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Original article

Risk of Traumatic Brain Injury Among Children, Adolescents, and Young Adults With Attention-Deficit Hyperactivity Disorder in Taiwan

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A B S T R A C T

Purpose: Previous studies suggested that patients with attention-deficit hyperactivity disorder (ADHD) were prone to health-risk behaviors and accidents. However, the relationship of ADHD with the risk of traumatic brain injury (TBI) remained uncertain.
Methods: Using the Taiwan National Health Insurance Research Database, 72,181 children (aged 3–11 years), adolescents (12–17 years), and young adults (18–29 years) with ADHD and 72,181 age-/sex-matched controls were enrolled between 2001 and 2009, and followed up to the end of 2011 in our study. Those who developed any TBI during the follow-up period were identified.
Results: Children, adolescents, and young adults with ADHD had a higher incidence of developing any TBI (9.8% vs. 2.2%, $p < .001$), such as skull fracture (.2% vs. .1%, $p < .001$) and concussion (4.3% vs. 1.0%, $p < .001$), than the controls did. Cox regression analysis with the adjustment of demographic data, psychiatric comorbidities, and ADHD medications showed that ADHD was related to an increased risk of subsequent TBI (hazard ratio: 4.57, 95% confidence interval: 4.31–4.85), and indicated that long-term use of ADHD medication was associated with a reduced likelihood of subsequent TBI (hazard ratio: .93, 95% confidence interval: .87–.99).
Conclusions: Patients with ADHD had an increased risk of developing any TBI compared with the controls. Long-term use of ADHD medications would reduce this risk. Our findings suggested that the public health government and clinicians should pay more attention to the TBI risk among patients with ADHD, and further indicated the importance of the optimal treatment for ADHD.

IMPLICATIONS AND CONTRIBUTION

Children, adolescents, and young adults with ADHD were prone to developing any TBI later in life. Use of ADHD medications was related to the reduced risk of subsequent TBI. Our study reminds clinical psychiatrists and public health officers to pay more attention to the risk of TBI among patients with ADHD.

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Attention-deficit hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder and is highly prevalent in children, adolescents, and young adults worldwide, affecting approximately 5%–7% of children and adolescents and 2% of young adults [1,2]. ADHD begins in childhood and persists up to adulthood. Individuals with ADHD manifest an inability to marshal and sustain attention, and modulate activity levels and impulsive actions [1,2].

Increasing evidence indicates a significant relationship between ADHD and different accidents, including driving, motorcycling, and bicycling accidents, falls, and fractures [3–7]. Chang et al. assessed the risk of serious transport accidents, including the proportion of emergency hospital visits and deaths due to a transport accident, among 17,408 adults with ADHD and reported that men with ADHD and women with ADHD had an increased risk of serious transport accidents compared with those without ADHD [4]. Kieling et al. observed that motorcycle riders with ADHD, especially those with additional conduct problems, had a higher number of traffic accidents [5]. An internet survey of 491,186 regular highway users revealed that drivers with ADHD symptoms were more likely to have accidents than were drivers without ADHD symptoms. Moreover, drivers with ADHD symptoms reported significantly more inattention-related near misses than did drivers without ADHD symptoms [7]. Nikolas et al. reported that adolescents with ADHD were more likely to have a risk of car–bicycle collision and to exhibit significant deficits in both the selection of gaps for crossing as well as in the timing of their movements while crossing intersections compared with non-ADHD youth [8]. Lee et al. assessed the risk of falls among fifth- and sixth-grade children, and demonstrated that ADHD was associated with the risk of falls [6]. These accidents, especially transport accidents, are regarded as a risk factor for traumatic brain injury (TBI) [9,10].

TBI is one of the leading causes of long-term disability in children, adolescents, and young adults, with serious sequelae and burdens on the lives of patients, their families, and society [10–12]. Every year, an estimated 10 million people worldwide are affected by a new TBI event. Furthermore, TBI is expected to become the third largest cause of global disease burden by 2020, especially in developing countries, where motor car use is increasing, leading to road traffic accidents, which are already a leading cause of TBI in many parts of the world [9,10,12].

Several studies have suggested the potential relationship between ADHD and TBI [13,14]. A cross-sectional sample of 3,993 adults aged ≥18 years with TBI and current or past ADHD revealed that adults with lifetime TBI had significantly greater odds of exhibiting positive scores on ADHD screening and of self-reporting a history of diagnosed ADHD than did those without TBI [14]. Alosco et al. demonstrated that 50.4% of athletes with ADHD reported a history of at least one prior concussion compared with 14.4% of athletes without ADHD [13]. Biederman et al. reported that adolescents and young adults with mild TBI had a significantly higher rate of ADHD than non-ADHD controls, and in all cases the onset age of ADHD was before TBI onset [15]. Mikolajczyk et al. determined via a case-only design whether ADHD medications would reduce the risk of TBI among patients with ADHD, and found that there was a preventive effect of ADHD medications on the risk of TBI [16]. Although the findings of cross-sectional studies have supported the significant relationship of TBI and its risk factors (i.e., transport accident and falls) with ADHD, the temporal relationship of whether ADHD may increase the risk of subsequent TBI and whether prompt intervention for ADHD may reduce the risk of TBI could not be determined.

In the current study, we used the Taiwan National Health Insurance Research Database, with a large sample size and a longitudinal follow-up study design, to investigate the risk of subsequent TBI, including skull fracture, concussion, and contusion, among patients with ADHD. We hypothesized that (1) patients with ADHD had an increased risk of developing any TBI later in life compared with the non-ADHD controls, and (2) prompt intervention for ADHD may reduce the risk of subsequent TBI.

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 manages the insurance claims database, namely the National Health Insurance Research Database (NHIRD), which consists of healthcare data from >99% of the Taiwanese population. The National Health Research Institutes 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 [17–20]. Taipei Veterans General Hospital Institutional Review Board approved the study.

Inclusion criteria for children, adolescents, and young adults with ADHD and the control group

Children aged between 3 and 11 years, adolescents aged between 12 and 17 years, and young adults aged between 18 and 29 years who had a diagnosis of ADHD (ICD-9-CM code: 314) given by board-certificated psychiatrists between January 1, 2001 and December 31, 2009 based on their clinical judgment and diagnostic interview and who had no history of any TBI (ICD-9-CM codes: 800–801, 803–804, 850–854, 959.01) before enrollments were included as the ADHD cohort. In Taiwan, the vast majority of ADHD care was provided by psychiatrists. The time of ADHD diagnosis was defined as the time of enrollment. The age-, sex-, and time of enrollment-matched (1:1) control cohort was randomly identified after eliminating the study cases, individuals who had been given a diagnosis of ADHD at any time, and individuals with any TBI before enrollment. Any TBI, including fracture of skull (ICD-9-CM codes: 800–801, 803–804), concussion (ICD-9-CM code: 850), contusion (ICD-9-CM code: 851), brain hemorrhage following injury (ICD-9-CM codes: 852, 853), and unspecified intracranial injury (ICD-9-CM codes: 854, 959.01), was identified during the follow-up (from enrollment to December 31, 2011 or to death). Psychiatric comorbidities, including disruptive behavior disorders, alcohol use disorders, and substance use disorders, were assessed as the confounding factors in our study. In addition, the use of ADHD medications (methylphenidate or atomoxetine) during the follow-up was also examined respectively, and divided into three subgroups: nonusers (cumulative defined daily dose [cDDD] during the follow-up < 90), short-term users (cDDD = 90–364), and long-term users (cDDD ≥ 365). Only methylphenidate and atomoxetine were approved for ADHD treatment