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Chapter 25

Nonepileptic seizures – subjective phenomena

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Abstract

Psychogenic nonepileptic seizures (PNES) superficially resemble epileptic seizures or syncope and most patients with PNES are initially misdiagnosed as having one of the latter two types of transient loss of consciousness. However, evidence suggests that the subjective seizures experience of PNES and its main differential diagnoses are as different as the causes of these three disorders. In spite of this, and regardless of the fact that PNES are considered a mental disorder in the current nosologies, research has only given limited attention to the subjective symptomatology of PNES. Instead, most phenomenologic research has focused on the visible manifestations of PNES and on physiologic parameters, neglecting patients' symptoms and experiences.

This chapter gives an overview of qualitative and quantitative studies providing insights into subjective symptoms associated with PNES, drawing on a wide range of methodologies (questionnaires, self-reports, physiologic measures, linguistic analyses, and neuropsychologic experiments). After discussing the scope and limitations of these approaches in the context of a dissociative phenomenon, we discuss ictal, peri-ictal and interictal symptoms described by patients with PNES. We particularly focus on impairment of consciousness. PNES emerges as a clinically heterogeneous condition. We conclude with a discussion of the clinical significance of particular subjective symptoms for the engagement of patients in treatment, the formulation of treatment, and prognosis.

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INTRODUCTION

p0005 Psychogenic nonepileptic seizures (PNES) superficially resemble epileptic seizures or syncope but are not associated with ictal electroencephalographic (EEG) discharges. They are episodes of impaired self-control associated with a range of motor, sensory, and mental manifestations. Studies using a wide range of different methodologies indicate that PNES are an experiential and behavioral response to internal or external stimuli (Reuber, 2009; Roberts and Reuber, 2014). The key symptoms of PNES, such as alterations in consciousness and the partial or complete loss of normal integration between memory, awareness of identity, and control of bodily movements, have increasingly been conceptualized as paroxysmal dissociative responses (Bowman, 2006).

p0010 Although different labels (including major hysteria and hysteroepilepsy) have been used to describe it, the clinical entity of what is today categorized as PNES has been recognized for a long time. However, especially since the introduction of synchronous video-EEG monitoring into routine care in the 1970s and 1980s, phenomenologic research about PNES has focused almost entirely on demonstrating the absence of the physiologic changes associated with epileptic seizures and on externally observable differences between PNES and epilepsy (Reuber, 2008). In contrast, the subjective symptomatology of PNES has largely been neglected, despite the current medical nosologies (*International Classification of Diseases*, 10th edition: ICD-10; *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition: DSM-5) categorizing PNES as a mental disorder (World Health Organization, 1992; American Psychiatric Association, 2013). Given that PNES may be a dissociative phenomenon, the reasons for this neglect may not be limited to

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the fact that visible PNES manifestations are easier to capture, objectify, analyze, and report than subjective experiences; they may also include that PNES usually involve subjective states or experiences that are particularly difficult for patients to share.

p0015 Nevertheless, research on the subjective experience of PNES is of great practical importance. Firstly, subjective symptoms may help with the differentiation of PNES and other paroxysmal disorders, especially epilepsy and syncope. Subjective PNES symptoms may also have implications for treatment. For example, the recognition of emotional triggers for PNES may help with patient engagement and an insight into the patient's subjective PNES experience is key to psychotherapeutic treatment, for instance, interventions which aim to enhance patients' tolerance of distress (LaFrance et al., 2013). Lastly, although this remains an area of ongoing study, patients' experiences of ictal and interictal states may co-determine their prognosis.

p0020 This chapter will review studies that have shed light on the subjective symptomatology of PNES using a range of different quantitative and qualitative approaches. The first section will focus on the methodologies that have been used to investigate subjective symptoms of PNES and outline their scope and limitations. The second section will address the temporal characteristics of subjective symptoms associated with PNES, i.e., differences between the ictal and the interictal state, including transition periods, warnings, triggers, and postictal symptoms. The third section will focus on alteration of consciousness, which is the key feature distinguishing PNES from other mental health problems more generally or other somatic symptom disorders more specifically. The fourth section will look at the clinical significance of subjective experiences, including diagnostic, therapeutic, and prognostic implications. The chapter will conclude with a discussion drawing on all previous sections and exploring what our current understanding of the subjective phenomenology of PNES tells us about the nature of this disorder.

s0010 METHODOLOGIC CONSIDERATIONS

p0025 In this section we discuss the methods used to study subjective PNES experiences, describing their merits and limitations. These are preliminary observations intended to provide readers with the ability better to judge the findings themselves, which will be discussed below.

p0030 Most studies examining PNES symptoms have used self-report questionnaires comparing the mean responses of different groups of participants, mainly patients with PNES and epilepsy, less commonly, healthy controls or other patient groups. This methodology has provided useful insights into the disorder and has been especially valuable in aiding the differentiation of PNES and epilepsy (and, to a much lesser extent, syncope). However, the narrow focus of this approach is prone to oversimplifying the complexity and heterogeneity of PNES disorders. Questionnaires only deliver the respondents' replies to their understanding of the exact questions asked; they give respondents little opportunity to qualify their responses or to communicate the finer subtleties of their experience.

p0035 The relative lack of studies involving other patient control groups than people with epilepsy also means that we know very little about differences in the subjective phenomenology of PNES and syncope or other mental disorders mainly characterized (at least in part) by subjective paroxysmal symptoms, such as panic disorder or posttraumatic stress disorder. Apart from the more general self-report limitation of social desirability biases (van de Mortel, 2008), there are also more specific problems with relying on the self-report of symptoms of a dissociative state. The neurobiologic mechanisms underpinning PNES may well interfere with patients' awareness of ictal symptom experiences, the storage and consolidation of ictal symptoms, memories, and postictal symptom recall (Bakvis et al., 2010; Roberts and Reuber, 2014). Last, but not least, patients may (at least prior to psychologic treatment) also be unwilling or emotionally unable to report unpleasant or unacceptable memories of PNES experiences, which must have been encoded successfully in long-term memory, and there is some evidence in support of this assertion, because patients are able to report them as psychologic treatment progresses (von Fabeck, 2010).

p0040 One well-established approach to getting around emotional blocks to the recall of unpleasant experiences has involved the use of hypnosis (Kihlstrom, 1985). Hypnosis was first used in somatoform disorders based on early theories suggesting that highly hypnotizable individuals are particularly prone to displaying "hysterical" symptoms (Schachter, 2011). Hypnosis has since been used in patients with PNES to aid the diagnostic differentiation from epilepsy and to contribute to treatment (Kuyk et al., 1999; Barry and Reuber, 2010). For instance, the phenomenon that patients who have had a PNES have a clearer recollection of ictal events under hypnosis than without hypnosis (and more complete recall than patients with epilepsy) has been used as a differential diagnostic method since World War I (Brown et al., 1999). Whilst this observation demonstrates that there is likely to be a significant difference between patients' actual PNES experience and their recall (or report) of ictal experiences, to date, hypnotic recall of subjective PNES symptoms has not been studied systematically. This means that we are currently unable to glean

as much information about patients' PNES experiences from studies using hypnosis as this method might yield.

p0045 Insights about subjective PNES symptoms are also available from a number of studies that have employed conversation analysis and other qualitative linguistic methods to address clinical questions about the disorder. The fact that patients used their own words to describe their experiences in these studies makes the findings harder to categorize, but means that, at least potentially, these studies can provide a more highly differentiated understanding of patients' individual subjective seizure manifestations compared to questionnaires. Most of these studies aimed to identify aspects of patients' interactional behavior in clinical encounters with neurologists, which might help with the differential diagnosis of epilepsy and PNES. However, these studies, in which researchers focused specifically on how patients described their problems to the doctor, have also yielded interesting insights into the etiology and experience of PNES (Reuber et al., 2014). Especially the analysis of patients' use of metaphors and diagnostic labels has enhanced our understanding of the subjective seizure experiences of PNES and how these differ from those of patients with epilepsy (Plug et al., 2009, 2010, 2011). Metaphors hold particular importance in phenomenology research: Lakoff (1993) argues that metaphors hold particular importance in phenomenology research as they are surface representations of mental domains that allow us to understand abstract unstructured matter in a more concrete manner by applying older, pre-existing concepts to new experiences. What is more, the examination of metaphors for seizure experiences used by patients in interactions with doctors are one example of how objective observations (such as interactional behavior or word choices) can provide clues about patients' subjective experience.

p0050 Clues about subjective PNES experiences can also be gathered from neuropsychologic experiments. Whilst there are obvious practical limitations to experimentation in the ictal state itself (which mean that no such studies have been undertaken to date), several studies have revealed important differences between patients with PNES or epilepsy in the interictal state, as well as between those with PNES, healthy controls, or volunteers with posttraumatic stress symptoms. On a group level, PNES patients have differed from these controls in terms of stimulus perception as well as cognitive, autonomic, and emotional stimulus processing. The differences that distinguish patients with PNES in the interictal state from the other groups listed may be less obvious or disabling than those that would be expected in the ictal state; however, their nature provides a plausible indication of the (much greater) differences, which might be observed in PNES patients during the ictal state. For instance, such studies found evidence for increased vigilance towards social stressors (Bakvis et al., 2009), an increased tendency to use avoidant responses to stressful stimuli (Bakvis et al., 2011), and a combination of an increased sensitivity to certain emotions with a reduced expressive response to the perceived emotion (Roberts et al., 2012). The findings from this type of research have been particularly enlightening when physiologic arousal levels were manipulated. However, given that none of these studies have captured PNES *per se,* the relationship between interictal findings and PNES remains inferential.

p0055 There is another important limitation of all studies investigating the subjective symptomatology of PNES. Temporal differences in terms of subjective symptoms are not limited to contrasts between ictal and interictal states but extend to differences of subjective PNES experiences between the earliest phases of the development of a PNES disorder and later stages, when PNES have become established and the seizure disorder has become more chronic. Unfortunately, very few studies have investigated or accounted for this factor, although there is a strong suspicion that the experience of PNES is dynamic and subject to change over the trajectory of the disorder's timeline. For instance, patients with PNES may originally experience typical panic attacks, but over time, symptoms of anxiety may diminish and manifestations of dissociation increase (Goldstein and Mellers, 2006). A study based on conversation analysis of a series of interviews with 4 patients with PNES undergoing inpatient or outpatient psychotherapy demonstrated that, as patients progressed through therapy, they used less projection, and fewer theoretic terms and preformed expressions such as "I feel really ill" to describe their PNES experiences. Instead, in their descriptions of PNES, they made increasing use of episodic reconstruction and more references to environmental stimuli or PNES-related subjective symptoms (von Fabeck, 2010).

p0060 These changes in patients' access to their PNES experiences mean that it would be best to describe subjective symptoms at different stages of the disorder rather than collating all patients together in one group. The fact that there is currently not enough evidence to pursue a more differentiated view does not mean that such an approach would not be more appropriate.

TEMPORAL CHARACTERISTICS OF SUBJECTIVE SYMPTOMS ASSOCIATED WITH PNES

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p0065 Even in epilepsy, when seizure states are defined by ictal EEG changes that markedly differ from "background" EEG activity, there is debate about the exact timing of seizure onset and offset. Although patients with PNES tend to speak of their disorder as characterized by

"seizures" (i.e., paroxysmal experiences) (Plug et al., 2009), the moment of transition from the interictal to the ictal state is often harder to define and associated with less dramatic physiologic arousal than the transition into an epileptic seizure (Ponnusamy et al., 2012). Nevertheless, we will use a temporal framework in this section, addressing subjective symptoms associated with PNES to discuss triggers, warnings, the ictal phase itself, postictal and interictal PNES manifestations.

PNES triggers

p0070 No research has specifically focused on subjective experiences of seizure triggers in patients with PNES. A study in which 100 patients with PNES (diagnosed by video-EEG) self-reported their experience of PNES manifestations demonstrated considerable heterogeneity of experiences of seizure triggers (measured by using a questionnaire listing 86 possible symptoms, including several questions relating to triggers or warnings). Only a small minority of patients (10%) stated that they were "always" aware of triggers, 57% were aware of triggers for some but not all of their PNES, and 31% claimed never to be aware of triggers. In the same study, 43% of patients stated that their PNES "always" "come on out of the blue without warning," 51% responded that at least some of their PNES came on in this way and 6% said this never happened. Whilst this study therefore suggested that PNES triggers may (at least at times) be experienced by just over one-half of patients, PNES witnesses questioned in the same study reported being aware of seizure triggers more often than patients themselves (Reuber et al., 2011) (this finding resonates with an observation made in a study in which the Illness Perception Scale-revisited was administered to patients with PNES and their caregivers and which demonstrated that caregivers of patients were more likely to perceive an association between psychologic factors (in particular, stress) and PNES than patients themselves) (Whitehead et al., 2015).

p0075 In an unpublished study in which a psychotherapist working in the Department of Neurology at the Royal Hallamshire Hospital, Sheffield, UK, prospectively questioned 58 consecutive patients with PNES attending a first appointment for psychotherapy about their symptoms (74% female, 19% reporting more than one type of PNES), 79% reported experiencing at least occasional PNES triggers. Recognized triggers included internal or external factors. The most commonly perceived triggers were emotional states (50%: feeling stressed, upset, anxious, aroused, neglected, nonspecific unwell). Bodily states (21%: illness, loss of sleep, feeling hot or cold, tiredness, pain, feeling dehydrated or exhausted after something energetic) and external stimuli (9%: crowded places, flashing lights, black and white patterns, blue light, flashing lights, smoke / flames / dogs / household objects acting as traumatic reminders, sun on surface, neon lights) were less commonly described potential triggers (S. Howlett, personal communication).

p0080 The facts that triggers cannot be recalled by all patients after all PNES and that about one-half of patients with PNES report having seizures from sleep do not mean that PNES are not always triggered by a particular internal or external stimulus (Duncan et al., 2004). Closer study of nocturnal PNES demonstrates that PNES happen when patients have actually been awake, and it is quite feasible that a completely "successful" dissociative response to an aversive trigger protects patients against the realization that they have difficulties with tolerating certain stimuli. In fact, one study demonstrated that, unlike in patients with epilepsy or healthy controls, patients with PNES showed discrepancies between a high number of explicitly self-reported anxiety symptom and normal implicit anxiety scores (measured by an Implicit Relational Assessment Procedure). This study suggests that, despite experiencing relatively high levels of anxiety symptoms, patients with PNES do not consider themselves as anxious individuals (Dimaro et al., 2014).

p0085 It is well recognized that PNES can be triggered during brief outpatient video-EEG recordings in a diagnostic setting with a number of provocation techniques, typically used in conjunction with verbal suggestion. Provocation with saline patches, vibration, and hypnosis has been described, but the most commonly used technique involves the suggestive intravenous injection of normal saline solution (Cohen and Suter, 1982). This procedure will provoke typical PNES in about three-quarters of patients (Reuber and Elger, 2003). However, over the last decade there have been increasing ethical concerns about the deceptive use of placebo to diagnose PNES (Bernat, 2010), and therefore, the combination of hyperventilation and photic stimulation with verbal suggestion has been proposed as a PNES provocation method instead. With this alternative method PNES can be triggered in about two-thirds of patients during a brief outpatient video-EEG recording (McGonigal et al., 2002).

p0090 Considering that a wide range of different stimuli seems to trigger PNES in the majority of patients, it is unlikely that the triggers used in these provocation procedures operate in a similar way to the highly specific stimuli that may trigger epileptic seizures (for instance, in musicogenic or photosensitive epilepsy). Instead, it is more likely that the provocation procedures for PNES cause physical or cognitive symptoms (for instance, physiologic arousal or anxiety) or anticipatory anxiety about a possible seizure, and that it is this state, combined

with excessive distress avoidance tendencies, which triggers PNES in this setting.

p0095 Evidence for increased avoidance tendencies in patients with PNES comes from self-report and experimental studies. For instance, a study using the Multiple Experiential Avoidance Questionnaire demonstrated increased levels of avoidance compared to healthy controls and patients with epilepsy in terms of behavioral avoidance, distress aversion, procrastination, distraction, and repression (Dimaro et al., 2014). An experimental study by Bakvis et al. (2011) used an affect evaluation task to assess avoidance. In their study, patients had to respond to happy or angry faces by making arm movements in response to the facial expression which were either consistent or inconsistent with usually preferred motor responses (extending the arm in response to a negative stimulus like an angry face, flexing the arm in response to a positive stimulus like a happy face). The findings in a group of 12 patients with PNES and 20 healthy controls signaled an instinctive avoidant action tendency towards social threatening cues (slower flexion / "approach" movements to angry faces).

PNES warnings

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p0100 Research on prodromal or warning symptoms of PNES is also very limited. The frequency with which prodromal or warning symptoms of PNES have been self-reported in patient cohorts varies widely, between 24% and 92% (Cohen and Suter, 1982; Gulick et al., 1982; Luther et al., 1982; Lancman et al., 1993; Vein et al., 1994; Goldstein et al., 2006). This wide range is likely to reflect differences in methodology and patient selection. Also, authors (and study participants) may not have separated clearly between "warning" and "ictal" symptoms. In the unpublished psychotherapy patient cohort mentioned above, 69% of patients reported symptoms that they (and the therapist) considered as seizure warnings (patients were able to report several warning symptoms, so the percentages add up to more than 100%). "Panic" (52% of patients) and "non-bodily panic" symptoms (38%) were reported most commonly, followed by "sensory non-panic" (24%) and "dissociative" symptoms (16%). The symptoms interpreted as indicating "panic" included dizziness, feeling hot, sweaty, shaky, panicky, light-headed, numb, tingly, cold, sick, nauseated, warm, clammy, as if going to pass out, short of breath, or frightened. The symptoms categorized as "bodily non-panic" included: muscle tightening or spasms, heavy-headedness, "thick" or "groggy" head, headache, head pain, feeling drained, weird, awkward, tired, lethargic, unable to stand up, as if falling asleep, drowsy, really ill, or as if energy was draining away. This category also included warnings such as limb weakness, beginning to stutter, developing slurred speech, or feeling the floor coming up. "Sensory non-panic" symptoms included white spots in peripheral vision, fuzzy eyesight, visual images moving sideways, spots and floaters, metallic or strange taste, taste of blood, horrible, strange, or burning smell or a high-pitched whine in ears. "Dissociative" symptoms included *déjà vu*, everything feeling distant, feeling as if stepping back, rushing past, as if things were slowing down, things going dark, and as if things were going distant (S. Howlett, personal communication).

p0105 The presence of particular subjective warning symptoms may depend on the subtype of PNES. A study based on a cluster analysis of patient-reported symptoms and seizure manifestations visible on video which had been rated by two independent experts suggested that PNES warnings were reported more often before "hyperkinetic prolonged attacks" (in 66.7% of cases) than in association with any of the other four semiologic subtypes ("dystonic attacks," "pauci-kinetic attacks," "pseudosyncope," and "axial dystonic prolonged attacks"). Sensory symptoms (34.5%) were only observed in "pauci-kinetic attacks" (Hubsch et al., 2011).

p0110 Clinical experience suggests that warning symptoms can last from seconds to many hours. Whilst most of these warning symptoms are unpleasant, patients may be more aware of the physical symptoms themselves than the fact that these symptoms are associated with emotional distress (or, indeed, that they may be symptoms of distress). In a study comparing ictal anxiety symptoms in patients with PNES and patients with epilepsy, both groups reported identical levels of cognitive or mental symptoms of anxiety; however, patients with PNES reported a significantly higher number of somatic anxiety symptoms (Goldstein and Mellers, 2006).

p0115 The fact that PNES warning states are subjectively distressing, even when patients may be unable to recognize or recall this fact, is supported by the observation that some patients admit to making a conscious effort in at least some of their PNES to black out and escape the sensation (Stone and Carson, 2013). This phenomenon of "willful submission" is perhaps not that surprising if PNES are a defense mechanism providing relief from a distressing emotional experience (the trigger), but also the aversive experience of anticipating the attack itself (and the fact that dissociation may be achieved in a way which appears subjectively "willful" to patients with PNES does, of course, not mean that the dissociation really was achieved by willed action or that the same dissociative mechanisms cannot also operate "automatically," i.e., without patients willing themselves to black out).

p0120 An effort not to contemplate the aversive experiences associated with PNES may also explain the observation made in sociolinguistic studies comparing diagnostic

discussions between doctors and patients about epilepsy or PNES. Whereas patients with epilepsy tend to be very happy to give detailed first-person accounts of their seizure experiences, those with PNES have a tendency to avoid discussing their symptoms, and to show conversational phenomena termed "detailing blocking" and "focusing resistance" as manifestations of avoidance instead (Schwabe et al., 2007, 2008; Reuber et al., 2009).

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Ictal symptoms

p0125 Behavioral manifestations tend to develop more gradually in PNES than in epileptic seizures (Meierkord et al., 1991; Syed et al., 2011). Whilst the speed of development of subjective symptoms in PNES has not been specifically examined, electrocardiographic studies also suggest that autonomic changes in epileptic seizures are typically more sudden than those seen in PNES (Opherk and Hirsch, 2002). Thus, it may be reasonable to assume that subjective symptoms also develop more slowly in PNES. Nevertheless, once the ictal PNES state has developed, it is associated with a significantly higher level of autonomic arousal than the resting state (even though arousal is less marked than that seen with epileptic seizures) (Ponnusamy et al., 2012).

p0130 The ictal state tends to last longer in PNES than in epilepsy (Luther et al., 1982; Ettinger et al., 1999b; Selwa et al., 2000). For example, one study based on the analysis of patients with epilepsy ($n=25$) and patients with PNES ($n=25$, actual number of recorded seizures was not disclosed) in a video-EEG unit showed that generalized tonic-clonic seizures lasted 50–92 seconds, whereas PNES lasted 20–805 seconds. Many PNES went on for more than 2 minutes (Gates et al., 1985). PNES continuing for over 30 minutes (also called pseudostatus or PNES status) occur in about one-third of patients, and more than one-quarter of patients diagnosed with PNES at epilepsy centers have received intensive care treatment for presumed status epilepticus at least once (Reuber et al., 2003c).

p0135 Evidence suggests that the ictal symptomatology of PNES is as heterogeneous as the preictal symptoms. Unfortunately, most studies do not separate clearly between preictal and ictal symptoms, so it is difficult to say how commonly patients are able to report subjective ictal symptoms. Only 19% of the 58 psychotherapy patients mentioned above could report any subjective ictal (as opposed to PNES warning) symptoms. Those who could report symptoms most commonly reported symptoms indicative of anxiety. Flashbacks, hallucinations, and dissociative symptoms were reported less frequently (S. Howlett, personal communication). In other studies, symptoms of anxiety were also most prominent: in the group of 100 patients with PNES studied by Reuber et al. (2011), patients most commonly reported disorientation (86%), fear (80%), and a feeling of disconnection (being conscious during the attack but unable to react to things: 77%) in at least some of their attacks. The next most common symptoms occurring in at least some attacks were rising bodily sensations (62%), nausea (59%), and a bad taste in the mouth (46%). Cognitive phenomena such as flashbacks (33%) and *déjà vu* (27%) were reported by fewer patients.

p0140 The questionnaire about ictal symptoms used in this study also included eight questions based on the Dissociative Experience Scale (DES) Taxon thought to reflect "pathological dissociation" experiences (Bernstein and Putnam, 1986; Waller et al., 1996). These eight symptoms were rarely endorsed: the proportion of people who reported that they were "always" or "frequently" present in their PNES ranged from 1% ("After an attack, I find things among my belongings which I don't remember buying") to 26% ("During an attack, I do not recognise my friends or family"), with the mean item response being 11%. In contrast, the number of people who reported that these symptoms were "never" or "rarely" present ranged from 43% ("During an attack, I do not recognise my friends or family") to 77% ("During an attack, I feel as if other people, objects, and the world are not real"), with the mean item response being 66.6%. This does not mean that the dissociative interpretation of PNES is incorrect. However, it shows that (for the majority of patients) the recalled ictal experience of PNES is materially different from the forms of dissociation captured by the DES Taxon.

p0145 Whilst this study showed that ictal PNES symptoms are very heterogeneous, it also demonstrated that symptom combinations are not randomly distributed. Reuber et al. (2011) used a correlation matrix to explore possible relationships between the DES Taxon, symptoms of anxiety, and other PNES symptoms. Significant positive correlations were seen between duration of seizures and seizures from reported sleep ($r=0.28$, $p=0.006$), seizure-related motor activity and seizures from reported sleep ($r=0.48$, $p<0.001$), flashbacks and anxiety ($r=0.44$, $p<0.001$), or dissociation ($r=0.66$, $p<0.001$), and between ictal symptoms of anxiety and dissociation ($r=0.53$, $p<0.001$).

p0150 A number of other studies have reported high levels of ictal anxiety symptoms in PNES as well: Vein et al. (1994) found that more than 90% of 15 patients with PNES reported experiencing dyspnea, palpitations, and dizziness during their attacks. Several other panic symptoms were reported by more than 70% of their patients. Another study (which did not distinguish between immediately pre-ictal, ictal, or immediately postictal symptoms) in which the authors compared the prevalence of 13 DSM-IV-TR (American Psychiatric Association, 2000) symptoms of panic disorder in 224 patients with PNES and 130 with epilepsy, showed that patients

with PNES described more panic symptoms than those with epilepsy, allowing the authors to classify up to 80% of patients with PNES correctly on the basis of these symptoms alone. In this study symptoms possibly related to hyperventilation were much more common in patients with PNES and separated particularly clearly between the two patient groups (shortness of breath: 55.8% in PNES vs. 13.8% in epilepsy; paresthesia: 58.0% in PNES vs. 23.1% in epilepsy) (Hendrickson et al., 2014).

p0155 Galimberti et al. (2003) found evidence of ictal autonomic arousal in more than half of their patients with PNES (although far fewer reported ictal fear or other affective symptoms) and ictal anxiety symptoms may be even more frequent (100%) in adolescents with PNES (Witgert et al., 2005).

p0160 Information about the ictal PNES experience can also be taken from linguistic findings. A study using metaphor analysis showed that patients with PNES were more likely to conceptualize their seizures as a "state/place" that they "enter" or "cannot come out of" and where the attack is a "passive location" or "state." Patients with epilepsy, on the other hand, depicted the seizure as an external "active/force" or "event/situation" and an independently acting entity that acts on their body (Plug et al., 2009). This is in keeping with a study by Watson et al. (2002), who asked patients with PNES and patients with epilepsy, who had experienced an earthquake in Seattle (6.8 on Richter scale), how this related to their seizure experiences. Only patients with epilepsy thought that there were similarities between their experience of the earthquake (i.e., an external independent entity impacting on them) and their seizures.

p0165 Another linguistic study looked at the labels (i.e., nouns) patients chose to use for their paroxysmal events. This study also yielded results supporting the analysis of metaphoric conceptualizations. In a diagnostic conversation with a neurologist, unlike those with epilepsy, patients with PNES showed interactional resistance to the use of the term "seizure," although this was still the label they most commonly used (Plug et al., 2009). Resistance could, for instance, manifest as a patient choosing a different term than "seizure" in their answer when the doctor had used "seizure" in the question, as hesitation before the use of the word "seizure," or through the addition of statements like "or whatever you want to call them." Whilst not apparent from this study, the fact that the word "seizure" conveys the impression of a person being seized by an independently acting force may have been one explanation for this observation.

Postictal symptoms

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p0170 Patients with PNES typically find it much easier to report postictal than ictal symptoms. In the study conducted by Reuber et al. (2011), involving 100 patients with PNES, 93% of patients said their muscles ached after the attack, 38% of patients said that they may wake from their attacks with a cut tongue, and 20% reported that they may have burned themselves after seizures. Similarly, in the series of psychotherapy patients reported above ($n = 58$), 74% said that they had at least one postictal symptom (fatigue 45%, memory problems 22%, emotional symptoms 22%, headache/pain 18%, altered sensation 17%, confusion 9%, altered speech 3%). It may be that the preferential recall of postictal symptoms is a manifestation of the tendency of patients with PNES to highlight the consequences of their seizures rather than the seizure experiences themselves (Schwabe et al., 2007, 2008).

p0175 However, not all studies have found symptoms in the postictal phase after PNES to be reported as frequently: Ettinger et al. (1999b) looked at spontaneous responses to the question "What symptoms do you have after a seizure?" This question was intentionally left vague to avoid endorsing specific symptoms. All patients with epilepsy ($n = 16$) reported having at least one postictal symptom, whereas 52% of 23 patients with PNES approached in this study had none ($p = 0.001$). Patients with PNES also reported a significantly lower prevalence of headaches ($p = 0.008$) and fatigue symptoms ($p = 0.004$). Although there were no differences between the groups in terms of any other symptoms or confusion, the authors of this study came to the conclusion that the aftermath of epileptic seizures tends to be more disabling or distressing than that of PNES.

p0180 In keeping with this finding, most studies investigating autonomic functioning in the postictal state suggest that disturbances are more marked in patients with epilepsy than those with PNES. Azar et al. (2008), for instance, compared postictal respiration after epileptic seizures and PNES and reported that deep, loud breathing, including snoring lasting approximately 5 minutes after the seizure, is common in epilepsy, whereas, quiet, shallow, and short irregular breathing patterns lasting 1 minute postseizure were associated with PNES. These findings were replicated by another study showing that patients with PNES have higher median respiratory rates postictally compared to patients with epilepsy ($p = 0.047$) and that abnormal respiration resolves more quickly after PNES than epileptic seizures (3.28 minutes compared to 6.34 minutes, $p < 0.0001$) (Rosemergy et al., 2013).

Interictal symptoms

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p0185 Many studies have explored symptoms in patients with PNES in the interictal state, although it is unlikely that the self-report methodology employed in most of these studies distinguished safely between symptoms, which are actually directly PNES-related, and symptoms not

directly related to seizures. Another difficulty that arises with the interpretation of interictal symptoms in patients with PNES is the high level of symptoms usually attributed to other mental health disorders. Patients most commonly fulfill the diagnostic criteria for other somatic symptom (22–84%), other dissociative (22–91%), posttraumatic stress (35–49%), depressive (57–85%), or anxiety disorders (11–50%) (Reuber, 2008). The likely presence of comorbid disorders (or the manifestation of PNES as features of other mental health disorders) makes it difficult to separate between symptoms attributable to the interictal state of PNES and more or less coincidental symptoms of other conditions.

p0190 Having said that, many studies have demonstrated significant elevations of interictal anxiety symptoms in patients with PNES compared to population norms. In addition, the prevalence of clinical anxiety disorders in patients with PNES is about twice as high as in the general population (Galimberti et al., 2003; Tellez-Zenteno et al., 2007). However, neither clinical diagnoses of anxiety disorders nor self-reported interictal anxiety symptom have been found to be persistently higher in patients with PNES than in those with epilepsy (Tojek et al., 2000; Owczarek, 2003; Bewley et al., 2005; Hixson et al., 2006; Dimaro et al., 2014).

p0195 Findings have been similar for symptoms of dissociation. Patients with PNES report more symptoms than the general population or healthy controls but symptoms of dissociation have not been found consistently more frequently than in patients with epilepsy (Goldstein et al., 2000; Prueter et al., 2002; Reuber et al., 2003a; Lawton et al., 2008; Ito et al., 2009). However, one study demonstrated that significantly fewer symptoms of dissociation were reported by seizure-free PNES patients compared to those with continuing seizures ($p < 0.05$) (Kuyk et al., 2008). Another study showed that self-reported dissociative symptoms are a significant predictor of health-related quality of life (HRQoL) in patients with PNES. Mitchell et al. (2012) found a strong negative correlation of symptoms to HRQoL and dissociative symptoms ($r = -0.64$, $p < 0.05$). After taking account of depressive symptoms (58.1%), Mitchell et al. found that dissociative symptoms explained an additional 14.4% of the variance in HRQoL ($p < 0.001$).

p0200 Somatization (i.e., a higher number of somatic symptoms other than seizures) may be slightly more specific for PNES than symptoms of anxiety or dissociation, in the sense that it differentiates not only between patients with PNES and healthy controls, but also between patient groups with PNES or epilepsy (Owczarek, 2003; Reuber et al., 2003a). High numbers of other somatic symptoms have been found to characterize patients with PNES regardless of whether they belonged to one cluster characterized by high levels of psychopathology, alexithymia, and emotional regulation problems (identifying, accepting, and describing feelings, accessing adaptive regulatory strategies, performing goal-directed behaviors, and controlling feelings / actions) or another cluster with elevated depression scores but comparatively normal levels of alexithymia and emotion regulation (Uliaszek et al., 2012; Brown et al., 2013). What is more, Reuber et al. (2003a) found that high somatization scores were correlated with a PNES severity score once dissociation and psychopathology had been controlled for. A high number of somatic symptoms also predicted poor prognosis in a naturalistic long-term outcome study (Reuber et al., 2003b).

p0205 Last but not least, LaFrance and Syc (2009) observed a significant association between the increased reporting of physical symptoms and lower HRQoL ($r = -0.73$, $p < 0.001$). Commonly reported somatic symptoms included headaches, insomnia, and memory difficulties. In another study, a higher number of somatic symptoms correlated negatively with the physical health component summary of the Short Form 36 (a measure of HRQoL), but not with the mental health component ($r = -0.45$, $p < 0.001$) (Lawton et al., 2009). In this study, the "bodily pain" subscale was rated particularly highly by patients with PNES, prompting the discussion about whether pain is a symptom, a trigger, or part of a comorbid pain condition (e.g., fibromyalgia) in patients with PNES (Benbadis, 2005).

IMPAIRMENT OF CONSCIOUSNESS s0045

p0210 In the context of seizure disorders, impairment of consciousness has been defined operationally as involving deficits in awareness and self-control or responsiveness (Lux et al., 2002). Although clinicians have applied the diagnosis of PNES when patients do not exhibit impairment of consciousness, awareness, self-control, or responsiveness, the apparent temporary reduction of the patient's level of consciousness is a key clinical feature of most PNES (Eddy and Cavanna, 2014). Much more than patients with epilepsy, those with PNES have been noted to highlight the complete and absolute nature of their impairment of consciousness when they talk about their seizures to a doctor. For instance, in linguistic studies patients with PNES showed a tendency to describe the gaps in their memory using uncontextualized negations, e.g., "I can't remember anything," or "I can't see, I can't hear, I can't move" (Schwabe et al., 2008; Plug and Reuber, 2009; Reuber et al., 2009). Caregivers may highlight patients' loss of awareness even more than patients themselves. In the self-report questionnaire study mentioned above, the 100 responses from patients with PNES were compared to responses from 86 caregivers. The caregivers' reports

demonstrated that they considered patients' loss of awareness as more profound than the individuals experiencing PNES themselves (Reuber et al., 2011).

p0215 Having said this, there are several indicators suggesting that loss of awareness in PNES is rarely (if ever) complete. During their PNES, patients often display purposeful movements, for instance reaching out for objects or people around them, or moving items out of the way. Patients whose eyes are usually closed in PNES often show resistance to eye opening and may move their eyes away from an examination torch (Reuber and Kurthen, 2011). One study demonstrated that, during their seizures, 48% of patients with PNES but only 18% of patients with epilepsy were able to follow simple commands, such as "shake my hand" (Bell et al., 1998). Similarly, in another study, verbal or motor responses to a nurse or doctor who approached patients during video-EEG examinations were observed in 58% of patients with PNES (Hubsch et al., 2011).

p0220 The 58 consecutive patients mentioned previously, who were interviewed about their PNES symptoms in their first appointment with a psychotherapist, were asked specifically about awareness and responsiveness during their seizures. Of these patients, only 46% stated that they were neither aware nor responsive in their seizures, 38% said they were aware during their seizures, although they were unresponsive, 19% said they were unaware, but responsive, and 2% said they were aware and responsive (19% had more than one seizure type and 5% had seizures fitting more than one of these categories) (S. Howlett, personal communication).

p0225 Whether or not patients report impairment of consciousness or loss of awareness in their PNES may be associated with certain visible PNES manifestations. In the semiology cluster analysis mentioned previously, "pauci-kinetic" attacks were particularly likely to be associated with maintained responsiveness (96.6% of cases), whereas "pseudosyncope" typically involved unresponsiveness (85.7%) (Hubsch et al., 2011).

p0230 Content and level of ictal impairment of consciousness have been explored using self-report questionnaires. Ali et al. (2010) conducted a quantitative evaluation of subjective experiences of ictal consciousness in patients with epilepsy ($n = 66$) and patients with PNES ($n = 29$). Using a bi-dimensional model plotting general level of awareness versus specific contents of consciousness, patients with PNES exhibited less impaired conscious profiles demonstrating greater levels of responsiveness, contents, and quality of consciousness than those with a range of different epileptic seizure types.

p0235 Others have demonstrated that patients with PNES are more likely to be able to recall ictal experiences than those with epilepsy. For example, Devinsky et al. (1996) demonstrated that, when 16 patients with both epilepsy and PNES were asked to remember a word or phrase during seizures, 15 patients were unable to recall the item after an epileptic seizure, whereas 14 patients were able to recall it after a PNES. Another study compared recall before and after hypnotic induction, finding that 17 of 20 (85%) patients with PNES but no patients with epilepsy recovered accurate seizure memories. Similarly, patients' reports of ictal memories were noted to become more detailed during the course of psychotherapy (von Fabeck, 2010). Taken together, this evidence suggests the initial amnesia resulting from PNES is, at least in part, the result of a postictal retrieval deficit rather than a learning impairment during the seizures themselves (Kuyk et al., 1999). Having said that, an interictal study has demonstrated working-memory impairments in patients with PNES, which were further exaggerated by stress (Bakvis et al., 2010). This suggests that postictal memory gaps may result from a combination of different factors.

CLINICAL SIGNIFICANCE OF SUBJECTIVE PNES EXPERIENCE s0050

Diagnostic implications s0055

p0240 In PNES, like many other disorders, the differential diagnosis is crucial because the most effective treatments of PNES and the paroxysmal disorders that PNES could be mistaken for (mainly epilepsy and syncope) is very different. This is particularly true for the distinction of PNES, epilepsy, and syncope. Delayed or incorrect diagnoses are likely to lead to patients being subjected to inappropriate, ineffective, and potentially iatrogenic treatments. Despite impressive developments in brain imaging and improved access to video-EEG, the act of taking and interpreting patients' narrative of their subjective experience is, arguably, still the most important diagnostic tool in patients who have lost consciousness (Plug and Reuber, 2009; Malmgren et al., 2012).

p0245 A better understanding of the typical interictal, ictal, and peri-ictal symptom profiles of patients with PNES should improve the diagnostic process. Batteries of self-report questionnaires which included questions about interictal somatic and mental health symptoms have already been shown to distinguish accurately between PNES and epilepsy with a sensitivity and specificity of 85% (Syed et al., 2009). One study used the Paroxysmal Event Profile mentioned above to examine whether subjective experience profiles could be used to differentiate between the three commonest causes of transient loss of consciousness (TLOC). One hundred patients with definite epilepsy, 100 with proven PNES, and 100 with physiologically documented recurrent syncope completed the questionnaire, eliciting responses to 86 symptom prompts. Respondents rated symptoms

on a five-point Likert scale (always to never). An initial exploratory factor analysis identified a five-factor structure based on 74/86 questionnaire items with loadings ≥ 0.4. In a confirmatory factor analysis goodness-of-fit statistics, including chi-square, root mean square error approximation, comparative fit index and Tucker Lewis index, were used to test the proposed model. The five resulting latent factors were named as "feeling overpowered," "sensory experience," "mind/body/world disconnection," "catastrophic experience," and "amnesia." Pairwise regression analysis based on these factors correctly classified 91% of patients with epilepsy versus those with syncope, 94% of those with PNES versus those with syncope, and 77% of those with epilepsy versus those with PNES. Thus, diagnostic distinction on the basis of symptoms was better between syncope and the other two common causes of recurrent TLOC than between epilepsy and PNES. These findings suggest that clusters of TLOC-associated symptoms can be used to direct patients to appropriate investigation and treatment pathways for syncope on the one hand, and seizures on the other, although additional information is required for definitive diagnoses, especially for the distinction between epilepsy and PNES (Reuber et al., in press).

p0250 In another analysis, the same dataset was used to explore whether the seven TLOC-associated panic symptoms included in the Paroxysmal Event Profile could differentiate between the PNES, syncope, and epilepsy groups ("During my attacks I feel very frightened"; "During my attacks I feel that something terrible might happen"; "During my attacks I am frightened that I am going to die"; "During my attacks I am frightened that I will lose control"; "During my attacks I am frightened that I will go crazy"; "During my attacks my heart pounds and I feel shaky and sweaty"; and "During my attacks I feel that I have to get out of the situation"). Patients with PNES reported more panic symptoms (median = 15.5) than those with epilepsy (median = 10, $p < 0.001$) and syncope (median = 9, $p < 0.001$). Panic symptoms were reported with similar frequency in the epilepsy and syncope groups ($p = 0.057$). Logistic regression demonstrated that differences in the subjective experience of panic could distinguish PNES from epilepsy and syncope (sensitivity 71.4%, specificity 65.6%), but not epilepsy from syncope (Rawlings et al., manuscript in preparation).

Links with etiology

s0060

p0255 Specific symptoms may also provide clues about etiologic factors. For example, Selkirk et al. (2008) demonstrated that patients with PNES who have a history of antecedent sexual abuse ($n = 64$) were more likely than those without this history ($n = 112$) to report emotional triggers (relative risk (RR), 1.46), attack prodromes (RR 1.33), urinary incontinence (RR 1.82), self-injuries (RR 1.81), nocturnal attacks (RR 1.42), internal experiences (RR 1.97), flashbacks (RR 3.9), and convulsions (RR 1.21) during their PNES. A logistic regression model based on these features correctly predicted whether sexual abuse had been reported in 77.5% of cases. The features accounted for 46.4% of the variance (R. Duncan, personal communication).

Treatment implications

s0065

p0260 A better understanding of subjective experiences is also likely to have implications for engagement and adherence to interventions. The engagement of patients with PNES in the treatment of choice, psychotherapy (LaFrance et al., 2013), is often difficult because patients perceive their disorder to be a "physical" rather than a "psychologic" problem (Whitehead et al., 2013).

p0265 For instance, several studies have demonstrated that patients who accept the diagnosis of PNES are more likely to have better treatment outcomes (Ettinger et al., 1999a; Duncan et al., 2014). It may well be easier for clinicians to convince patients (and caregivers) that they have PNES if the patient is aware of unpleasant warning symptoms, or at least of interictal mental health problems, and can accept that the seizures could be manifestations of arousal or distress (Thompson et al., 2009; Monzoni et al., 2011a, b). Indeed, there is one study which analyzed predictors of PNES cessation in 260 patients after the initial explanation of the diagnosis. This research demonstrated that those with evidence of anxiety and depression were 2.34 times more likely to become spell-free than those without symptoms of these disorders (McKenzie et al., 2010).

p0270 The identification of seizure triggers may also allow psychotherapists or other clinicians to assist patients in building up their tolerance of these stimuli. The presence of seizure warning symptoms and the retention of a degree of self-control during the PNES state may enable patients to learn seizure suppression or control techniques, such as distraction or sensory grounding approaches (Howlett and Reuber, 2009). The fact that HRQoL in patients with PNES is co-determined by other somatic and dissociative symptoms (as well as symptoms of depression) suggests that intervention aiming to reduce symptoms (or increase tolerance of these symptoms) rather than PNES themselves may improve patients' level of functioning (Birbeck and Vickrey, 2003; Szaflarski et al., 2003).

Prognostic implications

s0070

p0275 A naturalistic study of outcome in PNES (a mean of 4.1 years after diagnosis and 11.9 years after PNES

manifestation) suggested that better prognosis was predicted by a number of factors characterized by subjective symptoms, including fewer additional somatoform complaints, lower numbers of other dissociative symptoms, and lower scores of the higher-order personality dimensions ("inhibitedness," "emotional dysregulation," and "compulsivity"), as measured by the Dimensional Assessment of Personality Pathology Brief Questionnaire. Outcome was also poorer in those patients whose seizures involved "loss" of consciousness (Reuber et al., 2003b). Similarly, another study found that outcome after 6 months was worse if patients had symptoms of major depression, dissociative and personality disorders, or new somatic symptoms after disclosure of diagnosis (Kanner et al., 1999). Whilst no study has been undertaken to provide a comprehensive assessment of the value of ictal, peri-ictal, or interictal symptoms associated with PNES for the prediction of outcome (and whilst much more differentiated approaches of capturing symptoms and using them to characterize particular types of PNES would be desirable), somewhat less robust observations show that at least some subjective symptoms experienced by patients with PNES are relevant to how likely they are to become free of their seizures in the longer term.

CONCLUSION

s0075

p0280 Despite the fact that PNES are considered a manifestation of mental disorder, the subjective symptoms associated with this disorder have received much less attention from researchers than visible or physiologic features. Whilst this chapter demonstrates the challenges involved in studying the symptoms of a dissociative phenomenon, it also shows that they should not be ignored or devalued. Most of the studies which form the basis of this discussion only explore subjective symptoms in passing whilst focusing on another facet of PNES. However, this chapter shows how aspects of the subjective phenomenology of PNES can improve the diagnostic process, provide insights into the etiology of PNES in individual patients, help to shape treatment formulations, and allow for a better prognostication of likely treatment outcomes. This suggests that further research focusing more specifically on subjective PNES symptoms and their clinical relevance would be entirely justified and may allow us to understand and treat this complex disorder more successfully in the future. Having said that, even the limited knowledge base about subjective symptoms in PNES available thus far allows us to draw some conclusions.

p0285 The current psychiatric nosologies separate dissociative seizures or conversion seizures as a specific somatic symptom disorder from other manifestations of psychopathology and medical disorders (World Health Organization, 1992; American Psychiatric Association, 2013). However, a closer examination of the symptoms that patients experience (including those which they may not be able to recall during a first interaction with a clinician) demonstrates how indistinct the boundaries between PNES, other dissociative symptoms, somatic symptoms, and anxiety disorders are. We are not arguing that the categoric classifications need to be abandoned. However, it would be a serious misunderstanding of the current categoric classification systems for clinicians or researchers to use particular diagnostic categories as rigid pointers to particular interventions. Treatment formulations are likely to work best if they take account of the full range of a patient's personal PNES symptomatology and experience.

p0290 Another borderline of PNES, which emerges as rather indistinct, is that between the ictal and the interictal state. The differences between seizures and the interictal state are considerably less distinct in PNES than in epileptic seizure disorders. The onset and offset of PNES are often difficult to determine and there is considerable overlap between interictal, peri-ictal, and (when they can be reported) ictal symptoms. This observation suggests that PNES themselves are only the tip of an iceberg of a more pervasive disorder of perception and emotion processing.

p0295 Previous studies have demonstrated that the etiology and visible phenomenology of PNES are heterogeneous (Reuber, 2009; Hubsch et al., 2011). This overview shows that the subjective PNES experience is also rather varied. There are marked differences, not only between different patients but also between one patient's experiences of different seizures. Nevertheless, it is possible to describe some subtypes of PNES disorders, probabilistically characterized by combinations of etiologic factors and clinical features. To date, at least two such subtypes have been suggested: (1) patients with symptoms of marked emotional dysregulation, high levels of psychopathology, distress, and dissociation as well as high levels of alexithymia; and (2) patients with increased depressive and somatic symptoms but no increased number of symptoms of emotional or mental health problems (Uliaszek et al., 2012; Brown et al., 2013). Future research may well distinguish between more subtypes requiring different therapeutic strategies and associated with different outcomes. For instance, research into the warnings of PNES has, so far, only looked at anxiety and physiologic arousal. However, clinical experience suggests that patients may also dissociate in response to feelings of guilt, shame, anger, and other aversive emotions or states or experiences (Griffith et al., 1998; Reuber et al., 2007, 2014).

p0300 We hope that the approach we have pursued in this chapter, integrating patients' subjective seizure

experience with visible motor and measurable autonomic PNES manifestations but also with experimental insights into preconscious cognitive processing in the brain and relevant interictal findings, has not only demonstrated the scope of future PNES symptom research but also inspired readers to pay more attention to the subjective phenomenology of PNES in the meantime.

References

Ali F, Rickards H, Bagary M et al. (2010). Ictal consciousness in epilepsy and nonepileptic attack disorder. Epilepsy Behav 19: 522–525.

American Psychiatric Association (2000). Diagnostic and statistical manual of mental disorders (4th ed., text revision). American Psychiatric Association, Washington, DC.

American Psychiatric Association (2013). Diagnostic and statistical manual of mental disorders, American Psychiatric Association, Arlington, VA.

Azar NJ, Tayah TF, Abou-Khalil BW et al. (2008). Postictal breathing pattern distinguishes epileptic from nonepileptic convulsive seizures. Epilepsia 49: 132–137.

Bakvis P, Roelofs K, Kuyk J et al. (2009). Trauma, stress, and preconscious threat processing in patients with psychogenic nonepileptic seizures. Epilepsia 50: 1001–1011.

Bakvis P, Spinhoven P, Putman P et al. (2010). The effect of stress induction on working memory in patients with psychogenic nonepileptic seizures. Epilepsy Behav 19: 448–454.

Bakvis P, Spinhoven P, Roelofs K et al. (2011). Automatic avoidance tendencies in patients with psychogenic non epileptic seizures. Seizure 20: 628–634.

Barry J, Reuber M (2010). The use of hypnosis and linguistic analysis to discriminate between patients with psychogenic non-epileptic seizures and patients with epilepsy. In: S Schachter, C LaFrance (Eds.), Gates and Rowan's non-epileptic seizures. Cambridge University Press, Cambridge, pp. 82–90.

Bell WL, Park YD, Thompson EA et al. (1998). Ictal cognitive assessment of partial seizures and pseudoseizures. Arch Neurol 55: 1456–1459.

Benbadis Sr (2005). A spell in the epilepsy clinic and a history of "chronic pain" or "fibromyalgia" independently predict a diagnosis of psychogenic seizures. Epilepsy Behav 6: 264–265.

Bernat JL (2010). The ethics of diagnosing nonepileptic seizures with placebo infusion. Virtual Mentor 12: 854.

Bernstein EM, Putnam FW (1986). Development, reliability and validity of a dissociation scale. J Nerv Ment Dis 174: 727–735.

Bewley J, Murphy P, Mallows J et al. (2005). Does alexithymia differentiate between patients with nonepileptic seizures, patients with epilepsy, and nonpatient controls? Epilepsy Behav 7: 430–437.

Birbeck GL, Vickrey BG (2003). Determinants of health-related quality of life in adults with psychogenic nonepileptic seizures: are there implications for clinical practice? Epilepsia 44: 141.

Bowman ES (2006). Why conversion seizures should be classified as a dissociative disorder. Psychiatr Clin North Am 29: 185–211.

Brown P, van Der Hart O, Graafland M (1999). Trauma-induced dissociative amnesia in World War I combat soldiers. II. Treatment dimensions. Aust N Z J Psychiatry 33: 392–398.

Brown R, Bouska J, Frow A et al. (2013). Emotional dysregulation, alexithymia, and attachment in psychogenic nonepileptic seizures. Epilepsy Behav 29: 178–183.

Cohen RJ, Suter C (1982). Hysterical seizures – suggestion as a provocative EEG test. Ann Neurol 11: 391–395.

Devinsky O, Sanchezvillasenor F, Vazquez B et al. (1996). Clinical profile of patients with epileptic and nonepileptic seizures. Neurology 46: 1530–1533.

Dimaro LV, Dawson DL, Moghaddam NG et al. (2014). Anxiety and avoidance in psychogenic nonepileptic seizures: The role of implicit and explicit anxiety. Epilepsy Behav 33: 77–86.

Duncan R, Duncan M, Oto AJC et al. (2004). Pseudosleep events in patients with psychogenic non-epileptic seizures: Prevalence and associations. J Neurol Neurosurg Psychiatry 75: 1009–1012.

Duncan R, Grahamb CD, Oto M (2014). Neurologist assessment of reactions to the diagnosis of psychogenic nonepileptic seizures: Relationship to short- and long-term outcomes. Epilepsy Behav 41: 79–82.

Eddy CM, Cavanna AE (2014). Video- electroencephalography investigation of ictal alterations of consciousness in epilepsy and nonepileptic attack disorder: Practical considerations. Epilepsy Behav 30: 24–27.

Ettinger AB, Devinsky O, Weisbrot DM et al. (1999a). A comprehensive profile of clinical, psychiatric, and psychosocial characteristics of patients with psychogenic nonepileptic seizures. Epilepsia 40: 1292–1298.

Ettinger AB, Weisbrot DM, Nolan E et al. (1999b). Postictal symptoms help distinguish patients with epileptic seizures from those with non-epileptic seizures. Seizure 8: 149–151.

Galimberti CA, Ratti MT, Murelli R et al. (2003). Patients with psychogenic nonepileptic seizures, alone or epilepsy-associated, share a psychological profile distinct from that of epilepsy patients. J Neurol 250: 338–346.

Gates JR, Ramani V, Whalen S et al. (1985). Ictal characteristics of pseudoseizures. Arch Neurol 42: 1183–1187.

Goldstein LH, Mellers J (2006). Ictal symptoms of anxiety, avoidance behaviour, and dissociation in patients with dissociative seizures. J Neurol Neurosurg Psychiatry 77: 616–621.

Goldstein LH, Drew C, Mellers J et al. (2000). Dissociation, hypnotizability, coping styles and health locus of control: characteristics of pseudoseizure patients. Seizure 9: 314–322.

Goldstein LH, Goldstein JDC, Mellers JDC (2006). Ictal symptoms of anxiety, avoidance behaviour, and dissociation in patients with dissociative seizures. J Neurol Neurosurg Psychiatry 77: 616–621.

Griffith J, Polles A, Griffith ME (1998). Pseudoseizures, families, and unspeakable dilemmas. Psychosomatics 39: 144–153.

Gulick TA, Spinks IP, King DW (1982). Pesudoseizures – ictal phenomena. Neurology 32: 24–30.

Hendrickson R, Popescu A, Dixit R et al. (2014). Panic attack symptoms differentiate patients with epilepsy from those with psychogenic nonepileptic spells (PNES). Epilepsy Behav 37: 210–214.

Hixson JD, Balcer LJ, Glosser G et al. (2006). Fear sensitivity and the psychological profile of patients with psychogenic nonepileptic seizures. Epilepsy Behav 9: 587–592.

Howlett S, Reuber M (2009). An augmented model of brief psychodynamic interpersonal therapy for patients with nonepileptic seizures. Psychotherapy 46: 125–138.

Hubsch C, Baumann C, Hingray C et al. (2011). Clinical classification of psychogenic non- epileptic seizures based on video- EEG analysis and automatic clustering. J Neurol Neurosurg Psychiatry 82: 955–960.

Ito M, Adachi N, Okazaki M et al. (2009). Evaluation of dissociative experiences and the clinical utility of the Dissociative Experience Scale in patients with coexisting epilepsy and psychogenic nonepileptic seizures. Epilepsy Behav 16: 491–494.

Kanner A, Parra J, Frey M et al. (1999). Psychiatric and neurologic predictors of psychogenic pseudoseizure outcome. Neurology 53: 933–938.

Kihlstrom JF (1985). Hypnosis. Annu Rev Psychol 36: 385.

Kuyk J, Spinhoven P, van Dyck R (1999). Hypnotic recall: A positive criterion in the differential diagnosis between epileptic and pseudoepileptic seizures. Epilepsia 40: 485–491.

Kuyk J, Siffels MC, Bakvis P et al. (2008). Psychological treatment of patients with psychogenic non-epileptic seizures: An outcome study. Seizure 17: 595–603.

LaFrance W, Syc S (2009). Depression and symptoms affect quality of life in psychogenic nonepileptic seizures. Neurology 73: 366–371.

LaFrance WC, Reuber M, Goldstein LH (2013). Management of psychogenic nonepileptic seizures. Epilepsia 54: 53–67.

Lakoff G (1993). The contemporary theory of metaphor. In: A Ortony (Ed.), Metaphor and Thought, 2nd edition. Cambridge University Press, Cambridge, pp. 202–251.

Lancman ME, Brotherton TA, Asconapé JJ et al. (1993). Psychogenic seizures in adults: a longitudinal analysis. Seizure 2: 281–286.

Lawton G, Baker G, Brown R (2008). Comparison of two types of dissociation in epileptic and nonepileptic seizures. Epilepsy Behav 13: 333–336.

Lawton G, Mayor R, Howlett S et al. (2009). Psychogenic nonepileptic seizures and health-related quality of life: The relationship with psychological distress and other physical symptoms. Epilepsy Behav 14: 167–171.

Luther JS, McNamara JO, Carwile S et al. (1982). Pseudoepileptic seizures – methods and video analysis to aid diagnosis. Ann Neurol 12: 458–462.

Lux S, Kurthen M, Helmstaedter C et al. (2002). The localizing value of ictal consciousness and its constituent functions – A video-EEG study in patients with focal epilepsy. Brain 125: 2691–2698.

Malmgren K, Reuber M, Appleton R (2012). Differential diagnosis of epilepsy. In: S Shorvon, M Cook, R Guerrini et al. (Eds.), Oxford Textbook of epilepsy and epileptic seizures. Oxford University Press, Oxford, pp. 81–94.

McGonigal A, Oto M, Russell AJC et al. (2002). Outpatient video EEG recording in the diagnosis of non-epileptic seizures: A randomised controlled trial of simple suggestion techniques. J Neurol Neurosurg Psychiatry 72: 549–551.

McKenzie P, Oto M, Russell A et al. (2010). Early outcomes and predictors in 260 patients with psychogenic nonepileptic attacks. Neurology 74: 64–69.

Meierkord H, Will B, Fish D et al. (1991). The clinical feature and prognosis of pseudo seizures diagnosed using video-ERG telemetry. Neurology 41: 1643–1646.

Mitchell JW, Ali F, Cavanna AE (2012). Dissociative experiences and quality of life in patients with non-epileptic attack disorder. Epilepsy Behav 25: 307–312.

Monzoni CM, Duncan R, Grünewald R et al. (2011a). How do neurologists discuss functional symptoms with their patients: A conversation analytic study. J Psychosom Res 71: 377–383.

Monzoni CM, Grünewald R, Reuber M et al. (2011b). Are there interactional reasons why doctors may find it hard to tell patients that their physical symptoms may have emotional causes? A conversation analytic study in neurology outpatients. Patient Educ Couns 85: e189–e200.

Opherk C, Hirsch LJ (2002). Ictal heart rate differentiates epileptic from non-epileptic seizures. Neurology 58: 636–638.

Owczarek K (2003). Somatisation indexes as differential factors in psychogenic pseudoepileptic and epileptic seizures. Seizure 12: 178–181.

Plug L, Reuber M (2009). Making the diagnosis in patients with blackouts: It's all in the history. Pract Neurol 9: 4–15.

Plug L, Sharrack B, Reuber M (2009). Seizure metaphors differ in patients' accounts of epileptic and psychogenic nonepileptic seizures. Epilepsia 50: 994–1000.

Plug L, Sharrack B, Reuber M (2010). The use of diagnostic labels by patients with epileptic or non- epileptic seizures. Appl Linguist 31: 94–114.

Plug L, Sharrack B, Reuber M (2011). Metaphors in the description of seizure experiences: Common expressions and differential diagnosis. Lang Cogn 3: 209–233.

Ponnusamy A, Marques J, Reuber M (2012). Comparison of heart rate variability parameters during complex partial seizures and psychogenic nonepileptic seizures. Epilepsia 53: 1314–1321.

Prueter C, Schultz-Venrath U, Rimpau W (2002). Dissociative and associated psychopathological symptoms in patients with epilepsy, pseudoseizures, and both seizure forms. Epilepsia 43: 188–192.

Rawlings G, Jamnadas-Khoda J, Broadhurst M, et al. (manuscript submitted). Panic symptoms in transient loss of consciousness: frequency and diagnostic value in the differentiation of psychogenic nonepileptic seizures, epilepsy and syncope. Manuscript in preparation.

Reuber M (2008). Psychogenic nonepileptic seizures: Answers and questions. Epilepsy Behav 12: 622–635.

Reuber M (2009). The etiology of psychogenic non-epileptic seizures: toward a biopsychosocial model. Neurol Clin 27: 909–924.

Reuber M, Elger CE (2003). Psychogenic nonepileptic seizures: Review and update. Epilepsy Behav 4: 205–216.

Reuber M, Kurthen M (2011). Consciousness in non-epileptic attack disorder. Behav Neurol 24: 95–106.

Reuber M, House A, Pukrop R et al. (2003a). Somatization, dissociation and general psychopathology in patients with psychogenic non-epileptic seizures. Epilepsy Res 57: 159–167.

Reuber M, Pukrop R, Bauer J et al. (2003b). Outcome in psychogenic nonepileptic seizures: 1 to 10- year follow- up in 164 patients. Ann Neurol 53: 305–311.

Reuber M, Pukrop R, Mitchell AJ et al. (2003c). Clinical significance of recurrent psychogenic nonepileptic seizure status. J Neurol 250: 1355–1362.

Reuber M, Howlett S, Khan A et al. (2007). Non-epileptic seizures and other functional neurological symptoms: Predisposing, precipitating, and perpetuating factors. Psychosomatics 48: 230–238.

Reuber M, Monzoni C, Sharrack B et al. (2009). Using interactional and linguistic analysis to distinguish between epileptic and psychogenic nonepileptic seizures: A prospective, blinded multirater study. Epilepsy Behav 16: 139–144.

Reuber M, Jamnadas-Khoda J, Broadhurst M et al. (2011). Psychogenic nonepileptic seizure manifestations reported by patients and witnesses. Epilepsia 52: 2028–2035.

Reuber M, Micoulaud-Franchi JA, Micoulaud-Franchi E et al. (2014). Comment ce que disent les patients peut nous renseigner sur leurs crises non épileptiques psychogènes. Neurophysiol Clin 44: 375–388.

Reuber M, Chen M, Jamnadas-Khoda J, et al. (2016). Value of patient-reported symptoms in the differential diagnosis of transient loss of consciousness. Neurology (in press).

Roberts NA, Reuber M (2014). Alterations of consciousness in psychogenic nonepileptic seizures: Emotion, emotion regulation and dissociation. Epilepsy Behav 30: 43–49.

Roberts NA, Burleson MH, Weber DJ et al. (2012). Emotion in psychogenic nonepileptic seizures: Responses to affective pictures. Epilepsy Behav 24: 107–115.

Rosemergy I, Frith R, Herath S et al. (2013). Use of postictal respiratory pattern to discriminate between convulsive psychogenic nonepileptic seizures and generalized tonic-clonic seizures. Epilepsy Behav 27: 81–84.

Schachter SC (2011). Evidence-based Management of Epilepsy. TFM Publishing, Shrewsbury, UK.

Schwabe M, Howell SJ, Reuber M (2007). Differential diagnosis of seizure disorders: A conversation analytic approach. Soc Sci Med 65: 712–724.

Schwabe M, Reuber M, Schondienst M et al. (2008). Listening to people with seizures: how can linguistic analysis help in the differential diagnosis of seizure disorders? Commun Med 5: 59–72.

Selkirk M, Duncan R, Oto M et al. (2008). Clinical differences between patients with nonepileptic seizures who report antecedent sexual abuse and those who do not. Epilepsia 49: 1446–1450.

Selwa L, Geyer J, Nikakhtar N et al. (2000). Nonepileptic seizure outcome varies by type of spell and duration of illness. Epilepsia 41: 1330–1334.

Stone J, Carson AJ (2013). The unbearable lightheadedness of seizing: Wilful submission to dissociative (non-epileptic) seizures. J Neurol Neurosurg Psychiatry 84: 822–824.

Syed T, Arozullah A, Loparo K et al. (2009). A self-administered screening instrument for psychogenic nonepileptic seizures. Neurology 72: 1646–1652.

Syed T, Lafrance W, Kahriman E et al. (2011). Can semiology predict psychogenic nonepileptic seizures? A prospective study. Ann Neurol 69: 997–1004.

Szaflarski JP, Hughes C, Szaflarski M et al. (2003). Quality of Life in Psychogenic Nonepileptic Seizures, MA, USA, Boston.

Tellez-Zenteno JF, Patten SB, Williams J et al. (2007). Psychiatric comorbidity in epilepsy: A population-based analysis. Epilepsia 48: 2336–2344.

Thompson R, Isaac C, Rowse G et al. (2009). What is it like to receive a diagnosis of nonepileptic seizures? Epilepsy Behav 14: 508–515.

Tojek TM, Lumley M, Barkley G et al. (2000). Stress and other psychosocial characteristics of patients with psychogenic nonepileptic seizures. Psychosomatics 41: 221–226.

Uliaszek AA, Prensky E, Baslet G (2012). Emotion regulation profiles in psychogenic non- epileptic seizures. Epilepsy Behav 23: 364–369.

van de Mortel T (2008). Faking it: social desirability response bias in self- report research. Aust J Adv Nurs 25: 40–48.

Vein AM, Djukova GM, Vorobieva OV (1994). Is panic attack a mask of psychogenic seizures? A comparative analysis of phenomenology of psychogenic seizures and panic attacks. Funct Neurol 9: 153–159.

von Fabeck F (2010). Zur Dynamik narrativer (Re-) Konstruktionen im Behandlungsverlauf dissoziativer Patienten, Bielefeld Doctoral Thesis, Kurzvorstellung Elisabeth Gütlich, Germany.

Waller NG, Putnam FW, Carlson EB (1996). Types of dissociation and dissociative types: A taxometric analysis of dissociative experiences. Psychol Methods 1: 300–321.

Watson N, Doherty M, Dodrill C et al. (2002). The experience of earthquakes by patients with epileptic and psychogenic nonepileptic seizures. Epilepsia 43: 317–320.

Whitehead K, Kandler R, Reuber M (2013). Patients' and neurologists' perception of epilepsy and psychogenic nonepileptic seizures. Epilepsia 54: 708–717.

Whitehead K, Stone J, Norman P et al. (2015). Differences in relatives' and patients' illness perceptions in functional neurological symptom disorders compared with neurological diseases. Epilepsy Behav 42: 159–164.

Witgert ME, Wheless JW, Breier JI (2005). Frequency of panic symptoms in psychogenic nonepileptic seizures. Epilepsy Behav 6: 174–178.

World Health Organization (1992). The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. World Health Organization, Geneva.