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Psychogenic Nonepileptic Seizures: Diagnostic Challenges and Treatment Dilemmas

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Abstract

Psychogenic Nonepileptic Seizures (PNES) are episodes of movement, sensation or behavior changes similar to epileptic seizures but without neurological origin. They are somatic manifestations of psychological distress. Patients with PNES are often misdiagnosed and treated for epilepsy for years, resulting in significant morbidity. Video-EEG monitoring is the gold standard for diagnosis. Five to ten percent of outpatient epilepsy populations and 20 to 40 percent of inpatient and specialty epilepsy center patients have PNES. These patients inevitably have comorbid psychiatric illnesses, most commonly depression, Post-Traumatic Stress Disorder (PTSD), other dissociative and somatoform disorders, and personality pathology, especially borderline type. Many have a history of sexual and physical abuse. Seventy-five to 85 percent of patients with PNES are women. PNES typically begin in young adulthood. Treatment involves discontinuing antiepileptic drugs in patients without concurrent epilepsy and referring for appropriate psychiatric care. However, these patients, as compared to patients with epilepsy, are probably more difficult to manage and their management requires a multi-disciplinary team approach with long term follow up. Less than 50% of patents will have an excellent outcome on long-term follow up studies. More studies are warranted to determine the best treatment modality in these patients

Keywords

Conversion disorder, Diagnosis, Nonepileptic seizures, Video EEG

Introduction

Nonepileptic Seizures (NES) are involuntary episodes of movement, sensation or behavior similar to epileptic seizures that do not result from abnormal cortical discharges. They can mimic any kind of epileptic seizure, being mistaken for generalized tonic-clonic, absence, simple and complex partial seizures [1]. They have been recognized since ancient times as a form of hysteria; Jean Charcot first described nonepileptic seizures as a clinical disorder in the late 1800s, calling it "hysteroepilepsy" or "epileptiform hysteria" [2]. The term NES is preferable to the older terms hysterical seizure and pseudoseizure because those terms are considered pejorative [3].

NES are classified as physiologic or psychogenic in origin. (Table 1) Physiologic NES, which are less common than psychogenic NES, have multiple etiologies. More commonly, NES are psychogenic in origin. They are thought to be a form of physical manifestation of psychological distress. Psychogenic Non-Epileptic Seizures (PNES) are grouped in the category of psycho-neurologic illnesses like other conversion and somatization disorders, in which symptoms are psychological in origin but neurologic in expression [4]. The purpose of this review is to shed light on this common, but, often times, misdiagnosed problem. It has been estimated that approximately 20 to 30% of patients referred to epilepsy centers have PNES [5]. Still, it takes an average of 7 years before accurate diagnosis and appropriate referral is made [6]. Early recognition and appropriate treatment can prevent significant iatrogenic harm, and may result in a better outcome.

Epidemiology

Two to 33 per 100,000 people in the general population have PNES, making them about as common as multiple sclerosis and trigeminal neuralgia [7]. Five to 10 percent of outpatient epilepsy populations have PNES, compared to 20 to 40 percent in inpatient and specialty epilepsy centers [3,8]. Seventy-five to 85 percent of PNES patients are female [9]. PNES tend to begin in young adulthood similar to, conversion disorder, but are seen in a wide range of ages [9]. The prevalence of PNES is increased in patients with head injuries, learning disabilities and isolated neuropsychological deficits [10], and PNES patients have higher than average rates of abnormal MRIs and EEGs, suggesting that physical brain disease may play a role in development of PNES [11]. PNES are also seen in patients with CNS lesions that are associated with an increased risk of developing epilepsy, such as stroke, trauma, infection and malformation [12], as well as in patients with hippocampal sclerosis [13], an often-identified cause of temporal lobe epilepsy. The presence of abnormalities on MRI or EEG may therefore explain the delay in diagnosis and treatment of PNES.

Estimates of the co-existence of epilepsy and PNES have varied widely, from 5 percent to more than 60 percent depending on the study setting and diagnostic criteria used [3]. Recent studies using strict criteria for a diagnosis of epilepsy find that only 5 to 10 percent of patients with PNES have concurrent ES [8,14].

Etiology

All PNES function as a coping mechanism [15]. PNES patients

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Table 1: Classification of Nonepileptic Seizures

Nonepileptic Seizures	
Physiologic	**Psychogenic**
Cardiac arrhythmias	Misinterpretation of physical symptoms
Complicated migraines	Psychopathological processes:
Drug/Toxic effects	Conversion disorder
Dysautonomia	Somatization disorders
Hypoglycemia	Dissociative disorders
Movement disorders	Anxiety disorders (including PTSD)
Panic attacks	Hypochondriasis
Sleep disorders	Psychoses
Syncopal episodes	Reinforced behavior patterns in cognitively impaired patients
Transient ischemic attacks (TIAs)	Response to acute stress without evidence of psychopathology
Vestibular symptoms	

Table 2: Classification of PNES by Underlying Etiologies

Etiology	Description	Suggested Treatments
1. Acute/Situational Stresses	PNES develop after multiple and/or acute stressors overwhelm the patient's coping ability. There may not be an underlying psychopathology.	Supportive psychotherapy, lifestyle changes, group or family therapy as indicated.
2. Anxiety/Panic/ Physical Symptoms	Atypical symptoms of anxiety or panic are misdiagnosed as PNES, or the patient misinterprets physical sensations or symptoms.	Treatment of panic attacks; reassurance that physical symptoms are not seizures.
3. Depression/ Dissatisfaction	In this case, a specific stressor does not precipitate the PNES; rather, the patient is generally unhappy, and the PNES function as distraction or an acceptable way to get support and attention.	Antidepressant therapy for depression, CBT to challenge depressive thoughts and basic assumptions about self/illness, encourage active involvement in lifestyle changes and problem solving.
4. Poor interpersonal skills and affect regulation; disturbed family systems	Patients with this profile are often diagnosed with borderline personality disorder and often have history of abuse. The patient may come from a family with poor emotional expression, so he or she is unable to identify and effectively express strong emotions. The PNES function to resolve interpersonal crises or threatening emotions or situations.	Intensive psychodynamic psychotherapy to help identify and express threatening emotions (conflict, anger and rejection) and set realistic goals for relationships; family therapy when family systems support maintenance of PNES.
5. Psychosis	PNES can be a manifestation of psychosis; this is rarely the case and the diagnosis is clear.	Treatment of underlying psychosis.
6. PTSD/ Dissociation	Patients in this group have active, chronic PTSD and dissociative symptoms. Flashbacks, recollections or sensory triggers often trigger PNES. Often there is a history of severe childhood abuse, and/or current abuse.	Exposure-based therapies and SSRIs for PTSD.
7. Reinforced behavior pattern	Often seen in cognitively impaired people; they have developed because of the functional advantages that are reinforced by the PNES, e.g. attention or avoiding responsibility.	Behavior modification therapy.
8. Somatization/Somatoform/ Conversion disorders	The PNES represent emotional distress converted into physical symptoms; there is often a long history of medical attention for unexplained physical symptoms. The patient can often identify precipitating stressful events; the PNES are therefore a conversion symptom.	Cognitive behavioral therapy (CBT) to identify links between stress and NES and develop more adaptive coping; for severe somatization, regular visits not contingent on symptoms, focus on living with symptoms rather than investigating and treating them.

Adapted from Gates [3], Barry & Sanborn [41], Bowman & Markand [17], LaFrance &Devinsky [19], Reuber & House [27] and Rusch et al. [62]

consistently perceive their lives as stressful, and are more likely to use maladaptive coping strategies to handle stress [16]. In PNES, psychological conflicts are translated into a physical symptom, the seizure. In this way, intolerable distress is dissociated from the painful conscious experience of the trauma or forbidden emotions causing the distress [17,18]. Thus genuine PNES (as opposed to factitious disorder or malingering) are necessarily not intentional; they are created as a psychological defense mechanism to keep the internal stressors out of conscious awareness [17].

PNES do not have a single cause; rather, they are the product of several different causal pathways (Table 1). PNES may be the result of psychopathological processes; they may be a response to acute stress in a patient without evidence of psychopathology, or a reinforced behavior pattern in cognitively impaired individuals. Rarely, malingering or factitious disorder present as PNES [18]. Forty-three to 100 percent (median 73.5 percent) of PNES patients have a current psychiatric disorder [19]. These tend to be trauma-related disorders, including post-traumatic stress (PTSD) and other anxiety disorders; depressive disorders, and conversion, somatization and dissociation disorders. Personality pathology, particularly of the borderline type, is common [20]. Frequently these patients have other dissociative and somatization symptoms in addition to PNES [9,20].

There is often a history of, or current physical or sexual abuse [17] or significant psychosocial stressors for which the patient perceives no resolution [21-24] – what Griffith [23] called "unspeakable dilemmas". These dilemmas frequently involve dysfunctional family interaction and communication [9,16]. An often-cited prospective study [17] showed that 84 percent of the PNES patients had experienced trauma. More recent study [25], found a significantly higher rates of PTSD, childhood sexual abuse, dissociative symptoms and history of assaultive trauma in patients with PNES compared to epileptic controls. Physical and sexual abuse has been linked to increased rates of several somatization syndromes, including PNES [18].

To figure out why a particular patient is having PNES, the clinician must understand what the psychological function of the seizure is [26]. A detailed and systematic psychiatric evaluation and an assessment of family, social, financial and employment problems should provide insight [27]. Table 2 is a composite of several systems that classify PNES based on underlying etiologies.

Diagnosis

The search for easier and more cost-effective tools of differentiating epileptic seizures (ES) from PNES continues to be a real challenge. Early diagnosis of PNES is critical. Unfortunately,

Table 3: Historical and Clinical Details Suggesting a Diagnosis of Psychogenic Nonepileptic Seizures

Historical features
Associated (often multiple) psychiatric disorders
Flurries of seizures or recurrent "pseudostatus" epilepticus leading to multiple emergency visits or hospitalizations
High seizure frequency
History of sexual and physical abuse
Lack of concern ("*la belle indifference")* or excessive/exaggerated emotional response
Multiple unexplained physical symptoms
No history of injury from seizures
No response or paradoxical increase in seizures with AEDs
Personal, family or profession experience with epilepsy
Seizures occur only in presence of others or only alone

accurate diagnosis is often delayed; there is a mean latency of 7.2 years between manifestation and diagnosis of PNES [6]. This delay in diagnosis can be due to a low index of suspicion for PNES, lack of practical screening measures, cost, and limited availability of the vEEG or ambulatory EEG that would assist in reaching accurate diagnosis in a timely manner. PNES patients experience significant iatrogenic morbidity from inappropriate treatment of epileptic seizures, including adverse effects of Antiepileptic Drugs (AEDs) and emergency visits for pseduo-status, with associated aggressive and potentially harmful interventions including intubation. On the other hand, definitive diagnosis may be therapeutic as well; some patients will stop having PNES after being informed unambiguously of their diagnosis [28]. Furthermore, and from a healthcare costs point of view, it is important to diagnose PNES early in its course. One study [29] demonstrated an 84% reduction in total seizure-related medical charges in the six months after diagnosis: average diagnostic test charges decreased by 76 % and medication charges by 69 %, while outpatient visits decreased 80 % and emergency department visits by 97 %. Finally, it is worth mentioning that PNES have serious negative effects on patients' lives. Health-related quality of life is significantly lower in patients with PNES than patients with epilepsy, even when compared with patients with intractable epilepsy [30]. This decreased quality of life is associated with the presence of psychopathology and with adverse effects of antiepileptic drugs (AEDs) [31], further emphasizing the importance of early diagnosis, cessation of AEDs, and treatment of the underlying psychiatric illness.

Several factors have been considered when diagnosing PNES, but the gold standard for diagnosis remains the inpatient video-Electroencephalography (vEEG) monitoring. Several indicators have been used historically and, till today, they are only suggestive of PNES and they remain insufficient in themselves to make a definitive diagnosis. Example of these indicators are the presence or absence of self-injury and incontinence, ability to induce seizures by suggestion, psychological tests, historical factors and ambulatory EEG monitoring [1,32].

One of the suggested tools to differentiate ES from PNES is the Post-Ictal Prolactin (PRL) level measurement. Although Studies are conflicting on the reliability of this tool, one recent review study showed that elevated PRL levels 10-20 minutes post-ictaly were highly predictive of either generalized tonic–clonic or complex partial seizures. Pooled sensitivity was higher for generalized tonic–clonic seizures (60.0%) than for complex partial seizures (46.1%), while the pooled specificity was similar for both (approximately 96%). Data were insufficient, however, to establish validity for simple partial seizures. Two cited studies in this review were consistent in showing PRL elevation after tilt-test–induced syncope. Similarly, inconclusive data exist regarding the value of serum PRL following status epilepticus, repetitive seizures, and neonatal seizures. So it seems that elevated serum PRL assay, when measured in the appropriate clinical setting at 10 to 20 minutes after a suspected event, is a useful adjunct for the differentiation of generalized tonic–clonic or complex partial seizure from PNES among adults and older children. On the other hand, serum PRL assay does not distinguish ES from syncope. Moreover, the use of serum PRL assay has not been established in the evaluation of status epilepticus, repetitive seizures, and neonatal seizures [33].

Other tools have been tested that looked at the use of self-administered questionnaires. One particular questionnaire was found useful as a screening tool and can be used to hasten the referral of these patients for (vEEG) [34]. This 53 item questionnaire that were administered to 181 patients was found to accurately predict PNES diagnosis, with 94% sensitivity and 83% specificity at the training center, and 85% sensitivity and 85% specificity at the second tertiary referral center that was involved in the study.

Likewise, semiotics also can be used as a screening tool. Studies have shown that semiological differences between PNES and ES are reliable when performed by experts but, unfortunately, they are not as reliable, when obtained from relatives and lay persons [35]. Another suggested tool is the measurement of Heart Rate Variability in all suspected patients. A preliminary study has shown an increase of HRV in the ES patients when compared with the PNES group [36].

Definitive diagnosis can only be established by vEEG monitoring, in which, the patient is observed having his/ her habitual seizures, with lack of any accompanying abnormality on the ictal EEG recording. Family members or witnesses who are familiar with the patient's habitual events must agree that the recorded episodes are their typical habitual events and they are the only ones that they observe the patient is suffering from. The importance of using vEEG for diagnosis was underscored in a study [37] evaluating the diagnoses of patients referred to the inpatient vEEG-monitoring unit for characterization of their seizures. Twenty-four percent had been misdiagnosed: 22 patients previously diagnosed with epilepsy were found to have NES, and four patients previously diagnosed with NES were found to have epileptic seizures. Epileptologists or neurologists with experience in epilepsy referred all study patients. Interestingly, even epilepsy specialists misdiagnosed seizure types in nearly a quarter of cases. Despite the fact that the vEEG is the gold standard test, the inter-rater reliability of this tool was found in one study to be moderate in value when the test was used without any supporting historical and semiological data on the patients in question [38]. One way of increasing the diagnostic yield and reducing the waiting time of the vEEG is the administration of single placebo induction method, which has showed promising results in a preselected population in one study [39]. Similarly, another study showed that induction can be achieved without placebo [40]. This approach, however, remains a controversial issue and creates so much debate from an ethical point of view, which is not the scope of this review article.

On another note, historical details and clinical features that are suggestive (but not diagnostic) of PNES are reviewed in Table 3. Typical PNES features include a gradual onset, long duration, waxing and waning course, and disorganized, asymmetrical motor activity [41]. PNES seizures also lack the stereotypy of epileptic seizures; that is, the pattern of symptoms and sequence of events vary between seizures. Not all seizures with these features are PNES, however. Frontal lobe seizures are often mistaken for PNES because of their dramatic motor and vocal outbursts, possible retained consciousness

and short post-ictal period. They may be distinguished from PNES by their brief duration, stereotypical nature, and tendency to begin during sleep [41]. Likewise, gelastic seizures (in which the primary automatism is laughter), reflex epilepsies and myoclonic jerks have also been mistaken for PNES [41].

Indeed, a recent study attempted to come up with a new classification of PNES based on semiological characteristics and proposed a modified new classification: abnormal hypermotor response in 28% of their cohorts, abnormal partial motor response in 22%, affective/emotional behavior phenomena in 4.9%, dilaleptic type in 6.1%, nonepileptic aura in 6.1%, and mixed pattern in 32.9% [42]. This proposed classification has a potential to categorize PNESs which present in psychiatric settings as dissociative disorders. It is well established that nearly two-thirds of observers report that patients lose their awareness or the ability to react during their PNESs, and over half of observers endorse that patients' attacks "always" involve a "complete loss of consciousness or blackout". When compared with the observers of PNESs, patients themselves are less likely to state that they lose consciousness and almost a third of patients with PNES endorse that they "always" "have no idea what is happening around them during their attacks". They demonstrate greater general awareness/responsiveness, as compared to patients with ES and more subjective experiences during their seizures [43,44]. A recent review of dissociative seizures proposed that the current evidence and theory suggest that impairment of consciousness in PNESs is only "dissociative" in one subgroup of these seizures, when consciousness is suppressed as a collateral effect of the excessive inhibition of emotion processing based on early learning from coping with traumatic experiences, biologically-based tendencies, or other processes. It suggests that PNES to be classified as dissociative disorder and anticipated PNES to become a dissociative/functional disorder in ICD-11, and PNESs are often referred to as dissociative seizures [45]. On this basis, it could be argued that, by definition, the apparent alterations in consciousness associated with PNESs must be "dissociative" in nature.

However, vEEG is not available in some locations, and in some patients, events cannot be recorded. Some providers have limited access even to routine epilepsy diagnostic equipment [46]. Moreover, inpatient vEEG may not be practical in patients with infrequent events, and for patients whom seizures occur only in circumstances unlike those found in a clinical monitoring environment. Therefore, a group of researchers have come up with a model of diagnosis which is not entirely dependent on vEEG. They suggested a staged approach, where the diagnostic levels are stratified, based on level of certainty, into: possible, probable, clinically established, and documented [47]. Possible PNES is made when clinical history and descriptions of events from patient/witness (es) are suggestive of PNES and the patient has a normal interictal EEG). Probable diagnosis of PNES is made when clinical history is suggestive of the diagnosis and a clinician has reviewed the video recording of events or in person, provided that, the interictal EEG, did not show clear epileptiform discharges. On the other hand, clinically established PNES is made when clinician witness the events or upon review of the events with ambulatory EEG recording of habitual event(s) but without video. Generally, ambulatory EEG without video recording is more widely available than vEEG and has been used to differentiate epilepsy from PNES. However, as an adjunct to good clinical data, the vEEG recording of habitual events provides the most reliable diagnosis of documented PNES.

Finally, a recent review on this topic offers a concise review focusing on the practical aspects of clinical relevance in the v-EEG diagnostic work-up of inpatients with suspected epilepsy and calls for, rightly so, on the implication of both specific procedures e.g., activation maneuvers and interpersonal approach (e.g., monitoring protocols) during v-EEG on an individual basis according to the patient's presentation [48].

Obviously, neurologists have the most important role to play in the timely diagnosis of PNES through early referral of patients with apparently intractable seizures to epilepsy centers. About 60 percent of patients with newly diagnosed epilepsy will be controlled on a moderate dose of a single antiepileptic drug, usually the first or a second drug chosen; only about 10 percent with inadequate control of seizures on the first AED will become seizure-free [49,50]. Thus, the threshold for diagnosing a patient with intractable seizures should be low and a referral to an epilepsy center for clarification of the diagnosis should be prompt. As a matter of fact, a recently conducted first large scale qualitative study of providers' perspectives in a national, integrated health-care system utilizing semi structured interviews with 74 health-care clinicians and workers in the VA hospital, has revealed a variation in the level of care and two emergent domain themes of frustration and hope among health care providers caring for these patients. It calls for more resources to diagnose, and care for these patients, with emphasis on funding research in this area [51].

Disease Course & Prognosis

PNES is not a single entity or disorder, so the course is variable and depends on the underlying etiology. However, outcome studies allow generalizations about PNES patients as a group. Seizure cessation occurs in about 40 percent, seizure reduction occurs in a third of patients, and another third has chronic, unimproved PNES [52]. In a study assessing the 1 to 10 year outcomes of 164 patients with PNES [52] 44 percent had a poor outcome, (defined as not seizure-free and dependent – i.e. retired because of ill health or unemployed), 40 percent had an intermediate outcome, (seizure-free but dependent, or not seizure-free but living independently), and only 16 percent had a good outcome, (seizure-free and living independently). At more than 11 years after onset and 4 years after diagnosis, 71 percent were still having PNES, and 56 percent were still dependent. This is worse than the outcome for newly diagnosed epilepsy, and equivalent to the outcome for other somatoform disorders [50]. People having both epileptic and non-epileptic seizures may have less favorable outcomes, but there are still no long-term studies specifically evaluating that population. Prognostic factors vary among studies. As a matter of fact a recent review on prognosis of PNES has systematically assessed all published original studies on the prognosis and outcome predictors of patients with PNES. Out of 18 original studies meeting the search criteria, the prognosis was found to be poor in adults, but good in children. Fewer than 4 in 10 newly diagnosed adults with PNES can be expected to become seizure-free within 5 years after diagnosis. In children, however, the figure of patients achieving seizure remission appears to be around 70%. Predictors of poor outcome included the presence of coexisting epilepsy or psychiatric comorbidities, violent seizure phenomenology, dependent lifestyle, and poor relationships [53]. See Table 4 for a review of these factors.

Treatment

As mentioned in this article there is a proven therapeutic value for the mere communication of the diagnosis. From a pharmacological point of view, a single pilot randomized controlled trial (RCT) study on the use of SSRIs in the treatment of PNES have shown good positive preliminary results. Only one double-blind placebo controlled pilot RCT for PNES has been published [54]. Thirty-eight patients enrolled, and 26 (68%) completed the trial. Thirty-three subjects with nonzero baseline seizure rates were included in an intention to- treat analysis of the primary outcome. Patients assigned to the sertraline arm experienced a 45% reduction in seizure rates from baseline to final visit ($p = 0.03$) versus an 8% increase in placebo ($p = 0.78$). The pilot study was not powered for efficacy but showed feasibility for a pharmacologic RCT. Data from this RCT and other open label trials indicated that medications may help to reduce symptoms, but would likely require adjunctive psychotherapy to eliminate seizures. Clearly this finding needs to be replicated in a larger double blinded design to confirm this finding [54].

On the other hand, psychological treatments remain the preferred choice for clinicians involved with PNES as shown in a recent survey [55]. Unfortunately, there are still very limited numbers of RCT on psychological treatment of PNES [19,20].

Table 4: Prognostic factors implicated in favorable and unfavorable outcomes in patients with PNES

FAVORABLE	UNFAVORABLE
Children	Adults
Acceptance of nonepileptic nature of episodes	Co-existing epilepsy
Family structure that supports autonomy	Disbelief of diagnosis
Female	Family structure that supports dependency and illness
Having friends currently	Long history of psychiatric disorders
Having good relationships with friends as a child	Longer duration of PNES
Higher ability to express emotions	Male
Higher intelligence & education	Ongoing physical and/or sexual abuse
Independent lifestyle	Ongoing psychosocial stressors
Less dramatic PNES:	Pending litigation
- No positive motor features - No ictal incontinence or biting - No admissions to ICU - No pseudostatus with intubation	Persistently somatizing patient
Less extreme scores on traits defining emotional dysregulation	Reluctant self-disclosure
Less tendency to dissociate	Restricted expression of anger and positive feelings
Shorter duration of PNES	Unemployment/Disability
Younger age at diagnosis	

References: Barry & Sanborn [41], Reuber et al [52]. LaFrance &Devinsky [19], Durrant J [53], and Ettinger et al. [66].

Treatment recommendations are based on the logical but, unproven theory, that because the PNES are psychogenic in origin, they will respond to psychiatric treatment. Two uncontrolled studies [9,56], showed that psychotherapy was more effective than no intervention. Various psychotherapeutic techniques with proven efficacy for other disorders have been applied to PNES patients with similar psychiatric profiles. On the other hand, group psychotherapy which combines psychoeducation and behavioral and psychoanalytic techniques suggests that group psychotherapy might be a treatment option for chronic PNES. In this small powered study, they enrolled nine over 12 weeks of therapeutic sessions. After one year of follow-up, there was significant decrease in seizure frequency as well as significant improvements in the mental health subscale of the Spielberger State–Trait Anxiety Scale [57].

Furthermore, an open-label psychotherapy study for PNES used an epilepsy therapy workbook modified to target dysfunctional cognitions and behaviors in these patients. Eleven of 17 individual therapy intervention completers (65%) reported no seizures by the end of the 12-week trial. The 12-session, therapist-guided seizure treatment workbook focused on gaining control of seizures and included training in healthy communication, understanding medications, conducting functional behavioral analysis, and examining internal and external triggers. In addition to seizure reduction, mean scores on scales measuring depression, anxiety, somatic symptoms, quality of life (QOL), and psychosocial functioning showed improvement from baseline to the final session, suggesting that the intervention also improved psychiatric symptoms, QOL, and functioning [58].

Similarly, Cognitive Behavioral Therapy (CBT) seems a preferred choice of therapy among neurologists caring for these patients. Indeed, a small pilot study was undertaken to evaluate whether CBT-based group therapy would offer a feasible treatment option for patients with PNES and patients with other functional symptoms. Significant improvements were selectively reported in the 'emotional well-being and role limitation. However, improvements in overall quality-of-life scores, as well as in HADS anxiety and depression scores, did not reach statistical significance [59].

However, a recent Cochrane systematic review found insufficient evidence to recommend CBT or any other treatment for these patients [60]. In addition, some initial evidence suggests that patients who receive psycho education had a greater potential for improved social outcomes, but seizure frequency was not significantly reduced in open-label trials [61]. The role of psycho education may be to help reduce the loss to follow-up during patients' transition to the planned treatment. Group psycho education may have potential for reducing seizures, dissociative/posttraumatic symptoms, and reliance on emotion based coping strategies, as seen in an uncontrolled open-label study [62].

Finally, a recent level 1 trial for PNES randomized thirty-eight participants in a blocked schedule to 1 of 4 treatment arms: flexible-dose sertraline hydrochloride only, CBT informed psychotherapy (CBT-ip) only, CBT-ip with medication (sertraline), or treatment as usual. These patients were followed up for 16 weeks. At the end of trial, the psychotherapy (CBT-ip) arm showed a 51.4% seizure reduction (P =.01) and significant improvement from baseline in secondary measures including depression, anxiety, quality of life, and global functioning (P<.001). The combined arm (CBT-ip with sertraline) showed 59.3% seizure reduction (P=.008) and significant improvements in some secondary measures, including global functioning (P=.007). The sertraline-only arm did not show a reduction in seizures (P=.08). The treatment as usual group showed no significant seizure reduction or improvement in secondary outcome measures. The authors concluded that treatment with CBT-ip for PNES with and without sertraline can provide a significant seizure reduction and improved comorbid symptoms and global functioning in patients with PNES [63]. But the question remains here, whether this effect on PNES outcome was specific to the effect of CBT, or it was related to the nonspecific characteristics of general psychoeducational therapy, (e.g. higher education in CBT therapy and higher level of therapist/ patient interaction).

LaFrance and Devinsky [19] offer a model of neuropsychiatric treatment formulation for PNES. The first step is proper diagnosis with a thorough history and exam and inpatient video-EEG monitoring. Second, the diagnosis should be presented to the patient and family. Third, psychiatric treatment is determined by creating a problem list identifying predisposing factors, precipitants to seizures, and perpetuating factors; this list then informs the prescription of the appropriate psychotherapies. Finally, addressing pharmacotherapy involves tapering AEDs (in patients with exclusively PNES), which was shown to be safe when done under proper clinical surveillance [64], along with the titration of appropriate psychotropics for the management of psychiatric comorbidities. The importance of early AED withdrawal lies partly in communicating to the patient that they do not have epilepsy and thus that such medication is unwarranted. In view of the potential teratogenic effects of some AEDs, this assumes additional importance for women of child-bearing age, who make up

the majority of these patients.

Driving and PNES

A recent study approached this controversial issue from two aspects. Firstly neurologists were asked about their opinion regarding posing driving restrictions on patients with PNES. The opinion of this group of experts was quite mixed, 49% of the clinicians were in favor of placing the same restrictions as is the case of ES patients, and 32% were in favor with placing no restriction, while 19% were in favor of studying these patients on a case-by-case basis. The second part of the study showed that the patients with PNES do not differ from the general population in the rate of road traffic accidents [65]. Obviously this is a single and the only study, to our knowledge, reported so far in the literature. Additional studies, are urgently needed in order to make a meaningful recommendation to the society.

Conclusion

While we are able to reliably diagnose PNES and have an understanding of their psychological origins, diagnosis is often delayed and we still have much to learn about best treatment practices. Psychiatrists, and perhaps, neurologists, who understand the patient's psychosocial environment better than other specialists, can recognize factors like abuse history, other somatization symptoms and negative family environment that may lead to earlier diagnosis of PNES. Early recognition and referral to an epilepsy center will prevent harmful and costly interventions and will allow early treatment, which is associated with improved outcome. An excellent brochure on PNES for patients and their families can be found at: http://hsc.usf.edu/COM/epilepsy/PNESbrochure.pdf

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