REVIEW ARTICLE

Psychogenic Nonepileptic Seizures in Children and Adolescents

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Context: Though psychogenic non-epileptic seizures (PNES) are seen commonly during evaluation of children and adolescents with epilepsy, the literature regarding developmental changes in PNES is limited. **Evidence Acquisition:** Literature search was conducted in PubMed. Key search terms included: Pseudoseizure* OR PNES OR [(non-epileptic or nonepileptic or psychogenic or non-epileptic attack disorder) AND (seizure*)], resulting in 3,236 articles. Filters included human, ages 1-18 years, English language and last 15 years (2004-2019), resulting in 533 articles. We reviewed 33 articles, which included 19 articles that involved children (1-18 years), with 10 or more children with PNES in their study group. 21 articles obtained in cross references that were outside the filter setting (including time frame and age range) were also reviewed, for a total of 54 articles. **Results**: Majority of the studies were retrospective. We detail clinical features, predisposing factors and appropriate workup for children and adolescents with possible PNES. There is no consensus regarding frequency of psychiatric comorbidities in children with PNES. No controlled trials of treatment of PNES in children are available, but cognitive behavioral therapy is the consensus for adult PNES. Outcome appears to be better in children with PNES. **Conclusions:** There is a need for be long-term prospective studies to document various clinical features and outcome of pediatric and adolescent PNES, and also the comorbid conditions.

Keywords: Psychogenic seizures, PNES.

Psychogenic nonepileptic seizures (PNES) are a common problem in children and adolescents. They pose difficulties to the pediatrician because of diagnostic uncertainties. PNES are frequently difficult to distinguish from epileptic seizures on clinical grounds. The consequences of misdiagnosing PNES as epileptic seizures are significant. Financial ramifications include the expense of inappropriate, unnecessary costly treatments and needless emergency room visits or hospitalizations. Risk for iatrogenic complications include the adverse effects of unnecessary medications and exposure to invasive procedures such as intubation for management of prolonged events (nonepileptic/pseudo-status epilepticus). Psychosocial sequelae include strain on interpersonal and family dynamics. Most importantly, misdiagnosis results in delay in initiating the much needed psychiatric treatment and may contribute to a poor outcome.

PNES has been described extensively in adults. There remains a relative paucity of literature in the pediatric age. There has been recent progress in understanding the etiology of PNES and in defining appropriate treatments. Unfortunately, most of these studies have been done in adults with PNES

Few studies have assessed the semiology of PNES exclusively in children and even fewer more recent studies have reported differences in the clinical features of PNES between younger children and adolescents, with respect to the semiology of the episodes and types of stressors [1,2]. Studies pertaining to PNES in children reported over the past 15 years have been listed in **Web Table I**.

In this review, we will discuss the clinical manifestations, predisposing factors, and appropriate workup for children and adolescents with possible PNES. We will review the recent literature on semiology, etiology, and treatment, particularly pertaining to children and adolescents.

EPIDEMIOLOGY

Definitions

Psychogenic nonepileptic seizures (PNES) are defined as paroxysmal events of altered movement or behavior that resemble epileptic seizures but are not due to cerebral neuronal dysfunction and are not associated with epileptiform abnormalities on the electroencephalogram (EEG) [3]. They are related to an underlying psychogenic process, thus differing from other paroxysmal nonepileptic events that are physiologic in origin.

A variety of terms have been used in the literature to describe PNES. Previously used terms such as

hysteroepilepsy, pseudoseizures and pseudoepileptic or nonphysiologic seizures are considered pejorative or inappropriate, and have been replaced by more contemporary terms such as nonepileptic attacks, nonepileptic attack disorder and psychogenic nonepileptic seizures (PNES).

In the DSM-5 [4], they are listed in the somatic symptoms disorder section as conversion disorder or functional neurological symptom disorder with attacks. The term dissociative convulsions is used in the ICD 10 [5]. The term PNES, is non-judgmental, and is recommended as the preferred term to be used [6].

Demographics

PNES are common and seen in all age groups. The prevalence of PNES in the general population is estimated to be 2-33/100,000 [7]. They represent 5-20% of outpatient adult epilepsy clinics and 10%-20% of referrals to adult epilepsy centers [7]. However, reported estimates of the incidence or prevalence of PNES may represent an underestimation, as these reports include only cases for which the diagnosis was confirmed by video-electroencephalography (VEEG) [8].

There are no studies of prevalence or incidence of PNES in children. 3.5-20% of children undergoing VEEG monitoring [1,2,9] have PNES and it has been reported in 11-38% of children with all types of paroxysmal non-epileptic events [10,11].

PNES are seen in all age groups. The average age at diagnosis of PNES in children in India was 8 years [12] to 12 years [13], and the average delay in diagnosis was 5 months [14] to 3 years [13]. Overall, there is no significant difference in the demographics of age of onset and delay in diagnosis in the reports from India versus those from the Western world.

PNES are more common in adolescents than in children [15,16]. There is a female preponderance more apparent in adults and adolescents than in children [12,13,17]. Many of these children are given a diagnosis of epilepsy and are mistakenly placed on anti-seizure medications.

CLINICAL DIAGNOSIS

A definitive diagnosis of PNES can be secured if the patient satisfies the 'rule of 2s' consisting of the following three criteria, which yields a positive predictive value of 85% [18,19]:

i) At least 2 PNES per week;

ii) Refractory to at least 2 antiepileptic medications; and

iii) At least 2 EEGs without epileptiform abnormalities.

Accurate and prompt diagnosis of PNES can be a challenging task, especially since a proportion of these patients also have epilepsy. A detailed history is critical and important part of the evaluation. The interview should be customized accordingly.

PNES share some unique common features. These include frequent attacks that have not responded to appropriate medication, specific triggers (e.g. presence of stressors), occurrence of events only when spectators are present and recurrence in a particular setting. A detailed description of the episode by an eye witness or the patient should be obtained. The ready availability of smart phones and other digital recording devices allow for easy acquisition of video recordings as a useful tool in early diagnosis. Observation of the episode at bedside, or in the clinic by the physician aids in differentiating PNES from epileptic seizures and other paroxysmal non-epileptic events.

History of provoking factors, triggers or stressors of the events and associated psychiatric, neurologic and medical disorders should be obtained. There may also be presence of varied symptoms suggesting somatization.

Predisposing Factors (Stressors, Triggers)

A variety of risk factors have been identified as the etiologic basis of PNES. The most common risk factors in the pediatric age group are school related problems, seen in 21-46% of cases [1,14], reported more frequently in the adolescent age group [1,20] and exposure of the child to family dysfunction including parental divorce, sibling hostility and financial stress seen in 42-48% cases [1,14]. Interpersonal conflicts with teachers, peers and friends [1,20] are also seen frequently.

Physical and sexual abuse is reported less frequently in children, ranging from 0-32%, in contrast to a much higher frequency in adults [1,14,16,20,21]. Bereavement has been reported more frequently in adolescents [1]. One study reported a higher rate of suicidal attempts (13.5%) [16]. Self-related problems such as low self-esteem, body image issues and dependency, have also been reported [1,14].

Associated Psychiatric, Neurologic and Medical Disorders

Psychiatric comorbidity is common in children, adolescents, and adults with PNES. In patients of all age groups with PNES, emotional problems have been reported with varying frequency, from 13.8% to 84% [1,12,14-16,22]. The range may be due to differences in assessment for psychiatric comorbidity. Only a limited

number of studies used structured interviews or standard measures.

Depression and anxiety are most common associated psychiatric disorders.in adults with PNES. There is controversy regarding the prevalence of these psychopathologies in children with PNES. In children, major depression ranges from 2.5% [14] to 45% [1,16,22-24]. It is more common in the adolescent age group [1]. Anxiety disorders have also been reported with varying frequencies from 16% [13] to 83% [24]. Bipolar and dysthymic disorder [21], adjustment disorder (8.8%) [14], panic disorder (2.5%) [14], post-traumatic stress disorder [24], separation anxiety and disruptive behavioral problems such as temper tantrums and aggressive behavior have also been reported [1]. Overall, it appears that, in Indian literature, the reported percentages for psychiatric disorders in children with PNES are lower [12-14]. This may be related to cultural differences, variability in referral patterns and limitations related to easy accessibility of psychiatric evaluations in children.

Concurrent epilepsy is seen commonly, occurring with varying frequency from 15-90 % [1,13,15,16] with higher rates noted in children younger than 12 years [1]. Family history of epilepsy is a common finding seen in 25%-43% of patients [1,15]. It is thought that observation of a seizure in a family member may serve as a behavioral model for the child to shape expression of their own conversion symptoms. Frequently, these patients are mistakenly started on anti-seizure medications, and a large percentage ranging from 35-79% were reported to be unnecessarily treated. [1,13,14,25].

Pseudo-status epilepticus may occur and was reported in one study in 13.5% children with PNES [1]. This is a serious problem as it can be associated with iatrogenic complications and considerable distress to the child and family.

Coexisting neurologic illness has been reported in almost half of the children (55%), most frequently cognitive dysfunction (39%) which was significantly more common in the younger children (P<0.0001). Less frequent associated conditions include attention deficit hyperactivity disorder (20.3%), headaches (19%) and past head trauma (10%) [1].

Medical comorbidities have been reported in 7.5% of patients [14]. Children with PNES have more associated medical illnesses than their siblings and have been noted to be on more prescribed as well as over the counter medications than their siblings, suggesting that chronic illness may also act as a stressor for inducing PNES. These children are also exposed to more lifetime adversities such as bullying and domestic or community violence. Parents of children with PNES reported more somatization as compared to parents of children with epilepsy suggesting that this becomes an intergenerational family communication model [20].

ETIOLOGY

From the preceding two sections, one can see that PNES is a heterogeneous disorder with no uniform predisposing factors or comorbidity. Pathways exist for development of PNES. Some children may have significant pre-existing stressors whereas others may have no apparent etiology for PNES. Each child with PNES must be evaluated individually. Nevertheless, there is new information that helps improve understanding PNES. Reuber and Brown, et al. [26] proposed an integrated cognitive model. The motor manifestations of PNES are seen as an instinctual freeze or flight response or a learned motor pattern from experiencing or witnessing a seizure or seizure-like episode. These motor manifestations are triggered by threat or distress. The seizure-like episodes allow escape from the psychological distress and cause parasympathetic activation reducing stress. The seizure-like episodes thus become reinforcing. This neuropsychological model is supported by recent neuroimaging data that have shown changes in the limbic system and in the right inferior frontal cortex, a region involved in motor inhibition [27].

EVALUATION

Clinical

Differentiating PNES from epileptic seizures is the first and important step of the evaluation. Some of the major differences between the clinical features of nonepileptic and epileptic seizures has been summarized in **Table I**. PNES last longer than epileptic seizures in both adults and children [2,8]. Side to side head movements and disorganized, asynchronous, out-of-phase extremity movements suggest PNES. They have a gradual onset and termination, with preservation of consciousness during and immediately after events, even with generalized motor activity. Associated injury, tongue bite (usually involving the tip of the tongue) and urinary incontinence are infrequent. Negative emotions such as weeping, crying, or fear [2,13,14], may occur during and after the event, unlike the monotonous cry heard at the onset of some epileptic seizures. However, negative emotional signs have also been seen with epileptic seizures [28], and therefore does not categorically help with differentiating the two. The PNES episodes are often stereotypic, reported in up to 73% of the cases, suggesting that

Table I Difference in Clinical Features of Psychogenic Nonepileptic Seizures and Epileptic Seizures

	PNES	*Epileptic seizure*
Duration	Prolonged (> 2 minutes)	Briefer
Semiology	Fluctuating (may be stereotypic)	Stereotypic
Onset	Usually gradual	Abrupt
Consciousness	Preserved	Altered (especially with generalized seizures)[a]
Onset	Usually gradual	Abrupt
Head movements	Frequently side to side	Usually unilaterally turned
Extremity	Out-of-phase, bizarre	In-phase, rhythmic movements
Emotional signs	Usually negative (crying)	Cry at onset
Eyes	Closed, resisting eye opening	Open
Pelvic thrusting	Infrequent in children, forward	Retrograde
Incontinence	Rare	May be present
Cyanosis	Absent	May be present
Related injury	Inconsistent with fall	Consistent with fall
Tongue bite	Infrequent (tip)	More common (lateral aspect)
Postictal	None, even after generalized movements	Present (may be absent with frontal lobe seizure)
Other features	Preictal pseudosleep	Absent
	Forced downward eye deviation	Absent
	Postictal whispering	Postictal headache
Reaction	Histrionic	Deeply concerned

[a]*exception supplementary motor seizures.*

stereotypic nature of the episodes does not necessarily always suggest epilepsy [1,13,29].

Other features may also be seen. Commonly, eyes remain closed during the event whereas they are open in epileptic seizures [30], though this may not always be the case. It has been suggested that adolescents and adults who bring stuffed toys to the EMU, were more likely to be diagnosed with PNES and this has been referred to as the "teddy bear sign" [31]. However, this sign has not been found to be always reliable. Geotropic downward eye deviation, ictal stuttering [32], pre-ictal pseudo-sleep [13] and a postictal whispering tone [33] have also been noted.

The semiology of PNES in children differs from adults. Ictal eye closure, events lasting more than 2 minutes, postictal speech change, vocalization during the tonic clonic phase and tongue bite are seen more frequently in adults [29]. Pelvic thrusting is also more common in adults. This is rare in children, and when seen, occurs predominantly in the adolescent age group [13,22].

Varying descriptions of PNES in children are reported in the literature, ranging from unresponsiveness to disorganized motor activity. The features differ by age. Subtle motor activity (similar to hypokinetic or dialeptic seizures), commonly prolonged staring with unresponsiveness, is seen more commonly in children younger than 13 years of age. Prominent motor activity such as generalized arrhythmic jerking or flailing of extremities (similar to hyperkinetic seizures) is seen more frequently in adolescents and is similar to movements seen in adults [1,11,23,29,34]. The subtle behaviors noted in the younger children are more likely to be mistaken for epileptic seizures, thus contributing to a delay in diagnosis in the younger children as compared to the more overt, disorganized motor activity seen in adolescents.

One report further differentiates features of PNES in adolescents based on gender. Boys were more likely to demonstrate convulsive tonic-clonic like movements, whereas girls were more likely to experience atonic falls. Boys reported academic struggles significantly more frequently than girls, and girls more commonly reported difficulties with peer interactions. ADHD was more common in boys and major depression was more common in girls [22].

Electroencephalography and Laboratory Studies

Prolonged VEEG remains the gold standard of

evaluation. Recording of the habitual event of clinical concern that is not associated with epileptiform abnormalities on the EEG, along with the appropriate historical data, points to a diagnosis of PNES. If the initial study is normal and induction techniques fail to elicit an event, it would be very reasonable to consider repeating the study.

There exists a controversy regarding the use of provocative techniques. These have included placebo induction with intravenous saline, tuning fork and use of skin patches. However ethical concerns have been raised, given that these techniques involve deception, and risk compromise of patient-physician trust. Hyperventilation, photic stimulation and verbal suggestion were deemed more appropriate because these techniques are also used to induce epileptic seizures [35].

Short term VEEG along with induction techniques may be a reasonable option, especially in areas with limited resources [14,36]. It is more cost-effective, and more time efficient. However, interictal epileptiform abnormalities could potentially be missed. Therefore, it is not diagnostic for assessment of co-existing epilepsy.

The following measures have been studied but may only be considered ancillary and are certainly not diagnostic. Biologic markers such as serum prolactin have been studied in adults, with mixed results. Elevated postictal serum prolactin levels, 10-20 minutes after an event have been reported following generalized tonic clonic seizures. However, lack of elevation is not conclusive of PNES, as normal levels are also seen with other seizure types such as focal seizures and absence seizures [37,38]. Similarly, alterations in serum lactate levels [39] and serum creatine kinase (CK) levels [40] have also been studied but are not used routinely. Several other biomarkers that are still being investigated including Neuron specific enolase (NSE) and serum NT-proCNP (a fragment of C-type natriuretic peptide) [41].

Psychological Evaluation

The psychological assessment of the child with suspected PNES starts with a history, ideally taken form the parent and the child or adolescent separately. Questions about anxiety and depression are essential. Some children with PNES may have alexithymia, an inability to recognize emotions. Stress and trauma related disorder are covered with questions about discord at home, bullying or academic difficulties at school, and exposure to violence or displacement in the community. Screening instruments for emotional and behavioral problems such as the widely available Strengths and Difficulties Questionnaire, a free 25-item questionnaire normed for 4 to 16 year old children and available in multiple languages including Bengali, Hindi, Punjabi, Tamil, and Urdu, can be helpful. If academic difficulties are found, the child may need intellectual and achievement testing [42].

TREATMENT

Following the diagnosis of PNES, there should be immediate involvement with a mental health professional such as a therapist, psychologist, or psychiatrist who is familiar with this condition. The diagnosis should be presented to the parents by the clinician (pediatricians/ pediatric neurologist), reassuring the family that a diagnosis has been made and that the child has a type of disorder that will not require anti-seizure medications but will need mental health treatment. A similar discussion occurs next with the child. When possible, the pediatrician should offer to continue to be involved in care of the child.

Treatment should be multidisciplinary and include the mental health professional, the child, parents, school, and a pediatrician/ pediatric neurologist [19,43-45]. The first step of treatment is providing psychoeducation regar-ding PNES to the family and school [19,44]. Many children diagnosed with PNES have a decrease in their daily functioning. Therefore, gradual increase in their participation in school, extra-curricular activities, social interactions, etc. to return to previous level of activity and functioning is recommended. In order to increase the patient's success in school, accommodations should be implemented to minimize school absences [44]. Both the school and the parents should be taught selective attention (ignoring the episodes) and be given specific instructions of how to react to the episodes. For example, once the school and parents, have understood the concept that there is no underlying organic cause for the PNES, they need not seek emergency medical care for every subsequent episode. However, they should make efforts to ensure the patient is safe and will not sustain injury during a PNES. Parents and the school should be encouraged to decrease conversations regarding the PNES and provide positive attention to adaptive functioning [44].

Cognitive behavioral therapy (CBT) has empirical support for treatment of adults with PNES though not children [19,44]. A controlled trial in adults with PNES, showed decrease in seizure number [46]. In contrast, a recent controlled study of 368 adults found no reduction in seizure number but improvement in quality of life and psychosocial functioning [47]. We think that CBT may be helpful in children and adolescents with PNES, particularly when associated with anxiety or depression. In individual therapy, the child learns cognitive and

behavioral strategies to reduce episodes. The patient is taught how the body and mind are connected and is provided psychoeducation regarding how thoughts influence emotions, behavior, and somatic symptoms. The patient learns to identify these emotions and the associated somatic symptoms. The patient is then taught relaxation skills and mindfulness strategies to manage distress. The therapist teaches the patient to identify unhelpful thoughts (automatic thoughts) and how to label negative thinking patterns (cognitive distortions). The patient then learns how to challenge and change these unhelpful thoughts to positive thoughts through the use of cognitive techniques. As the patient changes these thoughts, there is an increase in positive emotions, thereby decreasing PNES. In addition to challenging thoughts, patients learn problem solving, exposure and response prevention, and activity scheduling [44]. Through a combination of parent and school interventions, teaching the child distress tolerance skills and cognitive restructuring, and resuming previous levels of functioning, the PNES should usually decrease.

OUTCOME

Though there are very few systematic studies reporting on the treatment of PNES in children, outcomes in children have been reported as more favorable than in adults [48-50]. According to a recent study, 36% of 90 children (5-18 years) with PNES who were followed up till 2 years, were symptom free at 6 months with sustained remission at 2 years. Another 33% did not achieve remission and this unfavorable outcome was attributed to delay in establishing their diagnosis and presence of comorbid epilepsy [50]. Chinta, et al. [49] reported that 35% were symptom free and an additional 50% experienced more than 50% reduction in frequency of symptoms on short-term follow-up of 3-6 months. Better outcome in these children was related to earlier diagnosis with lack of chronicity of complaints, as well as less severe associated psychiatric comorbidities.

CONCLUSIONS

There are still unmet needs. There should be more comprehensive assessment of comorbidity in children with PNES. There seems to be heterogeneity in the predisposing and precipitating factors for PNES occurrence in children. This might dictate difference in treatments. Advanced neuro-imaging techniques have been used to study adults with PNES and other functional neurological disorders but there is limited information on changes in children and adolescents. There are currently no controlled trials of treatments for children with PNES. Finally, outcome appears to be better in children with PNES, but there needs to be long-term follow ups for both PNES and the comorbid conditions. Families also need additional study for factors that may provoke or maintain PNES in children or assist with satisfactory resolution.

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