Psychogenic non-epileptic seizures: an overview on terminology, epidemiology and diagnostic features

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Abstract

Psychogenic non-epileptic seizures (PNES) are paroxysmal events which may be misdiagnosed as epileptic seizures. However, unlike epileptic seizures, PNES are not caused by an excessive and hypersynchronous electrical activity in the brain and therefore are not accompanied by ictal electroencephalographic changes; they are common disorders, considered as an involuntary response to emotional, physical, psychological or social distress. This review focuses on terminology, epidemiology, and diagnostic difficulties encountered by physicians facing with this condition. It also provides a comprehensive overview of the diagnostic accuracy values (sensitivity and specificity) for clinical signs commonly used to support the diagnosis of PNES.
The differential diagnosis between PNES and epileptic seizures may represent a diagnostic challenge, complicated by the coexistence of both conditions in some patients (up to 50%). The diagnostic delay for PNES is worrisome as a correct and prompt diagnosis is essential for an adequate therapy and to prevent unnecessary, costly and potentially harmful drug treatment. The diagnostic "gold standard" is a video-EEG recording of the paroxysmal event. Several physical signs have different sensitivity and specificity values in the differential diagnosis between PNES and epileptic seizures, but the diagnosis should never be driven by any single clinical sign alone. In doubtful cases, diagnosis should be carefully reconsidered checking event description and semiology at each visit, and not forgetting the possibility of a coexistence of both epilepsy and PNES.

KEY WORDS: epidemiology, epileptic seizures, psychogenic nonepileptic seizures, sensitivity, specificity.

Introduction

Unlike epileptic seizures, which are caused by an excessive and hypersynchronous electrical activity in the brain, psychogenic nonepileptic seizures (PNES) are paroxysmal events which may be misinterpreted as epileptic seizures, but are not accompanied by ictal electroencephalographic changes; PNES are considered an involuntary response to emotional, physical, psychological or social distress occurring in presence of inadequate or exhausted coping mechanisms (1). They are therefore currently categorized as dissociative or somatoform (conversion) disorders and as a somatic symptom disorder in DSM-5 (2). However, many patients also fulfill the criteria for mood and anxiety disorders, post-traumatic stress disorder, episodic dyscontrol and, in a minority, factitious disorder (3). Some PNES-like events are probably malingered but the overwhelming majority of patients are thought to have seizures which are not wilfully produced (4)
Because of their clinical resemblance to epileptic seizures, a diagnosis of PNES may represent a challenge for the clinician. They are typically, although not exclusively, diagnosed by epileptologists who needs to be well aware of their existence in order to recognize them promptly and accurately.
This review selectively focuses on terminology, epidemiology and diagnostic criteria of PNES and on the diagnostic difficulties encountered in daily practice by physicians (epileptologists, but also neurologists, psychiatrists, experts in movement disorders) facing with this condition. It also provides a comprehensive overview of the diagnostic accuracy values (sensitivity and specificity) for clinical signs commonly used to support the diagnosis of PNES.

Terminology: how should PNES be called?

Adopting a uniform, unequivocal terminology to refer to PNES has the potential of improving communication among epileptologists, other physicians without specific expertise in epilepsy, and patients. However, terminology and diagnostic criteria used by epileptologists for paroxysmal non-epileptic episodes differ considerably (5). Several terms are currently used, most frequently the term "psychogenic non-epileptic seizures" with its variants ("psychogenic seizures", "non-epileptic seizures", "pseudo-seizures", "psychogenic pseudo-seizures", "psychogenic non-epileptic attacks"). All these terms indicate the non-epileptic nature of these episodes which, unlike other "organic" based non-epileptic seizures, have a psychogenic origin. Conversely, other terms focus on the chronic condition underlying these paroxysmal episodes ("non-epileptic attack disorder", "pseudoepileptic attack disorder").

Recent literature has abandoned the use of older PNES terminology such as hysteroepilepsy, because of their ambiguity and pejorative meaning (6). Although the term "psychogenic non(-)epileptic seizure(s)" is the most commonly used in scientific literature, according to a survey of the American Epilepsy Society this term was reportedly used only by a small minority (7.9%) of clinicians, whereas terms most commonly used at diagnosis were "nonepileptic attacks" (61.9%), "nonepileptic attack disorder" (52.4%), and "nonepileptic seizures" (46.8%) (7). These findings suggest a discrepancy between the high information prevalence of the term "psychogenic non(-)epileptic seizure(s) in medical literature and its lower use in daily practice, where terms without the preceding adjective "psychogenic" and with use of the "lay" word "attack(s)" are most commonly used. The choice of these terms may reflect the tendency towards avoidance of the term "psychogenic" when communicating the diagnosis to patients. These "agnostic litotes" (7), i.e. expressions deriving their meaning from a negation of something else, may reflect the uncertainty of clinicians about the nature of the underlying mental processes, and the possibility of factitious episodes or malingering (8). The frequent use of terms including the word "attack(s)" may reflect clinicians´ attempt to explain epilepsy in less complex terms.

From patients´ perspective, some terms are more likely to be experienced as highly offensive, e.g. "hysterical seizures", whereas terms "non-epileptic attack disorder", "pseudoseizures" and "psychogenic seizures" are probably similar in their offensive potential (they may offend around one third of patients) (9). Overall, the use of term PNES is currently widely accepted among epileptologists, as it "provides clarity for patients, families and providers, while not estranging them and preparing them for appropriate treatments" (5).

A recent study has evaluated the most common English terms used to describe PNES on Google and in MEDLINE (accessed by PubMed) (5). In both Google and MEDLINE the term "psychogenic nonepileptic seizure" was the most commonly used. However, a broad spectrum of synonyms referring to PNES in MEDLINE was found, probably as a consequence of a lack of internationally accepted, uniform terminology for PNES. Furthermore, some obsolete terms, e.g., pseudoseizure(s), were found to be still used in the recent medical literature.

Recently, the question regarding the use of the term "functional nonepileptic event" as a substitute of PNES has been specifically raised (10). The proposal to use the term "functional" instead of "psychogenic" has been put forward, as the later propagates the anachronistic dualistic distinction of the mind from the brain and is not supported by the recent research advances providing increasing evidence supporting the "neurobiological model". In movement disorders the use of the alternative term "functional" has been proposed to indicate what was previously labelled "psychogenic movement disorders" (11, 12) and this change in terminology has been included in DSM-5 with regard to Conversion Disorder, given that relevant psychological factors may not be demonstrable at the time of diagnosis (2). However, the proposal of adopting the term "functional" to indicate PNES has been criticized, as recent neuroimaging data have provided growing evidence of cerebral abnormalities in patients with PNES, hence further supporting the neurobiologic model underpinning these phenomena (13).

Epidemiological features

Prevalence and incidence

The real prevalence of PNES is difficult to estimate. They are however commonly seen at epilepsy centers, where they represent up to 10-22% of referrals (14). Conversely, PNES are found in 5-20% of outpatient populations (15). An estimate yielded a prevalence of psychogenic non-epileptic seizures between 1/50 000 and 1/3000 (16). The only population-based study available yielded an incidence of PNES of 1.4 per 100,000, with highest age-specific incidence (3.4 per 100,000) in the 15 to 24 years age group (17). In this study half the patients also had epilepsy.

Around twenty percent of patients referred for outpatient evaluation of refractory seizures and up to 50% of patients in epilepsy monitoring units have PNES (18). Furthermore, it is estimated that 10 to over 50% of PNES have also epilepsy (19).

Gender

In PNES there is a predominance of the female gender (of about 75-90%) (20-22), although some studies showed a male prevalence up to 40% (23). Such gender distinction seems to appear only after the age of 13 (23). Reasons for this female preponderance are still unclear. It has been however argued that PNES occurring in women reflects rage, fear and helplessness against the male domination or abuse rather than sexual conflicts (23).

Age of onset

Age at onset of PNES is at about 20-30 years (20, 24, 25), although it can occur both in young (23) and old patients (26, 27). The age of PNES onset is later than for epilepsy, but earlier than for motor conversion patients (28, 29).

Risk factors

Several risk factors for PNES have been identified so far. They mainly include a history of sexual, emotional and physical abuse, which has been reported in up to 50% of patients with PNES (30). Other conditions increasing the risk of PNES are previous surgery or other physical trauma, dysfunctional family relationships and major emotionally stressful life events, such as divorce or death of a family member (31-34). A family history of substance abuse is also frequently encountered in patients with PNES (30). Finally, in up to 7% of patients with PNES a positive family history of neurological disease or exposure to individuals with neurological disease can be identified (35).

Diagnosis

How can PNES be diagnosed?

Internationally accepted, uniform diagnostic criteria and definitions for PNES do not currently exist. Definitions adopted in the literature vary widely, although they share several aspects. These include: 1. An observable abrupt, usually time-limited paroxysmal change in behavior or consciousness resembling an epileptic seizures. 2. The absence of electrophysiological changes which accompany an epileptic seizures (i.e. the absence of ictal or postictal EEG changes). 3. No evidence for other organic causes for the episodes. 4. Evidence or strong suspicion for psychogenic process(es) as causative factor(s) (35).

Based on these features, the International League Against Epilepsy proposed a staged approach to PNES diagnosis (35), with recording of the episode by means of video-EEG monitoring as gold standard for diagnosis.

Challenges in the differential diagnosis between PNES and epileptic seizures: when things are not as they appear

The differential diagnosis between PNES and epileptic seizures may represent a diagnostic challenge, which is complicated by the coexistence of both conditions in some patients (18, 36) and the high rates of psychiatric disorders in patients with epilepsy.

This explains the diagnostic delay often encountered in PNES. The diagnostic delay for PNES is worrisome as a correct and prompt diagnosis is essential for adequate therapy and to prevent unnecessary, costly and potentially harmful drug treatment (3, 29, 37, 38). Pseudostatus, a term which refers to prolonged non-epileptic attacks, can be erroneous diagnosed as status epilepticus. Inappropriate treatment of pseudostatus with intravenous anticonvulsants, general anaesthesia and intubation can cause injury and death (39).

On average, the diagnostic delay between onset of episodes and the final diagnosis is approximately 7 to 10 years (3, 25, 40, 41), although most data in the literature relate to patients referred to tertiary epilepsy centres. It has been hypothesized that such a diagnostic delay may be due to the fact that these paroxysmal episodes are firstly evaluated by general physicians in emergency units, rather than by epileptologists who are better equipped in the diagnosis of epileptic and non-epileptic seizures. Consequently, when faced with seizures, non-expert physicians may act “better safe than sorry”, hence treating these episodes as organic even if they may be uncertain about the final diagnosis (42). As reasonably expected, the diagnostic delay before establishing the correct diagnosis is significantly longer in patients with PNES suffering also from epileptic seizures and/or with interictal EEG abnormalities (43, 44). Furthermore, diagnosis appears to be significantly delayed for older patients (27).

Interestingly, a subgroup of patients with PNES and a remarkably short referral time to an epilepsy centre have been recently identified; these patients seem to be characterized by a more active attitude towards medical investigations of their symptoms, more previous psychological complaints and more previous psychological/psychiatric treatments (22).

The clinical suspicion for PNES relies mainly on an accurate history or on a description of the event given by witnesses, and the presence or absence of physical signs may provide additional information to support or rule out the initial diagnostic suspicion. Ideally, a diagnosis of PNES should be made based on a video-EEG recording of the paroxysmal event, which represents the “gold” diagnostic standard in the differential diagnosis between PNESs and seizures (35, 45, 46). However, in some patients a video-EEG may repetitively fail to capture a paroxysmal event, so the diagnosis of PNES relies on a careful integration of history, ictal signs and other clinical and investigational information.

Physical signs such as tongue biting or ictal eye closure have different sensitivity and specificity values in the differential diagnosis between PNES and epileptic seizure (Tab. 1) (47-53). However, evidence of accuracy for most of these signs comes from video-EEG studies, since eye witnesses account can be unreliable. Despite their diagnostic relevance, these signs should be used only to refine an initial probability of PNES, whose diagnosis should never be driven by any single clinical sign.

The patient’s subjective event experience should be taken into account, a sit may provide additional useful clues to the diagnosis. For instance, once frontal lobe seizures have been excluded, questioning patients with suspected generalized tonic-clonic epileptic seizures about whether they “remember the shaking” can be extremely helpful to support a diagnosis of PNES, avoiding unnecessary and expensive further diagnostic workup. Conversional features of

Table 1 - Sensitivity and specificity values of clinical signs for the diagnosis of PNES or generalized tonic-clonic epileptic seizures (GTCS) [values are obtained from (47-53)].

Clinical sign	Sensitivity (%) for PNES	Specificity (%) for PNES	Sensitivity (%) for GTCS	Specificity (%) for GTCS
Asynchronous movements	44-96	93-96		
Fluctuating course	69	96		
Ictal eye closure	58	80		
Memory recall	63	96		
Stertorous breathing	61-91	100		
Pelvic thrusting	1-31	96-100		
Side-to-side head or body movement	25-63	96-100		
Occurrence from sleep			31-59	100
Postictal confusion			61-100	88
Stereotypical ictal cry			13-85	100
Tongue biting (no further specifications)			38	75
Tongue biting (lateral)			22	100
Urinary incontinence			43	52

event description (e.g. the metaphors used by patients to define their seizures) can also be important in giving additional clues. For instance, patients with PNES may be reluctant to describe the paroxysmal symptoms, in detail, and may prefer to focus on the situations where the events occur and the consequences of these episodes (1, 54-56). Conversation analysis of patients' descriptions of their episodes during the communication with their neurologists appears therefore as a useful tool to differentiate the type of seizure.

However, in daily practice it is not always possible to reach a diagnosis of certainty about the nature of a paroxysmal event in all patients. In this case, diagnosis should be carefully reconsidered checking event description and semiology at each visit, and not forgetting the possibility of a coexistence of both epilepsy and PNES (9).

Provocative procedures: to use or not to use?

Provocative procedures may be used to support the clinical diagnosis of PNES or to confirm an initial clinical suspicion thereof. These procedures include placebo administration, usually intravenous saline administration or application of a patch over the skin (57), suggestion techniques based on verbal reinforcement of clinical symptoms (58, 59), or hypnosis (60). Other induction techniques such as compression of temple region, of tuning fork or moist swab application may also be used (61).

The use of provocative procedures to support a diagnosis of PNES should not be indiscriminate and in most cases may even be superfluous (62), as in approximately 50-85% of patients the paroxysmal episodes occur spontaneously during a (video)-EEG recording (63, 64), especially if hyperventilation and intermittent photic stimulation are used (65). Furthermore, PNES seem to occur more frequently if patients have been informed about the increased risk of seizures during hyperventilation and intermittent photic stimulation, suggesting that the adequate and explicit information about routine provocation techniques may alone increase the possibility of PNES to occur (65, 66).

Provocative procedures should be hence restricted to some specific circumstances. They have several advantages: inducing an attack may prove useful in providing conclusive diagnostic information especially in patients whose attacks do not occur spontaneously and can greatly shorten the length and costs of the electrophysiological evaluation (62). Their contribution to diagnosis is relevant also in terms of specificity: when correctly performed and interpreted under simultaneous EEG recording, their specificity is higher than 90% (58, 67). However, special attention should be paid to verifying with patients and family or caregivers that the recorded episode induced by provocative procedures was the habitual type; otherwise, a definite diagnostic conclusion cannot be made, as it is likely that the patient has different types of paroxysmal episodes which may be also epileptic seizures or non-epileptic paroxysmal events other than PNES (62).

Their use remains however controversial and has

been repetitively questioned by several ethical concerns, emphasizing the fact that these procedures can be interpreted as a violation of the relationship between patient and physician, which may be particularly serious in patients with a previous history of abuse (68). Furthermore, the use of deceptive provocative procedures can be seen as a limitation of the autonomy of the patients who have the right to provide their full informed consent and to be actively involved in any decisions which may affect their health (68). However, "it is far more unethical to not obtain a definitive diagnosis when it would be possible" (62), as perpetuating a wrong diagnosis of epilepsy has several serious consequences: patients continue taking AED which are ineffective, expensive, and carry the risk of adverse effects which may be serious and may negatively affect quality of life. Furthermore, if the wrong diagnosis is perpetuated patients do not receive specific treatment for their psychiatric disorder which ultimately remains unrecognized.

Indications for prolonged inpatient video-EEG recording

Most data on the diagnostic role of video-EEG available in the literature refers to long-term, inpatient procedure. It has proved to be a safe and cost-effective investigation strategy (69, 70). More specifically, a diagnosis of PNES based on results of prolonged inpatient video-EEG has been associated with substantial reductions in health care utilization (diagnostic and medication charges, outpatient and emergency visits) and costs (71-73).

The diagnostic role of a short-term outpatient EEG-video recording has been assessed only in one study conducted in a Veteran administration population with a clinical suspicion of PNES. In this study, outpatient video-EEG recording including an induction through hyperventilation, photic stimulation and verbal suggestion yielded conclusive results (i.e. recording of the habitual episode) in 67% of patients (74).

Video EEG monitoring represents therefore a valuable tool for differentiating between PNES and epileptic seizures. However, although the need to record all habitual types of paroxysmal episodes to make a conclusive diagnosis has been widely recognized (75), there is no agreement on the optimal duration of video-EEG monitoring required to achieve that goal. One retrospective study assessed the benefits of prolonged length of stay in an epilepsy monitoring unit for patients admitted for video-EEG monitoring (76). As expected, patients with clinical suspicion of PNES had more inconclusive admissions than other patients (20 *vs* 13%, respectively; p=0.033). In subjects with suspected PNES, a duration of stay equal or longer than 5 days was associated with higher risk of inconclusive admission (28 *vs* 12.5%, p=0.026) (76). These findings suggest that a prolonged duration of video-EEG monitoring may more beneficial to patients with presumed epileptic seizures than to subjects with suspected PNES. However, in this study a dichotomic pattern of presentation of PNES has been observed: some patients had their habitual paroxysmal episodes soon after admission whereas others did not have any attack, even with prolonged VEM (76). Consistently, previous studies reported that patients with PNES show a tendency towards a shorter time to first seizure compared to patients with epilepsy (77, 78). Consequently, taking into consideration the benefit-cost ratio, a prolonged inpatient video-EEG should be considered in patients suspected to have PNES but who did not have their habitual episodes recorded in short-term outpatient EEG-video recording comprehensive provocative procedures [limited to patients whose attacks do not occur spontaneously (62)].

Difficulties in management

Patients with PNES: children of a Lesser God?

Several issues complicate the management of patients with PNES.

Only a minority of patients (30%) achieve freedom from their paroxysmal episodes, whereas most continue to have episodes (79). Furthermore, patients may be reluctant to accept the diagnosis, adhere to treatment recommendations or return to follow-up visits.

Treatments for PNES are mostly based on uncontrolled studies and include educational and psychotherapeutic interventions. Unfortunately, to date adequately powered and methodologically rigorous randomised controlled trials to determine the efficacy of these treatments are still lacking (80).

To make things even worse, some mental health organizations (such as the American Psychiatric Association and the American Psychological Association) have not shown (at least to date) a special concern or interest towards patient education on somatoform, psychogenic, or somatic symptoms (81). Not surprisingly, most research concerning PNES has been and is still being published in the neurology/epilepsy field rather than in the psychiatric one. However, even among neurologists there is a widespread lack of training on how to appropriately manage psychogenic symptoms. Virtually each neurologist or epileptologist is aware of the need to make a correct diagnosis of PNES to avoid unnecessary, inefficacious, and sometimes harmful antiepileptic treatment, and to plan the most appropriate management (5). However, many physicians are not adequately trained in treating somatoform disorders (82), and may therefore experience frustration (83). Consequently, many patients with PNES may "find themselves caught between neurology and psychiatry" (81), with the risk of remaining untreated.

Ignorance and misperceptions still surround PNES even among physicians (84), and there is scarce amount of information and little public knowledge or interest about these phenomena (5). Hence, there remains a need for ongoing education about PNES both among patients and their caregivers, and among physicians. This need is far more relevant as prompt diagnosis of PNES and early psychoeducational inter-

ventions are associated with significant functional improvement (85), and may avoid exposing patients to unnecessary, expensive and potentially harmful medications.

Conclusions

Psychogenic non-epileptic seizures are paroxysmal episodes which may resemble epileptic seizures and may be misinterpreted as such. They are frequently encountered in clinical practice and are considered as an involuntary response to emotional, physical, psychological or social distress. The differential diagnosis between PNES and epileptic seizures is sometimes challenging, although an accurate and prompt diagnosis is essential for adequate therapy and to prevent unnecessary, costly and potentially harmful drug treatment. The diagnostic "gold standard" for PNES is a video-EEG recording of the paroxysmal event. Several physical signs have different sensitivity and specificity values in differentiating between PNES and epileptic seizures, but the diagnosis should never be driven by any single clinical sign. In doubtful cases, diagnosis should be carefully reconsidered checking event description and semiology at each visit, and not forgetting the possibility of a coexistence of both epilepsy and PNES.

Conflict of interest

None of the Authors has any conflict of interest to disclose with regards to the content of this article.

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