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Shame in patients with psychogenic nonepileptic seizure: A narrative review

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ABSTRACT

Psychogenic Nonepileptic Seizures (PNES) have been linked to dysregulated emotions and arousal. However, the question which emotions may be most relevant has received much less attention. In this multidisciplinary narrative review, we argue that the self-conscious emotion of shame is likely to be of particular importance for PNES. We summarize current concepts of the development of shame processing and its relationship with other emotional states. We demonstrate the potential of acute shame to cause a sudden disruption of normal cognitive function and trigger powerful behavioral, cognitive, physiological and secondary emotional responses which closely resemble key components of PNES. These responses may lead to the development of shame avoidance strategies which can become disabling in themselves. We discuss how excessive shame proneness and shame dysregulation are linked to several psychopathologies often associated with PNES (including depression and PTSD) and how they may predispose to, precipitate and perpetuate PNES disorders, not least by interacting with stigma. We consider current knowledge of the neurobiological underpinnings of shame and PNES. We explore how shame could be the link between PNES and a heterogeneous range of possible etiological factors, and how it may link historical aversive experiences with individual PNES events occurring much later and without apparent external trigger. We argue that, in view of the potential direct links between shame and PNES, the well-documented associations of shame with common comorbidities of this seizure disorder and the well-characterized relationship between chronic shame and stigma, there is a compelling case to pay greater attention to shame in relation to PNES. Its role in the treatment of patients with PNES is discussed in a separate, linked review incorporating case vignettes to highlight the complex interactions of different but interlinked shame-related issues in individual patients

1. Introduction

An emotion is the subjective experience of a mental state that directs our attention, guides our actions and is often accompanied by physiological and behavioral changes [1–3]. Traditional ideas of conversion and dissociation and more recent explanatory models based on emotion processing have linked Psychogenic Nonepileptic Seizures (PNES) closely with emotions [4]. In support of these theories, experimental studies have demonstrated abnormalities of emotion sensitivity, intensity, perception, tolerance, regulation and baseline arousal when comparing patients with PNES to those with epilepsy, healthy controls, or control groups with similar levels of trauma [5–8]. Clinical research has highlighted the overlap of manifestations of PNES with symptoms of arousal [9], and documented high levels of correlation of anxiety and avoidance as well as avoidance and seizure frequency in patients with PNES [10].

While observations like these firmly link dysregulated emotions and arousal with PNES, the question which emotions may be most relevant has received much less attention. In this article, we will argue that the self-conscious emotion of shame is likely to be of particular importance

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for PNES. While focussing on shame, we will also mention other self-conscious emotions such as guilt and embarrassment, although, for reasons discussed below, despite considerable subjective and neurobiological overlap with shame, these emotional states are likely to be less relevant in this clinical context.

We do not claim that shame is a necessary or sufficient factor in all PNES disorders or that our impression that PNES are commonly associated with shame is a novel discovery [11, 12]. However, given that there are few emotional states that are as comprehensively and deeply debilitating as shame, we argue that shame often makes a particularly important and – so far – relatively neglected contribution to PNES.

We note how the link between clinical symptoms and shame has been elucidated much more in relation to common PNES comorbidities such as posttraumatic stress disorder (PTSD) [13, 14], borderline personality disorder [15, 16], obsessive compulsive related disorders [17, 18] and depression [19], than it has in relation to PNES. It therefore strikes us that a discussion of the relationship between shame and PNES could provide a useful impetus to researchers and clinicians working in this field.

Importantly, we do not think that our call to pay more attention to shame means that our conceptual models of PNES have to be thrown overboard. Knowledge about the origins, development and effects of this emotion can easily be fitted into current biopsychosocial explanatory approaches and the 'Integrative Cognitive Model' of PNES [20, 21]. In fact, we will show how a fuller appreciation of shame can enhance these models and contribute to linking concepts, which focus on cognitive, emotional and physiological processes within one individual with PNES to the social and interpersonal environment in which these seizures arise. Shame can also help us understand how aversive experiences in early life may be linked to PNES disorders manifesting much later, or how recent stressors may trigger a PNES without externally perceptible triggers hours, days or weeks later.

2. Emotions: definitions and conceptual issues

Researchers have recognized an increasing number of more or less clearly separable emotions or "affective states" [22]. These states can be categorized in a number of ways, such as on a continuum of valence (how negative or positive the experience feels) and arousal (how 'strong' the experience feels), or as discrete emotions (e.g., basic emotions such as happiness, anger, fear). 'Social' or 'self-conscious' emotions, including shame, guilt, and embarrassment (as well as pride) are named as such because they require knowledge of the self and facilitate the maintenance of social goals, such as sustaining functioning of individuals within a group [23]. For similar reasons, shame, and guilt (along with certain forms of disgust) have also been described as 'moral' emotions [24].

2.1. Self-conscious emotions

An appraisal-based process model developed by Tracy and Robins suggests that experiencing any kind of self-conscious emotion requires focusing attention on public or private aspects of the self; appraising the eliciting event as relevant to one's personal goals; and attributing the cause of the event to internal factors that result in blaming or crediting the self [23]. For instance, failing an exam could cause feelings of shame or guilt if it was appraised as relevant to the person's identity and attributed to an internal failing, or feelings of anger, fear, or sadness if it was appraised as having an external cause.

This appraisal model draws on attribution theory (i.e., the causes people attribute to events). According to the model, the determination whether guilt or shame will be experienced in relation to an event requires a second level of appraisal: Whereas a negative event perceived to be due to internal, stable, uncontrollable and global causes (eg. "it happened because I'm a bad person'') would instill shame, an event attributed to internal, unstable, controllable and specific causes ("It happened because I did a bad thing'') causes guilt. In this context 'stable' refers to a part of the person that cannot change, 'global' to something likely to apply across different situations and 'uncontrollable' to something which is not an inherent characteristic of the person.

Put differently, whereas guilt is related to feeling bad about a particular act or omission, shame relates to the person one is. This understanding is in keeping with the established view that shame is a more aversive and potentially destructive state of self-criticism than guilt. It is consistent with the experience that shame can harm an individual's feeling of self-worth to such an extent that it only leaves them with the option of hiding away from their own inadequacy or of externalizing their perceived inadequacy through anger or hostility towards others [25].

This model accommodates the view and evidence that there is considerable overlap between shame and guilt and that it can be challenging to identify when someone is experiencing guilt versus shame [e.g., 26, 27, 28]. It is also consistent with the idea that shame is not *invariably* harmful or destructive. Indeed, while there is a large body of research linking chronic shame with "internalized" problems like depression, anxiety and low self-esteem, as well as "externalized" problems like hostility, aggression and anti-social behavior in children [29–31] adolescents [32–34], and adults [35–39], a theory-driven meta-analysis of 90 studies involving shame paradigms (N = 12,364) demonstrated that (similarly to guilt) shame *can* have positive consequences on thoughts or actions as long as failure or social image seem reparable. In contrast, negative consequences are likely when they are perceived as irredeemable [40]. In keeping with this, a number of recent studies have shown that recalled or current episodes of shame lead to a greater desire for self-improvement, cooperative behavior, and a more supportive orientation towards the victims of one's perceived moral failure [41–43].

2.2. Shame regulation

Whether emotions such as shame play protective or adaptive roles or are harmful depends not only on the emotional experience but also on timing, context, and how emotions are regulated. Emotion regulation describes a person's ability to respond and manage subjective, behavioral, and/or physiological responses, and includes seeking or avoiding emotion-eliciting situations [44]. As with other emotions, more frequent or intense shame experiences are likely to require greater effort to regulate this response [45]. Although emotion experience and regulation are therefore linked, it helps to distinguish 'emotion regulation' from 'emotion proneness'. More specifically, 'shame proneness' may be defined as a characteristic describing how likely an individual is to experience shame in response to a given situation [46]. One would talk of 'shame dysregulation' if there was inadequate regulation of the behavioral, cognitive, physiological and secondary emotional responses to the perceived shame. In individuals with excessive shame proneness and deficient shame regulation, compensatory interpersonal behaviors may become dominant and start to interfere with daily functioning. In contrast, if feelings of shame are insufficiently elicited, transgressions will not be followed by corrective behaviors and may cause interpersonal problems.

Schoenleber & Berenbaum [47], drawing on work on shame and emotion regulation, identified three broad maladaptive shame regulation strategies (see Fig. 1): 'prevention' (circumventing shame situations/experiences), 'escape' (disengaging from shame-eliciting situations), and 'aggression' (self- or other-directed acts attempting to manage shame experiences). This model was tested and received empirical support in individuals with borderline personality disorder, a condition characterized by emotion dysregulation and insecure attachment, which is often comorbid with PNES [48, 49]. All of the shame regulation activities included in this model are likely to be employed by patients with PNES. As argued below and illustrated in Fig. 1, PNES themselves usually involve a mixture of elements of escape and

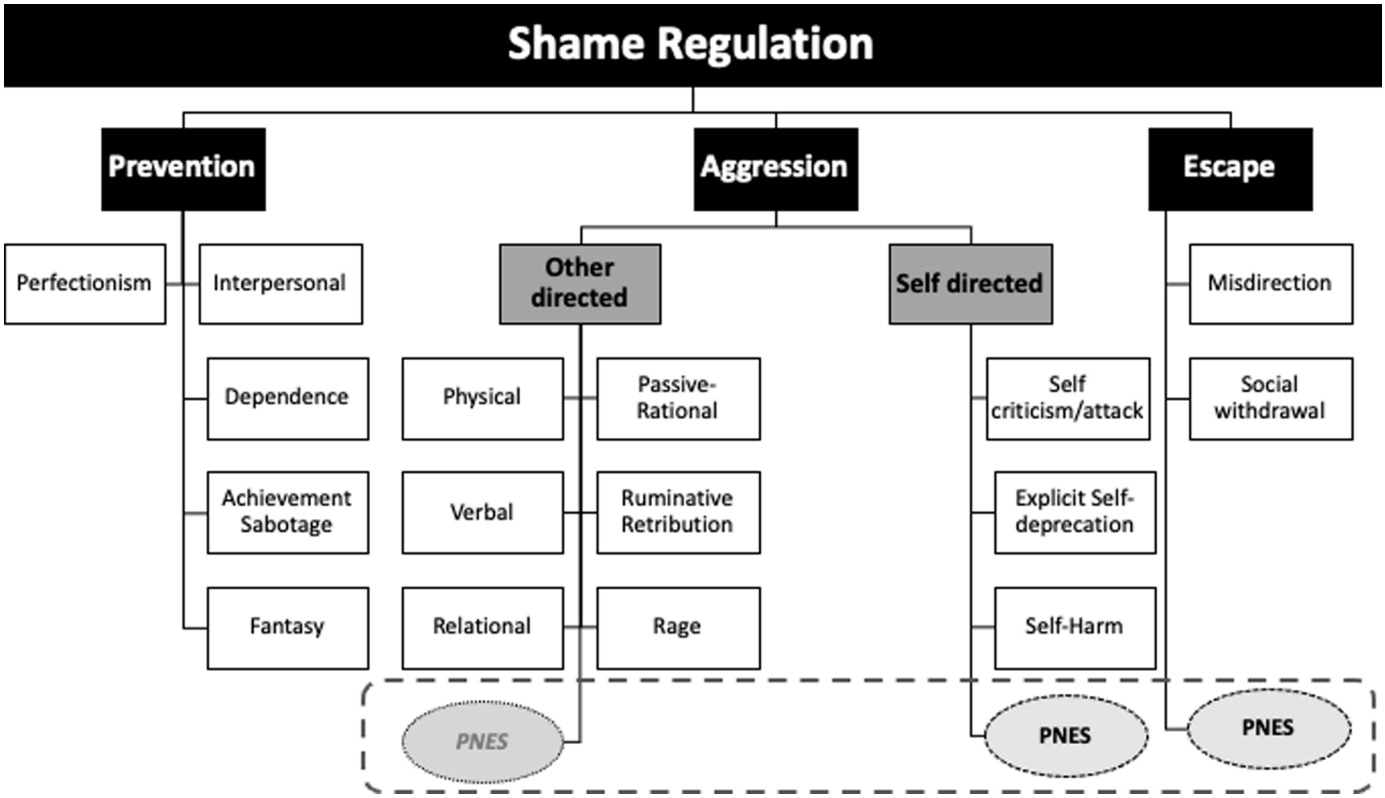

Fig. 1.. *Three broad maladaptive shame regulation strategies and their relation to PNES, where other-directed aggression is less prominent in PNES than self-directed aggression, as indicated by the lighter font (adapted from [47]).*

aggression (mostly self-directed, but also other-directed, typically in a passive-aggressive form).

3. Developmental aspects

The fact that shame processing plays a key role for healthy personal and social development but that dysregulated shame is also closely linked with psychopathology and abnormal social functioning underlines the importance of the developmental trajectory of shame [50].

3.1. Typical shame development

Basic emotions emerge very early in development. For instance, happiness is expressed at 6 weeks by the smile evoked by a human face. Self-conscious emotions, however, and initial manifestations of guilt-motivated behavior (e.g., reparations to mend transgressions; confessions for harmful acts, feeling badly about oneself, avoidance of the person who was transgressed upon) or shame reactions are not observed until 18–24 months of age [51–53]. These emotions can only occur once toddlers have become aware of themselves as separate individuals.

The self-concept [51, 54, 55] matures into a more stable set of self-representations around the age of 3 [56, 57]. In addition to the child's ability to evaluate the self and to differentiate between themselves and others, the processes underpinning the experience of shame and guilt depend on the capacity to empathize with others, and to understand social and moral standards [31, 58, 59]. Apart from self-awareness, the most important element for the normal development and processing of self-conscious emotions in young children is parental or caregiver input [31]. The experience of supportive parents tolerating missteps and perceived personal defects, and of parents providing comfort when children share such guilt- or shame-inducing experiences or perceptions, helps children to develop healthy levels of shame tolerance, regulation and management. In contrast, as described below, the lack of an appropriate parental response is likely to stifle the development of adequate shame management and regulation mechanisms, potentially leading to pervasive or hypersensitive shame reactions (i.e. excessive shame proneness), and/or avoidance or mislabeling of shame states.

As children grow older, observable shame responses become similar to those seen in adults. They involve cessation of movement, impassivity, and the child appearing to experience a disruption of behavior and thought processes [58, 60]. These responses become more pronounced during the preschool period as children's cognitive, language, social development and awareness advance and evolve further to late adolescence [59, 61]. In keeping with this, shame increases during adolescence. However, as individuals mature into adulthood they become better able to experience psychologically adaptive self-conscious emotions (such as guilt and authentic pride) and less prone to experiencing psychologically maladaptive ones (such as shame and hubristic pride) [62].

3.3. Atypical shame development: determinants and consequences

The level of shame proneness and tolerance as well as the triggers which elicit it are shaped by individual experiences, a person's sociocultural environment, and genetic factors [63]. In one study of healthy adolescents aged 14–17 years (N = 271) the association between self-reported early traumatic events and proneness to shame and guilt was moderated by the BDNF Val66Met status: trauma intensity was positively associated with guilt-proneness, but only in carriers of the low-expressing Met-allele of this gene [64]. The finding that levels of shame and guilt are higher in non-clinical and clinical samples of girls compared to boys could also be related to genetic factors (or gender-dependent gene-environment interaction), but experiential or sociocultural factors are also likely to play important roles [65, 66].

Poor parenting is the best studied determinant of excessive feelings

of shame. Adults who retrospectively report receiving low parental care and greater rejection are more prone to feel shame [67–69]. Studies with toddlers [70] and older children [71, 72] also suggest that children are at increased risk of shame expression if they have rejecting parents who provide little positive feedback. In a study on shame in young girls (aged 3–5), maternal and paternal authoritarian parenting predicted girls' shame responses [73]. Mills and colleagues also found that maternal shaming predicted shame responses in children from preschool to school age [74]. In addition, a longitudinal study has found that a history of paternal but not maternal depression and permissive parenting (measured when their children were 3 years old) predicted expression of shame and guilt by these children at the age of 6 [75].

Traumatic experiences in early life may compound the effects of unsupportive parenting and are often difficult to separate from it. This may be relevant in patients with PNES where studies have shown that sexual abuse is often associated with emotional neglect and broader family dysfunction [76][77–79].

Of course, the developmental aspects of shame perception need to be understood in the context of the development of an individual's broader emotion regulation capacity [80, 81]. Indeed, Szentágotai-Tătar & Miu [82] found that dysfunctional shame-proneness during adolescence was closely related to a broader pattern of maladaptive emotion regulation and to subsequent decreases in prosocial behavior.

The key role of dysregulated shame in the generation of manifestations of Borderline Personality Disorder has already been discussed (see Section 2.2). An inherited or acquired predisposition to excessive shame has also been linked to Posttraumatic Stress Disorder (PTSD), major depressive disorder (MDD), and obsessive-compulsive disorder (OCD) [83–86]. Similarly recurrent shame experiences, high shame proneness and inadequate shame regulation may lead to more frequent, prolonged or abnormally intense shame experiences in individuals with PNES, which could interact with anxious escape tendencies to promote excessively avoidant behaviors and a dynamic of increasing shame dysregulation. Depression research suggests that children excessively prone to shame (e.g., due to genetic factors and/or early life experiences) can enter self-reinforcing states of shame as they "focus attention on images of devaluation and rejection by others" [29, p.195]. Continual experiences of shame may reinforce these images and feelings over time, contributing to "feelings of helplessness and hopelessness about the self", increasing the risk of subsequent mood or behavioral disturbance [29, p.195]. Conceivably, shame-related erosion of the self could contribute to the lack of control patients with PNES report having over their seizures and to their very external health-related locus of control [87, 88].

4. Neurobiological underpinnings of shame

4.1. Brain regions associated with shame

In adults, a number of studies have examined neurobiological underpinnings of shame, most often alongside other self-conscious emotions - guilt and embarrassment; [89, 90], other negative emotions such as sadness [91], or positive self-conscious emotions such as pride [92]. In a review of 21 neuroimaging studies examining shame, guilt, and/or embarrassment [93], five specifically examined shame [86, 89, 90, 92, 94]. Neural activation unique to shame was observed in the dorsolateral prefrontal cortex, posterior cingulate cortex, and sensorimotor cortex [93]. Differences in neural activation were clearer when shame was compared with neutral conditions than in comparisons of shame and "control" emotions [93]. This is not surprising given the shared processes and neural substrates underlying emotional experience, such as language, conceptualization, and core affect [91].

In particular, one would expect overlap between shame and guilt. As described earlier, self-referential processing is a hallmark of both of these emotions; they require evaluation of or reflection on one's own behavior, as well as perspective-taking of another's state ("theory of mind"), and the integration of the two. As Zhu et al. [95] summarize, these processes are associated with activation of particular brain regions, specifically the anterior and posterior cingulate cortex for self-referential processing; superior temporal sulcus and temporo-parietal junction (TPJ) for theory of mind; and dorsomedial prefrontal cortex (dmPFC) for their integration, as well as anterior insular cortex and amygdala for salience and emotional processing. Indeed, during an interpersonal decision-making task designed to evoke shame or guilt both emotions were associated with greater (left) anterior insula and (bilateral) dmPFC activation, compared with experiences of happiness [95]. Comparing shame and happiness, shame showed greater activation in these regions than happiness - but guilt did as well. Further, Zhu et al. (2019) [95] found support for their prediction that guilt would show greater activation than shame in regions related to perspective-taking (left supramarginal gyrus, right TPJ) and cognitive control (right vlPFC/OFC and right dlPFC). Given that the right TPJ has been implicated in generating a sense of agency [96], it is possible that guilt responses – albeit subjectively uncomfortable – may coincide with greater feelings of agency, whereas shame-proneness may not yield this benefit.

Even if neural activation does not consistently and widely distinguish shame from other emotions, the neurobiological changes that occur during shame experience are noteworthy. For example, in Bastin et al.'s [93] review, anterior insular cortex was activated in all (100%) instances of shame elicitation, compared with neutral elicitation. The anterior insula facilitates mapping of interoceptive signals to conscious awareness and contributes to the experience of feelings [97–99]. Thus, shame may be linked to the essence of "self" in a very real way, which perhaps is what leads its experience to be so profound and self-defining.

Given the role of self-referential processing in shame as described above, shame-associated neural activation patterns could create a more negative (and shame-oriented) sense of self. Among those with remitted MDD, during a scripted (hypothetical scenario) imagery task, shame compared to guilt was associated with increased activation in the amygdala and posterior insula, whereas this was not the case among non-depressed controls [100]. This underscores the potential for shame to be integrated with one's neurobiology in ways that "outlast" overt signs and symptoms of a clinical syndrome such as MDD and could represent one particular link between shame-inducing traumas in early life and the emergence of PNES in adolescence or adulthood. Other clinical disorders offer further examples of how differences in neural processing associated with psychopathology may predispose to (or result from) pervasive shame states. Among women with PTSD, self-referential processing shows a different neural activation pattern than in controls - right amygdala activation, rather than the typical anterior cingulate cortex activation (perigenual region) – in response to positive self-descriptors (which the authors speculate might be beneficial in this context) [101]. Individuals with OCD not only endorse elevated, more pervasive shame on self-report measures than healthy controls, but also show different patterns of neural activation in response to shame- and guilt-inductions using sentences – such as greater parahippocampal gyrus, middle temporal gyrus, and hypothalamic activation to shame versus neutral conditions, as opposed to greater fronto-parietal activation for controls – perhaps suggesting heightened encoding and elaboration ("vividness") of shame in OCD, versus typical affect regulation and processing of shame stimuli [17].

4.2. Shame and activation of the autonomic nervous system

Studies of autonomic nervous system indicators of emotional arousal provide further insights into the neurobiology of shame. Respiratory sinus arrhythmia (RSA), or high-frequency heart rate variability, has received particular attention as an indicator of parasympathetic nervous system engagement (cardiac vagal control). Higher resting state RSA is associated with calm, regulated mood states [Reviewed in, 102]. Among healthy controls, greater RSA reactivity or "vagal flexibility" – higher

baseline RSA followed by greater RSA decreases (vagal withdrawal) to a stressful speech task – was associated with greater self-reports of shame in response to negative social evaluation, yet less shame in response to positive feedback [103]. This echoes the perspective that shame in itself is not problematic if it is linked to a specific, appropriate context and is relatively short-lived, whereas an undifferentiated and unrelenting experience of shame is potentially more harmful. In a study of females with PTSD due to interpersonal trauma (physical and/or sexual assault/abuse), shame proneness (self-reported shame during the past month) and current reports of shame/guilt (combined across ratings of these two emotions) were associated with lower RSA during a resting baseline, trauma-related images (10 slides presented 5 s each), and a 2-minute recovery period after trauma image-viewing. Further, shame/guilt but not fear/anxiety was associated with lower RSA during the post-trauma-image recovery period [104]. This suggests that shame/-guilt experiences in response to traumatic stress reminders may have longer-lasting physiological effects than other emotions. It is worth noting that shame-related alterations of heart rate variability may be associated with other biological factors capable of contributing to poor long-term physical and mental health, as threats to the "social self" resulting in shame are associated with greater HPA (cortisol) and proinflammatory cytokine responses [105].

5. Shame and PNES

In the next section of our review, we list arguments supporting the idea of a close link between PNES and shame. Any relationship between a putative emotional process and its visible manifestations – such as how shame might be associated with a seizure-like condition – is undoubtedly complex. We will argue that shame-inducing stimuli may not only trigger and shape individual seizures but that heightened shame proneness and shame dysregulation contribute to the etiology of PNES disorders as predisposing, precipitating or perpetuating factors (see Fig. 2).

Shame-stimulus processing may not only link trauma in early life with PNES in later life but shame-inducing memories could also explain the common temporal dissociation between acute stressors and the occurrence of PNES in a more reflective, apparently peaceful moment. In a specific PNES, shame-related involvement likely reflects a mixture of shame itself and the person's reaction to this intolerable emotional state (including dissociated awareness and rage).

5.1. Phenomenology of PNES and shame

PNES can present with a range of semiologies but the most common manifestations demonstrate at least some overlap with the behavioral changes associated with shame and its immediate processing in the form of self- or other aggression (or rage) and escape (see Fig. 1). The facial expressions of shame include downward gaze aversion and downward head movement [107–110]). The body is often lowered, shoulders slump; the upper torso seems to collapse [111]. This corporeal behavior seems consistent with the shame-associated urge to vanish, hide or die to escape the intense discomfort associated with shame. The realization that one's own practical or moral standards have not been met results in the halting of behavior. This may include the disruption of thought processes and an inability to speak.

In the best study of the observable semiology of PNES, two raters studied video recordings and looked for 22 signs in 145 PNES episodes collected from 52 patients [112]. The most commonly observed signs included axial immobility (72.3%), closed eyes (60.9%), tremor (43%) and sudden onset (41.4%). The mouth was often tightly closed. Other studies have demonstrated that 95% of patients with PNES exhibit impaired responsiveness in their seizures. Almost all patients with PNES report seizure-related memory gaps [113]. Vocalization is relatively infrequent in PNES - it was only observed in 18.6% of seizures examined in the study cited above [112].

Many of the differences in the visible manifestations of acute shame and the semiology of PNES may be explained by the immediate processing of the initial shame-trigger in terms of self- and other-directed aggression and escape (dissociation). While assaults on others (such has biting, hitting or scratching) are an infrequent manifestation of PNES, auto-aggressive acts (such has hitting the self or seizure-related self-injury) are relatively common and could be manifestations of levels of hostility or aggression which have been found to be higher in those with PNES than healthy controls of patients with other somatoform disorders [114]. PNES may also have a passive aggressive

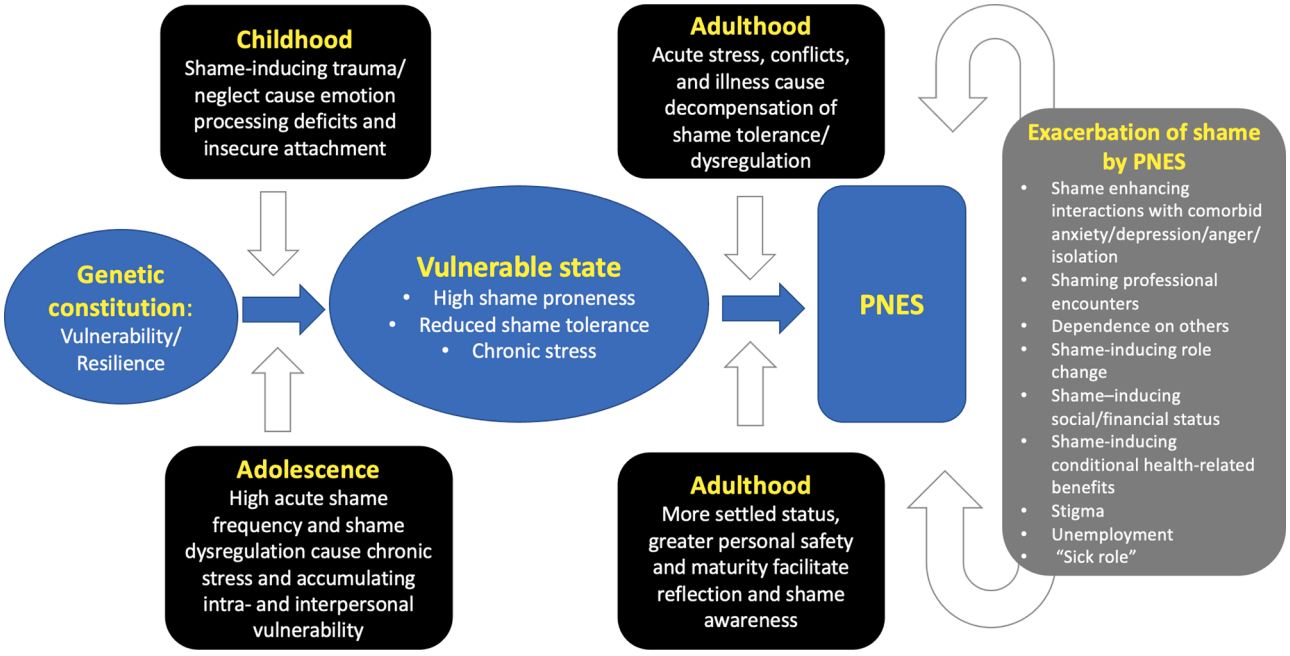

Fig. 2.. Model of how shaming experiences, shame proneness, shame dysregulation and stigma may contribute to the etiology of PNES disorders as predisposing, precipitating or perpetuating factors (adapted from [106]).

component (for instance by punishing or controlling others [114]).

Similarly to the autonomic manifestations of acute shame, PNES are associated with a 'fight / flight / freeze' response characterized by a reduction in parasympathetic and an increase in sympathetic tone [104, 115]. Like women with PTSD and elevated levels of shame proneness [116], patients with PNES (at group level) are characterized by reduced RSA and chronic hyperarousal in the interictal state [117, 118]. Although in one study RSA reactivity (change from baseline) did not differ between PNES and Trauma Controls while they relived a shameful memory, some individuals from the PNES group did not complete the task due to feeling overwhelmed, and therefore the greatest autonomic responders were likely excluded [119]. The process of dissociation of awareness may help individuals to switch from a hyperaroused 'ictal' state to one of recovery: studies of heart rate variability document physiological arousal before and during an episode (high sympathetic tone), and diminished arousal immediately afterward (an increase in vagal tone) [120, 121]. These observations are in keeping with the interpretation that dissociative seizures are a kind of cognitive and emotional 'reset' which stops the processes that have elicited the seizure.

Indeed, this switch may be one of the factors why some patients report 'wilfully submitting' to a PNES [122].

While PNES may bring relief from a distressing emotional state in the short term, the very nature of most seizures is likely to achieve the opposite effect of a 'normal' shame response: whereas the behavioral withdrawal associated with feeling shame makes a person less conspicuous, the visual manifestations and interpersonal consequences of PNES are likely to draw attention to the person, their seizures and their underlying causes. This may well increase the shame experienced by patients with PNES and make subsequent PNES more likely. It could be one of the reasons why PNES often occur in clusters [123] and why chronic PNES disorders are often particularly difficult to treat.

5.2. Shame as a trigger of PNES

As mentioned above, in one study exploring the relationship between shame and PNES, when asked to relive a shameful memory, a subset of those with PNES were unable or unwilling to do so. In other participants shameful memories triggered a PNES episode; this did not happen with other emotions (anger, happiness), nor were any noteworthy behavioral responses to the evocation of a shameful mempry observed among clinical controls (e.g., asking to stop the task, removing the physiological sensors, leaving the room) [119]. While further research still has to confirm the shame-PNES and shame-avoidance-PNES relationship in patients' daily lives, a relationship between shame, shame avoidance and PNES may be suggested by the observation of PNES during psychotherapy. Especially in early psychotherapy sessions, when, touching upon a traumatic and shameful memory, the patient may exhibit an almost immediate, visceral reaction, and go into a seizure [124]. Additional evidence may emerge as therapy progresses and patients become better able to tolerate and verbalize their emotional discomfort without seizing [125]. Often they can then describe the nature of their discomfort. As shame diminishes, PNES do as well.

5.3. Trauma, adversity, neglect and shame in the etiology of PNES

There is a well-documented association of PNES and trauma in early life, i.e., at a point in a child's development when the neurobiological and psychological mechanisms underpinning self-conscious emotions are evolving [126–128]. Although difficult to study, quantify or compare in terms of its relevance in relation to other aetiological factors, emotional neglect during this developmental stage may be even more prevalent than trauma [129, 130]. Excessive shame-proneness or the dysregulation of shame processing are plausible links between these developmental adversities and subsequent psychopathology including PNES, which may intersect with individual predisposing biological vulnerabilities as previously identified in stress-diathesis models of PNES [131]. As stated above, high levels of shame in early life are a risk factor for subsequent psychopathology.

Patients with PNES also report high rates of trauma in adulthood and symptoms of PTSD are common in this patient group [132, 133]. Shame has been identified as an important mediator between early experiences of trauma and subsequent PTSD [13]. Shame is also likely to be a key emotion in individuals whose PNES appear to be related to be related to experiences involving 'moral injury'. Such injuries have been described in veterans with PNES in whom they are often associated with PTSD [134]. They have been defined as the lasting psychological, biological, behavioral, spiritual, and social impact of "perpetrating, failing to prevent, bearing witness to, or learning about acts that transgress deeply held moral beliefs and expectations" [135]. Furthermore, shame could play a role in the substantial subgroup of patients with PNES who deny a history of major trauma or significant neglect. In some of these patients, PNES disorders may be precipitated by life events which do not have the characteristics of major trauma, although they are traumatizing for the individual concerned because of their previous life experiences or particular circumstances [136, 137]. Some of these life events – for instance the loss of employment or illness leading to a significant change in status or self-perception – could be linked to PNES through intolerable levels of shame [138]. Shame may also be the key mediator between "unspeakable" secrets and forced choices with no good outcome, which one research group identified as an underlying dynamic leading to PNES in 13 of 14 families [11].

5.4. Emotion processing abnormalities associated with PNES

As discussed above, early life experiences of trauma and neglect, as well as severe traumatic experiences in later life, are closely associated with the subsequent dysregulation of emotions. While PNES may arise in the context of over- or underregulated emotions [139, 140], and a broad range of abnormalities of emotion processing have been described in patients with PNES [4], avoidance and alexithymia are most prominent [141]. Avoidance could be considered universal for PNES if dissociation is interpreted as an acute avoidance mechanism. Excessive avoidance also characterizes the non-seizure thinking and behavior of many patients with PNES [10, 142]. Alexithymia has been identified in over 90% of patients with PNES [143]. These clinically important traits can arise as a consequence of the combination of trauma and shame. For instance, in individuals with eating disorders, shame has been shown to play a central role in the perception of an adverse self-image. Evidence suggests that, in this clinical context, alexithymia may result from previous unelaborated traumatic experiences and feelings of shame [144]. Shame has also been identified as a mediator between current distress and alexithymia [145]. In other words, it may explain why an important subgroup of patients with PNES have difficulties identifying or describing their emotions or acknowledging previous traumatic experiences [146].

PNES in patients with a history of trauma could be triggered by acute shame with dissociation functioning as a shame avoidance mechanism. This mechanism could effectively suspend these patients in a state of alexithymia, to which they may already have been predisposed, by 'protecting' them from fully realizing their own distress, vulnerability or helplessness [147]. In the absence of being able to adequately label one's own emotional state, other "safe" interpretations of bodily sensations – such as heightened attention to somatic cues (which in turn may trigger or perpetuate PNES episodes; [148]) – may fill the gap. This interpretation of PNES could explain the phenomenon that, compared to patients with focal epileptic seizures involving anxiety, those with PNES are more likely to acknowledge 'physical' ictal arousal than 'mental' anxiety symptoms, an observation which has given rise to the interpretation of PNES as attacks of "panic without panic" [149].

Paradoxically, the dissociation associated with PNES may also disrupt the individual's ability to fully "access" and process shame

experiences. Thus, it may require extra effort to do so, and, in some cases, an inability to do so without intervention and re-training. As studies with other clinical populations reveal (see Section 4.1), atypical neural processing of shame may result in its persistence or more consequential repercussions for emotional functioning.

5.5. Comorbid mental disorders

There is a complex relationship between PNES and "comorbid" mental disorders. Only about one third of patients with PNES do not meet DSM-4 diagnostic criteria for another current mental disorder [150]. While depression is the commonest mental disorder identified in patients with PNES, more specific links exist between PNES, anxiety disorders, PTSD and personality disorders [151], especially borderline personality disorder. In view of the role that increased chronic shame, shame-proneness and dysregulated shame may play in these disorders, shame could be a common mediator between the causes and manifestations of these mental illnesses and PNES. As such, shame could serve as a unifying etiological factor that helps to explain some of the clinical and psychopathological heterogeneity which characterizes PNES patient populations.

5.6. PNES and stigma

Over 90% of patients with PNES report being affected by stigma [152], and those who feel stigmatized have a lower Health Related Quality of Life [152, 153]. Among those with PNES, Stigma is most likely perceived by those people with high levels of anxiety and low self-control or education [154]. This stigma could be related to the lack of acceptability of mental disorders: many patients certainly experience the re-labeling of their seizure disorder from epilepsy – in itself a heavily stigmatized disorder – to a 'psychiatric' condition as stigmatizing [153, 155]. However, there are also bidirectional links between stigma and shame. Chronic shame can arise as a result of societal stigmatization based on salient aspects of one's identity, e.g., gender, health status, disability, race, sexuality, weight or ethnicity. However, high shame proneness and the low levels of self-esteem associated with it are also likely to increase vulnerability to stigma [147]: We note that the process of stigmatization [as described by, 156] has a lot in common with the experience of shame (cf guilt) - both involve the identification of a relevant difference from a norm that is taken to signify a flawed individual (in the case of stigma) or self (in the case of shame). Patients' self-perception of a 'spoiled identity' may therefore make those with PNES particularly vulnerable to the perception of stigma and interact with (very real) enacted societal stigma to drive levels of shame up to a level at which it becomes debilitating or pathological and affect a person's life chances, relationships and health outcomes [157].

5.7. Possible neurobiological links between PNES and shame

While our understanding of the neurobiological processes underpinning PNES remains incomplete, there is considerable overlap between patterns of regional activation and functional connectivity implicated in PNES pathophysiology or shame experiences. To date, knowledge of PNES and pathophysiology more broadly in Functional Neurological Symptom Disorder (FND) implicates multiple neural circuits and networks, including those underpinning sensorimotor, attentional, emotional, and cognitive control processes (i.e., sensorimotor and TPJ; salience; limbic; dorsal and ventral attention; cognitive control and motor planning) [158, 159]. Particular attention has been paid to the *salience* network [160], including the anterior and middle cingulate cortex, insula, amygdala, and periaqueductal gray [161]. Disruptions in these networks coincide with challenges appropriately attending to, prioritizing, and interpreting internal and external emotional/sensory information. These challenges may be magnified in shame, which is at the intersection of self- and other- evaluation because it involves self-reflection vis-à-vis social norms. Indeed, studies of functional connectivity in PNES (and functional movement disorders) point to alterations in connectivity among regions relevant to self-referential processing (TPJ, posterior cingulate cortex, precuneus) [159, 162].

Another possible account of the pathogenesis of PNES based on dysfunction in these networks and centres implicates poor interoception as a key factor [163]. Poor interoception, reflected in heightened attention to or misinterpretation of somatic cues [164], may be associated with generation of subsequent "prediction errors" [165], as well as a disrupted sense of self or self-agency (a sense of voluntary control over one's physical actions) [162]. Success in these latter domains requires appropriate recruitment of the anterior insula (sense of self) and TPJ (sense of self-agency), as is the case in shame and other self-conscious emotions (described earlier). Thus, we speculate that neurobiological vulnerabilities associated with disruptions in these other processes in PNES might coincide with disruptions in constructive experiencing and processing of self-conscious emotions also. For example, there is a lack of agency demonstrated in PNES and other FNDs [166, 167] – both behaviorally and in terms of neurobiological correlates (e.g. decreased connectivity in the right TPJ). We can speculate that those with PNES may be less likely to experience guilt, which also is associated with TPJ activation and is a relatively agentic state, often motivating reparations or corrective action. Instead, when confronted with a troubling interpersonal situation, neurobiological vulnerabilities may lead individuals with PNES to appraisals and response tendencies favoring shame and withdrawal.

6. Summary

This narrative review has drawn attention to the potential importance of the social emotion of shame to PNES, a disorder characterized by an episodic disruption of normal levels of self-control and awareness, in which seizures are usually interpreted as a dissociative response to internal or external triggers associated with aversive emotions. Although shame arguably pervades much of the literature on the presentation and etiology of PNES, it has rarely been explicitly named in previous writings on PNES. In this review, we have demonstrated how well much of what we know about the early development of shame and the factors which determine normal or abnormal shame development (like the presence or absence of healthy attachments in early life, and the experience of trauma in early or later life) matches what we know about factors predisposing to the development of PNES. What is more, excessive levels of shame and reduced shame tolerance or increased shame avoidance may also represent important links between predisposing and precipitating or triggering factors of PNES disorders. We argue that a close association of PNES with shame may interact with enacted stigma (which is clearly experienced by patients around the world [168] and thereby exacerbate disabilities directly related to seizure experiences.

As has been suggested for PTSD, an aetiological model centrally incorporating shame may compliment previous fear avoidance models of PNES. In such an aetiological model for PNES, potential genetic factors co-determining shame sensitivity and tolerance interact with life experiences (especially attachment experiences and traumatic life events in early childhood) to create a level of vulnerability characterized by elevated shame proneness, low shame tolerance, and dysregulated shame processing. Shame-related problems are exacerbated by the public exhibition of emotion processing which patients may perceive their dissociative seizures to represent, and by a vicious circle involving the stigma associated with having a mental disorder and the shame fostered by the self-perception of a 'spoiled identity'.

These ideas are in keeping with the current understanding of the neurobiological underpinnings of shame and PNES: Mounting evidence for connections between limbic and motor control circuits may help explain triggers of PNES [169]. Experiences of shame may be more central to these emotion-motor connections than previously recognized, given that shame is also associated with activation in motor-related

areas (SMA, cerebellum). In short, models of PNES suggest emotion-triggered unfiltered/ungated motor output. Shame may be one of the most important emotions triggering PNES, for physiological reasons based on the regions involved in self-conscious emotion processing, as well as the theoretical clinical reasons outlined above. In other words, the "pain" of shame may be physically and neuropsychiatrically embodied.

7. Limitations

We fully acknowledge the limitations of this review and of our understanding of the relationship between shame and PNES. The subjectivity, lack of universally accepted definitions (of shame or PNES) or widely used validated measures makes emotions such as shame difficult to study or discuss. These difficulties are compounded by the fact that patients are likely to find it much harder to talk about shame than about other emotions and a dearth of research specifically focusing on the role of shame in those with PNES. In view of the lack of directly informative studies, most of our arguments rely on associations or indirect evidence linking PNES with shame. Pending further research we admit that, even if associations between PNES and shame exist, relationships may not be directly causal but implicate other factors such as comorbidities of PNES or shared risk factors for chronic shame or abnormal shame responses and PNES such as early childhood trauma and neglect.

8. Conclusions

Despite these limitations we think that there is a compelling case for researchers to explore chronic shame and shame dysregulation in patients with PNES. Even in the absence of further evidence, the well-recognized links between excessive shame and common comorbidities of PNES such as depression and PTSD and the well-characterized relationships between chronic shame and stigma suggest that clinicians providing care for patients with PNES need to be alert to the importance of shame in patients with this disorder. Interested readers are referred to a linked review to learn more about the role of shame in the treatment of PNES disorders [170].

Declaration of Competing Interest

Markus Reuber: Payments from Elsevier as Editor-in-Chief of Seizure, educational grant from UCB Pharma. Markus Reuber and Lorna Myers: Income from book authorships (including books about PNES). None of these interests should have any bearing on the content of this article. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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