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Risk factors for comorbid psychopathology in youth with psychogenic nonepileptic seizures

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ABSTRACT

Purpose: To examine the risk factors for internalizing (anxiety, depression) and posttraumatic stress (PTSD) disorders, somatization, and anxiety sensitivity (AS) in youth with psychogenic non-epileptic seizures (PNES).
Methods: 55 probands with PNES and 35 siblings, aged 8–18 years, underwent a psychiatric interview, cognitive and language testing, and completed somatization and AS questionnaires. Parents provided the subjects' medical, psychiatric, family, and adversity history information.
Results: The risk factors for the probands' internalizing disorders (girls, older age of PNES onset), somatization (older age, epilepsy), and anxiety sensitivity (girls, adversities) differed from their siblings. The risk factors in the siblings, however, were similar to the general pediatric population. Proband depression was unrelated to the study's risk variables while PTSD was significantly associated with female gender and lower Full Scale IQ.
Conclusions: Knowledge about the specificity of the risk factors for comorbid psychopathology in youth with PNES might facilitate their early identification and treatment.

1. Introduction

Conversion disorders, such as psychogenic non-epileptic seizures (PNES), are poorly understood and difficult to diagnose. Their complex clinical presentation involves medically unexplained symptoms and internalizing disorders (anxiety and depression). PNES youth have more severe and prevalent comorbid psychopathology, such as internalizing disorders, posttraumatic stress (PTSD) disorder, anxiety sensitivity (identification of body sensations as dangerous), and somatization than their siblings [1]. The comorbid psychopathology contributes to the difficulties diagnosing PNES for three main reasons.

First, pediatric mood disorders, such as anxiety, depression, and PTSD, are more readily recognized than conversion disorder, as these disorders are more prevalent, well studied, and reliably diagnosed [2]. In contrast, PNES is a rare and under-investigated disorder, often misdiagnosed as epilepsy [3]. Furthermore, patients, parents, and some clinicians consider the comorbid depression and anxiety symptoms of youth with PNES as secondary to the distress caused by the seizures. Thus, when youth with seizure-like symptoms appear to be depressed and/or anxious, clinicians with little experience with PNES, omit the possibility of a conversion disorder and associated comorbid internalizing disorder(s).

Second, internalizing disorders frequently predate the onset of conversion disorder, and persist after its resolution [4,5]. Therefore, recognition of factors specifically associated with the comorbid psychopathology of pediatric PNES may help to better identify depressed and anxious youth that are at risk for development of conversion disorder and PNES. By differentiating

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between internalizing and conversion disorders, awareness of these risk factors might indirectly facilitate earlier PNES diagnosis. This, in turn, could reduce the excessive medical service use and improve outcomes [3–5].

Third, somatic and medically unexplained symptoms are common in internalizing disorders and PTSD [6,7]. Reif and Barsky's [8] biopsychosocial, perceptual filtering model of medically unexplained symptoms proposes that anxiety and depression change individual's perceptions of normal physical body sensations. Using this model, Lavigne et al. [9] demonstrated that somatization mediates the relationships between anxiety, depression, and medically unexplained symptoms in children. We previously found significant pre-existing medical histories in PNES youth than their siblings and significantly more somatization in PNES than epilepsy youth [1]. Identification of risk factors for somatization and the perception of bodily sensations as dangerous (anxiety sensitivity) in PNES might, therefore, facilitate diagnosis of this difficult to diagnose disorder.

In the general child population risk factors for internalizing disorders, PTSD, somatization, and anxiety sensitivity include female gender and older age [2], cognitive, and learning difficulties [10], life adversities, bullying, and single parent families [6,11,12]. However, there have been no studies on the risk factors for comorbid psychopathology in PNES youth.

To address this gap in our knowledge, we first identified the risk factors for internalizing disorders, somatization, and anxiety sensitivity in the PNES probands and their siblings. We posited that, despite shared genetic and family environment, PNES probands would have different demographic, cognitive, linguistic, adversity, and family structure risk factors than their siblings.

We then studied the profile of correlates of depression and PTSD only within the PNES group because only a few siblings had depression (14.3%) and PTSD (2.9%). Since anxiety disorders were present in almost all probands (83.6%), we could not determine their risk factors. Based on the previously described risk factors for depression and PTSD, we investigated the following hypotheses within the PNES group: (1) risk factors for depression and for PTSD include older age, female gender, lower Verbal IQ, higher somatization scores, single parent family structure, as well as more adversities and bullying, and (2) older age of PNES onset, impaired language skills, and anxiety sensitivity are additional PTSD risk factors.

2. Methods

2.1. Participants

This study included 55 youth with a video-EEG confirmed PNES diagnosis and their 35 sibling controls, who lived in the same families. We excluded probands and siblings from this study if they had known cognitive impairment (IQ < 70), other types of paroxysmal non-epileptic events (e.g., syncope, complex tics), a history of planned/past epilepsy surgery, and non-English-speaking parents.

The PNES group, aged 8.6–18.4 years, was significantly older than the siblings (14.8 ± 2.7 vs. 13.5 ± 2.4, $t(88) = 2.3$, $p = 0.02$). There were no statistically significant between group differences for gender, ethnicity, and family structure (Table 1). The mean age of PNES onset was 14.3 years (SD = 2.6). 30% of the probands but no siblings had epilepsy. For a detailed report of participant demographic, psychiatric, cognitive, academic, hassles, parenting, and coping profiles, see Plioplys et al. [1].

2.2. Recruitment and consent

PNES youth were recruited from seven USA tertiary epilepsy centers. At each site, a pediatric epileptologist confirmed the NES diagnosis, defined as paroxysmal events with semiology inconsistent with seizures due to epilepsy and without associated epileptiform discharges on v-EEG. A child psychiatrist/psychologist conducted a standardized psychiatric interview to confirm the psychogenic origin of the NES and diagnosis of conversion disorder.

2.3. Procedures

2.3.1. Instruments: demographic and family history questionnaire

The parents completed a questionnaire regarding their children's demographic information, medical and neurological illnesses, adversities, and their own marital status.

2.3.2. Psychopathology

Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL). This semi-structured instrument assesses current and past psychiatric diagnoses according to DSM-III-R and DSM-IV criteria [13].

Table 1
Demographic characteristics and psychiatric outcome measures in the PNES and sibling groups.

Variables[a]	PNES probands $N = 55$	Siblings $N = 35$	Statistics[b]	p-Value[b]
Age (years)	14.8 (2.7)	13.5 (2.4)	$t(88) = 2.3$	0.02
Gender				
Females (%)	39 (70.9)	18 (51.4)		0.08
Ethnicity				
Caucasian (%)	33 (60.0)	19 (57.6)		0.83
Family structure[c]				
Single parents	29 (54.7)	18 (55.5)		
Married	24 (45.3)	15 (45.5)		1
Epilepsy (%)	16 (29.1)	0 (0)		0.0002
Internalizing disorders				
Number of internalizing Dx	1.95 (1.18)	0.83 (1.25)	$F(1,87) = 13.5$	0.0004
Presence of internalizing Dx	51 (92.7)	14 (40.0)		0.0001
Anxiety	46 (83.6)	12 (34.3)		0.0001
Depression	24 (43.6)	5 (14.3)		0.005
PTSD	14 (25.5)	1 (2.9)		0.007
Somatization				
Total score	29.97 (19.58)	16.47 (16.94)	$F(1,87) = 11.28$	0.001
Anxiety sensitivity				
Total score	14.39 (7.13)	10.22 (5.57)	$F(1,87) = 8.13$	0.005

[a] Mean (SD) are presented for continuous variables and n(%) are presented for categorical variables.
[b] Statistics and p-values are from t-tests for age, ANCOVAs controlling for age, for other continuous variables and Fisher's exact test for categorical variables.
[c] Data missing for 2 families; single parents includes separated/divorced/widowed/never married.