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Pseudo-pseudo epileptic seizures: epilepsy or non epileptic seizures? An update

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Abstract

The concept of pseudo-pseudo seizures is often confused with epileptic seizures characterized by excessive or simultaneous anomalous neuronal activity, and with non-epileptic psychogenic seizures, which are known for their involuntary movements and decreased self-control that can mimic epilepsy, without presenting the previously described cortical alterations. Currently, these two types of seizures represent a challenge due to their similar clinical presentation, however semiology and precise office studies allow a correct clinical approach and differential diagnosis. Among epileptic seizures that generate further diagnostic difficulties and confusion are frontal lobe and temporal lobe seizures. Recognizing the semiological characteristics that can occur in these types of seizures and identifying the differences found between epileptic and non-epileptic psychogenic seizures is essential to avoid a misdiagnosis of a pseudo-pseudoseizure.

Keywords: *Epilepsy. Functional neurology. Not epileptic. Pseudoseizures. Psychogenic. Seizure.*

Introduction

The concept of pseudo-pseudo epileptic seizures, arises from the erroneous diagnosis on the part of doctors with a lack of experience, or not familiar with the unusual manifestations of the epileptic seizures of individuals and so the events presented were initially diagnosed as originating in epileptics, being catalogued as having functional origin (psychogenic) when these events actually arise due to epileptic activity[1]. Although the diagnosis can also be performed by doctors unfamiliar with epilepsy, the objectives of this review are to describe the current concept of pseudo-pseudo seizures, define the concepts of epileptic seizures (ES), epilepsy and psychogenic non-epileptic seizures (PNES) as well as to present their main differences and diagnostic characteristics to distinguish between them and mention the main diagnostic errors and types of epileptic seizures that could generate greater confusion in the diagnosis.

Development

Defining epileptic seizures and epilepsy

The International League Against Epilepsy (ILAE) defines epileptic seizures as "the appearance of transient signs and symptoms due to excessive or simultaneous

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anomalous neuronal activity in the brain"[2]. The manifestations of epileptic seizures depend on the neuronal network that is excited in a certain area of the cerebral cortex, and the determining factors include: the place of onset, the propagation pattern, the synaptic maturity, the sleep-wake cycle, medications, pathologies associated with the nervous system etc.[2]

Epilepsy is considered a brain disease defined by any of the following situations: a) appearance of at least two unprovoked (or reflective) seizures with a separation >24 h; b) appearance of an unprovoked seizures (or reflect) and a probability that more crises will appear during the following ten years similar to the risk of general recurrence (at least 60 %) after two unprovoked crises; c) diagnosis of an epileptic syndrome[3].

What are psychogenic non epileptic seizures?

In adults, the most common imitators of epilepsy are syncope and psychogenic non-epileptic seizures (PNES), followed by migraines, parasomnias, cerebrovascular disease and movement disorders such as paroxysmal dystonia and non-epileptic myoclonus[4].

Currently, PNES forms part of the spectrum of "Functional Neurological Symptoms Disorders (FNSD)"[5]. FNSD occupy a grey area between neurology and psychiatry, defining themselves as the manifestation of persistent and disabling symptoms, consistent with paroxysmal events, which include changes in movement control (for example, weakness, tremors, dystonic postures), episodes alterations in consciousness and alterations in sensitivity or behaviour[5,6].

The phenotypes that are present in FNSD are very varied and can be classified according to the manifestations presented in: motor, sensorial, axial, language alterations[1]. The classification proposed by Espay et.al. supports the diagnosis of FNSD based on the phenotype of the event, without depending on the exclusion of other disorders, grouping them into five categories, in patients with FNSD with motor, sensory, axial symptoms, with language alteration or with paroxysmal symptoms, facilitating for the observer the description of the crisis. This classification replaces the terms "Dissociative Disorders" and "Conversion Disorder" with "Functional Neurological Symptoms Disorders" which describe in a better way the phenomenon that gives rise to the events, separating the stigma that the previous terms represent[5]. In the international classification of diseases in its version number once (CIE-11) the FNSD are grouped within chapter number 6: "Mental disorders, behaviour or neurological development", where they are grouped under Dissociative Disorders as "Dissociative Disorders with Neurological Symptoms"[7]. On the other hand, in the DSM-V, a specifier can be added to the FNSD to emphasise the type of presentation[8] (Table 1).

On the other hand, the PNES, also called pseudo-seizures or psychogenic seizures were considered as events that occurred in people who found themselves under a strong psychological stress, and who showed signs or symptoms that could be confused with epileptic seizures, but did not account for hyperactivity in the cerebral cortex nor the predisposition to present recurrent seizures[6]. Recently, in the fifth edition of the diagnostic and statistical manual of mental disorders (DSM-5), the term "Conversion disorder with convulsive seizures" was replaced with "Conversion disorder (Disorder of functional neurological symptoms) with motor seizures or seizures", removing the need to count on a psychological trigger as a requirement to carry out the diagnosis, it being wrong to continue with the previous end of psychogenic seizures being a subtype of paroxysmal TSNF[5].

These events (PNES) are defined as episodes in which they refer to an experience of subjective alteration, involuntary movements and a reduced self-control that can mimic epilepsy, syncope or other paroxysmal disorders. PNES lack a structural basis for their appearance, they are the result of a complex neuropsychiatric dysfunction that does not necessarily require the presence of a stressful psychological factor as a detonating factor, because these are not always found despite the fact that the recent stress factors and histories are more common in patients with FNSD than in healthy and clinical control participants[5,9].

PNES are a frequent disorder recognised around the world[10]. It is estimated that annually PNES have an annual incidence of at least 1.5-6.17/100,000 inhabitants[11]. In the external consultation of general neurology, PNES provide 2% of new references[12]. In clinics specialised in "first seizure", PNES comprise 8-12% of the manifestations. Amongst patients who attend an emergency service due to epileptic seizures, PNES are recognised in 11% of cases. The proportion of those with apparent drug-resistant epilepsy referred to third-level centres is around 30%[9]. The prevalence of PNES in the general population has been estimated at 2-50/100,000 inhabitants[13]. Patients with the same disorder contribute around 5% of referrals to specialists in syncope or pseudosyncope. Women and girls

Table 1. Comparison between FNSD classifications from CIE-11, DSM-5 and classification proposed by Espay et al.[5]

CIE-11		DSM-5	Espay et al.[5]
6B60. Dissociative disorders with neurological symptoms		**Conversion disorder**	**Functional Neurological Symptoms Disorder**
6B60.0	With visual alteration	With weakness or paralysis	with motor symptoms
6B60.1	With hearing alteration	With anomalous movement	With sensitive symptoms
6B60.2	With vertigo or dizziness	With swallowing symptoms	With axial symptoms
6B60.3	With sensitive alterations	With speaking symptoms	With language alterations
6B60.4	With non-epileptic seizures	With seizures or seizures	With paroxysmal symptoms
6B60.5	With speech alteration	With anesthesia or sensory loss	
6B60.6	With paresis or weakness	With special sensitive symptom	
6B60.7	With a change of gear	With mixed symptoms	
6B60.8	With alteration of the movement		
6B60.80	With chorea		
6B60.81	With myoclonus		
6B60.82	Trembling		
6b60.83	With dystonia		
6B60.84	With facial spasm		
6B60.85	With parkinsonism		
6B60.8Y	With another specified movement change		
6B60.8Z	With non-specific movement alterations		
6B60.9	With cognitive symptoms		
6B60.Y	With other specific symptoms		
6B60.Z	With other non-specific symptoms		

CIE-11: international classification of diseases version 11; FNSD: functional neurological symptom disorder; DSM-5: diagnostic and statistical manual of mental disorders. *Adapted from CIE-11 and DSM-5*[5,7,8].

contribute to 60-80% of patients with this diagnosis; however, the gender disparity is smaller in older adults and in those with intellectual deficits[9]. The average and median age of initiation is around 28 years old (however, the age mode is at 19 years old). Young women have a greater risk[14,15]. As in epilepsy, PNES are more commonly diagnosed in individuals from lower socioeconomic strata[16].

Whilst semiological characteristics may suggest a diagnosis of PNES or ES, the gold standard for its diagnosis is the recording of these typical events on a video electroencephalogram (VEEG) noting a lack of epileptiform activity in the pericatal period, with semiology and history consistent with PNES, the case being analysed by a trained physician with extensive experience in epilepsy[17]. Recently, the International League Against Epilepsy (ILAE) in its working group on Neuropsychobiology of non-epileptic seizures published a consensus of clinical practice guides with the minimum requirements for the diagnosis of PNES (Table 2)[18].

Surface electromyography recordings can also potentially help in differentiating PNES from ES[17]. Approximately, the double of serum prolactin levels obtained 10 to 20 minutes after an ictal event can also help to differentiate a PNEC from an FB, although it is not 100% sensible nor specific, it supports more the diagnosis of motor FB[18].

Distinguishing ES from PNES

Differentiating PNES from epileptic seizures remains a difficult diagnosis for specialists with an error rate of

Table 2. Diagnostic levels of certainty for PNES

Diagnostic level	History	Witnessed event	EEG
Possible	Positive	By witness or self-report/description	Without epileptic activity during inter-ictal routine EEG or with sleep deprivation.
Probable	Positive	By clinician who reviews video recording or in person, showing typical semiology of PNES	Without epileptic activity during inter-ictal routine EEG or with sleep deprivation.
Clinically established	Positive	By experienced clinician in the diagnosis of epileptic seizures (on video or in person), showing typical semiology of PNES	No epileptic activity during routine EEG or ambulatory ictal EEG, capturing a typical ictus[The]
Documented	Positive	By clinic experienced in the diagnosis of convulsive disorders, showing typical PNES semiology during the realization of VEEG.	Without epileptic activity before, during or after the ictus captured in ictal VEEG with typical PNES semiology.

[a]Documented elictus should not be recalled to an ES nor should epileptic activity be found which correlates with the EEG.
PNES: psychogenic non-epileptic crisis; ES: epileptic seizure; EEG: electroencephalogram; VEEG: videoelectroencephalogram.
Adapted from LaFrance[18].

Table 3. Semiological characteristics that support the diagnosis of ES against PNES

Signs that favour the NES	Signs that favour ES	Intermediate signs
Long duration	Occurrence during physiological sleep	Gradual start
Floating course	Postictal confusion	Non-stereotyped events
Asynchronous movements	Stertorous breathing	Shaking or shattering movements
Pelvic thrusts*		Opisthotonos
Side-to-side movements of the head or body[†]		Tongue bite
Forced eyelid closure		Urinary incontinence
Ictal face		
Memory recovery		

*This sign may not reliably indicate between PNES and ES of the frontal and parietal lobe.
[†]This sign can only be useful to distinguish between PNES and ES
ES: epileptic seizures; PNES: seizures in psychogenic epileptics.
Adapted from Avbersek and Sisodiya[19,22].

approximately 20-30%.(2) Numerous studies have investigated the clinical signs that help in the diagnosis of PNES[19,20].

A retrospective review detailing the signs that reliably distinguished PNES from ES suggested that a diagnosis of PNES was favoured by events of long duration, fluctuating course, asynchronous movements or from side to side, closing the eyes at the beginning of the seizure, llanto ictal and retrieval of the information in the postictal state (Table 3). In addition, urinary incontinence and tongue biting do not reliably distinguish between the two[21].

A prospective study of 120 seizures in 35 consecutive subjects demonstrated that the video-documented preservation of the state of alert, the eye-rolling and the modulation of the event by the people who found themselves nearby were reliably predicted by the PNES; the abrupt onset, ictal eye opening and postictal confusion/sleep reliably predict the EC[22]. It is also worth mentioning that, apart from differentiating PNES from ES, other diagnoses must be considered and ruled out, including paroxysmal movement disorders, panic attacks and physiological forms of non-epileptic events such as syncope, cardiac arrhythmias, among other conditions[17].

Reasons for the misdiagnosis of epileptic seizures that lead to the end of pseudo-pseudo seizures

The fact that epilepsy and psychiatric illnesses can coexist in the same patient makes the diagnosis even more difficult. The lifetime prevalence of epilepsy is

3-4%, panic disorders are 1.5%, and both conditions have a considerable overlap of symptoms, such as sudden and unexpected fear and autonomic changes, in addition to the fact that many patients with epilepsy suffer anxiety and disorders of the state of mind with an incidence much greater than the population in general[1].

The manifestations of some types of epileptic seizures themselves can lead to confusion in the diagnosis of patients, especially when unusual, atypical and unusual manifestations are present, or when there is a minimal or null electrographic anomaly on the EEG. Some examples of these types of difficult-to-diagnose epileptic seizures originate in the frontal lobe and temporal lobe[1].

Types of ES that generate more confusion in the differential diagnosis

The ILAE classifies the epileptic seizures depending on the patient's onset symptoms: focal onset seizure, generalized onset seizure and unknown onset seizure[23]. Focal-onset seizures are those whose onset is limited to a neuronal network located in a cerebral hemisphere, the counterpart of generalized-onset seizures that start at a point in the brain and quickly compromise networks with a bilateral distribution[24]. Likewise, the focal seizures are subclassified depending on the state of consciousness if it is found with alteration of consciousness or without alteration of the same[23].

The seizures that present with cognitive alterations or emotional alterations are more difficult to differentiate from the presentation of some patients with psychiatric symptoms, frontal and temporal lobe epilepsy is more associated with this type of epileptic seizures, on occasions it is Continuous video-EEG recording is necessary, which manages to capture the appearance of epileptic graphelements in these cerebral regions during the event or, by default, to characterize the episodes, especially those that are stereotyped in the absence of abnormal graphelements[25].

Temporal lobe epilepsy:

The ILAE in 1989, described the main types of temporal lobe epilepsy: mesial temporal lobe epilepsy, related to alterations in the limbic system, comprising the hippocampus, the parahippocampal circumvolution, cingulum, longitudinal cleft and the amygdala; and the epilepsy of the lateral temporal lobe, a less frequent type, where the beginning of the seizure is located in the neo-temporal cortex[26].

Many patients with focal seizures with preserved consciousness have experiences (previously called auras) that simulate cognitive symptoms such as, for example, déjà vu, jamáis vu, episodes of depersonalization or derealization, somatosensory crises such as auditory, olfactory, visual, taste, painful hallucinations[1,24,27]. This type of seizure or "auras" are frequent in mesial temporal lobe epilepsy, and are mainly caused by sclerosis of the hippocampus[26].

Auditory and olfactory hallucinations have been described in mesial temporal sclerosis, due to the involvement of temporal olfactory structures, in particular the entorhinal cortex, pre-piriform cortex and the amygdala that are involved in the processing of olfactory information, in addition to the fact that these structures form part of the network of the limbic system[27].

Due to the anatomical proximity between neuronal networks of the limbic system, such as the fear circuit, composed of the amygdala, the insula and the anterior cingulate cortex, as the main components; in patients who present an epileptic network that involves the temporal-island-frontal areas, the epileptic activity can activate these fear circuits, or vice versa, causing patients with psychiatric disorders to present epileptic seizures, or otherwise patients with a type of seizure epileptics can undergo a change in the presentation of their seizure after a stressful psychogenic experience, as in patients with post-traumatic stress disorder[28].

Frontal lobe epilepsy:

A constellation of motor manifestations and behaviour can be described in frontal lobe crisis, which can be confused with some psychiatric illnesses and can be difficult to identify as manifestations of a frontal lobe seizure, due to their abrupt onset, hyper component. -motor, with frequency associated with vocalization at the beginning of the crisis (ictal scream) and short postictal. When these seizures are observed by personnel not familiar with this type of seizure, the diagnosis of epilepsy by PNES can easily be overlooked, especially those that present themselves with extraneous paroxysmal behavior and emotional changes with an inter-ictal or surface ictal EEG normal[29]. One of the events that could help to carry out the differential diagnosis, in addition to the stereotyped, hyper-motor behaviors and presentations during the sleep, would be the presence (if hubiera) of postictal psychosis of rapid resolution, since this has not been described as complication in CNEP[30,31].

There are PNES that can occur during sleep, (night) without embargo most of them come from a "pseudo-sleep"

this concept that was used in 1996 to refer to a state that has all the characteristics of a normal sleep, is to say patient is in a supine position, without moving and with closed eyes, but on the EEG there is evidence of being awake, including alpha rhythm, artifact of muscle activity by blinking and absence of slow eye movements[4].

In patients with PNES it is possible to appreciate a slight increase in the percentage of sleep MOR, which is similar to the changes in the architecture of sleep seen in patients with depression[32].

Conclusions

The Pseudo-pseudo seizure are those epileptic seizures that were initially erroneously cataloged as "psychogenic non-epileptic seizures", and after a more in-depth study by the doctor, with the help of the VEEG or experience, their correct identification was achieved.

ES and PNES are two of the diagnoses that have contributed to the end of the pseudo-pseudo-crisis and that generate difficulty and confusion at the time of establishing a clinical diagnosis. Due to the large number of symptoms that can appear in a person with epilepsy, the seizures that represent a greater diagnostic difficulty for the clinician are originated in the frontal and temporal lobes with the involvement of the mesial and lateral areas.

The use of the video electroencephalogram becomes the most important tool for the diagnosis of ES and PNES, without ruling out the existence of one of these until the case is not valued by a doctor specializing in epilepsy.

The characterization of the ES and PNES continues to represent a huge challenge, which only through a deep knowledge of the semiology of the different crises and the support in the diagnostic tools will be able to reduce this diagnostic difficulty and improve its accuracy.

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