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A Proposed Etiology of Psychogenic Nonepileptic Seizures

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Abstract

An estimated 20% to 50% of patients evaluated for ongoing seizures in epilepsy monitoring clinics walk away with a diagnosis of psychogenic nonepileptic seizures (PNES), not epilepsy. Seizures that do not produce an epileptiform discharge on the ictal video electroencephalogram (vEEG) garner a diagnosis of psychogenic nonepileptic seizures, or Conversion Disorder in modern nomenclature. The absence of an ictal epileptiform discharge is interpreted as proof that the seizure is hysterical, or psychological, in origin. The conspicuously high incidence of PNES shows that seizures with no concomitant electroencephalogram changes are common, but this constitutes an extreme and often chronic Conversion Disorder that is not identified outside of epilepsy clinics. A review of scientific literature reveals the use and limitations of the vEEG, the diagnostic practice and bias in epilepsy clinics, the complexity of epilepsies and seizure semiology, the global neurologic impact of epilepsy, and the parallel clinical profile observed in patients with epilepsy and patients with PNES. Although studies show that epileptic seizures can elude vEEG electrodes, the latter is still employed as a litmus test. The remarkably high incidence of PNES appears to be almost entirely an artifact of relying on the fallible vEEG. Patients with epilepsy and patients who undergo epilepsy surgery provide compelling evidence that PNES are simply undetected epileptiform discharges. Diagnostic practice in epilepsy clinics must be revisited.

Keywords: *Psychogenic nonepileptic seizures (PNES); Epileptic seizures (ES); Epileptiform discharge; Conversion Disorder; Video electroencephalogram (vEEG)*

Introduction

In recent decades, the high incidence of psychogenic nonepileptic seizures (PNES) coming out of epilepsy monitoring clinics implicates the practice of relying on video electroencephalogram (vEEG) test results. Psychogenic nonepileptic seizures are paroxysmal episodes that resemble epileptic seizures (ES) but do not show epileptiform discharges on the ictal vEEG, and thus are *presumed to be hysterical*, or psychological, in origin.

While research shows that epileptiform discharges can elude the vEEG, other studies reveal that the test has been declared the *gold standard* by experts for differentiating ES from PNES [1]. It does not capture all epileptiform discharges, but the vEEG is still employed as a litmus test.

In 2011, an international consensus clinical practice statement ranked PNES among the top three neuropsychiatric problems [2]. This finding reveals that epileptologists worldwide view PNES as common, and supports the inference that ongoing seizures in most patients who produce a negative ictal vEEG will be categorized as PNES.

The crux of the matter can be traced to the moment when the ictal vEEG does not show an epileptiform discharge. Then and there, the diagnosis of PNES is *confirmed* and the diagnostic phase is *over*. The body of research on PNES is extensive, but the theorizing and clinical investigations proceed from the *definitive diagnosis* which has already been established by the ictal vEEG. This diagnostic practice involves the adoption of a fantastic theoretical leap, at the expense of an ordinary and much more plausible hypothesis that is readily available. Either the seizure is hysterical in origin or it is an epileptic seizure that eluded the fallible gold standard (vEEG). Occam's Razor, the law of parsimony, would conclude it is the latter. If this hypothesis is accurate, and PNES are actually undetected ES, the clinical observations and comorbidities reported in PNES should mirror the clinical observations and comorbidities reported in epilepsy patients. Decades of research confirm that the seizure semiology and clinical profiles are so similar, that experts have proclaimed that PNES is just as disabling as epilepsy [3].

The misdiagnosis of ES as PNES leads to improper treatment and serious potential consequences. Patients are told that their seizures are not epileptic but psychological in origin, that anti-epileptic medication is not warranted or effective, and that the recommended treatment is psychotherapy. The crucial misdiagnosis can lead to ongoing seizures, injuries, progressive neurologic and psychiatric decline, risk of sudden death, and no possibility of epilepsy surgery. Diagnostic practice in epilepsy clinics must be revisited.

Literature Review and Analysis of Findings

Psychogenic nonepileptic seizures (PNES) are defined as paroxysmal episodes which clinically resemble ES, but are not caused by ictal epileptiform discharges [4], and are *presumed* to be of psychological origin [5,6]. The psychological mechanisms underlying PNES are poorly understood [7], but have been conceptualized in psychoanalytic terms as a manifestation of neurotic defense mechanisms [8]. In modern nomenclature, PNES meets the criteria for Conversion Disorder [9]. To generate and support this analysis, a wide sampling of PNES studies were reviewed.

An estimated 20% to 50% of patients evaluated in epilepsy monitoring units for ongoing seizures walk away with a diagnosis of PNES (Conversion Disorder), not epilepsy [10-13]. This conspicuously high incidence of Conversion Disorder is not identified outside of epilepsy clinics [14,15].

Studies show that epileptiform discharges can elude detection on scalp and intracranial vEEG electrodes. Around 10% of patients with epilepsy never show epileptiform discharges [16]. Patients with epilepsy can have persistently normal EEGs [17]. Not all epileptic seizures show visible changes in the scalp vEEG [18]. Frontal lobe seizures and seizures associated with Sturge-Weber Syndrome may not display ictal EEG abnormalities on scalp electrodes [19-22].

Intracranial and subdural electrodes can identify epilepsy surgery options, but engender risk because electrodes must be surgically inserted [23]. They are employed to tailor resection surgery but do not always capture seizures or improve localization [24]. They are considered more suitable for detecting deep-lying seizure foci [16,25]. There can be difficulties localizing seizure origin when intracranial electrodes are not close enough to the source [26].

Study after study shows the diagnostic preeminence of the vEEG. Psychogenic nonepileptic seizures are confirmed [27-29] and definitively diagnosed by vEEG [17,21,30]. The vEEG is the gold standard for differentiating ES from PNES [1,5,10,13,18,31,32-35]. PNES is only diagnosed via the negation of ES on the vEEG [36]. Apparently no patient is exempt from a diagnosis of PNES when the ictal vEEG is negative. Patients who show lesions with epileptogenic potential [21] and interictal EEG abnormalities [37], three year old children [38], and people with intellectual disabilities and autism [28,39,40], have been diagnosed with PNES. If infants had thick enough skulls to block epileptiform discharges from reaching scalp vEEG electrodes, they would be diagnosed with PNES because PNES is a diagnosis of *exclusion*.

Investigators are addressing the role of trauma in the genesis of PNES[41], but the presence of trauma is a non-specific finding, and there are patients whose PNES have been attributed to difficulties coping with stressors as common as parental discord and divorce [42]. While *any stressor or trauma* can be postulated as an underlying cause, triggers for initial PNES are often not apparent [43], and children and adolescents with PNES typically do not perceive themselves to be anxious, depressed or emotionally distressed [44].

The overall prognosis for patients with PNES is poor [45]. One follow-up study showed that 71% continued to have seizures, and 56% were receiving Social Security Disability benefits [46]. Another study showed that 25% to 33% of patients became chronic and continued to have PNES [47]. The generally poor outcome for patients with PNES mirrors the progressive decline seen in epilepsy patients [48]. One study suggested the poor prognosis could stem from the failure of PNES patients to participate in recommended psychiatric treatment [49], but if PNES are indeed misdiagnosed ES, the lack of appropriate assessments and treatment for epilepsy would almost certainly contribute to the generally poor prognosis.

Some PNES investigators claim that PNES only "superficially resemble" epileptic seizures [17,50], and experienced clinicians can differentiate ES from PNES with a high level of accuracy [50], but these claims are not supported by available evidence.

Studies show the clinical manifestations of PNES and ES are very similar [42,51,52]. Psychogenic Nonepileptic Seizures are "all too easily mistaken for epilepsy" and diagnostic error is the "rule rather than the exception [43]". Conversion Disorder (PNES) is the most common condition mistaken as epilepsy [6]. The most striking lesson from the vEEG is how often PNES has been misdiagnosed as ES [30]. Frontal lobe partial seizures can be bizarre and often mistaken for PNES [53]. Psychogenic nonepileptic seizures "can be deceptive" and masquerade as ES [34]. Previous "hallmarks"

of PNES included pelvic thrusting, violent thrashing, bicycling leg movements, but subsequent studies showed that frontal and temporal lobe seizures can produce these behaviors [11]. In a 2016 study, five experienced epileptologists (four blind) rated 23 videos of ictal events captured on the vEEG [51]. Seven events were accurately categorized by all raters. Semiologic features play a nonessential role in the diagnosis of PNES [35], and according to an international multidisciplinary board of experts on PNES, there is no specific symptom or sign that has diagnostic value [1]. *Without the vEEG*, experienced epileptologists cannot differentiate PNES from ES with a high level of accuracy.

A 2016 case study revealed the "strong bias" among staff at an epilepsy monitoring clinic [19]. They were *convinced*, based on seizure semiology, that a female patient was not having "true" ES, until day three when her vEEG showed epileptiform discharges [19]. Then her previous vEEG recordings, which had been interpreted as normal, were revisited and re-interpreted as consistent with epileptic activity. Another case report detailed "melodramatic" seizure semiology in a nine-year-old with temporal lobe epilepsy that initially impressed as PNES [52]. No matter how bizarre the seizure semiology, if the ictal vEEG shows an epileptiform discharge, the seizure will be categorized as an ES. Conversely, repeated exposure to bizarre ictal semiology that does not produce an epileptiform discharge (PNES) seems to reinforce the confidence of medical staff in their *perceived* ability to identify PNES based on semiology alone. Such confidence is prompting some investigators to support the practice of bypassing the expensive vEEG and relying on clinical judgement to diagnose PNES [34]. This practice would increase the already high incidence of PNES diagnoses.

An illuminating study looked at two adolescents with refractory ES who showed PNES recorded by invasive vEEG electrodes [42]. The 16-year-old female patient, who was suspected of having co-morbid PNES based on previous negative scalp vEEGs, generated three epileptiform discharges (ES) and four events with no concomitant changes (PNES). The 12-year-old male patient had one PNES that looked very similar to his ES. The most "remarkable" finding was the "striking resemblance" between ES and PNES in both adolescents [42].

Epilepsy is a condition that has global impact. The magnetic resonance imaging (MRIs) of patients with left and right temporal lobe epilepsy show equally distributed gray matter structural compromise [54]. The side of seizure focus did not differentially impact the degree of structural damage. Inflammatory processes in temporal lobe epilepsy appear chronically active or transiently re-induced by recurrent seizures [55]. There are patterns of shared grey matter reduction across epilepsy syndromes that indicate epilepsy is a network disorder, and certain epilepsies involve more widespread structural compromise than previously assumed [48].

To meet the criteria for Conversion Disorder, the presenting symptom is not explained by neurologic disease, and there must be clinical evidence of incompatibility with neurologic disease [9]. How do these criteria apply to epilepsy patients with co-morbid PNES? There is clinical evidence of brain pathology which research shows is not limited to abnormal electrical activity. In the two adolescent patients cited above [42], investigators would have been unable to differentiate ES from PNES without the vEEG, because the seizure semiology was identical. To assert that these PNES are not epileptic events, but look exactly like epileptic events, assumes a compartmentalization of brain function that is artificial, simplistic, and inconsistent with the global impact of epilepsy. The position for PNES in these patients is insupportable. The ES and PNES were generated by the same compromised neurologic system. The law of parsimony would conclude that both spring from the same brain pathology. That some seizures did not register on the vEEG is proof of the test's limitations, not proof of a Conversion Disorder, a diagnosis that rests on the absence of neurologic disease. In epilepsy with co-morbid PNES, *that absence is not present*. An organic disease with global neurologic impact is present which can account for all seizures.

Psychogenic nonepileptic seizures have been *eliminated and induced by epilepsy surgery*. In one study [56], nine of thirteen patients with co-morbid PNES stopped having PNES, and of those, seven also became free of ES. Overall, surgery produced a dramatic reduction in ES and PNES. In another study [57], five of nine patients diagnosed with co-morbid PNES became seizure-free and eight subsequently developed PNES. A case study reported a highly favorable response to surgery in a teen with temporal lobe epilepsy and comorbid PNES [58]. All of his PNES disappeared and there was a significant decrease in the frequency of his ES. Another case study described an excellent response to surgical intervention [59]. At the five year follow-up, the 17 year-old was free of both ES and PNES on a single antiepileptic medication. Why would hysterical seizures disappear or emerge following epilepsy surgery? Does epilepsy surgery remove neurotic defense mechanisms in some patients and induce them in others? The law of parsimony would conclude that the PNES and ES were significantly affected by epilepsy surgery because both were epileptic events. An undetected epileptiform discharge is not PNES, it's an epileptiform discharge that was not detected.

In one of the case studies cited above [58], investigators, perhaps unknowingly, hypothesized that the PNES in their patient

were actually undetectable ES. They suggested that both seizure types were secondary to "the presence of dysplasia and its associated epileptogenic focus," and the PNES stemmed from an "electrical discharge" that was "not powerful enough to be recorded as seizure at the cortical level, but continues to act as an emotional-cognitive dysfunction at the subcortical level" [58]. They promoted the "neurobiological hypothesis of PNES," and suggested PNES in epilepsy patients may be "less psychogenic" than PNES in patients without epilepsy [58].

Epileptic seizures inexplicably come and go, or persist, with or without intervention [60]. Spontaneous remission of ES occurs in a substantial proportion of untreated epilepsy patients [60-62], and 30% to 40% of patients with epilepsy fail to respond to antiepileptic drugs [63,64]. That some patients show a reduction or cessation of PNES after the psychological origin is explained to them [65,66], or following psychotherapy [3,67], is not proof that PNES exists. That PNES can persist in patients who are taking antiepileptic drugs is not proof the seizures are of psychological origin. The unpredictable and variable occurrence of PNES mirrors the variability of seizure activity observed in epilepsy.

The seizure semiology of PNES vis-à-vis ES is a major focus [30,34,35,68,69], but the clinical phenomenon is *rooted in the ictal vEEG test result*. Investigators are relying on vEEG studies to provide "detailed knowledge of the spectrum of visible PNES manifestations" [68]. The ictal vEEG dictates the diagnosis, and thus, categorizes the semiology as PNES or ES. The fact that ES and PNES can look identical in the same patient [42] garners little attention.

Intentional feigning is given scant attention, but it does contribute to the incidence of PNES diagnoses [70]. Potential "red flags" of PNES include self-reported very high frequency of seizures, and seizures that occur in front of an audience [71]. These are red flags, but not for PNES. Patients with these dramatic presentations and thoroughly intractable symptoms are characteristic of Factitious Disorders. This challenging population intentionally fabricates illness, impairment, or injury for psychological reasons [72].

Conclusion

The prevalent misdiagnosis of ES as PNES is primarily an artifact of disregarding neurologic disease and the exclusive reliance on a test with *known diagnostic limitations*. Clinicians and PNES researchers need to revisit diagnostic practice. In addition to epilepsy, PNES is associated with refractory seizures [18], cluster seizures [73], traumatic brain injury [74,75], memory impairments [76], a higher premature mortality rate [77], psychiatric symptoms [10], long-term disability [46], pseudo-status epilepticus [78,79], and a positive response to therapeutic interventions that enhance psychological wellbeing [3,67]. The same clinical profile is observed in epilepsy patients [63,80-87]. These objective findings constitute proof that the diagnosis of PNES is erroneous, and supports the argument that the seizures categorized as PNES over the years were in fact ES not detected by the vEEG.

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