Traumatic Brain Injury in Early Childhood and Risk of Attention-Deficit/Hyperactivity Disorder and Autism Spectrum Disorder:

A Nationwide Longitudinal Study

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ABSTRACT

Objective: Early childhood (< 3 years of age) is a critical period for neurodevelopment. This study investigated the correlation between early childhood traumatic brain injury (TBI) and subsequent risk of attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and developmental delay (DD) by analyzing a national-scale cohort.

Methods: Data from the National Health Insurance Research Database, which comprises health care information from > 99% of the Taiwanese population, were analyzed. Children with TBI in their early childhood were enrolled from 1998–2008, and the incidence of subsequent ADHD, ASD, or DD (according to *ICD-9* criteria) was assessed and compared with controls without TBI. Patients' age, number of TBI events, and TBI severity were investigated for the risk of ADHD, ASD, or DD.

Results: A total of 7,801 and 31,204 children were enrolled in the TBI and control cohorts, respectively. The TBI cohort exhibited a higher incidence of subsequent ADHD, ASD, or DD than the controls (all $P < .001$). Diagnoses of ADHD, ASD, or DD in the TBI cohort were made at a younger age compared with the controls. Cox regression demonstrated the highest hazard ratios (HRs) of ADHD, ASD, or DD with repeated TBI events, severe TBI, and TBI events before 1 year of age, with the exception that the HR of ASD did not significantly increase after repeated TBI ($P = .335$). In addition, cumulative HRs (> 10 years) of ADHD, ASD, or DD were increased after TBI (all $P < .001$).

Conclusions: Data from this study suggest that the incidence of ADHD, ASD, and DD significantly increased after TBI events in early childhood (< 3 years of age). The risk factors include severe TBI, repeated TBI events, and TBI at a younger age. The long-term follow-up demonstrated an increased cumulative risk of ADHD, ASD, and DD after TBI.

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Worldwide, head injury is one of the most common pediatric traumas requiring medical assistance. The annual incidence of pediatric traumatic brain injury (TBI) was estimated from 70 to 75 cases per 100,000 persons. A total of 475,000 children aged 0–14 years could be involved in TBI accidents annually in the United States.[1,2] Although pediatric TBI often results in less severe injury compared with that in adults,[1,3,4] the impact and consequence of neurologic injury in children can be enormous and long-lasting. The acute stage of TBI and the long-term sequelae are substantial concerns for public health because the consequences may manifest many years after the event. TBI is recognized as a major cause for long-term disability as well as cognitive deficit and neurodevelopment for children.[5,6]

Investigating the correlation between TBI and neuropsychiatric disorders has been a popular topic. Among the neuropsychiatric disorders, the associations of TBI with behavior disturbance and neurocognitive problems in children have been widely studied. TBI can result in memory, attention, learning, and developmental deficit in children, and these children are more likely to exhibit psychosocial delay.[7–9] In a meta-analysis, a significant association was found between mild TBI and attention-deficit/hyperactivity disorder (ADHD).[10] The sequence of TBI and ADHD and which one of them is responsible for the other remain unclear. Theoretically, attention deficit increases the risk of accidents and accompanying injury.[11] However, previous studies have proposed that a higher incidence of ADHD can result from TBI.[12,13]

ADHD is a neurodevelopmental disorder with an early childhood onset, and it can usually be diagnosed at the preschool age of 3–6 years.[14,15] Previous studies have demonstrated an increased risk of ADHD after TBI; however, they have focused on school-age children and adolescents.[8,9,12,13,16] Studies investigating TBI at a very early age and its influence on subsequent neurodevelopmental disorders are lacking.

Autism spectrum disorder (ASD) is another common neurodevelopmental disorder that is frequently diagnosed at the age of approximately 3–6

Clinical Points

- Early childhood (< 3 years of age) is a critical time for neurodevelopment. The correlations between early childhood TBI and subsequent risk of ADHD, ASD, and DD are unclear.
- The incidences of ADHD, ASD, and DD are significantly higher following TBI. The risks are highest among children with repeated TBI, severe TBI, and TBI before 1 year of age.

years.[17,18] The prevalence is approximately 1 in 88 children aged 8 years.[19] The diagnostic criteria of ASD for children aged ≥ 3 years are established in the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition. The etiology of ASD is multifactorial; however, accumulating evidence has demonstrated that the developmental disruption can occur as early as the first 3 years of life.[18] For the past few decades, a few reports have investigated the association between ASD and the dysfunction and injury of the frontal lobe, brain stem, and cerebellum.[20–22] However, no large epidemiologic study on the incidence of ASD following TBI is available.

The adverse consequences of pediatric TBI in cognitive, behavioral, and developmental outcomes are profound and warrant a more detailed investigation. Therefore, the current study assessed the correlation between early childhood TBI (< 3 years of age) and subsequent ADHD, ASD, and developmental delay (DD) in Taiwan using a large-scale national cohort. According to our review of relevant studies, this is the first study to investigate the risk of ASD following TBI. Moreover, multiple factors in relation to TBI and the risk of ADHD, ASD, or DD were analyzed.

METHODS

Data Source

Taiwan's National Health Insurance, a mandatory universal health insurance program, was implemented in 1995 and offers comprehensive medical care coverage to all Taiwanese residents. The National Health Research Institutes (NHRI) manages the insurance claims database, namely, the National Health Insurance Research Database (NHIRD), which consists of health care data from > 99% of the Taiwan population. The NHRI audits and releases the NHIRD for scientific study purposes. Individual medical records included in the NHIRD are anonymously maintained to protect patient privacy. Comprehensive information on insured individuals is included in the database, such as demographic data, clinical visit dates, disease diagnoses, and medical interventions. *The International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes are used for disease diagnosis. The NHIRD has been used extensively in many epidemiologic studies in Taiwan.[23–26]

Inclusion Criteria for Infants, Toddlers, and Children With TBI and the Control Group

The present study was conducted after approval from the Institutional Review Board of Taipei Veterans General Hospital, Taiwan. Infants, toddlers, and children aged < 3 years who had a diagnosis of TBI given by board-certified pediatricians, surgeons, internal medicine physicians, and emergency medicine physicians based on their clinical judgment or brain imaging assessment between January 1, 1998, and December 31, 2008, and who had no history of ADHD (*ICD-9-CM* code 314), ASD (*ICD-9-CM* code 299), or DD (*ICD-9-CM* code 315) before enrollment were included as the TBI cohort. The time of TBI diagnosis was defined as the time of enrollment. The age-, sex-, and time of enrollment–matched (1:4) control cohort was randomly identified after eliminating the study cases, individuals who had been given a diagnosis of TBI at any time, and individuals with ADHD, ASD, or DD before enrollment. ADHD, ASD, and DD were identified by board-certified psychiatrists based on their clinical judgment and diagnostic interview during the follow-up (from enrollment to December 31, 2011, or death). Comorbid perinatal conditions, including preterm birth or low birth weight, infections in the perinatal period, maternal causes of perinatal morbidity, birth trauma, and intrauterine hypoxia/birth asphyxia, were assessed as the confounding factors in our study. Level of urbanization (levels 1–5: level 1 = most urbanized region, level 5 = least urbanized region) was also assessed for our study.[27]

Statistical Analysis

For between-group comparisons, the *F* test was used for continuous variables and Pearson χ^2 test for nominal variables, where appropriate. Cox regression models with adjustment for demographic data (age, sex, level of urbanization) and comorbid perinatal conditions were performed to examine the risk of subsequent ADHD, ASD, and DD separately among children with TBI. Subanalyses stratified by age at TBI event (< 1 year, 1 year, 2 years) and number of TBIs (1 time, ≥ 2 times) were also performed to investigate the age effect of TBI and repeated TBI with the risk of developing ADHD, ASD, and DD. A 2-tailed *P* value of less than .05 was considered statistically significant. In addition, we also assessed the severity of TBI with the risk of subsequent ADHD, ASD, and DD. TBI severity was defined as follows: severe—receiving neurosurgical operation for TBI (craniotomy and craniectomy), moderate—being admitted due to TBI after brain imaging assessment, and mild—neither receiving operation nor being admitted due to TBI. All data processing and statistical analyses were performed with Statistical Package for the Social Sciences (SPSS) version 17 software (SPSS Inc, Chicago, Illinois) and Statistical Analysis Software (SAS) version 9.1 (SAS Institute, Cary, North Carolina).

RESULTS

Demographic data are summarized in Table 1. A total of 7,801 and 31,204 children aged < 3 years were enrolled in the TBI and control cohorts, respectively. The TBI event occurred, on average, at the age of 1.55 years. The majority of the TBI events were mild (93.8%), whereas moderate

Table 1. Demographic Data and Incidence of ADHD, ASD, and DD Among Children With TBI and Controls

	Children With TBI (n = 7,801)	Controls (n = 31,204)	*P* Value
Age at enrollment, mean (SD), y	1.55 (0.79)	1.55 (0.90)	.750
Sex, n (%)			1.000
Male	4,552 (58.4)	18,208 (58.4)	
Female	3,249 (41.6)	12,996 (41.6)	
Severity of TBI, n (%)			
Mild	7,317 (93.8)		
Moderate	444 (5.7)		
Severe	40 (0.5)		
Incidence			
ADHD, n (%)	480 (6.2)	1,239 (4.0)	< .001
Age at ADHD diagnosis, mean (SD), y	6.76 (2.37)	7.32 (2.14)	< .001
ASD, n (%)	64 (0.8)	125 (0.4)	< .001
Age at ASD diagnosis, mean (SD), y	5.36 (2.35)	6.45 (2.65)	.004
DD, n (%)	228 (2.9)	356 (1.1)	< .001
Age at DD diagnosis, mean (SD), y	4.38 (2.18)	5.38 (1.85)	< .001
Comorbid perinatal conditions, n (%)			
Preterm or low birth weight	202 (2.6)	749 (2.4)	.345
Infections in the perinatal period	508 (6.5)	1,605 (5.1)	< .001
Maternal causes of perinatal morbidity	85 (1.1)	256 (0.8)	.023
Birth trauma	49 (0.6)	92 (0.3)	< .001
Intrauterine hypoxia/birth asphyxia	30 (0.4)	102 (0.3)	.449
Level of urbanization, n (%)			.022
1 (most urbanized)	2,083 (26.7)	8,798 (28.2)	
2	2,475 (31.7)	9,599 (30.8)	
3	1,386 (17.8)	5,690 (18.2)	
4	1,141 (1.46)	4,278 (13.7)	
5 (most rural)	716 (9.2)	2839 (9.1)	

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, ASD = autism spectrum disorder, DD = developmental delay, SD = standard deviation, TBI = traumatic brain injury.

and severe TBI accounted for 6.2% of the events. The incidence of subsequent ADHD diagnosis was 6.2% in the TBI cohort, which is significantly higher than that in the control group (4.0%, $P < .001$). The mean ± SD age at ADHD diagnosis was 6.76 ± 2.37 years, which is younger than that of the control group (7.32 ± 2.14 years, $P < .001$). Similar trends were observed for ASD and DD. The incidence of ASD and DD following a TBI event (at an age of < 3 years) was higher than in the control group (0.8% vs 0.4% for ASD; 2.9% vs 1.1% for DD; both $P < .001$). The diagnoses of ASD and DD in the TBI cohort were made at a younger age compared with the controls (5.36 ± 2.35 vs 6.45 ± 2.65 years for ASD, $P = .004$; 4.38 ± 2.18 vs 5.38 ± 1.85 years for DD, $P < .001$).

After adjustment for demographic data and perinatal conditions, Cox regression analysis demonstrated that the risk of subsequent ADHD, ASD, or DD was significantly higher among children in the TBI cohort (Table 2). In terms of TBI severity, the more severe the TBI event was, the higher the hazard ratios (HRs) of ADHD, ASD, or DD are. The risks of ADHD and DD were the highest among children with severe TBI (adjusted HR = 2.75 and 9.79, respectively).

The risks of subsequent ADHD, ASD, or DD were also analyzed by stratifying the time of TBI (Table 3). The time of TBI is determined as the patient's age when the TBI occurred. Patients' age was divided into 3 intervals: < 1 year, 1 year, and 2 years. Patients who experienced TBI aged < 1 year exhibited a higher risk of subsequent ADHD, ASD, or DD than older patients. In general, when a patient experiences TBI at a younger age, the adjusted HR of subsequent ADHD, ASD, or DD is significantly higher.

Repeated TBI also resulted in a higher risk of ADHD and DD (Table 4). The adjusted HR of ADHD after repeated TBI (≥ 2 events) was 1.84 (95% confidence interval [CI], 1.58–2.14). The adjusted HR of DD after repeated TBI was 3.03 (95% CI, 2.40–3.81). The adjusted HR of ASD did not increase after repeated TBI events. Nevertheless, TBI still increased the risk of subsequent ASD irrespective of the number of events.

After a long-term follow-up (> 10 years) in this large cohort, the cumulative risks of ADHD, ASD, and DD among children with preexisting TBI differed substantially from those of the controls without TBI. Figure 1 presents the significant cumulative risks of subsequent ADHD, ASD, or DD after TBI compared with the control group after the long-term follow-up (all $P < .001$).

In addition, we also found that preterm birth or low birth weight was associated with an elevated risk of subsequent ADHD (adjusted HR = 1.35, 95% CI, 1.04–1.75) and DD (adjusted HR = 1.84, 95% CI, 1.24–2.74) (Table 2).

Table 2. Cox Regression Analysis of the Risk of ADHD, ASD, and DD Among Children With TBI vs Controls[a]

	ADHD, HR (95% CI)	ASD, HR (95% CI)	DD, HR (95% CI)
TBI (presence vs absence)	**1.59 (1.43–1.76)**	**2.06 (1.52–2.78)**	**2.61 (2.21–3.09)**
Mild	**1.54 (1.38–1.71)**	**2.03 (1.49–2.76)**	**2.52 (2.12–2.99)**
Moderate	**2.27 (1.66–3.11)**	**2.81 (1.15–6.88)**	**3.44 (2.11–5.60)**
Severe	**2.75 (1.14–6.61)**	NA	**9.79 (4.04–23.69)**
Comorbid perinatal conditions (presence vs absence)			
Preterm or low birth weight	**1.35 (1.04–1.75)**	0.78 (0.28–2.15)	**1.84 (1.24–2.74)**
Infections in the perinatal period	1.10 (0.91–1.34)	1.33 (0.77–2.31)	1.08 (1.78–1.50)
Maternal causes of perinatal morbidity	1.34 (0.91–1.99)	0.52 (0.07–3.81)	1.30 (0.68–2.50)
Birth trauma	1.83 (0.39–1.75)	1.12 (0.16–8.07)	0.93 (0.30–2.90)
Intrauterine hypoxia/birth asphyxia	1.23 (0.68–2.25)	1.23 (0.17–8.95)	1.70 (0.69–4.18)

[a]Boldface type indicates statistical significance ($P < .05$).
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, ASD = autism spectrum disorder, CI = confidence interval, DD = developmental delay, HR = hazard ratio, NA = not available, TBI = traumatic brain injury.

Table 3. Cox Regression Analysis of the Risk of ADHD, ASD, and DD Among Children With TBI vs Controls, Stratified by Age[a]

	ADHD, HR (95% CI)	ASD, HR (95% CI)	DD, HR (95% CI)
TBI (presence vs absence)	**1.59 (1.43–1.76)**	**2.06 (1.52–2.78)**	**2.61 (2.21–3.09)**
Age at enrollment			
< 1 year	**1.83 (1.50–2.23)**	**2.95 (1.78–4.89)**	**2.89 (2.19–3.81)**
1 year	**1.38 (1.16–1.65)**	**1.82 (1.07–3.09)**	**2.55 (1.95–3.45)**
2 years	**1.62 (1.35–1.94)**	1.58 (0.90–2.78)	**2.49 (1.78–3.47)**

[a]Boldface type indicates statistical significance ($P < .05$).
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, ASD = autism spectrum disorder, CI = confidence interval, DD = developmental delay, HR = hazard ratio, TBI = traumatic brain injury.

Table 4. Cox Regression Analysis of the Risk of ADHD, ASD, and DD Among Children With TBI vs Controls, Stratified by Number of TBI Events[a]

	ADHD, HR (95% CI)	ASD, HR (95% CI)	DD, HR (95% CI)
Non-TBI controls	1	1	1
1 TBI	**1.45 (1.28–1.65)**	**2.26 (1.61–3.18)**	**2.39 (1.97–2.92)**
≥ 2 (repeated) TBIs	**1.84 (1.58–2.14)**	**1.70 (1.05–2.75)**	**3.03 (2.40–3.81)**

[a]Boldface type indicates statistical significance ($P < .05$).
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, ASD = autism spectrum disorder, CI = confidence interval, DD = developmental delay, HR = hazard ratio, TBI = traumatic brain injury.

DISCUSSION

Many studies have addressed the associations between social behavior disturbance, neurocognitive deficit, and TBI. ADHD is one of the most prominent research areas. A series of classic prospective and retrospective studies conducted by Max et al[13,28–30] in the 1990s established the initial impression that children are more likely to develop ADHD after TBI. Recent research supports the concept that children are at a higher risk of ADHD following TBI.[5,7–10,12,16,31,32] Early reports have focused on the association between ADHD and TBI in school-age and adolescent children. However, ADHD can currently be recognized as early as 3–5 years of age, and school-age children and adolescents with ADHD may exhibit an increased risk of TBI.[14,33–35] By the time TBI occurred, the victims may have already had a predisposition to attention and neurocognitive deficit, however, the diagnosis was not made until older age.

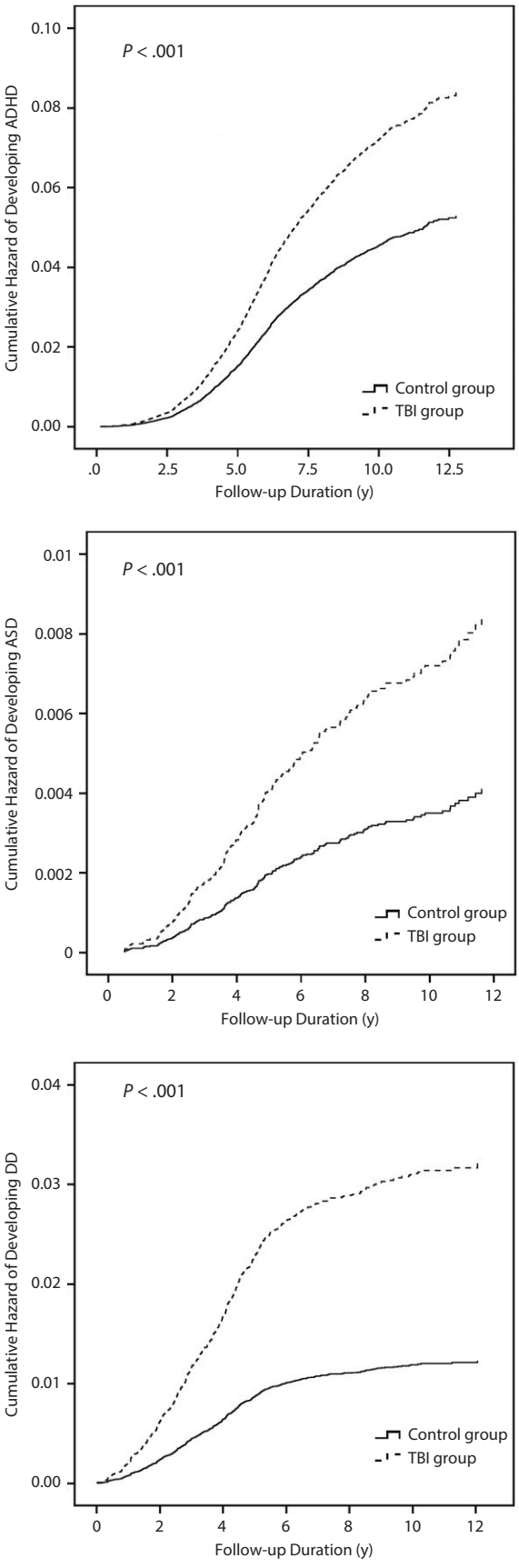
Our study enrolled children who sustained TBI in their early childhood (aged < 3 years) and assessed the subsequent risk of neurodevelopmental disorders such as ADHD, ASD, and DD. The aim of our study was the intention to clarify the sequence of TBI and diagnoses of neurodevelopmental disorders. In addition, because early childhood is a critical period for rapid neurodevelopment,[18,36,37] the investigation of TBI in early childhood and the associated subsequent neurodevelopmental disorders can be very meaningful. Our results demonstrated higher incidences of ADHD, ASD, and DD after early childhood TBI. The cumulative hazards (> 10 years) of developing ADHD, ASD, or DD after TBI were significant. Our data also revealed the highest risk of the neurodevelopmental disorders with severe TBI, repeated events, and the occurrence of TBI at ages of < 1 year. Additionally, preterm birth or low birth weight was identified as a risk factor of ADHD and DD; this was consistent with previous findings that established prematurity and low birth weight as risk factors of ADHD and DD.[38,39]

Unlike ADHD, few studies have investigated the association between autism and TBI. According to our review of relevant studies, no large epidemiologic study has been conducted. The prevalence of ASD among children aged 8 years increased from 1 in 250 in 1995 to 1 in 88 in 2008 in the United States.[19,40] This shift may be explained by the increasing awareness and diagnosis and by social-environmental contributions such as TBI. Notably, children diagnosed as having ASD and those who sustain TBI exhibit similar symptoms.[20] A study suggested that cerebellar injury can contribute to autism.[22] Executive function deficit and lack of inhibitory control, including self-regulation, were observed in patients with autism and children who sustained TBI.[41] Moreover, a neuroanatomic association between TBI and ASD has been suggested. Cortical thinning in the fusiform gyrus and the inferior parietal cortex has been associated with deficit in the early processing of faces, which may be responsible for autistic features in children following TBI.[42,43] Recent major research in autism has focused on the underlying genetic causes. However, an increasing contribution from environmental factors should not be ignored.[44] The present study provides a valuable perspective on the influence of environmental factors on ASD.

The mechanism underlying the contribution of TBI to the development of neurodevelopmental disorders remains elusive. Magnetic resonance imaging (MRI)–derived measurement revealed an alteration in the cortical thickness and activation of multiple areas after TBI, including the medial prefrontal and orbitofrontal regions, cuneus, and right anterior cingulated gyrus, which are related to the behavioral and emotional disturbance and cause symptoms similar to ADHD.[42] A comparison between boys with ASD and ADHD using functional MRI (fMRI) revealed an increased activation of the precuneus and decreased activation of the striatothalamic regions, prefrontal cortex, and superior parietal cortex in both groups.[45] Although the neuropathologies underlying TBI, ASD, and ADHD remain complex and vague, evidence of the association between the 3 exists based on the pathophysiologic changes within the brain.[46]

Various neurodevelopmental disorders such as ASD, ADHD, developmental language disorders, and schizophrenia have been proposed to result from an impairment of theory of mind (ToM), an incorporation of several neuropsychological functions and children's social interactions with peers and adults.[47] Traumatic injury to diffuse cerebral regions may also impair ToM.[48] The ToM system probably begins to operate from 13 to 15 months of age and rapidly develops until attaining ToM at approximately 3–4 years of age.[47] Injury to

Figure 1. Cumulative Hazards (> 10 Years) of Developing ADHD, ASD, and DD Among Children With TBI and Controls



Abbreviations: ADHD = attention-deficit/hyperactivity disorder, ASD = autism spectrum disorder, DD = developmental delay, TBI = traumatic brain injury.

the ToM system and its failure to mature may partially explain the mechanism by which TBI leads to neurodevelopmental disorders.

A study[49] that examined 125 children who sustained TBI in their early childhood (< 3 years of age) found that age and injury severity are likely to affect social and communication outcomes in children after TBI. Severe TBI and younger age were associated with less favorable outcomes in communication, social behavior, and social interactions, which may be early markers for cognitive and adaptive behavior difficulties.[49] Although numerous studies have investigated cognitive outcomes after TBI, few have stratified the outcomes according to severity and age groups.[31] Our study filled this gap and demonstrated a dose-response relationship between TBI severity and the risk of neurodevelopmental disorders.

Large-scale cohort studies such as ours have strengths and limitations. The present study enrolled thousands of children and tracked their records of seeking medical assistance for over decades. They were almost never lost to follow-up because the database coverage is more than 99% nationwide in Taiwan. Conducting a prospective, longitudinal study with thousands of children after birth with a high follow-up rate is challenging. Traditional studies have usually investigated the risk of ADHD following TBI in a short-term period of approximately ≤ 2 years. In addition, the sample size in these studies was relatively small (mostly < 100 patients).[12–14,28,29] Our study was able to accurately provide the longitudinal records of thousands of study subjects since birth.

A detailed review of medical charts and radiographic images cannot be obtained from a national database such as the NHIRD. Thus, the severity of TBI for each case cannot be determined using the Glasgow Coma Scale (GCS), a conventional scale for TBI classification.[50] Instead of the GCS, we defined severe TBI as the cases that required neurosurgical intervention.[51–53] Mild TBI was defined as cases that neither received neurosurgical intervention nor were admitted due to TBI. The treatment strategy followed the recommendations of the guidelines in the United States.[54] According to a previous World Health Organization survey, mild TBI accounted for approximately 90% of all TBIs in pediatric patients, whereas < 10% of the TBIs were classified as moderate to severe cases.[55–57] The prevalence of mild, moderate, and severe TBI in our study was similar to that reported in other studies. Therefore, the classification of TBI severity in our study can serve as a reliable alternative to conventional GCS scales.

The identification of TBI mechanisms and the early traits of neurodevelopmental disorders were also limitations of our study. Our study design captured the incidence of neurodevelopmental disorders only after diagnosis by a specialist using *ICD-9-CM* codes. Although our study demonstrated that children that had sustained TBIs in their early childhood developed greater risks of associated neurodevelopmental disorders, there remains a possibility of delay in diagnosis. At young ages, the symptoms and signs of ADHD, ASD, and DD can be easily overlooked. Theoretically, early traits of neurodevelopmental disorders may be associated with TBIs inflicted by parents or caregivers. The traits of neurodevelopmental disorders in early childhood and their relationships with assault remain unrecognized and require further efforts from research and clinical physicians.

CONCLUSION

Our study data suggested that the incidence of subsequent ADHD significantly increased when TBI events occurred in early childhood (< 3 years of age). Similar results were obtained for ASD and DD. The risks of ADHD, ASD, and DD increased after severe TBI compared with mild and moderate TBI. In addition, the risks of ADHD, ASD, and DD were significantly higher after repeated TBI events and the occurrence of TBI at a younger age, with the exception that the HR of ASD did not significantly increase after repeated TBI. Moreover, the long-term follow-up data (> 10 years) demonstrated that the cumulative risks of ADHD, ASD, and DD significantly increased after TBI.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Childhood and Adolescent Mental Health section. Please contact Karen D. Wagner, MD, PhD, at kwagner@psychiatrist.com.