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Periodic epileptiform discharges in mesial temporal lobe epilepsy with hippocampal sclerosis

Daniel San-Juan [a,g,*], Adriana Patricia M. Mayorga [a], Juan de Dios Del Castillo Calcáneo [a], Maricarmen Fernández González-Aragón [a], Mario Alonso-Vanegas [b,g], Carolina Domínguez Rico [c], Richard J. Staba [d], David J. Anschel [e], Andrew J. Cole [f]

[a] Neurophysiology Service, National Institute of Neurology, Mexico
[b] Neurosurgery Department, National Institute of Neurology, Mexico
[c] Facultad de Medicina, Universidad Nacional Autónoma de México, Mexico
[d] Department of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA
[e] Comprehensive Epilepsy Center of Long Island St. Charles Hospital, Port Jefferson, NY, USA
[f] Epilepsy Service, Massachusetts General Hospital, Boston, MA, USA
[g] Centro Neurológico, Centro Médico ABC, Santa Fe, Mexico

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ABSTRACT

Purpose: Periodic epileptiform discharges (PEDs) are an uncommon, abnormal EEG pattern seen usually in patients with acute diseases and less frequently in chronic conditions, such as mesial temporal lobe epilepsy (mTLE). Evaluate the clinical histories, neuroimaging findings, and serial electrophysiological studies prior to the appearance of PEDs in patients with mTLE secondary to hippocampal sclerosis (HS).
Methods: We searched 19,375 EEGs (2006–2012) for the presence of PEDs secondary to mTLE due to HS.
Results: 12 patients were included. The patients with PEDs had a high prevalence of psychiatric comorbilities, including major depression (50%), interictal psychosis (16%) and dementia (8%). All of the patients had intractable epilepsy with similar clinical findings. We observed a sequential neurophysiological worsening of the EEG patterns prior to the appearance of PEDs. Five patients with PEDs underwent epilepsy surgery and four were seizure free at follow-up 15 (±9) months.
Conclusions: PEDs are rare in patients with mTLE and HS and their presence in these cases could reflect clinical severity and neurophysiologic worsening, clinically manifested by intractable epilepsy and severe psychiatric comorbidities. The presence of PEDs in EEGs of patients with mTLE, however, was *not* associated with poor postsurgical seizure-freedom.

1. Introduction

Scalp electroencephalographic (EEG) findings in patients with temporal lobe epilepsy (TLE) commonly contain interictal blunt spikes, sharp waves, or sharp-slow waves complexes with maximal amplitude in basal anterior temporal electrodes (sphenoidal, zygomatic, mandibular notch $\geq$ T1/2 $\geq$ F7/8 $\geq$ T3/4).[1] These interictal epileptiform abnormalities are usually unilateral and may appear isolated or in short rhythmic trains lasting 1–2 s.[2] Other EEG patterns have also been reported in patients with TLE, such as interictal rhythmic delta activity[3] and frontal midline theta activity,[4] but the occurrence of interictal periodic epileptiform discharges (PEDs) in TLE is far less common.[5]

Periodic lateralized epileptiform discharges (PLEDs) were described initially by Chatrian et al.[6] and are considered abnormal indicating an increased risk for partial onset seizures.[7] Most often PEDs are found in patients with acute disease commonly caused by acute or subacute structural lesion of the cerebral cortex that can either diffuse or focal.[8,9] PEDs can also be observed in patients with static encephalopathy and epilepsy,[6,7,9] and some authors have postulated that chronic PLEDs may be a different entity than that occuring during acute illness.[10]

Studies have found PEDs in patients with symptomatic epilepsy,[9–12] with substantial controversy over whether PEDs and related discharges represent ictal phenomenon meriting aggressive treatment, or reflect a non-specific, self-remitting marker of brain injury.[9] To our knowledge no data has been

* Corresponding author at: Av. Insurgentes Sur 3877, Col. La Fama, Tlalpan, México, D.F. 14269, Mexico. Tel.: +52 5556063822x2527; fax: +52 5556064532.
E-mail address: pegaso31@yahoo.com (D. San-Juan).

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published on the occurrence of PEDs in patients with mesial TLE (mTLE) with hippocampal sclerosis (HS), which is the most common pharmacoresistant form of human epilepsy observed at surgical epilepsy centers.[13]

The classical pattern of HS is characterized by greater loss of principal neurons in the Sommer sector (CA1 and prosubiculum), CA3, and the hilus of dentate gyrus than CA2 sector and subiculum, and often accompanied by astrogliosis and axonal reorganization.[14,15] In the present study, we describe the clinical and neuroimaging findings in patients with mTLE and HS, as well as electrophysiological changes prior to the appearance of PEDs.

2. Methods

This is a case series study, which was carried out using the printed records of all EEGs and video-EEGs performed from January 1st, 2006 to October 31st, 2012 at the Department of Neurophysiology from the National Institute of Neurology (NIN) in Mexico City. Among 19, 375 EEGs and video-EEGs we found that 12 had PEDs and mTLE with HS.

For these 12 patients we reviewed and summarized clinical information (age, sex, physical findings, past history of febrile seizures, status epilepticus or perinatal hypoxia, age at onset of epilepsy, time since diagnosis of epilepsy, type of seizures, seizure frequency, psychiatric comorbilities, neuropsychological abnormalities, surgery, outcome, and time of follow-up). We used the Engel scale to describe the outcome in the follow-up.[16] The psychiatry department evaluated all patients with psychiatric comorbidities using a typical approach in the outpatient clinic not exactly during the time of EEG recordings showing PEDs.

Each patient had a workup that included routine laboratory tests, clinical neurological evaluation, neuroimaging, neuropsychological testing, nuclear medicine studies, interictal EEG and video-EEG. The neuropsychological testing and nuclear medicine studies were not performed simultaneously or on the same day as the EEG recordings showing PEDs. High-resolution 3.0 T MRI (T1, T2 and FLAIR acquisitions) was qualitatively reviewed using a standardized protocol by two neuroradiologists who were blinded to EEG findings. For each patient, seizure semiology was described using the Clinical and Electroencephalographic Classification of Epileptic Seizure, ILAE 1981.[17] Based on these results, all patients in the present study were diagnosed with unilateral mesial TLE with MRI evidence of mesial temporal sclerosis without other lesions. The pathological confirmation of HS was available only in the patients who underwent epilepsy surgery.

All patients had digital awake routine EEG (30 min) and video-EEGs recordings (6–72 h) with 24 scalp electrodes positioned according to the standard 10–20 system of electrode placement, reformatted to both bipolar and off-head referential montages. The filter setting were 0.3 s (0.53 Hz) and 70 Hz. All of the EEG and video-EEGs recordings (with 30–50% of antiepileptic withdrawals) were performed without sedative drugs. No patients had a seizure cluster within 48 h of the EEG or video-EEGs.

2.1. Patients with PEDs and mTLE with HS

All EEGs or video-EEGs that had been reported as repetitive or periodic discharges, PLEDs, PEDs or periodic epileptiform abnormalities were included in the present study. The following inclusion criteria were considered: (1) EEGs or video-EEGs that meet the criteria of PLEDs, bilateral independent PLEDS (BIPLEDs) or generalized periodic epileptiform discharge (GPEDs), (2) Both male and female patients aged more than 16 years and (3) complete clinical records and a follow-up until death or for at least one year. Patients with reports of triphasic sharp waves, status epilepticus, incomplete clinical records or with a follow-up of less than one year were excluded from the study. For each patient, we identified the first EEG or video-EEG study showing evidence of PEDs and then reviewed all previous EEG studies to evaluate changes in the previous EEGs done on the same patient.

For the purpose of this study, we classified PEDs as PLEDs, BIPLEDs or GPEDs, using strictly adhered-to definitions. PLEDs were characterized as lateralized or focal; periodic or near periodic; or spike, spike-wave, or sharp-wave complex presentations throughout most or all of the recording.[6] GPEDs were defined as the occurrence of periodic complexes occupying at least 50% of a standard 30-minute EEG over both hemispheres in a symmetric, diffuse, and synchronized manner[7,8,18] and BIPLEDs were defined as bilateral independent periodic lateralized epileptiform discharges.[7,19,20]

2.2. Statistics analysis

We used descriptive statistics, all the values are expressed in mean, percents and standard deviations.

3. Results

3.1. Patients with PEDs and mTLE with HS

From 2006 to 2012, we recorded 19, 375 EEGs and video-EEGs in inpatients and outpatients. We identified twelve patients who had EEGs that contained PEDs, and all had mTLE with HS based on EEG, neuroimaging and epileptic semiology. In these twelve patients, BIPLEDs, GPEDs, PLEDs or PLED-like activity were captured on at least 1 available EEG or video-EEG, which represents a prevalence of 0.061% among the inpatient and outpatient EEG and video-EEG recordings. Complete clinical information, EEGs, video-EEGs and neuroimaging findings were available in all the patients. Tables 1 and 2 show the clinical, neurophysiological and neuroimaging findings of these patients. All the patients with hypoperfusion in the SPECT study were concordant with the PEDs localization, ictal onset recorded in the video-EEG and the HS side indicated by brain MRI, except two patient with PLEDs that showed bi-temporal hypometabolism in the SPECT.

The mean age of the patients was 39 (±12) year-old and 50% (6/12) were female. All patients were righthanded and 58% (7/12) of them had right mTLE. One patient with BIPLEDs had a past history of status epilepticus. The mean of the age at onset of epilepsy was 12 (±9) years old and the mean frequency of seizures monthly was 13 (±14). Also, all the patients had pharmacoresistant epilepsy and were taking 3 or more antiepileptics drugs, had normal physical and general neurological exams, but had moderate-to-severe neuropsychological deficits and were diagnosed with severe psychiatric diseases that included major depression 50% (6/12) or interictal psychosis 16% (2/12). Five patients underwent epilepsy surgery and four were seizure free at follow-up 15 (±9) months. The pathological analysis showed HS in these patients. Of the seven patients that had not had surgical treatment at the time of this study, two had interictal psychosis and dementia and their guardians declined surgical treatment, one patient refused the surgery, while the remaining four patients are scheduled for epilepsy surgery.

Fig. 1, illustrates the evolution of the EEG abnormalities before BiPLEDs were first observed. Table 2 shows the progression for an increase from slowing focal to generalized disturbances in the EEG of 5/12 patients. No patient had status epilepticus during the EEG recording. Among the 12 patients we had prior EEG or video-EEG recordings, which dated back to a median of 3 years (range 1–19 years). The PLEDs disappears in the postsurgical EEGs in patients who underwent epilepsy surgery.