Epilepsy & Behavior 54 (2016) 40–46

Contents lists available at ScienceDirect

Epilepsy & Behavior

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

Clinical Research

Improving first responders' psychogenic nonepileptic seizures diagnosis accuracy: Development and validation of a 6-item bedside diagnostic tool

Luciano De Paola [a,b,*], Vera Cristina Terra [a,b], Carlos Eduardo Silvado [a,b], Helio Afonso Ghizoni Teive [c], Andre Palmini [d], Kette Dualibi Valente [e,f], Márcia Olandoski [g], W. Curt LaFrance Jr. [h,i]

[a] Epilepsy and EEG Service, Hospital de Clínicas, Federal University of Paraná, Brazil
[b] EPICENTRO, Comprehensive Epilepsy Center, Hospital N S das Graças, Curitiba, Paraná, Brazil
[c] Movement Disorders Service, Hospital de Clínicas, Federal University of Paraná, Brazil
[d] Service of Neurology, Porto Alegre Epilepsy Surgery Program, The Brain Institute (InsCer), Pontificia Universidade Católica do Rio Grande do Sul, Porto Alegre, Brazil
[e] Psychiatric Department, Clinic's Hospital, University of São Paulo, Brazil
[f] Clinical Neurophysiology Laboratory, Clinic's Hospital, University of São Paulo, Brazil
[g] Medical School, Pontificia Universidade Católica do Paraná, Brazil
[h] Psychiatry Department, Brown Medical School, Rhode Island Hospital, Providence, RI, USA
[i] Neurology Department, Brown Medical School, Rhode Island Hospital, Providence, RI, USA

ARTICLE INFO

Article history:
Received 27 September 2015
Revised 24 October 2015
Accepted 26 October 2015
Available online 29 November 2015

Keywords:
Seizures
Nonepileptic seizures
Nonepileptic attacks
Seizure semiology
Video-electroencephalography

ABSTRACT

Objective: Epileptic seizures (ES) are often seen as a medical emergency, and their immediate and accurate recognition are pivotal in providing acute care. However, a number of clinical situations may mimic ES, potentially leading to misdiagnosis at the emergency room and to inappropriate prescription of antiepileptic drugs (AED) in the acute and chronic settings. Psychogenic nonepileptic seizures (PNES) play a major role in this scenario and often delay the correct diagnosis and increase treatment morbidity and cost. First responders often conduct the initial assessment of these patients, and their impression may be decisive in the prehospital approach to seizures. We sought to investigate and improve the accuracy of PNES diagnosis among professionals involved in the initial assistance to patients with seizures.
Methods: Fifty-three registered nurses, 34 emergency physicians, 33 senior year medical students, and 12 neurology residents took a short training program consisting of an initial video-based seizure assessment test (pretest), immediately followed by a 30-minute presentation of a 6-item bedside diagnostic tool and then a video-based reassessment (posttest). Baseline status and learning curves were determined.
Results: The distinct professional categories showed no significant differences in their ability to diagnose PNES on both pretests and posttests. All groups improved diagnostic skills after the instructional program.
Significance: The findings helped determine the best identifiable PNES clinical signs and to provide initial validation to a novel diagnostic instrument. In addition, our results showed that educational measures might help in the identification of PNES by first responders, which may decrease the treatment gap.

1. Introduction

Epilepsy is currently defined as a disease of the brain diagnosed on the bases of a single unprovoked seizure plus a probability of further seizures similar to the general recurrence risk (~60%) after two unprovoked seizures [1]. This updated conceptualization has increased the relevance of a correct diagnosis of the nature of a first seizure, particularly the differentiation of epileptic seizures (ES) from psychogenic nonepileptic seizures (PNES). We have evolved from Hippocrates' description of convulsions "similar to those of epilepsy" [2] to recently reported minimum requirements for the diagnosis of PNES [3]. Still, unrecognized PNES not only delay correct diagnosis by a mean of 7 years, but also increase treatment cost and morbidity [4,5].

As convulsions are often considered an emergency, ambulance personnel and emergency room (ER) staff are frequently involved in the primary assessment [6,7]. Diagnostic errors in this setting may bias the next steps in the evaluation and treatment, including unnecessarily aggressive treatment of prolonged PNES mistaken as status epilepticus [8,9]. Thus, it is important to train 'first responders' in the clinical hallmarks of PNES and to develop tools to aid these professionals in the suspicion of a diagnosis of PNES. Here, we report first responders'

* Corresponding author at: Epilepsy Service, Neurology Department, Hospital de Clínicas, Universidade Federal do Paraná, Rua General Carneiro, 181, Curitiba 80.060-900, Brazil.
E-mail address: luciano.depaola@gmail.com (L. De Paola).

http://dx.doi.org/10.1016/j.yebeh.2015.10.025
1525-5050/

diagnostic performance on a suspicion of PNES and present a novel instrument designed to improve accuracy in the initial approach. We hypothesized that this instrument would considerably enhance first responders' awareness of PNES, as well as their ability to identify clinical clues that may lead to this diagnosis. This study was designed with two components to be carried out together: one, to identify a useful diagnostic instrument and two, to assess the value of an educational measure. In this paper, we describe the findings as they inform both parts.

2. Methods

2.1. Developing a bedside seizure semiology identification tool

We reviewed video-EEG recordings of documented PNES from the archives of epilepsy monitoring units (EMU) of two tertiary epilepsy centers (Hospital de Clínicas, Federal University of Paraná and EPICENTRO, Hospital Nossa Senhora das Graças, Curitiba, Paraná, Brazil), between 2004 and 2014. Cases in which the PNES had motor features resembling generalized tonic–clonic epileptic seizures (ES) were selected, and PNES with pure immobility, subtle random movements, or hypotonia and unresponsiveness were excluded. Fifty patients were selected, 30 with "lone" PNES and 20 "mixed", with documented coexistence of PNES and ES. A mean of 3 (ranging from 1 to 12) PNES were recorded per patient. All seizures were analyzed, and one representative sample per patient was selected and edited, based upon the quality of both the video and the interaction with the patient during the episode. Semiology in patients with lone and mixed PNES was analyzed, compared, and proven similar. The 50 patients with PNES were compared with 20 patients with video-EEG documented ES, randomly assigned from the same databases. A mean of 2.8 (ranging from 1 to 10) ES were recorded per patient, and one representative episode was selected and edited. All 70 videos were then reviewed for the presence or absence of 27 semiological signs considered as potential discriminators between PNES and ES according to the pertinent literature [3,10–12]. Comparison between PNES and ES allowed us to select six practical semiological features with potential to distinguish PNES from ES and to build a rapid assessment instrument. We aimed to include signs that were easily and promptly identifiable at the emergency site, assuming that, if present, they would not be missed, even in the distressful environment of seizure-like events. Recognition of these signs and consequent consideration of PNES into the differential diagnosis may prevent the "error on the safe side" effect that leads to starting antiepileptic drugs for any event resembling an epileptic seizure. To optimize recognition, these signs were plotted on cartoon figures displaying the positions or features of each chosen sign, favoring either PNES or ES. This layout was loosely inspired by Gates' [2] classical paper on "ictal characteristics of pseudoseizures" (Fig. 1).

2.2. Testing and validation of PNES diagnostic tool among first-responders

We tested and validated the usefulness of this rapid seizure assessment instrument by analyzing performance on a group of first responders. In our setting, 'first responders' encompass distinct categories of professionals, as opposed to the exclusive emergency medical technicians (EMTs) seen on other countries. Subjects were 53 nurse clinicians (RN), 34 emergency physicians (MD), 33 senior medical students (MS), and 12 neurology residents (NR), all related to emergency care. The RN and MD were recruited from a pool of professionals working at the city public emergency medical ambulance system. The MS were at their senior year of medical school, attending subinternship activities and routinely taking calls at emergency rooms under staff supervision. The NR group encompasses both neurology and child neurology residents. All participants signed an informed consent form and were presented with a random selection of 6 videos, 3 of PNES and 3 of ES. Before any specific training, participants were pretested by watching each video and selecting either "PNES" or "ES" as a primary diagnosis. Accuracy of responses was established for all responders and for each professional category. Following the pretest, subjects immediately attended a 30-minute live slide- and video-based group educational activity covering concepts of PNES, the importance of their recognition,

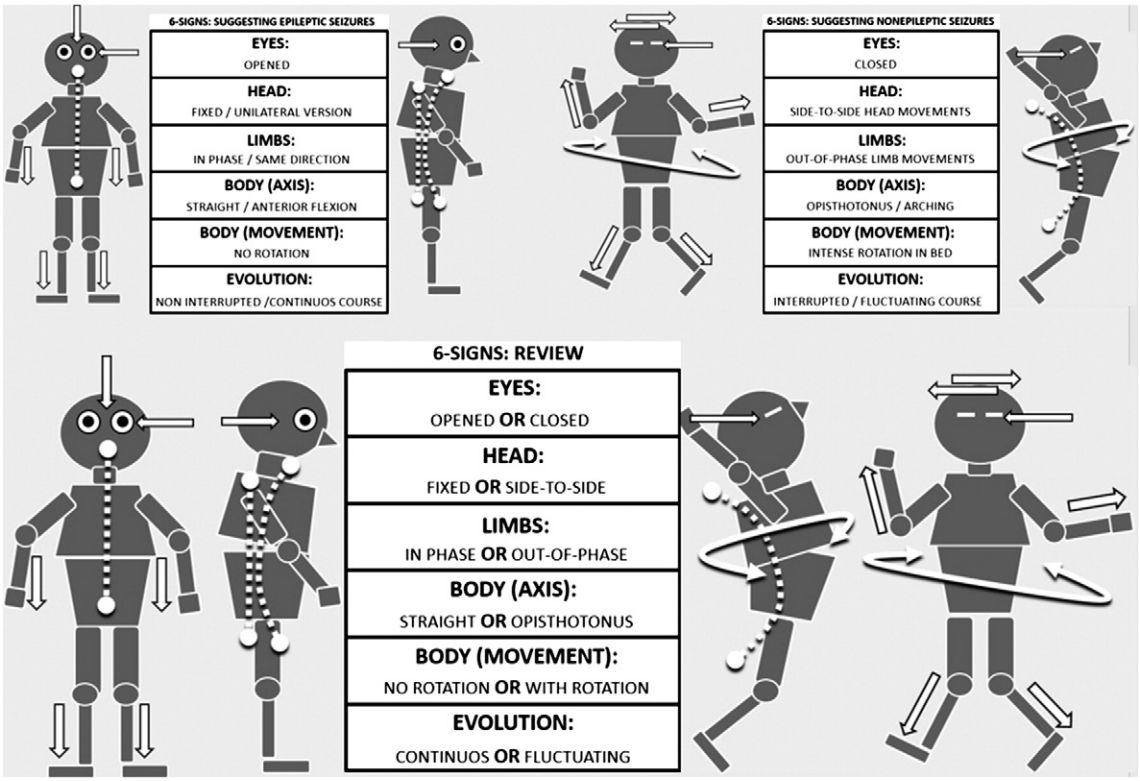

Fig. 1. Cartoon figures shown during the teaching sessions displaying the 6 signs used as ES/CNEP discriminators.

and the 6-item bedside diagnostic instrument for practical discrimination between PNES and ES. Subsequently, they took a posttest, i.e., a new round of videos with 6 seizures, 3 PNES and 3 ES, different from the first test and presented randomly. Participants were requested to once again check "PNES" or "ES" and also to acknowledge the presence or absence of each of the 6 signs previously discussed. Answer sheets had the six signs listed for each seizure and the subjects could mark either its presence or absence or leave it blank if not recognized or unsure. Participants were unaware of the test–retest nature of this activity to avoid previous preparation, thus, achieving maximum baseline legitimacy. Baseline knowledge, learning curves, and overall performance were analyzed, as well as the signs that were more consistently identified, and therefore, deemed most useful in teasing out PNES and ES.

2.3. Statistical analysis

Student's t-test for independent samples was used to compare the clinical sign identification in lone PNES, mixed PNES–ES, and ES-only cases. Nonparametric Mann–Whitney test was used for the analysis of seizure durations, Wilcoxon signed-rank test for performance in pre- and post-instruction tests, and Spearman's coefficient of correlation for the analysis of correct answers based on correct recognition of each clinical sign. The different professional groups had their performances compared by Kruskal–Wallis nonparametric test. For all statistical analyses, p values of less than 0.05 were considered significant. All data were analyzed with IBM's SPSS Statistics v.20 Program.

2.4. Ethics committee approval

All patients signed informed consents regarding to the use of their videos for research and teaching purposes. All subjects in this study signed informed consents allowing the interpretation of results on their pre and post tests. This study was approved by the local ethics committee (approval number CAAE47899715.5.000.5689).

3. Results

3.1. Semiology samples

Demographic and medical features of PNES and ES groups did not differ concerning age, gender (in spite of a trend towards predominance of women in the group with PNES), or medication profiles (Table 1). Moreover, no significant differences were found regarding any of the 27 clinical signs when comparing patients with lone PNES and mixed PNES–ES. Thus, these 50 patients with PNES could be combined and systematically compared with the 20 patients with ES on the presence or absence of the 27 clinical signs (Table 2). Eight signs did not prove useful in differentiating PNES and ES: eye fluttering, mouth position (opened/closed), ictal crying/weeping, rigidity throughout the seizure, persistently clenched fists, ictal hyperventilation, and stereotypy of the attacks. The remaining 19 clinical signs were valid discriminators and deserved further analysis. Given that the aim of this study was to provide a quick, objective, and easily identifiable set of clinical signs to be used at the emergency site, six signs best suited these requirements and therefore defined the clinical diagnostic instrument. Table 2 also summarizes the inclusion and exclusion criteria for the short-listing process. Sensitivity, specificity, and accuracy were determined for each clinical sign (Table 3) and compared with data from papers using similar methodology [10–12]. These comparisons showed similar sensitivity and specificity for fluctuating course, forceful eye closing, asynchronous movements, and side-to-side head movements between our study and others. Opisthotonus and rotation in bed showed excellent specificity for PNES (100%), but, respectively, low sensitivity of 38% and 26%, and overall accuracy of 55.7% and 47%. A combination of opisthotonus and rotation in bed was seen in 22% of patients with PNES, leading to a diagnostic accuracy of 55.7%. Psychogenic nonepileptic seizures averaged 10.8 min in duration, whereas ES were significantly shorter (average 1.1 min). Although this feature constitutes a highly significant discriminator ($p < 0.001$) and is consistent with the literature [3], we did not include it in this study, as we focused on immediate recognition, as opposed to longer clinical observation.

Table 1
Main demographic and clinical characteristics of the seizure semiology groups.

Demographic or clinical feature	Pure PNES N = 30	Mixed PNES N = 20	ES N = 20	p value (1)	p value (2)
Age (years)	16–52 (m: 35.2)	20–58 (m: 36.4)	17–49 (m: 31.8)	0.7	0.18
Gender (M/F)	8/22	5/15	10/10	1.0	0.08
On AEDs (Y/N)	26/4	20/0	20/0	0.2	0.3
On AD (Y/N)	13/17	9/11	1/19	1.0	0.02*
On AP (Y/N)	1/29	2/18	2/18	0.5	0.6

Pure PNES — patients presenting with psychogenic nonepileptic seizures only.
Mixed PNES — patients presenting with both psychogenic nonepileptic seizures and epileptic seizures.
ES — patients presenting with epileptic seizures only.
AEDs (antiepileptic drugs), AD (antidepressants), AP (antipsychotics).
p value (1): variable comparisons between group with Pure PNES and group with Mixed PNES.
p value (2): variable comparisons between combined groups with PNES (Pure PNES plus Mixed PNES) and group with ES.
* Statistical analysis: Student's t-test significance ($p < 0.05$).

3.2. Clinician sample testing

We then determined the accuracy for the PNES diagnosis among a group of first responders in conjunction with preseizure and postseizure PNES identification training. Nine participants (5 MD and 4 RN) were excluded because of incorrect filling of the test forms. The remainder 132 showed similar diagnostic skills for PNES and ES with no statistically significant differences between pretest and posttest results among the professional categories (Table 4). Although absolute numbers for identification of signs suggest poorer performances for RN, the difference did not reach statistical significance. The groups of MD, MS, and NR had a remarkably similar performance. About 65–70% of the seizures were correctly diagnosed on pretest. Overall excellent effort of the participants in trying to identify and check the clinical sign boxes during posttest was noted, with filling of 86 to 100% of these requested boxes in the test cards, across different professional categories. The vast majority (78.8–94.1%) of responders improved their diagnostic skills (Table 4). There were differences between professional categories on the accuracy of interpretation of each clinical sign individually (Table 5), which did not affect the overall diagnostic accuracy for PNES or ES.

4. Discussion

We provided data on the use of a seizure semiology identification tool for bedside differentiation of ES and PNES. To the authors' knowledge, this represents the first study of its kind to develop a bedside 6-sign diagnostic tool, test the tool, and validate a seizure differentiation education program specifically designed for clinicians, nurses, and senior medical students, all involved in acute care delivery. This study is borne out of the great need for accurate diagnosis, which directly informs intervention in the acute care setting.

Fifteen years ago, an iconic editorial by John Gates praised 20 years of work in the PNES field and called for multicenter population-based studies, an effort that would uncover the economic impact of PNES and justify more aggressive research programs [13]. An international PNES workshop in 2005 sponsored by the NINDS, NIMH, and AES established the research benchmarks for PNES [14]. While significant progress has been made both in PNES diagnosis and treatment [15], this borderland disorder remains misdiagnosed, wrongly treated, and even actively avoided by many health-care providers [16]. The antidote

Table 2
Incidence and significance of each clinical sign as a discriminator between Pure PNES, Mixed (PNES and ES), and pure ES.

Clinical sign	Pure PNES (N = 30)	Mixed PNES (N = 20)	p value	PNES (N = 50)	ES (N = 20)	p value	Inclusion/ exclusion	Rationale
Occurrence from sleep	0 (0)	0 (0)	1.00	0 (0)	6 (30)	<0.001	Excluded	Requires EEG for sleep assurance
Fluctuating course	27 (90)	20 (100)	0.26	47 (94)	0 (0)	<0.001	Included	Ictal feature/easily identified
Closed eyes/opened eyes/both	19 (63.3)/7 (23.3)/4 (13.3)	16 (80)/3 (15)/1 (5)	0.42	35 (70)/10 (20)/5 (10)	0 (0)/20 (100)/0 (0)	<0.001	Included	Ictal feature/easily identified
Eye fluttering	3 (10)	0 (0)	0.26	3 (6)	0 (0)	0.55	Excluded	Not significant
Closed mouth	25 (100)	19 (95)	0.38	44 (88)	15 (75)	0.27	Excluded	Not significant
Asynchronous (limb) movements	24 (80)	18 (90)	0.45	42 (84)	0 (0)	<0.001	Included	Ictal feature/easily identified
Side-to-side head movements	21 (70)	12 (60)	0.54	33 (66)	0 (0)	<0.001	Included	Ictal feature/easily recognized
Pelvic thrusting	12 (40)	9 (45)	0.77	21 (42)	0 (0)	<0.001	Excluded	Sometimes unclear/not easily identified
Opisthotonus	10 (33.3)	9 (45)	0.55	19 (38)	0 (0)	<0.001	Included	Ictal feature/easily recognized
Rotation in bed	6 (20)	7 (35)	0.32	13 (26)	0 (0)	<0.001	Included	Ictal feature/easily recognized
Responsiveness during attack (Y/N/partially)	8 (26.7)/21 (70)/1 (3.3)	5 (25)/11 (55)/4 (20)	0.15	13 (26)/32 (64)/5 (10)	0 (0)	0.01	Excluded	Requires interaction
Ictal crying/weeping	2 (6.7)	3 (15)	0.38	5 (10)	0 (0)	0.31	Excluded	Not significant
"Epileptic cry" (classic)	0 (0)	0 (0)	1.00	0 (0)	16 (80)	<0.001	Excluded	Not sustained/mostly at onset
Ictal rhythmic grunting	0 (0)	0 (0)	1.00	0 (0)	20 (100)	<0.001	Excluded	Not sustained/mostly at offset
Persistent rigidity	5 (16.7)	2 (10)	0.68	7 (14)	0 (0)	0.18	Excluded	Not significant
Persistent clenched fist	5 (16.7)	5 (25)	0.49	10 (20)	0 (0)	0.053	Excluded	Not significant
Persistent ictal hyperventilation	6 (20)	1 (5)	0.21	7 (14)	0 (0)	0.18	Excluded	Not significant
Stertorous breathing	1 (3.3)	0 (0)	1.00	1 (2)	20 (100)	<0.001	Excluded	Post ictal feature
Urinary incontinence	0 (0)	1 (5)	0.40	1 (2)	0 (0)	1.00	Excluded	Not significant
Sialorrhea/hypersalivation	5 (16.7)	1 (5)	0.38	6 (12)	20 (100)	<0.001	Excluded	Draws attention & prevents recognition of other signs
Cyanosis	0 (0)	0 (0)	1.00	0 (0)	20 (100)	<0.001	Excluded	Draws attention & prevents recognition of other signs
Duration in minutes (min/max/average)	0.2/120/10.9	0.2/60/10.7	0.94	0.2/120/10.8	1.0/1.6/1.1	<0.001	Excluded	Requires timing
Stereotyped attacks	30 (100)	20 (100)	1.00	13 (26)	20 (100)	<0.001	Excluded	Requires clinical history
Postictal confusion	5 (16.7)	2 (10)	0.68	7 (14)	20 (100)	<0.001	Excluded	Post ictal feature
Postictal unresponsiveness	0 (0)	0 (0)	1.00	0 (0)	20 (0)	<0.001	Excluded	Post ictal feature
Postictal flaccidity	8 (26.7)	1 (5)	0.06	9 (18)	20 (100)	<0.001	Excluded	Post ictal feature
Recall for the period when patient appears unconscious	15 (50)	15 (75)	0.14	30 (60)	0 (0)	<0.001	Excluded	Post ictal feature

Statistical analysis: Fisher's exact test or Chi-square test (categorical variables), Mann–Whitney nonparametric test (for duration), significance $p < 0.05$, Pure PNES — patients presenting with psychogenic nonepileptic seizures only, Mixed PNES — patients presenting with both psychogenic nonepileptic seizures and epileptic seizures, ES — patients presenting with epileptic seizures only.

to this adverse scenario largely relies on a change of attitude, ultimately based on education. We aimed to aid bedside PNES diagnosis, targeting selected professionals who are indeed the people most frequently confronted with patients with PNES in emergency situations. Considering that setting, we prioritized ictal semiology, as it constitutes the foundation for an initial suspicion of the diagnosis when confronting putative PNES. We acknowledge that video-EEG remains the gold standard of PNES diagnosis.

Well-conducted studies have addressed semiological features of PNES, endorsing their cross-cultural nature and similar clinical presentations [2,16–25]. In order to establish a local database, we collected clinical data on 50 PNES cases and compared ictal semiology with 20 ES cases. Evidence suggests that clinical history, taken either during a formal interview or through structured questionnaires, may be useful as an adjunctive discriminator between PNES and ES [26–28]. We purposefully did not use clinical history and focused exclusively on ictal features, systematically comparing the presence or absence of 27 clinical signs, ranging from classic overt signs to more subtle presentations, all listed among the most commonly reported [2,3,10–12,29].

The ILAE Nonepileptic Seizures Task Force summarized the literature and provided minimum requirements for the diagnosis of PNES [3]. Several notes of caution emerged: (i) individual elements of seizure semiology are unreliable as diagnostic discriminators; (ii) traditional tables with semiologic elements and their frequency in PNES and ES generally disregard semiologic subdivisions, for instance GTC-like events vs "swoon" events; (iii) it is not always clear whether conclusions are drawn from video-based data or witnesses' reports. Nonetheless, the Task Force provided a list of signs from the literature favoring either

Table 3
Comparison of sensitivity, specificity, and accuracy of selected clinical seizure signs among different series.

Clinical sign	Avbersek & Sisodiya [10]	Syed et al. [12]	Present study (CI 95%)*
	Sensitivity/specificity (%)	Sensitivity/specificity (%)	Sensitivity/specificity/accuracy (%)
Fluctuating course	69 (events)/96	42/96	94/100/95.7
Closed eyes	34–88 (events)/74–100 52–96 (patients)/97	33/100	80/100/85.7
Asynchronous (limb) movements	44–96 (events)/93–96 9–56 (patients)/93–100	17/78	84/100/88.6
Side-to-side head movements	25–63 (events)/96–100 15–36 (patients)/92–100	25/87	66/100/75.7
Opisthotonus	Insufficient	8/96	38/100/55.7
Rotation in bed	n/a	n/a	26/100/47.1

Abbreviation: n/a — not applied.
Sensitivity/specificity/accuracy refers to 'patients', unless otherwise discriminated.
* Fisher's exact test, $p < 0.05$.

Table 4
Accuracy on diagnosis on baseline (pretest) and post-instruction program (posttest) according to professional category.

Category	PNES (average correct answers/min: 0, max: 3)			ES (average correct answers/min: 0, max: 3)			Total (average correct answers/min: 0, max 6)		
	Pretest	Posttest	p-Value*	Pretest	Posttest	p-Value*	Pretest	Posttest	p-Value*
RN (N = 53)	1.8	2.9	<0.001	1.8	2.6	<0.001	3.6	5.6	<0.001
MD (N = 34)	1.9	3.0	<0.001	2.1	2.8	<0.001	3.9	5.8	<0.001
MS (N = 33)	1.8	2.9	<0.001	2.2	2.8	0.004	4.1	5.7	<0.001
NR (N = 12)	2.3	2.9	0.018	1.9	2.8	0.024	4.3	5.8	0.005
p-Value**	0.070	0.886		0.143	0.257		0.141	0.276	

Abbreviations: RN, registered nurse; MD, medical doctor; MS, medical student; NR, neurology resident; PNES, psychogenic nonepileptic seizure; ES, epileptic seizure.
* Comparing pretest × posttest; Wilcoxon nonparametric test, $p < 0.05$.
** Comparing professional categories; Kruskal–Wallis nonparametric test, $p < 0.05$.

PNES or ES (the "good" signs), plus a list of "insufficient" signs. Our study used very strict definitions for each sign. We limited our sampling to events with a predominance of motor features (i.e., resembling GTC seizures), and our database was entirely documented on video-EEG. With these narrow criteria, our results matched those indicated by the Task Force, with two exceptions: (i) ictal crying, considered a "good" discriminating sign, did not reach statistical significance, in spite of its occurrence in 5 of our cases with PNES, and (ii) opisthotonus, a Task Force "insufficient" sign, was highly significant in our series. A plausible explanation could rest on our inclusion criteria which required unquestionable crying, as opposed to soft weeping and a more classic opisthotonus position, with sustained and forced arching, occurring at any given moment during a seizure. Interestingly, in spite of its perceived relevance, there are only two uncontrolled studies reporting on opisthotonus, which constituted the basis for its consideration as an "insufficient" diagnostic sign [10]. The first phase of the study was to develop the bedside diagnostic tool. Table 2 details our process of shortlisting the 19 potentially discriminant signs into the 6 that we believed to be more appropriate for the purpose of this project. In addition to assessing their significance, we took into account the literature consensus (fluctuating course, asynchronous movements, forceful closing of the eyes, and side-to-side head movements) and the readiness of their recognition (opisthotonus and rotation in bed). We believe that the closest equivalent to our 'rotation in bed' sign would be 'flailing' or 'thrashing' movement signs. The latter have been traditionally associated with oscillatory, side-to-side, out of phase, or just chaotic movements and are considered "insufficient" as a discriminator [3]. Just like rotation in bed, these movements may be seen with frontal lobe seizures with a rather bizarre clinical presentation and be associated with a negative EEG [30,31]. In our report, 'rotation in bed', although occasionally associated with flailing or thrashing, defines a rolling movement from belly up to belly down or whole body movements from side to side. We found this to be a highly sensitive, poorly specific, and moderately accurate sign, but overall very easy to distinguish. Other signs were ruled out because they (a) were not immediately recognizable, (b) were subjected to confusion, (c) required time for definition during the seizure, or (d) were mostly postictal phenomena. A recent review suggested that between 56 and 81% of PNES are associated with motor events [32]. Thus, by choosing 6 readily recognizable motor signs, we hypothesized that our instrument could efficiently be applied to the majority of cases.

The next phase of the study was assessing an education module to identify seizure types. We tested this hypothesis on a group of first responders, who in our setting are represented by various professionals, as previously described. Our short teaching program included a pretest, brief instruction with presentation of the 6 signs that was taken immediately following the pretest, and a posttest. Three relevant results were immediately evident. First, we found a better-than-expected performance in all professional categories, with correct interpretation of

Table 5
Assessment of correct recognition of each clinical sign according to professional category on posttest evaluation.

Clinical sign	Professional category	N	Correct recognition for PNES[a]			Correct recognition for ES[a]		
			Mean	SD	p value	Mean	SD	p value
Eyes (opened/closed)	RN	53	1.7	1.1	0.12	2.1	1.1	0.14
	MD	34	2.0	1.0		2.4	0.8	
	MS	33	2.2	0.9		2.5	0.9	
	NR	12	2.3	0.5		2.6	0.8	
Head movements (side-to-side)	RN	53	1.9	1.0	0.04	1.8	1.2	0.001
	MD	34	2.4	0.7		2.4	1.0	
	MS	33	2.4	0.6		2.8	0.5	
	NR	12	2.3	0.7		2.3	0.8	
Limbs movements (synchronous/asynchronous)	RN	53	1.7	1.0	<0.001	1.9	0.9	<0.001
	MD	34	2.6	0.7		2.7	0.6	
	MS	33	2.7	0.6		2.8	0.5	
	NR	12	2.9	0.3		2.8	0.6	
Body position (opisthotonus)	RN	53	0.4	0.7	<0.001	0.7	1.1	<0.001
	MD	34	1.2	1.2		1.2	1.2	
	MS	33	1.6	0.9		2.3	1.0	
	NR	12	0.8	0.9		1.5	1.2	
Seizure evolution (fluctuating/continuous)	RN	53	1.0	0.9	<0.001	1.4	1.1	<0.001
	MD	34	1.6	0.6		2.2	0.9	
	MS	33	2.1	0.7		2.8	0.5	
	NR	12	1.8	0.8		2.4	1.0	
Rotation in bed	RN	53	0.9	1.0	<0.001	0.9	1.1	<0.001
	MD	34	1.4	1.2		1.5	1.2	
	MS	33	2.3	0.6		2.4	0.8	
	NR	12	1.5	1.1		1.4	1.3	

Kruskal–Wallis nonparametric test, $p < 0.05$.
Abbreviations: RN, registered nurse; MD, physician (ER and GP); MS, medical students; NR, neurology residents; PNES, psychogenic nonepileptic seizures; ES, epileptic seizures; SD, standard deviation.
[a] Based on the number of correct answers (0 to 3 for PNES, 0 to 3 for ES).

signs in 60–70% at pretest. That may be secondary to the seizure sample selection, purposefully using major motor PNES and overt ES, as opposed to more subtle presentations. Still, our study population missed the correct diagnosis on nearly a third of these very representative examples. Second, there was a surprising similarity of performance among the distinct professional categories. Although we did not control for experience, it could be intuitively expected that physicians would outperform residents, medical students, or nurses. Finally, all categories benefited from training, with improvement rates ranging from 79 to 94%, across different professional categories. These data suggest that a live, video-based teaching program does improve accuracy of diagnosis of the nature of seizure events. There are only a few studies with a similar design but targeting different populations. A proof-of-concept study, also video-based training, was conducted by Seneviratne and colleagues and aimed to improve seizure recognition skills among medical students in Australia, using emergency medical trainees as controls. It shows that targeted video-based training increases the accuracy of visual discrimination of seizures. Although, prior to instruction, trainees had a higher rate of diagnostic accuracy, the difference disappeared following video-based training. However, as compared with ours, they used a longer and more detailed training module and a larger test–retest interval [33]. In another diagnostic study, O'Sullivan and colleagues offered video-based teaching to 261 subjects, including medical students and physicians from various medical disciplines and showed that diagnostic accuracy, clinical confidence, as well as sensitivity and specificity for diagnosing PNES increased for the entire group on the posttest [34]. An interesting finding in our study is that in spite of similar accuracy among responders, there have been some differences in the recognition of each individual sign. The most uniformly recognized sign was forceful eye closing, confirming our perception that this would be an easily identifiable and effective diagnostic sign. The diagnostic value of this sign has been both supported and rejected [35,36]. This variability may be related to the overly simplistic designation of eyes open/eyes closed. Other studies have shown that eyes open *at ictal onset* was associated with epilepsy. This specific sign was not designated for this study. Short sets of signs make a useful tool, as recently demonstrated on a study for the validity of bedside signs for functional weakness and sensory and gait abnormalities in conversion disorders, which short-listed 38 into 6 "highly reliable", thus, practically efficient signs [37].

Patients receiving the diagnosis of PNES often report "being left in limbo land" [38]. Regretfully, neurologists and psychiatrists sometimes encounter the same destination [39,40]. A lack of knowledge about PNES by patients and providers appears to be the fundamental nature of this conundrum, which could be reversed by teaching interventions.

Limitations of the study include the following: (i) the focus was only on generalized semiology. We did not include focal dyscognitive (complex partial or simple partial) semiologies, which may result in less generalizability to nongeneralized motor seizures. The latter, however, may even challenge the diagnostic skills of experienced epileptologists. We were looking at a basic level of seizure distinction among a nonspecialist population, that is, more exposed to error and to inducing iatrogenicity. (ii) Eye closure sign was not designated as being at ictal onset or during ictus, which have been shown to inform diagnosis of ES and PNES; (iii) also, our study focused on recognition of one specific sign at a time, rather than a combination of signs. Likewise, we did not take into account the difference between directly observed and witness-described signs. Our goal was to assist decision making during seizure occurrence, using minimal relevant information, not dependent on clinical history, interaction, witnesses, or longer observations. We acknowledge the fact that patients still in a seizure represent the minority of cases when medical attention is called. But these are also the ones in which the diagnosis should definitely not be missed, thereby avoiding unnecessary procedures, such as sedation and intubation; (iv) the increasing availability of smartphones with video cameras provide a number of documented events, and these lesser quality, yet important vignettes, were not included on our study; as for teaching purposes we aimed for best quality documentation. A specific study using home videos is currently in progress; (v) a longer intervention effect was not measured in our study, as this was not the focus on the brief education format we proposed. (vi) Finally, EMTs were not included in the test sample but, because EMTs are the primary first responders, assessing how they evaluate seizures will be important.

5. Conclusions

Psychogenic nonepileptic seizures are indeed common, misdiagnosed, and wrongly treated, leading to increased health-care cost and morbidity and less than optimal outcomes. Part of the burden relies on its borderline status, reluctantly managed by insecure ER doctors at the start and somewhat uncomfortable neurologists and psychiatrists later along the care. Changing concepts start with a good diagnosis. We presented data supporting ictal semiology as an adjunctive approach to generalized motor seizure differentiation for PNES diagnosis. We proposed a simple diagnostic instrument based on easily and quickly identifiable clinical signs that proved useful in video-based teaching programs. We hope this provides a more solid argument to first responders when formulating an initial diagnostic impression of a seizure-like event. We believe education is key, not only to allow practical and safer approaches to these patients, but also to enlighten health-care providers with the overall concept of PNES.

Roles of each author in the study

Luciano De Paola, MD — concept, patient selection, group discussion, writing, editing.

Vera C Terra, MD — concept, patient selection, group discussion, writing, editing.

Carlos Silvado, MD — concept, patient selection, group discussion, writing, editing.

Helio Teive, MD — concept, group discussion, review.

Andre Palmini, MD — concept, group discussion, writing, editing.

Kette Valente, MD — concept, group discussion, writing, editing.

Márcia Olandoski, PhD — concept, group discussion, statistical analysis.

William Curt LaFrance,Jr, MD — concept, group discussion, writing, editing.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in the ethical publication and affirm that this report is consistent with those guidelines.

Acknowledgments

The authors would like to express their gratitude to Monica Parolin, MD and Gerson Albuquerque, RN from the Medical Emergency Ambulance Service, City of Curitiba, Paraná, Brazil for providing data and allowing interaction with the medical and paramedic personnel on their teams. The authors would also like to express their gratitude to Rubens Cat, MD, head of the Pediatrics Department, Hospital de Clínicas, Federal University of Paraná, Brazil, for involving the senior year medical students in this project.

Potential conflicts of interest

Luciano De Paola, MD has nothing to disclose.

Vera C. Terra, MD has nothing to disclose.

Carlos Silvado, MD has nothing to disclose.

Helio Teive, MD has nothing to disclose.

Andre Palmini, MD has nothing to disclose.

Kette Valente, MD has nothing to disclose.

Márcia Olandoski, PhD has nothing to disclose.

William Curt LaFrance, Jr., MD receives grants from Brown/NPNI and the Siravo Foundation. He receives author's royalties from Oxford University Press, and editor's royalties from Cambridge University Press with royalties.

References

[1] Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. A practical definition of epilepsy. Epilepsia 2014;55:475–82.
[2] Gates JR, Ramani V, Whalen S, Loewenson R. Ictal characteristics of pseudoseizures. Arch Neurol 1985;42:1183–7.
[3] LaFrance Jr WC, Baker GA, Duncan R, Goldstein RH, Reuber M. 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.
[4] LaFrance Jr WC, Benbadis SR. Avoiding the costs of unrecognized psychological nonepileptic seizures. Neurology 2006;66:1620–1.
[5] Jirsch DJ, Ahmed SN, Maximova K, Gross DW. Recognition of psychogenic nonepileptic seizures diminishes acute care utilization. Epilepsy Behav 2011;22:304–7.
[6] Shneker BF, Elliott JO. Primary care and emergency physician attitudes and beliefs related to patients with psychogenic nonepileptic spells. Epilepsy Behav 2008;13:243–7.
[7] Siket MS, Merchant RC. Psychogenic seizures: a review and description of pitfalls in their acute diagnosis and management in the emergency department. Emerg Med Clin North Am 2011;29:73–81.
[8] Reuber M, Baker GA, Gill R, Smith DF, Chadwick DW. Failure to recognize psychogenic nonepileptic seizures may cause death. Neurology 2004;62:834.
[9] Holtkamp M, Othman J, Buchheim K, Meierkord H. Diagnosis of psychogenic nonepileptic status epilepticus in the emergency setting. Neurology 2006;66:1727–9.
[10] 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.
[11] Seneviratne U, Rajendran D, Brusco M, Phan TG. How good are we at diagnosing seizures based on semiology? Epilepsia 2012;53:e63–6.
[12] Syed TU, LaFrance Jr WC, Kahriman ES, Hasan SN, Rajasekaran V, Gulati D, et al. Can semiology predict psychogenic nonepileptic seizures? A prospective study. Ann Neurol 2011;69:997–1004.
[13] Gates JR. Nonepileptic seizures: time for progress. Epilepsy Behav 2000;1:2–6.
[14] LaFrance Jr WC, Alper K, Babcock D, Barry JJ, Benbadis S, Caplan R, et al. Nonepileptic seizures treatment workshop summary. Epilepsy Behav 2006;8:451–61.
[15] LaFrance Jr WC, Baird GL, Barry JJ, Blum AS, Frank Webb A, Keitner GI, et al. Multicenter pilot treatment trial for psychogenic nonepileptic seizures: a randomized clinical trial. JAMA Psychiatry 2014;71:997–1005.
[16] Smith BJ. Closing the major gap in PNES research. Finding a home for a borderland disorder. Epilepsy Curr 2014;14:63–7.
[17] Ettinger AB, Devinsky O, Weisbrot DM, Ramakrishna RK, Goyal A. A comprehensive profile of clinical, psychiatric, and psychosocial characteristics of patients with psychogenic nonepileptic seizures. Epilepsia 1999;40:1292–8.
[18] 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;42:398–401.
[19] De Paola L, Palmini AL, Yacubian EM, Sakamoto AS, Guerreiro CA, Arruda F, et al. Nonepileptic seizures (NES) in Brazil: results on a national survey. J Clin Neurophysiol 2004;10:109–11.
[20] De Paola L, Silvado CES, Mader MJ, Minhoto GR, Werneck LC. Clinical features of psychogenic nonepileptic seizures (PNES): analysis of a Brazilian series. J Clin Neurophysiol 2006;12:37–40.
[21] O'Sullivan SS, Spillane JE, McMahon EM, Sweeney BJ, Galvin RJ, McNamara B, et al. Clinical characteristics and outcome of patients diagnosed with psychogenic nonepileptic seizures: a 5-year review. Epilepsy Behav 2007;11:77–84.
[22] Reuber M. Psychogenic nonepileptic seizures: answers and questions. Epilepsy Behav 2008;12 [622:35].
[23] Brown RJ, Syed TU, Benbadis S, LaFrance WC, Reuber M. Psychogenic nonepileptic seizures. Epilepsy Behav 2011;22:85–93.
[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 2011;20:308–11.
[25] Alessi R, Valente KD. Psychogenic non-epileptic seizures at a tertiary care center in Brazil. Epilepsy Behav 2013;26:91–5.
[26] Syed TU, Arozullah AM, Loparo KL, Jamasebi R, Suciu GP, Griffin C, et al. A self-administered screening instrument for psychogenic nonepileptic seizures. Neurology 2009;72:1646–52.
[27] Schramke CJ, Kay KA, Valeriano JP, Kelly KM. Using patient history to distinguish between patients with nonepileptic and patients with epileptic events. Epilepsy Behav 2010:478–82.
[28] Azar NJ, Pitiyanuvath N, Vittal NB, Wang L, Shi Y, Abou Khalil BW. A structured questionnaire predicts if convulsions are epileptic or nonepileptic. Epilepsy Behav 2010;19:462–6.
[29] Ali S, Jabeen S, Arain A, Wassef T, Ibrahim A. How to use your clinical judgment to screen for and diagnose psychogenic nonepileptic seizures without video electroencephalogram. Innov Clin Neurosci 2011;8:36–42.
[30] LaFrance Jr WC, Benbadis SR. Differentiating frontal lobe epilepsy from psychogenic nonepileptic seizures. Neurol Clin 2011;29:149–62.
[31] Pillai JÁ, Haut SR. Patients with epilepsy and psychogenic nonepileptic seizures: an inpatient video-EEG monitoring study. Seizure 2012;21:24–7.
[32] Mostacci B, Bisulli F, Alvisi L, Licchetta L, Baruzzi A, Tinuper P. Ictal characteristics of psychogenic nonepileptic seizures: what we have learned from video/EEG recordings — a literature review. Epilepsy Behav 2008;22:144–53.
[33] Seneviratne U, Ding C, Bower S, Craig S, Leech M, Phan TH. Video-based training improves accuracy of seizure diagnosis. J Neurol Neurosurg Psychiatry 2014;85:466–70.
[34] O'Sullivan S, Redwood R, Hunt D, McMahon EM, O'Sullivan S. Recognition of psychogenic non-epileptic seizures: a curable neurophobia? J Neurol Neurosurg Psychiatry 2013;84:228–31.
[35] Chung SS, Gerber P, Kirlin KA. Ictal eye closure is a reliable indicator for psychogenic nonepileptic seizures. Neurology 2006;66:1730–1.
[36] Syed TU, Arozullah AM, Suciu GP, Toub J, Kim H, Dougherty ML. Do observer and self-reports of ictal eye closure predict psychogenic nonepileptic seizures? Epilepsia 2008;49:898–904.
[37] Daum C, Gheorghita F, Spatola M, Stojanova V, Medlin F, Vingerhoets F, et al. Inter-observer agreement and validity of bedside "positive signs" for functional weakness, sensory and gait disorders in conversion disorder: a pilot study. J Neurol Neurosurg Psychiatry 2014. http://dx.doi.org/10.1136/jnnp-2013-307381 [pii: jnnp-2013-307381].
[38] Thompson R, Isaac CL, Rowse G, Tooth CL, Reuber M. What is it like to receive a diagnosis of nonepileptic seizures? Epilepsy Behav 2009;14:508–15.
[39] Kanner AM. When did neurologists and psychiatrists stop talking to each other? Epilepsy Behav 2003;4:597–5601.
[40] Kanner AM. Is the neurologist's role over once the diagnosis of psychogenic nonepileptic seizures is made? No! Epilepsy Behav 2008;12:1–2.