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Original Article

Risk Factors for Diagnostic Delay in Psychogenic Nonepileptic Seizures Among Children and Adolescents

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ABSTRACT

BACKGROUND: This study aims to analyze a series of pediatric patients with psychogenic nonepileptic seizures (PNES) to establish the diagnostic gap and possible risk factors for the delayed diagnosis in this age group. **METHODS:** We evaluated all children with PNES documented by video electroencephalography. None had a previous diagnosis of PNES. In total, we included 53 children (interquartile range: seven to 17 years; mean age 12.81 years [S.D. 3.15]; 60.4% girls) who underwent a protocol consisting of neurological and psychiatric interviews. **RESULTS:** The average time between seizure onset and referral was 17.76 months (interquartile range: 0.5 to 48 months; S.D. ± 12.62). Earlier age of onset correlated with a later diagnosis ($P < 0.001$). The late referral group also presented with a history of psychological abuse ($P = 0.018$). **CONCLUSION:** Youth with PNES represent a diagnostic challenge. Identification of children at risk might lead to earlier diagnosis of PNES.

Keywords: nonepileptic seizures, psychogenic, children, adolescents, diagnosis

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Introduction

Psychogenic nonepileptic seizures (PNES) are paroxysmal episodes that resemble epileptic seizures. However, they are caused by a psychogenic process and not by epileptiform activity.[1] There is considerable variability in the number of patients with a diagnosis of PNES seen in tertiary institutions.[2,3] Referral delay is worrisome since diagnosing PNES prevents hospitalization and leads to unnecessary medical procedures for diagnosis, treatment, and excessive costs.[4] There is uncertainty regarding the factors that preclude early diagnosis and treatment. According to Reuber et al.,[5] physician-related factors such as incorrect diagnosis of epilepsy are the primary reason for treatment delay in adults with PNES. Bodde et al.[2] observed that patient-related factors are relevant since patients with psychological complaints and previous psychological or psychiatric treatments favor earlier interventions.

In children, one associates PNES with school-related difficulties and significant psychopathology.[6] It is undeniable that correct recognition, referral, and treatment could save health resources and alleviate great distress for affected children and their families.[6,7] Although there have been few systematic studies on the treatment of children with PNES, it is possible that outcomes might be more favorable in this age group.[8]

The few studies addressing PNES in children show that the treatment gap is highly variable, and ranges from one week to five years.[9] As previously noted, the longer the duration of untreated PNES, the less optimal the response to therapy and the higher the recidivism rate.[8-10]

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There are scarce data on the time until diagnosis of PNES in children. In addition, no previous studies assess the factors that delay the diagnosis in this population. We analyzed the average interval until a definite diagnosis was established among youth with PNES and attempted to identify the factors that contributed to diagnostic delays.

Methods

Study population

We included individuals less than 18 years of age with PNES who were consecutively referred to a tertiary medical center for epilepsy treatment. We included only patients and families who agreed to undergo video electroencephalography (VEEG) monitoring and psychiatric and neurological evaluations. We excluded children whose parents were unable to understand the protocol and to give precise and accurate information. We excluded youth with PNES if they had other paroxysmal nonepileptic events, panic attacks, or degenerative or metabolic disorders affecting the central nervous system. Coexisting epilepsy was not a criterion for exclusion. However, we analyzed patients with PNES and epilepsy as a subgroup. We did not include patients who presented with PNES and epileptic seizures with similar features that could not be distinguished. We excluded patients who had only homemade videos, and whose events could not be documented by VEEG at our center. Nonadherence to protocol was also a criterion of exclusion of patients with documented PNES.

Study procedures

The study was approved by our institutional review board, and all subjects and their parents provided informed consent before enrollment.

Diagnosis of PNES

Video electroencephalography. Long-term inpatient VEEG, a gold standard for diagnosing PNES,[11] was mandatory for diagnosis. During monitoring, we favored recording spontaneous events. After the diagnosis of PNES was confirmed with VEEG monitoring, the same epilepsy specialist analyzed the events and confirmed the diagnosis of PNES. We performed provocative methods such as verbal induction (suggestion), hyperventilation, and photic stimulation if we could not obtain a spontaneous event. Documented PNES had to be the typical or habitual event experienced by the individual and witnessed by parents and/or caretakers.

We classified PNES semiology into major motor, minor motor, dialeptic (characterized by unresponsiveness), and aura.[12]

Clinical evaluation. After the diagnosis, we informed families about the nonepileptic nature of these events. In case of coexisting epilepsy, we showed both, epileptic and non-epileptic events, to the families and explained the differences. We referred the patients and families for further evaluation using the standard protocol.

The same child psychiatrist, who was aware of the diagnosis of PNES, evaluated all patients using a psychiatric interview. The Schedule for Affective Disorders and Schizophrenia for School-Age Children—Epidemiological Version (K-SADS-PL),[13] a semi-structured diagnostic interview, was administered to all patients and parents. To improve the data reliability of the K-SADS-PL, an experienced and well-trained child psychiatrist, familiar with Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition (DSM-IV) criteria, applied it. It was performed separately with each informant (first with the child and then with the parents).

The patients were classified according to the DSM-IV, and Classification of Mental and Behavioral Disorders: Diagnostic Criteria for Research (ICD-10). This evaluation was done to establish coexisting psychiatric conditions including depression and anxiety.

Parents were questioned about the presence of somatic complaints that occurred without a clear etiologic diagnosis despite the proper investigation, were related to environmental stressors, and occurred only under particular circumstances. This included spontaneous complaints or asking direct questions about nonspecific headaches, recurrent abdominal pain, nausea or vomiting, and episodes of hyperventilation. These questions were posed in a standard manner based on the K-SADS-PL[13] interview and adapted from the Child Behavior Checklist.[14]

Additional biographic information, details of medical and seizure history, diagnosis, previous ancillary examinations, and treatment details were retrieved from patients' records and obtained from contact with patients and families.

The parents also completed a questionnaire regarding: (1) child's past and current neurological history (epilepsy, brain infections, head injury, developmental delay, migraine); (2) medical illnesses (non-neurological chronic medical conditions); (3) previous and current medications; (4) past and present emotional, behavioral, and learning problems; and (5) frequency of emergency room visits and hospitalizations over the past year (especially considering history of possible PNES status in patients without coexisting epilepsy). Additionally, the parents responded to questions about child's health condition and family history of medical conditions including epilepsy and psychiatric illness.

Details about stressors and risk factors such as head trauma, physical or sexual abuse, family discord, and school problems were collected using a standardized protocol. This protocol was previously developed by our group[15] and has been used for follow-up psychiatric interviews by our group and others.[16]

Criteria for diagnosis of epileptic syndromes. For patients with coexisting epilepsy, the parents and patients were interviewed by two epileptologists to classify the seizures and epileptic syndromes. All patients with epilepsy, except those with genetically determined epilepsy, as determined by history and confirmed by electroencephalography (EEG), underwent brain magnetic resonance imaging (MRI) for etiologic diagnosis as part of our standard protocol. We reviewed available previous ancillary examinations such as EEG and MRI. The data of seizure semiology and ancillary examinations had to be congruent to confirm the diagnosis of epilepsy. For patients who did not have epileptic events recorded during VEEG, parents had to be able to differentiate and point out the differences between the PNES semiology recorded by VEEG, and the epileptic seizures witnessed by the family.

Statistical analysis

Mean diagnostic delays were calculated for variable categories such as gender, coexisting epilepsy, psychiatric and neurological comorbidities (other than epilepsy), semiology, use of antiepileptic drugs (AEDs), family history of epilepsy, family history of psychiatric disorders, family history of neurological or other chronic illness, presence of stressors, history of possible psychogenic status, presence of epileptiform discharges, and MRI abnormalities.

Association with referral delay was assessed using the Wilcoxon-Mann-Whitney test (homoscedastic case), Brunner-Munzel test (heteroscedastic case) for binary variables, Kruskal-Wallis test for other categorical variables, and Spearman correlation for numeric variables. We entered variables with significant association into a linear regression model. We inspected graphically linear model assumptions of residual normality, homoscedasticity, and independence. We conducted all analyses on R 3.2.2,[17] and we set the type I error at 5%.

Results

Patient characterization

Demographics

Fifty-three children and adolescents with PNES fulfilled the inclusion and exclusion criteria and composed the study group. There was a female predominance (60.4%), and the age at diagnosis ranged from seven to 17 years (mean was 12.81 years; median 13 years; S.D. $\pm$ 3.15 years).