

PNES Epidemiology: what is known, what is new?

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Structured abstract

Psychogenic non-epileptic seizures (PNES) are clinically defined as events resembling epileptic seizures but presumed to be not conscious and an involuntary expression of emotional distress similar to panic attacks. Their neurobiological physiopathology is different. However, PNES-like states are recognized in some cultures as a cultural phenomenon.

PNES rank among the top three neuropsychiatric problems and are targeted by an International League Against Epilepsy Task Force that published in 2017 an actualization concerning PNES epidemiology renewing the interest concerning PNES. Studies concerning PNES are complicated: these patients are difficult to identify, and a have tendency to disengage from medical services after diagnosis.

The incidence and prevalence estimates in the literature are based on diagnoses from tertiary care epilepsy monitoring units, where approximately 20 to 40% of adult patients and 10 to 23% of children presenting with "drug-resistant epilepsy" are diagnosed with PNES, making the incidence of PNES to be 1.4–4.9 cases per 100,000 people per year and the prevalence range of 2–33/100,000 However, epilepsy can be associated with PNES with estimated comorbidity range from 5 to 50%.

75% of patients with PNES are young adult women. PNES are uncommon under 6 and after 50 years of age. The female predominance is classically not found in children, late-onset or intellectual disability (ID) subgroups (about 10% PNES patients). Psychiatric comorbidities such as anxiety, post traumatic stress disorders and history of trauma are frequent in PNES patients.

One recent change concerning the epidemiology of PNES is the awareness that this condition is present worldwide, and not only in western developed countries.

Highlights

- 1) PNES epidemiology study is of growing interest after ILAE task force publication.
- 2) PNES are found worldwide and sometimes recognized as a cultural phenomenon.
- 3) New studies are warranted to improve PNES epidemiology knowledge worldwide.

Keywords

PNES, depression, epilepsy, anxiety, epidemiology, functional disorder.

INTRODUCTION

Psychogenic Non-Epileptic Seizures (PNES) are clinically defined as events resembling epileptic seizures but presumed to be not conscious and involuntary expression of emotional distress similar to panic attacks. They mimic epileptic seizures, but their neurobiological physiopathology is different. PNES are the most common type of conversion disorders or functional neurologic symptom disorders, both terms used interchangeably in the Diagnostic and Statistical Manual - Fifth Edition (DSM-5) (1). The Scottish Neurological Symptom study (2) stated that functional and psychological symptoms are the second most frequent referral symptom in neurology (after headache), PNES being the most frequent motive in this category.

The International League Against Epilepsy (ILAE) established that "gold standard" diagnosis of PNES is based on a history consistent with PNES and the recording of a typical event with semiological features of PNES such as resistance to eye opening but no epileptiform activity on the electroencephalogram (EEG) **before, during, or after** the ictus. The combination of a history, semiology, and video EEG findings consistent with PNES provides the level "**documented**" PNES (3).

It is estimated that 20–30% of patients referred to epilepsy centers with intractable seizures have been misdiagnosed with epilepsy. The vast majority of these patients are eventually diagnosed with PNES (4).

An international consensus clinical practice statement issued in 2011 (5) ranked PNES among the top three neuropsychiatric problems : Assessment and management of nonepileptic seizures and imitators of epilepsy was preceded by assessment and management of depressive disorders in epilepsy and assessment and management of concomitant anxiety disorders in epilepsy. Followingly, an ILAE PNES Task Force published in 2017 an actualization concerning PNES epidemiology in adults and in patients subgroups, such as children, older adults, and those with intellectual disability (3). We searched PubMed central using the keywords "psychogenic non epileptic seizure", "PNES", "epidemiology" on August 27th, 2019. We obtained 122 results. We selected among the results reviews and studies in French or English that we considered of interest, concerning aspects of PNES epidemiology. We were careful that the methodology of PNES diagnosis in the selected papers used Video-EEG exploration.

Findings

PNES epidemiology is a topic of growing interest. The most ancient publication we found dated from 1984. Between 1984 and 2009, there were less than 10 publications per year. This number increased in the last years with a maximum of 25 publications in 2018.

PNES are a topic of interest not only from the medical and caregiver point of view but also from the societal and economical health aspect. Studies concerning PNES **medico-economic consequences** report a heavy burden for healthcare systems and societies at large, as well as for affected individuals and their families (6). The lack of money for treatment concerns 70% and 50% of the low and middle-income countries respectively and is identified as one of the major hurdles to the diagnoses and treatment of PNES (7). In addition to the direct healthcare costs associated with PNES, indirect costs to patients and caregivers caused by loss of employment and reduced availability for household work have great societal impact (8). Several studies have found that direct healthcare costs decline following the diagnosis of PNES because of substantial reductions in healthcare resource utilization (9)(10).

The early reduction in healthcare use is often sustained over the longer term, although long-term employment outcomes do not seem favorable (11) (12).

Studying PNES epidemiology is complicated. One major recent improvement is the publication of clearly defined diagnostic criteria after ILAE interest in this domain, that allowed to harmonize PNES patient's definition around the world.

PNES **diagnosis delay** from first seizure to definitive diagnosis of PNES is usually reported (13) (14)(15) (16) between 3 and 8,4 years. Two recent studies (15) (17) noticed that the presence of antiseizure medication is associated with longer diagnostic delay (odds ratio 6,1) and each anti-seizure medication trial extends this diagnostic delay. Younger age at onset and the presence of ictal injury (odds ratio 3,6) are also associated with longer diagnostic delay in PNES patients (17). This long diagnosis delays and a tendency for patients with PNES to disengage from medical services after diagnosis are two issues that make patients with PNES disorders difficult to identify, even in developed countries.

One limitation concerning PNES epidemiology, clearly underlined by ILAE, is the absence of wellresourced, formal population-based epidemiological studies. Most estimates of the **incidence and prevalence** in the literature are based on diagnoses from tertiary care epilepsy monitoring units (EMU), where approximately 20 to 40% of adult patients and approximately 10 to 23% of children presenting with "drug-resistant epilepsy" are diagnosed with PNES (18)(19) (20) (21). A study in Tanzania (22) observed a higher proportion with half the patients referred to a tertiary medical center with functional neurological disorders presenting PNES. A study by Salinsky et al. indicated that up to 25% of veterans entering epilepsy monitoring units were finally diagnosed with PNES (23).

The incidence of PNES has recently been determined to be 4.09/100,000 in a study based in the United Kingdom (24). Other studies estimated the incidence of PNES to be 1.4–4.9 cases per 100,000 people per year (25) (26).

Two prevalence estimates are suggested by ILAE (3): one based on the number of patients referred to epilepsy centers who are thought to have severe epilepsy but who turn out to have PNES. This solution yields a possible prevalence range of 2-33/100,000 (0.002-0.033%) (27).

The second one is based on the assumption of a similar long-term course for PNES and epilepsy and an extrapolation from incidence figures. Following this approach, an incidence figure of 5/100,000/year would yield an estimated prevalence of approximately 1/10 that of epilepsy, or 5/100,000.

There is a **predominance of female gender** among patients with PNES with a ratio classically considered of 3 to 1 in favor of women. This may vary as published in a recent study concerning 330 patients retrospectively included over 10 years (17), in which sex ratio was only 1,89 in favor of women. The female sex preponderance occurs after puberty but is also found in some pediatrics studies (28) and does not vary with the country development status ((7),(29) (30) (31). This sex ratio is also found in other conversion disorders such as functional movement disorders (32). Neurobiological, social and vulnerability differences may explain why PNES are predominantly seen in female gender (33)(34) (35) (36)(37) : many of the PNES risk factors are more common in women (1). Studies have reported differing but high rates of previous sexual abuse in women with PNES in Eastern and Western countries (38) (39) (21) (30). (33). Yet, one study comparing men and women with PNES found similar overall rates of psychiatric comorbidity between the two genders (40). Interestingly, another study using a personality profile evaluation showed worse emotional adjustment in men compared with women with PNES (41).

The clinical course of PNES in men and women may differ : a recent study including 41 video-EEG diagnosed PNES patients found that PNES started later in women compared to men (24,3 versus 17,5 years), with longer PNES episode duration in women (10 versus 2 minutes) and no gender specific difference in the semiologic expression of PNES (42).

PNES occur mainly in **young adults** (second and third decades) but are also reported **in children** (43). A recent study in Brazil (28) about 53 children aged between 7 to 17 with video-EEG documented PNES showed an average delay until referral of 17,76 month (elongating with an earlier age of onset), and a female predominance (60,4%). However, there is a lack of population-based data on the prevalence or incidence of PNES in the pediatric population.

Studies of children up to 12 years of age have identified the following patient characteristics:

- PNES have been reported from the age of 3 years but are uncommon under 6 years of age (44);

- Unlike in adults, there is no female predominance (45);
- Motor inhibition (dialeptic attacks) are more common than hyper-motor-type events (46) (47);
- A history of physical or sexual abuse is reported less commonly by pediatric than by adult patients (43);
- School phobia or difficulties in school (including bullying, specific learning difficulties, or unrealistic expectations) are the most common precipitating or perpetuating factors (43);
- A better outcome for children than for adults with PNES (48).

Concerning older patients, PNES are uncommon after the age of 50 years and little is known about patients with **late onset PNES**. In Duncan et al. (24) cohort, late onset PNES were more likely to be male, less likely to report history of sexual abuse and more likely to have severe physical health issues and to report health-related traumatic experiences. PNES semiology and mental health status seemed similar between early and late onset PNES.

Psychiatric comorbidities are very common in PNES, with estimates ranging between 53 and 100% of PNES patients with at least one comorbid psychiatric disorder (49).

When compared to patients with conversion disorders such as functional movement disorders (32), PNES patients have more anxiety disorders (56% versus 44%), and similar rates of mood disorders. Study using personality measure scales (such as the Personality Assessment inventory) (50)(51) have found significantly higher somatic, conversion, depressed, anxious and suicidal symptoms in PNES patients.

In comparison with epileptic patients, PNES patients have significantly elevated risks found for Post-Traumatic Stress Disorder (PTSD), personality disorder, and anxiety but not depression (52) but this result is not consistent in every study (53). In a recent review (53), considering only video EEG proven PNES and ES, Walsh et al. concluded that PNES patient's depression level was better explained by interpersonal factors whereas epileptic patient's depression level were influenced by illness related factors. When PNES are associated with depression (21% to 60% patients) (54), patients have lower level of functioning and worse quality of life (55) (56). The reduction in quality of life experienced by people with PNES is well documented and is a major global public health issue (57).

Traumatic life experiences in childhood or adulthood are associated with PNES :

Adverse childhood experiences have been identified as a factor predisposing to the development of PNES in later life (58) (59). Childhood sexual abuse is reported between 5,9 to 84,6% PNES patients (PNES patients are three time more likely to report sexual abuse than controls) (59). In a study comparing subjects with epilepsy or PNES, using the 28-item brief screening version of the Childhood Trauma Questionnaire, the prevalence of childhood trauma was significantly higher (36% vs 16%) in PNES patients than epilepsy patients (60). Patients with PNES scored significantly higher across all childhood trauma domains, including emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. Patients with PNES and a history of childhood repeated trauma have more frequent dissociative experiences and psychiatric comorbidities, with an association between their psychiatric symptoms and diagnosis criteria of complex PTSD (61).

Concerning trauma in adulthood, a review of 7 studies by Fiszman et al (38) indicated that 82,6% PNES patients report trauma in adult life ("general traumatic events other than abuse") (38). Among veterans, in a retrospective study including 50 PNES confirmed patients, PTSD was the most frequent DSM-axis 1 diagnosis preceding admissions (58%), followed by depression (46%) and alcohol abuse. These axis 1 diagnosis were frequently associated in those patients (34% had all 3 diagnoses and 58% had at least 2). In addition, 36% patients had a personality disorder (62).

PNES clinical presentation is close from epileptic seizure. Video-EEG is key to differential diagnosis between those conditions. However, it is not unusual to find both epileptic seizure and PNES in a single patient : the **association of PNES and epilepsy** is not consistently reported in the literature, with estimates ranging from 5 to 50% (21) (27) (63) (64) (65) (66) (18) (67) (68). The criteria for diagnosis of concomitant epilepsy are not consistent among studies. Some considered interictal spikes sufficient to define epilepsy even if interictal epileptiform abnormalities have been reported in nonepileptic conditions (69) and even in normal people (67).

After temporal lobe epilepsy surgery, patients presenting with epileptic seizures and PNES improve in both (70), but rarely PNES occur de novo after epilepsy surgery (>5%).

A recent study from Wissel et al. (71) used video-EEG proven events to separate patients with combined epileptic (ES) and psychogenic nonepileptic seizures (PNES) and age- and gender-matched patients with ES-only and PNES-only. The study (138 patients) showed that in patients with PNES and ES, ES antedated PNES in 70% cases. The PNES-ES patients had higher depression and anxiety scores and had more often epileptic discharges originating the right hemisphere.

The proportion of patients with **PNES and comorbid intellectual disability (ID)** is similar to that of patients with PNES and additional epilepsy (i.e., about 10%) (72) (73). In a recent study (74) that focused on patients living at an epilepsy day-care facility in the Netherland, the prevalence of PNES in patients with ID was 7,1%.

One study focusing on patients with PNES and ID suggested differences from patients with PNES without ID : trend towards a male preponderance, relative paucity of antecedent sexual abuse, frequent episodes of psychogenic nonepileptic status, as well as a greater proportion of patients in whom situational or emotional triggers immediately preceding individual PNES were reported (75). Another study (74) showed that they had more depressive symptoms, experienced more negative life events and had more often an ID discrepancy (ID profile with one domain particularly more impaired than another).

Gates and Erdahl proposed "a reinforced behavior pattern" as a particularly important pathogenetic factor leading to PNES in patients with comorbid ID (76) (77).

Unfortunately, no other data are available about PNES in these specific subgroups from less highly developed regions of the world. (3)(78).

Discussion:

PNES is a chronic and not rare medical condition that implies long term care and follow-up.

Before PNES diagnosis criteria were clearly defined, PNES patients were mistakenly thought to have drug resistant epilepsy and were treated with anti-seizure medication (62). After ILAE interest in this

condition, our knowledges are increasing with numerous studies associating neurologists, psychiatrists, and epilepsy specialists located around the world.

The sex ratio in favor of women, the highest prevalence among young adults, the association with a history of trauma and psychiatric comorbidities is more and more established. Our knowledges concerning PNES in less frequent patients' subgroups such as children, older adults, or ID subjects improve slowly.

The better knowledge of PNES patients' characteristics improves our understanding of this condition. In a study that investigated and compared psychiatric features of 25 consecutive patients with PNES on the basis of presence of reported trauma, Hingray et al. (79) observed two different patients profiles : patients with trauma antecedents correlated with a high rate of psychiatric comorbidity and a strong dissociative mechanism. Patients without trauma had a weaker dissociative mechanism, lower female predominance, less psychiatric comorbidities, more frequent "frustration situations" as a factor triggering PNES and sick leaves as perpetuating factors. Another study observed 2 clusters of patients on the basis of differences concerning alexithymia and emotion regulation (80). Theoretical models are developed to increase the understanding of PNES (81).

One recent change concerning the epidemiology of PNES is the awareness that this condition is not present only in western developed countries but present worldwide, as suggested by some authors since 2000 (29)(30). In addition to presentations closely resembling those observed in western and other highly industrialized societies, PNES-like states are also recognized in some cultures around the world as a cultural phenomenon (82).

PNES repartition among a single country population can be heterogenous as in Georgia, where PNES are more frequent in the minority religions and ethnic groups (3)

ILAE publication encouraged studies describing PNES in several countries increasing our knowledge concerning PNES patients' care discrepancies : in Subsaharian Africa, diagnosis is more difficult due to the frequent lack of national healthcare and PNES diagnoses rely mostly on clinician expertise (22). But western countries findings are also found in other part of the world : in South Africa (83) a retrospective study comparing video-EEG diagnosed PNES and epilepsy patients showed a high rate

of initially misdiagnosed patients (50% epilepsy, 50% PNES), a female predominance, and a tendency toward overmedication with antiepileptic drugs in PNES patients.

The future challenge concerning PNES epidemiology study is the elaboration of well-resourced, formal epidemiological studies with strong methodology, issued from less highly developed regions of the world.

References

1. Dworetzky BA, Baslet G. Psychogenic Nonepileptic Seizures in Women. Semin Neurol. 2017;37(6):624–31.

2. Stone J, Carson A, Duncan R, Roberts R, Warlow C, Hibberd C, et al. Who is referred to neurology clinics?--the diagnoses made in 3781 new patients. Clin Neurol Neurosurg. 2010 Nov;112(9):747–51.

3. Kanemoto K, LaFrance WC, Duncan R, Gigineishvili D, Park S-P, Tadokoro Y, et al. PNES around the world: Where we are now and how we can close the diagnosis and treatment gaps-an ILAE PNES Task Force report. Epilepsia Open. 2017;2(3):307–16.

4. Jirsch JD, Ahmed SN, Maximova K, Gross DW. Recognition of psychogenic nonepileptic seizures diminishes acute care utilization. Epilepsy Behav EB. 2011 Oct;22(2):304–7.

5. 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 Nov;52(11):2133–8.

6. LaFrance WC, Benbadis SR. Avoiding the costs of unrecognized psychological nonepileptic seizures. Neurology. 2006 Jun 13;66(11):1620–1.

7. Hingray C, El-Hage W, Duncan R, Gigineishvili D, Kanemoto K, LaFrance WC, et al. Access to diagnostic and therapeutic facilities for psychogenic nonepileptic seizures: An international survey by the ILAE PNES Task Force. Epilepsia. 2018;59(1):203–14.

8. Stone H. The burden of psychogenic nonepileptic seizures (PNES) in context: PNES and medically unexplained symptoms. In: Gates and Rowan's nonepileptic seizures. In Schachter SC, LaFrance WC Jr (Eds);

9. Martin RC, Gilliam FG, Kilgore M, Faught E, Kuzniecky R. Improved health care resource utilization following video-EEG-confirmed diagnosis of nonepileptic psychogenic seizures. Seizure. 1998 Oct;7(5):385–90.

10. Razvi S, Mulhern S, Duncan R. Newly diagnosed psychogenic nonepileptic seizures: health care demand prior to and following diagnosis at a first seizure clinic. Epilepsy Behav EB. 2012

Jan;23(1):7–9.

11. Duncan R, Graham CD, Oto M, Russell A, McKernan L, Copstick S. Primary and secondary care attendance, anticonvulsant and antidepressant use and psychiatric contact 5-10 years after diagnosis in 188 patients with psychogenic non-epileptic seizures. J Neurol Neurosurg Psychiatry. 2014 Sep;85(9):954–8.

12. Reuber M, Pukrop R, Bauer J, Helmstaedter C, Tessendorf N, Elger CE. Outcome in psychogenic nonepileptic seizures: 1 to 10-year follow-up in 164 patients. Ann Neurol. 2003 Mar;53(3):305–11.

13. Reuber M, Fernández G, Bauer J, Helmstaedter C, Elger CE. Diagnostic delay in psychogenic nonepileptic seizures. Neurology. 2002 Feb 12;58(3):493–5.

14. Bodde NMG, Lazeron RHC, Wirken JMA, van der Kruijs SJ, Aldenkamp AP, Boon P a. JM. Patients with psychogenic non-epileptic seizures referred to a tertiary epilepsy centre: patient characteristics in relation to diagnostic delay. Clin Neurol Neurosurg. 2012 Apr;114(3):217–22.

15. Kerr WT, Janio EA, Le JM, Hori JM, Patel AB, Gallardo NL, et al. Diagnostic delay in psychogenic seizures and the association with anti-seizure medication trials. Seizure. 2016 Aug;40:123–6.

Asadi-Pooya AA, Tinker J. Delay in diagnosis of psychogenic nonepileptic seizures in adults:
A post hoc study. Epilepsy Behav EB. 2017;75:143–5.

17. Bahrami Z, Homayoun M, Asadi-Pooya AA. Why is psychogenic nonepileptic seizure diagnosis missed? A retrospective study. Epilepsy Behav EB. 2019 Aug;97:135–7.

18. Martin R, Burneo JG, Prasad A, Powell T, Faught E, Knowlton R, et al. Frequency of epilepsy in patients with psychogenic seizures monitored by video-EEG. Neurology. 2003 Dec 23;61(12):1791–2.

Asadi-Pooya AA, Emami Y, Emami M. Psychogenic non-epileptic seizures in Iran. Seizure.
2014 Mar;23(3):175–7.

20. Alsaadi TM, Marquez AV. Psychogenic nonepileptic seizures. Am Fam Physician. 2005 Sep 1;72(5):849–56.

21. Asadi-Pooya AA, Sperling MR. Epidemiology of psychogenic nonepileptic seizures. Epilepsy Behav EB. 2015 May;46:60–5.

22. Dekker MCJ, Urasa SJ, Kellogg M, Howlett WP. Psychogenic non-epileptic seizures among patients with functional neurological disorder: A case series from a Tanzanian referral hospital and literature review. Epilepsia Open. 2018;3(1):66–72.

23. Salinsky M, Spencer D, Boudreau E, Ferguson F. Psychogenic nonepileptic seizures in US veterans. Neurology. 2011 Sep 6;77(10):945–50.

24. Duncan R, Razvi S, Mulhern S. Newly presenting psychogenic nonepileptic seizures: incidence, population characteristics, and early outcome from a prospective audit of a first seizure clinic. Epilepsy Behav EB. 2011 Feb;20(2):308–11.

25. Sigurdardottir KR, Olafsson E. Incidence of psychogenic seizures in adults: a populationbased study in Iceland. Epilepsia. 1998 Jul;39(7):749–52.

26. Szaflarski JP, Ficker DM, Cahill WT, Privitera MD. Four-year incidence of psychogenic nonepileptic seizures in adults in hamilton county, OH. Neurology. 2000 Nov 28;55(10):1561–3.

27. Benbadis SR, Allen Hauser W. An estimate of the prevalence of psychogenic non-epileptic seizures. Seizure. 2000 Jun;9(4):280–1.

28. 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.

29. Silva W, Giagante B, Saizar R, D'Alessio L, Oddo S, Consalvo D, et al. Clinical features and prognosis of nonepileptic seizures in a developing country. Epilepsia. 2001 Mar;42(3):398–401.

30. Lazarus JP, Bhatia M, Shukla G, Padma MV, Tripathi M, Shrivastava AK, et al. A study of nonepileptic seizures in an Indian population. Epilepsy Behav EB. 2003 Oct;4(5):496–9.

31. Pretorius C, Cronje G. People with psychogenic non-epileptic seizures: A South African perspective. Afr J Disabil. 2015;4(1):176.

32. Ekanayake V, Kranick S, LaFaver K, Naz A, Frank Webb A, LaFrance WC, et al. Personality traits in psychogenic nonepileptic seizures (PNES) and psychogenic movement disorder (PMD): Neuroticism and perfectionism. J Psychosom Res. 2017;97:23–9.

33. Thomas AA, Preston J, Scott RC, Bujarski KA. Diagnosis of probable psychogenic nonepileptic seizures in the outpatient clinic: does gender matter? Epilepsy Behav EB. 2013 Nov;29(2):295–7.

34. Noe KH, Grade M, Stonnington CM, Driver-Dunckley E, Locke DEC. Confirming psychogenic nonepileptic seizures with video-EEG: sex matters. Epilepsy Behav EB. 2012 Mar;23(3):220–3.

35. Asadi-Pooya AA. Psychogenic nonepileptic seizures are predominantly seen in women: potential neurobiological reasons. Neurol Sci Off J Ital Neurol Soc Ital Soc Clin Neurophysiol. 2016 Jun;37(6):851–5.

36. Lesser RP. Psychogenic seizures. Neurology. 1996 Jun;46(6):1499–507.

37. Asadi-Pooya AA, Emami M, Emami Y. Gender differences in manifestations of psychogenic non-epileptic seizures in Iran. J Neurol Sci. 2013 Sep 15;332(1–2):66–8.

38. Fiszman A, Alves-Leon SV, Nunes RG, D'Andrea I, Figueira I. Traumatic events and posttraumatic stress disorder in patients with psychogenic nonepileptic seizures: a critical review. Epilepsy Behav EB. 2004 Dec;5(6):818–25.

39. An D, Wu X, Yan B, Mu J, Zhou D. Clinical features of psychogenic nonepileptic seizures: a study of 64 cases in southwest China. Epilepsy Behav EB. 2010 Mar;17(3):408–11.

40. Oto M, Conway P, McGonigal A, Russell AJ, Duncan R. Gender differences in psychogenic non-epileptic seizures. Seizure. 2005 Jan;14(1):33–9.

41. Holmes MD, Dodrill CB, Bachtler S, Wilensky AJ, Ojemann LM, Miller JW. Evidence That Emotional Maladjustment Is Worse in Men Than in Women with Psychogenic Nonepileptic Seizures. Epilepsy Behav EB. 2001 Dec;2(6):568–73.

42. Korucuk M, Gazioglu S, Yildirim A, Karaguzel EO, Velioglu SK. Semiological characteristics of patients with psychogenic nonepileptic seizures: Gender-related differences. Epilepsy Behav EB. 2018;89:130–4.

43. Reilly C, Menlove L, Fenton V, Das KB. Psychogenic nonepileptic seizures in children: a review. Epilepsia. 2013 Oct;54(10):1715–24.

44. Mayor R, Howlett S, Grünewald R, Reuber M. Long-term outcome of brief augmented psychodynamic interpersonal therapy for psychogenic nonepileptic seizures: seizure control and health care utilization. Epilepsia. 2010 Jul;51(7):1169–76.

45. Kotagal P, Costa M, Wyllie E, Wolgamuth B. Paroxysmal nonepileptic events in children and adolescents. Pediatrics. 2002 Oct;110(4):e46.

46. Szabó L, Siegler Z, Zubek L, Liptai Z, Körhegyi I, Bánsági B, et al. A detailed semiologic analysis of childhood psychogenic nonepileptic seizures. Epilepsia. 2012 Mar;53(3):565–70.

47. 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 Jul;59:60–6.

48. Wyllie E, Friedman D, Lüders H, Morris H, Rothner D, Turnbull J. Outcome of psychogenic seizures in children and adolescents compared with adults. Neurology. 1991 May;41(5):742–4.

49. Turner K, Piazzini A, Chiesa V, Barbieri V, Vignoli A, Gardella E, et al. Patients with epilepsy and patients with psychogenic non-epileptic seizures: video-EEG, clinical and neuropsychological evaluation. Seizure. 2011 Nov;20(9):706–10.

50. Hill SW, Gale SD. Predicting psychogenic nonepileptic seizures with the Personality Assessment Inventory and seizure variables. Epilepsy Behav EB. 2011 Nov;22(3):505–10.

51. Thompson AW, Hantke N, Phatak V, Chaytor N. The Personality Assessment Inventory as a tool for diagnosing psychogenic nonepileptic seizures. Epilepsia. 2010 Jan;51(1):161–4.

52. Diprose W, Sundram F, Menkes DB. Psychiatric comorbidity in psychogenic nonepileptic seizures compared with epilepsy. Epilepsy Behav EB. 2016 Mar;56:123–30.

53. Walsh S, Levita L, Reuber M. Comorbid depression and associated factors in PNES versus epilepsy: Systematic review and meta-analysis. Seizure. 2018 Aug;60:44–56.

54. Kanner AM, Schachter SC, Barry JJ, Hesdorffer DC, Hersdorffer DC, Mula M, et al. Depression and epilepsy, pain and psychogenic non-epileptic seizures: clinical and therapeutic perspectives. Epilepsy Behav EB. 2012 Jun;24(2):169–81.

55. Szaflarski JP, Szaflarski M. Seizure disorders, depression, and health-related quality of life. Epilepsy Behav EB. 2004 Feb;5(1):50–7.

56. Myers L, Lancman M, Laban-Grant O, Matzner B, Lancman M. Psychogenic non-epileptic seizures: predisposing factors to diminished quality of life. Epilepsy Behav EB. 2012 Nov;25(3):358–

57. Jones B, Reuber M, Norman P. Correlates of health-related quality of life in adults with psychogenic nonepileptic seizures: A systematic review. Epilepsia. 2016 Feb;57(2):171–81.

58. Bakvis P, Roelofs K, Kuyk J, Edelbroek PM, Swinkels WAM, Spinhoven P. Trauma, stress, and preconscious threat processing in patients with psychogenic nonepileptic seizures. Epilepsia. 2009 May;50(5):1001–11.

59. Sharpe D, Faye C. Non-epileptic seizures and child sexual abuse: a critical review of the literature. Clin Psychol Rev. 2006 Dec;26(8):1020–40.

60. Johnstone B, Velakoulis D, Yuan CY, Ang A, Steward C, Desmond P, et al. Early childhood trauma and hippocampal volumes in patients with epileptic and psychogenic seizures. Epilepsy Behav EB. 2016;64(Pt A):180–5.

61. Hingray C, Donne C, Cohn A, Maillard L, Schwan R, Montel S, et al. Link between psychogenic nonepileptic seizures and complex PTSD: A pilot study. Eur J Trauma Dissociation. 2017 Apr 1;1(2):131–6.

62. Salinsky M, Evrard C, Storzbach D, Pugh MJ. Psychiatric comorbidity in veterans with psychogenic seizures. Epilepsy Behav EB. 2012 Nov;25(3):345–9.

63. Alessi R, Valente KD. Psychogenic non-epileptic seizures at a tertiary care center in Brazil. Epilepsy Behav EB. 2013 Jan;26(1):91–5.

64. Asadi-Pooya AA, Emami M. Demographic and clinical manifestations of psychogenic nonepileptic seizures: the impact of co-existing epilepsy in patients or their family members. Epilepsy Behav EB. 2013 Apr;27(1):1–3.

65. Benbadis SR, Agrawal V, Tatum WO. How many patients with psychogenic nonepileptic seizures also have epilepsy? Neurology. 2001 Sep 11;57(5):915–7.

66. Marchetti RL, Kurcgant D, Gallucci-Neto J, Von Bismark MA, Fiore LA. Epilepsy in patients with psychogenic non-epileptic seizures. Arq Neuropsiquiatr. 2010 Apr;68(2):168–73.

67. Binnie CD, Stefan H. Modern electroencephalography: its role in epilepsy management. Clin Neurophysiol Off J Int Fed Clin Neurophysiol. 1999 Oct;110(10):1671–97.

68. Reuber M. The etiology of psychogenic non-epileptic seizures: toward a biopsychosocial model. Neurol Clin. 2009 Nov;27(4):909–24.

69. Kollar B, Carnicka Z, Siarnik P, Krizova L, Sutovsky S, Traubner P, et al. The importance of interictal electroencephalography in paroxysmal states. Bratisl Lek Listy. 2014;115(3):168–70.

70. González Otárula KA, Tan Y-L, Dubeau F, Correa JA, Chang E, Hall JA, et al. Psychogenic nonepileptic seizures in patients with surgically treated temporal lobe epilepsy: Presurgical and de novo postsurgical occurrence. Epilepsy Behav EB. 2017;75:252–5.

71. Wissel BD, Dwivedi AK, Gaston TE, Rodriguez-Porcel FJ, Aljaafari D, Hopp JL, et al. Which patients with epilepsy are at risk for psychogenic nonepileptic seizures (PNES)? A multicenter case-control study. Epilepsy Behav EB. 2016;61:180–4.

62.

72. Guberman A. Psychogenic pseudoseizures in non-epileptic patients. Can J Psychiatry Rev Can Psychiatr. 1982 Aug;27(5):401–4.

73. Krumholz A, Niedermeyer E. Psychogenic seizures: a clinical study with follow-up data. Neurology. 1983 Apr;33(4):498–502.

74. van Ool JS, Haenen AI, Snoeijen-Schouwenaars FM, Aldenkamp AP, Hendriksen JGM, Schelhaas HJ, et al. Psychogenic nonepileptic seizures in adults with epilepsy and intellectual disability: A neglected area. Seizure. 2018 Jul;59:67–71.

75. Duncan R, Oto M. Psychogenic nonepileptic seizures in patients with learning disability: comparison with patients with no learning disability. Epilepsy Behav EB. 2008 Jan;12(1):183–6.

76.Gates and Rowan's Nonepileptic Seizures [Internet]. Cambridge Core. [cited 2019 May 14].Availablefrom:/core/books/gates-and-rowans-nonepileptic-seizures/7E0D35DC86710D5C49154CC215FDA63F/listing?q=Hamilton&_csrf=J8J9gEX6-

S07CH7cKTuElC2DGh3Q38W6oAFA&searchWithinIds=7E0D35DC86710D5C49154CC215FDA6 3F&aggs%5BproductTypes%5D%5Bfilters%5D=BOOK_PART

77. Magaudda A, Gugliotta SC, Tallarico R, Buccheri T, Alfa R, Laganà A. Identification of three distinct groups of patients with both epilepsy and psychogenic nonepileptic seizures. Epilepsy Behav EB. 2011 Oct;22(2):318–23.

Plioplys S, Doss J, Siddarth P, Bursch B, Falcone T, Forgey M, et al. A multisite controlled study of risk factors in pediatric psychogenic nonepileptic seizures. Epilepsia. 2014 Nov;55(11):1739–47.

79. Hingray C, Maillard L, Hubsch C, Vignal J-P, Bourgognon F, Laprevote V, et al. Psychogenic nonepileptic seizures: characterization of two distinct patient profiles on the basis of trauma history. Epilepsy Behav EB. 2011 Nov;22(3):532–6.

80. Brown RJ, Bouska JF, Frow A, Kirkby A, Baker GA, Kemp S, et al. Emotional dysregulation, alexithymia, and attachment in psychogenic nonepileptic seizures. Epilepsy Behav EB. 2013 Oct;29(1):178–83.

81. Brown RJ, Reuber M. Towards an integrative theory of psychogenic non-epileptic seizures (PNES). Clin Psychol Rev. 2016;47:55–70.

82. Martinez-Taboas A, Lewis-Fernandez R, Sar V. Cultural aspects of psychogenic nonepileptic seizures. In Schachter SC, LaFrance WC Jr (Eds). In: Gates and Rowan's nonepileptic seizures 3rd Ed. Cambridge University Press; p. 2010:121–130.

83. Anderson DG, Damianova M, Hanekom S, Lucas M. A comparative retrospective exploration of the profiles of patients in South Africa diagnosed with epileptic and psychogenic non-epileptic seizures. Epilepsy Behav EB. 2017;69:37–43.