

**Unraveling the Seizure Spectrum: Differentiating Between Psychogenic
and Epileptic Seizures**

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Abstract:

Psychogenic non-epileptic seizures (PNES) present a unique clinical challenge, sitting at a crossroads of neurology and psychiatry. This thesis explores the potential pathophysiological and psychological framework of PNES, comparing them to epileptic seizures to outline the differences and similarities between these two distinct conditions. Through an in-depth literature review, this will examine the physical manifestations of PNES, the diagnostic criteria, and factors contributing to these event misclassifications. Additionally, this work investigates the root causes of PNES, particularly the role of psychological stress, trauma, and mental health disorders in their onset. Key research questions focus on understanding the mechanism of PNES both physiologically and psychologically, identifying the criteria for precise diagnostic practices, and exploring the complex relationship between mental health and seizure manifestations. By analyzing current literature on both PNES and epilepsy, this research aims to clarify the boundaries between neurological and psychiatric diagnoses, while also addressing the stigma associated with PNES. The findings are expected to inform future research directions, diagnostic approaches, and treatment strategies, ultimately expanding the literature exploring the understanding and management of PNES in medical and psychological contexts.

Introduction:

Seizures are neurological events characterized by sudden and uncontrolled bursts of electrical disruption in the brain's nervous tissue that cause a broad spectrum of changes in behavior, sensation, locomotion, or consciousness. Epileptic seizures are a widely recognized neurological condition within medicine and society, caused by rapid and excessive electrical disruptions in the brain. Psychogenic non-epileptic seizures (PNES) are not associated with any measurable electrical disruption. Instead, PNES are thought to be the result of psychological

factors, often assumed to be a reaction to severe stress and trauma, or other mental health conditions.

Psychogenic non-epileptic seizures mimic epileptic seizures in their subjective manifestations, such as changes to speech or movement, but have not been proven to have a similar physiological causation. PNES is categorized as a functional neurological disorder, in which psychological components, such as trauma or underlying mental health conditions, trigger physical manifestations that resemble epileptic seizures. PNES episodes can involve shaking, convulsions, loss of consciousness, and many more symptoms, similar to epileptic seizures. Nonetheless, during a PNES episode or collection of symptoms, there is no measurable change to the electrical activity of the brain via neurological monitoring. Scientific experts, such as Dr. Elaine Wyllie (2024) of the Cleveland Clinic Lerner College of Medicine at Case Western Reserve University explain in further detail that cerebral activity of the brain continues during a typical episode of PNES symptoms, proving that these events are not due to neurological fault. The deficit of any abnormal neural markers, during intense PNES symptoms, allows us to differentiate PNES from epilepsy and points to the root of the disease not relating to dysfunction of the neural firing in the brain.

Epileptic Seizures are classified as neurological events resulting from abnormal, excessive electrical impulses in the brain, due to inappropriate and untimely activity of neurons. These seizures can arise from a multitude of origins, including but not limited to brain injury, genetic factors, or metabolic abnormalities. The physical signs and symptoms of epileptic seizures are widely inconsistent and varying, depending on the part of the brain affected and whether it is a focal (localized) or generalized (widespread) seizure. They may involve convulsions, loss of consciousness, sensory disturbances, and loss of motor function. Diagnosis

is typically confirmed through an electroencephalogram (EEG) recording - a test that measures the electrical activity within the brain, which indicates distinct electrical disruptions during epileptic seizure activity.

Both epileptic seizures and PNES can present with similar outward symptoms, such as convulsions, unresponsiveness, or changes in awareness, making it difficult to distinguish between the two conditions based on observation alone. However, PNES often presents with more variable, prolonged, or abnormal seizure characteristics that are rarely seen in epilepsy. In the *Seminars in Pediatric Neurology* journal, Albert (2022) explains how psychogenic seizures have distinct characteristics that indicate a psychological origin, rather than epileptic. A typical PNES episode will present with a fluctuation of symptoms, prolonged seizure duration, asynchronous and arrhythmic movement of the limbs, forced closure of the eyes, thrusting of the hips or shoulders, shaking the head side-to-side, and emotional disruption shown through crying or grimacing. While many patients who experience epileptic seizures will experience a loss of memory following an event, PNES patients will typically retain memory and be able to recall the event afterward. Emotional stressors can trigger PNES, while epileptic seizures often occur without an immediate psychological trigger. Ultimately, many distinguishing signs and symptoms between PNES and epilepsy help guide professionals in uncovering the mechanisms of both conditions.

Despite significant advancements in diagnostic methods such as EEG and neuroimaging, major gaps remain in the comprehensive understanding of both epileptic seizures and PNES. In epilepsy, the etiology of this condition can be easily identified through imaging or genetic analysis, but in many cases, the exact causal agent remains unknown. For PNES, the exact pathophysiological mechanisms that relate psychological distress to seizure-like manifestations

are still poorly understood by medical professionals. The physiological and psychological complexity of both PNES and epilepsy causes slowed development of innovations for treatment or diagnostics that may better the quality of life for patients.

Although PNES and epileptic seizures share outward physical phenomena, their underlying causes appear to be fundamentally different. However, in some patients, both conditions may coexist, and the diagnostic process can be challenging due to overlapping symptoms. Precise differentiation is critical, as the treatments and management for these two conditions differ significantly. In this literature review, I aim to better explain the complexities of the seizure spectrum by analyzing, combining, and comparing known information on these conditions from a variety of peer-reviewed sources.

Literature Review:

Overview of PNES:

Psychogenic non-epileptic seizures (PNES) are episodes of muscle convulsion, with varying triggers based on the individual patient. These seizures are presumed to be of psychological origin, arising from the conversion of emotional or mental stress into physical symptoms, without resulting in changes in neurological signaling of the brain. These events, which fall into the category of functional neurological disorders, occur without detectable abnormalities in brain structure or electrical activity. PNES is commonly associated with underlying trauma, anxiety, depression, or chronic psychological distress, with episodes acting as a dysfunctional response to overwhelming emotions. Patients frequently experience these seizures in patterns that appear episodic, where unique symptoms appear suddenly and last far longer than typical epileptic seizures, often exceeding ten minutes. Although many medical

professionals predict that PNES is a purely psychological event, no scientifically confirmed mechanism explains how PNES occurs on a physiological level.

Symptoms and Episode Patterns:

PNES symptoms often only occur for limited periods of time, when many symptoms overlap and appear in a patterned manner, these are called episodes. Experts have noted that during these episodes, individuals generally exhibit physical behavior resembling epileptic seizures, including rapid and disorganized jerking of the limbs, which may move in opposite directions. Unlike epilepsy, patients may remain cognitively aware during the event and are capable of retaining memories of the seizure experience. Other typical behaviors, such as pelvic thrusting, rhythmic shaking, dystonic positioning, or abrupt shifts in movement, are commonly observed. Some episodes involve vocalizations, with patients groaning, screaming, or weeping while presenting distinct changes in the pitch of their voice. These symptoms can occur regardless of whether the patient's eyes are open or closed, further complicating the clinical presentation (Jafari et al., 2020).

A prominent difficulty in expanding the understanding of PNES is due to patients exhibiting a diverse range of symptoms with varying intensity and triggers. Many patients report a strong connection between increased emotional, mental, or physical stress and the onset of these episodes. Stressors often include unresolved trauma, interpersonal conflict, fatigue, or periods of heightened anxiety, and it is common for individuals with PNES to have co-morbid conditions such as post-traumatic stress disorder (PTSD) or generalized anxiety disorder (GAD), emphasizing the complexity of the disorder.

Pathophysiology of Epilepsy:

Despite their similar appearance, PNES is distinct from epilepsy, a neurological condition marked by abnormal electrical activity in the brain. Epilepsy involves improper or excessive discharge from neurons, which creates faulty electrical stimuli that can affect the entire brain or specific regions, resulting in symptoms like loss of consciousness, convulsions, or other motor and sensory disturbances. Epilepsy originates from damage to normal conversion processes of neurological information in the brain, which results in hyperactivity of neuronal discharge. Disruptions to ion homeostasis, defective proteins causing abnormalities in receptor function, and subsequent improper binding of neurotransmitters provide a cellular explanation for the failure of neuronal processes within epilepsy patients.

Notably, the excessive production and release of excitatory glutamic acid stimulates a drastic increase in intracellular calcium ion (Ca^{2+}) concentration in neurons, ultimately activating proteases - enzymes that degrade proteins, destroying important cellular architecture. Increased concentration of glutamic acid also triggers an increase in the release of nitric oxide (NO), initiating oxidative stress and causing the production of toxic free radicals that cause irreversible DNA injury.

Alan W.C. Yuen, Mark R. Keezer, and Josemir W. Sander (2018) discuss this issue in their article in the *Epilepsy and Behavior* journal, titled *Epilepsy Is a Neurological and a Systemic Disorder*. They state, "Oxidative stress is thought to disrupt intracellular calcium homeostasis gradually, leading to increased neuronal excitability, seizure susceptibility, and vulnerability to additional stress and neuronal cell loss" (p. 59). The combination of these

biological processes can eventually lead to cell death of brain and nerve tissue in cases of severe and consistent seizures, often in patients who do not receive proper epilepsy treatment.

The large-scale death of neurons resulting from epileptic seizure episodes further exasperates symptoms and serves as an etiological factor for the majority of comorbidities. Yuen, Keezer, and Sander also explore these comorbidities in their article for the *Epilepsy and Behavior* journal. They explain that people with epilepsy are more likely to experience both neurological and non-neurological conditions in tandem. Key neurological associations include issues like stroke, dementia, and migraines, while non-neurological conditions such as heart disease, hypertension, chronic obstructive pulmonary disease, and cancer also occur at higher rates compared to the general public. This further demonstrates the widespread consequences of severe epilepsy, which can be traced to a distinct pathophysiological factor.

Classification of PNES:

Conversely, psychogenic non-epileptic seizures (PNES) cannot be traced back to a distinct neurological dysfunction. PNES is classified as a conversion disorder, also called a functional neurological disorder (FND), which results from the conversion of psychological stress into visible physical manifestations. Conversion disorders are diagnosable by clinical examination based on specific criteria. As seen in Figure 1, the criteria are as follows: There must be an indicator of at least one neurological symptom that disrupts the peripheral nervous system's typical motor or sensory function. Additionally, the onset of symptoms must have a direct correlation to some emotional stressors. Physical manifestations must be involuntary and uncontrollable - not a result of an external factor, like substance use or another medical

condition. Lastly, conversion disorders must cause a significant increase in psychological stress during or following a symptomatic period (McCutcheon, 2022).

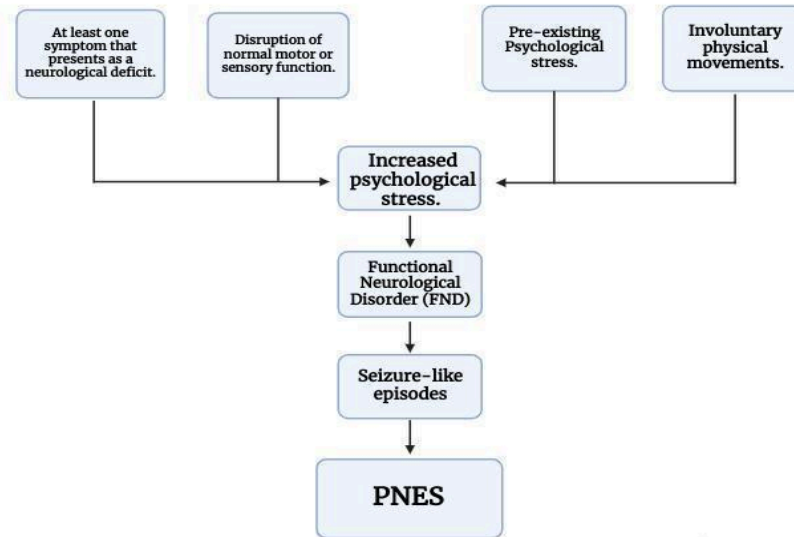


Figure 1: Depiction of the relationship between FND and PNES by Kennedy Jones, created with BioRender.com (2024).

There is a well-recognized connection between PNES and improper signaling to the peripheral nervous system, responsible for innervating skeletal muscle which maintains out-of-phase muscle contractions seen in this condition. Although this relationship is crucial to the mechanism of these seizures, the exact pathophysiological mechanism remains unknown.

Proposed Mechanisms for PNES:

Although the exact biological mechanism for PNES remains unknown, many scientists have developed hypothetical models that attempt to explain the relationship between

psychological overwhelm and physical convulsions. For some time, scientists and clinical professionals alike have debated whether PNES is a psychological or neurological condition. However, many conclude that this condition is likely a stress response that alters the communication of neurological processes. The following information provides several mechanisms proposed by scientific experts to explain this condition, although, this is not a comprehensive list of all existing theories.

a. PNES and Stress Conversion:

Ian E. McCutcheon (2022), of The University of Texas M. D. Anderson Cancer Center, hypothesizes that convulsions can be thought of as a means to express or relieve extreme psychological stress, functioning as an involuntary act of self-expression. McCutcheon further explains his theory on the relationship between psychological and neurological processes in his article titled *“Seizures and Pseudoseizures: The Great Divide”*. McCutcheon states: “Such conversion of inner distress to an outward expression of clinical symptoms allows patients to relieve that conflict, at least to some degree. Often, depression and/or anxiety underlie the conversion of emotional pain to physical pain. In this sense, pain without any apparent physical trigger can manifest as a form of conversion disorder; so too can pseudoseizures.” (p. 145).

b. Dissociative Mechanism:

Gaston Baslet (2011) proposes two models to explain these phenomena in his article titled *“Psychogenic Non-Epileptic Seizures: A Model of their Pathogenic Mechanism”*. Baslet first suggests that PNES symptoms may originate from dissociation, which impairs the integration of information in cognitive processing. Dissociation often occurs due to unresolved mental distress, and many patients exhibit alexithymia - an impaired ability to distinguish

between psychological emotions and bodily sensations. The consequences of dissociation in PNES patients can lead to cognitive deficits, ultimately triggering the use of pre-wired behavioral tendencies. Supporting this dissociation model, Baslet explains that individuals with PNES have consistently heightened cortisol levels throughout the day, regardless of whether they experience an event. This pattern aligns with what is observed in dissociative disorders, where basal diurnal cortisol levels are elevated, and there is reduced cortisol suppression in response to the dexamethasone suppression test (DST). The similarities in cortisol patterns between PNES patients and those with dissociative disorders suggest a direct co-morbidity, indicating that both conditions arise as a direct consequence of increased stress.

Cortisol is widely considered to be the “stress hormone” that initiates a variety of physiological processes in response to psychological stress. The dexamethasone suppression test (DST) measures the ability of the adrenal gland to secrete cortisol. In this test, patients are given dexamethasone - a synthetic corticoid intended to inhibit the release of cortisol from the adrenal glands. In patients with severe stress-linked psychological disorders, dexamethasone will fail to inhibit cortisol release, indicating hyperactive dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis (Crespo et al., 2020).

c. Selective Attention Mechanism:

The second model Baslet theorizes involves excessive, selective attention, where patients concentrate the vast majority of their cognitive resources on a single distressing thought or sensation, with limited ability to shift their attention. This mechanism is thought to resemble the process of intrusive thoughts, which is a common co-morbid condition to PNES. Somatization supports this model, proposing that the symptoms arise from bypassing the cognitive processing

of emotions. Clarifying this concept, Baslet explains that in somatization, emotional states and arousal are believed to manifest physically as movements of the body without engaging neurocognitive processing. In contrast, conversion or dissociation is thought to involve neurocognitive processing in the development of symptoms. This perspective supports the idea that somatization functions as an avoidance mechanism. Thus, when PNES originates from somatization, it may represent a psychological mechanism to avoid processing emotional distress by converting it into physical symptoms.

d. Anticipated Seizure Scaffold:

Richard J. Brown and Markus Reuber (2016), in their article titled “*Towards an Integrative Theory of Psychogenic Non-Epileptic Seizures (PNES)*” for the *Clinical Psychology Review*, theorize that PNES is due to an anticipatory psychological mechanism. This mechanism suggests that PNES occurs when a patient experiences elevated threat perception in response to pre-conditioned or external cues, such as reminders of traumatic experiences or increased anxiety in unfamiliar or overwhelming environments. An increase in perceived threat triggers the patient to have a latent anticipation that a seizure episode may develop under stressful conditions. The increased stress of predicting the onset of seizures will activate the seizure scaffold and PNES symptoms will occur. As seen in Figure 2, their theory suggests that PNES is a repeated cognitive behavior, a vicious cycle that continuously validates PNES symptoms as their seizure behavior consistently aligns with the patient's foreseeing of events.

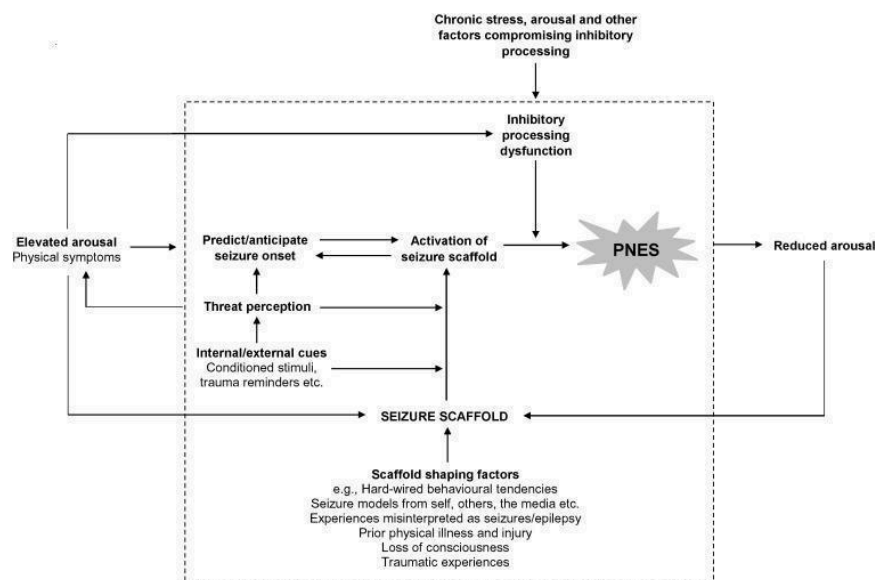


Figure 2: Visualization of the anticipated seizure scaffold mechanism (Brown, Reuber, 2016).

Comparison of Epilepsy and PNES Mechanism:

When someone falls to the ground and exhibits convulsive movements, it is often assumed to be epilepsy; however, conditions like PNES reveal that this assumption is not always accurate. Epileptic seizures are marked by symptoms such as convulsion, shaking, and abnormal limb movement, resulting from neurological overload that disrupts standard brain function, causing abnormal physical behavior. Although psychogenic non-epileptic seizures (PNES) may resemble epileptic seizures in appearance or sensation, they are not caused by the same electrical overload. Instead, PNES is typically triggered by psychological disorders or other sources of extreme mental stress. While these two conditions may appear similar, they differ fundamentally and require distinct diagnosis, treatment, and management methods (Chen, 2019).

Diagnostics:

In both conditions, outward symptoms may appear similar, but their diagnostic processes vary. Epilepsy is diagnosed through electroencephalogram (EEG) testing, which records abnormal electrical discharges during seizures. In contrast, PNES does not exhibit such electrical abnormalities. Even during episodes involving dramatic physical symptoms, EEG results for PNES patients remain within relatively normal limits, indicating the absence of neurological dysfunction. Unlike epilepsy, PNES diagnosis requires rigorous psychological evaluation alongside EEG testing. This distinction highlights the importance of comprehensive diagnostic approaches to differentiate between the two conditions, as accurately identifying the underlying cause is crucial for effective treatment. Understanding these diagnostic methods in detail can provide greater insight into how clinicians distinguish between neurological and psychogenic seizure events.

Diagnosis of Epilepsy:

Clinical evaluation may suggest to a physician that a patient may have epilepsy, presenting with seizure-like muscular convulsions, and staring spells, with subsequent periods of temporary confusion, anxiety, or fear. Patients may also exhibit stiffness and soreness following seizures. While these symptoms are often associated with epilepsy, clinical evaluation alone is insufficient to provide a definitive epilepsy diagnosis, as conditions like PNES can present nearly identical symptoms. A conclusive diagnosis of epilepsy requires video EEG, which allows for simultaneous observation of physical symptoms and corresponding brain activity.

A patient suspected of having epilepsy will undergo video EEG monitoring, in which brainwaves will be recorded simultaneously with a video of the patient's physical behavior. EEG leads are placed on the patient's scalp to capture the brain's electrical activity. This procedure is conducted while the patient experiences seizure-like symptoms, allowing medical professionals to analyze the brainwave patterns concerning the onset, duration, and conclusion of seizure-like episodes. Physicians may need to provoke seizures to occur, by having the patient undergo sleep deprivation, exposure to flashing lights, or engage in strenuous exercise.

In epilepsy, the video EEG reveals distinct abnormal brainwaves, such as short-duration spikes or longer-duration sharps, both indicating a patterned, hypersensitive neuronal discharge. Prabhu D. Emmad and Arayamparambil C. Anilkumar (2023) reflect on the source of epileptic seizure activity, in their article "*EEG Abnormal Waveforms*". The authors explain that Interictal epileptiform discharge (IED) is an irregular synchronous electrical secretion from a collection of neurons in the region where epileptic abnormalities occur, that occur in between seizure episodes - which will often be seen in the EEG of epilepsy patients. However, these discharges have low sensitivity during routine 30-minute EEG recordings, and epilepsy diagnostics may improve with repeated or prolonged EEG monitoring. IED is a major indicator that seizure activity is a result of epilepsy, although several other EEG abnormalities may also contribute to an epilepsy diagnosis.

Diagnosis of PNES:

The diagnostic process for PNES shares many similarities with that of epilepsy. Patients with a PNES diagnosis may also present with convulsions and staring spells, followed by periods

of heightened mental distress and muscle soreness. However, factors such as a history of chronic stress, mental health disorders, or severe trauma may lead physicians to suspect PNES rather than epilepsy. Additional diagnostic clues include patterned out-of-phase limb movements or rapidly changing patterns of convulsion. Despite these indicators, a video EEG test and psychological evaluation are essential for confirming a diagnosis. In patients with PNES, the video EEG will show no epileptogenic brainwave activity during or after seizure episodes. Video EEG monitoring, which combines continuous EEG recording with real-time video observation of seizures, distinguishes it from epilepsy. When used appropriately, it prevents misdiagnosis and avoids unnecessary treatments that might otherwise be prescribed under the assumption of epilepsy.

Ian McCutcheon (2022), in his article *“Seizures and Pseudoseizures: The Great Divide”* explains that subtle yet noticeable changes in EEG patterns may occur during PNES episodes - however, while abnormal, they do not indicate epileptic seizure. He states: “During continuous EEG monitoring of the patient with intermittent pseudoseizures, the onset of a clinical episode typically correlates with a very sudden switch from normal background waking rhythm to a more chaotic EEG tracing in which the waveforms are obscured by movement and muscle artifact.” (p. 148). This suggests that the distinctive muscle convulsion seen during PNES episodes produces abnormal EEG patterns. Nevertheless, these EEG irregularities are minimal and distinct from epileptic patterns.

Other experts, such as Dr. Elaine Willie (2024), MD, emphasize that EEG recordings during PNES episodes typically show no considerable change in brainwave patterns. Unlike many conditions resulting from neurological deficits, video EEG serves as a highly effective diagnostic tool for PNES, as normal cerebral rhythms during seizures confirm that the events are

non-epileptic. The potential for brainwave irregularities in PNES is a topic that remains under investigation, although the general professional belief is that EEG irregularities should not be present in PNES. This lack of detectable neurological disruption on EEG helps differentiate PNES from epilepsy, further solidifying its classification as a functional, rather than structural, neurological disorder.

Co-Morbid Epilepsy and PNES:

While distinguishing between epilepsy and psychogenic non-epileptic seizures (PNES) is essential for developing an effective treatment plan for the individual patient, it is important to recognize that co-occurrence of both epilepsy and PNES is possible, although not extremely common. Typically, when the two conditions co-exist, PNES is thought of as a co-morbidity to epilepsy. When the conditions are comorbid, PNES is suspected to be a repeated behavior that has a weaker relationship to mental health conditions.

A recent study titled “*Psychogenic non-epileptic (functional) seizures in adults with intellectual disability and epilepsy: A matched case-control study*” examined a population of 540 adults who had been diagnosed with both intellectual disability and epilepsy, that were screened for PNES. The study found that out of 540 participants, 42 (7.8%) were also diagnosed with PNES. Notably, PNES in individuals with intellectual disability and epilepsy was primarily described as a reinforced behavioral pattern, with limited associations with psychiatric disorders (Kloosterman et al., 2024). These findings highlight the complexity of diagnosing comorbid PNES and epilepsy, which can complicate the curation of effective long-term treatment plans.

Treatment:

Although PNES and epilepsy share some symptomatic similarities, their treatment approaches differ significantly. Epilepsy is primarily managed through pharmaceutical interventions, particularly anticonvulsant medications that work by modulating neuronal activity. In contrast, PNES treatment emphasizes an integrated pharmaceutical and psychotherapy approach. Moreover, the types of medications used for these conditions differ in classification - while epilepsy is treated with anticonvulsants, PNES treatment often involves selective serotonin reuptake inhibitors (SSRIs) to address underlying psychological distress. Diagnostic differentiation between PNES and epilepsy is crucial, to avoid mistreatment and avoidable complications.

Mistreatment for both epilepsy and PNES patients can pose significant risks. Epilepsy patients receiving improper care may face an increased risk of life-threatening or disabling seizures, placing the patient in an extremely vulnerable state. In contrast, while PNES patients do not typically experience life-threatening symptoms, mistreatment often causes a drastic worsening of their symptoms and quality of life. Therefore, accurate differential diagnosis and the development of an appropriate treatment plan are of great importance.

Treatment of Epilepsy:**a. Pharmaceutical:**

Treatment for epilepsy involves a combination of pharmacological and non-pharmacological approaches customized to the patient's seizure type, frequency, and overall state of health. The primary form of treatment is anti-epileptic drugs (AEDs), which modulate neuronal excitability through mechanisms such as sodium channel inhibition, GABA enhancement, and glutamate antagonism. Common AEDs include carbamazepine and lamotrigine which lessen seizure severity by stabilizing sodium channels in an inactive state. Other medications such as valproate stimulate the production of Gamma-aminobutyric acid (GABA), ultimately modifying the flow of chloride ions into the cell, resulting in a more stable cell membrane. Regardless of their specific mechanism, all AEDs minimize seizure activity by inhibiting or modulating the electrochemical gradient across the cell membrane and stabilizing neuronal excitability (Ochoa, 2024).

Determining which AED will be used is based on the patient's seizure profile. However, a significant portion of epilepsy patients will benefit from alternative treatments in tandem with their AEDs. Notably, some epilepsy patients may be resistant to treatment with AEDs, showing no changes in seizure activity when taking their medication.

b. Non-Pharmaceutical:

Non-pharmaceutical approaches are crucial for patients who exhibit drug-resistant epilepsy, as these patients present with a high incidence of life-threatening complications of their epileptic seizures. A comprehensive review published in *Biomedicines* outlines various pharmacological and non-pharmacological approaches to epilepsy treatment, emphasizing the evolving role of anti-epileptic drugs, surgical interventions, and alternative therapies. The authors highlight that options such as surgery, dietary interventions, and neurological therapies

are considered. Surgery may be recommended on a case-by-case basis and is dependent on a variety of factors. Dietary changes, such as switching to a ketogenic diet, have been shown to modify neurotransmitter balance and gene expression causing positive results in epilepsy patients. Additionally, a medical device may be used to stimulate the Vagus nerve, delivering programmed electrical impulses to the brain via the Vagus nerve, in an attempt to reduce seizure frequency in patients who respond poorly to medication (Ghosh et al., 2021).

c. Surgical:

The most common form of surgery to treat epilepsy is resective surgery, which is used for focal seizures that only affect a portion of the brain. In this procedure, the surgeon will remove a small segment of brain tissue in the affected area. Typically, the resected portion will be in the temporal lobe which is responsible for visual memory, comprehension of language, and emotions, as this is where focal seizures occur most often. Other surgical procedures may include deep brain stimulation where an electrical stimulation device is permanently placed on the brain to disrupt seizure-inducing neuronal activity, or laser interstitial thermal therapy (LITT) where a laser is used to destroy the portion of the brain associated with seizure mechanisms. Additionally, corpus callosotomy or hemispherectomy procedures may be performed to remove larger pathogenic portions of the brain (Mayo Clinic, 2024).

Treatment of PNES:

In treating PNES, the approach aligns with that of many mental health conditions, often incorporating psycho-education, therapy or mental health counseling, and pharmacological

intervention. Given the condition's strong association with stress, trauma, and overall mental well-being, the most critical aspect of an effective treatment plan is to begin by approaching the diagnosis with respect, empathy, and patient education. This process starts with the neurologist, whose role extends beyond simply providing a diagnosis using EEG and psychological evaluation. Neurologists will ensure that patients and their families understand that PNES is not epilepsy, that the events will not cause brain damage, and that seizure episodes do not need to be treated with emergency medical care. Ongoing involvement from the neurologist should support the patient's care and help prevent unnecessary medical intervention, such as inappropriate usage of anti-seizure medications (LaFrance et al., 2023). Ideally, the neurologist's care integrates into a multidisciplinary team - including psychiatrists and psychologists - to develop a comprehensive treatment plan.

a. Cognitive Behavioral Therapy:

In a study by LaFrance et al. (2014), titled "*Multicenter Pilot Treatment Trial for Psychogenic Nonepileptic Seizures: A Randomized Clinical Trial,*" researchers examined the effectiveness of cognitive behavior therapy (CBT) and pharmacological treatment with serotonin reuptake inhibitors (SSRIs) for managing PNES symptoms. The study concluded that CBT resulted in a significant reduction in the frequency of seizure episodes and the intensity of associated symptoms, whether administered alone or in combination with SSRI medication.

CBT is a psychological treatment approach aimed at reducing symptoms of various mental health conditions. This method focuses on identifying and reframing mental stressors as a combination of learned behaviors and self-reinforcing negative thoughts (Society of Clinical Psychology, 2017). The primary goal of CBT is to equip patients with effective coping strategies

to help manage stress, trauma, or other mental health challenges with greater effectiveness. Since PNES is a functional disorder often rooted in significant mental stress, CBT is a highly effective component of symptom management - although it does not cure the condition.

b. Pharmaceutical:

The use of SSRIs in the treatment of PNES is further supported by a study published in the *Journal of Neuropsychiatry and Clinical Neurosciences*, titled “*Efficiency of Venlafaxine in Patients With Psychogenic Nonepileptic Seizures and Anxiety and/or Depressive Disorders*”. In this study, researchers administered PNES patients with increasing doses of venlafaxine, a commonly prescribed SSRI, over a five-month period while monitoring seizure activity. The results indicated that after five months of treatment, 88.2% of participants experienced a 50% reduction in seizure frequency compared to baseline levels (Pintor et al., 2010). These findings suggest that SSRI usage can be remarkably effective in reducing PNES symptoms, although the exact mechanism by which SSRIs exert this effect remains unclear.

SSRIs work to alleviate symptoms of anxiety and depression through their action on the serotonin transporter (SERT), which is responsible for the reuptake of serotonin from the synaptic cleft into the pre-synaptic neurons. By inhibiting SERT, SSRIs allow for an increase in the concentration of serotonin in the synaptic cleft. Additionally, SSRIs cause downregulation of 5-HT receptors which disinhibits the neuron and causes an increase in the electrical firing rate, resulting in an increased serotonin release that further contributes to serotonin accumulation in the synaptic cleft (Guzman, 2016). The elevated serotonin concentration in the synaptic cleft is thought to help reduce feelings of depression, hopelessness, and anxiety. Given that PNES patients see a drastic reduction in symptoms when treated with SSRI medications, it suggests a

potential underlying dysfunction in the serotonin pathway. While SSRIs demonstrate great benefits for PNES patients and enhance their quality of life, they have yet to provide insight into the etiology of PNES. Additionally, SSRIs are not intended to be used as the sole treatment for patients. Treatment of PNES is most effective with a combination of pharmaceuticals, psychological therapy, and lifestyle changes, alongside other methods.

c. Patient Education:

Effective treatment for PNES patients greatly depends on how medical professionals convey the diagnosis. In her article, *“Psychogenic Nonepileptic Seizures: A Neurologist’s Perspective”*, Dr. Elaine Wyllie (2024), MD, offers insights into the role of neurologists in the diagnosis and management of PNES. She highlights that a neurologist’s approach can either facilitate patient acceptance and accelerate the treatment process or, conversely, lead to the patient feeling shamed or frustrated, which can worsen symptoms by increasing stress and emotional turmoil. Dr. Wyllie describes her approach to initiating the diagnosis conversation: “We are happy that we are not dealing with a new diagnosis of epilepsy, and that there is no need for treatment with antiseizure medication. The next step is for us to consult our expert colleague in psychiatry, who will help you develop a plan to stop the episodes by quieting and controlling the mind-body reflex that is causing the problem.” (p. 261). This highlights the major impacts of perceived judgment on PNES patients, a topic that scientific experts have begun investigating with more consideration.

Ensuring that patients feel supported, free from shame, and clearly understand their condition during the diagnostic process is essential. Many individuals with PNES may initially reject the diagnosis and continue seeking an epilepsy diagnosis due to the stigma associated with

psychological conditions. This denial can result in delayed or inappropriate treatment, often exacerbating their symptoms.

Stigma and PNES:

There is a clear link between PNES and psychiatric disability, with one of the most challenging aspects of the condition being the effects of societal stigma and shame often associated with psychological disorders. For PNES patients, misunderstandings about the condition frequently lead to the assumption that their symptoms are exaggerated or fabricated, for the patient to gain attention. While well-educated individuals know this to be false, the pressure and shame resulting from these misconceptions can still place a large amount of stress on PNES patients. This increased stress may exacerbate symptoms and delay patients' willingness to seek help and treatment for their condition, ultimately hindering their ability to effectively manage their symptoms.

A group of researchers conducted a study, titled "*Stigma in Psychogenic Nonepileptic Seizures*", which examined the stigma experienced by PNES patients and caregivers through an in-depth survey. Among 43 PNES patients and 165 epilepsy patients, 75.6% of those with PNES and 59.5% of those with epilepsy reported feeling stigmatized due to their condition. Similarly, among 28 caregivers of PNES patients and 99 caregivers of epilepsy patients, 72% of PNES caregivers and 47% of epilepsy caregivers reported feeling stigmatized in their caregiving role (Karakis et al., 2020). These findings highlight the drastic impact of stigma on those with seizure disorders, with PNES patients and caregivers more likely to feel judged by society.

PNES patients may experience greater levels of stigma due to pervasive misconceptions about mental health, often causing doubts about the validity of their condition and subsequent symptoms. Epilepsy, on the other hand, is widely recognized as a legitimate medical condition, backed by extensive research and public awareness, which creates validation and support from both peers and healthcare professionals alike. Furthermore, the lack of a well-defined etiology and effective treatment plan for PNES may lead some to doubt the authenticity of the condition, whereas epilepsy's established etiology and treatment contribute to greater acceptance and understanding.

PNES patients who experience chronic shame or embarrassment related to their condition, or who have co-morbid psychological conditions, may find that their PNES symptoms are aggravated as a result. It is presumed that these patients may enter a self-perpetuating cycle in which shame elevates stress levels, leading to an increase in the frequency and intensity of seizure symptoms, which in turn promotes further shame and emotional distress.

In a 2022 study, investigators explored shame as a component of the mechanism of PNES in their article "*Shame in Patients with Psychogenic Nonepileptic Seizure: A Narrative Review*". They inspect various factors that may contribute to shame and embarrassment in patients and delve into how shame development may relate to symptom expression. The authors conclude that shame is likely the most important emotion involved in triggering PNES symptoms, based on the regions of the brain that are associated with self-conscious processing of emotions and clinical evidence combined. They propose that the emotional impact of shame may manifest both physically and psychologically, deepening the complexity of PNES symptomology (Rueber et al.).

Results:

The information presented above reveals the complexities of psychogenic non-epileptic seizures (PNES), encompassing disease mechanisms, symptomatology, diagnostics, treatment approaches, and influential psycho-social factors, including stigma. This analysis supports the classification of PNES as a stress-related conversion disorder, associated with maladaptive stress management, leading to the somatization of seizure-like episodes. Importantly, PNES is not driven by neurological impairment; patients consistently demonstrate normal neuronal activity across all stages of the disorder, in contrast to epilepsy, where distinct neurological dysfunction underlies epileptic seizures.

The absence of neurological pathology differentiates the treatment pathways for these conditions. Management of PNES should involve a combination of cognitive behavioral therapy (CBT), pharmacological support, and social support utilizing a multidisciplinary approach. Epilepsy, conversely, requires anticonvulsant medications and is primarily managed through neurological interventions. Accurate differentiation between these conditions prevents misdiagnosis and inappropriate treatment, as PNES may be misidentified as epilepsy. Misdiagnosis may lead to unnecessary emergency medical interventions and unwarranted treatment.

Stigma and social shame associated with seizure disorders impact both PNES and epilepsy patients, often exacerbating the condition. In PNES specifically, heightened stigma and shame may further intensify symptoms. Despite this comprehensive analysis of contributing

factors and resultant impacts of PNES, the precise pathological mechanisms and consistently effective treatments remained undetermined.

Discussion:

Existing literature contributes to a differential understanding of psychogenic non-epileptic seizures (PNES), highlighting the complex interplay between psychological and physiological factors that distinguish them from epileptic seizures. This thesis affirms that while PNES and epileptic seizures may present with overlapping symptoms, their underlying causes are profoundly different, making it necessary to distinguish diagnostic and treatment approaches. Notably, this work confirms the identification of stress and trauma as primary influences on the manifestation of PNES, which can inform future interventions that aim to address the underlying pathophysiological triggers. However, substantial gaps remain, specifically regarding how these triggers are translated into PNES seizures. Understanding this psycho-physiological process remains essential for advancing treatment methods that may effectively mitigate symptoms and improve patient quality of life.

Future research on PNES should focus on uncovering the biological mechanism of the disorder, aiming to bridge the gap between psychological origins and physical manifestations. One of the most important unanswered questions is how this condition occurs at the pathophysiological level, especially as there is no evidence of neurological abnormalities. Additionally, refining diagnostic criteria to ensure accurate and early identification of PNES remains vital, as misdiagnosis can lead to ineffective treatment. Further studies should also consider the long-term efficacy of various treatment methods, such as new pharmaceuticals, forms of behavioral therapy, and other mindfulness-centered interventions, to better determine

which approaches offer the most effective and sustainable improvements.

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