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A novel scale for suspicion of psychogenic nonepileptic seizures: development and accuracy

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ABSTRACT

Objective: : The differential diagnosis between epileptic and psychogenic nonepileptic seizures (PNES) is challenging, yet suspicion of PNES is crucial to rethink treatment strategies and select patients for diagnostic confirmation through video EEG (VEEG). We developed a novel scale to prospectively suspect PNES.
Methods: : First, we developed a 51-item scale in two steps, based upon literature review and panel expert opinion. A pilot study verified the applicability of the instrument, followed by a prospective evaluation of 158 patients (66.5% women, mean age 33 years) who were diagnosed for prolonged VEEG. Only epileptic seizures were recorded in 103 patients, and the other 55 had either isolated PNES or both types of seizures. Statistical procedures identified 15 items scored between 0 and 3 that best discriminated patients with and without PNES, with a high degree of consistency.
Results: : Internal consistency reliability of the scale for suspicion of PNES was 0.77 with Cronbach's Alpha Coefficient and 0.95 with Rasch Item Reliability Index, and performance did not differ according to the patient's gender. For a cut-off score of 20 (of 45) points, area under the curve was 0.92 (95% IC: 0.87–0.96), with an accuracy of 87%, sensitivity of 89%, specificity of 85%, positive predictive value of 77%, and negative predictive value of 94% (95% IC) for a diagnosis of PNES.
Conclusions: : The scale for suspicion of PNES (SS-PNES) has high accuracy to a reliable suspicion of PNES, helping with the interpretation of apparent seizure refractoriness, reframing treatment strategies, and streamlining referral for prolonged VEEG.

1. Introduction

Psychogenic nonepileptic seizures (PNES), also known as dissociative seizures, are paroxysms of altered subjective experience, involuntary movements or reduced self-control resembling epileptic seizures, yet unrelated to ictal epileptiform discharges [1]. Early identification shortens disease duration, optimizes counseling and improves prognosis. Despite this, accurate diagnosis of PNES may take up to 8 years, a fact mainly associated with health care providers' education and inadequacies of the health care system [2,3].

Video electroencephalography (VEEG), the gold-standard method to diagnose PNES, is time-consuming and costly, demands inpatient monitoring and is often not available in poor-resource settings [4,5]. Thus, sensitive tools to suspect PNES on clinical grounds could improve patient selection for VEEG monitoring and significantly shorten diagnostic delay. Previous attempts have sought to identify demographic,

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semiological, psychologic, somatic, and etiological elements that could contribute to a suspicion of PNES [6–11]. However, the scope of such initiatives was limited by an excessive emphasis on motor signs, specifically on the differentiation of PNES from generalized tonic-clonic seizures, largely neglecting "nonconvulsive" presentations (e.g., prolonged unresponsiveness) [8,12,13]. Furthermore, strategies such as conversational analysis, video monitoring, and linguistic differences. [14–16] However, the use of variables that are often not consistent with one another, are often related to the experience of the examiner with the pathology and are developed from a broad range of methodologies in fact indicates a fragmentation of the available instruments [17].

In short, despite widely held views of PNES as related to childhood trauma, current psychological distress and history of overt psychiatric disorders, a scheme integrating these negative life events with broader semiological elements in a rigorously developed scale is clearly lacking.

Neurologists and psychiatrists are often eager to use scales that allow diagnostic suspicion or confirmation of a number of entities, but seldom realize the laborious psychometric process of developing reliable instruments. Here, we present a novel instrument, the scale for suspicion of psychogenic nonepileptic seizures (SS-PNES), that follows the recommended guidelines of establishing a theoretical framework, developing a preliminary version with items analyzed by an expert panel, testing the scale in a pilot study and, lastly, applying the instrument in a prospective patient cohort, testing its usefulness against a gold standard for the diagnosis – in this case, prolonged VEEG monitoring with ictal recording.

Here, the process of elaborating the SS-PNES is described, with emphases on the statistical approaches to abridge the scale from 51 items to a straightforward instrument composed of a 'pure culture' of 15 highly discriminating items, and on its performance to raise a solid suspicion that a given patient has PNES, compared to VEEG data prospectively obtained. We hypothesized that combining objective epileptological questions with present and past emotional and psychiatric features would frame a useful scale to suspect PNES.

2. Methods

We developed the SS-PNES according to theoretical and methodological procedures recommended by the Standards for Educational and Psychological Testing [18]. Its accuracy was prospectively tested and described according to the Standards for Reporting Diagnostic Accuracy Studies [19].

The methodology is presented in three sequential steps: (1) development of the scale, (2) empirical study, and (3) statistical analysis. Flowchart of validation steps performed with their respective results and changes is presented in Supplementary Material 1.

The study followed regulations for research involving humans and was approved by the Institutional Committee on Ethics in Research (#573.300). The authors obtained written and informed consent from all subjects or legal representatives.

2.1. Development of the scale

A review of the literature preceded the elaboration of the items. As the first step, we conducted a broader search using the following keywords: "pseudoseizure," "pseudoseizures," "psychogenic seizures," "psychogenic non-epileptic," "psychogenic nonepileptic," "psychogenic nonepileptic seizures," "psychogenic non-epileptic seizures," "non-epileptic attack disorder," "epilepsy," and "seizures." We considered articles that were published from 1995 to 2014; the database was PUBMEB. We included articles that allowed us to identify the main differences between PNES and ES (epileptic seizures). The PRISMA is presented in Supplementary Material 2.

The scale was developed using etiological and biopsychosocial understanding, [20] and combining elements from several dimensions: neurological, psychiatric and somatic complaints, interpersonal relations, history of traumatic events in childhood, and family history. Items were elaborated from the following: (i) review of the literature focused on the distinction between PNES and ES; (ii) face-to-face meetings between three experts—a psychiatrist (G.B.) and two epileptologists (A.P., K.D.V.) — well-versed in history-taking from patients with PNES and ES and their relatives.

Initially, we formulated 49 items. Each item was scored on a Likert scale from zero to three, with higher scores suggesting PNES. This initial version of the scale was then revised by a specialist in the Portuguese language and underwent validation through independent analysis of three experts in PNES from two other tertiary epilepsy centers for content validity. The scale was sent by email individually to a panel of experts. To avoid influence, the experts were unaware of others' opinions. The responses were collected by the senior author. Participants remained anonymous. Their identity and comments were not revealed, even after the completion of the final report. This prevented the authority, personality, or reputation of some participants from dominating others during the process. Since the facilitator observed no disagreement, a second round with the experts was unnecessary.

Following this procedure, two items were added to the original 49 — "feeling of super-protection" and "episodes of self-harm and aggression toward others." Two criteria were modified to avoid repetition.

A 51-item scale was consolidated and tested in a pilot study of 20 consecutive patients with ages ranging from 16 to 62 years (mean, 35.1; SD = 11.6; 60% female) who had prolonged VEEG monitoring (24–260 hours; mean, 89.30; SD = 61.72) at the Porto Alegre Epilepsy Surgery Program for (i) presurgical evaluation, (ii) diagnosis of the epilepsy syndrome, or (iii) suspicion of PNES.

Two independent evaluators (GB, VP) applied the scale during the VEEG monitoring, blinded to clinical and neurophysiological diagnoses, and at this stage the application of the instrument was standardized and issues such as the sheer applicability of the scale, adequacy of the content, level of comprehension of the questions, and distribution of the answers were addressed. Mean time of application of this extended version was 30 minutes. Intraclass Coefficient (ICC) was also performed from five aleatory cases scored independently, and ICC indicated 100% agreement in all items (ICC = 1.000), except for the item seizure duration (ICC = 0.966; IC = 0.669 – 0.996; p = 0.003).

At the onset of each interview, participants were informed about the study's objectives and were given a brief explanation of the possible types of seizures: epileptic, psychogenic, or both, in that order.

2.2. Empirical study

Two hundred and twenty individuals who had VEEG monitoring from May 2016 to June 2019 were identified as potential participants. Inclusion and exclusion criteria were applied in two different moments, as described in figure 1. Initially, 43 patients were excluded based on previous surgery, psychiatric comorbidities, or cognitive difficulties. Of the remaining 177 participants, 19 were additionally excluded after VEEG, either due to the impossibility of establishing a definitive diagnosis or because their final diagnoses were neither ES nor PNES (figure 1).

The study had a transversal design, comparing the 51-item scale with VEEG data.

At the moment of the VEEG, two researchers (GB, VP), blind to the VEEG findings, applied the 51-item scale. The data obtained by this interview was compared with the electroclinical evaluation by VEEG.

During the VEEG, the epilepsy team decided the type of seizures (ES, PNES, mixed ES and PNES, or other) on the basis of the available ictal EEGs and with the support of clinical and neuroimaging data. The VEEG was obtained with the partial or complete withdrawal of antiseizure medications, ranging from 24 to 180 hours (mean 96 hours) and lasted until at least one typical event, recognized by patients and families, was captured. When more than one seizure type was reported, the VEEG monitoring continued until all seizure types were recorded. If the family

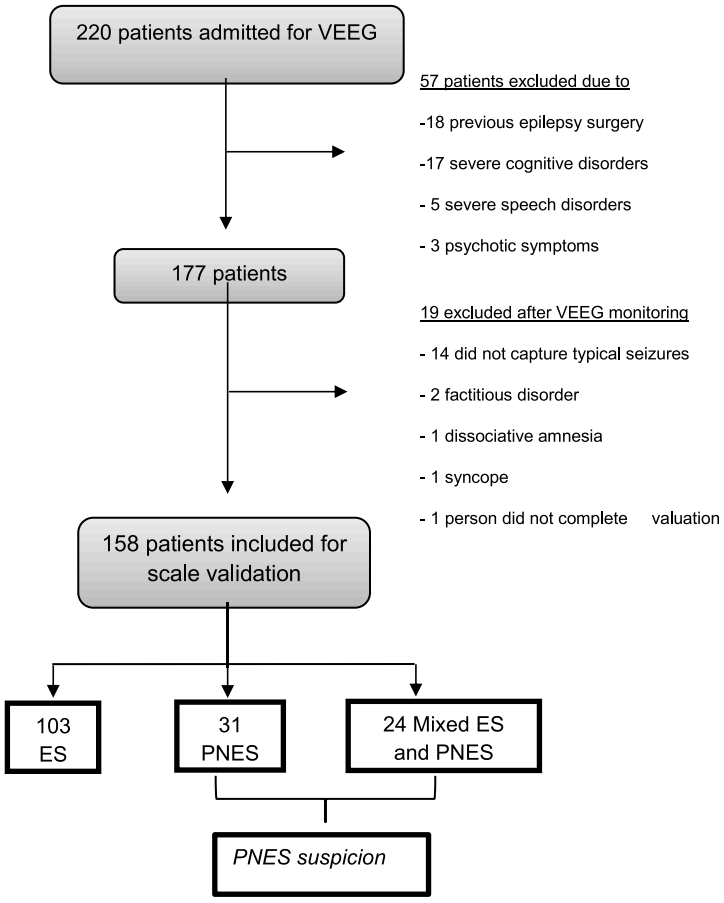

Fig. 1. Participants Selection Flowchart. Abbreviations: ES = Epileptic Seizures; PNES = Psychogenic Nonepileptic Seizures; VEEG = Video EEG

or the patient mentioned one seizure type that was not captured during VEEG, the video was considered inconclusive and was not considered for this analysis. Evidence of diagnoses other than ES or PNES were also excluded.

Following this comprehensive evaluation, the initial instrument of 51 items was compared with VEEG findings using a stepwise method for discriminant analysis and a chi-square test. After statistical analysis, we identified the items with the highest impact on the differential diagnosis, which led to a straightforward, simplified 15-item scale. The Rasch item response theory and expertise of the authors were used to ascertain the most efficient set of items that correctly identify PNES patients according to VEEG diagnosis (see below).

2.3. Statistical analysis

The sample size was calculated using PEPI (Programs for Epidemiologists) 4.0, based on data from Dixit R et al, [21] Noe KH et al, [22] and Benbadis SR [23]. We calculated a minimum of 80 patients for a level of significance of 5%, a power of 90%, and a risk ratio of 2.5 for an estimate of PNES between 10% and 40% of the sample. We also considered variables including seizure frequency; a history of sexual, physical, or emotional abuse; and clinical and psychiatric comorbidities.

Item selection was based on Chi-square tests, using VEEG as the gold standard and focusing on the capacity to discriminate the presence of PNES. From the 15 selected items, we used a Rasch item response theory (IRT) (rating scale model) to estimate the items' psychometric parameters [24]. The Rasch model is useful to estimate items and person parameters in the same linear continuum of log odds units or logits. In the present study, the continuum represents suspicions of PNES, ranging from low to high indicative of this condition. The linking function between those parameters is a normal ogive (logistic) probabilistic curve, and the parameters are represented through a log odds unit (logit). In order to evaluate the fit of the measurement model, we describe fit statistics (infit- and outfit-detection, ideal to have values between 0.0 and 1.5).

The differential function (DIF) of the scale to analyze differences between man and woman was assessed by means of contrast measure (i.e., differences in item's difficulty parameter to discriminate the presence of PNES). Contrast statistics have two complementary rules for interpretation. First, contrast statistics should not have a significant probability associated with them. Second, once the p-value is lower than the alpha, the absolute value of the contrast should not be higher than .64, which means that its effect size is not noticeable [24].

The dimensionality of the instrument was assessed through parallel analysis with two methods: Monte Carlo (parametric) and a permutation test (non-parametric). Rasch principal-contrast analysis was realized by estimating a principal-component analysis of the residuals of the main measurement dimension. Eigenvalues with values of 2.0 or larger are indicative of a possible second dimension in the data [24].

The internal consistency reliability was assessed by Cronbach's alpha coefficient and the Rasch item-reproducibility index. Cronbach's alpha expresses the degree of consistency of the scores across individuals, and it models the random error from the item selection by modeling shared covariance in relation to the total variance of the items. An alpha coefficient of 0.70 or higher is desirable for reliable measures [25]. The Rasch item reliability index expresses the adequate item's difficulty variance (latent trait coverage), and the sample size is informative enough to adequately set the item's location. Values of 0.9 or higher are indicative of the high reproducibility of the item's parameters.

To estimate sensibility and specificity parameters to the modeled scores (rating scale model), we used a receiver operating characteristic curve (ROC Curve) analysis using VEEG as the gold standard. We

identified cut-points for screening based on sensibility and specificity values, the area under the curve (AUC), and accuracy levels.

2.4. Data Availability Statement

All documents and data not appearing in the publication will be made available upon direct request to the first author. Documents will be available from 9 to 36 months following publication of the original article. Data requestors will need to sign a data access agreement.

3. Results

The final sample was composed of 158 participants, with an average age of 33 years old (SD ± 12 years) and a female predominance (66.5%). Fifty-five (35%) had PNES, which was isolated (31 participants) or associated with ES (24 participants) (table 1).

Prevalence and univariate analyses of the 51-items scale elaborated to suspect PNES were analyzed and compared in the three groups classified according to the VEEG diagnosis. The three groups were: ES (n = 103), PNES (n = 31), and mixed ES/PNES (n = 24). Patients with PNES and mixed ES/PNES had similar results and therefore were grouped. Chi-square identified 22 items with a major power of distinction between the groups, and we used Cronbach's alpha and the total area of the ROC curve to keep the 15 that best discriminated patients with PNES. Table 2 highlights items with frequencies that were higher than expected.

The IRT Rasch analysis revealed 15 items of the SS-PNES that present better discrimination of PNES and ES. The model identified a scale measurement structure, in which each item was classified according to its severity level in the continuum of PNES suspiciousness (table 3). This means that items with higher levels are more indicative of PNES. Table 3 exhibits the selected item sets and their adjustment statistics (infit and outfit) within an expected range (0.5 to 1.5). The scale demonstrated no difference in performance between sex groups; the male sex Dif contrast value was < 0.64 in all items ($p < 0.05$) (Table 3).

The unidimensionality of the set of the 15 items was confirmed by parallel analysis. With Monte Carlo (simulated) and sample-permutation (resampled) techniques, the analysis identified up to four factors with explanatory power greater than that of the simulated ones. Only one factor presented an Eigenvalue above 1. The principal contrast analysis showed a second dimension, with an eigenvalue of 2.0 at the cutoff point exactly; however, this dimension was judged to be meaningless due to its content. Therefore, the instrument is understood as being

Table 1
Demographic characteristics of the study sample (n=158)

Characteristics	ES n=103	PNES/mixed n=55	*p* value
Age at evaluation (years)Mean ± SD	35.2±11.5	29.3±12.6	0.004*
Female Sex, n (%)	60 (58.3)	45 (81.8)	0.005**
Marital Status; n (%)			0.10**
Single	49 (47.6)	35 (63.6)	
Married	44 (42.7)	16 (29.1)	
Divorced	10 (9.7)	3 (5.5)	
Widowed	-	1 (1.8)	
Ethnicity, n (%)			0.60**
Caucasian	59 (57.3)	37 (67.3)	
Afro-descendent	3 (2.9)	2 (3.6)	
Asiatic	14 (13.6)	5 (9.1)	
Mixed	27 (26.2)	11 (20.0)	
Education, n (%)			0.63**
Elementary	36 (35.0)	16 (29.1)	
High school	48 (46.6)	30 (54.5)	
Some college or technical school	19 (18.4)	9 (16.4)	
Religion	92 (89.3)	53 (96.4)	0.22**

* Student's T-Test for independent samples;
** Chi-square test or Fisher's exact test.Abbreviations: ES= Epileptic Seizures; PNES= Psychogenic Nonepileptic Seizures; mixed= ES+PNES

Table 2
Items that best discriminated patients with PNES

Questions	ES n=103 n (%)	PNES/mixed n=55 n (%)	*p* value
Main seizure type			<0•001
Pure disconnection	49 (47•6)	2 (3•6)	
Impaired awareness with automatism	24 (23•3)	11 (20•0)	
Repetitive motor movements	30 (29•1)	33 (60•0)	
Prolonged unresponsiveness	-	9 (16•4)	
Seizure frequency			<0•001
Rare or eventual	7 (6•8)	2 (3•6)	
Monthly	29 (28•2)	5 (9•1)	
Weekly	36 (35•0)	13 (23•6)	
Daily	31 (30•1)	35 (63•6)	
Seizure duration			<0•001
Less than 1 minute	32 (31•1)	2 (3•6)	
From 1 to 2 minutes	34 (33•0)	8 (14•5)	
From 3 to 5 minutes	27 (26•2)	19 (34•5)	
More than 5min	10 (9•7)	26 (47•3)	
Duration of seizure disorder			<0•001
More than 20 years	57 (55•3)	14 (25•5)	
From 11 to 20 years	28 (27•2)	10 (18•2)	
From 5 to 10 years	11 (10•7)	10 (18•2)	
Less than 5 years	7 (6•8)	21 (38•2)	
Seizures-related injuries			<0•001
Frequently	44 (42•7)	7 (12•7)	
Occasionally	14 (13•6)	4 (7•3)	
Rarely	28 (27•2)	16 (29•1)	
Never occurred	17 (16•5)	28 (50•9)	
Emergency department visits			0•001
Never occurred	23 (22•3)	2 (3•6)	
Rarely	33 (32•0)	14 (25•5)	
Occasionally	14 (13•6)	5 (9•1)	
Frequently	33 (32•0)	34 (61•8)	
Weekly generalized seizures			<0•001
None	74 (71•8)	21 (38•2)	
One or two	10 (9•7)	9 (16•4)	
Three or four	9 (8•7)	3 (5•5)	
Five or more	10 (9•7)	22 (40•0)	
First seizures related to emotional stress			0•007
No	71 (68•9)	26 (47•3)	
Unlikely related	6 (5•8)	1 (1•8)	
Probably related	14 (13•6)	11 (20•0)	
Clearly related	12 (11•7)	17 (30•9)	
Psychiatric treatment			<0•001
Never	39 (37•9)	10 (18•2)	
Yes, in the past	37 (35•9)	12 (21•8)	
Yes, currently without medication	6 (5•8)	4 (7•3)	
Yes, currently with medication	21 (20•4)	29 (52•7)	
Number of psychotropic drugs in use*			<0•001
None	71 (68•9)	18 (32•7)	
One	18 (17•5)	16 (29•1)	
Two	8 (7•8)	15 (27•3)	
Three or more	6 (5•8)	6 (10•9)	
Other physical symptoms			<0•001
None	31 (30•1)	5 (9•1)	
One	40 (38•8)	9 (16•4)	
Two	20 (19•4)	11 (20•0)	
Three or more	12 (11•7)	30 (54•5)	
Relationship struggles with the caregiver			0•009
Never	57 (55•3)	16 (29•1)	
Rarely	12 (11•7)	6 (10•9)	
Occasionally	15 (14•6)	15 (27•3)	
Often	19 (18•4)	18 (32•7)	
History of emotional neglect			<0•001
None	74 (71•8)	21 (38•2)	
Only once	6 (5•8)	3 (5•5)	
More than once, but rarely	7 (6•8)	9 (16•4)	
Recurrent	16 (15•5)	22 (40•0)	
History of parental separation			0•001
Never occurred	72 (69•9)	21 (38•2)	
Only once- short period	1 (1•0)	4 (7•3)	
Multiple episodes	12 (11•7)	10 (18•2)	
For a long time	18 (17•5)	20 (36•4)	
Family history of psychiatric disorder			0•014
None	43 (41•7)	14 (25•5)	

(*continued on next page*)

Table 2 (*continued*)

Questions	ES n=103 n (%)	PNES/mixed n=55 n (%)	*p* value
Not sure	8 (7•8)	4 (7•3)	
Yes, caregiver not included	37 (35•9)	17 (30•9)	
Yes, caregiver included	15 (14•6)	20 (36•4)	

Data presented by n (%) and compared using Chi-Square test. Frequency data highlighted in **bold** symbolize categories with value more frequent than expected, according to the adjusted analysis.

* Psychiatric medications included any psychopharmacological compound, except AED.Abbreviations: ES= epileptic seizures; PNES= psychogenic non-epileptic seizures; mixed= ES+PNES; AED= antiepileptic drug

Table 3
IRT- Rasch analysis

Items	Difficulty	Infit*	Outfit*	Dif contrast**
Number of psychotropic drugs in use	0•57	0•81	0•71	0•03
Weekly generalized seizure	0•39	1•24	1•17	-0•25
First seizures related to emotional stress	0•36	1•38	1•36	0•49
History of parental separation	0•34	1•31	1•33	-0•16
History of emotional neglect	0•28	1•29	1•22	0•31
Disease duration in years	0•22	0•98	0•94	0•07
Main seizure type	0•07	0•62	0•63	-0•16
Relationship struggles with the caregiver	0•06	1•13	1•09	-0•12
Psychiatric treatment	-0•12	0•91	0•93	0•03
Family history of psychiatric disorder	-0•15	1•13	1•16	-0•27
Other physical symptoms	-0•22	0•79	0•77	0•23
Seizures-related injuries	-0•25	1•14	1•14	-0•26
Seizure duration	-0•25	0•71	0•69	0•02
Emergency department visits	-0•51	0•98	0•97	0•16
Seizure frequency	-0•80	0•81	0•85	-0•02

Abbreviations: DIF= differential function

unidimensional. Standardized factorial loads of items were estimated using the minimum rank method and presented factorial loads that varied from 0.36 to 0.66 (the minimum expected value is 0.32). Furthermore, according to the Rasch Item Reliability Index (0.95) and Cronbach's alpha (0.77), the instrument showed a good level of reliability.

Each item scored between 0 and 3 points. The mean score of the whole sample (n = 158) was 19.1 (SD 8.4), ranging from 3 to 41 points. There was no significant difference in the average score between the two groups with PNES (pure PNES 28.8 [SD 7.0], Mixed 25.3 [SD 6.2]; $p = 0.075$), with minimal effect size (0.53). In contrast, there was a significant average scoring difference between the joint groups with PNES (27.3 [SD 6.8]) and that of the group with pure ES (14.8 [SD 5.4]; $p < 0.001$) with a large effect size (2.11).

In addition, we assessed the convergent validity within VEEG. The area under the ROC curve was 0.92 ($p < 0.001$, CI 95%: 0.87–0.96), showing a significant discriminating power (figure 2). The best cut-off was 20 points.

The SS-PNES cutoff score of 20 points, according to the gold standard VEEG (95% CI), led to the sensitivity, specificity, positive, and negative predictive values and accuracy described in table 4.

4. Discussion

We prospectively developed the SS-PNES (scale for suspicion of psychogenic nonepileptic seizures) - a novel screening scale to raise suspicion of PNES - through a stepwise selection of items that proved to be valid and reliable. The result was a simple, straightforward scale that could be used by healthcare providers. Our scale comprehensively addresses clinical features and the neuropsychiatric etiology (figure 3).

Of note, that to develop a scale for PNES that follow recommended guidelines: A systematic literature review leading to a theoretical model, which informed the construction of the items before an independent analysis of the judges [18]. Moreover, accuracy and reliability was confirmed by the high inter-rater agreement in the pilot study and the psychometric properties of the SS-PNES. The high inter-rater agreement also suggested that the scale is simple to apply and grade, and the IRT Rasch model analysis confirmed the individual reliability of all 15 items constituting the definitive scale. None of the items showed differences

Table 4
Score performance measure compare to VEEG

Performance measures	% (95%CI)
Sensitivity	89•1 (78•2-94•9)
Specificity	85•4 (77•4-91•0)
Positive predictive value	76•6 (64•9-85•3)
Negative predictive value	93•6 (86•8-97•0)
Accuracy	86•7 (80•5-91•1)

95% CI: confidence interval of 95%

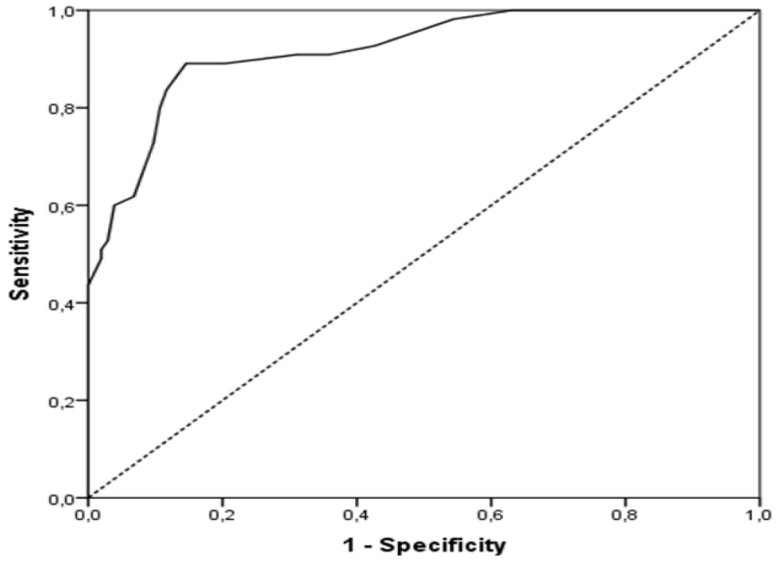

Fig. 2. ROC curve of the SS-PNES with VEEG as the gold standard

SCALE FOR SUSPICION OF PSYCHOGENIC NONEPILEPTIC SEIZURES (SS-PNES)

For each item, check the one alternative that best matches the patient's situation.

	Zero	One	Two	Three
1 - Main seizure type in the past 3 months	Pure disconnection, short-lasting (< 30 seconds)	Impaired awareness with automatisms and/or unilateral motor signs	Repetitive motor movements, affecting both sides of the body	Prolonged unresponsiveness
2 - Seizure frequency	Rare or occasional	Monthly	Weekly	Daily
3 - Duration of the main seizure type	Less than 1 min	From 1 to 2 min	From 3 to 5 min	More than 5 min
4 - Disease duration in years	More than 20 years	From 11 to 20 years	From 5 to 10 years	Less than 5 years
5 - Weekly frequency of generalized seizures, on AED	None	One or two	Three or four	Five or more
6 - Presence of seizure-related injuries	Frequently*	Occasionally**	Rarely***	Never occurred
7 - Emergency department visits for seizures	Never occurred	Rarely***	Occasionally**	Frequently*
8 - First seizure is clearly related to an episode of emotional stress	No	Unlikely to be related	Probably related	Clearly related
9 - Presence of other physical symptoms	None	One	Two	Three or more
10 - Psychiatric or psychological treatment: If yes, the diagnosis is _____	Never	Yes, only in the past	Yes, currently without psychotropic drug use	Yes, currently with psychotropic drug use
11 - Number of psychotropic drugs currently in use (other than AEDs)	None	One	Two	Three or more
12 - Family history of psychiatric disorder. Please describe: _____	None	Not sure	Yes, but not the primary caregiver	Yes, the primary caregiver
13 - Parental separation (abandonment, death, divorce, and other conflict situations)	Never occurred	Only once, for a short period of time	Multiple episodes	For a long period of time or estrangement
14 - History of emotional neglect during childhood and adolescence	None	Only once	More than once, but rarely	Recurrent
15 - Relationship struggles with the primary caregiver	Never	Rarely	Occasionally	Often

* More than five occasions,
**Three or four occasions
***One or two occasions

Total score ☐

Fig. 3. SS- PNES

based on gender [24]. A manual explaining the application of the scale is detailed in the supplementary material 2.

We attempted to translate into specific and simple questions the distinguishing features between PNES and ES. Using VEEG as the gold-standard method for the diagnosis, the scale had a discriminating power of 0.92 for a score equal to or greater than 20 points and good accuracy in 87% of patients. A score below 20 points, indicative of ES, diminishes the probability of PNES in 94% of the patients, even in those with the mixed disorder. This ability to reduce or increase the suspicion of a PNES diagnosis, with a predictive value of 76.6%, sensitivity of 89%, and specificity of 85%, strengthens the screening power of the SS-PNES compared to other instruments. [6,7,9,10,11] Furthermore, unlike other instruments designed to guide professionals trained in detailed observation of seizure semiology, the integrative nature of the SS-PNES makes it readily applicable by other health care providers [12,13].

Our scale used an integrated approach combining neurological, psychiatric, somatic, and other (interpersonal relations, traumatic events, and family history) variables, reflecting authors' understanding of PNES is a complex condition.

The use of non-linear evaluation methods provided an interaction of heterogeneous factors, including those considered potentially predisposing to PNES that tend to be valid and relevant in different cultures [26]. Moreover, the sample was evaluated through a prospective, blind, independent, and standardized process, and the final diagnosis was

established by the gold-standard method.

Previous studies attempted to create a score for PNES suspicion [6–13]. Despite the apparent similarity with other self-administered screening instrument, prospective design, the SS-PNES had all items originally developed and did not incorporate parts of other scales [8]. Moreover, the instrument takes into account the history of episodes with minimal motor abnormalities and investigates different types of traumatic childhood events.

The lack of gold-standard interviews or questionnaires for this purpose does not allow us to compare our instrument with others in this respect. Recently, Giussani and colleagues provided a comprehensive review of the available instruments for the diagnosis of PNES [17]. Only seven of the studies used structured questionnaires tailored for the differential diagnosis between epileptic and nonepileptic seizures. The other studies included in that review explored either single items or aspects specific for PNES, such as clinical comorbidities, chronic pain, history of stressful events, and loss of consciousness during the episodes. The authors suggested that a careful selection of a range of distinct variables could facilitate the diagnosis and allow a clinical history centered on the key aspects of PNES [17]. We posit that this was exactly what we had in mind when developing the SS-PNES.

A major criterion to maintaining items in the scale's final format was the confirmation that PNES groups had a higher score statistically different from the ES group.

We investigate each type of childhood traumatic experience. Emotional neglect appeared to be more relevant in the distinction of the items and was confirmed in a systematic review and meta-analysis of case-control studies.[27] The decision not to include the item "history of sexual abuse" took into account the fact that despite historically being regarded as an etiology of PNES, discriminatory power was not statistically significant [10]. Also, our perception during the application of the instrument confirmed previous data that this item is surrounded by recall and reporting biases [8,28].

Although PNES's underlying psychopathology is not yet entirely understood,[29],[30]Fig. 1 items referring to direct and indirect psychiatric aspects were relevant to the distinction between the groups. Items based on the evidence that patients with PNES come from stressful families with potentially pathological patterns of adaptation and thus have symptoms of somatic distress and high prevalence of psychiatric disorders were important discriminators in our scale [31].

It remains controversial whether semiology alone can differentiate epileptic from nonepileptic seizures because of their similarities [15,32]. However, our scale suggests that semiology is important when viewed as part of the integrative model proposed to PNES [33]. In this context, our findings regarding motor phenomena, duration, and frequency corroborate previous research.

From a broad perspective, the SS-PNES has several unique features which single it out from other instruments. It probes in a straightforward, and simple fashion - using only 15 items - both psychiatric and neurological aspects pertaining to the differential diagnosis. The latter are missing in many scales [6,7,9]. It was originally designed to specifically evaluate psychogenic nonepileptic seizures, being presented in a Likert format with cut-offs established through ROC curves. Furthermore, the fact that it was originally developed to support diagnosis and clinical applicability through a focus on family and psychiatric history could facilitate the communication of the diagnosis of PNES, streamlines the necessary discussion of associated mental health issues, and the referral to mental health professionals.

Like other instruments, The SS-PNES has the potential to optimize the duration of the interview. We suggest that it can be used for screening, optimizing referral to VEEG, and also as an ancillary instrument to help decisions in patients for whom, for whatever reason, VEEG was not definitive. Furthermore, the scale may also prove helpful in patients for whom, although a diagnosis of epileptic seizures was established, changes in semiology or unexplainable loss of seizure control raised the suspicion of co-occurrence of PNES. Finally, the SS-PNES may help practioners when VEEG is not readily available. Because PNES is a common cause of pseudo-refractoriness of seizures, having a strong suspicion of such nonepileptic phenomena may redirect the approach to treatment [30].

We believe these differentiating features make the scale important in clinical practice, irrespective of whether in primary, secondary, or tertiary care settings. It is widely acknowledged that once patients receive a diagnosis of 'epilepsy' it is much more difficult to revert to an alternative diagnosis, even as the individual progresses along the ladder of more specialized care. Thus, helping primary care and emergency room physicians, nurses and psychologists to raise a PNES suspicion may prove highly beneficial to the trajectory of the patient. Taking this into consideration, the scale be implemented into clinical practice, and not be solely reserved for clinical research.

This study has some limitations. Despite including patients from different Brazilian regions, the sample was derived from a single tertiary center. In addition, it was not possible to distinguish patients with "pure PNES" from the mixed group, which is a clinically relevant issue because the latter must be treated for both conditions. Second, the abridged 15-item scale was not specifically tested, but resulted from the statistical treatment of the more extensive 51-item instrument. However, the 51-item original instrument already discriminated patients with and without PNES and the final 15-item scale is a 'pure culture' of the items with the best discriminating power, following exhaustively analyses with state-of-the-art psychometric procedures. Finally, a limitation of any novel diagnostic procedure is the inevitable need for independent replication. Hence, future single and multicenter studies will be needed to confirm that the final 15-item version of the SS-PNES delivers what it proposes, that is, a reliable, objective tool to raise suspicion of PNES before VEEG.

5. Conclusion

We designed and prospectively validated the SS-PNES, a new instrument crafted to facilitate early suspicion of PNES. Hopefully, this instrument, will help avoid the situation of neglecting this diagnostic possibility in centers where access to VEEG is limited or nonexistent, used in conjunction with the homemade seizure videos, thus avoiding far-reaching negative consequences, including patient exposure to inappropriate treatments leading to increased morbidity and mortality [33-35].

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Declaration of Competing Interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.seizure.2021.04.025.

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