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Authors

Lowet, Daniel

Vaida, Florin

Hesselink, John

et al.

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Novel Oppositional Defiant Disorder 12 months after Traumatic brain injury in children and adolescents

Daniel S. Lowet, BS[1], **Florin Vaida, Ph.D.**[2], **John R. Hesselink, M.D.**[3], **Harvey S. Levin, Ph.D.**[4], **Linda Ewing-Cobbs, Ph.D.**[5], **Russell J. Schachar, M.D.**[6], **Sandra B. Chapman, Ph.D.**[7], **Erin D. Bigler, Ph.D.**[8,9], **Elisabeth A. Wilde, Ph.D.**[9], **Ann E. Saunders, M.D.**[5], **Tony T. Yang, M.D., Ph.D.**[10], **Olga Tymofiyeva, Ph.D.**[11], **Jeffrey E. Max, MBBCh**[1,12]

[1.]University of California, San Diego, Department of Psychiatry

[2.]University of California, San Diego, Department of Family Medicine and Public Health, Division of Biostatistics & Bioinformatics

[3.]University of California, San Diego, Department of Radiology

[4.]Baylor College of Medicine, Department of Physical Medicine and Rehabilitation

[5.]University of Texas Health Science Center at Houston

[6.]The Hospital for Sick Children, University of Toronto

[7.]Center for BrainHealth® -The University of Texas at Dallas

[8.]Brigham Young University, Department of Psychology

[9.]University of Utah, TBI and Concussion Center, Department of Neurology

[10.]University of California, San Francisco, Department of Psychiatry and Behavioral Sciences, Division of Child and Adolescent Psychiatry, Weill Institute for Neurosciences

[11.]University of California, San Francisco, Department of Radiology and Biomedical Imaging

[12.]Rady Children's Hospital, San Diego

Abstract

Objective: To investigate the factors predictive of novel Oppositional Defiant Disorder (ODD) in the interval 6-12 months following traumatic brain injury (TBI).

Methods: Children ages 5 to 14 years who had suffered a TBI were recruited from consecutive admissions to five hospitals. Participants were evaluated soon after injury (baseline) for pre-injury characteristics including psychiatric disorders, adaptive function, family function, psychosocial

Corresponding Author: Jeffrey E. Max, MBBCh (University of California, San Diego, Department of Psychiatry; Rady Children's Hospital, San Diego; Address: 5755 Oberlin Drive, Suite 301, San Diego, CA 92121; Phone: 858-625-0025; Fax: 858-622-1265; jmax@health.ucsd.edu).

Disclosures: Drs. Max provides expert testimony in cases of traumatic brain injury on an ad hoc basis for plaintiffs and defendants on a more or less equal ratio. This activity constitutes approximately 5-10% of his professional activities. Dr. Bigler Dr. Bigler is retired but still provides expert testimony in cases of traumatic brain injury. Dr. Ewing-Cobbs provides expert testimony in cases of traumatic brain injury on an ad hoc basis largely for plaintiffs at < 5% of professional activities. Dr. Schachar is a consultant to Highland Therapeutics and Ehave. The other authors report no competing interests.

adversity, family psychiatric history, socioeconomic status (SES), and injury severity to develop a biopsychosocial predictive model for development of novel ODD. MRI analyses were conducted to examine potential brain lesions. Psychiatric outcome including that of novel ODD was assessed 12 months after the injury.

Results: While 177 children were recruited for the study, 120 children without pre-injury ODD or conduct disorder (CD) or disruptive behavior disorder, not otherwise specified (DBD NOS) returned for the 12-month assessment. Of the 120 children, 7 (5.8%) exhibited novel ODD and none developed CD or DBD NOS in the interval of 6 to 12 months post-injury. Novel ODD was significantly associated with lower SES, higher psychosocial adversity, and lower pre-injury adaptive functioning.

Conclusion: The results demonstrate that novel ODD following TBI impacts selectively and negatively impacts an identifiable group of children. Both proximal (pre-injury adaptive function) and distal (SES and psychosocial adversity) psychosocial variables significantly increase risk for this outcome.

Keywords

Pediatric traumatic brain injury; Oppositional Defiant Disorder; prospective longitudinal study

Introduction

Children 17 years of age and younger experienced over 837,000 TBI-related emergency department visits, hospitalizations, and deaths in 2014 alone in the United States, qualifying TBI in this population as a major public health problem {1}. New-onset post-injury psychiatric disorders, otherwise termed novel psychiatric disorders, occur commonly and the biopsychosocial predictors or correlates of these disorders have been well studied {2–7}. However, studies of post-injury onset of oppositional defiant disorder (ODD), conduct disorder (CD), or disruptive behavior disorder, not otherwise specified (DBD NOS) are sparse and needed to better understand and proactively address deficits that could emerge from TBI. The current investigation is an extension to a 12-month follow up of our published work that examined “novel ODD or CD or DBD NOS” in the first 6-months post-injury. This work, which is informed by a biopsychosocial model {8}, is the first prospective study of a consecutively hospitalized sample of children with TBI that examines DSM-IV-TR “novel ODD or CD or DBD NOS” assessed 12-months post-injury {9}. We chose to study children with any of these new-onset disorders as a single group due to the anticipated low incidence and phenomenological similarities between these diagnoses. However, as will be discussed, in the 6-12-months post-injury interval there were no cases of novel CD or DBD NOS. Therefore, we have simplified our outcome of interest to “novel ODD”.

Our investigation of predictors of novel ODD in the first 6-months post-injury in the same cohort examined here, revealed that 11/134 (8.2%) of prospectively studied children developed novel ODD {10}. The significant correlates of novel ODD were lower socioeconomic status (SES), lower pre-injury family functioning, and higher pre-injury psychosocial adversity, as well as lower post-injury processing speed which was associated

with severity of injury {10}. Besides the current study, there are only two prospective longitudinal psychiatric standardized-interview pediatric TBI studies have investigated novel ODD or novel CD symptomatology. One study examined post-injury ODD symptom counts and change in ODD symptom counts in consecutively hospitalized children with mild to severe TBI (n=50) over the first two years post-injury {11}. The other study investigated symptom counts and categorical diagnoses of novel ODD and novel CD using parent report in a referred sample of inpatient rehabilitation center patients with severe TBI (n=94) and one-year post-injury {4}. While these studies differed in design, both found overlapping psychosocial risk factors (e.g., SES, pre-injury family function, psychosocial adversity, pre-injury ODD symptomatology, pre-injury aggression and delinquency) and comorbidities (e.g., emotional lability and/or personality change due to TBI, novel attention-deficit/hyperactivity disorder (ADHD)) implicated in novel ODD symptomatology {4, 11–15}. Only one study found a potential biological risk factor: a smaller bicaudate ratio identified on the day-of-injury CT scan in exploratory analyses {11}. Neither study had a significant relationship between first-year post-injury ODD and lowest post-resuscitation Glasgow Coma Scale (GCS) score {16}, a primary acute measure of brain injury severity. However, another prospective study--which did not use a psychiatric interview assessment approach--suggested that preschool children with mild TBI (mTBI) who were hospitalized for their injury had increased ODD/CD symptomatology as adolescents compared with outpatient-treated children with mTBI and children with no history of mTBI {17}. The assumption was that the inpatient-outpatient treatment difference reflected severity of injury which was associated with adverse outcomes.

The current literature of pediatric TBI and novel ODD symptomatology is limited in several regards. Among the limitations are that 1) only three relevant studies exist {4, 11, 17}, only one of which studied consecutively treated children presenting with TBI; 2) the TBI sample sizes are relatively small (<100); and 3) there are minimal data on a relationship between novel ODD and brain injury indices. The current investigation attempts to address these limitations and current knowledge gaps in the field. Therefore, we endeavored to extend the follow up of our existing cohort from 6-months post-injury to 12-months post-injury as well as replicate findings from earlier studies with respect to the pre-injury psychosocial variable relationship with novel ODD in a larger sample of consecutively treated injured children. In addition, we planned to study the relationship of novel ODD to injury severity.

Consistent with a biopsychosocial model of risk for novel psychiatric disorders {8}, the following hypotheses were tested: 1) Novel ODD will be significantly related to pre-injury distal psychosocial variables (SES, psychosocial adversity, family function) and a pre-injury proximal psychosocial variable (adaptive function). 2) Novel ODD will be significantly related to severity of TBI (lowest post-resuscitation GCS score). 3) Given the dearth of prospective longitudinal psychiatric studies of pediatric TBI, we designed exploratory analyses focusing on the relationship of novel ODD with demographic variables (age, sex, race), other psychosocial variables (family psychiatric history, pre-injury ADHD, pre-injury lifetime psychiatric disorder, comorbid novel anxiety disorder and novel depressive disorder, and other injury variables (frontal lobe white matter/network lesions, baseline post-injury processing speed).

Methods

Recruitment:

There were 177 participants recruited between the ages of 5 and 14 who suffered a TBI between 1998 and 2003 and were identified from admissions to three academic medical centers in Texas (Baylor College of Medicine, Houston; University of Texas, Houston; University of Texas, Dallas); Rady Children's Hospital in San Diego, California; and The Hospital for Sick Children in Toronto, Canada. Children with mild-to-severe TBI were recruited at all hospitals except San Diego, where only complicated mild-to-severe TBI patients were included in the study. Children with pre-existing autistic disorder or schizophrenia, intellectual deficiency, and injury due to child abuse or penetrating-missile injury were excluded from the study. In San Diego only, children were excluded if they had pre-existing ADHD. Parents/guardians of children were not required to answer eligibility questions before deciding to participate in the study; therefore, data regarding the number of children approached, the proportion eligible for recruitment, and participation rate of those who were eligible for recruitment are missing. As required by the Institutional Review Boards, all children signed assent or consent forms to participate in the study, and their legal guardians provided informed consent. Table 1 shows demographic information, pre-injury psychosocial variables and injury indices for these participants studied at the 12-month follow-up point.

Measures

PSYCHOSOCIAL ASSESSMENTS

Psychiatric Outcome (Novel ODD) and Psychiatric Mediating Diagnoses: DSM-IV {9} psychiatric diagnoses including our outcome psychiatric measure of novel ODD, several potential pre-injury psychiatric predictor variables (pre-injury ADHD, pre-injury lifetime psychiatric disorder), and concurrent novel psychiatric disorder mediator variables (novel anxiety disorder, novel depressive disorder) were made using the *Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (K-SADS-PL)* {18} and the *Neuropsychiatric Rating Schedule (NPRS)* {19}. Baseline measurements (soon after injury) recorded pre-injury diagnoses, and assessments were repeated at 6 months and 12 months post-injury to record any diagnoses that were not present before injury but were present in the 6-12-month post-injury interval. The K-SADS-PL is a semi-structured, integrated parent/child interview developed to make diagnoses in both children and adolescents using DSM-IV criteria {9}. While the NPRS is structured similarly to the K-SADS-PL, it is more specific in that it assesses for personality change due to TBI. All interviewers were Master's- and Ph.D.- level clinicians trained by the last author in a pre-study workshop and a mid-study workshop. A child psychiatrist supervised the assessments at four sites, and a child psychologist oversaw one site. In addition to this supervision, the last author reviewed written summaries compiled by the interviewer and also held monthly teleconferences with the interviewers to discuss the cases. The central questions of the study involved present and lifetime symptoms and timing of the onset of these symptoms in relation to the TBI. Novel ODD in the 6-12-month post-injury interval was recorded if the child had no pre-injury disorder but later developed ODD after the

injury. Novel ODD also could occur when a child developed the disorder but had a different pre-injury psychiatric disorder such as generalized anxiety disorder or ADHD.

Socioeconomic Status: The *Four-Factor Index* was used to measure SES {20}. Classification is based on a formula that accounts for both maternal and paternal educational and occupational levels. The scores range from 8 to 66, with a higher score representing a higher SES.

Family Function: The *Family Assessment Device General Functioning Scale (FAD)* assesses global family functioning {21}. The scale consists of 12 questions, each on a 4-point scale, with lower scores representing healthier family functioning. The child's primary caretaker completed this scale. Pre-injury family function was rated at the baseline assessment. Scores in families of nonclinical, psychiatric, and medical probands were 1.89 (.43), 2.27 (.51), and 1.89 (.45) respectively.{22}

Psychosocial Adversity: The *Psychosocial Adversity Measure* used was similar to that used in a pioneering pediatric TBI study {2}. Six areas of adversity were assessed: (1) child not living with biological or adoptive parents, (2) sibship of at least four children or a person: room ratio exceeding 1, (3) family difficulties leading to admission of the child into local authority care, (4) maternal "malaise inventory" score of 7 or more, (5) paternal criminality, and (6) father or mother with an unskilled or semiskilled job. A score of 1 indicated adversity and a score of 0 indicated no adversity in each area.

Family Psychiatric History: The *Family History Research Diagnostic Criteria* interview was conducted by trained research assistants at the baseline assessment {23, 24}. At least one parent for each child answered questions that were aimed at documenting the presence and severity of psychiatric disorders in the child's first-degree relatives. Scores range from 0 to 3 with increasing severity {5}.

Adaptive Function: The *Vineland Adaptive Behavior Scales* were used to measure adaptive functioning at baseline assessment after the injury {25}. This assessment is a structured interview done with the child's primary caretaker. It accounts for the kinds of behaviors a child displays in his or her environment and then provides an overall adaptive-behavior composite score (mean +/− standard deviation is 100 +/− 15).

NEUROLOGICAL ASSESSMENTS—The *Glasgow Coma Scale* (GCS), which is the standard measure of severity of acute brain injury associated with closed head trauma, was used to assess the severity of the children's brain injuries {16}. The GCS has three different classifications with their respective score ranges: severe (3-8), moderate (9-12), and mild (13-15).

MRIs (1.5T) were completed in the vast majority of subjects about 3 months post-injury. The procedure included a T1 volumetric spoiled gradient-recalled echo (1.5 mm slices) and fluid-attenuated-inversion recovery sequences (3 mm slices) obtained in coronal and sagittal planes per research protocol guidelines. A neuroradiologist coded the different lesions from a list of brain structures using the multiple-slice, hard-copy films at each site.

The anatomical locations included white matter, cortical gray matter (frontal, temporal, parietal, occipital), and subcortical gray matter (thalamus, basal ganglia) {12}. Images were not registered, tissues types were not segmented, nor were volumetric analyses performed.

NEUROPSYCHOLOGICAL ASSESSMENT—The *Wechsler Intelligence Scale for Children (3rd Edition)* Coding and Symbol Search subtests were performed to measure processing speed {26}. In the Coding subtest, children are requested to transcribe the correct geometric designs below numbers guided by a key. The number of symbols transcribed correctly in 2 minutes was recorded. The Symbol Search subtest required the participant, when presented with target stimuli, to check a "yes" or "no" box as quickly as possible to specify whether or not the target or targets appeared among the presented stimuli (n=45 total trials). The Symbol Search score was the number of correct responses minus the number of errors completed in 120 seconds. A scaled Processing Speed score was obtained and averaged for both subtests.

Statistical Analyses

To assess the representativeness of the cohort that participated versus that did not participate in the 12-month assessment, independent sample t-tests and χ^2 analyses or Fisher's Exact tests were performed depending on whether the variables of interest were continuous or categorical variables respectively. To test the associations of 12-month novel ODD with the hypothesized continuous and categorical variables, logistic regression univariable analyses were conducted. To determine the relative importance of variables associated with novel ODD, a stepwise logistic regression analysis was conducted with novel ODD as the dependent variable. The independent baseline predictors were included in the model using backwards model selection with a $p < 0.15$ inclusion criterion using the likelihood ratio test. Statistical significance was considered at level $\alpha = 0.05$. All tests were two-sided. All analyses were conducted in SPSS.

Results

Occurrence

Of the original 177 children, 11 were excluded from the analyses because their pre-injury ODD (n=7 including 3 resolved), CD (n=2), and DBD NOS (n=2) precluded them from developing a novel ODD/CD/DBD NOS diagnosis. Additionally, one child suffered a second TBI between the 6- and 12-month assessments, and thus was excluded from the analyses. One hundred twenty of the remaining 165 children (72.7%) returned for the 12-month psychiatric assessment. However, termination of the funding cycle resulted in 9 children who did not return; therefore, the effective participation was 120/156 (76.9%). Female participants were more likely to participate at the 12-month follow-up relative to male participants (41/48 [85%] vs 79/117 [68%], Fisher's Exact test p-value = 0.021). Participation was significantly related to race (Fisher's Exact test p-value = .028), and inspection of the data suggested higher attrition among African-Americans (14/30; 47%). Those lost to follow up had significantly lower baseline post-injury processing speed standard score (91.8 +/− 20.3; n=36 versus 100.1 +/− 18.5; n=102; t=−2.2; df=136; p=.027). Participation was not significantly related to age of injury, injury severity (lowest post-

resuscitation GCS score), SES, psychosocial adversity, family function, pre-injury lifetime psychiatric disorder, pre-injury ADHD, pre-injury depressive disorder, pre-injury anxiety disorder, or pre-injury adaptive function (p>.05). Of the 120 children who returned for the 12-month assessment, 7 (5.8%) developed novel ODD/CD/DBD NOS. The specific novel psychiatric disorder in these children included ODD (n =7), CD (n=0), and DBD NOS (n=0). Therefore, we shall refer to the outcome of interest as novel ODD. Six of the 7 cases of novel ODD documented in this 6-12-month post-injury interval also had novel ODD in the first 6 months post injury. The seventh case of novel ODD developed de novo during the second 6 months post injury. The following analyses are limited to the seven patients who had novel ODD during the 6-12 months post-injury interval. Of the 11 cases of novel ODD documented in the first 6-month post-injury interval, 9 participated in the 12-month assessment. Three of those 9 cases (33%) evidenced resolution of their novel ODD.

Psychosocial and Biological Correlates of Novel ODD

Table 2 shows the relationship of psychosocial variables and novel ODD. Logistic regression univariable analyses demonstrated that SES (OR=0.871; 95%CI [0.795, 0.953]; p<.0005), pre-injury adaptive function (OR=0.929; 95%CI [0.867, 0.996]; p=.025), and psychosocial adversity score (OR=2.367; 95%CI [1.217, 4.604]; p=.011) were significantly associated with novel ODD. Furthermore, the logistic regression univariable analysis examining the relationship of pre-injury family function to novel ODD had a p-value under the predetermined threshold for additional multivariable analyses (OR=1.104; 95%CI [0.977, 1.246]; p=.131).

Table 2 also shows the relationship of injury severity and novel ODD. The logistic regression univariable analysis examining the relationship of the lowest post-resuscitation GCS score and novel ODD had a p-value under the predetermined threshold for additional multivariable analyses (OR=0.869; 95%CI [0.724, 1.044]; p=.127).

As planned, a backwards stepwise likelihood ratio logistic regression analysis was conducted with novel ODD as the dependent variable, and the independent variables consisted of the baseline measures that were associated with novel ODD at the p<.15 level in univariable analyses (SES, pre-injury adaptive functioning, psychosocial adversity score, pre-injury family function, and lowest post-resuscitation GCS score) to determine which of these variables were independently related to developing novel ODD. The regression produced a significant final model (χ^2=11.055; *df*=1; *p*=.001) which included only lower SES (Wald χ^2=6.285; *df*=1; *p*=.012) (OR=0.845; 95%CI [0.741, 0.964]; *p*=.001). This result suggests that of the array of significant individual pre-injury and injury biopsychosocial predictors, SES is the most important variable predictive of novel ODD outcome at 12 months.

Exploratory Analyses

Table 3 provides the planned exploratory analyses related to novel ODD. Novel ODD was not significantly related to demographic variables (age, sex, race), family psychiatric history, pre-injury lifetime psychiatric disorder, pre-injury ADHD, novel anxiety disorder, novel

depressive disorder, presence of a frontal lobe white matter lesion, and baseline post-injury processing score (all p-values > .05).

Post-injury Outcome for Children with Pre-injury ODD/CD/DBD NOS

Since the effect of TBI on children with pre-existing ODD/CD/DBD NOS is of interest to clinicians and researchers, these data are provided. Two of the 4 children with unresolved pre-injury ODD continued to manifest ODD, and a third progressed to CD by 12 months. The fourth child with unresolved pre-injury ODD did not return for the 12-month assessment. None of the 3 children with resolved pre-injury ODD returned for assessment at 12 months. Two children had pre-injury CD, one of whose CD resolved while the other did not return for assessment. Similarly, two children had pre-injury DBD NOS, one of whose disorder resolved following TBI and the other did not return for assessment.

Discussion

The main finding of this prospective study of pediatric TBI is that clinically significant novel ODD present in the 6-12-month post-injury interval has significant pre-injury psychosocial predictors that 1) coincide generally with, and 2) expand results of the scarce related existing studies. Specifically, novel ODD was present in 6% of children who were ages 5-14 years when they were injured and was significantly associated with pre-injury psychosocial risk factors (lower SES, higher psychosocial adversity, lower adaptive function). There was no significant association of novel ODD with injury severity.

The rate of novel ODD was similar to that documented at the 1-year follow up of a consecutively-treated rehabilitation center cohort (6% versus 9%). This similarity is noteworthy especially because of study design differences. The respective differences between the current study and the rehabilitation center study include 1) consecutively hospitalized children for TBI compared with children consecutively treated at a rehabilitation facility; 2) TBI severity ranging from mild to severe compared with severe only; and 3) novel ODD diagnoses made using- compared with not-using impairment criteria. An important divergent finding between studies was the 0% versus 8% rate of novel conduct disorder in the present- versus rehabilitation-sample study respectively. We suspect this divergence is related to methodological differences in the application of impairment criteria.

The significant relationship of novel ODD with pre-injury psychosocial variables (hypothesis 1) extends the timeline of this association from the first 6-months post-injury to 12-months post-injury in the current cohort. Our 12-month follow up findings were that, in univariable analyses, novel ODD was significantly predicted by distal pre-injury psychosocial variables (lower pre-injury SES, higher pre-injury psychosocial adversity), and a proximal pre-injury psychosocial variable (lower pre-injury adaptive function). These results are similar to our 6-month follow up findings except for the earlier finding of a significant relationship of novel ODD and pre-injury family function, whereas the relationship with pre-injury adaptive function was just short of significance. At both 6-month and 12-month assessment points, the only independently significant pre-injury psychosocial predictor of novel ODD in multivariable analyses was lower SES {10}.

The current predictive variable findings replicate the few previous related studies. Novel ODD in a rehabilitation study was significantly related to psychosocial adversity in univariable analyses, but only pre-injury history of special education was associated in multivariable analyses {4}. Our earlier study of consecutively hospitalized children with mild to severe TBI examining ODD symptoms post-injury rather than novel ODD found that total ODD symptoms 12-months post-injury were significantly related to pre-injury family function, SES, and pre-injury ODD symptom count in a regression analysis with model R^2 increasing from .23 to .32 to .49 with addition of each significant predictor {11}. A closer comparison of our earlier study with the current study was the examination of change in ODD symptom count from pre-injury to 12-months post-injury which was significantly associated with only SES in a regression analysis with model R^2 = .36 {11}.

To our knowledge, the significant association of novel ODD and pre-injury adaptive function, a proximal pre-injury psychosocial predictor, has previously not been detected. This adaptive functional domain may be considered as a measure of behavioral “reserve” not unlike the construct of “cognitive reserve” {13, 27}. Thus, we offer the operative principle that in the face of a given level of brain insult, behavioral reserve measured as higher pre-injury adaptive function serves as a buffer or protective factor in terms of transcending the level of impairment threshold for the categorical diagnosis of novel ODD. This principle may encompass protective behavioral trajectories that reach beyond prevention of the development of novel ODD. Other empirically testable trajectories could include a scenario in which children with greater pre-injury learned socialization, communication, and daily living skills recover more readily, resulting in improved behavior, modulation of affect, and aggression following TBI. It is also conceivable that pre-injury adaptive function may not be directly involved from a mechanistic point of view but rather may be a marker for the ability to relearn inhibitory control of aggression or irritability and regulation of mood. The delayed emergence of significance for pre-injury adaptive function in the 6–12-month post-injury interval rather than the injury-6-month post-injury interval suggests that over time, behavioral reserve may become a more cogent variable determining novel ODD outcome. This behavioral reserve concept is not unique to novel ODD, as pre-injury adaptive function has been found to significantly predict other novel disorders including personality change due to TBI and novel ADHD at various post-injury intervals {13, 14}.

Hypothesis 2, that novel ODD would be significantly associated with severity of TBI measured by the lowest post-resuscitation GCS score, was not supported. This is generally consistent with previous studies, the findings of which are characterized by significant pre-injury psychosocial predictive variables {4, 11}, but inconsistent with others {17}. It is likely that the current study had insufficient power to detect a significant difference. This is suggested by the observation of a moderate effect size (Cohen’ d = 0.52) with regard to the comparison of lowest post-resuscitation GCS scores between children with and without novel ODD. Exploratory analyses of post-injury baseline processing score, which is reflective of injury severity {10, 28}, was also not significant. However, limited power was also likely responsible for this result since there was a comparable moderate effect size (Cohen’s d = 0.53). Furthermore, the fact that the children lost to attrition had significantly lower baseline post-injury processing speed scores suggested that this injury

severity-related variable should not be ruled out as a potential predictor of novel ODD in adequately powered studies.

Other exploratory analyses did not show any significant association between novel ODD and age, sex, race, family psychiatric history, pre-injury lifetime psychiatric disorder, pre-injury ADHD, and presence of a frontal lobe white matter lesion. While we did not find a significant association of novel ODD with novel depressive disorder and novel anxiety disorder, we have previously shown significant comorbidity of novel ODD with personality change due to TBI and also with novel ADHD in the 6–12 month post-injury interval with the current cohort {13, 14}.

The findings of this study must be viewed within its limitations. First, we did not include a non-brain related injury control group to compare to the TBI group. Establishing causality between TBI in children and developing ODD is difficult without a control group. Second, interrater reliability for psychiatric diagnoses was not directly tested within and across testing sites. However, the outlined specific quality control and training procedures diminished this issue. Third, neuroimaging analyses were rudimentary and did not include volumetric or tissue-segmentation measures. Fourth, sample attrition was approximately 27% due to attrition of a 12-month follow-up. Attrition was significantly related to sex and race (more males and African Americans were lost to follow up), and non-participants had lower post-injury processing speed performance. However, the participants and non-participants were no different on multiple variables such as age, SES, pre-injury psychosocial adversity, pre-injury adaptive function, pre-injury family function, pre-injury psychiatric status, and injury severity. Fifth, DSM-IV diagnostic criteria, the version that was current at the time of this study, were used to define each diagnosis. However, the classification of ODD, including meeting at least four of eight criteria to qualify for ODD, remained the same between the DSM-IV and DSM-5 aside from minor semantic differences {29}. Sixth, the natural history of post-injury treatment-seeking by the families of participants may be variable and could influence outcome. Finally, this study is limited to only measuring the impact of TBI at one time point, 12-months post-injury, as opposed to multiple time points as some other studies have done.

This study also had several notable strengths. Importantly, to our knowledge, this is the largest prospective pediatric TBI study to use a clinician-administered semi-structured psychiatric assessment on a consecutively admitted non-referred population assessing outcomes considered to be clinically significant. The extensive range of measures included interview assessments of psychopathology, adaptive function, and family psychiatric history, in addition to rating scales measuring injury and other psychosocial risk factors for new-onset psychopathology. Additionally, lesion analysis was based on readings by expert neuroradiologists, despite lesion correlates being a negative finding. Finally, the results from this study are generalizable to a wide pediatric TBI population due to examining a spectrum of mild to severe TBI.

In conclusion, the post-injury sequela of clinically-significant novel ODD occurred in a small (6%) but important proportion of children who were consecutively admitted for mild to severe TBI. A proportion of cases of novel ODD (3/9; 33%) resolved after the

6-month post-injury mark and de novo novel ODD after the 6-month mark occurred but was rare. These findings suggest that clinicians can offer reassurance to some degree regarding resolution of novel ODD but should also be vigilant for delayed onset of novel ODD after 6-months post-injury, and perhaps follow more closely at regular intervals to intervene as indicated. Earlier data have established an association of novel ODD with both novel ADHD and personality change due to TBI. Therefore, to facilitate comprehensive treatment, clinicians should be on high alert for all three of these novel disorders when one of the disorders is more readily apparent. Novel ODD was significantly associated with pre-injury distal psychosocial risk factors (lower SES, higher psychosocial adversity) and with a pre-injury proximal psychosocial risk factor (lower adaptive function). Although the biological risk factor, severity of injury, was not significantly related to novel ODD, it should not be ruled out because of the present study's insufficient power. Finally, an important implication of our biopsychosocial risk factor findings is that children who are at higher risk for developing novel ODD may be identified soon after injury and monitored for the purposes of decreasing this specific complication with timely interventions.

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29. DSM-IV to DSM-5 Oppositional Defiant Disorder Comparison. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016. p. Table 18.

Table 1.

Demographic, Psychosocial, And Injury Variables Among Children Assessed 12-Months After Traumatic Brain Injury Cohort (n=120)

Demographic Variables		
Age at Injury (mean years +/− SD)	9.99	2.78
Gender: male, N (%)	79	65.8%
Socioeconomic Status (mean +/− SD)	37.23	12.65
Psychosocial Variables		
Pre-injury Lifetime Psychiatric Disorders, N (%)	28	23.3%
Pre-injury Vineland Adaptive Behavior Composite Score (mean +/− SD)	95.78	14.26
Pre-Injury Family Assessment Device Score (mean +/− SD) *	1.62	0.50
Injury Variables		
Glasgow Coma Scale Score (Lowest Post-resuscitation) (mean +/− SD)	10.93	4.14
Glasgow Coma Scale Score, N (%)		
3-8	44	36.7%
9-12	15	12.5%
13-15	61	50.8%

SD = standard deviation;

* See methods section for average scores in reference populations.

Table 2.

Results of Logistic Univariable Regression Analyses of Psychosocial and Biological Correlates of Novel ODD

	Novel ODD (N=7)			No Novel ODD (N=113)			OR	95% CI	p
Socioeconomic Status (mean +/− SD)	20.50	11.24		38.28	12.02	n=111	0.871	(0.795, 0.953)	<0.0005
Pre-injury Family Functioning (mean +/− SD)	1.98	0.43	n = 5	1.61	0.50	n=105	1.104	(0.977, 1.246)	.131
Pre-injury Psychosocial Adversity score (mean +/− SD)	1.86	1.35		0.75	.95	n=110	2.367	(1.217, 4.604)	.011
Pre-injury Adaptive Functioning	83.67	10.73	n=6	96.46	14.17	n=107	.929	(0.867, 0.996)	.025
Glasgow Coma Scale score	8.57	5.53		11.08	4.02		0.869	(0.724, 1.044)	.127

The values are expressed for children with novel ODD (n=7) and for children with no novel ODD (n=113) unless otherwise indicated due to missing data.

Table 3.

Exploratory Logistic Univariable Regression Analyses of Relationship of Demographic, Family Psychiatric History, Psychiatric Diagnoses, and Injury Variables with Novel ODD

	Novel ODD (N=7)			No Novel ODD (N=113)			OR	95% CI	p
Age at Injury (SD)	9.69	2.64		10.01	2.81		0.959	(0.727, 1.265)	NS
Sex (male), N (%)	5	71%		74	66%		0.759	(0.141, 4.093)	NS
Race									.086
White, N (%)	2	29%		66	58%		1		
Hispanic, N (%)	4	57%		23	20%		5.739	(0.985, 33.441)	.052
Black, N (%)	0	0%		16	14%		-	-	NS
Asian, N (%)	1	14%		3	3%		11.000	(0.766, 158.008)	.078
Other, N (%)	0	0%		5	4%		-	-	NS
Family Psychiatric History	1.50	1.22	n=6	1.11	1.06	n=92	1.395	(0.653, 2.979)	NS
Pre-injury Lifetime Psychiatric Disorder	1	14%	27	24%			1.884	(0.217, 16.346)	NS
Pre-injury ADHD, N (%)	1	14%		17	15%		1.062	(0.120, 9.389)	NS
Novel Anxiety Disorder, N (%)	1	14%		11	10%		0.647	(0.071, 5.878)	NS
Novel Depressive Disorder, N (%)	1	14%		6	5%	N=111	2.917	(0.301, 28.267)	NS
Injury Variables									
Frontal White Matter Lesion, N (%)	0	0%		21	20%	n=106	-	(0.000, -)	0.084
Baseline Processing Speed standard score (mean +/− SD)	91.00	17.22	n=5	100.53	18.54	n=97	.971	(0.923, 1.022)	NS