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Focal EEG features and therapeutic response in patients with juvenile absence and myoclonic epilepsy

Giorgi Japaridze [a,*], Sofia Kasradze [a], Giorgi Lomidze [a], Lali Zhizhiashvili [a], David Kvernadze [a], Kakha Geladze [a], Sándor Beniczky [b,c,1]

[a] Institute of Neurology and Neuropsychology, Tbilisi, Georgia
[b] Danish Epilepsy Centre, Department of Clinical Neurophysiology, Dianalund, Denmark
[c] Aarhus University, Department of Clinical Neurophysiology, Aarhus, Denmark

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HIGHLIGHTS

- We have prospectively scored focal EEG features in 168 consecutive patients with juvenile myoclonic and juvenile absence epilepsy.
- One-hundred-eighteen patients (70.2%) had focal EEG features: 89 patients (53%) had focal epileptiform discharges, and 80 patients (47.6%) had focal slowing.
- None of the focal features influenced the therapeutic outcome.

ABSTRACT

Objective: To investigate the characteristics of focal EEG features in patients with juvenile absence epilepsy (JAE) and juvenile myoclonic epilepsy (JME), and to assess their possible influence on therapeutic response.
Methods: Focal EEG features were prospectively scored in 168 consecutive patients. Ninety-six patients were drug-naïve and 72 patients were already on antiepileptic drugs (AEDs): 38 on adequate medication and 34 on inadequate medication. Therapeutic response was assessed one year after starting adequate therapy.
Results: One-hundred-eighteen patients (70.2%) had focal EEG features: 89 patients (53%) had focal epileptiform discharges, and 80 patients (47.6%) had focal slowing. Most often, these were multifocal and localized in frontal and temporal regions. Among patients already on AEDs, patients with focal EEG features were more often treated with inadequate medication due to misdiagnosis, than patients without focal features. Data on therapeutic response were available for 118 patients; most of them (90.7%) were seizure free. None of the focal EEG features affected therapeutic response.
Conclusion: Focal EEG features are common in patients with JME and JAE, but they do not influence the therapeutic response.
Significance: It is important that physicians are aware of the focal EEG features in order to avoid misdiagnosis and inadequate therapy.

1. Introduction

Typical EEG findings in patients with idiopathic/genetic generalized epilepsies (IGE) are bilateral, synchronous generalized spike-and-wave or polyspike-and-wave discharges, with normal background activity (Janz, 1985, 1998; Betting et al., 2006).

They may also include focal abnormalities and asymmetries particularly in those with juvenile myoclonic epilepsy (JME), juvenile absence epilepsy (JAE) (Betting et al., 2006; Aliberti et al.,

* Corresponding author at: Institute of Neurology and Neuropsychology, 83/11, Vazha-Pshavelaave., 0186 Tbilisi, Georgia. Tel.: +995 32 291 29 47 (O); fax: +995 32 2 95 89 72.
E-mail addresses: gjaparidze58@gmail.com (G. Japaridze), sbz@filadelfia.dk (S. Beniczky).
[1] *Address during processing of manuscript*: Department of Clinical Neurophysiology, Aarhus University Hospital and Danish Epilepsy Centre, Visby Allé 5, 4293 Dianalund, Denmark. Tel.: +45 26981536.

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1994; Panayiotopoulos et al., 1994; Lancman et al., 1994) and childhood absence epilepsies (AE) (Betting et al., 2006; Lombroso, 1997) which may result in diagnostic errors and inappropriate treatment (Panayiotopoulos et al., 1991; Grünewald et al., 1992; Grünewald and Panayiotopoulos, 1993; Murthy et al., 1998; Seneviratne et al., 2014).

There are only few studies addressing the possible influence of focal EEG features on therapeutic response in patients with IGE, and the results are controversial (Seneviratne et al., 2014). Most of the studies are retrospective and based on datasets that were not standardized (widely varying duration of follow-up, different type and number of EEG recordings for the included patients). In addition, diagnostic criteria, characteristics of focal EEG features and the outcome measures were not or poorly defined.

The goal of this study was (1) to elucidate the EEG characteristics of the focal features in patients with JAE and JME, and (2) to assess whether these features influence therapeutic response.

2. Methods

2.1. Data acquisition and evaluation

One-hundred-sixty-eight consecutive patients (99 female patients), diagnosed with JME or JAE, in the period January 2008 to October 2014, at the Institute for Neurology and Neuropsychology (INN), Tbilisi, Georgia, were recruited. Patients gave their informed consent, and the study was approved by the institutional ethics committee. The age of the patients was between five and 63 years (mean: 22.8 years; median: 19.5 years).

As INN has both regional function, as primary referral centre, and national function for epilepsy program (tertiary referral centre), we had two different patient-populations: untreated, drug-naïve patients ($n = 96$) and patients who had previously been diagnosed and treated for epilepsy ($n = 72$).

All patients had standard EEG recordings at the time of the initial consultation in our institute. These were standard, awake recordings of 20 min duration and included hyperventilation (3 min for children, 4 for adolescents and 5 for adults) and intermittent photic stimulation. Electrodes were placed according to the 10–20 system (Recommendations for the Practice of Clinical Neurophysiology: Guidelines of the International Federation of Clinical Neurophysiology, 1999). Out of the 168 recordings, drowsiness was present in 39 recordings. None of these standard, awake recordings contained sleep – stage N2, N3 or REM.

JME and JAE were diagnosed according to the ILAE criteria (Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes, 1989). Only unequivocal cases, fulfilling the diagnostic criteria at the initial consultation were included. We diagnosed 110 patients (63 females) with JME (mean age: 25 years) and 58 patients (36 females) with JAE (mean age: 18.5 years). Supplementary material 1 shows the seizure-types in our patients.

The age of onset was between 10 and 23 years in the JME group (mean: 15.7 years) and between 5 and 19 years for the JAE group (mean: 10.7 years).

Seventy-two patients were already on AEDs at the time of the first consultation in our institute. We categorized them into groups with adequate therapy (AT) and inadequate therapy (IAT). AT groups included valproate, levetiracetam, lamotrigine (Machado et al., 2013) and phenobarbital. Phenobarbital was considered AT only for JME, not JAE. Patients on carbamazepine monotherapy or in combination with other AEDs were considered IAT (Seneviratne et al., 2014). We noted the cases in which patients experienced exacerbation while on AEDs, before the first consultation in our institute, and before being changed to adequate therapy.

EEGs were prospectively evaluated by one of the authors (GJ). The characteristics of epileptiform discharges and of focal EEG features in these recordings were then scored and logged in a database together with another author (SB) who was blinded to the clinical data. Both authors are board certified clinical neurophysiologists, with more than 10-year experience in epileptology. Recordings were inspected both in bipolar montages and in common average. In addition, 3D voltage maps were constructed using BESA software (Figs. 1 and 2).

Epileptiform discharges (spike/polyspike and slow wave complexes) and slowing (rhythmic delta or theta activity) were defined according to the IFCN glossary of terms (Recommendations for the Practice of Clinical Neurophysiology: Guidelines of the International Federation of Clinical Neurophysiology, 1999).

All patients had "generalized" (bilateral synchronous) spike/polyspike and slow wave complexes (Fig. 1), since this was part of the inclusion criteria (Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes, 1989; Kasteleijn-Nolst Trenité et al., 2013).

EEG graphoelements were considered focal, when they were only seen over one side, in bipolar montages (allowing though for midline electrodes) and when the distribution of the negative potentials over the head was strictly unilateral and confined to 1–3 regions. Asymmetric bilateral graphoelements were not considered focal.

For the focal EEG features, the following characteristics were scored: morphology, spatial distribution and location. Morphology was scored either as epileptiform discharge (spike, polyspike, sharp-wave) or as slowing (delta or theta activity) (International Federation of Clinical Neurophysiology et al., 1999). Spatial distribution was scored as single focus, bilateral independent foci or multifocal graphoelements (two or more independent foci provided they were not bilateral-independent).

Follow-up: one year after the initial consultation, therapeutic response was classified as seizure-free, >50% seizure-reduction (but not seizure-free), no/minor change.

2.2. Statistical analysis

Descriptive statistics were used. Pearson's chi square test was used to identify associations between the categorical variables. Two-sided probabilities of less than 0.05 were considered statistically significant. The statistical analysis was performed with SPSS, version 21.0 (SPSS, Chicago, Illinois, USA).

3. Results

3.1. Incidence of focal EEG features

One-hundred-eighteen patients (70.2%) had focal EEG features in the initial EEG recording. Focal epileptiform discharges were recorded in 89 patients (53%), while focal slowing was recorded in 80 patients (47.6%) (Fig. 2). There was no significant difference between JME and JAE in the incidence of the focal EEG features (Table 1).

3.2. Characteristics of focal features

Characteristics of focal EEG features (morphology and location) are summarized in Table 2. Examples of focal EEG features are illustrated in Fig. 2. Most often, focal EEG features were multifocal,

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