Epilepsy & Behavior 70 (2017) 135–139

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Risk factors for learning problems in youth with psychogenic non-epileptic seizures

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ARTICLE INFO

Article history:
Received 24 October 2016
Revised 14 February 2017
Accepted 7 March 2017
Available online 17 April 2017

Keywords:
Epilepsy
Psychogenic non-epileptic seizures
Learning problems
Adolescents
Risk factors

ABSTRACT

Objectives: This study examined the risk factors for learning problems (LP) in pediatric psychogenic non-epileptic seizures (PNES) and their specificity by comparing psychopathology, medical, cognitive/linguistic/achievement, bullying history, and parent education variables between subjects with PNES with and without LP and between subjects with PNES and siblings with LP.
Methods: 55 subjects with PNES and 35 siblings, aged 8–18 years, underwent cognitive, linguistic, and achievement testing, and completed somatization and anxiety sensitivity questionnaires. A semi-structured psychiatric interview about the child was administered to each subject and parent. Child self-report and/or parent report provided information on the presence/absence of LP. Parents also provided each subject's medical, psychiatric, family, and bullying history information.
Results: Sixty percent (33/55) of the PNES and 49% (17/35) of the sibling subjects had LP. A multivariable logistic regression demonstrated that bullying and impaired formulation of a sentence using a stimulus picture and stimulus word were significantly associated with increased likelihood of LP in the PNES youth. In terms of the specificity of the LP risk factors, a similar analysis comparing LP in the youth with PNES and sibling groups identified anxiety disorder diagnoses and bullying as the significant risk factors associated with LP in the PNES youth.
Conclusions: These findings emphasize the need to assess youth with PNES for LP, particularly if they have experienced bullying, have linguistic deficits, and meet criteria for anxiety disorder diagnoses.
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1. Introduction

Psychogenic non-epileptic seizures (PNES) in youth is a form of conversion disorder with a complex risk factor profile and a long lag in diagnosis [1,2]. Learning problems (LP) are one of the more common risks for pediatric PNES [1,3]. Nevertheless, there have been no studies on the risk factor profile for LP in youth with PNES, and whether it differs from LP in the general youth population and in youth with other medically unexplained symptoms. Delineation of the risk factors and their specificity for PNES may both aid in earlier diagnosis of PNES and inform treatment approaches.

Risk factors for LP in the general population include below-average IQ scores [4], language difficulties [4], lower socioeconomic status [5], and comorbid psychopathology [6]. Attention deficit hyperactivity disorder is the most well studied psychiatric comorbidity of LP in the general population [6]. Learning problems are also associated with increased risk for anxiety and depression [7]. Although more than 50% of youth with medically unexplained symptoms were found to have undiagnosed LP in a recent study [7], no studies have examined the risk factors associated with their LP.

Studies of youth with medically unexplained symptoms have found comorbid psychopathology risk factors similar to those in PNES [1] including depression [8], generalized anxiety [9,10], social anxiety [11], performance anxiety [12], and anxiety sensitivity (the tendency to be fearful of physical sensations) [9,10]. Internalizing disorders (depression, anxiety) and anxiety sensitivity also distinguish youth

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http://dx.doi.org/10.1016/j.yebeh.2017.03.016
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with PNES from their siblings [1]. Thus, internalizing disorders, found in LP in the general population, in youth with medically unexplained symptoms, and in those with PNES, as well as anxiety sensitivity, evident in the two latter disorders [13], might play a role in the observation of perceived/reported LP of PNES youth.

Bullying and learning difficulties (variably determined through formal testing, language testing, non-standardized measures designed by the study team, parent report, and self-report) are bi-directionally related so that bullying appears to increases the likelihood of LP and vice versa [14,15]. Youth with LP who experience bullying are also at greater risk for the development of functional symptoms, especially medically unexplained pain [9,16]. Children who struggle with language-related learning difficulties might be at particular risk for bullying [14,15]. In a previous study we examined a range of childhood adversities and found that history of bullying played a role in differentiating youth with PNES from their siblings [1].

To examine risk factors for LP in PNES and their specificity on our previously studied youth with PNES and sibling subjects [1], we compared (a) youth with PNES with and without LP, and (b) youth with both PNES and LP and the siblings with LP. We explored if the following variables were risk factors for the LP in PNES: lower IQ, language, and achievement scores; parents with fewer years of education; ADHD, anxiety disorder, and depression diagnoses; higher somatization and anxiety sensitivity; and history of bullying. Since 29.1% of the youth with PNES had epilepsy, and 29.1% were on anti-seizure drugs, variables that might contribute to learning difficulties [17], we also examined the role of these variables in the LP of PNES. We then compared youth with PNES and sibling subjects with LP on all of the above variables to determine if youth with PNES and LP had specific risk factors compared to their siblings.

2. Methods

2.1. Participants

This multi-site study included 55 youth with a confirmed video-EEG (vEEG) diagnosis of PNES and 35 of their siblings as a control group. The mean age of PNES onset was 14.3 years. We excluded participants from this study if they had known cognitive impairment (IQ < 70), history of epilepsy surgery, other types of non-epileptic events, and if they had non-English speaking parents. Youth with PNES were recruited from seven USA tertiary epilepsy centers. At each site, a pediatric epileptologist confirmed the PNES diagnosis, defined as paroxysmal events with semiology inconsistent with seizures due to epilepsy and without associated epileptiform discharges on v-EEG in concert with the ILAE diagnostic levels [18]. A child psychiatrist or psychologist conducted a semi-structured psychiatric interview to assess psychiatric diagnoses associated with the PNES symptoms. Youth were not excluded from the study if they had past psychiatric diagnoses, including autism.

We categorized a child as having LP if during the semi-structured psychiatric interview, described below, a child and/or parent reported poor grades, difficulty with specific or all subjects, boredom in subjects with poor grades, or not completing or handing in homework. Follow-up questions for youth who reported these problems determined if they reflected learning or social problems at school. School-related social difficulties were not categorized as LP. Of the 55 PNES probands, 33 had LP and 17 of the 35 siblings had LP.

Table 1 presents demographic, educational, and clinical characteristics of the study groups. The age range for the PNES group was 8.6–18.4 years. There were no statistically significant differences between the groups with regard to age, gender, ethnicity, mother's education, and special education. While probands with LP missed significantly more school days in the month prior to testing than those without LP, there were no significant differences in this variable in the siblings with and without LP. Table 1 does not include information on father's education since only a few fathers participated in the study. For a detailed report of the participant demographic, psychiatric, cognitive, academic, hassles, parenting, and coping profiles, see Plioplys et al. (2014).

Table 1
Demographic characteristics and outcome measures of PNES proband and sibling groups.

Variables[a]	PNES probands		Siblings	
	LD (N = 33)	No LD (N = 22)	LD (N = 17)	No LD (N = 18)
Age (years)	14.3 (2.8)	15.5 (2.3)	13.7 (2.6)	13.3 (2.2)
Gender				
Females (%)	22 (66.7)	17 (77.3)	7 (41.2)	11 (61.1)
Ethnicity				
Caucasian (%)	17 (51.5)	16 (72.7)	11 (68.8)	8 (47.1)
Mother education[b]				
College grad (%)	10 (30.3)	10 (50.0)	6 (37.5)	5 (29.4)
Number of school days missed (past month)[c]	4.9 (5.4)	10.4 (8.4)	1.4 (1.8)	1.9 (2.3)
Special education (%)[d]	8 (25.8)	3 (13.6)	2 (13.3)	2 (11.8)
Full scale IQ	98.0 (14.5)	105.0 (13.5)	103.3 (14.1)	109.4 (23.0)
WIAT achievement	98.2 (15.3)	102.2 (10.1)	103.8 (12.6)	103.1 (17.7)
CELF				
Formulated sentences	10.0 (3.4)	11.5 (2.1)	11.0 (2.8)	15.4 (12.0)
Word associations	8.9 (3.3)	10.8 (2.4)	10.1 (2.7)	10.3 (2.4)
Epilepsy-related				
Epilepsy present (%)	9 (27.3)	7 (31.8)	0 (0)	0 (0)
On anti-seizure drugs (%)	8 (24.2)	8 (36.4)	0 (0)	1 (5.6)
Experienced bullying (%)	18 (54.6)	5 (22.7)	2 (11.8)	4 (22.2)
Psychiatric diagnoses				
ADHD (%)	13 (39.4)	3 (13.6)	5 (29.4)	2 (11.1)
Anxiety (%)	27 (81.8)	19 (86.4)	6 (35.3)	6 (33.3)
Depression (%)	13 (39.4)	11 (50.0)	1 (5.9)	4 (22.2)
Somatization				
Total score	27.7 (19.4)	35.7 (19.2)	14.0 (14.4)	15.9 (19.4)
Anxiety sensitivity				
Total score	13.9 (7.3)	15.5 (6.9)	11.1 (5.4)	9.0 (5.7)

[a] Mean (SD) are presented for continuous variables and n(%) are presented for categorical variables.
[b] Mother education data are missing for 2 proband and 2 sibling families.
[c] Data on number of school days missed are unavailable for 8 proband and 5 sibling families.
[d] Special education data are missing for 2 proband and 3 sibling families.

2.2. Procedures

The parents completed a questionnaire about their children's demographic information, illnesses, epilepsy, medications, adversities, family composition, as well as parents' years of education and marital status. Institutional review board approval was obtained for all co-authors at each site.

2.2.1. Psychopathology

2.2.1.1. Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version (K-SADS-PL) [19]. This semi-structured instrument assesses current and past psychiatric diagnoses according to the DSM-IV-TR criteria. The study's child psychiatrists/psychologists, trained to administer the K-SADS-PL, interviewed each subject and parent, separately, about the child. A study co-investigator (RC), blinded to the subjects' group assignment, reviewed all the video-recorded interviews. The interviewer and reviewer reached a consensus diagnosis on cases for which there was diagnostic disagreement. The interview yielded summary diagnoses based on both the child and parent interviews. As described above, self-report by the study subjects and/or by the parents during the interview provided information on the presence/absence of LP.

2.2.1.2. Childhood Anxiety Sensitivity Index (CASI) [20]. This 18-item self-report scale measures the tendency to view anxiety-related bodily sensations as dangerous. Items are scored on a 3-point scale (none, some, a lot); total scores are calculated by summing all items. The

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