



## Brief Communication

# Psychogenic nonepileptic seizures in patients with surgically treated temporal lobe epilepsy: Presurgical and de novo postsurgical occurrence



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## ARTICLE INFO

## Article history:

Received 28 June 2017

Revised 3 August 2017

Accepted 5 August 2017

Available online 1 September 2017

## Keywords:

Temporal lobe epilepsy

Psychogenic nonepileptic seizures

Epilepsy surgery

## ABSTRACT

Whether occurring before or after an epilepsy surgery, psychogenic nonepileptic seizures (PNES) impact treatment options and quality of life of patients with epilepsy. We investigated the frequency of pre- and postsurgical PNES, and the postsurgical Engel and psychiatric outcomes in patients with drug-resistant temporal lobe epilepsy (TLE). We reviewed 278 patients with mean age at surgery of  $37.1 \pm 12.4$  years. Postsurgical follow-up information was available in 220 patients, with average follow-up of 4 years.

Nine patients (9/278 or 3.2%) had presurgical documented PNES. Eight patients (8/220 or 3.6%) developed de novo PNES after surgery. Pre- and postsurgery psychiatric comorbidities were similar to the patients without PNES. After surgery, in the group with presurgical PNES, five patients were seizure-free, and three presented persistent PNES. In the group with de novo postsurgery PNES, 62.5% had Engel II–IV, and 37.5% had Engel I. All presented PNES at last follow-up.

Presurgical video-EEG monitoring is crucial in the diagnosis of coexisting PNES. Patients presenting presurgical PNES and drug-resistant TLE should not be denied surgery based on this comorbidity, as they can have good postsurgical epilepsy and psychiatric outcomes. Psychogenic nonepileptic seizures may appear after TLE surgery in a low but noteworthy proportion of patients regardless of the Engel outcome.

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## 1. Introduction

Psychogenic nonepileptic seizures (PNES) may coexist with epileptic seizures (ES) in the same patient. Previous studies showed variable frequency of coexisting epilepsy in patients with PNES, ranging from 5.3% [1] to 10%–30% [2–4]. These differences are probably related to the use of different criteria in the diagnosis of epilepsy and PNES. Higher prevalence (30%) was reported when the diagnosis of PNES was based on expert observation only, without EEG recording of the events, and when the diagnosis of epilepsy was made with presence of interictal EEG abnormalities and concordant clinical history [4]. Lower frequency (5.3%) was reported when the criteria included video-EEG-documented PNES and ictal recording of epileptic seizures [1].

Occasionally, these patients are diagnosed with focal drug-resistant epilepsy and need to be evaluated for surgery. The association of ES

and PNES can be particularly challenging in the decision toward epilepsy surgery. There is scarce information about the surgery outcomes in this group of patients [5]. A concern about performing surgery in the presence of psychiatric comorbidities and the assumption that these conditions do not result in significant impact on quality of life altogether might have precluded the development of any type of standardized approach. Further, the presence of PNES may be perceived as a relative contraindication for epilepsy surgery. When surgery is considered, there is not a clear guideline as to whether it would be best to observe a good span of time after clarification of the dual diagnosis and appropriate psychotherapy or, as a result of an underlying mechanism that is different from that in ES, whether surgery should proceed without delay is the best option of care.

Conversely, a proportion of patients with surgically treated epilepsy may develop de novo PNES after surgery, which may be underdiagnosed and confound the assessment of postsurgical seizure outcomes and clinical management [6,7].

To address this gap in knowledge, this study analyzes a large cohort of consecutive patients surgically treated for drug-resistant TLE. The aims are to assess the frequency of presurgical PNES and that of

Abbreviations: PNES, psychogenic nonepileptic seizures; TLE, temporal lobe epilepsy; ES, epileptic seizures; AEDs, antiepileptic drugs.

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postsurgically occurring de novo PNES and to evaluate the frequency of persistent PNES along with postsurgical Engel and psychiatric outcomes.

## 2. Methods

This is a retrospective observational study.

### 2.1. Participants

Consecutive patients with TLE who underwent surgery from 1999 to 2014 were identified from the database at the University of California San Francisco and from one neurosurgeon's database at the Montreal Neurological Hospital and Institute. This study was approved by each institution's Research and Ethics Boards.

Only patients with ictal recordings for their ES and documented PNES were included. We used the definition proposed by the ILAE considering documented PNES as events witnessed by a clinician experienced in diagnosis of patients with seizure disorders, while on video-EEG, without epileptiform activity immediately before, during, or after the ictus was captured [8].

### 2.2. Data collection

All the patients that underwent surgery for drug-resistant temporal lobe epilepsy were classified into one of the following groups: presurgical PNES, postsurgical de novo PNES, and ES only.

Demographic information, presence of intellectual disability, age at seizure onset, seizure frequency, presurgical psychiatric comorbidities, duration of epilepsy until surgery, age at surgery, number of antiepileptic drugs, and side of surgery were reviewed. The diagnosis of personality disorder and history of sexual abuse were not included in this study, as they were not systematically documented in the charts. Postsurgical psychiatric comorbidities were reviewed and seizure outcomes were observed at last follow-up using Engel's classification [9].

### 2.3. Data analysis

Presurgical clinical and demographic characteristics, and surgery information were summarized descriptively to characterize the cohort. For not normally distributed quantitative variables, we reported median and interquartile range (25% percentile–75% percentile).

Factors for comparison between the groups with presurgical PNES, postsurgical de novo PNES, and ES only that might potentially be associated with the presence of presurgical or de novo postsurgical PNES included the following: gender, presence of intellectual disability, age at seizure onset, frequency of focal seizures with impaired awareness, presence of psychiatric comorbidities, age at surgery, epilepsy duration until surgery, number of AEDs at surgery, and side of surgery. Kruskal–Wallis test was used for comparisons for continuous variables. Fisher exact test was used for comparison for categorical variables. Significance was set at  $p < 0.05$ .

Postsurgical seizure outcomes and psychiatric comorbidities were summarized for the three groups. For the group with postsurgical de novo PNES, the time of PNES onset after surgery was reported. For the group with presurgical PNES, the presence of persistent PNES was described at last follow-up after surgery.

## 3. Results

### 3.1. Sample characteristics

Two hundred seventy-eight patients who had surgical resection for drug-resistant TLE were reviewed, including 150 females (54%), with mean age at surgery  $37.1 \pm 12.4$  years. Postsurgery outcome

information was available for 220/278 patients. The average follow-up time after surgery was 4 years (range, 1–16).

Nine patients (9/278 or 3.2%) had a presurgical diagnosis of documented PNES. Eight patients (8/220 or 3.6%) developed de novo PNES after surgery.

### 3.2. Comparison of presurgical and surgery factors among the groups with presurgical PNES, postsurgical de novo PNES, and ES only

We found no significant presurgical clinical or demographic differences between the groups with presurgical PNES, postsurgical de novo PNES, and ES only (Table 1). Age at surgery, side of surgery, and epilepsy duration until surgery were similar among the three groups (Table 1). In the group with presurgical PNES, there were a higher proportion of patients receiving polytherapy with 4–5 antiepileptic drugs (AEDs) at the time of surgery.

### 3.3. Postsurgical outcomes

Postsurgical Engel outcome and psychiatric comorbidities at last follow-up are summarized in Table 2. Follow-up was available for eight of nine patients in the group with presurgical PNES (Table S1): five patients (62.5%) were completely seizure-free (Engel Ia), and only one continued to have occasional PNES. Two of the three patients with bad seizure outcome (Engel II–IV) also continued to have frequent PNES. None of the eight patients experienced worsening of the PNES after surgery, nor did they show higher incidence of postoperative mood disorders or psychosis when compared to the ES-only patients.

Development of postsurgical de novo PNES was reported most often ( $n = 6$ ; 75%) within the first year after surgery but occurred during the third postoperative year in one patient and 7 years after surgery in another patient (Table S2). At last follow-up, only three patients (37.5%) had Engel I, and five patients (62.5%) had a poor seizure outcome with Engel II–IV. All eight patients had unresolved PNES.

## 4. Discussion

Whether occurring before or after an epilepsy surgery, PNES impact treatment options and quality of life of patients with TLE, a disorder that is potentially curable with surgery. The frequency of presurgical and postsurgical de novo PNES has been scarcely reported in patients with TLE. A better understanding of the relationship between persistent or de novo PNES after surgery and postsurgical seizure outcome may help clarify whether epileptic seizures play a role in PNES occurrence, regardless of other psychiatric comorbidities.

### 4.1. Presurgical PNES and TLE

In our study population of TLE surgical cases, only 3.2% had coexisting presurgical PNES confirmed by video-EEG. A previous study reported a higher proportion of PNES in patients with TLE (8%), but most had controlled epilepsy [10]. Our patients represent a special population given that they are a cohort of confirmed drug-resistant TLE that was surgically treated. A report in patients with surgically treated epilepsy found a 1.3% incidence of coexisting PNES and drug-resistant epilepsy [5]. Frequency differences might also be related to different criteria considered by each center when offering surgery to these patients. In particular, the two centers evaluated in our study do not impose the presence of PNES as a contraindication for TLE surgery.

Among patients with presurgical PNES and TLE, we observed an increased proportion of patients receiving four to five AEDs, despite having similar seizure frequency, a finding that is in agreement with previous reports [11]. This finding probably reflects the poor diagnostic distinction between PNES and ES made by both patients and physicians, a problem that is likely to result in increased prescription of AEDs.

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