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Patients with epilepsy and psychogenic non-epileptic seizures: An inpatient video-EEG monitoring study

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ABSTRACT

Seizure and EEG characteristics of patients with epilepsy and concomitant psychogenic non-epileptic seizures (PNES) were compared to age and sex matched controls with epilepsy alone in a retrospective case control study. 39 patients with clearly documented epileptic and non-epileptic events were compared to 78 age and sex matched controls, sequentially admitted for video-EEG monitoring with documentation of epilepsy alone. Frontal seizures were higher in prevalence in patients with PNES who had concomitant epilepsy ($P < 0.001$), while temporal seizures were higher in prevalence in patients with epilepsy alone ($P < 0.04$). On regression analysis, the odds of having a frontal seizure was found to be significantly lower in the epilepsy alone group compared to the epilepsy + PNES group (odds ratio 0.13, 95% CI, 0.033–0.51). This significant association between frontal lobe epilepsy and PNES may be related to misattribution of frontal seizures for PNES events, or may reflect frontal lobe cortical dysfunction in this subgroup.

1. Introduction

Psychogenic non-epileptic seizure disorder (PNES) is a behavior pattern mimicking epileptic events without the concomitant EEG pattern of an electrical seizure. Non-epileptic seizures occurs both in patients with and without epilepsy.[1] Previous studies report coexisting PNES and epilepsy in 10–13% of cases reviewed.[2–5] Higher numbers (10–40% of epilepsy patients) are reported in tertiary epilepsy centers, likely due to the higher rates of intractable epilepsy, and due to the pertinent diagnostic facilities available, namely video-EEG monitoring.[6–9]

While most studies have addressed PNES alone, a few studies have focused on the subgroup of patients with both epilepsy and PNES.[10,11] Currently, progress is being made towards understanding comorbid psychiatric diagnoses and neuropsychological characteristics of this subgroup. Physiological changes including presence of multifocal or generalized seizures, interictal EEG changes[11,12] and hemispheric localization[13] have also been investigated. The aim of our study was to extend previous analyses and examine if specific seizure syndromes were more commonly noted in the subjects with epilepsy and PNES compared to subjects with epilepsy alone.

2. Methods

We performed a retrospective case control study comparing the ictal and interictal EEG characteristics of patients with epilepsy and PNES events and patients with epilepsy alone admitted for video-EEG monitoring. All cases and controls were 16 years or older and with full epilepsy history available for review. The study protocol was reviewed and cleared by the Montefiore Medical Center Institutional Review Board. The video-EEG evaluation consisted of digitized EEG and audiovisual data recorded on site. The video monitoring sessions ranged 2–7 days. Patients were admitted for one of three reasons: (1) undiagnosed events, uncertain whether epileptic seizures or psychogenic events (2) probable epileptic seizures, diagnosis of seizure type needed to select and modify therapy (3) Phase 1 or 2 evaluation for epilepsy surgery.

Electrodes were placed in accordance with the International 10–20 system, and included anterior temporal (FT9 and FT10) electrodes. All EEG were recorded in accordance with the American Clinical Neurophysiology Society guidelines. Ictal EEG characteristics along with interictal awake and sleep EEG were analyzed. Diagnosis of PNES was made by an epileptologist, based on the absence of electrographic paroxysmal changes during, after or prior to a typical event along with review of their clinical history to include semiology of events, previous events, comorbid diagnosis and laboratory data including electrocardiogram (ECG). Multiple typical PNES events were noted during monitoring in each patient. Episodes due to other medical and neurologic disorders were

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Table 1
Epilepsy localization in patients with epilepsy + PNES and patients with epilepsy alone when undergoing video-EEG monitoring.

Epilepsy localization	Epilepsy + PNES ($n = 39$)	Epilepsy alone ($n = 78$)	Independent samples t-test
Localization related epilepsy: Frontal lobe	23.07% ($n = 9$)	3.84%($n = 3$)	$P < 0.001$
Localization related epilepsy: Temporal lobe	43.58% ($n = 17$)	64.1% ($n = 50$)	$P < 0.04$
Other Extratemporal	5.12% ($n = 2$)	3.84% ($n = 3$)	$P < 0.7$
Multifocal (>2 foci)	0.00%	5.12% ($n = 4$)	$P < 0.2$
Non localizable	5.12% ($n = 2$)	2.56% ($n = 2$)	$P < 0.7$
Idiopathic generalized epilepsy (IGE)	25.64% ($n = 10$)	21.79% ($n = 17$)	$P < 0.6$

Note: One patient in both groups had seizure localizable to both temporal and one other area in the same hemisphere (Parietal, Central or Occipital) at the same time but was not multifocal (>2 foci).

excluded. The events in question were confirmed as the patient's typical events. Diagnosis of epilepsy was made by an epileptologist, confirmed by clinical episodes with accompanying electrographic seizure patterns seen during monitoring. Benign variants were not considered epileptiform. In cases of regional focal onset epilepsy, localization of the seizure onset was based on ictal and interictal EEG evidence during video-EEG recordings, seizure semiology (onset during sleep or when awake, motor or sensory semiology) and neuroimaging evidence for focal brain lesions when present. Each patient's clinical diagnosis of seizure foci and seizure type during video-EEG monitoring had formed the basis of their subsequent clinical treatment plan.

All available Epilepsy monitoring unit (EMU) electronic records from 1999 to 2008 were searched using a computerized search protocol. The records of 91 patients with search hits for concomitant epilepsy and PNES were obtained. These were further reviewed by one of us, a board certified epileptologist (SH) who identified 39 patients with clearly documented epileptic and non-epileptic events during the video monitoring period alone on careful review of the initial records and monitoring EEG. Of note, these video-EEG records had been reviewed earlier by a panel of senior epileptologists at our customary institutional video-EEG case conferences during each patient visit. All 39 patients identified by SH to have had epileptic and non-epileptic events during the present review of their video-EEG records were retrospectively also noted to carry the same diagnosis at their initial review, confirming the robustness of these diagnoses. Subjects in a 1:2 ratio of cases to controls were identified from sequential EMU admissions for video-EEG monitoring 2007–2009. As there is a female predominance for PNES,[14] controls were age and sex matched to cases. The 78 controls had a diagnosis of epilepsy with seizures confirmed during video-EEG monitoring, no PNES events ever noted on video monitoring or in their clinical history. Final statistical analysis was performed on SPSS™ (Chicago, IL) statistical software package.

3. Results

The mean age at monitoring for patients with epilepsy and PNES was 37.4 years (Standard deviation, SD 12.7) and mean age at monitoring for patients with epilepsy alone who were age matched was 37.5 years (SD 13.1). The age of onset of PNES could not consistently and reliably be determined from the monitoring records. 3 patients with epilepsy + PNES and 11 patients with epilepsy alone underwent video-EEG as part of pre-surgical evaluation, the rest were admitted to capture and characterize their seizure events towards medical management.

Seizures with onset in the frontal lobe were more likely to occur during sleep compared to temporal lobe onset (89% vs. 41%). 77.7% ($n = 7$) subjects with frontal epilepsy had electrographic seizures localized to the frontal lobe and 64.7% ($n = 11$) of subjects with temporal epilepsy had electrographic seizures localized to the temporal lobe during video-EEG monitoring concurrent with their clinical semiology, with the rest in both epilepsy syndromes being non localizable electrographic seizures with their corresponding seizure diagnosis supported by clinical history and semiology. Details of epilepsy localization in patients with concomitant epilepsy and PNES and patients with epilepsy alone are summarized in Table 1. Idiopathic generalized epilepsy (IGE) was not significantly associated with the presence or absence of PNES. Focal seizures with PNES were predominantly either of frontal or temporal lobe onsets. Frontal lobe epilepsy was significantly more frequently diagnosed in patients with epilepsy and PNES (23.07% vs. 3.84%, Independent samples t-test, 2 tailed (equal variance, $P < 0.001$), while temporal lobe epilepsy was significantly more common in patients with epilepsy alone (64.1% vs. 43.58%, Independent samples t-test, 2 tailed (unequal variance, $P < 0.04$) (see Table 1). Other extra-temporal localizations (parietal, central or occipital) were quite small to warrant further analysis between the groups.

Details of interictal EEG changes captured during video monitoring are documented in Table 2. The interictal EEG findings showed a similar predominance of temporal epileptic EEG characteristics (spikes and sharp waves) in the epilepsy alone group when compared between patients with concomitant epilepsy and PNES and patients with epilepsy alone. The PNES events concomitant with seizure syndromes were distinguishable from typical seizure semiology of the patients and the nature of PNES events did not significantly differ between frontal and temporal seizure syndromes in frequency of occurrence of aura, unresponsiveness following the event, motor or sensory symptoms. Ictal and interictal variables when entered into a conditional forward logistic regression model to predict epilepsy + PNES. Frontal lobe epilepsy remained significant in the model. On conditional logistic regression analysis, the odds of having frontal seizures was found to be more than 80% lower in the epilepsy alone

Table 2
Interictal EEG characteristics in patients with epilepsy + PNES and patients with epilepsy alone while undergoing video-EEG monitoring.

Interictal epileptiform activity	Epilepsy + PNES ($n = 39$)	Epilepsy alone ($n = 78$)	Independent samples t-test
Frontal Epileptiform (Spikes and sharp waves)	20.51% ($n = 8$)	8.97% ($n = 7$)	$P < 0.14$
Temporal Epileptiform (Spikes and sharp waves)	33.33% ($n = 13$)	57.69% ($n = 45$)	$P < 0.02$
Other Epileptiform (Parietal, Central, Occipital) (Spikes and sharp waves)	12.82% ($n = 5$)	7.69% ($n = 6$)	$P < 0.5$
Generalized spike and wave	25.64% ($n = 10$)	21.79% ($n = 17$)	$P < 0.6$

group compared to the epilepsy + PNES group (odds ratio 0.13, 95% CI, 0.033–0.51, $P < 0.003$).

4. Discussion

In this study, frontal lobe epilepsy was more common in patients with epilepsy and concomitant PNES than in patients with epilepsy alone. The result suggests that at least in the subgroup of epilepsy patients with concomitant PNES, PNES symptoms may be often related to frontal seizures.

Diagnostic errors of mistaking epileptic seizures for PNES have been reported.[15–18] Previous studies have noted that many signs that have been considered typical for PNES appear not to be specific to it but can also be found in epileptic seizures, especially of frontal lobe onset.[19–21] Frontal lobe seizure patients and PNES patients also are not thought to differ with respect to history of psychiatric disorder, ictal pelvic thrusting, rocking of body, side-to-side head movements, or rapid postictal recovery, all of which previously have been reported as characteristic features of PNES.[19] In addition, seizures characterized by general motor agitation are known to be associated with lesions of the orbitofrontal and frontopolar cortices.[22] Difficulty in localizing these ictal events by scalp EEG monitoring could possibly add to their misattribution as PNES events. The present study meanwhile was limited to patients with clearly documented PNES + epilepsy and epilepsy alone. In the specific sub group of patients with epilepsy and concomitant PNES, we note a larger number of frontal epilepsy than temporal epilepsy unlike patients with epilepsy alone, raising a possibility that some PNES events in the PNES + epilepsy group could in fact be episodes of frontal seizures.

Epilepsy is related to neuronal dysfunction while PNES are thought to have psychological causes. A few studies have shown a higher prevalence of PNES in patients with epilepsy than the general population.[10–13] Nonepileptic seizures have been noted to occur almost immediately after epileptic seizures, suggesting that the experience of having a seizure can, in susceptible individuals, provoke PNES.[23,24] A possibility has subsequently been raised that disorders including epilepsy that impair emotional or self-monitoring functions may contribute to conversion disorder and thereby PNES.[24] Impaired emotional and self-monitoring functions noted in orbitofrontal cortical dysfunction[25] and seizures characterized by general motor agitation[22] make this a region of interest in future studies of PNES. While the higher prevalence of ictal frontal EEG abnormalities in patients with epilepsy and PNES in our study might be simply due to the misattribution of frontal seizures for PNES events, given the resemblance of seizures from orbitofrontal cortical dysfunction and PNES like events, other possibilities which have been raised needs further investigation.

As the study was retrospective, variables of interest including, age of onset of epilepsy, age of first diagnosis of epilepsy and family history of psychiatric disorders were occasionally unavailable to be appropriately analyzed. Additionally a selection bias could exist if the criteria were different for inclusion in video-EEG monitoring for epilepsy patients with and without PNES over the duration of the study. There was however no formal directive for change in admission guidelines for monitoring. A larger number of pre-surgical candidates (Phase 1 and 2) with temporal epilepsy syndromes could suggest a selection or referral bias towards temporal lobe localization in the epilepsy alone group influencing our results. In our series, the pre-surgical candidates with temporal lobe seizure localization were 22% among epilepsy alone and 17.6% among epilepsy + PNES groups. The larger number of temporal lobe localization subjects in the epilepsy group therefore could not be satisfactorily explained by the preferential selection of patients for epilepsy surgery alone. Alternatively, lower numbers of IGE subjects in both groups could be due to a possible referral bias towards subjects with localization related epilepsy for video-EEG monitoring. Even as video-EEG is an important technique in differentiating between epileptic seizures and PNES, it has significant limitations in the diagnosis of PNES that have been well described ([26], review) which also pertain to our study. Among other limitations, the inter-rater reliability of video-EEG when used alone in the diagnosis of PNES is known to be moderate,[27] care was therefore taken to account for a combination of patient history, examination and video-EEG monitoring which includes semiology, EEG and ECG data. Despite these limitations, we feel that the results are clinically relevant, as clinical decisions of epilepsy and PNES are now widely made using the techniques used in our study, video-EEG and clinical history, to guide diagnosis and therapy.

Our results suggest that frontal seizures are more commonly noted in patients with epilepsy and concomitant PNES than in those with epilepsy alone during video-EEG monitoring. Future studies in this subgroup of patients, including a larger number of patients and methodology to better localize frontal lobe physiological changes are warranted to confirm and extend the findings of the present report.

Conflicts of interest

Dr. Haut receives funding unrestricted grant from Endo. She is a consultant for Acorda; Jazz; Vivus; King. Dr. Pillai has no conflicts of interest to declare.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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