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Clinical Semiology and Comparative Analysis of Different Classification Systems of Psychogenic Nonepileptic Seizures

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Abstract

Objective Only a few studies have compared the different classification systems of psychogenic nonepileptic seizures (PNESs). A universally acceptable classification system for PNES will aid in the early diagnosis and may lead to better standardization for future studies. This study aimed to describe the clinical semiology and provide comparative analysis of PNES classification systems described by Hubsch et al, Wadwekar et al, Dhiman et al, and Asadi-Pooya.

Methods Prospectively, patients provisionally diagnosed clinically as PNES were confirmed on video electroencephalography and their semiology was classified according to the classification systems mentioned earlier. Patients were additionally evaluated for coexisting anxiety or depression using Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria and its severity assessed using Hamilton's depression/anxiety rating scales.

Results A total of 104 PNES patients were included in the study. Mean age at presentation was 24.5 ± 10.4 years with females as the predominant proportion (76.9%). Whole body flaccidity was the commonest clinical presentation of PNES seen in 60.58% cases. All PNES cases could be classified using the Asadi-Pooya's classification, while 8.7, 47.1, and 53.8% PNES events remained unclassified, respectively, using the classification system as described by Dhiman et al, Wadwekar et al, and Hubsch et al; 33(31.73%) PNES patients had depression and 8 (7.7%) had generalized anxiety disorder in our study.

Conclusion Nonmotor manifestations were the most frequent semiology in our cohort. Of the PNES classification systems studied, Asadi-Pooya's classification was easier to apply and could classify all the patients in the study.

Keywords
- psychogenic
- nonepileptic
- seizures

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Introduction

Psychogenic nonepileptic seizures (PNESs) are paroxysms of altered movement or behavior, resembling epileptic seizure, with underlying psychogenic basis, but without concurrent electroencephalographic abnormalities.[1] There are no isolated clinical characteristics which are sensitive or specific for PNES, and the events are typically described based on the semiology of the events.[2,3] Distinguishing PNES from true seizures is essential not only to prevent prolonged treatment with antiseizure medications but also mistreatment can be detrimental in further exacerbating the PNES semiology.[4] Video electroencephalography (VEEG) is considered to be the gold standard for diagnosis of PNES. However, it is often delayed in low-resource settings because of long waiting lists and limited centers offering this facility.[5] In such clinical scenarios, detailed semiological analysis, in the meantime may help in diagnosing and classifying PNES that may assist in management of these patients. In an earlier study, the clinical semiologies of ictal stuttering and "teddy bear sign" (age inappropriate behavior like bringing a teddy bear to the clinic) were moderately specific for PNES, while pelvic thrusting and ictal eye closure could not differentiate PNES from true seizures.[4] Only a few studies have attempted to describe different types of PNES as a conjunction of clinical signs. The classification systems as described by Hubsch et al,[6] Wadwekar et al,[7] Dhiman et al,[8] and Asadi-Pooya[9] are among a few that have attempted to classify PNES events clinically. An earlier retrospective analysis of 248 patients with PNES events could classify all semiologies as per the schemes by Asadi-Pooya and Wadwekar et al.[10] A universally accepted and appropriate semiology-based classification system for PNES may lead to better standardization of future studies. This study aimed to describe the clinical semiology and provide a comparative analysis of PNES classification systems.

Materials and Methods

This prospective observational study was conducted in Department of Neurology, Dr Ram Manohar Lohia Institute of Medical Sciences Lucknow, a tertiary care referral institute in North India, over a period of 18 months. Newly diagnosed cases of PNES with age >14 years were included in the study. Medically unstable patients and those not giving the consent were excluded. The demographic data of all PNES patients were recorded, and a clinical semiology of the event was noted. Short-term VEEG was done for all patients using 23 EEG electrodes according to the 10/20 International system, at a 1-kHz sampling rate (Natus system). No antiseizure medications were withdrawn or any dose modification made prior to the VEEG. Patients lied in a dorsal recumbent position in a semi-illuminated quiet room and were asked to close their eyes or gently relax during the recording. As provocative techniques, hyperventilation for 3 minutes and intermittent photic stimulation (using a photic strobe lamp at 10 different frequencies ranging between 1 and 25 Hz, for 5 seconds at each frequency followed by 5 seconds of rest) was done as per the standard protocols. The duration of short-term VEEG was at least 30 minutes to a maximum duration of 8 hours and was terminated when the patient had an episode of PNES or was induced. The use of verbal induction was done for cases that did not have spontaneous events. In short, during the process of verbal induction, the patient was asked to close the eyes, concentrate about the event and verbally re-enforced that this might bring an attack. The safety of the procedure was told beforehand, and the process was continued arbitrarily for 90 seconds before documenting induction failure as has been described previously.[11] PNES was identified in VEEG as either of the following: events without concurrent cortical discharges, sudden onset of completely obscured EEG with mixture of movement and muscle artifacts or no postepisode slowing or suppression of background.[12] Patients with a high suspicion of PNES but those that could not be induced nor had no episode over this duration of 8 hours of VEEG were excluded from the study. Type (flexion, extension, dystonic movements, rotation, tremors, tonic, clonic, myoclonic, complex movements, and immobility), distribution (head, limbs, trunk, and pelvis), symmetry and synchrony of the movements were noted. Responsiveness to stimuli, presence or absence of eye opening, vocalization, hyperventilation, and fluctuations during the attacks were recorded. Based on the PNES semiology and VEEG analysis, the episode was classified as per the schemes by Hubsch et al, Wadwekar et al, Dhiman et al, and Asadi-Pooya's classification systems. Patients were also evaluated for any coexisting anxiety or depression using Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria,[13] and their severity was assessed using Hamilton's depression[14] and anxiety rating scales.[15] One neurologist was assigned the role of evaluating the semiology and analyze the VEEG and another neurologist classified these patients as per each classification system.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 21. Categorical data were expressed as frequency and percentage. Continuously distributed data were expressed as mean $\pm$ standard deviation. For comparing proportions, Fisher's exact test was used. Analysis of variance was used to compare means with normal distribution, while Kruskal–Wallis' test was used for nonparametric variables. A p-value <0.05 was considered statistically significant. The study was approved by the institutional ethics committee (IEC No. 21/21).

Results

One hundred and four patients were diagnosed as PNES as per the clinical semiology and after VEEG and included in the study with a female preponderance (80 females, 76.9%). The mean age of the patients at presentation was 24.5 ± 10.4 years. In 6 patients (5.8%), epilepsy and PNES coexisted and 20 patients in total were on at least one antiseizure medication. On analyzing the PNES semiology, whole body flaccidity was noted most commonly in 63 patients (60.58%). Other semiologies observed are as described in ►**Table 1**. Hyperventilation was seen in 15.4% and no patient had tongue bite;

Table 1 Clinical semiology of PNES

Sl. no.	Semiology	No of patients (%)
1	Whole body flaccidity	63 (60.58%)
2	Tonic posturing	12 (11.54%)
3	Out of phase limb movements	9 (8.65%)
4	Clonic upper limb movements	7 (6.73%)
5	Clonic lower limb movements	6 (5.8%)
6	Neck flexion and extension	5 (4.8%)
7	Pelvic thrusting	4 (3.85%)
8	Tremors and irregular jerky movements	4 (3.85%)

Abbreviation: PNES, psychogenic nonepileptic seizure.

86.54% patients were unresponsive during the episode and of these, 4.44% had eye blinking and 6.67% had their eyes open during the episode. The median (interquartile range) duration of the PNES event in our study was 2.86 (6.58) minutes. Classification of PNES as per different schemes is as outlined in ►**Table 2**. Using Asadi-Pooya's classification, all PNES events could be classified. On the contrary, 8.7, 47.1, and 53.8% PNES events remained unclassified by applying Dhiman et al, Wadwekar et al, and Hubsch et al's classification, respectively (►**Table 2**). Thus, the sensitivity of Asadi-Pooya's classification was 100%, Dhiman et al 91.3%, Wadwekar et al 52.88%, and Hubsch et al 46.15% in our study. Thirty-three (31.73%) PNES patients had depression and eight (7.7%) had generalized anxiety disorder in our study. Twenty-nine patients had mild depression as per the Hamilton's depression rating scale and all patients with anxiety had mild anxiety according to the Hamilton's anxiety rating scale.

Discussion

In this observational study, we analyzed the clinical semiology of PNES and categorized it as per the known classification systems to determine which scheme could best classify PNES; 76.9% patients in our study were females which were in accordance with the existing literature.[7,10] Coexistent true seizures were seen in 5.8% of our patient group, similar to an earlier study by Garg et al[10] where 4% had coexistent seizures. Coexistence of PNES with epileptic seizure ranges from 10 to 50% in various studies.[16] This broad range is probably related to clinical and electrophysiological criteria used to diagnose epilepsy that varies among studies.[17,18] In our study, this coexistence was established based on typical history, ictal or interictal VEEG abnormality, and imaging findings. The most common semiology noted in our study was whole body flaccidity (60.58%). This presentation, often described as "fall and lying still" phenomena has been reported in Indian studies to be the most common presentation.[19] Garg et al[10] also reported nonmotor, paucikinetic manifestations as the most frequent semiology. Likewise, Patidar et al had 62% of their patients with PNES with limp attacks.[20] The whole body flaccidity is a paucikinetic semiology rather than a true nonmotor phenomena as these patients have mild tremors or jerks limited to the limbs or head without any trunk movement.[6] However, on a global scale, PNES events with hyperkinetic movements and increased motor manifestations are commoner than the aforementioned subcontinent presentation. Studies by Abubakr et al[21] and Hovorka et al[22] from the United States and the Czech Republic, respectively, noted that the most frequent PNES symptomatology was motoric. This difference in PNES semiology can be best described by the integrative cognitive model of PNES by Reuber and Brown.[23,24] They have suggested that complex interactions between physiological hyperarousal, involuntary conditioned responses, and central processing problems lead to activation of a latent seizure

Table 2 Classification of PNES events by various classification schemes ($N = 104$)

Asadi-Pooya's classification (no. of patients, %)	Dhiman et al's classification (no. of patients, %)	Wadwekar et al's classification (no. of patients, %)	Hubsch et al's classification (no. of patients, %)
Generalized motor (20, 28.8%)	Hypermotor (6, 5.8%)	Dystonic attacks with primitive gestural activity (2, 1.9%)	Dystonic attacks with primitive gestural activity (2, 1.9%)
Focal motor (2, 2%)	Partial motor (25, 24%)	Paucikinetic attacks with preserved responsiveness (3, 2.9%)	Paucikinetic attacks with preserved responsiveness (3, 2.9%)
Nonmotor akinetic (71, 68.2%)	Affective/emotional behavioral phenomenon (0, 0%)	Pseudosyncopes with/without hyperventilation (33, 31.7%)	Pseudosyncopes (26, 25%)
Nonmotor subjective symptoms (0, 0%)	Dialeptic (57, 54.8%)	Hyperkinetic prolonged attacks ± trunk involvement (13, 12.5%)	Hyperkinetic prolonged attacks (13, 12.5%)
Mixed (1, 1%)	Nonepileptic aura (0, 0%)	Axial dystonic prolonged attacks (4, 3.8%)	Axial dystonic prolonged attacks (4, 3.8%)
Unclassified (0, 0%)	Mixed (7, 6.7%)	Unclassified (49, 47.1%)	Unclassified (56, 53.8%)
	Unclassified (9, 8.7%)		

Abbreviation: PNES, psychogenic nonepileptic seizure.

"scaffold" which is determined by previous encounters and understanding and shaped by previous experiences and perceptions. Cultural and religious factors also modulate the PNES semiology and may explain the differences between our studies and the Western world.[25] Of the classification schemes selected, Hubsch et al employed a statistical clustering analysis to classify the semiologies of their patient group, while the other three classification systems used a more subjective interpretation of the semiology based on the event morphology. We used the same classification system as was done in a previous retrospective study from our group.[10] The present study could classify all the PNES events with Asadi-Pooya's classification, while 8.7, 47.1, and 53.8% PNES events remained unclassified by applying Dhiman et al, Wadwekar et al, and Hubsch et al's classification, respectively. The number of unclassified events in the Hubsch et al and Wadwekar et al system are related to their strict confinement to the duration of pseudosyncope of < 5 minutes. Asadi-Pooya scheme does not have such distinction and these cases could be classified using the latter's scheme into the nonmotor akinetic group. Among the 56 patients who remained unclassified by using Hubsch et al's classification, 42 patients were classified as nonmotor akinetic subtype, 11 as generalized motor, 2 as focal motor, and 1 as mixed subtype by Asadi-Pooya's classification. Similarly, of the 49 patients who remained unclassified using Wadwekar et al's classification, 35 patients were classified under nonmotor akinetic, 11 as generalized motor, 2 as focal motor, and 1 as mixed subtype under Asadi-Pooya's classification.

A classification system for PNES should be clinically easy to apply, should have less variables and subclasses and not be very confusing. Hubsch et al's classification was modified in the Indian population and Wadwekar et al and Dhiman et al's classification schemes were put forth.[6–8] Hubsch et al's classification group had patients with comorbid epilepsy and hence cannot be generalized to the population. Asadi-Pooya's classification system is the latest and simplifies the previous classifications.[10] In our study, though Asadi-Pooya's and Dhiman et al's classification system had the least unclassified patients, in practical application, the former classification system was easiest to apply. Inclusion of a mixed category where patients with multiple and complicated semiologies can be classified is an additional advantage in both Asadi-Pooya and Dhiman et al's classification system.

In the subcontinent, where access to tertiary centers is not always possible and access to VEEG is also not feasible, an easy to apply classification for PNES where most patients can be classified as per the semiology would best suit the clinical setting and the confusion on the true nature of the episode and PNES in unclassified groups could be minimized. Thus, we feel that of the four classifications studied, Asadi-Pooya is the easiest to apply and can be used as a uniform classification system for PNES.

Our patients with PNES had coexistent mild depression and anxiety, as has been reported earlier.[22,26] However, this is in sharp contrast to the study by Patidar et al, where depression and anxiety coexisted in 62 and 90% cases, respectively.[20] We did not exclude patients on medications for depression and anxiety, and this could be a reason for relatively low scores on Hamilton's rating scale in our study. It has been found that emotional dysregulation (a core psychological construct in disorders such as major depression, anxiety, and borderline personality disorders) is an independent psychopathology in PNES,[27] and the emotional pain created by the comorbid psychiatric illnesses is expressed via PNES.[16,28,29]

Our study has some limitations. Being conducted in a tertiary care referral center, the results are not reflective of general population. We excluded children younger than 14 years from the study as these patients are evaluated under pediatrics as per the institute protocol and are referred only for opinion. A detailed psychiatry evaluation could have further classified the associated psychiatry comorbidities beyond anxiety and depression. VEEG analysis, though considered to be the gold standard in diagnosing PNES, can sometimes miss out on patients with frontal lobe epilepsy where the semiology resembles PNES and the interictal scalp EEG findings are usually normal. This is an important limitation of VEEG and should always be borne in mind when evaluating a patient with PNES.

Conclusion

Semiological assessment and VEEG monitoring of the patient is more reliable as the eye witnesses often provide unreliable accounts of the episode semiology. Of the PNES classification systems studied, Asadi-Pooya's classification was easiest to apply and could classify all the patients in the study. A universally accepted and appropriate semiology-based classification system for PNES may lead to better understanding and reduce the confusion with regard to the multiple and complex schemes of classifying PNES. Assessment of associated psychiatric comorbidity is a prerequisite in PNES management and can improve the outcome and overall quality of life in these patients.

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Conflict of Interest
None declared.

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