cobbs et al., 1990) to record pre-injury diagnoses and repeated 6 months after injury to record new-onset diagnoses. The K-SADS-PL is a semi-structured diagnostic integrated parent-child interview designed to generate diagnoses in children and adolescents based on DSM-IV-TR criteria. The questions address present and lifetime symptoms and timing of the onset of psychiatric symptoms in relation to TBI. The NPRS is structured similarly to the K-SADS-PL and assesses specifically for Personality Change due to TBI.

The category of definite/subclinical depressive disorder consisted of children who met full criteria or had a subclinical depressive disorder including: major depressive disorder (MDD), depressive disorder not otherwise specified, dysthymia, or adjustment disorder with depressed mood. A designation of subclinical depressive disorder was made in situations where there was no clear functional impairment even though participants met or were one symptom short of meeting criteria for a specific depressive disorder. Children with anxiety were diagnosed with at least one of the following definite and/or subclinical disorders: general anxiety disorder (GAD), post traumatic stress disorder (PTSD), adjustment disorder with anxious mood, separation anxiety disorder, obsessive compulsive disorder (OCD),

simple phobia, social phobia, or panic disorder. Children with an adjustment disorder with depressed or anxious mood were considered subclinical cases in our classification because although the DSM-IV-TR does not include the respective adjustment disorders under the depressive or anxiety disorder classification, depressive symptoms or anxious symptoms are specifically noted. We chose to investigate subclinical depression and anxiety because of the compelling empirical data supporting the validity of these constructs and their relationship with corresponding full clinical disorders with naturalistic follow up (Klein et al., 2009; Shankman et al., 2009).

Definite/subclinical depressive disorders and definite/subclinical anxiety disorders were further classified as “preinjury” or “novel”. Consistent with the pediatric TBI literature, we use the term “novel” rather than “new” to draw a distinction from studies that exclude children with preinjury psychiatric disorders from analysis in studies focused on postinjury psychiatric disorders (Max et al., 1997b). Novel definite/subclinical disorders refer to new-onset disorders that occurred within the first 6 months after TBI. Children with preinjury MDD were ineligible to develop novel definite/subclinical depressive disorders because they already had the most severe form of depressive disorder. However, children with preinjury definite/subclinical depressive disorders who developed a more severe form of depressive disorder (e.g., preinjury history of adjustment disorder with depressed mood who then developed a postinjury MDD) were classified as having a novel definite/subclinical depressive disorder. An example of a novel definite/subclinical anxiety disorder would be a participant with no preinjury definite/subclinical anxiety disorder or with preinjury separation anxiety disorder who then developed a different anxiety disorder such as panic disorder after the injury.

Children identified as having a novel definite/subclinical depressive disorder were further categorized as either having *anxious depression*, i.e., comorbid novel definite/subclinical depressive disorder and novel definite/subclinical anxiety disorder, or *non-anxious depression*, i.e., no comorbid definite/subclinical anxiety disorder.

Interviews were conducted by Ph.D. and Master’s level clinicians who were trained by the first author in a pre-study workshop and a mid-study workshop. A child psychiatrist (4 sites) or a child psychologist (1 site) supervised the assessments at each center. The next level of supervision involved the first author reviewing written summaries composed by the interviewer and discussion of cases at monthly teleconferences between the interviewers and the first author. All disagreements about diagnosis were resolved through consensus among the interviewer and the first author. This expert quality of interview and supervision is necessary to minimize the potential of spurious diagnoses of depression considering that brain injury, in the absence of a depressive disorder, can generate symptoms that overlap with depressive disorder such as irritability, anhedonia, sleep disturbance, psychomotor changes, fatigue, and concentration difficulties.

2.2 Family Psychiatric History

The Family History Research Diagnostic Criteria (Andreasen et al., 1977) interview was administered by trained research assistants. At least one parent of each child was interviewed regarding psychiatric disorders for every first-degree relative of the child with TBI. Criteria were modified to conform to DSM-IV-TR. Family history of mood disorder (MDD, dysthymia, mania, or cyclothymia) and family history of anxiety disorder was coded present/absent depending if a first-degree relative met diagnostic criteria.

2.3 Adaptive Function

The Vineland Adaptive Behavior Scales (Sparrow et al., 1984) was used to assess adaptive function. The instrument is a nondirective interview conducted with the child's primary caretaker surveying behaviors that the child habitually demonstrates in the environment giving an overall adaptive behavior composite score.

2.4 Family Function

An assessment of global family functioning was made using the Family Assessment Device general functioning scale (Miller et al., 1985). The scale is a self-report questionnaire of 12 items with a four-point scale. The questionnaire is completed by the primary caretaker of each child. Every response is given a number from a range of 1-4. Lower scores represent better functioning.

2.5 Socioeconomic Status

The Four Factor Index (Hollingshead, 1975) was used to assess socioeconomic status (SES). Scores take into account both the maternal and paternal educational and occupational levels. The scores range from 8-66 with higher scores indicating higher SES.

2.6 Neurological Assessments

Magnetic Resonance Imaging (MRI) was conducted 3 months after the injury, a timeframe sufficient for the major aspects of trauma-related pathology to be expressed (Bigler et al., 1997). The protocol included fluid attenuated-inversion recovery sequences (3mm slices) and T1 volumetric spoiled gradient recalled echo (1.5mm slices), acquired in coronal and sagittal planes according to a research protocol applied uniformly across sites. Of the 177 enrolled children, 162 (92%) returned to complete their research MRI. A study neuroradiologist at each center coded each lesion from the multiple slice hard copy films. Pathology (e.g., shearing, encephalomalacia, hemorrhage) was coded from a list. Anatomical location was coded from a list of brain structures including cortical gray matter (frontal, temporal, parietal, occipital), subcortical gray matter (basal ganglia, thalamus), and white matter (Max et al., 2005). Specific coding of frontal lobe gyri was made only when gray matter lesions were present in those gyri. Since lesion coding was by judgment of expert neuroradiologists, and volumetric analyses were not conducted, there was no attempt to register images or to segment tissue types.

The Glasgow Coma Scale (GCS) (Teasdale and Jennett, 1974), recorded from clinical notes, was used to classify the severity of TBI based on the lowest post-resuscitation score. Score ranges for mild, moderate, and severe TBI are respectively 13-15, 9-12, and 3-8.

2.7 Statistical analyses

The outcome variables of interest were novel definite/subclinical depression (all), novel definite/subclinical non-anxious depression, and novel definite/subclinical anxious depression. These will be referred to hereafter as depression (all), non-anxious depression, and anxious depression, respectively. The association of 6-month post-injury depression (all), non-anxious depression, and anxious depression with the hypothesized predictive variables was tested by independent sample t-tests for continuous variables and Fisher's exact Test and chi-square statistics for categorical variables. The hypothesized associated variable analyzed with an independent sample t-test was age at injury. The hypothesized associated variables analyzed with Fisher's exact Test were family history of anxiety disorder, family history of mood disorder, Personality Change due to TBI, pre-injury definite/subclinical anxiety disorder, and neuroimaging lesions.

3. Results

One hundred forty one of the original 177 children (80%) returned for the 6-month psychiatric assessment. The children who did not return were not significantly different from the children who did with respect to age, gender, race, SES, or GCS score. The children who returned had significantly higher pre-injury adaptive function measured by the Vineland Adaptive Behavior Composite than those who did not return (95.6 $\pm$ 14.6 versus 89.5 $\pm$ 18.0; $t=-2.02$; $df=163$; $p<.05$). Children with basal ganglia lesions were more likely to be in the group not returning versus those returning (4/20 versus 6/131; Fisher's exact = .028), however lesion distribution was not significantly different in the other 21 areas coded. Participants in the 6-month psychiatric assessment had MRI lesions visualized in 34/63 (54%) of mild TBI cases, 12/17 (71%) of moderate TBI cases, and 48/51 (94%) of severe TBI cases.

3.1 Incidence

Analyses were done on three different groups of subjects; (1) *depression (all)*, which included all subjects with a novel definite/subclinical depressive disorder, (2) *non-anxious depression*, which consisted of those diagnosed with a novel definite/subclinical depressive disorder but without a comorbid novel definite/subclinical anxiety disorder, and (3) *anxious depression*, which included those with both a novel definite/subclinical anxiety and a novel definite/subclinical depressive disorder. Three of the children returning for the 6-month follow up had preinjury major depressive disorder (the most severe form of depressive disorder) and were therefore ineligible to develop a novel definite/subclinical depressive disorder. Fifteen (11%) of the remaining 138 subjects had a novel definite/subclinical depressive disorder at 6 months following TBI of which 9 (60%) had novel definite/subclinical non-anxious depression and 6 (40%) had novel definite/subclinical anxious depression. Of the non-anxious depressed subjects 5 were diagnosed with adjustment disorder depressed mood, 3 were diagnosed with major depressive disorder (MDD), and one with subclinical dysthymia. Of the subjects with anxious depression 4 were diagnosed with MDD (one subclinical diagnosis), 1 with adjustment disorder depressed mood and 1 with depressive disorder not otherwise specified. The anxiety diagnoses for this group were as follows (1 subject had 3 diagnoses); 2 with separation anxiety, 2 with adjustment disorder anxious mood, 3 with PTSD (two of which were subclinical), and 1 with simple phobia.

Analyses of each of the depression groups (all; non-anxious; anxious) showed no significant differences from children without depression regarding demographic variables (gender, race, SES) and preinjury psychosocial variables (family function, adaptive function) as outlined in Table 2. There were no significant between-group differences in injury severity between those with and without novel definite/subclinical depressive disorder. The numbers of mild and moderate/severe TBI in the respective depression groups (all; non-anxious; anxious) were 7 and 8, 6 and 3, and 1 and 5.

3.2 Predictors of Depression (Table 3)

Age at injury was significantly greater in children with depression (all) versus no depression and also in non-anxious depression versus no depression. The mean (SD) age in years of children with depression (all) was 11.9 (2.2) while those without depression 9.9 (2.8) ($t=-2.55$; $df=136$; $p=.012$). For example, there was a 5-fold increase in the rate of depression for children with age of injury ≥ 12 years (18.2%) compared with age of injury < 9 years (3.5%). The mean (SD) age in years of children with non-anxious depression was 12.7 (1.8) while those without depression was 9.9 (2.8) ($t=-4.25$; $df=11.2$; $p=.001$). Similarly, the rate of non-anxious depression in children with age of injury ≥ 12 years was 14% compared with 0% with age of injury < 9 years.

Family history of anxiety disorder significantly predicted novel depression (all) (Fisher's exact = .008) and novel anxious depression (Fisher's exact = .006), but not novel non-anxious depression. Family history of a mood disorder including depressive disorders was not a predictor for novel depression (all), non-anxious depression or anxious depression. Comorbid Personality Change due to TBI at 6 months post injury was significantly correlated with novel anxious depression only (Fisher's exact = .020). Preinjury anxiety did not predict any category of novel depression.

3.3 Lesion Correlates (Table 3)

Depression (all) was significantly correlated with lesions in the left and right hemispheres specifically in the left inferior frontal gyrus (IFG) (lesion present in 5/15 versus 8/114 children with versus without depression; Fisher's exact = .008) and right frontal lobe white matter (lesion present in 5/15 versus 12/114 children with versus without depression; Fisher's exact = .029). There was a non-significant trend association between depression (all) and lesions in the left temporal pole.

Non-anxious depression was significantly correlated with only left hemisphere lesions, specifically lesions of the left IFG (lesion present in 4/9 versus 8/114 children with versus without depression; Fisher's exact = .005) and the left temporal pole (lesion present in 2/9 versus 2/114 children with versus without depression; Fisher's exact = .027).

Anxious depression was significantly correlated with right frontal white matter lesions (lesion present in 3/6 versus 12/114 children with versus without depression; Fisher's exact = .025) and with left parietal lesions (lesion present in 3/6 versus 10/114 children with versus without depression; Fisher's exact = .014).

3.4 Logistic Regression examining significant demographic, psychiatric, and lesion correlates

The demographic, psychiatric, and lesion correlates of depression which were significant in the univariate analyses were entered into logistic regression analyses to determine the relative independence and significance of these variables in accounting for depression. In the first logistic regression, depression (all) was the dependent variable and age at injury, family history of anxiety disorder, left inferior frontal gyrus lesions, and right frontal white matter lesions were the independent variables. The regression was significant ($-2 \log \text{likelihood } \chi^2 = 21.16$, $df=4$, $p=.0003$) and correctly predicted 90% of cases. The significance was accounted for independently by left inferior frontal gyrus lesions (Wald $\chi^2 = 6.27$, $df=1$, $p=.012$), family history of anxiety (Wald $\chi^2 = 4.24$, $df=1$, $p=.039$), age at injury (Wald $\chi^2 = 4.21$, $df=1$, $p=.040$), but not by right frontal white matter lesions.

In the second logistic regression, non-anxious depression was the dependent variable and age at injury, left inferior frontal gyrus lesions, and left temporal pole lesions were the independent variables. The regression was significant ($-2 \log \text{likelihood } \chi^2 = 17.58$, $df=3$, $p=.0005$) and correctly predicted 95% of cases. The significance was accounted for independently by left inferior frontal gyrus lesions (Wald $\chi^2 = 6.13$, $df=1$, $p=.013$), by age at injury (Wald $\chi^2 = 4.54$, $df=1$, $p=.033$), but not by left temporal pole lesions.

In the third logistic regression, anxious depression was the dependent variable and right frontal white matter lesions, left parietal lesions, Personality Change due to TBI, and family history of anxiety were the independent variables. The regression was significant ($-2 \log \text{likelihood } \chi^2 = 18.02$, $df=4$, $p=.0012$) and correctly predicted 97% of cases. The significance was accounted for independently by left parietal lesions (Wald $\chi^2 = 4.33$, $df=1$, $p=.038$), by family history of anxiety disorder (Wald $\chi^2 = 4.96$, $df=1$, $p=.026$), but not by right frontal white matter lesions or Personality Change due to TBI.

4. Discussion

This is the first prospective psychiatric interview study of pediatric TBI that investigated the occurrence and phenomenology of new-onset depression and its demographic, psychiatric, and lesion correlates. Our most important finding is that the pathophysiological mechanisms of TBI-associated depression may be robust and common across the lifespan. We found non-anxious depression to be associated with left inferior frontal gyrus and left temporal pole lesions and anxious depression to be associated with right frontal white matter lesions and left parietal lesions. These laterality distinctions and lesion-behavior correlates are similar to the findings of depression studies of adult TBI (Jorge et al., 1993b; Jorge et al., 2004).

The second important finding relates to the relationship between depressive and anxiety disorders. Forty-percent of children with novel definite/subclinical depressive disorder had a comorbid novel definite/subclinical anxiety disorder. This comorbidity is typical in children and adolescents who have not been injured (Moffitt et al., 2007), as well as in adults with depression post-TBI (Jorge et al., 2004). Research has shown that there are both similarities and distinctions in the neural correlates of these disorders (Beesdo et al., 2009). It is not surprising therefore that lesion correlates of depression vary depending on the presence of comorbid anxiety because emotional reactivity is both a neurobiologic risk factor for, and hallmark of, non-anxious depression as well as anxious depression (Pine et al., 2001). We extend this observation with the new finding that emotional reactivity appears to be broader in the case of anxious depression evidenced not merely by the presence of comorbid depression and anxiety, but by its significant association with Personality Change due to TBI. Personality Change due to TBI is the classic example of affective dysregulation after TBI and most commonly is characterized by clinically significant irritability and anger (Max et al., 2005; Max et al., 2006). Postinjury anxiety, we have found, is related to lesions of the superior frontal gyrus, younger age at injury, and to other manifestations of affective dysregulation including depression and Personality Change due to TBI (Max et al., 2011).

An additional new finding was that family history of anxiety disorder was significantly related to new-onset depression (combined non-anxious and anxious depression), as well as to anxious depression although not to non-anxious depression. Family history of mood disorder was not related to new-onset depression. These findings again demonstrate that there are similarities in the pathophysiology of depression and anxiety and that genetic factors likely influence the expression of depression after pediatric TBI.

Older age at injury was significantly related to new onset depression (all) and to non-anxious depression, but not to anxious depression, consistent with the pattern of increasing rates of depression from childhood to adolescence (Birmaher et al., 1996). We have previously shown that younger age at injury is associated with new-onset anxiety in this cohort (Max et al., 2011) and this likely neutralized the influence of age at injury on anxious depression.

Assessment of the relative importance of demographic (age at injury), psychiatric (family history of anxiety disorder, Personality Change due to TBI), and lesion correlates (left IFG, left temporal pole, right frontal white matter lesions, left parietal lesions) were instructive. In adults with TBI, abnormal magnetic resonance spectroscopy findings in left temporal and cingulate areas are related to mood disorder (Capizzano et al., 2010). It is likely that disturbance of critical limbic areas and their relationship to emotional control underlie important neuropathological determinants in the development of post-TBI depression (Maller et al., 2010), especially given the commonness of frontotemperolimbic damage in pediatric TBI (Bigler et al., 2010). The association of anxious depression with left parietal

lobe lesions was unexpected, however anxious depression in adults has been associated with absence of frontal lesions (Jorge et al., 1993b).

Our findings must be appreciated within its limitations. Despite the fact that this is the largest prospective psychiatric interview of pediatric TBI, the total number of children with depression was small and subgroups of non-anxious and anxious depression were yet smaller. As with almost all prospective studies, attrition is an important limitation and was 20% of the sample, although, to be sure, we identified few differences between participants and non-participants. Specifically, children with lower preinjury adaptive function and children with basal ganglia lesions were less likely to follow up. We might have expected a higher rate of depression if not for this pattern of attrition. Another limitation relates to how neuropathology was identified, i.e., coding of lesions from hard copy films from different scanners. It is possible that even more insightful markers of neuropathology as it relates to novel onset depressive disorder following TBI would be observed with advanced neuroimaging analysis methods. The San Diego sample was different in terms of exclusion of mild TBI participants with no lesions and exclusion of children with pre-injury ADHD. However, the findings are unlikely to be skewed because the San Diego contingent was relatively small accounting for 19/141 (13%) of 6-month follow up participants. Another limitation was the lack of an injured control group which could provide a comparison of new-onset depression in brain-injured versus orthopaedic injured children. However, a control group would not be relevant to the important lesion findings.

In conclusion, non-anxious depression after pediatric TBI appears to be linked to specific left-sided (IFG and temporal pole) lesions and anxious depression is related to different specific left-sided lesions (parietal lobe) and right-sided lesions (frontal white matter). This lesion-behavior relationship is similar to that occurring after adult TBI and suggests a common pathophysiology despite that fact that depression is less common after pediatric versus adult TBI. Older age at injury independently accounts for depression, probably because of the increased incidence of depression noted between childhood and adolescence/adulthood in the general population. Finally, familial factors in the form of family psychiatric history of anxiety disorder, independently accounts for post-TBI depression.

Acknowledgments

This study was supported by National Institute of Mental Health (NIMH) Grant K-08 MH01800 (Dr. Max) and National Institute of Neurological Disorders and Stroke (NINDS) Grant NS-21889 (Dr. Levin). Disclosures: Dr. Schachar is a consultant for Eli Lilly Corporation and Purdue Pharma (Canada). None of the other authors has financial disclosures to make relative to for-profit enterprises.

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Highlights

- This prospective study of pediatric TBI investigated the development of depression postinjury.
- Non-anxious depression is associated with older age, left sided lesions.
- Anxious depression is linked to familial anxiety, mood lability, and left and right lesions.

Table 1

Demographic, psychosocial, and injury data of enrolled participants.

Demographic Variables	
Age at injury mean (SD)	10.13 (2.77)
Socioeconomic Status mean (SD) n=173	37.01 (12.90)
Gender: males (%)	125 (71%)
Psychosocial Variables	
Pre-injury Lifetime Psychiatric Disorder cases (%)	56 (31.6%)
Pre-injury Family Functioning mean (SD) n=160	1.62 (.47)
Pre-injury Vineland Adaptive Behavior Composite Standard Score mean (SD) n=165	94.37 (15.43)
Injury Variables	
Lowest post-resuscitation Glasgow Coma Scale Score mean (SD)	10.85 (4.20)
Severity of Injury	N (%)
Severe (lowest post-resuscitation Glasgow Coma Scale Score 3-8)	54 (38)
Moderate (lowest post-resuscitation Glasgow Coma Scale Score 9-12)	18 (13)
Mild (lowest post-resuscitation Glasgow Coma Scale Score 13-15)	69 (49)
Mechanism of Injury	N (%)
Fall	41 (23.2)
Auto, truck, bus passenger	40 (22.6)
Recreational vehicle/Off-road vehicle	10 (5.6)
Bicycle	9 (5.1)
Motorcycle-moped	5 (2.8)
Assaulted	1 (.6)
Other	2 (1.1)
Hit by motor vehicle	49 (27.7)
Sports or play	15 (8.5)
Hit by a falling object	5 (2.8)

Legend: n=177 unless otherwise specified because of missing data.

Table 2

Demographic and psychosocial characteristics of novel depressive disorder and no novel depressive disorder groups.

	Novel Definite/Subclinical Depressive Disorder (n=15)	No Novel Definite/Subclinical Depressive Disorder (n=123)	t	df	sig
Gender (males)	8 (53%)	88 (72%)			ns
Race					ns
Caucasian	10 (67%)	68 (55%)			
Hispanic	2 (13%)	24 (20%)			
Black	3 (20%)	21 (17%)			
Asian	0	4 (3%)			
Other	0	6 (5%)			
Socioeconomic Status	40.2 (13.8)	37.5 (12.6) ^a	-.79	134	ns
Pre-injury Family Function	1.74 (.70)	1.61 (.45) ^b	-.69	15.6	ns
Pre-injury Adaptive Function	99.7 (10.7)	95.0 (15.0) ^b	-1.18	128	ns
	Novel Definite/Subclinical Non-Anxious Depression (n=9)	No Novel Definite/Subclinical Non- Anxious Depression (n=123)			
Gender (male)	5 (56%)	88 (72%)			ns
Race					ns
Caucasian	7 (78%)	68 (55%)			
Hispanic	0	24 (20%)			
Black	2 (22%)	21 (17%)			
Asian	0	4 (3%)			
Other	0	6 (5%)			
Socioeconomic Status	45.7 (11.0)	37.5 (12.6) ^a	-1.89	128	.061
Pre-injury Family Function	1.69 (.79)	1.61 (.45) ^b	-.45	122	ns
Pre-injury Adaptive Function	97.1 (10.9)	95.0 (15.0) ^b	-.41	122	ns
	Novel Definite/Subclinical Anxious Depression (n=6)	No Novel Definite/Subclinical Anxious Depression (n=123)			
Gender (male)	3 (50%)	88 (72%)			ns
Race					ns

	Novel Definite/Subclinical Depressive Disorder (n=15)	No Novel Definite/Subclinical Depressive Disorder (n=123)	t	df	sig
Caucasian	3 (50%)	68 (55%)			
Hispanic	2 (33%)	24 (20%)			
Black	1 (17%)	21 (17%)			
Asian	0	4 (3%)			
Other	0	6 (5%)			
Socioeconomic Status	32.1 (14.3)	37.5 (12.6) ^a	1.02	125	ns
Pre-injury Family Function	1.82 (.58)	1.61 (.45) ^b	-1.09	119	ns
Pre-injury Adaptive Function	103.7 (10.0)	95.0 (15.0) ^b	-1.39	119	ns

^a Legend: N=121

^b N=115

Table 3

Age, injury severity, psychiatric, and lesion characteristics of novel depressive disorder and no novel depressive disorder groups.

	<u>Novel Definite/Subclinical Depression (all) (n=15)</u>	<u>No Novel Definite/Subclinical Depression (n=123)</u>	t	df	sig
Age at Injury (mean;SD)	11.9 (2.2)	9.9 (2.8)	-2.55	136	.012
Glasgow Coma Scale Score (mean;SD)	11.3 (3.7)	10.8 (4.3)	-.42	136	ns
Personality Change due to TBI (cases;%)	6 (40%)	24 (20%)			.094 ^e
Family History of Anxiety Disorder (cases;%)	8 (62%) ^c	27 (24%) ^d			.008 ^e
Family History of Mood Disorder (cases;%)	8 (62%) ^c	37 (33%) ^d			.065 ^e
Pre-injury definite/subclinical Anxiety Disorder (cases;%)	4 (27%)	18 (15%)			ns
Left Hemisphere					
		n=114			
Frontal White Matter Lesion (cases; %)	3 (20%)	16 (14%)			ns
Inferior Frontal Gyrus Lesion (cases %)	5 (33%)	8 (7%)			.008 ^e
Middle Frontal Gyrus Lesion (cases; %)	1 (7%)	11 (10%)			ns
Superior Frontal Gyrus Lesion (cases; %)	3 (20%)	16 (14%)			ns
Temporal Pole (cases;%)	2 (13%)	2 (2%)			.066 ^e
Parietal Lobe (cases; %)	3 (20%)	10 (9%)			ns
Right Hemisphere					
Frontal White Matter Lesion (cases; %)	5 (33%)	12 (11%)			.029 ^e
Inferior Frontal Gyrus Lesion (cases %)	0	18 (16%)			ns
Middle Frontal Gyrus Lesion (cases; %)	2 (13%)	11 (10%)			ns
Superior Frontal Gyrus Lesion (cases; %)	1 (7%)	19 (17%)			ns
Temporal Pole (cases;%)	1 (7%)	3 (3%)			ns
Parietal Lobe (cases; %)	3 (20%)	17 (15%)			ns
	<u>Novel Definite/Subclinical Non-Anxious Depression (n=9)</u>	<u>No Novel Definite/Subclinical Non- Anxious Depression (n=123)</u>			
Age at Injury (mean;SD)	12.7 (1.8)	9.9 (2.8)	-4.25	11.2	.001
Glasgow Coma Scale Score (mean;SD)	12.8 (3.3)	10.8 (4.3)	-1.37	130	ns

	Novel Definite/Subclinical Depression (all) (n=15)	No Novel Definite/Subclinical Depression (n=123)	t	df	sig
Personality Change due to TBI (cases; %)	2 (22%)	24 (20%)			ns
Family History of Anxiety Disorder (cases; %)	3 (43%) ^f	27 (24%) ^d			ns
Family History of Mood Disorder (cases; %)	4 (57%) ^f	37 (33%) ^d			ns
Pre-injury definite/subclinical Anxiety Disorder (cases; %)	2 (22%)	18 (15%)			ns
Left Hemisphere					
		n=14			
Frontal White Matter Lesion (cases; %)	1 (11%)	16 (14%)			ns
Inferior Frontal Gyrus Lesion (cases; %)	4 (44%)	8 (7%)			.005 ^e
Middle Frontal Gyrus Lesion (cases; %)	1 (11%)	11 (10%)			ns
Superior Frontal Gyrus lesion (cases; %)	1 (11%)	16 (13%)			ns
Temporal Pole (cases; %)	2 (22%)	2 (2%)			.027 ^e
Parietal Lobe (cases; %)	0 (0%)	13 (11%)			ns
Right Hemisphere					
Frontal White Matter Lesion (cases; %)	2 (22%)	12 (11%)			ns
Inferior Frontal Gyrus Lesion (cases; %)	0	18 (16%)			ns
Middle Frontal Gyrus Lesion (cases; %)	1 (11%)	11 (10%)			ns
Superior Frontal Gyrus lesion (cases; %)	0	19 (17%)			ns
Temporal Pole (cases; %)	1 (11%)	3 (3%)			ns
Parietal Lobe (cases; %)	1 (11%)	19 (17%)			ns
	Novel Definite/Subclinical Anxious Depression (n=6)	No Novel Definite/Subclinical Anxious Depression (n=123)			
Age at Injury (mean;SD)	10.7 (2.3)	9.9 (2.8)	- .61	127	ns
Glasgow Coma Scale Score (mean;SD)	9.0 (3.4)	10.8 (4.3)	1.24	5.79	ns
Personality Change due to TBI (cases; %)	4 (66%)	24 (20%)			.020 ^e
Family History of Anxiety Disorder (cases; %)	5 (83%)	27 (24%) ^d			.006 ^e
Family History of Mood Disorder (cases; %)	4 (67%)	37 (33%) ^d			ns
Pre-injury definite/subclinical Anxiety	2 (33%)	18 (15%)			ns

	Novel Definite/Subclinical Depression (all) (n=15)	No Novel Definite/Subclinical Depression (n=123)	t	df	sig
Disorder (cases; %)					
Left Hemisphere		n=14			
Frontal White Matter Lesion (cases; %)	2 (33%)	16 (14%)			ns
Inferior Frontal Gyrus Lesion (cases; %)	1 (17%)	8 (7%)			ns
Middle Frontal Gyrus Lesion (cases; %)	0	11 (10%)			ns
Superior Frontal Gyrus lesion (cases; %)	2 (33%)	16 (13%)			ns
Temporal Pole (cases; %)	0	2 (2%)			ns
Parietal Lobe (cases; %)	3 (50%)	10 (9%)			.014 ^e
Right Hemisphere					
Frontal White Matter Lesion (cases; %)	3 (50%)	12 (11%)			.025 ^e
Inferior Frontal Gyrus Lesion (cases; %)	0	18 (16%)			ns
Middle Frontal Gyrus lesion (cases; %)	1 (17%)	11 (10%)			ns
Superior Frontal Gyrus Lesion (cases; %)	1 (17%)	19 (17%)			ns
Temporal Pole (cases; %)	0	3 (3%)			ns
Parietal Lobe (cases; %)	2 (33%)	18 (16%)			ns

^cLegend N=13

^dN=112

^eFisher's exact test

^fN=7

^gN=12