Abstract

Psychogenic nonepileptic seizures (PNES) superficially resemble epileptic seizures, but are not associated with ictal electrical discharges in the brain. PNES constitute one of the most important differential diagnoses of epilepsy. However, despite the fact they have been recognized as a distinctive clinical phenomenon for centuries and that access to video/EEG monitoring has allowed clinicians to make near-certain diagnoses for several decades, our understanding of the etiology, underlying mental processes, and, subsequently, subdifferentiation, nosology, and treatment remains seriously deficient. Emphasizing the clinical picture throughout, the first part of this article is intended to “look and look again” at what we know about the epidemiology, semiology, clinical context, treatment, and prognosis of PNES. The second part is dedicated to the questions that remain to be answered. It argues that the most important reason our understanding of PNES remains limited is the focus on the visible manifestations of PNES or the seizures themselves. In contrast, subjective seizure manifestations and the biographic or clinical context in which they occur have been relatively neglected.

Keywords: Nonepileptic seizures; Dissociative disorder; Conversion disorder; Anxiety disorder; Phenomenology

1. Introduction

Based on our current understanding, psychogenic nonepileptic seizures (PNES) are episodes of paroxysmal impairment of self-control associated with a range of motor, sensory, and mental manifestations, which represent an experiential or behavioral response to emotional or social distress. The overwhelming majority of PNES are considered as beyond patients’ voluntary control [1,2]. However, it is recognized that PNES occur in malingering and factitious disorders [3], and that, short of confession, there are no definitive tests to identify simulated seizures [4].

I have previously contributed to richly referenced review articles that focused on the diagnostic process and the psychological treatment of PNES [5,6]. These topics have also been very capably reviewed by others [7–11]. I refer to our previous reviews when they contain information discussed in less detail here. The emphasis on the clinical picture means that theoretical models are relatively neglected in this manuscript. The continuing controversy surrounding the labeling and nosology of PNES is side-stepped completely [12,13]. In as much as this article is about seizures that neurologists have diagnosed as “nonepileptic” and that they suspect as having a “nonorganic” or “psychogenic” cause, PNES seems an appropriate term for the condition that is being discussed.

2. What we know about PNES

2.1. Epidemiology

2.1.1. Prevalence

The incidence of PNES has been reported as 1.4 per 100,000 [14], or 3 per 100,000 per year [15]. However, given the setting of these studies in neurology centers and the fact that only video/EEG-proven cases were counted, this is likely to be an underestimate. An audit of 659 consecutive new patients in a first-seizure clinic reported that 12% had a
clinical diagnosis of PNES (which was not confirmed with video/EEG in all cases) [16]. The authors of another study, which reportedly captured all patients with a blackout first presenting to a neurologist, emergency room, or primary care physician, thought that 57.4% had epilepsy, 22.3% had fainted, and 18.0% had PNES [17]. On this uncertain basis, the prevalence of PNES has been estimated as 2 to 33 per 100,000 [18]. PNES may be identified more commonly in specialized clinical settings. For instance, 24% of patients with refractory seizures referred to a typical U.S. epilepsy center for video/EEG monitoring [19] and up to 50% of patients with refractory “status” have been diagnosed with PNES rather than epilepsy [20]. In most patients, there is a delay of several years between the manifestation of PNES and the correct diagnosis. Two studies documented mean diagnostic delays of 7 to 16 years. Three quarters of patients with PNES (and no additional epilepsy) were treated with antiepileptic drugs initially [21,22].

PNES are not unique to diversified health systems in developed countries. Although there may be important differences in etiology, PNES have also been described in Argentina and rural India [23–25].

2.1.2. Gender
Lesser examined the sex distribution in 21 studies and found descriptions of 734 women and 250 men with PNES [26]. A number of studies suggest that men and women develop PNES for different reasons. Two studies found that sexual abuse is more commonly a factor in women, and work-related problems, in men [27,28]. However, a posttraumatic etiology may still be important in selected male patient groups such as veterans [29].

2.1.3. Age
PNES typically start in the second or third decade of life [30–32], although seizure onset below age 4 and above 70 has been described [33,34]. The age distribution in Fig. 1 is based on a group of patients diagnosed with PNES in Bonn, Germany [21]. Several studies indicate that seizures in children and younger adults are associated with a better prognosis [35–39]. However, older patients may be better able to engage in a psychotherapeutic process [40]. PNES with onset at an older age are equally common in men and women, less likely linked to sexual trauma, and more likely related to health-related traumatic experience [41,42].

2.2. Semiology

2.2.1. Behavioral seizure manifestations
Studies using cluster analysis suggest that several types of PNES can be differentiated [43]. The commonest semiology involves excessive movement of limbs, trunk, and head [30,31,39,43,44]. Seizures with stiffening and tremor [30,43,44] or seizures with atonia [39,45–47] are less frequent in most series. PNES are diagnosed most commonly in patients whose attacks involve impairment of consciousness [30,31,39,44]. However, the diagnosis has also been applied to purely motor, sensory, or experiential attacks akin to simple partial seizures [26].

Although PNES can start abruptly, seizure onset is more commonly gradual than in epilepsy [31,33,47,48]. In convulsive PNES, shaking is often asynchronous and asymmetrical [30,44]. Phases of vigorous and less vigorous motor activity can come and go [46]. Whereas tonic–clonic epileptic seizures are characterized by a gradual decline in the frequency of limb jerks during the course of the seizure, muscle twitches in PNES tend to vary in terms of amplitude but not frequency [49]. Pelvic thrusting occurs in epileptic seizures, but is seen more commonly in PNES [30,50–54]. Ophisthotonus (arc en cercle) may be seen [44,52–55]. The head may shake from side to side [30,56]. Eyes and mouth are much more likely to be closed than in epileptic seizures [57,58]. Ictal crying or verbal communication may be observed [30,59,60].

Eye opening may be resisted [30,44,46,47,61]. The pupillary light response is preserved [61]. Purposeful movements or signs of reactivity may be observed while patients appear unconscious [31,44]. In an ictal assessment procedure in individuals with seizure-related impairment of consciousness, 48% of patients with PNES but only 18% of patients with complex partial seizures were able to follow simple commands [62].

PNES typically last longer than epileptic seizures [47,63–65]. One study found that generalized tonic–clonic seizures lasted from 50 to 92 seconds, whereas PNES lasted 20 to 805 seconds. Many PNES went on for more than 2 minutes [30]. Prolonged PNES treated as status epilepticus (pseudo-status, PNES status) occur in about one-third of patients with PNES, and more than one-quarter of patients diagnosed with PNES at an epilepsy center have received intensive care treatment for presumed status epilepticus at least once [66].
Postictal recovery may be unexpectedly rapid or slow and is less commonly associated with temporary neurological deficits than epileptic seizures [47, 64, 65].

### 2.2.2. Autonomic/systemic seizure manifestations

More than one-quarter of patients with PNES give a history of ictal incontinence of urine; fecal incontinence is also reported [66]. Sinus tachycardia is common, but is more gradual in onset, less marked, and less persistent postictically than in epileptic seizures [67, 68]. In PNES, tachycardia is more likely if seizures are convulsive; in epilepsy, it is also a common feature of nonconvulsive attacks [67, 69]. Cyanosis is unusual [70]. Although stress hormone increases are much commoner in the context of epileptic seizures [71], they have been reported in PNES [72]. Historical accounts describe increases in body temperature in epileptic seizures but not in PNES [73]. PNES (unexplained by heart rate or blood pressure changes) have been reported during tilt-table examinations [45, 74]. As far as this evidence goes, these autonomic changes seem to be in line with what might be expected on the basis of the visible seizure manifestations.

### 2.2.3. Subjective seizure manifestations

Many patients describe physical symptoms of panic or hyperventilation during their seizures without feeling anxious [75–77]. It has been suggested that panic symptoms are more common in adolescents with PNES than in adults [78]. Even in the absence of panic symptoms, most patients experience their seizures as confusing and beyond their control [79]. At the same time, patients with epilepsy are more likely to conceptualize their seizure as a hostile agent acting of its own volition [80–82].

Typically, PNES impair recall for ictal experiences to a lesser extent than epileptic seizures. One study demonstrated that the recall for events that took place during a seizure under hypnosis had a sensitivity of 100% and specificity of 85% in the differentiation of PNES and epileptic seizures [83]. Even without hypnosis, at least two memory items of an ictal neuropsychological testing procedure were recalled by 63% of patients immediately after a PNES, but by only 4% of patients who had had a complex partial seizure [62].

### 2.3. Clinical context

#### 2.3.1. Multifactorial etiology

Only a small minority of patients (perhaps 1 in 20) seem to have seizures without any other psychiatric symptoms, and in the absence of personal or social circumstances that could explain a dissociative or conversion process [84, 85]. A range of interacting etiologic factors are observed with such regularity that one would be somewhat concerned about making the diagnosis of PNES in their absence. However, patients may resist the idea of a link between psychosocial problems and seizures, or their self-representation may lack coherence, and it may be difficult to get a full idea of their biographic or social background and emotional symptomatology.

#### 2.3.2. Predisposing factors

##### 2.3.2.1. Trauma

Around 90% of patients with PNES report significant traumatic experiences in their past [84, 86–89]. A trauma history may be associated more closely with PNES than with other functional neurological symptoms [84]. However, trauma appears to be a less important etiologic factor in important subgroups of patients, for instance, men, individuals with a seizure onset in late adulthood, or individuals with learning difficulties [27, 41, 42, 90].

The most intensively studied form of trauma is childhood abuse. In larger patient series, 32.4–88.0% of patients with PNES, but only 8.6–37.0% of patients with epilepsy, claimed to have been abused sexually or physically in childhood [77, 89, 91–95]. In the largest study, the difference between the two patient groups was significant for the prevalence of both a history of sexual abuse (24.0% vs 7.1%) and a history of physical abuse (15.5% vs 2.9%) in childhood [94], suggesting that this particular form of trauma is an important predisposing factor for PNES [96].

##### 2.3.2.2. Family dysfunction

It has been argued that PNES are not so much a consequence of childhood abuse, but that both PNES and childhood abuse are the result of family dysfunction [97]. Patients with PNES are also more likely than patients with epilepsy to report a family history of psychiatric disorder or epilepsy [98, 99]. Three studies demonstrated that patients with PNES experience their families as less supportive and communicative than do patients with epilepsy [100–102]. Two studies reported a greater number of conflicts within PNES than epilepsy families [92, 101]. Another study revealed that the families of patients with PNES are characterized by high levels of criticism and stronger somatization tendencies [103].

##### 2.3.2.3. Personality

Studies using the Minnesota Multiphasic Personality Inventory (MMPI) show that PNES are not associated with a single personality profile [104]. However, many patients have elevations on the axes hysteria, hypochondriasis, and schizophrenia. Unfortunately, the relationship of the MMPI to modern concepts of personality or personality pathology is a little unclear, because it also measures affective, somatization, and other psychopathologic disorders. However, evidence for personality pathology has also been gathered using other means. Clinically, 25–67% of patients with PNES fulfill the DSM-III or DSM-IV criteria for personality disorder [99, 100, 105–112]. Personality characteristics that may be found in association with PNES have also been described as ego-structural deficits in psychodynamic terms [113]. Psychometric tests other than the MMPI reveal a range of abnormal personality profiles in the majority of patients [106, 114, 115]. In most studies, the largest group of patients with PNES have features of borderline personality disorder [116]. We found evidence of a borderline-like personality profile in 40% of...
patients with PNES [115]. A further large group had a personality profile characterized by an unusually tight control of emotional regulation [115]. The severity of the PNES disorder and long-term outcome correlate with the degree of abnormality of the personality profile [39,66,108,117].

2.3.2.4. Psychopathology. PNES are associated with high levels of psychiatric comorbidity. Patients most commonly fulfill the diagnostic criteria for other somatoform (22–84%), other dissociative (22–91%), posttraumatic stress (35–49%), depressive (57–85%), or anxiety disorders (11–50%) [89,107–109,118–120]. The degree of psychopathology correlates positively with the severity of the PNES disorder [121].

2.3.2.5. Illness perceptions and coping styles. What characterizes patients with PNES more than the presence of psychopathology is their difficulty in recognizing this pathology as a relevant factor. They are less likely than patients with epilepsy to endorse stress or emotional factors as a possible cause of seizures [100]. In fact, more than 90% of patients score as alexithymic on a self-report instrument [122]. Perhaps not surprisingly, patients with PNES report a more external locus of control than patients with epilepsy [123,124]. In keeping with this, they have a stronger tendency to use escape or avoidance to deal with problems they encounter than do patients with epilepsy [124]. Two studies found that patients with PNES experience their lives as more stressful than patients with epilepsy, but that they also use less effective coping mechanisms [125,126]. Several studies have documented higher levels of anger or hostility in patients with PNES [79,118,127,128].

2.3.2.6. Cognitive factors. Many studies show that patients with PNES tend to perform below expectation in neuropsychological tests. In our own study, 60.6% of all patients with PNES and (no additional epilepsy) performed at least 1.5 SD below norm populations in at least one domain of testing [129]. In another study, 63% of patients had a Halstead Impairment Index in the impaired range [130]. Many studies comparing performance in patients with PNES with that of patients with epilepsy (i.e., a neurologic brain disorder) found no differences between the two groups when corrections were made for education and age [131–135]. In some studies, patients with PNES actually did worse than patients with epilepsy [136]. We compared patients with PNES and epilepsy with patients with epilepsy alone and found that global neuropsychological deficits and low IQ were commoner in the PNES group [137]. Others have described learning difficulties as a possible risk factor for PNES [32,90,111,138]. Most researchers have failed to identify a characteristic pattern of deficits in patients with PNES [104]; one study described motor deficits as an indication of frontal lobe dysfunction [139].

It has been suggested that some of these findings could be related to variable effort (or malingering) [133,140,141]. In fact, one study showed that patients with PNES will do better on neuropsychological tests than patients with epilepsy if the subgroup who fail an effort test are excluded [142]. However, another study in nonlitigant patients with neurologically unexplained symptoms (including PNES) did not find much evidence of malingering, and documented variable effort in only 11% of participants [143].

2.3.2.7. Neurobiological factors. A number of studies have demonstrated an unexpectedly high prevalence of abnormal brain imaging or nonspecific EEG abnormalities [129,144,145]. Right-sided hemispheric abnormalities predominated in one series [146], but not in another [129]. Although abnormal findings are much commoner in patients with epilepsy as a group, we found that 22.3% of our patients with PNES (and no additional epileptic seizures) had interictal epileptiform EEG abnormalities, MRI lesions, or neuropsychological deficits. Given that not all patients had been fully investigated, the true prevalence of such abnormalities would have been even higher [129]. In a blinded comparative study, we found nonspecific EEG changes in 18% of patients with PNES (and no epilepsy) and 10% of age-matched healthy controls [144].

Many patients with PNES report antecedent mild head injuries [130,147,148]. Although only a minority of patients with PNES have a history of severe head injury, up to one-third of individuals whose seizures are investigated with video/EEG after moderate to severe brain injuries turn out to have PNES rather than epilepsy [149,150].

The percentage of patients with concurrent epilepsy has varied from 3.6 to 58% in different series [137], but it is generally accepted that the prevalence of epilepsy is greater among patients with PNES than in the general population [151]. In our own series, the clinical history suggested additional epilepsy in 119 of 329 patients with PNES (36.2%). Of these patients, 90 (27.4%) also had interictal EEG changes, and additional epileptic seizures with ictal EEG changes had been recorded in 58 (17.6%) [137]. Notably, PNES are always preceded by epilepsy [137]. PNES can stop after epileptic seizures have been fully controlled [152]. On the other hand, PNES may first manifest after epilepsy or other brain surgery [153–155], or when epileptic seizures have been controlled by antiepileptic drugs [156].

2.3.3. Precipitating factors and seizure triggers
2.3.3.1. Stress and dilemmas. Many patients with PNES experience stress or unresolvable dilemmas in their home environment. Often the problems center around sexual or physical abuse [28,95,98,125]. PNES can manifest in temporal relation to traumatic life events [88,89,91,157]. Factors that have been described as precipitating PNES include rape [89,158], injury [109], “symbolic” traumatic experience in adulthood after childhood abuse [89,98], surgical procedures, giving birth, and undergoing anaesthetics [159–163], death of or separation from family members or friends [164], job loss [28], road
traffic and other accidents [28], earthquakes [82], relationship difficulties [28], and legal action [165].

One study in which patients were interviewed soon after seizures had first started showed that (while patients with PNES reported more negative life events overall than patients with epilepsy), there was no higher incidence of such events within the 3 months before seizure manifestation [100]. The authors of one descriptive study of PNES and life events were able to identify a precipitating event in all but 9% of patients. However, in 76% of patients, the event was significant only in the context of a history of other trauma or previous or ongoing conflict [28]. Psychodynamic explanations for the common delay between a traumatic event and the manifestation of PNES (stressing the cumulative effect of negative life events) have been elaborated since Freud first stated: “No hysterical symptom is ever caused by a real experience alone. The associative triggering of earlier memories always makes a contribution to the causation of the symptom” [89,113,166].

2.3.3.2. Triggers for seizure recurrence. Recurrent seizures can be triggered by much less significant events or stimuli, for instance, visits to the doctor [31,33,47,48] and sudden noise or flashing light [47,52]. In around two-thirds of patients, PNES can be provoked during (video/) EEG monitoring by a range of suggestion or provocation techniques [167–171].

PNES can also arise directly from physiologically explained mental states: it has been demonstrated that (epileptic) simple partial seizures can trigger PNES [172–174]. PNES have also been reported from EEG-documented sleep [175], although PNES from “pseudosleep” (with EEG appearance of wakefulness) are much more common [176,177].

2.3.4. Perpetuating factors
2.3.4.1. Health care contacts. Like other patients with medically unexplained symptoms, most patients with PNES are frequent users of health care services [178–180]. Many have other medically unexplained physical symptoms including chronic pain, fibromyalgia, irritable bowel syndrome, and menstrual problems [181–183]. Each health care contact can exacerbate the problem [116]. Frequent health care contacts mean that some patients are being repetitively investigated and hear different explanations from the many doctors they encounter [184].

2.3.4.2. Social/financial illness gain. We found evidence of isolation, family dysfunction, or unusual life pressures in 54% of patients with functional neurological symptoms (most of whom had PNES) [84]. However, it is also possible that financial or social benefits related to the seizures play a perpetuating role, especially in more chronic cases [1,2]. For instance, patients may acquire a “sick role” and offload unpleasant responsibilities onto others [185]. A number of studies have shown how commonly patients with PNES rely on the support of others. For instance, 69% of 84 patients with PNES had a job when their seizures first started. At the time they underwent video/EEG monitoring, only 20% of these patients still worked [179]. Our own study conducted in Germany demonstrated that at a mean of 4.1 years after diagnosis (range: 1–10 years), 41.4% of patients had retired on health grounds and another 12.4% were unemployed. The mean age of these patients was 38.6 years [39]. Two studies suggested that patients with PNES are more likely to receive health-related state benefits than patients with similarly disabling epileptic seizures [136,186].

2.3.5. Diagnosis
2.3.5.1. History
2.3.5.1.1. Factual features. One study showed that patients reporting a seizure warning with a choking sensation or palpitations were three times more likely to have PNES than epilepsy [17]. On the other hand, it has been shown that ictal injury, tongue biting, incontinence, pelvic thrusting, and nocturnal seizures, which are often used by doctors to distinguish between epilepsy and PNES, are only of limited differentiating value [50,176,187]. This may explain the low specificity of a differentiation of seizures into epileptic and nonepileptic based on facts: one study, in which two epileptologists, who were unaware of any other clinical information, were asked to rate detailed written seizure descriptions from patients with temporal lobe epilepsy or nonepileptic seizures, found that the sensitivity of this approach for the detection of epileptic seizures was 96% although the specificity was only 50% [188].

2.3.5.1.2. Background. The background history may contribute more to the differentiation of epilepsy and PNES than the seizure description. A history of other physical symptoms or illnesses [121,181,189,190] or operations without abnormal histopathological findings (such as laparoscopies, appendectomies, hysterectomies, or cholecystectomies) [160,183,191] may be particularly strong indicators, although the predictive value of this observation is uncertain. One report suggested that patients with PNES were nine times more likely than those with epilepsy to have received psychiatric treatment [17].

2.3.5.1.3. Interactional features. A number of recent studies have demonstrated that patients with PNES differ from those with epilepsy in terms of their communication behavior [192]. Using a linguistic approach inspired by Conversation Analysis, a number of differentiating interactive, topical, and linguistic features have been described, which can best be elicited if the doctor adopts a receptive stance, avoids early interruption, and begins the encounter with an open question (such as “What was your expectation when you came to see me?”). Table 1 provides an overview of discriminating linguistic features [192]. The described features may not only help doctors to distinguish better between epileptic and nonepileptic seizures; they may also reflect the patient’s underlying psychopathology and coping resources in terms of emotional reactivity, biographic coherence, and ego organization. An attentive
listener may pick up relevant psychodynamic indicators such as emotional instability, tendency toward projection, and a lack of distinct boundaries between self and others that can inform the choice of the most appropriate therapy.

2.3.5.2. Tests. Several reviews on the usefulness and limitations of tests in the diagnosis of PNES have been published recently. Cuthill and Espie found that no procedure (seizure induction, MMPI assessment, postictal prolactin, SPECT, establishment of pre-ictal pseudosleep, and ictal/postictal characteristics) had sufficiently high sensitivity and specificity and adequately replicated findings. High levels of specificity were more commonly reported than high levels of sensitivity, suggesting that procedures were generally better at excluding an alternative diagnosis [7]. Cragar et al. also concluded that none of the diagnostic methods they reviewed was likely to replace video/EEG monitoring as the definitive investigation [8].

2.3.5.3. Video/EEG monitoring. When undertaken as a brief outpatient test, video/EEG monitoring captures PNES in about 50% of patients [167]. The likelihood of a seizure rises to at least two-thirds if photostimulation and hyperventilation are combined with verbal suggestion [193–195]. The seizure yield can be increased to more than 75% with stronger suggestion methods such as placebo injections [5]. PNES can also be induced by hypnosis [171,196].

2.3.6. Treatment

2.3.6.1. Dealing with seizures. Historical references suggest that “hysterical seizures” were reliably stopped by injections of apomorphine potent enough to cause vomiting within minutes or by closing the patient’s mouth and nose for 20 to 30 seconds. The compression of different abdominal organs (especially the ovaries) favored by Charcot failed to work in British patients [73]. PNES can be terminated by placebo (e.g., saline injections) in some patients [197]. A more acceptable approach, which is likely to increase the patient’s self-control rather than strengthen dependence on others, involves the removal of individuals increasing the patient’s distress from the scene of the seizure and calm conversation [198]. Patients who experience seizure warnings can often be shown how to control seizures by using external focusing or abdominal breathing techniques [6].

2.3.6.2. Communicating the diagnosis. The successful communication of the diagnosis is a significant challenge [199]. Most patients have a clearly dualistic concept of illness [79]. This means that patients may interpret the statement that there is “no physical cause” as meaning that seizures must be “all in the mind”. This may be unacceptable and is unlikely to match the patients’ subjective illness experience. Many patients are left confused or angry when the neurologist has explained the diagnosis to them [128]. On the other hand, the successful communication of the diagnosis can stop seizures in at least 10% of patients [200]. It also has the potential to change patients’ health care utilization behavior significantly, leading to health care cost reductions over the 6 months after diagnosis with video/EEG [180]. The message that the seizures are not related to a brain disorder may be enhanced by the withdrawal of AEDs, which was associated with the emergence of different (epileptic) seizures in only 3 of 64 patients in one prospective study [201].

2.3.6.3. Specific treatment. The treatment of PNES has been reviewed by several groups of authors recently [6,9–11]. Many describe single cases or small series; few were adequately powered or included randomization procedures or credible control treatments. Only one recent study used...
a pharmacological intervention. In this study, a psychological intervention delivered during an inpatient stay (paradoxical intention, PI) was compared with the effectiveness of outpatient treatment with diazepam (5–15 mg/day). PI treatment proved more effective overall in terms of anxiety reduction and symptom control, although 9 of 15 patients in the diazepam group were also characterized as “responders” [202]. The use of antidepressant drugs has not been studied in patients with PNES, although they can be effective in patients with other medically unexplained symptoms [203].

All other studies use psychological treatments delivered on an in- or outpatient basis to individuals or patient groups [6]. The range of approaches described includes cognitive behavioral therapy (CBT), variants of psychodynamic interpersonal therapy, operant conditioning, eye movement desensitization and reprocessing, biofeedback, hypnotherapy, family therapy, and multidisciplinary inpatient management [6,9–11].

The best study so far described a prospective, open treatment trial with 12 sessions of CBT targeting fear and avoidance. Treatment was associated with significant improvements in seizure frequency, psychosocial functioning, anxiety, and depression [204]. Our own (uncontrolled) pilot study of an individualized brief integrative therapy derived from a psychodynamic interpersonal intervention showed that at least one patient-centered measure (SF-36, CORE [Clinical Outcomes for Routine Evaluation] outcome measure, or somatic symptom count) improved significantly in one-half of all patients [205].

2.3.7. Prognosis

One prospective study reporting outcome 6 months after diagnosis found that PNES had stopped in 29% of patients. A second demonstrated that 42% of patients had become seizure-free 1 year after diagnosis [206]. Another showed that 50% of patients were free of seizures after 2 years [207]. However, in keeping with the prognosis in other somatoform disorders [208,209], most longer-term studies suggest that seizure and social outcome is poor [5]. The largest study revealed that at a mean of 11 years after seizure onset, two-thirds of patients continued to have seizures, and more than half were dependent on social security. Only 16% of patients had a good outcome (economically active and seizure-free), although at least 42% had had some therapeutic intervention [39].

A number of studies describing PNES outcome have identified factors that may affect the prognosis: the rapid recognition of PNES, a younger age at seizure onset or diagnosis, higher level of intelligence, and higher socioeconomic class have been associated with better prognosis. Outcome was worse in patients with more dramatic PNES (tonic-clonic-like seizures, history of ictal incontinence, tongue biting, or PNES status), a wider range of physical symptoms, greater dissociative tendencies, and more significant personality pathology [5].

3. What we don’t know about PNES

3.1. Epidemiology

We know much more about the frequency with which neurologists diagnose PNES in specialist settings than about the incidence or prevalence of nonepileptic seizure-like expressions of psychological or social distress in the general population. However, one cannot assume that PNES always present as refractory seizure disorders likely to trigger referral to an epilepsy specialist. There may be a group of patients with PNES with much less troublesome seizure disorders. It is also possible that some patients’ seizures are so obviously related to an upsetting event that they do not seek the advice of a doctor. In view of the indistinct margins between the manifestations of panic or hyperventilation attacks and PNES or between PNES and syncope [45,75,76,78], it is quite likely that such patients exist. If they do, our current understanding about the etiology and prognosis of PNES disorders could be seriously flawed.

Along similar lines, our understanding of the sociological or health system contribution to PNES disorders is very limited. Historical or anthropological accounts of PNES-like events are typically used to argue that PNES are a “real” disorder that has existed “always and everywhere” [210]. However, closer inspection reveals very important differences between the significance placed on seizures, their management, and consequences, which, by their nature and number, are likely to outweigh the superficial similarities.

3.2. Semiology

There is a marked contrast between our knowledge of the visible manifestations of PNES and patients’ subjective seizure experience. This is surprising. Given that PNES are thought to result from a psychological or mental process, one might have expected researchers to have focused especially on subjective or mental states rather than patients’ behavior. What is more, no serious attempt has been made to investigate the link between particular ictal mental states and certain motor or autonomic seizure manifestations. Thus, our understanding of the meaning or clinical significance of the notable interindividual differences between seizure manifestations remains very limited.

We also know little about the biographical or interactional role of PNES. A single case study of a patient with panic disorder has shown how revealing a detailed sociolinguistic analysis of patients’ interaction with others in their home environment can be [211]. No equivalent work exists for patients with PNES.

3.3. Clinical context

Many factors that could predispose to or precipitate PNES have been suggested, but our knowledge of the prevalence of these factors in the general population is limited.
This means that we are still not certain about the real significance of these factors for PNES. Even when a factor has been identified (e.g., female gender), it is often not specific. What is it about being female that increases the risk of developing PNES? Our knowledge of factors conferring resilience is largely limited to psychodynamic theory.

Another important issue, which we do not understand, is how different constitutional, developmental, environmental, and social factors interact. Of course, there are legitimate reasons for this. Many of the proposed factors are difficult to define or objectify. Their number is so great that it is difficult to capture them adequately. The relationship of PNES to “comorbid” psychiatric symptoms illustrates this complexity. In some patients, PNES seem intimately linked to an underlying psychiatric disorder. A patient with psychosis, for instance, may have PNES only when he is particularly paranoid or troubled by hallucinations. In others, the coexistence of PNES and other psychiatric symptoms appears more coincidental, or comorbid psychopathology develops only as a consequence of PNES.

3.4. Diagnosis

Despite the great number of studies describing certain features as typical of PNES or more common in PNES than epilepsy, we are left with a surprisingly large number of questions. Whereas we know about the discriminating value of symptom clusters reported by patients with syncope versus those with generalized epileptic seizures [212], or by patients with parasomnias versus those with nocturnal epilepsy [213], it has not been established how we can maximize our ability to distinguish between epilepsy and PNES on the basis of the patient’s history. Even the diagnostic value (including the interrater reliability) of ictal video/EEG monitoring, the diagnostic “gold standard,” remains uncertain.

However, the most significant knowledge gaps do not relate to the distinction of PNES from epilepsy, but the more precise characterization of PNES disorders. There is strong evidence suggesting that PNES are clinically heterogeneous, but the methodology of the DSM-IV [214], which splits a complex neuropsychiatric syndrome into multiple comorbid mental and personality disorders, does not yield meaningful subgroups of patients with PNES. Alternative methods that could produce a differentiation of patients with PNES with a clearer relationship to suitable treatment modalities and prognosis may exist: the Operationalized Psychodynamic Diagnostic Manual has been reported to have impressive interrater reliability but has not been used in the context of PNES [215].

3.5. Treatment

In view of the lack of adequately controlled and sufficiently powered studies, it is currently impossible to state with certainty that the benefits described are not entirely nonspecific or attributable to phenomena such as “regression to the mean”. Skeptics might feel confirmed by the observation that so many different psychotherapeutic approaches seem similarly effective. On the other hand, it could be argued that this observation simply reflects the heterogeneous nature of the disorder and that complex behaviors can be tackled in different ways.

We also do not know whether it would be possible to develop an effective treatment for “all comers”, or whether management needs to be individualized, or whether patients should be divided into different groups depending on the likely etiology or manifestations of PNES [6,89,113,216–220]. Future treatment studies could include the evaluation of a diagnostic paradigm allocating subgroups of patients to particular treatment streams, or a “stepped care” approach in which more complex individualized interventions were preceded by simpler “generic” treatments.

3.6. Prognosis

We cannot explain the reason for the apparent discrepancy between the relatively encouraging outcomes in short term follow-up and the poorer prognosis in longer-term outcome studies. It may be that the apparently conflicting results merely reflect differences in terms of outcome measures or patient selection. Notably the more positive short-term studies focused on seizure outcome, not more comprehensive measures. We have previously demonstrated that seizure cessation is a reasonable marker of psychopathology in patients who have only PNES, but that the achievement of full seizure control was not associated with reduced levels of psychopathology in more complex patients, for instance, those thought to have additional epilepsy at the time of PNES diagnosis [221].

If both findings were true, two more interesting explanations could be considered: First, outcome (at least in terms of seizures) may be quite good in the short term. However, patients may relapse in the longer term or develop other health problems causing disability. Second, the outcome of PNES may have a bimodal distribution. A proportion of patients may get better quickly. A slightly larger group could be considered: First, outcome (at least in terms of seizures) may be quite good in the short term. However, patients may relapse in the longer term or develop other health problems causing disability. Second, the outcome of PNES may have a bimodal distribution. A proportion of patients may get better quickly. A slightly larger group may have a more entrenched and etiologically different disorder that is unlikely to improve, even over the longer term [116]. In the absence of longer-term studies charting the course of a sufficiently large group of patients prospectively, we cannot determine which of these explanations comes closer to the mark.

4. Conclusion

Our knowledge of the clinical picture and context of PNES has made only modest progress since Gowers summarized his understanding of “hysteroid” seizures in 1885 [73]. The most significant developments since this time were the clinical introduction of the EEG in the 1930s and video/EEG monitoring in the 1970s. However, these developments have only increased the level of certainty with which PNES can be distinguished from epileptic seizures and have not had much impact on our understanding of PNES themselves.
or the differences between different PNES syndromes. Nearly 70 years after his death, the psychodynamic theories that underpin most modern thinking about PNES can still be traced back to Freud’s writings on the subject [222,223]. Although Kretschmer has since suggested that learned or reflex behavior may be relevant to the pathogenesis of PNES [224], most modern psychological theories continue to follow Freud’s essentially dualistic approach to mind and brain. An integrative psychosocial model of PNES that goes beyond overly simplistic hardware/software analogies and that embraces our understanding of the scope and limitations of neuroplasticity and neuronal modulation in health and disease has yet to be developed.

Much of the research conducted into PNES has been reactive or opportunistic—often based on data collected routinely in epilepsy centers in the course of evaluating patients for epilepsy surgery. The studies examining the mental or psychodynamic processes leading to PNES are greatly outnumbered by studies describing visible or behavioral phenomena. Far too many studies have used patients with epilepsy as the only controls. Only a handful of studies can be considered prospective and hypothesis-driven. Most of our knowledge is derived from retrospective studies open to all the biases associated with “data trawling”. Although this is disappointing, it also means that there is still much to be learned about PNES by testing the many hypotheses that have been generated by retrospective studies and psychodynamic thinking through carefully constructed prospective studies.

To date, many well-established investigational methods have hardly been used in this area. Only a small number of focused neuropsychological experiments have been carried out. Although the recent technological advances in structural and functional neuroimaging have provided intriguing insights into posttraumatic stress disorder and functional hemiplegia [225,226], neuroimaging techniques have not made a significant contribution to our understanding of PNES. The same is true of the rapidly developing field of psychogenetics. Having said this, it is unlikely that we will be able to benefit fully from these investigational methods without a clearer understanding of the subjective seizure manifestations and the biographic or clinical context in which PNES occur.

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