

Updated Review on the Diagnosis and Primary Management of Psychogenic Nonepileptic Seizure Disorders

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Abstract: Psychogenic nonepileptic seizures (PNES) are paroxysmic and episodic events associated with motor, sensory, mental or autonomic manifestations, which resemble epileptic seizures (ES), but are not caused by epileptogenic activity. PNES affect between 20% and 30% of patients attending at epilepsy centers and constitute a serious mental health problem. PNES are often underdiagnosed, undertreated and mistaken with epilepsy. PNES are diagnosed after medical causes (epilepsy, syncope, stroke, etc.) have been ruled out, and psychological mechanisms are involved in their genesis and perpetuation. For psychiatry, there is not a single definition for PNES; the DSM-IV and ICD-10/11 describe the conversion and dissociative disorders, and the DSM-5 describes the functional neurological disorders. However, patients with PNES also have a high frequency of other comorbidities like depression, particularly trauma and post-traumatic stress disorder. It has been postulated that PNES are essentially dissociations that operate as a defensive psychological mechanism that use the mind as a defense to deal with traumas. With the advent of VEEG in the 90s, the recognition of PNES has significantly increased, and several psychological treatments have been developed. In this manuscript, we carried out a state-of-the-art review, with the aim to provide a critical approach to the extensive literature about PNES, focusing on diagnostic aspects, the primary management, and the available treatments that have been shown to be effective for the improvement of PNES.

Keywords: psychogenic nonepileptic seizures, conversion disorder, dissociative disorder, diagnosis, treatment

Introduction

Psychogenic nonepileptic seizures (PNES) are sudden and involuntary episodic events (paroxysmic), associated with motor, sensory, mental or autonomic manifestations. During PNES, normal functioning of central nervous system is altered, and self-control is reduced.^{1,2} PNES frequently resemble epileptic seizures (ES) but the symptoms are not caused by epileptogenic activity. PNES are diagnosed when medical causes (ie, epilepsy, syncope, stroke), have been ruled out and psychological mechanisms are involved in their genesis and perpetuation. PNES are often underdiagnosed, undertreated and mistaken with epilepsy.²⁻⁴

The term PNES was coined by contemporary neurologists after the implementation of the video-electroencephalogram (VEEG) in epilepsy centers. In 1964, Liske and Forster created the term pseudo-seizures to refer to the paroxysmal events similar to epileptic seizures but without the electroencephalographic changes of

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epilepsy.^{5,6} Several other names have received the PNES over time: “psychogenic seizures,” “nonepileptic seizures,” “pseudo-seizures,” “psychogenic pseudo-seizures,” “psychogenic nonepileptic attacks”, however currently, the most widespread term in the scientific literature is “psychogenic nonepileptic seizures”.^{7–9} Recently, some researchers have proposed to mention this condition as “dissociative seizures” or “functional seizures”.^{10–12} In this regard, is important to achieve to an international consensus on the terminology used. It has been found that the methods of communicating the PNES diagnosis to patients, produce different effects on their understanding, acceptance and/or rejection.^{13–15} Therefore, a consensus on the terminology could favor the improvement of the relationships between the health professional and the patients, the inter-professional communications, and enhance the therapeutic relationship in the execution of treatments.^{14–16}

Different theories according to psychopathological models have been developed to explain the etiology and phenomenology of PNES.^{1–3,17} In addition, with the advent of VEEG in the 90s, the recognition of these entities has significantly increased and several mental health interventions and psychological treatments have been developed in the last years.^{18–25} In this article, we present an updated review of the main diagnostic aspects, primary management and available treatments of patients with PNES. We have made special emphasis on mental health approaches and psychological treatments, which have been shown to be effective for the improvement of PNES. The aim of this manuscript is to review the main data of PNES in order to recognize PNES and to implement the correct psychotherapeutic treatment early.

Methods

We carried out a state-of-the-art review, narrative type. This type of review aims to provide a critical approach to the extensive literature about PNES, emphasizing on those articles produced in the last decades. The search strategy was made through different scientific databases (PubMed, Medline, PsycInfo), using the following descriptors: “PNES”, “psychogenic nonepileptic seizures”, OR “pseudoseizures”, and “prevalence”, “semiology”, “differential diagnosis”, “diagnosis”, “psychiatric comorbidities”, “psychotherapy”, “treatment”, and “psychological treatment”. The most recent and important articles were selected, through pair debriefing, in order to include the most updated information about each topic. This work

will provide useful information to contribute to an adequate approach to the diagnosis and treatment of patients with PNES.

Prevalence of PNES

The prevalence of PNES is approximately 1.5% per 100,000 inhabitants per year.^{26,27} However, the frequency tends to rise, and it is present among 20–30% of the patients admitted at specialized epilepsy centers. Patients with PNES are referred to epilepsy centers with suspected epilepsy with poor response to treatment and are frequently misdiagnosed as having drug resistant epilepsy (DRE).^{26,27} In addition, between 5% and 40% of patients with PNES have comorbid epilepsy, generating a complex situation during therapeutic management.^{27–29} In turn, a delay to reach PNES diagnosis is about seven to nine years on average, according different studies.^{29,30} In our experience, a delay of seven to eleven years has been found among patients with PNES, and most of the patients were previously suspected to have drug resistant epilepsy.²² The trouble to identify subpopulation of patients with PNES may be due to various factors: The difficulty in accessing to VEEG due to the high costs and low availability in primary health centers; the difficult of patients with PNES to connect with mental health services after having received the diagnosis; and the difficult in recognizing epileptic seizures versus PNES.^{24,26,27}

Regarding sex, women presented PNES with a higher prevalence compared to men in all studies.^{21,22,24,31–33} In addition, multicenter studies showed approximately a 70% of women among patients with PNES.^{34–36} Several authors linked the gender differences with a history of physical and sexual trauma, suffered more frequently by women in different cultures.^{32,37,38,39} In this regard, it has been postulated that PNES are essentially dissociations, that operate as a defensive psychological mechanism that use the mind as a defense to deal with traumas. In our casuistic, the trauma history was present among 48% of patients with PNES, and 22% of the patients met full-criteria for post-traumatic stress disorder.²² In this regard, a higher prevalence of trauma and sexual trauma was found among adults comparing to pediatric populations of PNES, suggesting more severe presentations associated with trauma in adult-onset PNES compared with younger ages.⁴¹

Clinical Semiology of the PNES; Differential Diagnosis with Epileptic Seizures and the Role of VEEG

The clinical confirmation of PNES is through the complementary method of VEEG, based on the exclusion of epilepsy and other medical diseases. VEEG consists of the continuous monitoring of the patient's behavior during the paroxysmal episodes, while the electrical activity of the brain is simultaneously recorded through the surface electrodes of the electroencephalogram (EEG).^{19,42} In medical practice, VEEG is indicated to study the clinical and topographic aspects of the epileptic discharges in patients with epilepsy, and also to study the possibility of epilepsy surgery. However, VEEG is also indicated to carry out the differential diagnosis between ES (epileptic seizures) and PNES when there are diagnostic doubts.^{19,29,42–44} The aim of VEEG is to corroborate the existence of an electro-clinical correlation during the paroxysmal events. PNES is confirmed when the typical episodes described by the patients or relatives, are present during VEEG, without associating any ictal epileptiform activity, and psychological aspects are involved.^{19,43,44}

As well VEEG is the gold standard to define the differential diagnosis, some semiological differences are described between PNES and epileptic seizures. The longer time duration of episodes is a common finding among patients with PNES. However, there are no pathognomonic signs that allow us to totally rule out epileptic seizures.^{21,44–46} Furthermore, studies have shown that certain signs that were considered typical of PNES (ie, non-synchronic hypermotor symptoms), were not actually specific since they could also be seen in epileptic seizures originated in the frontal lobe.^{47,48} On the other hand, between 8% and 31% of patients with PNES have suffered injuries during seizures such as tongue biting, bumps and falls. This situation had traditionally been linked to epilepsy.^{34,35,46} Loss of sphincter control and the appearance of seizures during sleep, have been also described in some patients with PNES, although they are more frequent in epilepsy.^{46–48} Thus, many times in clinical practice, the diagnosis of PNES cannot be reached only by the clinical manifestations, being the VEEG the method of choice to confirm the differential diagnosis.^{44,45}

Table 1 resumes the main semiological characteristics observed among patients with PNES, according to the studies based on VEEG analysis.^{34,35,44,49–56} If PNES compromise motor functions (ie, hypermotor), they may

resemble epileptic generalized tonic-clonic seizures or frontal lobe epilepsy. Those PNES that compromise the state of consciousness (lack of responsiveness, psychic symptoms, aura), or some localized sensory-motor function (focal motor, akinetic), may resemble partial epileptic seizures with automatisms and/or generalized absence seizures.^{21,44} Some types of PNES (ie, psychogenic atonic seizures, dialeptic or pseudosyncope), may present behavioral arrest, immobility, psychic auras, depersonalization, derealization, unusual somatic sensations and auditory, visual and olfactory hallucinations resembling complex partial epileptic seizures of temporal lobe origin.^{21,44,49–56}

Psychiatric Diagnosis of Patients with PNES

There is not a single definition of what neurologists called PNES. Different diagnostic categories defined by the contemporary psychiatric nosographies represent the so-called PNES. For the fourth revised version of the Diagnostic and Statistical Manual of Mental Disorders (DSM IV-TR), PNES with motor symptoms are mainly represented in the category of conversion disorders (somatoform disorders).⁵⁷ The DSM-IV subdivides conversion disorders into four categories: conversion with sensory symptoms or deficit, with motor symptoms, with seizures, and mixed presentation with more than one type of conversion symptom.⁵⁷ However, when symptoms affect consciousness, PNES would be better represented within dissociative disorders. In relation to these differences between conversion and dissociation, some controversies have arisen. While conversion is regarding at a purely descriptive level, the role of dissociation implies a psychological mechanism that affects the processing and integration of objective and subjective data of the experience. In this sense, all conversion disorders also imply dissociation of motor experiences.^{58,23} In addition, it has been postulated that dissociation is the central mechanism that explains the disturbances of consciousness and cognitive control.⁶⁰ Therefore, contemporary authors have been proposed the dissociation term to unify and refer to the PNES.^{10,11,59} Recently, the diagnostic category of functional neurological disorders (FND) have been replaced the conversion and dissociative categories in the Diagnostic and Statistical Manual of Mental Disorders 5 version, DSM-5 and encompassed all PNES types.⁶⁰ In this definition, the term “functional”, describes a group of disorders in which

Table 1 Clinical Manifestations of PNES Based on VEEG Analysis

Author (n=Number of Patients with PNES)	Gröppel et al 2000 ⁴⁹ (n=27) Vienna, Austria	Selwa et al 2000 ⁵⁰ (n=85) Michigan, USA	Seneviratne et al 2010 ⁵¹ (n=61) Melbourne, Australia	Hubsch et al 2012 ⁵² (n=55) Nancy, France	Dikmen et al 2013 ⁵³ (n=37) Istanbul, Turkey	Wadwekar et al 2013 ⁵⁴ (n=65) Pondicherry, India	Magaudda et al 2016 ⁵⁵ (n=55) Messina, Italy	Ali Assadi Pooya 2017 ³⁴ Multicenter International Study (n=89)	Ali Assadi Pooya 2019 ³⁵ Multicenter International Study (n=389)	Madaan et al 2018 ⁵⁷ (n=80, paediatric) New Delhi, India	Lombardi et al 2020 ⁴⁴ (n=32) Argentina
Motor symptoms	Psychogenic motor seizures	Intermittent 4.7% Trashing 22.3%	Hypermotor (limb and trunk movements, hyperventilation) 3.3% Complex motor (51.5% trunk extensions) 10% Mixed pattern 5.2%	Hyperkinetic prolonged attack with hyperventilation and auras (limb movements, without trunk, hyperventilation) 11.7% Axial dystonic prolonged attack (85% trunk extension) 16.4% Dystonic attack with primitive gestural activity 31.6%	Complex motor attack (hypermotor, tonic-clonic, versive.)	Hyperkinetic prolonged attacks with movements of limbs and trunk, hyperventilation 25.9% Axial dystonic attacks 14.8% (87.5% trunk extension/12.5% flexion) Dystonic attacks with primitive gestural activities 5.6%	Hypermotor Focal motor	Hypermotor (53–27%) Focal motor (10–8%)	Hypermotor (89 –79%)	Hypermotor 1.2% Complex motor 3.7% Mixed 28.8%	Hypermotor/ hyperkinetic (limb and trunk movements) (81%)
	Psychogenic minor motor or trembling seizures (100% lack of responsiveness)	Automatisms 3.5% Tremor 4.7%	Rhythmic motor (83.8% lack of responsiveness) 46.7%	Paucikinetik attack with preserved responsiveness (3.4% lack of responsiveness) 23.4%	Simple motor attack (myoclonic, tremor-like)	Paucikinetik attacks with or without preserved responsiveness 9.3% (80% lack of responsiveness)	Akinetic	Akinetic (28–29%)	Akinetic (11–18%)	Rhythmic motor 10%	Automatisms 21.8% Akinetic (31%)

Other Symptoms (psychic symptoms, awareness, sensorial)	Psychogenic atonic seizures 25.9% (100% lack of responsiveness)		Catatonic Symptoms 22.3%	Dialeptic (16% hyperventilation, 100% lack of responsiveness)	Pseudo-syncope (85% lack of responsiveness)	Dialeptic attack Special PNES (atonic, astatic, hypotonic)	Pseudosyncope 38–9% (19% hyperventilation, 80% lack of responsiveness)			Lack of responsiveness (32 – 82%)	Dialeptic 42.5%	Lack of responsiveness (28%)
			Subjective Symptoms 11.7%	Non-epileptic psychic Aura 23.6%		Non-epileptic aura (psychic/ somatosensory)	Unclassified type 5.6%	Subjective symptoms (55–10%)	Subjective symptoms	Non-epileptic Auras (23–89%)	Non-epileptic aura 13.8%	Non-epileptic Auras (6.5%)

Note: Resume of the most important reports about semiological manifestations of PNES, according to the clinical studies based on VEEG analysis.

there is a functional rather than a structural disturbance of the nervous system.⁶⁰

On the other hand, the International Classification of Diseases 10 version (ICD-10) includes the category dissociative (conversion) disorders, which comprises the diagnoses of hysteria, conversion hysteria, hysterical psychosis, conversion reaction, and dissociative seizures from other nomenclatures.⁶¹ Regarding the ICD-10, PNES are classified within mental and behavioral disorders as somatoform disorders and dissociative (conversion) disorders, a category of neurotic disorders and stress-related disorders. Dissociative (conversion) disorders are characterized by the partial or complete loss of normal integration between certain memories of the past, awareness of one's own identity and sensations of loss of control of body movements.⁶¹ However, some differences in the diagnostic categories were proposed by the International Classification of Diseases 11 version (ICD-11).⁶² In the chapter about mental, behavioral or neurodevelopmental disorders, dissociative disorders were included to separate somatic symptoms from those related to the perception or awareness, of the individual identity and the environment. The ICD 11 also added the dissociative identity disorder and the partial dissociative disorder, as separated diagnoses. The ICD 11 deleted any reference to multiple personality disorder and the conversion classification, including the neurotic, the somatoform and the stress-related disorder.⁶²

Psychiatric Comorbidities in Patients with PNES

Patients with PNES comprise a heterogeneous group from a psychiatric point of view^{3,17,21,22} and may be considered as a clinical syndrome that is frequently associated with psychiatric comorbidities. These comorbidities constitute the underlying cause of PNES in many cases, such as PTSD (post-traumatic stress disorder), however in other patients a psychiatric comorbidity may be a trigger for PNES or a consequence of chronic PNES.^{4,8,17,22}

Among psychiatric comorbidities, depression is the most frequent psychiatric disorder which can occur in approximately 60% of PNES or more.^{17,22,63–65} Secondly, traumatic experiences and the post-traumatic stress disorder (PTSD) have been found in approximately 50% of patients with PNES, followed by anxiety disorders in 45%, according to different studies.^{22,63–66} In addition, the clinical presentation of patients with PNES is even

more complex when personality disorders are presented as a psychiatric comorbidity since they can contribute to the poor psychosocial functioning.^{22,64} Within the personality disorders, cluster B disorders (borderline personality disorder), are the most frequently reported. Cluster C personality disorders have been also reported among patients with PNES.^{22,64}

Although the causes of PNES are multifactorial and they result from the combination of biological, psychological, environmental and social factors, patients with PNES report high rates of general trauma. Traumatic experiences constitute the most important factor involved in the etiology of the PNES. The history of traumatic events were found between 44% and 100% and the prevalence of sexual abuse has been reported ranging between 23% and 77% of patients with PNES.^{17,34,37,65} Trauma was associated with the activation of dissociation mechanisms and with a high prevalence of comorbid depression and personality disorders.^{1,21,22,65,66}

Therapeutic Approaches of Patients with PNES

The first therapeutic strategy after confirming the diagnosis of PNES consists of informing to the patient and his family of the nonepileptic origin of the seizures, through a psychoeducation intervention.⁶⁷ This type of initial intervention seeks to raise awareness of the diagnosis and the psychogenic origin of the problem. In a pioneering study in 1998, the use of the health system before and after carrying out the VEEG, was compared in patients with PNES.⁶⁸ In this report, a clear explanation on PNES diagnosis, combined with immediate psychological treatment, markedly reduced the use of medical services. In addition, a brief and clear communication of the diagnosis can remit the symptoms in a certain proportion of patients.⁶⁹ It is important that the communication of the diagnosis refers to an adequate, clear and understandable explanation for the patient and relatives, and ideally, both neurologist and mental health professionals should participate.^{4,8,28} In sum, how the diagnosis is communicated is very important. Communication with the new diagnosis has been reported to have consequences on the evolution of seizures.^{70,71} In our experience, patients who did not accept the newly diagnosis have shown a worse outcome.¹⁹

Since PNES are frequently mistakenly considered as epileptic seizures, most patients with PNES have received

antiepileptic medication (AE) for long periods.²² The International League Against Epilepsy (ILAE) defines drug-resistant epilepsy (DRE) when seizure control fails with at least two AE schemes (either in monotherapy or in combination).⁷² Patients with PNES are usually diagnosed as DRE, and they also tend to suffer the imposition of stigma and restrictions on the lifestyle of patients with DRE.^{3,21,22} On the other hand, AE can generate adverse effects, toxicity and unnecessary high costs for the patient and/or the health system. Once the diagnosis of PNES is made, and as long as there are no comorbid epileptic seizures, the treating neurologist will gradually discontinue the AE medication while the patient simultaneously starts the treatment of choice (mental health treatment, psychotherapy and/or psychotropic medication, interdisciplinary approach).⁸

After the diagnosis has been explained to the patient and the family, patients with PNES should be addressed by the mental health team.⁷⁴ The core symptoms of PNES (types of conversion and dissociation symptoms), the presence of comorbid psychiatric disorders potentially treatable with specific medication (ie, depressive disorders, anxiety disorders and post-traumatic stress disorders), and the presence of comorbidity with personality disorders, should be evaluated in each case in particular.^{8,17,67,73} Antidepressants are frequently indicated when depression comorbidity is present, and also to treat post-traumatic stress disorder. Sertraline showed reduction of PNES after patients received sertraline in combination with cognitive behavioral therapy.⁷⁵ At the moment, there are no specific drugs with efficacy to treat conversion and/or dissociative symptoms (the core symptoms of PNES), and the treatment of choice is psychotherapy.^{76–89}

Psychotherapeutic Interventions for Patients with PNES

Psychotherapy is a priority for treating PNES. The therapeutic approaches for patients with PNES are varied and depends on the diagnoses and comorbidities presented by these patients. Psychotherapeutic interventions and coping strategies specially oriented to PNES have been developed with the aim to improve the quality of life of the patients. The main studies reported in the literature about psychotherapeutic interventions for patients with PNES are summarized in Table 2.

Table 2 Psychotherapeutic Interventions in Patients with PNES

Study	Type of Study	Study Participants	Intervention and Duration	Intervention Outcome (Seizure Frequency)
Cognitive-Behavioral Therapies (CBT)				
Goldstein et al (2004) UK ⁸²	Before-after, non-controlled study	n=16	Individual CBT (12x1/week or fortnightly)	25% reported seizure freedom 81% reported seizure reduction
Goldstein et al (2020) UK ⁸⁵	Pragmatic, parallel-group multicentre randomised controlled trial	n=313	CBT plus standardised medical care (12x1/week or fortnightly) (n=186) vs standardised medical care alone (n=182)	At 12 months, no significant difference in monthly dissociative seizure frequency was identified between the groups
LaFrance et al (2009) USA ⁸⁶	Before-after, non-controlled study	n=21	Individual CBT (12x1/week)	65% reported seizure freedom. 94% reported seizure reduction
LaFrance et al (2014) USA ⁸⁷	Multicenter pilot randomized controlled trial	n=34	CBT-only: individual CBT (60 min/week x12) TAU; CBT w/ Sertraline; Sertraline-only	33% reported seizure freedom. 55% reported seizure reduction
Myers et al (2017) USA ⁸⁸	Before-after, non-controlled study	n=16	Prolonged exposure psychotherapy. 12–15 90 min weekly sessions	81% reported seizure freedom
Mindfulness				
Baslet et al (2020) USA ⁹³	Prospective uncontrolled trial	n=26	Individual mindfulness-based psychotherapy (12x1/week or fortnightly)	50% reported seizure freedom. 23% reported sustained cessation of PNES
Interpersonal therapy				
Mayor et al (2010) UK ⁹²	Before-after, non-controlled study	n=108	Psychodynamic IPT (19x50 min/ week or fortnight)	25% reported seizure freedom
Psychoeducation				
Mayor et al (2013) UK ⁹⁶	Multicentre before-after, noncontrolled study	n=13	Manualized psychoeducation (4x 60 min/week)	31% reported seizure freedom. 54% reported seizure reduction
Chen et al (2013) USA ⁹⁵	Randomized controlled trial	n=64	Three successive monthly, 1.5 h long group sessions	No significant group difference in seizure frequency/intensity between groups was found
Zaroff et al (2004) USA ⁹⁴	Before-after, non-controlled study	n=10	Group psychoeducational program 3 groups (10x1h/week)	75% reported seizure freedom
Cope et al (2017) UK ⁹⁷	Before-after, non-controlled study	n=19	3-session cognitive-behavior therapy-informed psychoeducation group	40% reported seizure freedom at the end of treatment. 63% reported seizure reduction during the intervention period
Sharpe et al (2011) UK ⁹⁸	Randomized controlled efficacy trial	n=125	CBT-based self-help workbook and face-to-face guidance sessions	No data available about seizure frequency
Sarudiansky et al (2020) Argentina ⁹⁹	Before-after non-controlled study	n=12	3- group session cognitive behavioral based psychoeducation	42% reported a reduction in seizure frequency after the intervention

(Continued)

Table 2 (Continued).

Study	Type of Study	Study Participants	Intervention and Duration	Intervention Outcome (Seizure Frequency)
Group therapy				
Barry et al (2008) USA ¹⁰⁰	Before-after, non-controlled study	n=7	Group psychodynamic therapy (1x week for 32 weeks)	57% reported seizure freedom
Other Interventions				
de Oliveira Santos et al (2014) Brazil ¹⁰⁷	Before-after, non-controlled study	n=37	Individual psychoanalysis (1x50 min/week for 12 months)	30% reported seizure freedom
Kuyk et al (2008) Netherlands ¹⁰¹	Before-after, non-controlled study	n=22	Eclectic psychotherapy (individual, group and family). Duration not reported	27% reported seizure freedom 68% reported seizure reduction
Metin et al (2013) Turkey ¹⁰²	Before-after, non-controlled study	n=9	Group psychoanalytic and behavioural therapy (12 sessions, 90 min/week)	67% reported seizure freedom
Paradoxical Interventions				
Ataoglu et al (2003) Turkey ¹⁰⁸	Randomized controlled trial	n=30	Individual PIT (2x/day for 3 weeks)	93% reported seizure freedom

Note: Resume of the main psychotherapeutic intervention trials reported in the literature and performed in patients with PNES.

Cognitive-Behavioral Therapies

Cognitive-Behavioral Therapy (CBT) has been effective in the treatment of somatoform disorders of DSM-IV according randomized and controlled studies.⁸⁰ Also, CBT has a proven effectiveness for depression and anxiety disorders,⁸¹ frequently associated with the development and maintenance of PNES. Thus, different manualized cognitive-behavioral treatments have been developed for patients with PNES.

Goldstein et al developed a treatment based on the fear, escape or avoidance model, which considers PNES as dissociative responses to different signals (cognitive, emotional, physiological or environmental).^{82,83} Such responses would be associated with extremely stressful or dangerous experiences, for example, abuse or trauma, which have produced unbearable feelings of fear and discomfort in early life.^{82,83,82,83} With this theoretical foundation, based on the research of Chalder,^{85,84} Goldstein presented a 12-session model focused on the cognitive, emotional, physiological and behavioral aspects of

PNES.^{84,83} This treatment proposes home works and psychoeducational bibliography about PNES and has five clearly differentiated stages: 1) Commitment to treatment and rational explanation; 2) Techniques for controlling pseudo-seizures; 3) Exposure techniques to reduce avoidance; 4) Management of cognitions and emotions related to seizures; and 5) Relapse prevention. This model has a randomized and controlled study in which cognitive-behavioral therapy is compared with Standard Medical Care (SMC). SMC included supervised withdrawal of antiepileptic drugs, and supportive sessions in which explanations about the psychological bases of seizures were provided. Results indicated that CBT in addition to SMC, significantly reduced seizure frequency in patients with PNES, in comparison to SMC alone.

Recently, the CODES group – Cognitive and Behavioral Approach for the treatment of Dissociative [non-epileptic] Seizures – published the results of a multicenter randomized controlled trial, which compared the effectiveness of a 12-session CBT protocol plus

standardized medical care with SMC alone, for the reduction of dissociative seizure frequency. The authors concluded that although CBT did not show benefit to seizure frequency after 12 months, improvements in other outcome measures, such as psychosocial functioning were reported.^{86,85}

The model developed by LaFrance was based on the assumption that patients with PNES have had traumatic experiences that lead them to develop maladaptive core beliefs, cognitive distortions and somatic symptoms. The 12-session treatment aimed to promote behavioral changes generate greater self-control and self-efficacy. It has been specially designed for patients with PNES for the treatment of seizures and their comorbidities. The results showed that, of 21 participants, 16 had managed to reduce seizures by 50% and 11 of the 17, were seizure-free at the end of treatment.⁸⁶ In a subsequent study, a randomized controlled trial was conducted with 35 patients with a diagnosis of PNES confirmed by VEEG. These patients were assigned to four treatments: Antidepressant Medication (Sertraline), CBT, CBT and Medication, and Standard medical treatment. The CBT intervention showed a significant reduction in seizures, and an improvement in general functioning and symptoms. The combination of CBT and Medication showed improvements, but less than the application of antidepressant alone. Medication showed signs of improvement, while standard medical treatment did not show any decrease of PNES.⁸⁷

Also, based on trauma as a key aspect for PNES occurrence, Myers et al⁸⁸ applied a modified protocol of Prolonged Exposure (PE) psychotherapy to 16 adult patients with VEEG-confirmed PNES and PTSD. PE consisted of 12–15 90-minute sessions, which included psychoeducation about trauma an PTSD, different techniques such as breathing retraining, sensory grounding, deep breathing, and exposure to real life situations, places, and activities associated to the traumatic event. Authors affirm that PE was effective in reducing seizure frequency, and also improving symptoms related to PTSD and mood disorders.⁸⁸

Interpersonal Therapy

A brief psychodynamic interpersonal therapy was developed for patients with PNES.⁸⁹ The authors adapted the brief psychodynamic interpersonal therapy model and combined it with an adapted model for functional somatic disorders.^{90,91} They proposed an empathetic approach, aimed at improving coping styles and promoting patient

collaboration. This model assumes that the patient's problems originate or are exacerbated by disturbances in their significant personal relationships, with dysfunctional interpersonal patterns, which are related to the patient's symptoms. This approach uses different types of hypotheses: "comprehensive hypotheses", to promote awareness of feelings; "Linking hypothesis", to establish connections between current feelings and other feelings; and "explanatory hypotheses", aimed at looking for possible underlying reasons for the patient's behaviors. These hypotheses seek to facilitate the identification and change of dysfunctional patterns in interpersonal relationships, and a more effective processing of current and past painful emotions. Treatment consists of an initial 2-hour semi-structured interview, followed by up to nineteen therapy sessions of approximately 50 minutes, weekly or at two-week intervals. In the first session, it is expected to a) Create an initial commitment; b) Develop a case formulation. To do this, an individualized PPPT (predisposing, precipitating and perpetuating factors and seizure triggers) model is used, based on the history of symptoms, life chronology, interpersonal relationships, current life stressors, coping resources; c) Change the illness perception; d) Control of symptoms, through breathing and relaxation techniques. The objectives of the subsequent sessions are increase independence, introducing strategies that promote autonomy and self-care; to include caregivers and other health professionals; to improve the emotional process encouraging patients to communicate their feelings; trauma processing. When evaluating the efficacy of this model on 108 patients, the authors found that between 12 and 60 months after the end of therapy, 25% of the patients were seizure-free and 40% presented a 50% reduction; furthermore, the use of health services had decreased significantly.⁹³

Mindfulness

Mindfulness-based therapies (MBT) are those psychotherapeutic approaches that promote self-regulation of attention, and the adoption of an attitude of curiosity, openness, and acceptance towards one's own experience at each moment. Baslet et al developed a manualized 12-session MBT program for PNES. The program is organized in 5 modules and includes psychoeducation, stress management strategies, mindfulness for everyday life, emotion management, and relapse prevention. The results indicated improvements, with a lower seizure frequency and intensity, and a better quality of life.⁹³

Psychoeducation

Psychoeducation is one of the central aspects of treatment for patients with PNES. Given the difficulties that many patients have in understanding this condition, explanatory and educational modules about PNES have been included in most of the interventions. Interventions aimed solely to promoting understanding of PNES, have also been proposed. Also, most psychoeducational approaches are designed in a group format, which in turn, support a better efficiency of mental health resources.

One of the first psychoeducational interventions has been proposed by Zaroff et al in USA.⁹⁴ It consisted of 10 weekly sessions, aimed to explaining the psychogenic origin of seizures and the associated aspects such as anxiety and depression. In addition, the role of trauma was also introduced and explained. This intervention was conducted with 7 patients with PNES, but the authors did not report a significant decrease in seizure frequency. However, they reported improvements in PTSD symptoms and dissociation, as well as in patients' perceived quality of life.

Also, in USA, Chen et al developed an intervention that consisted of 3 monthly meetings. They offered information regarding the relationship between physical symptoms and emotions, and strategies oriented to promote frustration tolerance and relaxation, among others.⁹⁵ The authors compared the effects of the intervention, with a control group. Similar to Zaroff et al, the authors did not report a significant reduction in the frequency or in the intensity of the PNES. However, they did find that patients who participated in the psychoeducational intervention showed improvements in psychosocial aspects, and reduced the use of health services.

In the UK, Mayor et al reported the results of a before-and-after study of a four-session psychoeducational treatment.⁹⁶ This study included explanations regarding the mind-body relationship, relaxation, distraction exercise, execution of avoided activities, among other interventions. In this study, almost half of the patients reported a significant decrease in the frequency of PNES.

Another psychoeducational intervention has been proposed by Sharpe et al, who used a CBT intervention that included both face-to-face sessions and bibliotherapy. When comparing this intervention with the usual treatment, the authors reported improvements of the symptoms. Nevertheless, no reports regarding seizure frequency were exposed.⁹⁷

Also based on CBT, Cope et al have proposed a three-session group psychoeducational intervention for patients with functional neurological disorders, with and without epilepsy. The authors reported that almost 40% of the patients finished the treatment without PNES, and that approximately 75% reported a significant decrease in seizure frequency.⁹⁸ They also reported improvements in illness perception, especially regarding concerns about duration, and a better understanding of the condition.

Psychoeducational interventions have also been applied in other cultures. For example, in our casuistic in Argentina, Sarudiansky et al investigated the effects before and after of a psychoeducational intervention for low-income patients with PNES.⁹⁹ The results reported in 12 patients indicate that there was a significant reduction in seizure frequency in 40% of participants. Furthermore, in line with Cope et al, the patients also reported a reduction in the negative illness perception.⁹⁸ Nevertheless, more studies in other non-Western (non-Caucasian) populations are needed, in order to provide cross-cultural evidence about the efficacy of psychoeducational interventions in patients with PNES.

Group Therapy and Family Interventions

Group therapies have shown variable results regarding the reduction of seizures, but have demonstrated improvements in psychological well-being in patients with PNES.^{100–102}

Other studies evaluated the efficacy of family therapy in patients with PNES. It has been found that the families of patients with PNES would be more conflictive than those of patients with epilepsy.^{103,104,105} McMaster's family therapy model has been applied to patients with PNES,¹⁰⁶ yielding positive results.¹⁰⁶

Psychodynamic Therapies for Patients with PNES

The treatments for patients with PNES based on the psychoanalytic concept of trauma, using principles of Anna Freud's ego psychology and object relations theory, have been also reported. De Oliveira Santos et al applied individual psychoanalysis, and reported a 30% of seizure-freedom in patients with PNES.¹⁰⁷

Eye Movement Desensitization and Reprocessing, and Paradoxical Interventions for Patients with PNES
EMDR has been proposed for the treatment of PNES given its use as a therapeutic strategy in patients with post-traumatic stress disorder (PTSD). However, it has not shown sufficient positive results in the treatment of PNES, either as a first-line treatment or as part of

a battery of interventions.⁸⁹ Paradoxical interventions showed a reduction in conversion seizures and in the anxiety levels.¹⁰⁸ Nevertheless, the research carried out on this type of interventions is still scarce.

Discussion

In this manuscript, we carried out a state-of-the-art review, with the aim to provide a critical approach to the extensive literature about PNES, focusing on diagnostic aspects, the primary management, and the available treatments that have been shown to be effective for the improvement of PNES.

As well the recognition of PNES increased significantly in the last years following the setting-up of VEEG, PNES still constitute a serious mental health unresolved problem. PNES are prevalent among patients admitted for intractable seizures or referred to epilepsy centers. However, the interdisciplinary approach, involving the neurologist, the psychiatrist and the psychologist, is essential for the correct diagnosis and treatment of patients with PNES.^{26–29} Furthermore, there is a delay of several years to reach PNES diagnosis in different countries, which is still too long and too late to implement the correct treatment.^{22,29,30} The difficulties accessing to VEEG which is privative of specialized centers of epilepsy make this access even more difficult.^{22,29,30} The PNES syndrome constitute a mental health problem to be treated by psychiatrists and psychologists, nevertheless a misdiagnosis between PNES and epilepsy is very frequent.^{29,30,34–36} According to the semiology, PNES may have some clinical differences comparing epileptic seizures nevertheless, differential diagnosis based only on clinical semiology is sometimes very difficult and the VEEG is the complementary method of choice, to confirm the differential diagnosis.^{44,45}

Most patients with PNES present at least one current and recognizable psychiatric disorder and many studies showed high rates of somatization, conversive and dissociative disorders, in combination with other comorbid disorders such as depression. The history of sexual abuse, trauma and posttraumatic stress disorder (PTSD) have been considered etiopathogenic factors.^{3,17,21,22,63–65} Indeed, a mental health approach for patients with PNES is mandatory. In addition, for treating PNES, psychotherapy is the first-line treatment.^{67,69}

In the last decades psychotherapeutic interventions have been proposed from different theoretical models (cognitive behavioral therapy, psychoanalysis, interpersonal therapy, etc.). However, more controlled studies are

needed to increase empirical support for these treatments. Likewise, increasing cross-cultural researches are desirable to enhance representation of other countries and cultures.^{25,99} Despite this, patient improvements continue to be partial and different lines of research should be continued in the future. For sum, the individualization of the treatment for each patient, is highly recommended.

Disclosure

The authors reported no conflicts of interest for this work.

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