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Psychiatric Disorders in Children and Adolescents 24 Months After Mild Traumatic Brain Injury

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Abstract

This study aimed to better understand the occurrence of novel psychiatric disorders (NPDs) in children with mild traumatic brain injury (mTBI) in relation to preinjury variables, injury-related variables, and concurrent neurocognitive outcome. Eighty-seven children aged 5–14 years who had experienced mTBI were studied from consecutive hospital admissions with semistructured psychiatric interviews soon after injury (baseline). Fifty-four children were reassessed 24 months postinjury. Standardized instruments were used to evaluate injury severity, lesion characteristics, preinjury variables (lifetime psychiatric disorder, family psychiatric history, family function, socioeconomic status, psychosocial adversity, adaptive function, and academic function), and finally, postinjury neurocognitive and adaptive function. At 24 months postinjury, NPDs had occurred in 17 of 54 (31%) participants. NPD at 24 months was related to frontal white matter lesions and was associated with estimated preinjury reading, preinjury adaptive function, and concurrent deficits in reading, processing speed, and adaptive function. These findings extend earlier reports that the psychiatric morbidity after mTBI in children is more common than previously thought, and moreover, it is linked to preinjury individual variables and injury characteristics and is associated with postinjury adaptive and neurocognitive functioning.

Traumatic brain injury (TBI) is a major public health issue in the United States, leading roughly one-half a million children aged, 15 years to the emergency room every year[1] with >300 cases per 100,000 child-years.[2] Most of these cases (80%–90%) are considered to be mild.[1] Although more severe cases may cause greater levels of dysfunction, mild traumatic

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Dr. Max and Dr. Bigler independently provide expert testimony in cases of TBI on an ad hoc basis for plaintiffs and defendants on a more or less equal ratio. This activity constitutes approximately 5% of their respective professional activities. Dr. Schachar is a consultant for Eli Lilly Corporation and Purdue Pharma (Canada). All other authors report no financial relationships with commercial interests.

brain injury (mTBI) occurs in much larger numbers and its consequences are not trivial. With hundreds of thousands of cases of mTBI in children each year and up to a 20% prevalence of psychiatric disorder in children, establishing a connection between the two occurrences is extremely relevant,[3] and it is essential to understand whether mTBI is associated with new-onset psychiatric disorders in children and to recognize which variables are associated with these disorders. Greater awareness and insight into the development of novel psychiatric disorders (NPDs) in children who have experienced mTBI can considerably enhance the ability to predict and treat these disorders.

NPDs can manifest in two different situations.[4] NPDs can occur after a TBI in a child without a preinjury lifetime psychiatric disorder, or they can occur after a TBI in a child who has already been diagnosed with a different preinjury lifetime psychiatric disorder (e.g., a child with a preinjury diagnosis of attention deficit hyperactivity disorder [ADHD] experiences mTBI and subsequently develops major depressive disorder). Our previous study assessing children with mild/moderate TBI at 3, 6, 12, and 24 months postinjury found that 22%, 10%, 23%, and 20% of the children developed NPDs, respectively.[5] Other results from a birth cohort study found that mTBI resulting in inpatient as opposed to outpatient treatment was significantly related to the development of hyperactivity, inattention, and conduct disorders, especially in children injured before 5 years of age.[6] Retrospective studies, by nature of weaker design, tend to report substantial behavioral morbidity after mTBI[7] in contrast with some prospective studies.[8]

Recent work investigating postconcussion symptomatology, although not specifically psychiatric outcome, found that a high acute level of postconcussion symptomatology was particularly likely in children with mTBI whose acute clinical presentation reflected more severe injury.[9] The follow-up interval in prior research was limited to 12 months postinjury; thus, the current work extends prospective follow-up by assessing children up to 2 years postinjury. An earlier study found that children with mTBI whose specific symptoms increased after injury experienced relatively poor preinjury behavioral adjustment.[10] One of our earlier publications investigating psychiatric outcome 24 months after mild-severe TBI focused specifically on personality change due to TBI.[11] We found that preinjury adaptive function and frontal white matter lesions were correlated with this specific NPD. The cohort in this current mTBI study which uses any NPD as the outcome variable, is a subset of participants from our larger mild-severe TBI study in which the more specific diagnosis of personality change due to TBI served as the outcome variable.

In addition to behavioral symptoms that relate to mTBI, neurocognitive and academic sequelae of injury are also clinically important.[12] The association between NPDs and neurocognitive and academic deficits is understudied. In one of our studies examining a population of hospitalized children that included a broader range of TBI as well orthopedic injury, we found that NPDs related significantly to neurocognitive outcome.[13] Memory and intellectual function were each independently related to a “neuropsychiatric factor” composed of both injury severity and the presence of NPD. Furthermore, these two cognitive measures were also independently related to a “psychosocial disadvantage factor,” which encompassed socioeconomic status, family functioning, and family psychiatric history. By contrast, some reports have failed to find a connection between cognitive function and NPDs

after mTBI. One study found that children with mTBI with persisting behavioral problems did not exhibit significantly lower measures across memory, processing speed, executive function, or memory tests.[14] Other reports have suggested that mTBI was associated with benign cognitive outcome.[15–17] Nonetheless, mTBI was more likely to result in postconcussion symptomatology compared with orthopedic injury among children of lower versus higher cognitive ability. This was especially the case for children with complicated mTBI (lesion evident on MRI).[18] Of interest, children with milder forms of TBI have deficits in social cognition, even when general intelligence is age appropriate,[19] and deficits in social cognition help predict social competence.[20] The fact that cognitive difficulties related to the social world are beginning to be reported in children with milder forms of TBI emphasizes the need to further define the relationships between mTBI, NPD, and neurocognitive function in children.

In psychiatric studies, including our own, the typical predictors of NPDs include constructs from within the broad categories of 1) injury variables (e.g., injury severity; lesions), 2) individual preinjury characteristics (e.g., preinjury adaptive function), and 3) preinjury family characteristics (e.g., family function; socioeconomic status). Furthermore, we examined and found a significant relationship between concurrent neurocognitive function and NPDs.[21–23] This association may reflect that both NPDs and neurocognitive deficits are common complications of TBI. It is also possible that postinjury neurocognitive deficits may actually predate the injury and act as risk factors for NPD onset. This study further examines these concurrent correlates of NPDs after mTBI.

This investigation extends our prospective longitudinal psychiatric study of children and adolescents with mTBI into the second year after injury following reports addressing NPDs at 6 and 12 months postinjury.[21,22] NPDs were common at both 6-month and 12-month assessments, occurring in 25 of 70 (36%) and 17 of 60 (28%) of children, respectively. We found that NPDs were associated with relatively low concurrent cognitive function across several measures at both 6-month and 12-month assessments. At 6 months postinjury, frontal white matter lesions were related to onset of NPDs. Although this lesion correlate did not remain significant at the 12-month assessment, family measures were found to be risk factors for NPDs at this time period. The significant family correlates included psychosocial adversity and socioeconomic status. Low estimated preinjury reading ability also related to NPDs at a trend level at the 6-month assessment and significantly at the 12-month assessment. This study investigates the rate of NPDs in children 24 months after mTBI. We examine the relationships between NPDs and different risk variables from the three broad general categories mentioned above as well as concurrent neurocognitive and adaptive function. Based on the reviewed literature, we hypothesized that NPDs in children at 24 months after mTBI would relate to frontal white matter lesions, estimates of preinjury reading ability, preinjury adaptive functioning, and preinjury family measures. We further hypothesized that NPDs at 24 months would be associated with lower levels of both concurrent adaptive and neurocognitive function.

Methods

Participants

Participants included 87 children from consecutive hospital admissions, recruited at five different hospitals during initial hospitalization after an mTBI. Recruitment occurred between 1998 and 2002, and was from one of three academic medical centers in Texas, the Hospital for Sick Children in Toronto, and Rady Children's Hospital in San Diego, California. mTBI was considered to have occurred in children if an mTBI was sustained, the lowest Glasgow Coma Scale score upon emergency room examination was ≥13,[24] and if a history of an altered state or loss of consciousness no longer than 30 minutes was experienced.[25] Because we did not require patients to answer eligibility questions before deciding to participate in the study, we are lacking precise data regarding the number of approached children or participation rate among all eligible children. Children were not excluded if they experienced a linear skull fracture, which was consistent with inclusion in another study of pediatric mTBI neurobehavioral outcome.[9] Injuries that were excluded were those from child abuse or penetrating missiles. Children with autism spectrum disorder, mental deficiency, or schizophrenia were excluded. Parents or guardians of all children provided informed consent for participation and each child gave consent to participate in accordance with the institutional review board requirements at each study site. Enrolled participants were evaluated within 2 weeks postinjury. One participant suffered a second TBI before the 24-month assessment and was excluded from the analyses. Of the remaining 86 children, 54 (63%) returned for the 24-month evaluation. Termination of the funding cycle accounted for 18 children who did not return and thus the effective participation was 54 of 68 (79%) patients. This returning group did not differ significantly from the nonreturning group regarding gender, age, race, socioeconomic status, Glasgow Coma Scale scores, preinjury lifetime psychiatric disorder, preinjury family psychiatric history, preinjury family functioning, estimated preinjury reading ability, or preinjury adaptive function. However, the returning group did have significantly higher psychosocial adversity (mean ± SD 0.83±0.92 [N=52] versus 0.39±0.56 [N=31]; $t=-2.71$; $df=80.97$; $p<0.01$).

Table 1 represents demographic data (age, gender, and socioeconomic status), injury indices (cause of injury, depressed skull fracture, and Glasgow Coma Scale scores), and preinjury psychosocial variables (lifetime psychiatric disorder, adaptive functioning, family functioning, family psychiatric history, and psychosocial adversity) for the entire cohort. Race of participants was as follows: Caucasian, 54 (62%); African American, 13 (15%); Hispanic, 13 (15%); Asian, 3 (3%); or other, 4 (5%).

Measures

Psychiatric assessment—*DSM-IV* psychiatric diagnoses[26] were made via a semistructured interview, using the Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Present and Lifetime Version.[27] This is an integrated parent-child interview in which a clinician compiles data, collected separately from parent and child, regarding concurrent and lifetime symptoms (at baseline) and symptoms present or past from 12 months postinjury to 24 months (at the 24-month assessment).

The Neuropsychiatric Rating Schedule,[28] another semistructured interview, was also employed to identify symptoms and subtypes of personality change due to TBI. Children and parents were interviewed both at baseline and at 24 months postinjury.

Parent and child Neuropsychiatric Rating Schedule, Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Present and Lifetime Version interviews and, when available, the Survey Diagnostic Instrument[29] completed by the teacher (56 of 87, 65% at baseline; 39 of 54, 72% at 24 months) were all incorporated to help interviewers give "best estimate" diagnoses, which meets the gold standard of child psychiatric assessment, by including data from several sources.[30] Master's- and doctoral-level clinicians trained by the first author in both prestudy and midstudy workshops served as interviewers. A child psychiatrist (four sites) or a child psychologist (one site) supervised evaluations. The first author, responsible for a second level of supervision, then reviewed written summaries from the interviewers, and held case discussions at monthly teleconferences to reach consensus diagnoses.

Neurological assessments—TBI severity was established via the patient's lowest score on the Glasgow Coma Scale,[24] a standard measure of acute brain injury related to TBI. Scores ranging from 3 (unresponsive) to 15 (normal) indicate a child's level of verbal, motor, and eye-opening responsiveness.

The Abbreviated Injury Scale provided an Injury Severity Score,[31] delineating overall extracranial injury severity The Injury Severity Score is the sum of the squares of the highest Abbreviated Injury Scale score in each of the three most severely injured body areas (chest, abdominal, or pelvic regions, extremities, and external areas) when applicable.

At 3 months postinjury, MRI (1.5 T) was performed in most participants. The procedure included both T1-weighted volumetric spoiled gradient recalled echo and fluid-attenuated inversion recovery sequences acquired in sagittal and coronal planes. Lesion coding performed by expert project neuroradiologists at each site included gray/white matter pathology (e.g., shearing injury, hemosiderin, gliosis), and anatomical location. Specific coding of frontal lobe gyri was conducted only if gray matter lesions appeared in these gyri. Lesions in frontal lobe white matter were recorded as either present or absent. Of the 87 enrolled children, 73 (84%) returned to undergo the research MRI. Table 2 displays the lesion distributions. Lesion presence and location did not differ significantly in children who did and did not attend the 24-month assessment.

Psychosocial assessments—Trained research assistants at each site conducted the Family History Research Diagnostic Criteria[32] assessment. These criteria were altered to conform to *DSM-IV* criteria. At least one parent gave information about psychiatric disorders in the participant's first-degree relatives. Subsequently, family ratings were summarized using a four-point scale of increasing severity.[5]

The Family Assessment Device–General Functioning Scale, a self-report survey with 12 items[33] was used to evaluate global family functioning at baseline. Each family's primary

caretaker answered each question on a 4-point Likert scale. A higher total score denoted increased dysfunction.

The Four Factor Index evaluated socioeconomic status.[34] Assessments were made using scores derived from a formula that integrated educational and occupational levels of the child's mother and father. The scores ranged from 8 to 66, with lower scores representing lower socioeconomic status.

Psychosocial adversity was classified using a psychosocial adversity index modified from a seminal study of pediatric TBI.[4] Six domains were assessed and 1 point was given for every area suggesting adversity. A score of zero was assigned when adversity was absent in a specific domain.

Adaptive function was measured using the Vineland Adaptive Behavior Scale interview.[35] Trained research assistants interviewed primary caretakers in semistructured interviews. Preinjury adaptive functioning was retrospectively estimated within 2 weeks after injury (baseline) and concurrent adaptive functioning was assessed 24 months postinjury using the same measurements.

Neurocognitive Assessments

Estimate of preinjury academic function—The Woodcock-Johnson Revised Letter-Word Identification subtest[36] was performed within 2 weeks of injury to estimate baseline academic function. The test judges how accurately a child is able to read letters and words aloud. Data produced a standard score that represented the total number of items a child read properly. Other research has indicated that in children that have experienced mTBI, this baseline assessment of reading ability, although given after the injury, can be used to estimate preinjury reading ability.[37]

Concurrent Academic and Neurocognitive Function (Processing Speed, IQ, Academic Function, Memory, and Language) 24 Months Postinjury

Processing speed—Processing speed was assessed using the WISC-III Symbol Search and Coding subtests.[38] The Symbol Search subtest consisted of 45 trials in which children were presented with target stimuli and ask to check yes or no as quickly as possible to signify whether the targets appeared among a variety of stimuli. Subtracting the number of errors from the number of correct responses made in 120 seconds yielded the test score. During the Coding Subtest, children used a key to identify certain geometric designs beneath numbers. The number of symbols correctly transcribed in 2 minutes yielded this score. A Processing Speed scaled score was calculated and averaged for both subtests.

IQ—The Wechsler Abbreviated Scale of Intelligence[39] assessed intellectual function. Full-scale IQ was estimated through the administration of the Vocabulary, Similarities, Block Design, and Matrix Reasoning subtests.

Academic function—Postinjury academic function at 24 months was measured using the previously described Woodcock-Johnson Revised Letter-Word Identification subtest.[36]

Memory—The California Verbal Learning Test–Children's Version was given to evaluate verbal learning and memory.[40] Standard procedures for alternate forms were followed. Children were told to learn 15 different words from three categories across five learning trials and one distraction trial. Verbal memory was assessed for delayed recall and given a z score.

Language—Expressive language was evaluated using the Clinical Evaluation of Language Fundamentals–Third Edition Formulated Sentence Subtest[41] consisting of 22 items. Children were shown an image with a target word/phrase and they were instructed to construct a sentence in response.

Data Analysis

Independent-sample t tests or chi-square analyses and effect size analyses[42] were conducted as appropriate. Alpha levels were set at 0.05. Tests analyzed the association of 24-month postinjury NPDs with injury variables (frontal lobe white matter lesion, presence of any lesion), preinjury individual variables (lifetime psychiatric disorder, adaptive function, estimated reading ability), preinjury family variable (socioeconomic status), and concurrent neuropsychological function (processing speed, IQ, processing speed, reading, verbal memory, language) and concurrent adaptive function. Furthermore, exploratory analyses tested variables potentially associated with NPDs including demographics (age at injury, race, gender), injury severity (Glasgow Coma Scale scores, abnormal CT scan, depressed skull fracture), and other preinjury family variables (preinjury family functioning, family psychiatric history, preinjury psychosocial adversity).

Results

Preinjury and NPDs

Thirty-three of the 87enrolled children (38%) had a history of one or more preinjury psychiatric disorders. The specific disorders occurred as follows: ADHD (N=20), simple phobia (N=8 including two in remission), separation anxiety disorder (N=5 including two in remission), oppositional defiant disorder (N=3 including one in remission), obsessive-compulsive disorder (N=2), generalized anxiety disorder (N=2), major depressive disorder (N=1 in remission), chronic motor tic disorder (N=1), social phobia (N=1), encopresis (N=1), disruptive behavior disorder not otherwise specified (N=1), and eating disorder not otherwise specified (N=1).

Seventeen of the 54 children (31%) who returned for the 24-month assessment showed NPD. The NPD in 10 of these children had been present at an earlier assessment, whereas the remainder developed de novo in the second postinjury year. The specific disorders recorded were as follows: ADHD (N=9), disruptive behavior disorders including oppositional defiant disorder, conduct disorder, and disruptive behavior disorder not otherwise specified (N=5), personality change due to TBI (N=4), depressive disorders including dysthymia, major depressive disorder, and depressive disorder not otherwise specified (N=3, with the depressive disorder not otherwise specified resolved), anxiety

disorders (N=3) including generalized anxiety disorder and one child with social phobia, and lastly, adjustment disorder with depressed mood (N=2, both resolved).

Preinjury and Injury Correlates of NPDs

Results displaying the variables associated with NPDs at 24 months after mTBI are in Table 3 and Table 4. Of the variables hypothesized to be associated with NPD, estimate of preinjury reading ability and preinjury adaptive function both showed significance but preinjury family variables (socioeconomic status, psychosocial adversity, family psychiatric history, or family functioning) were not significantly related. Other demographic (age, race), psychosocial (preinjury psychiatric disorder), and injury (lowest Glasgow Coma Scale score, depressed skull fracture, and abnormal CT scan) variables tested in exploratory analyses were not significantly associated with NPD. However, there was a nonsignificant trend of females more commonly developing NPD.

Concurrent Neurocognitive and Adaptive Function Correlates of NPDs at 24 Months

Neurocognitive and adaptive function scores at 24 months postinjury are displayed in Table 4 according to the status of NPD. Processing speed (WISC-III), reading (WJ-R Letter-Word Identification test), and adaptive function were significantly associated with NPD. A logistic regression analysis with NPD as the dependent variable showed that when preinjury and postinjury reading scores were entered, the regression was significant but neither of the independent variables significantly and independently accounted for NPD. The same pattern was evident in a regression analysis with NPD as the dependent variable and with preinjury and postinjury adaptive function scores as independent variables. This pattern of results suggests that the preinjury and postinjury scores were highly correlated. Intellectual function (Wechsler Abbreviated Scale of Intelligence full-scale IQ) and language (Clinical Evaluation of Language Fundamentals–Third Edition formulated sentences) were associated with NPD at a trend level. Verbal memory (California Verbal Learning Test-Children's Version long delay z score) was not significantly associated with NPD.

Lesion Characteristics

Table 2 displays the lesions distributions obtained from MRI. The presence of frontal white matter lesions was found to be significantly associated with NPD. Frontal white matter lesions were present in four of 16 children with NPDs and in only one in 32 children that did not develop NPDs. The existence of any lesion was not significantly associated with NPD: a lesion was present in 11 of 16 children with NPDs versus in 16 of 32 of the children who did not develop NPDs.

Discussion

The most important finding in this study is that mTBI in children is associated with NPDs that are present in the second postinjury year, including some that emerged in the first weeks postinjury. Not only do the NPDs persist, but they are surprisingly common (31%) in this prospectively studied cohort. The results address poten-tial pathophysiological mechanisms, risk factors, and concurrent correlates for NPDs by demonstrating significant associations

with frontal network damage, preinjury vulnerabilities in reading and adaptive function, and lower postinjury processing speed, reading, and adaptive function.

The rate of NPDs in this study is higher than that reported by a previous psychiatric study, which found that 6 of 30 (20%) children and adolescents developed NPDs 24 months after mild and moderate brain injuries.[5] As previous studies showed, the specific NPDs were heterogeneous[4,5] and included novel ADHD, personality change due to TBI, anxiety disorders, depressive disorders, and disruptive behavior disorders. Rates of NPDs in control children with orthopedic injury are lower than rates in this study and range from 4% to 14%.[4,23,43] Larger studies are necessary to determine whether the trend of more females with NPDs found here and in a previous cohort is meaningful.[43]

In addition to the high rates of NPDs after mTBI, we found, as in the earlier assessment at 6 months postinjury, that the specific presence of frontal white matter lesions significantly correlated with NPD.[21] This finding highlights the important role of frontal white matter damage in post-TBI behavioral outcome.[44] The likely mechanism is that frontal white matter injury leads to a less connected and subsequently damaged and less efficient complex of neural systems.[45]

In addition to the injury-related (frontal white matter damage) correlate of NPD, we found that two indices of children's preinjury function (adaptive function and estimated reading ability) were significantly related to NPD. Preinjury adaptive function is a measure of a child's overall abilities in the domains of socialization, communication, and daily living skills. It is not surprising that children with lower adaptive function (although still within the normal range) than their peers would experience greater difficulties adapting to the stressors associated with mTBI and ultimately develop behavioral or emotional problems. One may think of preinjury adaptive function as a type of “behavioral reserve” such that children with greater reserve than their peers will require larger insults to reach the threshold of functional deficits such as NPDs.

Our finding that the estimate of preinjury reading ability negatively correlated significantly with NPDs suggests that the construct of “cognitive reserve” plays a role in behavioral outcome after mTBI. The cognitive reserve hypothesis states that regardless of injury severity psychometric intelligence may preserve functional capacity.[46] Reading ability is just one important component of the diverse construct of cognitive reserve. Therefore, a relatively low reading proficiency could be a marker of a generally low cognitive reserve and/or can specifically complicate learning, increase frustration, and limit one's ability to cope with trauma.

Clearly there is a link between NPDs 2 years postinjury adaptive function, and reading ability We found that this link was not limited to preinjury status but extended to concurrent adaptive function and reading skills 24 months after mTBI. Furthermore, processing speed measured 2 years postinjury was also significantly related to NPD. The pattern of results from our analyses suggested that preinjury and 24-month postinjury scores within the same measures (i.e., adaptive function; reading) were highly correlated and not independently significantly related to NPD. Notwithstanding that adaptive function and reading

assessments were derived after the mTBI, the parsimonious explanation for this is that on average, adaptive function and reading scores did not change substantially and that differences with regard to NPDs preceded the injury. The processing speed measure did not have a preinjury estimate; therefore, it is unclear whether the significant association with NPDs represents a complication of the mTBI or a preinjury risk factor.

This investigation concerns the final wave of data collection within a prospective longitudinal study of children with mTBI. We are now able to review and interpret the shifting pattern of the relationship of NPDs at progressive epochs (0–6, 6–12, and 12–24 months postinjury) and injury child, family, and neurocognitive variables.[21,22] Changes in the statistical relationships among variables are not surprising because the groups of children with NPDs overlapped only partially at each assessment, and the NPDs themselves varied over time. With regard to injury correlates of NPDs, frontal white matter lesions were significantly related at the 6-month and 24-month assessments. Inspection of individual cases revealed that the 12-month frontal white matter finding was lost primarily because of fluctuating NPD diagnoses in two cases with frontal white matter lesions. NPDs and child variables (aside from neurocognitive function) were seldom associated. For example, only preinjury adaptive function predicted NPDs and did so only at 24 months. However, NPDs and family variables (socioeconomic status and psychosocial adversity) were significantly associated, but only at the 12-month assessment. Finally NPDs and neurocognitive function were significantly associated on multiple measures and at all follow-up assessments. Specifically, NPDs were related to an estimate of preinjury reading at 6 months at a trend level, and significantly at 12 and 24-month assessments. In addition, NPDs were significantly related to concurrent measures of processing speed at every follow-up. Furthermore, NPDs and language function were significantly associated at 6 and 12 months postinjury and were related at a trend level at 24 months. The important overarching conclusion is that NPDs after mTBI are not a static or homogeneous entity; therefore, the significant injury, child, family, and neurocognitive correlates also shift.

This study should be considered within its limitations. Our mTBI sample consisted exclusively of hospitalized children, excluding children with mTBI that were discharged from the emergency room after treatment. This limitation is particularly relevant because the rate of emergency room discharge in children with mTBI is growing[47] and thus our sample does not represent the entire population of children with mTBI. Furthermore, the study sample could have possessed certain injury or psychosocial characteristics that contributed to decisions to hospitalize rather than discharge these children. For example, the rate of abnormal MRI (any lesion detected) in our sample was 58%, which is substantially higher than that in a cohort of injured children who were not selected based on hospitalization status.[9] Another limitation is the absence of videotaping for interrater reliability assessments for NPD diagnoses. However, licensed child psychiatrists or psychologists closely supervised all clinical evaluations and other levels of surveillance as noted in the methods section were in place to maintain fidelity in reliability and validity of assessments. The attrition rate was another limitation of our study. Thirty-eight percent of eligible mTBI participants did not return for the 24-month psychiatric assessment. Because termination of funding accounted for 17% of attrition, the effective participation was 79%. There were no differences in demographic, injury, or psychosocial variables in children who did versus did

not return for the 24-month assessment except for a higher level of preinjury psychosocial adversity in those who returned. Nevertheless, psychosocial adversity was not significantly related to NPDs. It is important to consider that even if none of these children lost to attrition developed NPDs, the rate of those that did would still be high (17 of 86; 20%). Another limitation is the image analysis we used, which did not utilize volumetric measurements or diffusion tensor imaging that might have more clearly outlined NPD imaging correlates. We did not have a measure of parental expectation of psychiatric outcome, which could be informative in future studies. The final limitation to consider for this study is the absence of an orthopedic injury comparison group, which could control for NPDs in children predisposed and exposed to injuries in general.

The strengths of this study should also be acknowledged. To our knowledge, this is the largest prospective psychiatric interview study of a consecutively admitted pediatric mTBI population. The scope of evaluation was extensive and included interview assessments of psychopathology and adaptive function. In addition, potential risk factors for NPDs were investigated comprehensively by consideration of standardized injury, child, and family variables. Finally, expert neuroradiologists at each site carried out the lesion analyses to evaluate injury correlates of the NPDs.

Conclusions

After suffering an mTBI, children should be screened and observed for the development of NPDs in the 2 years after the injury. Specifically, individuals with evidence of frontal white matter injury, with low preinjury neurocognitive or adaptive function, or who show a decline in academic function during recovery should be examined carefully and monitored longer term. Given that mTBI is extremely common, we are currently conducting an additional study to determine whether this high rate of NPDs among initially hospitalized children is replicated in the more common group of children with mTBI who are treated and discharged from emergency rooms.

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Table 1

Demographic, Injury, and Psychosocial Data of the Mild Traumatic Brain Injury Cohort (N=87)

Variable	Value	N
Demographic variables		
Male gender, N (%)	58 (66.7)	87
Age at time of injury (years)	10.02 (2.99)	87
Socioeconomic status	40.13 (11.81)	85
Injury variables, N (%)		
Lowest postresuscitation Glasgow		
Coma Scale score		
13	6 (7)	
14	20 (23)	
15	61 (70)	
Depressed skull fracture	8 (9.2)	87
Mechanism of injury		87
Passenger in car, truck, or bus	17 (19.5)	
Off-road or recreational vehicle	3 (3.4)	
Bicycle riding	6 (6.9)	
Fall	29 (33.3)	
Hit by a falling object	3 (3.4)	
Sports or play	11 (12.6)	
Hit by motor vehicle	16 (18.4)	
Other	2 (2.3)	
Psychosocial variables		
Preinjury lifetime psychiatric disorder, N (%)	33 (37.9)	87
Preinjury Vineland Adaptive Behavior Scale composite standard score	94.62 (15.34)	79
Preinjury family functioning	1.55 (0.42)	80
Family psychiatric history	1.09 (1.03)	69
Preinjury psychosocial adversity	0.65 (0.83)	84

Data are presented as means (standard deviations) unless otherwise specified.

Table 2

Lesion Distribution Based on Research MRI in the Entire Cohort (N=73) and in Children With and Without NPDs 24 Months After Injury

Lesion Location	All Subjects (N=73)	Subjects With NPD (N=16)	Subjects Without NPD (N=32)	p Value
Any lesion[a]	38 (52.1)	11 (68.8)	16 (50.0)	n.s.
Frontal lobe white matter[a]	8 (11.0)	4 (25.0)	1 (3.1)	0.04
Distribution of other lesions				
Frontal lobe				
Any frontal lobe gray matter	16 (21.9)	6 (37.5)	6 (18.8)	
Superior frontal gyrus	7 (9.6)	2 (12.5)	3 (9.4)	
Middle frontal gyrus	8 (11.0)	4 (25.0)	2 (6.3)	
Inferior frontal gyrus	6 (8.2)	3 (18.8)	2 (6.3)	
Orbital gyrus	2 (2.7)	1 (6.3)	1 (3.1)	
Gyrus rectus	5 (6.8)	2 (12.5)	2 (6.3)	
Temporal lobe	7 (9.6)	0	5 (15.6)	
Parietal lobe	12 (16.4)	4 (25.0)	6 (18.8)	
Basal ganglia	1 (1.4)	0	1 (3.1)	
Cerebellum hemisphere	1 (1.4)	1 (6.3)	0	

Data are presented as N (%). White matter lesions were recorded specifically only in the frontal lobes. NPD, novel psychiatric disorder.

[a]Fisher's Exact Test.

Table 3

Preinjury and Injury Correlates of NPDs 24 Months After Mild Traumatic Brain Injury

Variable	NPD (N=17)	No NPD (N=37)	t	df	p Value
Demographic variables					
Age at injury (years)	10.2 (3.5)	9.6 (2.8)	−0.69	52	n.s.
Male gender, N (%)[a]	8 (47)	27 (73)		1	0.08
Race[b]				4	n.s.
Caucasian	11	24			
African American	2	4			
Hispanic	2	6			
Asian	2	1			
Other	0	2			
Psychosocial variables					
Preinjury lifetime psychiatric disorder, N (%)[a]	7 (41)	14 (38)			n.s.
Preinjury Vineland Adaptive Behavior Scale composite score	88.1 (14.8) (N=16)	98.7 (16.1) (N=36)	2.24	50	0.03
Preinjury family functioning	1.63 (0.44) (N=16)	1.59 (0.44) (N=36)	−0.26	50	n.s.
Family psychiatric history	1.2 (1.1) (N=15)	1.0 (1.1) (N=34)	−0.51	47	n.s.
Preinjury psychosocial adversity	1.0 (1.0) (N=16)	0.8 (0.9) (N=36)	−0.90	50	n.s.
Socioeconomic status	35.7 (11.1) (N=16)	39.0 (12.5)	0.912	51	n.s.
Injury variables					
Lowest postresuscitation Glasgow Coma Scale score[c]				2	n.s.
Glasgow Coma Scale score, no. of participants					
13	2	2			
14	4	11			
15	11	24			
Abnormal CT scan, N (%)[a]	9 of 16 (56)	13 of 33 (39)			n.s.
Depressed skull fracture, N (%)[a]	2 (12)	4 (11)			n.s.
Abbreviated Injury Scale–Injury Severity score	1.4 (2.5)	1.6 (4.8)	0.15	52	n.s.

Values are expressed as means (standard deviations) unless otherwise indicated. NPD, novel psychiatric disorder.

[a]Fisher's exact test.

[b] $\text{Pearson } \chi^2=2.81$.

[c] $\text{Pearson } \chi^2=0.80$.

Table 4

Neurocognitive Correlates of NPDs 24 Months After Mild Traumatic Brain Injury

Correlate	NPD (N=17)	No NPD (N=37)	t	df	p Value	Effect Size
Estimates of preinjury cognitive function (conducted after injury)						
WJ-R Letter-Word Identification standard score	95.8 (17.0)	106.7 (16.8)	2.21	52	0.03	0.64
Neurocognitive correlates 24 months postinjury						
WISC-III Processing Speed scale score	102.5 (17.4) (N=15)	114.1 (16.9) (N=36)	2.22	49	0.03	0.68
WASI full-scale IQ standard	99.8 (12.3) (N=16)	107.8 (14.9)	1.89	51	0.07	0.59
WJ-R Letter-Word Identification standard score	96.6 (20.6) (N=16)	109.8 (13.2)	2.80	51	0.01	0.76
CVLT Monday List-Long Delay z score	0.43 (0.59) (N=15)	0.63 (0.96) (N=36)	0.87	41.4	n.s.	0.25
CELF-3 Formulated Sentences scale score	8.5 (3.2) (N=16)	10.2 (3.2)	1.77	51	0.08	0.53
Adaptive function 24 months postinjury						
Vineland Adaptive Behavior Scale composite standard score	84.1 (13.3) (N=16)	95.5 (14.2)	2.74	51	0.01	0.83

Values are expressed as means (standard deviations) unless otherwise indicated. CELF-3, Clinical Evaluation of Language Fundamentals–Third Edition; CVLT, California Verbal Learning Test–Children's Version; NPD, novel psychiatric disorder; WASI, Wechsler Abbreviated Scale of Intelligence; WJ-R, Woodcock-Johnson–Revised.