Epilepsy & Behavior 90 (2019) 90–92

Contents lists available at ScienceDirect

Epilepsy & Behavior

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

Psychogenic nonepileptic seizures in children and adolescents: An international cross-cultural study

Ali A. Asadi-Pooya [a,b,*], Raidah AlBaradie [c], Tyson Sawchuk [d,e], Zahra Bahrami [a], Abeer Al_Amer [c], Jeffrey Buchhalter [d,e,f]

[a] Neurosciences Research Center, Shiraz Medical School, Shiraz University of Medical Sciences, Shiraz, Iran
[b] Jefferson Comprehensive Epilepsy Center, Department of Neurology, Thomas Jefferson University, Philadelphia, PA, USA
[c] King Fahd Specialist Hospital, Dammam, Saudi Arabia
[d] Children's Comprehensive Epilepsy Center, Alberta Children's Hospital, Calgary, Canada
[e] Alberta Children's Hospital Research Institute, Calgary, Canada
[f] Cumming School of Medicine, University of Calgary, Alberta, Canada

ARTICLE INFO

Article history:
Received 12 October 2018
Revised 12 November 2018
Accepted 12 November 2018
Available online 2 December 2018

Keywords:
Adolescents
Children
Nonepileptic seizures
PNES
Psychogenic

ABSTRACT

Purpose: We compared various clinical characteristics of psychogenic nonepileptic seizures (PNES) between young patients from Iran, Saudi Arabia, and Canada, three nations with significantly different socioeconomic and demographic characteristics. This international cross-cultural comparative study may advance our knowledge and understanding of PNES in children and adolescents across the cultures and borders.
Methods: In this retrospective study, we investigated all patients 16 years of age or younger, with PNES admitted to the epilepsy monitoring units at one center in Iran, one center in Saudi Arabia, and one center in Canada. Age, gender, age at seizure onset, seizure semiology, seizure frequency, factors potentially predisposing to PNES, and video-electroencephalography (EEG) recording of all patients were registered routinely and compared between the nations.
Results: Fifty-one patients were studied (22 from Iran, 14 from Saudi Arabia, and 15 from Canada). Age at the diagnosis was 13.4 ± 2.2 years (range: 8–16 years), and age at the onset of seizures was 12.3 ± 2.7 years (range: 5–16 years). Demographic and clinical characteristics of and associated factors in the patients among the three nations were not significantly different. Twenty-six (51%) patients were taking antiepileptic drugs at the time of diagnosis; the difference was not statistically significant between the nations (13 patients in Iran, 6 in Saudi Arabia, and 7 patients in Canada; $P = 0.5$).
Conclusion: Young patients with PNES across borders and between cultures share more similarities than differences with regard to their demographic and clinical characteristics.

1. Introduction

Psychogenic nonepileptic seizures (PNES) tend to begin in young ages, although the seizures can begin at any ages; there are reports about PNES in children as young as five years [1–5]. In one study of juvenile- and adult-onset PNES, age at onset did not correlate with clinical manifestations, although factors potentially predisposing to PNES were different in patients with juvenile-onset compared with those with adult-onset PNES (e.g., history of being abused, academic failure, epilepsy or family history of epilepsy were more frequent in patients with juvenile PNES while medical comorbidities were more frequent among patients with adult-onset PNES) [2]. Therefore, investigating clinical characteristics of PNES in children and adolescents could be revealing and may shed light on important aspects of PNES in this age group.

There are only few studies on the cross-cultural and international differences of PNES in the literature [6]. In specific, comparative studies on the cross-cultural and international differences of PNES in children and adolescents do not exist in the literature. Psychogenic nonepileptic seizures occur in a heterogeneous patient population with common social life experiences (e.g., sexual abuse or physical abuse) and psychiatric comorbidities [1]. Therefore, it is plausible to assume that there would be differences and clinical variability in different cultures and among different nations. In the current study, we compared various clinical characteristics of PNES between young patients from Iran, Saudi Arabia, and Canada, three nations with significantly different socioeconomic and demographic characteristics. This international

* Corresponding author at: Neuroscience Research Center, Shiraz Medical School, Shiraz University of Medical Sciences, Shiraz, Iran.
E-mail addresses: aliasadipooya@yahoo.com (A.A. Asadi-Pooya), raidah_albaradie@hotmail.com (R. AlBaradie), tyson.sawchuk@albertahealthservices.ca (T. Sawchuk), bahrami.zahra1368@gmail.com (Z. Bahrami), dr.abeer1409@gmail.com (A. Al_Amer), jeffrey.buchhalter@albertahealthservices.ca (J. Buchhalter).

https://doi.org/10.1016/j.yebeh.2018.11.005
1525-5050/

cross-cultural comparative study may advance our knowledge and understanding of PNES in children and adolescents across the cultures and borders.

2. Methods and materials

In this retrospective study, we investigated all patients 16 years of age or younger with PNES admitted to the epilepsy monitoring units at one center in Iran (i.e., Shiraz Comprehensive Epilepsy Center, from 2008 to 2018), one center in Saudi Arabia (i.e., Comprehensive Epilepsy program, King Fahd Specialist Hospital, Dammam, from 2009 to 2016), and one center in Canada (i.e., Comprehensive Children's Epilepsy Center at Alberta Children's Hospital, from 2009 to 2015). Epileptologists with experience in making the diagnosis of seizures confirmed the diagnosis when the typical seizures were captured on video-EEG monitoring and no epileptiform activity before, during, or after the seizure was captured. There were no exclusions.

The epileptologists and psychologists interviewed all the patients, and if they agreed to share their information in the study, it was used. All the data were kept confidential. Age, gender, age at seizure onset, seizure semiology, seizure frequency, factors potentially predisposing to PNES [history of physical abuse (i.e., corporal punishment or any physical injury resulted from aggressive behavior towards the patient), sexual abuse (rape), child abuse (i.e., neglect), dysfunctional family (i.e., divorce, single parent, etc.), academic failure, any medical comorbidities, and family history of epilepsy], and video-EEG recording of all patients were registered routinely. We classified the psychogenic seizures into four distinct classes, as follows:

1. Generalized motor: seizures mainly characterized by tonic, clonic, or dystonic generalized movements, tremors, rigor-like movements, whole body rigidity, pelvic thrusting, pedaling, and/or side-to-side head movements.
2. Akinetic: seizures mainly characterized by unresponsiveness and the absence of movement. Minor distal limb tremors were permitted.
3. Subjective symptoms: seizures were mainly characterized by experiential phenomena reported by the patients. Eyelid myoclonia and minor distal limb tremors were permitted.
4. Focal motor: seizures with focal movements.

Demographic variables and relevant clinical variables were summarized descriptively to characterize the study populations. The Pearson Chi-Square, one-way Analysis of Variance (ANOVA), and Bonferroni correction tests were used for statistical analyses. P value less than 0.05 was considered significant. This study was conducted with the approval by Institutional Review Boards of all centers.

3. Results

Fifty-one patients were studied (22 from Iran, 14 from Saudi Arabia, and 15 from Canada). Age at the diagnosis was 13.4 ± 2.2 years (range: 8–16 years), and age at the onset of seizures was 12.3 ± 2.7 years (range: 5–16 years). Table 1 shows the demographic characteristics of the patients. Table 2 describes the clinical characteristics of seizures in the patients. Table 3 shows the associated factors in the patients among three nations. Thirty-nine patients (76%) reported auras before their seizures; the most common types of auras were dizziness (10 patients; 20%) and headache (9 patients; 18%). Twenty-six (51%) patients were taking antiepileptic drugs at the time of diagnosis; the difference was not statistically significant between the nations (13 patients in Iran, 6 in Saudi Arabia, and 7 patients in Canada; P = 0.5).

Table 1
Demographic characteristics of children and adolescents with PNES in three nations.

Demographic characteristic	Iran	Saudi Arabia	Canada	P value
Sex ratio (female:male)	13:9	10:4	9:6	0.7
Age at diagnosis (years)	14.2 ± 1.9	12.1 ± 1.8	14.1 ± 2.2	0.01
Age at onset (years)	12.9 ± 2.3	10.7 ± 2.8	13.5 ± 2.5	0.03*
Delay in diagnosis (years)	1.3 ± 2.2	1.2 ± 2.2	0.4 ± 1	0.3

* Loses its significance after Bonferroni correction.

Table 2
Clinical characteristics of seizures in children and adolescents with PNES in three nations.

Clinical characteristic	Iran	Saudi Arabia	Canada	P value
Aura before seizures	16	8	15	0.02*
Unresponsiveness	17	8	12	0.3
Prolonged seizures (>10 min)	5	3	5	0.7
Urine incontinence	2	1	0	0.5
Nocturnal seizures	3	2	2	0.9
Ictal injury	3	0	3	0.2
Generalized motor seizures	16	6	8	0.2
Akinetic seizures	4	5	5	0.3
Subjective seizures	1	2	3	0.3
Focal motor seizures	1	0	2	0.3
Seizure frequency (per month)	197 ± 650	44 ± 41	39 ± 53	0.4

* Loses its significance after Bonferroni correction.

4. Discussion

This study investigated 51 children and adolescents with PNES across the borders and between the cultures. The demographic variables of the patients with PNES, particularly the sex ratio of the patients, were more or less similar between these three nations (Iran, Saudi Arabia, and Canada). Age at onset was statistically earlier in patients from Saudi Arabia, but the difference did not look clinically significant (11 versus 13 years; adolescence in all nations); in addition, it lost its significance after Bonferroni correction. Seizure characteristics, with the exception of auras, were very similar between these patients. The significant finding that preictal aura was reported more often among the Canadian sample (100% of them) may reflect the differences in clinical assessment practices between the nations, rather than semiology variability; in addition, it lost its significance after Bonferroni correction. Most of the auras described in the Canadian dataset related to self-reported autonomic features of anxiety (e.g., hyperventilation, chest pain, etc.), which were carefully explored during standardized assessment by a clinical psychologist embedded within the epilepsy monitoring unit. Seizure types and dramatic seizure manifestations (e.g., ictal injury, prolonged seizures, and urinary incontinence) were similar between patients from these three nations. Factors potentially predisposing to PNES had also similar patterns between these patients.

Studies on the cross-cultural comparisons of PNES are scarce. In one previous study of 89 adult patients with PNES (49 from the USA and 40 from Brazil) [6], the authors observed that patients from the two countries were not significantly different with regard to sex and age, but patients from Brazil had earlier age at onset (26 years vs. 34 years; P = 0.004). Some characteristics of seizures were different between patients from the two nations; patients from the USA had generally more seizure types and more often reported subjective seizures (55% in the USA vs. 10% in Brazil; P = 0.0001). However, clinical and historical characteristics of the patients were not significantly different [6]. These findings

Table 3
Associated factors in children and adolescents with PNES in three nations.

Associated factor	Iran	Saudi Arabia	Canada	P value
Family history of seizures	10	4	2	0.1
History of physical abuse	5	0	0	0.02*
History of sexual abuse	2	0	1	0.5
History of child abuse	1	0	0	0.6
Dysfunctional family	7	2	7	0.1
Academic failure	8	4	6	0.8
Comorbid epilepsy	6	1	6	0.1

* Loses its significance after Bonferroni correction.

from an adult study are very similar to the findings from the current study on children and adolescents. It appears that patients with PNES across borders and between cultures share more similarities than differences. These findings might endorse the concept that PNES may result from neurobiological dysfunctions at specific brain networks and abnormal connectivity of the networks [7]. Researchers may learn more about the pathophysiology of PNES by investigating the effects of genetic factors, intrinsic factors, and environmental factors on functional and structural brain connectivity, particularly in multicenter international studies.

Interestingly, delay in making a final diagnosis of PNES was much shorter in all three nations compared with that in most previous adult studies (approximately, 1 year in this study versus 5 years in adults) [8]. This is similar to a previous study on children, in which the median delay in making the diagnosis was 5 months [4]. Although PNES are one of the most common and important differential diagnoses of epilepsy, misdiagnosis and delay in making a definite diagnosis are common. As a result, patients with PNES are at risk of iatrogenic harm, as they are more likely to receive unnecessary treatments (e.g., antiepileptic drugs) [8–11]. In our study, about half of the patients were taking antiepileptic drugs at the time of diagnosis, and the difference was not statistically significant between the nations; this was similar to the finding from a previous study [4]. Early and definitive diagnosis of PNES has prognostic significance with regard to outcome, because it can lead to appropriate therapy [12]. In one previous study [5], outcome was less favorable in children/adolescents who presented with chronic PNES and in those with a chronic comorbid mental health disorder that failed to resolve with treatment. This highlights the significance of early diagnosis in suspected patients, followed by prompt multidisciplinary assessment, engagement, and treatment plans [5,13].

In conclusion, young patients with PNES across borders and between cultures share more similarities than differences with regard to their demographic and clinical characteristics. This study has some limitations including its retrospective design, lack of some important data such as psychiatric comorbidities of the patients, and a relatively small sample size. In addition, because of existence of different definitions for child molestation in different cultures, we considered sexual abuse as rape only; this would cause underestimation of the real frequency of sexual abuse in this study.

Conflict of interest

Ali A. Asadi-Pooya, M.D.: Honoraria from Cobel Daruo; Royalty: Oxford University Press (Book publication). Others have no conflict of interest.

Acknowledgment

This was a nonfunded study.

References

[1] Asadi-Pooya AA, Sperling MR. Epidemiology of psychogenic non-epileptic seizures. Epilepsy Behav 2015;46:60–5.
[2] Asadi-Pooya AA, Emami M. Juvenile and adult-onset psychogenic non-epileptic seizures. Clin Neurol Neurosurg 2013;115(9):1697–700.
[3] Szabó L, Siegler Z, Zubek L, Liptai Z, Körhegyi I, Bánsági B, et al. A detailed semiologic analysis of childhood psychogenic non-epileptic seizures. Epilepsia 2012;53:565–70.
[4] Madaan P, Gulati S, Chakrabarty B, Sapra S, Sagar R, Mohammad A, et al. Clinical spectrum of psychogenic non epileptic seizures in children; an observational study. Seizure 2018;59:60–6.
[5] Kozlowska K, Chudleigh C, Cruz C, Lim M, McClure G, Savage B, et al. Psychogenic non-epileptic seizures in children and adolescents: part II — explanations to families, treatment, and group outcomes. Clin Child Psychol Psychiatry 2018;23(1):160–76.
[6] Asadi-Pooya AA, Valente K, Alessi R, Tinker J. Semiology of psychogenic nonepileptic seizures: an international cross-cultural study. Epilepsy Behav 2017;75:210–2.
[7] Asadi-Pooya AA. Neurobiological origin of psychogenic nonepileptic seizures: a review of imaging studies. Epilepsy Behav 2015;52(Pt A):256–9.
[8] Asadi-Pooya AA, Tinker J. Delay in diagnosis of psychogenic nonepileptic seizures in adults: a post hoc study. Epilepsy Behav 2017;75:143–5.
[9] Kerr MP, Mensah S, Besag F, de Toffol B, Ettinger A, Kanemoto K, et al. International consensus clinical practice statements for the treatment of neuropsychiatric conditions associated with epilepsy. Epilepsia 2011;52:2133–8.
[10] Valente KD, Alessi R, Vincentiis S, Santos BD, Rzezak P. Risk factors for diagnostic delay in psychogenic nonepileptic seizures among children and adolescents. Pediatr Neurol 2017;67:71–7.
[11] Asadi-Pooya AA, Emami M. Reasons for uncontrolled seizures in children; the impact of pseudointractability. Epilepsy Behav 2012;25(3):341–4.
[12] Farias ST, Thieman C, Alsaadi TM. Psychogenic nonepileptic seizures: acute change in event frequency after presentation of the diagnosis. Epilepsy Behav 2003;4:424–9.
[13] Sawchuk T, Buchhalter J. Psychogenic nonepileptic seizures in children — psychological presentation, treatment, and short-term outcomes. Epilepsy Behav 2015;52(Pt A):49–56.