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Neuropsychiatric features of the coexistence of epilepsy and psychogenic nonepileptic seizures

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ABSTRACT

Objective: To investigate demographic, epidemiologic and psychiatric features suggestive of the coexistence epilepsy (ES) and psychogenic nonepileptic seizures (PNES) that may contribute to precocious suspicion of the association.

Methods: In this exploratory study, all patients older than 16 years admitted to prolonged video-electroencephalogram monitoring were evaluated about demographic, epileptological and psychiatric features. Detailed psychiatric assessment using M.I.N.I.-plus 5.0, Beck Anxiety Inventory, Beck Depression Inventory and the Childhood Trauma Questionnaire (CTQ) was performed. Data were collected previous to the final diagnosis and patients with ES-only, PNES-only or coexistence of ES/PNES were compared.

Results: Of 122 patients admitted to epilepsy monitoring unit, 86 patients were included and 25 (29%) had PNES. Twelve (14%) had PNES-only, 13 (15%) had ES/PNES and the remaining 61 (71%) had only ES. A coexistence of ES and PNES was associated with clinical report of more than one seizure type ($p^{<}0.001$), non-specific white matter hyperintensities on MRI ($p < .001$) and a past of psychotic disorder ($p = .005$). In addition, these patients had significantly more emotional abuse and neglect ($p < .002$ and 0.001, respectively). Somatization (including conversion disorder) was the most common diagnosis in patients with PNES- only (83%) and co-existing of PNES and ES (69.2%), differentiating both from ES-only patients ($p < .001$).

Conclusion: The high prevalence of this coexistence ES/PNES in this study reinforces a need to properly investigate PNES, especially in patients with confirmed ES who become refractory to medical treatment with antiepileptic drugs. The neuropsychiatric assessment may help to diagnostic suspicion and in the planning of therapeutic interventions.

1. Introduction

Psychogenic nonepileptic seizures (PNES) are paroxysmal episodes without concomitant ictal electrical discharges, caused by a psychological dysfunction. They represent the most common cause of nonepileptic phenomena in adults, can be confused with epilepsy (ES) [1,2] and are categorized by the Diagnostic and Statistical Manual (DSM-5) as a functional neurological disorder of the conversion type [3]. The combination of ES and PNES represents quite well how neuropsychiatric interconnection and biopsychosocial vulnerabilities connect physical and psychological illnesses.

Neurologists need to differentiate epileptic from nonepileptic seizures on a regular basis. For instance, among patients referred for a first episode of loss of consciousness, 57% received a diagnosis of ES, 18% of PNES and 22% of a syncopal episode [4]. The prevalence of coexistence ES/PNES has been estimated to be 5 and 50% [5] and a precise diagnosis of ES, PNES or their coexistence remains a clinical challenge, inasmuch as timely diagnosis reduces chronicity and increases the likelihood of a favorable prognosis [6,7]. Once a diagnosis of PNES is established, accurate treatment may lead to remission or improvement

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in 75–95% of patients, significantly reducing health care costs and overall morbidity [8,9].

Patients with co-existing ES and PNES are often excluded from PNES studies and in the last years only few studies differentiating patients with PNES-only from those with PNES + ES were published [10–15]. They were all retrospective and thus open to selection biases. This study aimed to investigate demographic, epidemiologic and psychiatric features suggestive of co-existing epilepsy (ES) and psychogenic non-epileptic seizures (PNES) that may contribute to precocious suspicion of the association.

2. Methods

2.1. Participants

This is a cross-sectional study. Patients were consecutively recruited from the inpatient VEEG monitoring unit of the Porto Alegre Epilepsy Surgery Program, Hospital São Lucas, PUCRS, between March 2014 and November 2015. Because only few centers in Brazil perform presurgical evaluation and epilepsy surgery through the public health system, referrals of people with refractory epilepsy are from general neurologists all over the country, through a 'high complexity procedure code'.

A total of 122 potential participants were admitted in the V-EEG monitoring unit for (1) diagnostic investigation/classification of seizures; (2) optimization of antiepileptic drugs (AEDs) for refractory ES and (3) evaluation for eligibility to ES surgery.

All patients were approached for participation prior to stabilizing the diagnosis. Twenty-five patients were excluded: ten for significant limitation in adaptive behavior or mental retardation, nine for previous epilepsy surgery, four because of acute psychosis during evaluation and two for severe language deficits. Ninety-seven were evaluated, prior to a diagnosis related to their seizures.

This study was approved by the local ethics committee and written informed consent was obtained from all participants and no monetary incentive was provided for participation.

2.2. Procedures

Participants were informed that this research would evaluate their seizure type(s) and received an explanation about their possible diagnoses (ES, PNES or a combination of both). Two different groups of examiners, who were blind to each other's findings, obtained neuropsychiatric and epileptological data prior to final diagnosis.

Neuropsychiatric evaluation was performed by the senior author (GB), a certified psychiatrist. Demographic variables included gender, age, marital status, ethnics, education and occupation. Age at seizure onset, duration of illness, number and type of antiepileptic drugs (AEDs), as well as description of the type of clinical events were obtained from patients and relatives. Seizure frequency was assessed by historical recall by patients and family members, for whom we asked to perform an estimate of seizure frequency for 3 months prior to the evaluation. Seizure triggers included sleep deprivation, stress, menstrual cycle variation, alcohol and drug use.

The Mini International Neuropsychiatric Interview plus– M.I.N.I. (DSM-IV) 5.0 [16], probed the main psychiatric diagnoses in axis I. In addition, M.I.N.I.-plus tool also analyses presence of antisocial personality disorder, which is the only axis II diagnosis assessed. Beck Anxiety Inventory (BAI) [17] and Beck Depression Inventory II (BDI II) [18] scales evaluated severity of anxiety and depression symptoms. Childhood Trauma was measured using Childhood Trauma Questionnaire (CTQ) [19]. History of seizure triggers, previous personal contact with epilepsy and family history of psychiatric disorders were obtained during interview.

Prolonged V-EEG monitoring was recorded digitally on a 21-channel polygraph (Siemens-Elema), with electrodes placed according to the 10–20 system. Time under Video-EEG monitoring, therefore, varied from each patient, since it is our practice to capture all typical seizures or events reported by the patients and their family members. Duration of recordings ranged from 24 to 178 h and was extended until all typical attacks were registered. Time under Video-EEG monitoring, therefore, varied from each patient. The latter was routinely reviewed with caregivers or relatives to assure a typical spell. During recording, no atypical spells were captured. Activation methods were used in a case-by-case basis, including hyperventilation, photic stimulation, sleep deprivation and partial or total withdraw of AEDs. Verbal suggestion or placebo was not used to induce PNES. If the typical seizures could not be recorded, patients would receive an inconclusive diagnosis and be excluded from the study. Epileptological data included the presence of focal or diffuse background slowing interictal as well as localization ictal epileptiform discharges. These were classified as lobar: frontal, temporal and other. MRI was classified as normal, lesional or presenting nonspecific white matter alterations.

When evaluation was concluded, two senior neurologists (AP, LP) and a senior psychiatrist (GB) reviewed all data. Definitive diagnosis, including putative localization of the epileptogenic zone, when feasible, was based on the convergence of multimodal localizing data, including clinical history, ictal scalp EEG and MRI. Ictal events were classified as epileptic or non-epileptic.

Following this initial selection, we excluded 11 further cases: 8 (8.2%), which did not present a seizure or a typical paroxysmal episode on V-EEG, therefore precluding an unequivocal diagnostic confirmation, and 3 subjects that had documented disorders other than ES or PNES: factitious disorder or syncopal episodes.

All 86 patients, in whom it was possible to establish a diagnosis of PNES-only, ES-only or co-existing ES/PNES, through V-EEG recording of typical episodes, validated by clinical history and confirmed by family members or patients were included.

2.3. Definition of specific groups

- Group ES-only: Diagnosis was made when a patient presented ictal epileptiform discharges during a seizure.
- Group PNES-only: During a typical episode, V-EEG did not show epileptiform discharges or change in baseline background – despite muscle artifacts– nor electroencephalogram (EEG) abnormalities.
- Group co-existing ES/PNES: V-EEG with typically ictal and interictal epileptiform discharges during ES, associated with documentation of at least one PNES, validated as a typical attack.

2.4. Statistical analysis

Data are presented as mean ± standard deviation (SD) or median and interquartile range for continuous variables and as absolute and relative frequencies for categorical variables. For comparison between groups, Chi-square and one-way analysis of variance (ANOVA) adjusted by Bonferroni test or Kruskal-Wallis tests were used. To use the Bonferroni correction in non-parametric data, logarithmic transformation was applied. Statistical analyses were performed by SPSS v 21.0 and statistical significance was set at $p < 0.017$.

3. Results

Demographic characteristics are summarized in Table 1. Mean age at presentation was 33.7 ± 11.5 (16 to 62) years and patients with PNES-only were younger at evaluation than those ES-only ($p = .01$). Female patients comprised 70% of the sample and predominated in both PNES groups ($p = .01$).

Time under V-EEG monitoring did not differ between groups. ES-only were recorded in 61 patients (71%), while the other 25 (29%) had PNES. Thirteen (52%) of the latter had both ES and PNES.

Age at seizure onset did not differ among the groups. Onset of each seizure semiology was assessed. Epileptic seizures preceded PNES in all