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Auras in psychogenic nonepileptic seizures

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ABSTRACT

Purpose: The aim of this study was to investigate the frequency and characteristics of auras in patients with psychogenic nonepileptic seizures (PNES) and to characterize the patients' historical and clinical risk factors that may be associated with such manifestations.

Methods: In this retrospective database study, all patients with PNES, who were investigated at Shiraz Comprehensive Epilepsy Center at Shiraz University of Medical Sciences, from 2008 until 2018, were studied.

Results: During the study period, 258 patients were investigated. One hundred and seventy-three patients (67.1%) reported having auras. Auras were associated with multiple variables, including sex ratio, history of head injury, ictal injury, and taking antiepileptic drugs, in univariate analyses. We then performed a logistic regression analysis, assessing these four variables. The model that was generated by the regression analysis was significant ($p = 0.0001$) and could predict the possibility of auras in 72% of the patients. Within the model, sex ratio (OR: 0.498; 95% CI: 0.282 − 0.878; $p = 0.01$) and a history of head injury (OR: 0.096; 95% CI: 0.020 − 0.465; $p = 0.004$) retained their significance.

Conclusion: Patients with PNES may frequently report auras including some auras which are often seen in patients with focal epilepsies; as a result, they are at great risk of receiving wrong diagnosis and unnecessary treatments. Health care professionals involved in the management of patients with seizures should be aware of this risk and prescribe an antiepileptic drug only after making a definite diagnosis of epilepsy in a patient with a paroxysmal event.

1. Introduction

In clinical practice auras are often associated with epilepsy; they are subjective ictal events that may precede a seizure in patients with epilepsy, particularly those with focal epilepsies [1]. On the other hand, psychogenic nonepileptic seizures (PNES) comprise of paroxysmal changes in responsiveness, movements, or behavior that seemingly look like epileptic seizures, but lack a neurobiological origin similar to epileptic seizures and are not associated with electrophysiological epileptic changes [2]. Epilepsy and PNES have various distinguishing signs and symptoms; but, none is pathognomonic to either PNES or epilepsy [2–4].

The aim of this study was to investigate the frequency and characteristics of auras in patients with PNES and to characterize the patients' historical and clinical risk factors that may be associated with such manifestations. This was an exploratory study; we tried to generate a hypothesis on whether some demographic variables (e.g., sex) or risk factors (e.g., a history of sexual abuse) have associations with the presence of auras in patients with PNES. Identifying and characterizing auras in patients with PNES could have important clinical implications in the diagnosis and management of patients with paroxysmal events.

2. Methods and materials

In this retrospective database study, all patients with PNES, who were diagnosed at Shiraz Comprehensive Epilepsy Center at Shiraz University of Medical Sciences, Iran, from 2008 until 2018, were investigated. The diagnosis was made by the epileptologist through a careful clinical assessment and documented by ictal recording during video-EEG monitoring in all patients. The epileptologist interviewed all the patients. At the time of interpretation of the recorded ictal event, we reviewed the video with their relatives or care-givers to make sure that we have captured the patient's habitual events. We make a diagnosis of PNES if history is compatible with the diagnosis of PNES; events are witnessed by the epileptologist, showing semiology typical of PNES while on video-EEG monitoring; and finally, no epileptiform activity is detected immediately before, during or after the attack that has been captured during video-EEG recording. We also always obtain a detailed

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clinical history in order to investigate the existence of any possible comorbid epileptic seizures in patients with PNES [e.g., presence of other seizure types, different from what we have captured during their video-EEG monitoring, if their description is compatible with epileptic seizures (e.g., staring episodes for a few seconds as absences)]. We also review the recorded interictal EEG carefully to search for any possible epileptiform discharges. Patients with comorbid epilepsy, abnormal EEG (e.g., ictal or interictal epileptiform discharges), or incomplete data were not included in this study.

Age, gender, age at seizure onset, seizure semiology [including auras (defined as the very first subjective event that the patient has, preceding the onset of their seizure)], seizure frequency, factors potentially predisposing to PNES [a history of physical abuse (i.e., corporal punishment or any physical injury resulted from aggressive behavior towards the patient), a history of sexual abuse, a history of child abuse (i.e., neglect, emotional/verbal abuse), family function (i.e., divorce, single parent, significant family disputes, etc.), academic failure (school dropout or repeated grades), any medical comorbidities, and a family history of seizures], and video-EEG recording of all patients were registered routinely. In clinical practice it is often the case that patients with PNES report that some, but not all, of their attacks are preceded by auras. In the current study was considered aura to be present if the patient reported that they have an aura with most of their attacks. We did not quantify this as this was a retrospective study.

Demographic variables and relevant clinical variables were summarized descriptively to characterize the study population. Initially, we performed univariate analyses using Pearson Chi-square, Mann-Whitney, Kolmogorov-Smirnov, and t-test. Variables that were significant ($p < 0.05$) were assessed in a logistic regression analysis. Odds ratio (OR) and 95% confidence interval (CI) were calculated. P value less than 0.05 was considered as significant. This study was conducted with the approval by Shiraz University of Medical Sciences Review Board.

3. Results

During the study period, 258 patients (out of 325 patients in our database) had the inclusion criteria and were studied. One hundred and seventy-three patients (67.1%) reported having auras with their seizures and 85 patients (32.9%) did not have any auras. The most common auras were as follows: headache, dizziness or vertigo, palpitation, breathing difficulty, and weakness (Table 1). However, a few patients reported more specific auras, such as nausea and abdominal discomfort, warm sensations, cold sensations, visual auras, and finally, even auditory aura (hearing voices).

Auras were associated with multiple variables, including sex ratio, a history of head injury, ictal injury, and taking antiepileptic drugs (AEDs), in univariate analyses (Table 2). We then performed a logistic regression analysis, assessing these four variables (i.e., sex ratio, a history of head injury, ictal injury, and taking AEDs) in patients with or without auras. The model that was generated by the regression analysis was significant ($p = 0.0001$) and could predict the presence of auras in 72% of the patients. Within the model, sex ratio (OR: 0.498; 95% CI: 0.282 − 0.878; $p = 0.01$) and a history of head injury (OR: 0.096; 95% CI: 0.020 − 0.465; $p = 0.004$) retained their significance. Auras were more frequently reported by women and less frequently by those with a history of head injury.

4. Discussion

Current literature has only given limited attention to the subjective symptomatology of PNES [5,6]. Instead, most phenomenological research has concentrated on the visible manifestations of PNES and on physiological parameters; they often neglect patients' symptoms and experiences [5]. In this study, we observed that two-thirds of the patients with PNES-only reported having auras associated with their seizures. Previous studies in patients with PNES have found rates of 25–60% [6]. Some authors have suggested that patients with PNES do have prodromal symptoms, but generally do not want to talk about them [6]. Therefore, we should specifically inquire about auras and prodromal symptoms when interviewing patients with paroxysmal events, including those with PNES. We observed a wide range of subjective ictal experiences (auras) in patients with PNES. Even specific auras, which are often associated with focal epilepsies [e.g., abdominal (in mesial temporal epilepsy), auditory (in temporal neocortical epilepsy), visual (in occipital lobe epilepsy), and sensory (in parietal lobe epilepsy) auras], were reported by patients who just had PNES in our study. Previous studies have reported a greater range of subjective ictal experiences in patients with PNES than those with epilepsy [7,8].

Table 1
Auras in patients with psychogenic nonepileptic seizures.

Aura	Number	Percent
Headache	40 (28 females/ 12 males)*	16
Dizziness or vertigo	26 (19 females/ 7 males)**	10
Palpitation	11 (8 females/ 3 males)***	4
Breathing difficulty	10 (7 females/ 3 males)****	4
Weakness	10 (9 females/ 1 males)*****	4
Warm/burning sensation	8	3
Vague sensation	8	3
Nausea	4	2
Cold sensation	4	2
Flashing lights	4	2
Fear	3	1
Dry mouth	2	1
Blurred vision	2	1
Anxiety (rush)	2	1
Focal (right or left) paresthesia	2	1
Auditory aura (hearing voices)	1	0.4
Abdominal discomfort	1	0.4
Others (e.g., slurred speech, malaise, yawning, etc.)	35	14

*P value for sex difference = 0.3; ** P value for sex difference = 0.3; ***P value for sex difference = 0.5; ****P value for sex difference = 0.6; *****P value for sex difference = 0.08.

Table 2
Factors associated with auras in psychogenic nonepileptic seizure in univariate analyses.

	Having auras (173 patients)	No auras (85 patients)	P value
Sex ratio (Female: Male)	121: 52	44: 41	0.006
Age (years)	28 ± 9	30 ± 11	0.1
Age at onset (years)	24 ± 9	25 ± 11	0.2
Duration of the condition (years)	4.5 ± 7	5 ± 7	0.7
Loss of responsiveness	143	77	0.09
Urinary incontinence	20	11	0.8
Generalized motor seizures	145	77	0.3
Akinetic seizures	21	7	0.3
Ictal injury	43	32	0.04
Seizure frequency per month	36 ± 62	32 ± 77	0.6
History of head injury	2	10	0.0001
Family history of seizures	50	26	0.8
History of physical abuse	20	12	0.6
History of childhood abuse	13	11	0.1
History of sexual abuse	17	5	0.3
Family dysfunction	56	33	0.3
Academic failure	13	5	0.7
Medical comorbidities	44	20	0.7
Taking antiepileptic drugs	90	58	0.02

Reporting auras (particularly some specific auras) may be mistakenly associated with epileptic seizures and may lead to misdiagnosis and mismanagement in clinical practice. A previous study showed that the majority of patients with PNES may report some phenomena, which have traditionally been attributed to epilepsy (e.g., seizures from sleep, experiencing a rising sensation in their body, and postictal myalgia) [9]. Physicians who are taking care of patients with paroxysmal events and seizures should be aware that while epilepsy and PNES have various distinguishing signs and symptoms, none is pathognomonic to either diagnosis. The correct diagnosis of epilepsy vs. PNES can be made based on different combinations of data including, clinical history (e.g., panic attack symptoms, a history of antecedent factors, etc.), witness reports, clinician observations, interictal EEG and ictal video-EEG recordings [10–15]. We would like to draw the reader's attention to the large number of patients in this PNES-only cohort who were taking AEDs (58%). This would support the widespread belief that misdiagnosis of PNES is common. It also lends some weight to our theory that diagnosis may be sometimes based on individual features like an aura, that are reminiscent of those seen in epilepsy, rather than looking at all of the available information; one should bear in mind that much of the information we get from the seizure history does not differentiate these two conditions.

We also observed that auras more frequently reported by women (in 73%) compared with that in men (in 56%). However, the frequency of the most common types of auras (i.e., headache, dizziness or vertigo, palpitation, breathing difficulty, and weakness) was not significantly different between women and men (Table 1). We are not aware of any direct evidence to explain this finding; but, recent evidence suggests that altered functional and structural brain connectivity may be an underlying pathophysiological mechanism in patients with PNES [16]. On the other hands, gender plays an important role in the anatomy and function of the human brain. The literature provides convergent evidence for a substantial gender difference in brain connectivity that possibly underlies gender-related cognitive, emotional and behavioral differences [17–19]. This should be studied in future international cross-cultural studies.

Finally, we observed that a history of head injury was inversely associated with PNES-associated auras (odds ratio: 0.09). We do not have any clear explanation for this observation and this should be verified and investigated in future studies.

In conclusion, patients with PNES may frequently report auras including some auras which are often expected in patients with focal epilepsies; as a result, they are at great risk of receiving wrong diagnosis and unnecessary treatments. Health care professionals involved in the management of patients with seizures and paroxysmal events should be aware of this risk and prescribe an AED only after making a definite diagnosis of epilepsy in a patient with a paroxysmal event. In addition, identifying and characterizing auras in patients with PNES could have important clinical implications. For example, the presence of aura might influence treatment approaches (e.g. by training patients to recognize warning symptoms and employ cognitive or behavioral strategies aimed at averting a seizure). This hypothetical strategy should be tested in future studies.

This study has some limitations including its retrospective design and the possibility of recall bias and also lack of some important data such as psychiatric comorbidities of the patients. We inquired the factors potentially predisposing to PNES (history of physical abuse, sexual abuse, child abuse, family dysfunction, academic failure, any medical comorbidities, and family history of seizures) by taking history from the patients and no validated tool was used.

Conflict of interest

Ali A. Asadi-Pooya, M.D.: Honoraria from Cobel Daruo; Royalty: Oxford University Press (Book publication). Zahra Bahrami, M.D.: none.

Contributions

Ali A. Asadi-Pooya, M.D.: Study design, data collection, statistical analysis, manuscript preparation. Zahra Bahrami, M.D., Data collection, manuscript preparation.

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References

[1] Blume WT, Lüders HO, Mizrahi E, et al. Glossary of descriptive terminology for ictal semiology: report of the ILAE task force on classification and terminology. Epilepsia 2001;42:1212–8.
[2] Asadi-Pooya AA, Sperling MR. Epidemiology of psychogenic nonepileptic seizures. Epilepsy Behav 2015;46:60–5.
[3] Müller T, Merschhemke M, Dehnicke C, et al. Improving diagnostic procedure and treatment in patients with non-epileptic seizures (NES). Seizure 2002;11:85–9.
[4] Asadi-Pooya AA, Emami M. Demographic and clinical manifestations of psychogenic non-epileptic seizures: the impact of co-existing epilepsy in patients or their family members. Epilepsy Behav 2013;27:1–3.
[5] Reuber M, Rawlings GH. Nonepileptic seizures - subjective phenomena. Handb Clin Neurol 2016;139:283–96.
[6] Stone J, Carson AJ. The unbearable lightheadedness of seizing: willful submission to dissociative (non-epileptic) seizures. J Neurol Neurosurg Psychiatry 2013;84:822–4.
[7] Ali F, Rickards H, Bagary M, Greenhill L, McCorry D, Cavanna AE. Ictal consciousness in epilepsy and nonepileptic attack disorder. Epilepsy Behav 2010;19:522–5.
[8] Reuber M, Chen M, Jamnadas-Khoda J, et al. Value of patient-reported symptoms in the diagnosis of transient loss of consciousness. Neurology 2016;87:625–33.
[9] Reuber M, Jamnadas-Khoda J, Broadhurst M, et al. Psychogenic nonepileptic seizure manifestations reported by patients and witnesses. Epilepsia 2011;52:2028–35.
[10] LaFrance WC, Baker GA, Duncan R, et al. Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: A staged approach; A report from the International League Against Epilepsy Nonepileptic Seizures Task Force. Epilepsia 2013;54:2005–18.
[11] Avbersek A, Sisodiya S. Does the primary literature provide support for clinical signs used to distinguish psychogenic nonepileptic seizures from epileptic seizures? J Neurol Neurosurg Psychiatry 2010;81:719–25.
[12] Hendrickson R, Popescu A, Dixit R, Ghearing G, Bagic A. Panic attack symptoms differentiate patients with epilepsy from those with psychogenic nonepileptic spells (PNES). Epilepsy Behav 2014;37:210–4.
[13] Duncan R, Oto M. Predictors of antecedent factors in psychogenic nonepileptic attacks: multivariate analysis. Neurology 2008;71:1000–5.
[14] Asadi-Pooya AA, Emami M, Ashjazadeh N, et al. Reasons for uncontrolled seizures in adults; the impact of pseudointractability. Seizure 2013;22:271–4.
[15] Asadi-Pooya AA, Emami M. Reasons for uncontrolled seizures in children: the impact of pseudointractability. Epilepsy Behav 2012;25:341–4.
[16] Asadi-Pooya AA. Neurobiological origin of psychogenic nonepileptic seizures: A review of imaging studies. Epilepsy Behav 2015;52:256–9.
[17] Gong G, He Y, Evans AC. Brain connectivity: gender makes a difference. Neuroscientist 2011;17:575–91.
[18] Yang X, Wang S, Kendrick KM, et al. Sex differences in intrinsic brain functional connectivity underlying human shyness. Soc Cogn Affect Neurosci 2015;10:1634–43.
[19] Asadi-Pooya AA. Psychogenic nonepileptic seizures are predominantly seen in women: potential neurobiological reasons. Neurol Sci 2016;37:851–5.