



## Review

# Variables associated with co-existing epileptic and psychogenic nonepileptic seizures: a systematic review



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## ABSTRACT

**Purpose:** Epileptic seizures (ES) have many mimickers, perhaps the most relevant being psychogenic nonepileptic seizures (PNES). The picture is even more challenging when PNES are associated with ES in a given patient. The aim of this research paper was to delineate the demographic, epileptological and psychiatric profile of that specific population.

**Methods:** A systematic review was carried out from 2000 to 2015 for articles in English, French, Italian, Spanish and Portuguese in PUBMED and EMBASE. Cohort or case-control studies reporting prospective or retrospective original data comparing patients with co-existing ES and PNES with those who had PNES only and ES only have been included. In retained studies, the presence of PNES was confirmed by video-electroencephalography (V-EEG). Forty-eight abstracts were identified.

**Results:** Nine studies were retained. Most showed that female gender predominated in both groups with PNES. Patients with co-existing ES and PNES take higher number of antiepileptic drugs (AEDs) than PNES alone. Two studies showed association of concomitant ES and PNES with earlier age of seizure onset. Localizing EEG features and ES type were evaluated in only two studies and their association with either group was inconclusive. Somatoform, conversion or cluster B personality disorders were more frequent in subjects with PNES than with ES.

**Discussion:** Patients with concomitant ES and PNES are highly heterogeneous, challenging differentiation on clinical grounds. A diagnosis of conversion or somatoform, anxiety disorders, and the use of a higher number of AEDs than psychiatric medications may have an association with co-existing ES and PNES.

Further studies are warranted to differentiate patients who only have PNES from those with co-existing ES and PNES.

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## 1. Introduction

Epileptic (ES) and psychogenic nonepileptic seizures (PNES) share a number of features, despite distinct mechanisms and clinical meaning. Both lead to physical, social and occupational impairment, meet with significant stigmatization and are associated with a high prevalence of comorbid psychiatric disorder [1,2]. PNES are the most common cause of nonepileptic ictal events and present as unintentional physical symptoms mediated by psychological factors, usually triggered by stressful situations [3,4]. DSM-V has

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PNES as a conversion disorder with functional neurological symptoms and several studies relate PNES to maladaptive behavior, personality traits and major psychiatric comorbidities, particularly depressive, or anxiety and somatoform disorders [4–6]. Thus, PNES are likely to be the result of a complex interaction between psychiatric disorders, coping style and cerebral vulnerability [2,7].

Some patients, however, have both epileptic seizures and PNES. Ictal semiology varies accordingly and a correct differential diagnosis between epilepsy, a psychiatric disorder manifesting PNES or a combination of both is pivotal to their management. Because only ES respond to antiepileptic drugs (AEDs), failing to diagnose PNES or the co-existence of ES and PNES, may lead to unnecessary modifications and/or escalation of AEDs regimens to the point that patients with frequently recurring episodes may be totally sedated. Given such practical relevance, it is somewhat surprising that such association is of uncertain prevalence - reported figures vary widely from 5.3 to 50% of patients with confirmed PNES [8,9] - and the factors associated with the co-occurrence of ES and PNES are far from clear.

To set the stage for future research, we have carried out a systematic review of articles published since the year 2000, which aimed to uncover demographic, epileptological and psychiatric factors suggestive of co-existing ES and PNES in the same patient.

## 2. Method

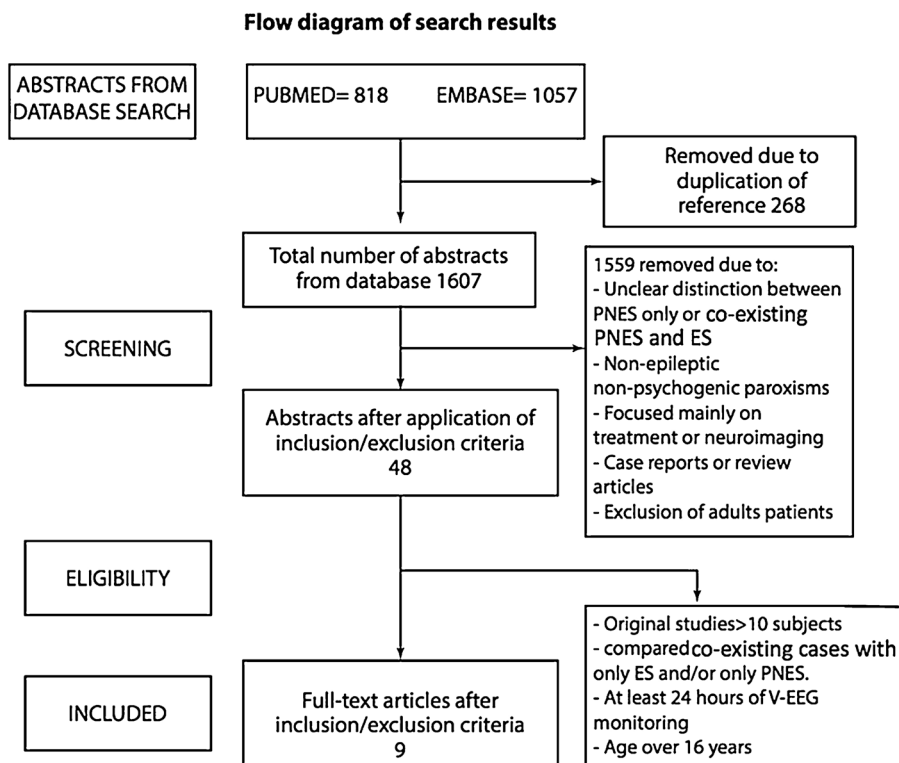
### 2.1. Search strategy and study selection

A systematic review using the methodology outlined in the Cochrane Handbook for Systematic Reviewers was carried out [10]. Data were reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [11]. Several synonyms for PNES were initially identified and then a systematic search for articles in English, French, Italian, Spanish and

Portuguese in PUBMED (818 abstracts) and EMBASE (1057) abstracts, from January 2000 to October 2015, was carried out. Search words/terms were pseudoseizure OR pseudoseizures\* OR pseudoseizures epilepsy OR psychogenic seizures OR psychogenic non-epileptic OR psychogenic nonepileptic OR psychogenic non-epileptic OR psychogenic nonepileptic seizures OR psychogenic non-epileptic seizures OR psychogenic non-epileptic seizures OR nonepileptic attack disorder AND (epilepsy OR seizures).

The senior author reviewed all abstracts and selected, for further review, those reporting (I) original research (II) related to diagnostic evaluation of (III) adult patients (IV) and the association of ES and PNES. Abstracts thus selected underwent a second round of independent review by the senior author (GB) and the co-author VP to confirm initial findings. When both reviewers agreed that pre-requisites had been met, the abstract was retained. When abstract data were unclear, the full article was assessed for further analysis.

Forty-eight abstracts were identified and then full texts independently reviewed by one certified psychiatrist (GB, senior author) and one certified neurologist (LP). A third reviewer (AP) resolved divergences in data interpretation. Based upon the main goals, these 48 manuscripts were further 'screened' and retained if they (a) reported prospective or retrospective original observational data or were cohort or case-control studies with ten or more subjects; (b) compared patients with co-existing ES and PNES with those with PNES only and ES only; (c) had a confirmation of the diagnosis of PNES by video-electroencephalography (V-EEG) monitoring, with or without induced events. A concomitant diagnosis of ES in these studies was based either upon ictal confirmatory recordings or convergent semiology and interictal epileptic discharges. Nine articles [12–20] met the inclusion criteria. A list of excluded articles can be found as supplementary material (S1). The screening process is described in Fig. 1.



Psychogenic Nonepileptic Seizure (PNES); Epileptic Seizure (ES)

**Fig. 1.** Psychogenic Nonepileptic Seizure (PNES); Epileptic Seizure (ES).

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