Assessment of the neuropsychiatric comorbidities in Chinese children with epilepsy using the MINI-KID tool

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ABSTRACT

This study aimed to assess neuropsychiatric comorbidities and analyze risk factors in Chinese children with epilepsy. Children with epilepsy aged between 6 and 16 years from the Children’s Hospital of Fudan University were included. Children with asthma and typically developing children were matched for age and gender, and served as control groups. Neuropsychiatric disorders were assessed by interviewing the parents or guardians using the Mini International Neuropsychiatric Interview for children (MINI-KID) (parent version). Basic information and clinical data were also collected using an author designed questionnaire. Multiple logistic regression analysis was done to identify the risk factors associated with neuropsychiatric comorbidities. In this study, 140 children with epilepsy, 70 children with asthma and 70 typically developing children were recruited. Neuropsychiatric disorders were significantly more common in children with epilepsy (41.4%) as compared with the asthma group (15.7%) and the control group (10.0%). Of the 58 children with epilepsy who had neuropsychiatric comorbidities, only 29.3% had been diagnosed before our study. Multivariate analysis revealed that a younger age at seizure onset (OR = 0.877, 95%CI: 0.773−0.996), seizures occurring more than once monthly during the past year (OR = 3.526, 95%CI: 1.177−10.562), polytherapy (OR = 2.632, 95%CI: 1.066−6.501) were all significantly associated with neuropsychiatric comorbidities in children with epilepsy. In conclusion, children with epilepsy are more likely to have neuropsychiatric comorbidities, and up to 70% of them were undiagnosed. Early screening, diagnosis and treatment of neuropsychiatric comorbidities in children with epilepsy may improve the long-term prognosis.

1. Introduction

Epilepsy is a common neurological disorder, approximately 70 million people have epilepsy worldwide, and about half of the epilepsy in the population first happens in childhood (Baca, Vickrey, Caplan, Vassar, & Berg, 2011; Singh and Trevick, 2016). Children with epilepsy are more likely to have psychiatric disorders and behavior problems than typically developing children (Reilly et al., 2014a; Reilly et al., 2014b; Russ, Larson & Halfon, 2012), and even compared to children with other chronic illness such as diabetes and asthma (Davies, Heyman & Goodman, 2003). In an epidemiological study conducted by Davies et al. (Davies et al., 2003), the prevalence of psychiatric disorders was higher in children with epilepsy (37%), compared with diabetes (11%) and a control group (9%). In a population-based survey involving 91,600 children from the USA, Russ et al. (Russ et al., 2012) reported that children with epilepsy or seizures were more likely than those who had never had a seizure to experience attention deficit/hyperactivity (ADHD) (23% vs. 6%), depression (8% vs. 2%), anxiety (17% vs. 3%) and autism spectrum disorder (ASD) (16% vs. 1%).

These neuropsychiatric comorbidities not only complicate the diagnosis and treatment of epilepsy, but also have a serious impact on the quality of life for patients and families, and are even more disabling than seizures themselves (Baca et al., 2011; Hamiwka and Wirrell, 2009). Researches suggest that major risk factors associated with neuropsychiatric disorders in children with epilepsy include common neurological abnormalities, genetic factors, epilepsy-related factors, polytherapy of anti-epilepsy drugs (AEDs) and socioeconomic deprivation (Austin and Caplan, 2007; Hamiwka and Wirrell, 2009). The rates of neuropsychiatric comorbidities in children with epilepsy range from 37% to 80%, however, these comorbidities are typically undiagnosed (Alfstad et al., 2011; Davies et al., 2003; Reilly et al., 2014b; Russ et al., 2012). Reilly et al. (Reilly et al., 2014b) reported only 1 in 3
of children with epilepsy with neuropsychiatric disorders had been diagnosed before the study, which could be due to the lack of screening and standardized assessment for psychiatric conditions in children with epilepsy. Both diagnosis and early intervention of comorbid disorders are essential to improve quality of life in children with chronic disorders. In China, few studies have investigated the full spectrum of neuropsychiatric disorders in children with epilepsy and the application of standardized interview protocols is limited (Choudhary, Gulati, Sagar, Kabra, & Supra, 2014). Therefore, in this present study, a structured diagnostic interview—MINI-KID—was used to assess the neuropsychiatric disorders in children with epilepsy, compared with children with asthma and typically developing children. Possible risk factors for neuropsychiatric comorbidities in children with epilepsy were also analyzed.

2. Methods

2.1. Study Populations

This cross-sectional study was conducted from October 2016 to January 2017. We recruited children with epilepsy aged 6 to 16 years from the pediatric neurology clinics at the Children’s Hospital of Fudan University in China. Criteria for the children with epilepsy included: (1) diagnosis of epilepsy according to the International League Against Epilepsy (ILAE) 2014 (Robert and Carlos, 2014), (2) no other chronic disease (e.g., diabetes and asthma), (3) no intracranial operation within the past month, and (4) no family history of psychosis.

Children with asthma and typically developing children were recruited as control groups and matched for age and gender. Children with asthma were recruited from the pediatric respiratory Medicine Clinic. Criteria for the children with asthma included: (1) diagnosis of asthma according to the 2016 Guidelines for the Prevention and Treatment of Asthma in Chinese Children (The Group of Respiratory, Chinese Pediatric Society, Chinese Medical Association, 2016), (2) no history of seizure and other neurological disorders and (3) no other chronic disease (e.g., epilepsy, diabetes, and tumor). Typically developing children were recruited from the physical examination center. Criteria for typically developing children included: (1) no history of seizure and other neurological disorders and (2) no other chronic disease (e.g., epilepsy, asthma, diabetes, and tumor).

Written informed consent was obtained from all parents or guardians. The protocol was approved by the Research Ethics Committee of Children’s Hospital of Fudan University.

2.2. Assessment Instruments

The neuropsychiatric disorders were assessed by interviewing the parents or guardians by using the Mini International Neuropsychiatric Interview for children and adolescents (MINI-KID) (parent version). The MINI-KID is a structured diagnostic interview, which was designed on the basis of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) and International Classification of Disease, 10th version (ICD-10) by epidemiologists and clinicians. The instrument includes 25 modules and diagnoses 24 psychiatric disorders and suicidality in children and adolescents between 6-16 years of age concisely and comprehensively (Sheehan et al., 2010). Each module includes both screening questions and diagnostic sections, and diagnostic questions are asked only when the screen questions are positive. All questions are answered in a “yes/no” format (Sheehan et al., 2010).

The MINI-KID has been translated into many languages and is widely used in epidemiological studies (Adamowska, Adamowski, Frydecka, & Kiejna, 2014; Sheehan et al., 2010). The Chinese version of MINI-KID (parent version) 5.0 was translated by Liu YX et al. of the Peking University Institute of Mental Health in 2010 (Liu, Liu & Liu, 2010). The research conducted by Liu YX et al. suggested that the Chinese version of MINI-KID (parent version) present favorable reliability and validity and is suitable for epidemiological studies (Liu et al., 2010). Furthermore, the sensitivity of the parent-rated version in all disorders is higher than the child version (Liu et al., 2011), leading to the selection of the Chinese version MINI-KID (parent version) in this study with Dr. Liu’s approval.

2.3. Study procedure

After obtaining informed consent from parents or guardians, each parent or guardian was invited to receive an interview using the MINI-KID to assess current neuropsychiatric disorders. An author designed questionnaire was prepared to collect socio-demographic details and clinical data. Socio-demographic details included date of birth, gender, education, family income, parents’ occupation, parents’ educational background, and registered residence. Clinical data primarily contained birth history, growth and development, family history of seizures, age of seizure onset, duration of epilepsy, current AEDS, electroencephalogram (EEG) findings within the past 6 months, neuroimaging findings, comorbidities diagnosed previously, and intelligence test results.

2.4. Statistical Analysis

Statistical analyses were conducted using Stata 11.0 software (version 11.0, college station, Texas 77845, United States). Continuous variables were compared using the Mann-Whitney U test. Chi-square and fisher tests were carried out to compare categorical variables. Binary logistic regression analysis was performed to identify the risk factors associated with neuropsychiatric comorbidities, and p < 0.05 was considered to be significant.

3. Results

3.1. Socio-demographic and clinical characteristics

From October 2016 to January 2017, 155 outpatient children (aged 6-16 years) with epilepsy were included in this study, 90.3% (140/155) of the parents of children with epilepsy who provided informed consent were invited to participate in this research. The sample included 92 boys (65.7%) with a mean age of 9.8 ± 2.5 years, with 130 children (92.9%) attending mainstream schools, and 57.8% receiving monotherapy. Twenty-seven children had intellectual disability (IQ < 70). The mean age of seizure onset was 5.7 ± 3.1 years, and the duration of epilepsy ranged from 1 to 7.2 years. Twenty (14.3%) children had a family history of seizures, and the general seizure was predominant in the epilepsy type; 63 (45%) children were seizure free for more than 1 year, 62 (45.6%) children had no epileptic discharge in EEG, and 39 cases had an abnormal brain MRI. The socio-demographic and clinical characteristics of children with epilepsy are shown in the Table 1. Seventy children with asthma and 70 typically developing children matched for age and gender were recruited as control groups. Socio-demographic characteristics of the 3 groups are shown in Table 2. Most variables were matched except for paternal education (Table 3).

3.2. The prevalence of neuropsychiatric disorders in the epilepsy, asthma and control group

The prevalence of neuropsychiatric disorders in the epilepsy group was compared with those of the children in the other two groups, which was shown in Table 3. Neuropsychiatric disorders were more common in children with epilepsy (41.4%) compared to the asthma group (15.7%) and typically developing children (10.0%). There was a significant difference between the epilepsy group and the asthma group ($\chi^2 = 13.987, P < 0.001$), as well as between the epilepsy group and the control group ($\chi^2 = 21.568, P < 0.001$). The difference between
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