Curr Treat Options Neurol (2015) 17: 41
DOI 10.1007/s11940-015-0371-4

Epilepsy (E Waterhouse, Section Editor)

A Therapeutic Approach to Psychogenic Nonepileptic Seizures

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Published online: 8 August 2015

This article is part of the Topical Collection on *Epilepsy*

Keywords Psychogenic nonepileptic seizures · PNES · Seizure monitoring unit · SMU · Cognitive behavioral therapy · CBT · Video-EEG · Selective serotonin-reuptake inhibitors · SSRIs

Opinion statement

The diagnosis of psychogenic nonepileptic seizures (PNES) is usually made in the seizure monitoring unit (SMU; also commonly named the epilepsy monitoring unit) after PNES are recorded on video-EEG. The diagnosis should be discussed with the patient thoroughly. The discussion should focus on how the diagnosis was reached and that the diagnosis is real and treatable. When the diagnosis is communicated well, some patients may improve significantly without further interventions. Next, a psychiatric evaluation should be completed, ideally before discharge from the SMU. After discharge, the patient should undergo cognitive behavioral therapy (CBT), the only treatment for PNES that is supported by high-quality evidence. Other therapies, including psychodynamic therapy and different types of group therapy can be considered in some patients, although high-level evidence to support their use is lacking. Some patients may benefit from selective serotonin-reuptake inhibitors (SSRIs), especially when psychiatric comorbidities are present. This should be considered on a case-by-case basis.

Introduction

Psychogenic nonepileptic seizures (PNES) are defined as episodes of paroxysmal change in behavior, motor activity, or sensation that may clinically resemble epileptic seizures but are attributed to a psychological rather than an organic neurological cause [1, 2]. Although demographic data on prevalence and incidence is limited, PNES are believed to be common, occurring in 20–40 % of patients admitted to seizure monitoring units (SMUs) [3] with an estimated prevalence of 2 to 33 per 100,000 [4]. One population-based study [5] suggested an incidence of 1.4/100,000. Studies based on referrals to an epilepsy center reported an incidence of 3.3–4.9/100,000 [6, 7]. In these studies, women represented the majority of patients with PNES (73–81.5 %) [7, 5, 6].

Mandeville, who documented the first full description of a nonepileptic seizure in 1730, suggested treating one of his patients with a "course of exercise! And no medicines at all" [8]. Charcot recommended ovarian compression for acute treatment of PNES. Gowers proposed more drastic techniques to abort seizures, using "strong sensory impression of any kind" such as faradization, pouring water in the patient's mouth, "closing the mouth and nose with a towel until the patient is at the point of asphyxia," and even "a vigorous tug at the pubic hair' [2]. Freud suggested the use of hypnosis and dream interpretation [8].

The diagnosis of PNES is usually based on clinical history and video-EEG monitoring, which is considered the gold standard for diagnosing the condition [9]. Prolonged video-EEG monitoring (usually performed in a SMU) should document habitual seizure types and investigate whether the patient has PNES alone or with co-existent epilepsy, which can be present in up to 9.5 % of cases [10]. Misdiagnosis may occur when based on history alone or observation of a singular event [9].

Most patients with PNES report history of significant traumatic experience [11]. A relationship between PNES and a history of sexual abuse is supported by a large body of research [12]. This seems to be a less important factor in some subgroups of patients, including men, patients with late adulthood seizure onset and patients with learning difficulties [11]. Family dysfunction seems to play a role [13, 14], especially in males [15]. Psychiatric comorbidities are common in patients with PNES, most notably depression, anxiety, posttraumatic stress disorder, and personality disorders [16].

Despite the increasing interest in PNES and significant increase in related publications, treatment of PNES continues to prove challenging. This could be due to the limited understanding of mechanisms underlying PNES and the lack of sufficiently powered randomized controlled trials (RCTs) evaluating the efficacy of different treatment modalities [17, 9]. A major barrier to performing RCTs for PNES treatment is the limited funding [9]. Nevertheless, the recent publication of the results of three pilot RCTs [18, 19, 20••], including a well-conducted study with high-quality evidence for cognitive behavioral therapy (CBT) [20••], is quite promising.

Treatment

Communicating the diagnosis

The first therapeutic intervention

This is the first step in treatment and most often takes place in the SMU after PNES are recorded on video-EEG. Unfortunately, the importance of this step in the treatment process is sometimes underestimated. This first therapeutic step may subsequently determine the patient's outcome and hence it should be handled carefully [17]. The therapeutic potential of this discussion was demonstrated in a few studies. One study demonstrated significant decrease of psychogenic seizures in the first day following the presentation of the diagnosis [21]. In a study by McKenzie et al., where communication of the diagnosis was the only therapeutic intervention, 38 % of patients were seizure-free for at least 2 months at 6–12-month follow-up. In addition, 23 had significant reduction in their seizure frequency [22]. In another study, 88.9 % of patients who were seizure-free at 3-month follow-up stopped having seizures immediately after presentation of the diagnosis [7].

What should be discussed?

In a multicenter study by Hall-Patch et al., a standardized protocol was used to present the diagnosis of PNES in 50 newly diagnosed patients [23]. The protocol consisted of 14 core points: Explain that the seizures are real; give the seizures a label; discuss alternative names for the condition; reassure the patient

that this is a common and recognized condition; discuss that this is not epilepsy; discuss predisposing, precipitating, and perpetuating factors; provide a model for the attacks (e.g., brain becomes overloaded and shuts down); discuss that antiepileptic medications are not effective; discuss evidence that psychological treatment is effective; discuss referral to a specialist; and discuss that the condition can resolve and that improvement can be expected. With this communication as the only therapeutic intervention, 14 % of patients were seizure-free at 3-month follow-up and 63 % reported more than 50 % reduction in seizure frequency. There are other published protocols for communicating the diagnosis that follow similar outlines [24–26]. However, the clinical efficacy of these protocols has not been evaluated.

Is this enough?

Many studies suggest that the positive effect from a comprehensive communication of the diagnosis may not be sustained in the long run, and many patients still need further active psychological or psychiatric treatment [27•]. A multicenter study [28] evaluated the longer-term outcomes after presenting the diagnosis to 44 patients using the standardized communication strategy described by Hall-Patch et al. [23]. At 6-month follow-up, only 16 % of patients were seizure-free while 23 % showed >50 % reduction in seizure frequency [28]. The majority of patients continued to demonstrate high levels of distress according to self-reported measures of psychological well-being.

Terminology

Terminology used to describe PNES has been a subject of controversy [27•]. The term PNES is the most commonly used term in English language literature published on PubMed [29]. In a US survey, the majority of neurologists (60 %) used the term "nonepileptic seizures" [30] while 10.7 % of physicians used the term "spells" and 4.5 % still used the old-fashioned term "pseudoseizures." In one study, the terms "pseudoseizures," "hysterical seizures," and "symptoms all in the mind" were perceived most offensive by patients [31]. These terms should be avoided when presenting the diagnosis to the patient. Some neurologists prefer the term "nonepileptic attacks" [32] which seems to be popular in the UK, where it was used by 62 % of physicians in one survey [33]. This term risks associating seizures with a physically or emotionally traumatic attack previously experienced by patients [27•]. We prefer the term PNES at our institution. What is more important than the term used, however, is how the diagnosis is explained to the patient [27•].

Who presents the diagnosis?

The diagnosis should be presented by the neurologist, who is most qualified to discuss the results of video-EEG monitoring and explain how the diagnosis was made. A team approach involving the neurologist, psychiatrist, psychologist, and nurse can create a collaborative environment where the transition into mental health care can be facilitated [34]. A mental health-care provider (psychiatrist or psychologist) should discuss with the

patient the diagnosis of PNES as it relates to stressful factors and psychiatric comorbidities.

Transition to mental health care

Psychiatric assessment

A psychiatric evaluation is recommended early after diagnosis is made [27•]. Ideally, the assessment should be carried out while the patient is still in the SMU [35]. However, this is not a routine practice at more than half of epilepsy centers, and it was suggested that inpatient psychiatric consult may not be needed in all cases [36].

The mental health professional performing the evaluation should have some experience and confidence in the diagnosis of PNES [27•]. The severity and complexity of the psychiatric comorbidities in the majority of patients with PNES may require the use of pharmacological therapy [35]. If the initial evaluation was not initially done by a psychiatrist, other providers have the obligation to recognize the need for pharmacological therapy and referral to psychiatry [27•].

Who should be involved?

The team involved in the patient's long-term care may involve neurologists, psychiatrists, psychologists, neuropsychologists, and social workers. Communication with the primary care physician is essential to ensure proper coordination of care. The composition of the team should be tailored according to the patient's individual needs.

Neurologist's role

The involvement of the neurologist does not end with the establishment of the diagnosis of PNES [35]. We recommend at least one follow-up clinic visit with the neurologist following the presentation of diagnosis in the SMU. Both the neurologist and primary care physician should be involved in coordinating care with mental health providers. Premature discharge from neurological care may contribute to patients' resistance to accept the diagnosis [37]. We agree with the recommendation [35] that neurological supervision should be discontinued depending on the following factors: (a) the understanding and acceptance of the diagnosis by the patient and family; (b) the presence of co-existing epilepsy; (c) the timing of complete withdrawal of AEDs; (d) the existence of comorbid neurological conditions; and (e) a joint decision by the patient, neurologist, mental health providers, and primary care provider that neurological supervision is no longer needed. It should be noted that these are recommendations based on anecdotal experience; evidence-based guidelines are lacking.

Cognitive behavioral therapy

What is CBT?

Cognitive behavioral therapy (CBT) is the treatment that has most reliable evidence for efficacy in PNES thus far. It is the only treatment that was studied in pilot randomized controlled trials (RCT). CBT is based on the hypothesis that

patients use dysfunctional thought processes (such as generalizations, selective focusing, and "catastrophizing") which can result in misperception of reality. CBT attempts to help the patient identify these distortions and decrease anxiety and depression [38].

LaFrance's CBT model for treatment of PNES is based on the assumption that life experiences and trauma in PNES patients lead to maladaptive core beliefs resulting in cognitive distortions and somatic symptoms. [27•] The 12 treatment sessions involved contextualization of patient's environment; identifying mood and thoughts; training in healthy communication, support seeking and goal setting; understanding seizures and neuro-active medications; identifying auras; conducting functional behavioral analysis; learning relaxation techniques; examining external stressors/triggers; promoting health and wellness; and preparing for life after completing the intervention [27•].

The CBT method described by Goldstein et al. [39] is based on a fear escape-avoidance model. PNES are viewed as dissociative responses to stimuli or cues associated with extremely distressing or life-threatening experiences and which had produced unbearable feelings of fear and distress earlier in life. Treatment is also delivered over 12 sessions, utilizing seizure-directed techniques, attention refocusing, relaxation, dealing with avoidance behaviors, negative cognitions, and other factors contributing to development of PNES and the involvement of family members [27•].

Pilot RCTs

The first pilot RCT study was published by Goldstein et al. [18]. Sixty-six PNES patients were randomized to CBT and standard medical treatment (SMC) or SMC alone. SMC consisted of clinic visits with a psychiatrist that are mainly supportive in nature, focusing on education about PNES and tapering of antiepileptic drugs. The active group was offered up to 12 weekly 1-hour sessions with CBT-trained nurse therapist. Following treatment, patients had follow-up sessions at 1, 3, and 6 months. Seizure frequency was significantly lower for the CBT group than the SMC group at the end of treatment (p=0.002). At the end of the follow-up period, the CBT group was significantly more likely to have resulted in three consecutive months of seizure freedom. However, the difference in seizure frequency between the CBT and SMC groups at the end of the follow-up period was not statistically significant.

The pilot multicenter RCT by LaFrance et al. [20••] provides the highest quality evidence for the efficacy of CBT in treatment of PNES. It randomized 38 patients to 4 treatment arms: CBT only, CBT with medication (sertraline), medication only, and treatment as usual (TAU). CBT was administered in 12 weekly 1-hour sessions. Significant reduction in seizure frequency was seen at 16-week follow-up in the CBT group (51.4 %) and the CBT with medication group (59.3 %). There was also improvement in psychiatric comorbidity and measures of functioning and quality of life. The medication only and TAU groups did not show significant reduction in seizures. The main limitations of this pilot study is the sample size and length of the follow-up period. It is yet to be clarified (in a larger sample) whether CBT with medication is superior to CBT alone.

Other studies

Other small open-label studies have also supported the use of CBT to treat PNES [40, 39, 41, 42].

Psychodynamic therapy

Introduction

According to the psychodynamic theory, symptoms and behaviors are presumed to be external manifestations of internal processes, with childhood experiences being crucial to the development of persistent maladaptive behavioral patterns. Psychodynamic therapy focuses on the role of dissociation, defined as a "failure to integrate aspects of perception, memory, identity and consciousness" [2].

Clinical evidence

One of the first psychodynamic therapy models used to treat PNES was that described by Kalogjera-Sackellares. In this model, traumatic experiences are considered a key feature [43]. Therefore, the goal of therapy is to recognize the role of trauma and the response to trauma in developing maladaptive behavior patterns [27•]. No data on the outcomes of this therapy model has been published.

A brief augmented psychodynamic interpersonal therapy (PIT) was developed by Howlett and Reuber [44]. It was based on the assumption that the patient's problems arise from disturbances in personal relationships, with dysfunctional interpersonal patterns developing early in life. It includes an encouraging and supportive approach from the therapist to help the patient change unhelpful interpersonal patterns. The therapy is delivered over 20 sessions to change illness perceptions, achieve symptom control, improve emotional processing, increase independence, encourage self-care, and process trauma. Long-term follow-up (average 42 months) of 47 patients who underwent PIT showed 25.5 % became seizure-free and 40 % achieved more than 50 % reduction in seizure frequency [45]. A significant decrease in healthcare utilization was also reported. To date, there have been no randomized controlled trials evaluating the role of psychodynamic therapy in PNES.

Group therapies

An open-label trial of group therapy with emphasis on psychoeducation was reported [46]. Ten patients participated in weekly sessions over 10 weeks. Two patients experienced decline in seizure frequency, one reported an increase, and four had no change. There was, however, significant decrease in posttraumatic and dissociative symptoms.

Another uncontrolled trial [47] reported outcomes of psychodynamically oriented group therapy. Six of 7 patients who completed the 32 weekly sessions experienced a decrease in frequency of PNES.

Efficacy of a 6-month group psychotherapy program was also studied [48]. A reduction in seizure frequency was noted in six out of nine subjects.

More recently, one controlled study evaluated the efficacy of monthly psychoeducation sessions started early after diagnosis and provided by the

team who confirmed and communicated the diagnosis of PNES [49]. Patients were randomized to participation in the program or routine outpatient follow-up visits. No significant difference in seizure frequency was seen between the two groups, but patients who received psychoeducation showed significant improvement in work and social adjustment scores (p=0.038) and were less likely to use emergency services or be hospitalized again after discharge from the SMU (p=0.0184).

Other psychological treatments

Hypnosis

The use of hypnosis for PNES has been suggested [50]. Two RCTs evaluated the efficacy of hypnotherapy in the treatment of conversion disorder of the motor type [51, 52]. One study [51] included 49 patients including 7 who were described as having "paroxysmal myoclonic outbursts" and 8 patients who had "seizures or convulsions." Both active and control groups followed a group psychotherapy program. Hypnosis was used as adjunctive therapy in the active group. At 8-month follow-up, there was a reduction in conversion symptoms in both groups, but there was no additional benefit of hypnosis. Detailed data on the outcome in PNES patients was not provided.

Paradoxical intention therapy

One RCT [53] evaluated the efficacy of paradoxical intention therapy (PIT) in PNES. Thirty patients were randomized to PIT or treatment with diazepam. In the PIT group, patients were asked to imagine seizure-provoking situations. The PIT group had greater improvement in anxiety scores (p<0.015) and conversion symptoms (p=0.034). However, in this study, seizure frequency measures were not considered a primary outcome and were not reported.

A recent Cochrane review provides an excellent summary of published studies that evaluated the efficacy of different types of psychological therapy [54].

Pharmacological treatment

Pharmacological therapy is often indicated for the treatment of comorbid psychiatric conditions accompanying PNES. There is currently no high-quality evidence to support the use of antidepressants in treatment of PNES. However, some evidence for potential efficacy of serotonin reuptake inhibitor sertraline comes from two studies [20••, 19]. One study [19] randomized 38 patients to flexible-dose sertraline or placebo. PNES frequency declined by 45 % over a 12-week treatment course, while the control group experienced 8 % increase in seizures. However, the change in seizure frequency was not statistically different between the sertraline and placebo groups (RR, p=0.29). There was also no significant difference in secondary outcomes related to psychological well-being. The second study was the previously referenced pilot RCT France et al. [20••], which had four treatment arms including two pharmacological treatment ones: CBT with sertraline and sertraline alone. There was a trend of seizure reduction of 26.5 % in the sertraline group but this was not statistically significant (p=0.8). It was also shown that secondary outcome measures improved in CBT-only arm compared to CBT with sertraline. A larger sample size will hopefully better clarify the role of this

selective serotonin-reuptake inhibitor (SSRI) in the management of PNES.

An open-label trial evaluated the efficacy of venlafaxine in patients with PNES and comorbid depression and/or anxiety disorder. Nineteen patients were treated with venlafaxine 75 mg/day for 5 months. At the end of this period, >50 % seizures reduction was seen in 88.2 % of subjects. There was also improvement in measures of secondary measures [55].

Pediatric considerations

PNES are not uncommon in children and adolescents, where they are often associated with school-related difficulties and significant psychopathology [56]. Precipitating factors might differ in the pediatric population, and this should be considered when formulating a treatment intervention. School-related problems and interpersonal/family problems are commonly reported underlying stressors [56]. Physical and sexual abuse are believed to be common, but one recent study found no statistical difference in frequency of abuse between children with PNES and controls [57]. Chronic medical illness was found to be common compared to controls [57]. Unfortunately, the literature on management of pediatric PNES is sparse compared with adult studies [58]. Irwin et al [59] suggested prompt intervention from a child mental health professional with initial focus on exploring precipitating factors and "living safely" with seizures. The management should aim at helping the family and child develop a better understanding of PNES and to control precipitating factors [59]. The use of stress management techniques, including relaxation therapy and cognitive approaches, has been suggested [59]. The efficacy of CBT and other psychotherapeutic interventions in pediatric PNES has not been thoroughly evaluated. Further research in this population is needed.

Compliance with Ethics Guidelines

Conflict of Interest

M. Ayman Haykal and Brien Smith declare no conflicts of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by the authors.

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