Long-Term Clinical and Electroencephalography (EEG) Consequences of Idiopathic Partial Epilepsies

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Background: Idiopathic partial epilepsies of childhood (IPE) affect a considerable proportion of children. Three main electroclinical syndromes of IPE are the Benign Childhood Epilepsy with Centro-temporal Spikes (BECTS), Panayiotopoulos Syndrome (PS), and Childhood Epilepsy with Occipital Paroxysms (CEOP). In this study we investigated the long-term prognosis of patients with IPE and discussed the semiological and electroencephalography (EEG) data in terms of syndromic characteristics.

Material/Methods: This study included a group of consecutive patients with IPE who had been followed since 1990. Demographic and clinical variables were investigated. Patients were divided into 3 groups – A: Cases suitable for a single IPE (BECTS, PS and CEOP); B: cases with intermediate characteristics within IPEs; and C: cases with both IPE and IGE characteristics. Long-term data regarding the individual seizure types and EEG findings were re-evaluated.

Results: A total of 61 patients were included in the study. Mean follow-up duration was 7.8±4.50 years. The mean age at onset of seizures was 7.7 years. There were 40 patients in group A, 14 in group B, and 7 in group C. Seizure and EEG characteristics were also explored independently from the syndromic approach. Incidence of autonomic seizures is considerably high at 2–5 years and incidence of oromotor seizures is high at age 9–11 years. The EEG is most abnormal at 6–8 years. The vast majority (86%) of epileptic activity (EA) with parietooccipital is present at 2–5 years, whereas EA with fronto-temporal or multiple sites become more abundant between ages 6 and 11.

Conclusions: Results of the present study provide support for the age-related characteristics of the seizures and EEGs in IPE syndromes. Acknowledgement of those phenomena may improve the management of IPEs and give a better estimate of the future consequences.

MeSH Keywords: Epilepsies, Partial • Epilepsy, Rolandic • Seizures

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Background

Benign idiopathic partial epilepsies of childhood (IPE) affect a considerable proportion of children with non-febrile seizures and pose some difficulties in decision-making about treating or not treating the patient, as well as about anticipating the long-term prognosis. There are 3 main electroclinical syndromes recognized by the International League Against Epilepsy (ILAE) [1]: the Benign Childhood Epilepsy with Centro-temporal Spikes (BECTS), Panayiotopoulos Syndrome (PS), and Childhood Epilepsy with Occipital Paroxysms (CEOP) [2].

BECTS is the best known and most common form, with a prevalence of 15% in children with non-febrile seizures and between ages 1–15 years [3–7]. The main features of BECTS are focal seizures as unilateral facial sensory-motor symptoms, oro-pharyngo-laryngeal symptoms, and speech arrest [8–12]. Spike-wave (SW) activity, mainly in central regions, is typical in the electroencephalography (EEG) and is activated by non-REM sleep [13,14].

PS is characterized by seizures, often prolonged, with predominately autonomic symptoms, as autonomic status epilepticus (ASE), but convulsive SE may be also seen [15]. The onset of seizures is 3–6 years in 76% of patients with PS [16]. In the majority of cases, spike-wave complexes present with intra- or interhemispheric shifting loci, in the same or in successive EEGs. Occipital spikes may predominate. SW activity shows increase in non-REM sleep.

CEOP is a form of occipital epilepsy characterized by positive visual hallucinations and/or attacks of vision loss [17,18]. Ictal headache and orbital pain are common ictal symptoms, and may be associated with deviation of the eyes. CEOP is a relatively rare form of IPE, with an age range of seizure onset of 3–15 years. The inter-ictal EEG shows occipital paroxysms [17].

Focal or multifocal spike-wave abnormalities with fluctuating abundance and migratory characteristics are frequently found throughout the long-term epileptic process in IPEs. Although the differential diagnosis between the main phenotypes of IPEs is frequently not difficult in their typical presentations, cases with symptoms pertaining to 2 or more phenotypes or with distinctive EEG signs may lead to diagnostic suspicion. In such cases it can be useful to perform a meaningful synthesis of quality and quantity, chronological sequence, consistency, relation to other seizure manifestations, the circumstances of their appearance, and the overall clustering of clinical EEG manifestations [16].

In this study, we selected the common and discrete clinical and EEG characteristics in a group of patients with IPEs and questioned the age-relatedness of individual seizure types and their significance in relation to syndromic conception.

Material and Methods

This study includes data pertaining to a group of patients with IPE who have been followed in a private child neurology clinic since 1990. Patient selection criteria were: presence of partial seizures with or without secondary generalization, normal physical and mental development, presence of sleep and waking EEGs, normal EEG background activity, presence of normal phasic elements in non-REM sleep, normal cranial magnetic resonance imaging (cMRI) findings, and having regular follow-ups and good compliance. At least 2 years of seizure-free was also mandatory for inclusion. Diagnosis and classification of epileptic seizures and syndromes were based on the 2010 ILAE report [2].

Demographic and clinical variables questioned were gender, presence or absence of febrile seizures in the history, presence or absence of family members with relevant medical conditions, consanguineous parents, and age at onset and at the remission of seizures. Data from long-term follow-up were enrolled and evaluated. Only EEGs and cMRIs fulfilling the international technical requirements were included in the evaluation.

Patient groups according to the epilepsy syndromes were PS, BECTS, and CEOP. Patients with a single IPE syndrome were placed in the typical IPE group (group A). The atypical IPE group (group B) included patients with features relating to more than 1 of those IPE syndromes or evolving into atypical benign partial epilepsy (ABPE) on clinical and EEG grounds [19,20]. The minimum percentage of SW activity in non-REM sleep was accepted as 50% in continuous spike-wave (CSWS) patients. Patients in group C (the IPE + group) had initial features of IPEs with additional clinical or EEG features relating to idiopathic generalized epilepsies (IPEs) [21].

Two main groups of seizure symptoms were evaluated in relation to age at first occurrence. Those were autonomic seizures and oro-motor seizures. First, individual seizure types supported with temporally-related (maximum 6 months apart) abnormal EEG findings were recorded. Second, from this pool, particular seizure types were selected for evaluation due to their predominance and consistent stereotypical repetition in the afflicted individuals, as well as their well-established relationships to certain epileptic syndromes of childhood and adolescence. Presence or absence of peri-ictal headache was also noted. Those data were evaluated on the basis of 4 stages of development. Those age groups were 2–5, 6–8, 9–11, and ≥12 years.
Continuous variables are expressed as the mean ±SD; categorical variables are presented as frequencies and percentages. The chi-square test was used to compare the differences in categorical variables between the groups. SPSS 17.0 statistical software was used for statistical analysis. A value of $p<0.05$ was considered statistically significant.

### Results

A total of 61 patients were included in the study. Twenty-three (38%) were female and 38 (62%) were male. The mean age at onset of seizures was 7.7 ± 2.81 years (2–12). Age at the first visit to a physician was 8.51 ± 2.94 years (2–14). Age of the patient at the latest visit was 15.3 ± 5.29 years (6–28). Mean follow-up duration was 7.8 ± 4.50 years (2–20 years). Twenty-three patients were followed for more than 10 years and 44 patients were followed for more than 5 years. Twenty-one patients had at least a single individual with epilepsy within the family. Five patients had consanguineous parents (Table 1).

Among patients with at least 1 occurrence, autonomic symptoms were the most frequent manifestations, followed by oromotor signs, present in 39% and 36% of patients, respectively. They were followed by unilateral motor involvement of the extremities (28%), positive or negative visual signs (24.5%), and staring with or without versive ocular/head movement (19%). Other complaints were, in decreasing order of frequency, headache, apathy, ictal syncope, loss of consciousness, and TV sensitivity, as well as other variable, isolated events.

Two main seizure groups were categorized as autonomic seizures and oromotor seizures. Table 2 shows the incidence of autonomic seizures and oromotor seizures on the age scale. Incidence of autonomic seizures is considerably higher (60%) in the youngest age group (2–5 years) and displays a steady decline later, as 30%, 19%, and 7%, in age groups as 6–8, 9–11, and ≥12, respectively. The relation between seizure types and age groups was statistically significant ($p<0.0001$). A graphical representation of this relation is demonstrated in Figure 1. Oromotor seizures were present in all age groups. They were more frequent than autonomic seizures in age groups 9–11 and ≥12. The peak incidence of oromotor seizures is at age 9–11 years.

The number of patients distributed in syndromic sub-groups included a total of 40 patients in group A, with characteristics typical for BECS in 18 patients, for PS in 11, and for CEOP in another 11 patients. Group B included 14 patients with atypical features. Three patients in this group evolved into ABPE, with later amelioration of EEGs at ages 9, 10, and 11 years in each patient. A total of 7 patients with additional IGE traits fell into Group C, the IPE+ group. Age at the development of

### Table 1. Demographic features of patients.

| N: 61          |  |
|----------------|---|
| Sex (F/M)      | 23/38 |
| First visit to physician (year) | 8.51±2.94 (2–14) |
| Age at onset of seizures (year) | 7.7±2.81 (2–12) |
| Follow-up duration (year) | 7.8±4.50 (2–20) |

### Table 2. Distribution of seizure types and EEG findings in different age groups.

| Age Groups | 2–5 year | 6–8 year | 9–11 year | ≥12 years | p     |
|------------|----------|----------|-----------|-----------|-------|
| Seizure types* |         |          |           |           |       |
| Autonomic seizures | 33 | 22 | 20 | 4 | <0.0001 |
| Oro-motor seizures | 3 | 19 | 31 | 5 |       |
| EEG characteristics* |      |        |           |           |       |
| Normal | 6 | 5 | 21 | 64 |       |
| FCT SW | 4 | 13 | 24 | 31 | <0.0001 |
| PO SW | 11 | 15 | 14 | 13 |       |
| Multiple loci | 0 | 6 | 12 | 15 |       |

SW = Spike-wave; FCT = frontocentrotemporal; PO = parieto occipital. * Some pts have more than 1 seizure types or EEG characteristics.
clinical or EEG features of IGE was 15 years in 5 of 6 patients in group C (Table 1).

A total of 39 patients (63.93%) were seizure free and without treatment for at least 2–14 years (mean 7.03±4.581). Only 20 patients (32.78%) were on treatment during the latest visit and 14 of those were at or older than age 13. That group included 6 patients with characteristics pertaining to groups with atypical IPE, or, IPE + (Groups B and C), 5 patients with CEOP, and 3 patients with BECTS.

There were a total of 254 sleep-waking EEGs evaluated. All but 6 patients had multiple EEGs. All repetitive EEGs of 2 patients displayed normal results. Epileptogenic activity (EA) was detected in only a single EEG in 8 patients. Most (36) of the remaining patients showed varying spatial, quantitative, and less frequently, propagational characteristics of the EA in different control EEGs.

The topical distribution of EA in different age groups is shown in Figure 2. The EEG is most abnormal at 6-8 years and improvement becomes evident by age 12, when more than a half of non-REM sleep was noted in 5 patients.

The majority (86%) of EA with patients showed varying spatial, quantitative, and less frequently, propagational characteristics of the EA in different control EEGs.

The topographical distribution of EA in different age groups is shown in Figure 2. The EEG is most abnormal at 6-8 years and improvement becomes evident by age 12, when more than half of the EEGs became normal. The majority (86%) of EA with patients showed varying spatial, quantitative, and less frequently, propagational characteristics of the EA in different control EEGs.

Bilateral, synchronous, interhemispheric representation of focal EA was most prominent in the 6–8 age group. Continuous SW activity in ≥50% of non-REM sleep was noted in 5 patients (0.8%); bilateral, mostly short-lasting, generalized SW discharges, or spiky K-complexes in at least 1 EEG were documented in 14 (22.9%) patients.

The EEG findings common for both PS and BECTS out of a group of patients with PS and BECTS, a form of rolandic epilepsy with onset at a similar age with PS is claimed to present features typical of “benign childhood seizure susceptibility syndrome” (BCSSS), since they share both age-related and age-limited characteristics, as well as possible genetic determination [22]. Most of these conditions present spontaneous resolution before or around puberty, possibly due to cases with overlapping features in discrete IPE syndromes, of family members with other IPEs, and of common EEG features. Some patients with PS have rolandic type oro-motor seizures concurrent with autonomic seizures or at distant times [23,24]. The topography of interictal spikes may overlap in some cases with PS and BECTS [25]. Reports on siblings of a child with rolandic seizures and another PS, as well as a high prevalence of febrile seizures in both groups, exist in the related literature [23,26–28]. Fourteen patients out of a total of 61 (22.9%) had characteristics pertaining to more than 1 IPE (excluding FS) in this study. Covanas et al. described a total of 9 (37.5%) patients with either clinical or EEG findings common for both PS and BECTS out of a group of 24 with IPE. Although many common features do exist between PS and BECTS, a form of rolandic epilepsy with onset at a similar age with PS is claimed to present features typical for BECTS [29]. Visual seizures in CEOP are the sole symptom; they are mostly diurnal and short-lasting. EEG abnormalities are mainly unilaterally or bilaterally occipital and reactive to eye-opening. Although few clinical or EEG similarities exist between either PS, BECTS, and CEOP, some cases with such IPEs may later develop occipital seizures [23,30,31]. In our study, 6 patients (3 PS, 3 BECTS) developed visual symptoms typical of focal EA.
for CEOP in later years. Such cases are considered to indicate the intimate links of these disorders within the framework of BCSSS [32]. Six patients (9.8%) in the present study developed EEG features characteristic for IGE in the long term. All those patients developed more than 1, bilateral, diffuse SW discharge in their EEGs at or later than 15 years of age, except for one at age 10. Two of them had asymmetrical continuous spike-wave activity in nearly 50% of non-REM sleep (CSWS) in some EEGs before puberty. A single patient in this group developed juvenile myoclonic epilepsy (JME) associated with generalized spike-wave activity in the EEG after puberty. A genetic relationship with idiopathic photosensitive occipital lobe epilepsy (POLE) and IGEs, including JME, is reported in the current literature [33]. Some cases of partial epilepsies within the CSWS spectrum may share some common genetic traits with IGEs. There are also a few cases with both absence and partial seizures [34], but most of BCSSS do not have any clinical or EEG resemblance to idiopathic generalized epilepsies [32].

Two main groups of seizure symptoms were evaluated in relation to the age at their first occurrence – autonomic seizures and oro-motor seizures. Figure 1 is a diagram which shows the incidence of autonomic seizures versus oro-motor seizures on the age scale. Incidence of autonomic seizures is considerably higher (60%) in the youngest age group (2–5 years) and displays a steady decline later. The preferential involvement of emetic and other autonomic manifestations in PS is attributed to a maturation-related susceptibility of the central autonomic network [23]. The authors claim that, as seizures primarily involve a particular system (the autonomic), PS may be considered as an electroclinical example of ‘system epilepsy’ [34].

The epileptogenic zone in BECTS involves neuronal networks within the rolandic cortex, possibly due to a lower threshold for seizure susceptibility at later ages than the autonomic centers. As suggested the seizure onset curve in our study and the variations in quantity and spatial characteristics of the EA in the EEGs in different ages, an age-related, dynamic re-arrangement of functional systems with a possible genetic vulnerability for seizures may provide a favorable setting for IPEs. EA with occipital localization was found to have a shifting tendency to other sites, or become multifocal by time, in around half of patients in a study by Oguni et al. [36]. Koutroumanidis reported a similar incidence of EA with occipital versus centro-temporal/parietal localization in the initial EEGs of patients with PS. In a detailed analysis of a symptomatic case with PS, multifocal extra-occipital SW foci were shown as representing rapid diffusion of epileptogenic activity related to the lesion in the inferior parietal lobe [37].

**Conclusions**

The results of the present study provide support for the age-related characteristics of both the seizures and EA in the EEGs in IPE syndromes and the interrelation between those conditions. Acknowledgement of those phenomena may improve the clinician’s ability to manage IPEs and estimate prognosis in individual cases.

**Conflict of Interest**

The authors declare that there are no conflicts of interest.

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