The clinical-electrographic expression of infantile seizures

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Abstract

Purpose: To describe the electro-clinical expression of seizures in infants (1–24 months).
Methods: We reviewed the video and EEG files of all infantile seizures recorded at Children’s Memorial Hospital, Chicago, IL, from 2000 to 2005. Electrographic and clinical features were entered into separate databases. The electrographic component of the database analyzed the predominant location and pattern at onset, the evolution, the termination and the duration of each seizure. The clinical data sheet included 25 items. Each seizure was assigned to a specific category according to its most prominent clinical feature, according to the opinion of both observers.
Results: Thirteen seizure types were identified. In a significant number of cases, the EEG correlate could not be predicted on the basis of clinical observations only. Generalized seizures were observed, on average, at a later age than focal seizures. Excluding spasms, the mean duration of seizures was short (36 s).
Conclusions: The results of this study are useful in describing the clinical and electrographic repertoire of infantile seizures. The findings show that video-EEG recordings in infants with frequent, recurrent seizures are useful by fully allowing complete recognition of subtle events, and in fully categorizing the true nature of the ictus. Video-EEG findings and accurate seizure classification may add fundamental information with regards to epilepsy syndrome diagnosis and specific treatment options, including surgery.

Keywords: Seizures; Infants; Electro-clinical expression

1. Introduction

The incidence of epilepsy in infancy is high and the prognosis may be unfavorable regarding seizure control and future neurodevelopment (Cavazzuti et al., 1984; Battaglia et al., 1999; Vanderlinden and Lagae, 2004). Work-up and effective treatment could be aided by an accurate, adapted classification of seizures and their associated epilepsies.

The epilepsy syndrome classification system, derived from studies done on adults and adopted by the (ILAE) in 1989 (Commission of the ILAE, 1989), has been shown to be reliable and applicable to children...
in large community-based studies (Berg et al., 1999). However, seizures in infants younger than 2 years show certain peculiarities that make classification more complex and challenging (Nordli et al., 1997; Engel, 2002). For instance, the state of consciousness during a focal seizure in a pre-verbal infant is very difficult to assess with certainty. It is therefore often impossible to verify the complex or simple character of a seizure (Luna et al., 1989; Nordli et al., 1997). Moreover, in this age group, clinically generalized seizures are frequently correlated to focal electrographic abnormalities, whereas clinically focal seizures may demonstrate generalized features on the EEG (Acharya et al., 1997; Nordli et al., 1997; Hamer et al., 1999). This makes the clinical subdivision into generalized or focal categories confusing, and sometimes arbitrary. An accurate diagnosis of the true nature of a seizure sometimes requires correlation with electrographic features. In that perspective, a new clinical classification scheme based exclusively on semiology has been proposed (Lüders et al., 1998), and a scheme for a diagnostic approach of patients with epilepsy consisting of five axes (ictal phenomenology, seizure type, syndrome, etiology and impairment) has been outlined (Engel, 2002). Both illustrate the importance of a step-wise approach in the diagnosis of seizures and highlight the usefulness of thoroughly analyzing both the clinical and electrographic features of ictal events. An orderly approach begins with the clinical description of the event. In some circumstances the characteristics of the event are so declarative that no other information is required to arrive at a seizure diagnosis. Other times, the characteristics are rather ambiguous and EEG data is necessary to classify. Knowledge of the precise electro-clinical relationships of infantile seizures would enhance the ability to accurately classify seizures. Such information could be used to identify those instances when EEG data are needed for classification and those times when the clinical features alone are distinctive enough to allow diagnosis of the seizure type.

In previous work it was clear that a semiological clinical classification of infantile seizures resulted in a high consensus between different observers, but the question whether there were consistent EEG correlates to these clinical patterns was not addressed (Nordli et al., 1997). Likewise, Hamer et al. described the symptomatology of seizures in the first three years of life, but focused their electrographic analysis on the focal or generalized character of the ictus (Hamer et al., 1999). Acharya et al. described the seizure symptomatology and electrographic correlates in infants with localization-related epilepsy (Acharya et al., 1997) but precise clinical-electrographic correlates for the entire seizure repertoire in infants has yet to be described.

We therefore reviewed the video-EEG files of seizures in infants recorded at a tertiary care pediatric epilepsy center, and report the details of their electro-clinical correlate.

2. Methods

The database of the Epilepsy Center at Children’s Memorial Hospital (CMH), Chicago, IL, includes patients aged from 1 day to 18 years, who present with a great diversity of indications, ranging from new-onset paroxysmal spells to intractable epileptic seizures. Twenty-three gold electrodes are used for all recordings, including reference and ground electrodes, and placed according to the rules of the 10–20 international system.

All seizures recorded at CMH in children older than 1 month and younger than 2 years were analyzed by both authors. If several seizures of the same type were recorded during the same EEG, only one of them was considered for review. If a similar seizure was observed during a subsequent recording, it was included in the study as well. One child could therefore have several seizures included, as long as they were of a different type or observed during separate recordings. The entire video and EEG files were systematically reviewed throughout the ictus. We entered the clinical and electrographic features into separate datasheets.

The clinical database contained many detailed descriptors. Multiple entries were possible for each seizure. A modification of the 1981 ILAE seizure classification system (Commission of the ILAE, 1981) was used to categorize the clinical features with more accuracy. In particular, a category of focal seizures, with “undetermined alteration of consciousness” was added. This group contained several subcategories: clonic, tonic, tonic–clonic, pure behavioral arrest, behavioral arrest with version, hypermotor and mixed seizures. Mixed seizures were those in which both generalized and focal features were observed, but where the complete analysis of the ictus, using both
clinical and electrographic features strongly suggested a focal ictus. Spasms were separated into generalized and mixed categories: spasms that exhibited unequivocal generalized clinical and electrographic features were classified under generalized seizures, whereas if generalized and focal features were noted, the spasm was considered as a mixed seizure. This latter category also included seizures that showed diffuse tonic posturing and focal clonic jerks.

The electrographic component of the database analyzed the predominant location and pattern at onset, the evolution, the termination and the duration of each seizure in order to allow for a complete electrographic characterization.

Each seizure was classified according to its most prominent clinical feature according to the opinion of both observers.

3. Results

From a total of 2112 patients monitored in our video-EEG lab from May 2000 through January 2005, 109 distinct seizures in 77 infants were reviewed. Eight events in 8 patients were excluded: five had a poor video quality and three were purely electrographic seizures in heavily sedated and paralyzed patients. We retrospectively analyzed the clinical-electrographic correlate of the remaining 101 seizures in 69 infants (Table 1). Thirteen seizure types were identified.

3.1. Seizure types

A summary of the most characteristic electroclinical correlates of each seizure type is presented in Table 2. Details are described hereafter.

3.1.1. Generalized seizures

1.3 Clonic (C) (n = 6): These seizures were characterized by generalized clonic jerks. In all six of them (100%), the EEG ictal features consisted of runs of repetitive generalized sharp waves or spikes with occipital predominance in one of them, and frontal predominance in two. Since the seizures were rather diffuse, no spread was observed on evolution. Four (66%) stuttered (repeated epochs of ictal features mixed with epochs of usual background activity), and two (33%) had an abrupt termination (clear-cut instant change in EEG features from ictal activity to post-ictal features, such as attenuation, slowing or return to the usual background activity).

1.5 (Clonic)–tonic–clonic (CTC) (n = 1): “Classic” generalized tonic–clonic seizures were not observed. However, one similar seizure was captured in a 9-month-old patient with Dravet syndrome. The seizure was characterized by bilateral symmetric myoclonic jerks, followed by blinking, symmetric tonic posturing, erratic myoclonic jerks and orolalimentary automatisms. Its electrographic correlate began with a run of generalized sharp waves, which was followed by a brief epoch of diffuse attenuation then bicentral rhythmic theta–alpha (RTA) pattern with subsequent spread over the entire hemispheres, further evolution of generalized rhythmic spikes and, finally, abrupt termination.

1.6 Atonic (A) (n = 5): These seizures were characterized by isolated or repeated head drops associated or not to generalized hypotonia. Their electrographic correlate was a run of slow waves in one patient (20%), or generalized sharp waves or spikes in four patients (80%), with occipital predominance in one and frontal predominance in two of them. These features stayed generalized or predominantly confined to the same region before progressively fading in all of them (100%).

1.7 Spasms (S)(n = 13): These seizures were characterized by clusters of a sudden bilateral symmetric jerk of the limbs, neck and trunk followed by a brief bilateral symmetric tonic posture, sometimes accompanied by crying (classic infantile spasms). Electrographically, a generalized sharp wave was observed in 12 cases (92%), whereas a bilateral symmetric occipital sharp wave was noted in one case (8%). These initial features were immediately followed by attenuation and low voltage fast activity (electrodecrement) in all cases (100%). The termination was stuttering in 12 patients (92%) and fading (progressive and continuous disappearance of ictal features and evolution to the usual background activity) in one patient (8%).
<table>
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<td>Spread</td>
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<tr>
<td>1.3 Clonic</td>
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<td>Bilateral symmetric clonus</td>
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<td>1</td>
<td>Bilateral symmetric clonus, symmetric tonic posture, and erratic clonus</td>
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<td>Unilateral or bilateral asymmetric clonus</td>
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<td>2.4 Tonic</td>
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<td>Asymmetric tonic posture</td>
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<td>2.4 Spasms with partial seizures/asymmetric</td>
<td>28</td>
<td>Generalized or focal spasms associated or not to focal clonus, asymmetric tonic posture, or both</td>
<td>Generalized or focal spike, electrodecrement; occasional focal spikes or low voltage fast activity</td>
</tr>
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</table>
3.1.2. Focal seizures

2.3 Tonic-clonic with secondary generalization (TCSG) (n = 3): These seizures were characterized by an asymmetric tonic posture in one patient, and a symmetric tonic posture in another patient. The onset was off video in the third patient. These features were followed by unilateral or bilateral asymmetric clonus in the three children (100%). Eye or head version was also noted in two patients (66%). The electrographic onset was a run of unilateral spikes in two patients (66%), RTA in the third (33%). Secondary generalization was present in all (100%). Abrupt termination was noted in two children (66%), and fading was present in the third (33%).

2.4 Uncertain impairment of consciousness

2.4 Clonic (n = 11): These seizures were characterized by unilateral or bilateral asymmetric myoclonic jerks of the limbs in all patients (100%). Erratic jerks were also noted in one patient. The electrographic onset was focal in all patients (100%), and more specifically anterior (frontal, central or frontal–central) in eight of them (73%). In two patients, only (18%) the onset was posterior (parietal–temporal–occipital); it was hemispheric in one (9%). Repetitive spikes were observed in the majority of children with this seizure type (eight children 73%); the remaining three patients showed low voltage fast activity, attenuation or rhythmic delta (one pattern 9% for each). The abnormal activity was confined in five patients (45%), spread to the contralateral homotopic region in five (45%), and to the posterior region in the same hemisphere in one (9%). Termination was fading in seven patients (64%) and stuttering in four of them (36%). Overall, the EEG pattern of these seizures was often distinctive with a localized “crescendo” of rhythmic spikes or sharp waves in the central region followed by a “decrescendo” of ictal activity (Fig. 1).

2.4 Tonic (T) (n = 11): These seizures were characterized by a predominant asymmetric tonic posture in nine patients (81%). Two patients (19%) showed a symmetric tonic posture that was accompanied by head or eye version. On one occasion, these features were

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**Fig. 1.** Focal clonic seizure. Fifteen-month-old girl, awake. Longitudinal bipolar montage. Left parietal run of spikes, no spread, fading termination (crescendo–decrescendo pattern).
preceded by a brief behavioral arrest. Their electrographic onset was unilateral in seven patients (63%), bilateral symmetric in one (9%), and generalized in three (27%). Predominant features were observed in the frontal region in two (18%), in the frontal–temporal region in one (9%), in the frontal–central in two (18%), in the temporal–occipital in one (9%), and purely occipital in one (9%). It was unilateral hemispheric in one patient (9%) and generalized in the remaining child (9%). Onset features involved rhythmic activity in 7 patients (63%), and were composed of low voltage fast activity in four (36%), of RTA in one (9%), of delta waves and RTA in one (9%) and of RTA and attenuation in one (9%). Three patients (27%) had a run of spikes, and one had pure attenuation. On evolution, five events (45%) were electrographically confined to the same region, two (18%) spread to the contralateral homotopic region, one (9%) spread to the posterior region of the same hemisphere, and two (18%) which were initially diffuse converged to a more restricted area. One event (9%) independently migrated to the contralateral hemisphere. Termination was fading in seven patients (63%), abrupt in two (18%) and stuttering in two (18%).

2.4 Focal tonic–clonic (TC) (n = 3): These three seizures (100%) were characterized by unilateral myoclonic jerks and asymmetric tonic posturing, which either preceded or followed the former. Head version in one patient and blinking in the other were also observed. Electrographically, one seizure had a clear focal onset and the two others had a predominant initial ictal pattern felt to be focal, although not as certain. Initial features were predominant in the temporal region in two (66%), in the frontal region in one (33%). The three seizures (100%) involved rhythmic activity at onset, one RTA (33%) and two in the beta range (66%). One seizure (33%) showed anterior spread on the same hemisphere, another one (33%) stayed confined, and the third (33%) showed independent migration to the contralateral hemisphere. Termination was stuttering in one (33%) and abrupt in the two others (66%).

2.4 Pure behavioral arrest (BA) (n = 1): this seizure was characterized by an isolated behavioral arrest without any iversive signs, followed by rare bilateral sym-
metric myoclonic jerks. Electrographic onset was composed of unilateral parietal–temporal–occipital spikes. The ictal pattern then spread to the anterior region of the same hemisphere and had a fading termination.

2.4 Behavioral arrest with version (BAV) \((n = 14)\): In addition to the prominent behavioral arrest previously described, these seizures also showed pronounced version of the head, eyes, or both. Electrographically, thirteen (93%) had a unilateral focal onset and one (7%) had bilateral asymmetric involvement. Four (29%) had hemispheric onset, one (7%) was predominantly frontal, two (14%) were frontal–temporal, two (14%) were temporal, two (14%) were parietal–occipital, and three (21%) were purely occipital (Fig. 2). Twelve seizures (86%) involved rhythmic activity at onset: low voltage fast activity in four, RTA in four, delta waves in three, and beta waves in one. One showed irregular slowing, and one showed a run of spikes. Ten seizures (71%) showed confinement to the same hemisphere, two with anterior spread, and three with posterior spread. One spread to the contralateral homotopic region. Three showed independent migration to the contralateral hemisphere. Termination was fading in eleven patients (79%) and abrupt in three (21%). The ictal discharge was contralateral to the version in nine patients (64%), and ipsilateral in the five remaining ones (36%).

2.4 Hypermotor \((H) (n = 1)\): This seizure was characterized by incessant non-purposeful and disorganized movements. Its electrographic correlate was a unilateral hemispheric onset of rhythmic delta waves, which stayed confined to the same region, and progressively faded away.

2.4 With mixture of focal and generalized elements (mixed)

2.4 Diffuse tonic–focal clonic (DTFC) \((n = 4)\): These seizures were characterized by a bilateral symmetric tonic posture that followed or preceded unilateral or bilateral asymmetric myoclonic jerks. Two patients also exhibited versive signs, and one of them showed oroolimentary automatisms. Electrographically, three (75%) had a unilateral onset, and

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Fig. 3. Diffuse tonic–focal clonic seizure. One-month-old girl, awake. Longitudinal bipolar montage. Right frontal–temporal predominant sharp wave, diffuse attenuation, followed by right frontal–temporal rhythmic delta sharp waves, with posterior and homotopic spread, stuttering termination (not shown).
one (33%) had a bilateral asymmetric onset. Features were predominant in the frontal region in one child, in the frontal–temporal region in the second, in the parietal–temporal–occipital region in the third, and in the central region in the remaining. Onset was composed of spikes in two patients (50%), of fast waves and spikes in one (25%), and of low voltage fast activity in one of them (25%) (Fig. 3). Homotopic spread was noted in two patients (50%), regional posterior spread was observed in the third (25%), and independent contralateral migration was noted in the fourth (25%). Termination could be fading (25%), abrupt (25%) or stuttering (50%).

2.4 Spasms (n = 28): This category included spasms that were accompanied by independent focal seizures, and spasms that had markedly asymmetric features, either clinical or electrographic.

Spasms with focal seizures (SFS) (n = 16): three patients (19%) had spasms with focal clonic seizures, nine patients (56%) had spasms with focal tonic seizures (Fig. 4), and four patients (25%) had spasms with focal tonic–clonic seizures. Blinking was occasionally also observed. The electrographic onset was generalized in five patients (31%), bilateral symmetric in four patients (25%), bilateral asymmetric in four patients (25%), and focal in three patients (19%). If any location predominance was observed, it was anterior in four patients (25%), parietal–temporal–occipital in two patients (13%), and purely occipital in two patients (13%). The onset was characterized by a sharp wave and electrodecrement in 15 cases (94%). One patient who showed eye blinking and myoclonic jerks before the spasms had an RTA electrographic correlate at onset. Ten patterns (63%) stayed confined to the same region, five converged to a more restricted region on evolution, and one showed posterior and contralateral homotopic spread. Termination was stuttering in 11 patients (69%), fading in four (25%), and abrupt in one (6%).

Asymmetric spasms (AS) (n = 12): These seizures were similar to generalized spasms but exhibited clear asymmetric clinical features. Their electrographic

Fig. 4. Spasm with focal tonic seizure. Six-month-old boy, awake. Longitudinal bipolar montage. Generalized high amplitude sharp wave and attenuation, followed by run of bilateral asymmetric F predominant run of spikes, stuttering termination (not shown).
correlate was generalized in four patients (33%), bilateral asymmetric in five patients (42%), bilateral symmetric in two patients (17%), and focal in one patient (8%). Initial features were predominant in the posterior region in four children (33%), involved an entire hemisphere in three children (25%), they were located in the frontal–central area in two patients (17%), and in the frontal–parietal region in one (8%). They were composed of a sharp wave and electrodecrement in nine patients (75%), of isolated sharp waves in two patients (16%), and of low voltage fast activity in one patient (8%). All of the AS (100%) were confined to the same region on evolution. Termination was stuttering in 10 children (83%), and fading in two patients (16%).

Six seizures showed the peculiar electrographic characteristic of independently migrating to the contralateral hemisphere, a second asynchronous seizure of a different pattern starting while the first seizure progressively faded (Fig. 5). Predominant clinical manifestations were BAV in three patients (50%), DTFC in two patients (33%), and unilateral tonic posturing in one patient (17%). Electrographically, they were all (100%) unilateral at onset, with posterior predominance in three of them (50%), frontal in one of them (17%), central in one of them (17%) and hemispheric in one of them (17%). Initial features were low voltage fast waves and RTA in three cases (50%), low voltage fast waves in one (17%), fast waves and spikes in one (17%), and rhythmic delta and RTA in the remaining (17%).

3.2. Age

Overall, median age at the time of seizure recording was 9 months. Fig. 6 shows the age at the time of recording for each seizure type. Certain types of seizures showed a tendency to appear earlier in life and were not observed after a certain age, such as DTFC (up to 14 months), BAV and partial clonic seizures (up to 18 months). On the other hand, other seizure categories were not observed before a certain age and showed a tendency to appear at a later median age, such

![Fig. 5. Seizure with migratory features. Five-month-old girl, awake. Longitudinal bipolar montage. Right hemispheric rhythmic delta sharp waves, evolving to a more focalized parietal run of spikes, fading and independent migration to the contralateral temporal region, abrupt termination (not shown).](image)
as generalized seizures (spasms excluded, 7 months), generalized atonic seizures (7 months), and generalized clonic seizures (8 months). Spasms were observed at a median age of 8–8.5 months. Spasms with focal seizures were the only seizure type recorded throughout the age spectrum of 1–23 months.

In the group of patients aged 1–6 months, there was predominance of focal clonic seizures and of spasms with focal seizures. Both categories accounted for 50% (15 seizures) of the 30 seizures observed in this group. Moreover, four of the six seizures with migratory features that we recorded were observed in this group of age. With the exception of rare generalized spasms, no primary or secondary generalized seizures were noted.

In the group of patients aged 7–12 months, there was predominance of spasms, which accounted for 41% (13 seizures) of the 32 seizures recorded. The first generalized seizure other than spasms was an atonic seizure recorded at 7 months. The first generalized seizure with tonic and clonic components was recorded at 9 months, and was a CTC seizure in a child with Dravet syndrome.

Spasms also predominated in the group of patients aged 13–18 months. They accounted for 37% (11 seizures) of the 30 seizures recorded. Seizures with behavioral arrest were second in frequency, and accounted for 20% (6 events) of the seizures. Both categories accounted for 57% of all seizures in this group.

Finally, in the group of patients aged 19–24 months, only nine seizures of five types were observed, with a predominance of spasms with focal seizures (4 events, 44% of all seizures).

3.3. Duration

Five seizures had either onset or termination off video, whereas electrographic onset or termination data were missing in two cases. Overall, seizures were short. Spasms excluded, the median clinical duration was 36 s (range: 1–1512 s; standard deviation: 3 min 51 s) and the median electrographic duration was 49 s (range: 1–1515 s; standard deviation: 3 min 57 s). If we included spasms, which for the majority lasted for 1–2 s, the clinical and electrographic duration dropped to 11 s (range: 1–1512 s; standard deviation: 3 min 5 s) and 12 s (range: 1–1515 s; standard deviation: 3 min 12 s), respectively. Only 2 seizures out of 96 (Fig. 7A)
and two seizure types (CTC and BAV) out of 14 (Fig. 7B) lasted clinically for more than 5 min. One of them was a generalized CTC seizure that lasted for more than 25 min in a patient with Dravet syndrome; the second one was a BAV seizure manifest as a behavioral arrest with eye deviation and focal hypotonia that lasted for almost 15 min in a patient with migrating partial seizures in infancy. On average, focal and mixed seizures showed a clear tendency to last longer (EEG duration: median: 29 s, range: 1–888 s, standard deviation: 2 min 19 s; clinical duration: median: 25 s, range: 1–833 s, standard deviation: 2 min 2 s) than generalized seizures (EEG duration: median: 3 s, range: 1–1515 s, standard deviation: 5 min 3 s; clinical duration: median, 13 s; range, 1–1512 s, standard deviation 5 min), spasms included in both groups. Fig. 8 shows the median clinical and electrographic duration of each seizure type.

3.4. State of awakening

State of awakening of the patient could not be determined during one seizure, and two seizures were recorded in sedated patients. Of the remaining 98 seizures, 74 (76%) were observed in awake patients, and 24 (24%) were observed out of sleep.

4. Discussion

4.1. Seizure types

Our findings are consistent with those described previously, namely that the seizure repertoire in infants is rather limited (Hamer et al., 1999)—we observed 13 distinct seizure types but, even smaller number of seizure types (spasms, focal clonic, focal tonic, and BAV) account for the majority of seizures observed (76% of the total).

The clinical and electrographic characteristics of these infantile seizures differ from those seen in older children and adults, and some (e.g., spasms) are very rarely seen outside of infancy (Personal observations from our entire dataset).

A remarkable finding was that there were a limited number of clinical and electrographic patterns, allowing us to group all seizures into these thirteen categories. In many cases, the clinical features can be used to predict the ictal EEG correlates, but in some circumstances it is impossible to infer the ictal patterns from even detailed analysis of the videotapes (Table 3).

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<th>Seizures with predictable EEG features</th>
<th>Seizures with unpredictable EEG features</th>
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<td>2.4 Focal tonic</td>
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<td>1.6 Generalized atonic</td>
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Fig. 8. Median electrographic (A) and clinical (B) duration of each seizure type. A, atonic; AS, asymmetric spasms; BA, behavioral arrest; BAV, behavioral arrest with version; C, clonic; CTC, clonic–tonic–clonic; DTF, diffuse tonic–focal clonic; H, hypermotor; S, spasms; SFS, spasms with focal seizures; T, tonic; TC, tonic–clonic; TCSG, tonic–clonic with secondary generalization.
Of the seizures with predictable electrographic correlates, generalized spasms were the most important. Here, all seizures were consistently accompanied by electrodecrements consisting of a diffuse slow wave discharge followed by profound attenuation, sometimes with superimposed posteriorly predominant low voltage fast activity. The ictal discharges, like the spasms themselves, recurred in an almost periodic fashion so that the evolution was best described as stuttering.

Generalized clonic seizures also showed a highly predictable electrographic correlate. A majority showed runs of repetitive generalized spikes or sharp waves, which either ended abruptly or concluded after a short epoch of stuttering activity.

Others, however, had much more heterogeneous EEG findings with regards to onset location and pattern, evolution and termination. This was the case for focal tonic seizures, in which varying associated electrographic patterns could start in any location, evolve or stay confined, and end abruptly, fade or stutter. BAV also showed varying onset locations. However, the electrographic pattern and termination mode were more homogeneous, and involved rhythmic patterns that progressively faded.

A striking finding is that most seizure types may exhibit simultaneous generalized and focal clinical or electrographic features, an observation made by others (Acharya et al., 1997; Engel, 2002; Nordli et al., 1997). This, added to the short seizure duration, may prevent an accurate observation, and highlights the necessity to perform video-EEG monitoring in infants with certain clinical presentations. This ability of focal seizures in infants to express both diffuse and focal elements is a particular characteristic that makes clinical diagnosis of focal seizures in the very young somewhat problematic. Fortunately, the electrographic characteristics of the seizures are quite distinctively focal.

Seizures with migratory EEG features were another important seizure type. They were so-called because they appear to “migrate” from one hemisphere to the other, but this may not be an accurate description of the true electrographic nature of the events. On careful analysis the “migrating” seizure develops an independent focus of ictal activity, often with a different electrographic pattern and almost always at different frequency in the contralateral hemisphere, suggesting that these seizures actually independently arise and are not due to electrographic spread of the discharge. The duration of seizures with migratory features was among the longest of all seizures in our study, whatever their clinical presentation: these six events had a median duration of almost 2 min, with a range of 49 s to nearly 15 min. Clinical manifestations were heterogeneous, and included BAV, DTFC and focal tonic seizures. All of the patients who showed these characteristics in our group were severely delayed, had intractable seizures, and were suspect of having the malignant syndrome of migrating partial seizures in Infancy. This syndrome was initially reported in 1995 in 14 children with normal development at seizure onset, seizure onset before 6 months, nearly continuous multifocal intractable seizures, lack of a demonstrable etiology and severe developmental delay on follow-up (Coppola et al., 1995). Neuropathological investigations showed hippocampal neuronal loss and gliosis in two patients (Coppola et al., 1995), but not in a third child (Wilmshurst et al., 2000). The clinical and EEG characteristics suggest a genetic or a metabolic origin, but a specific etiology remains to be discovered (Coppola et al., 1995; Gross-Tsur et al., 2004). Additional investigations and case descriptions are of utmost importance in this syndrome, but given the negative evaluations to date it is conceivable that this represents an extreme manifestation of an idiopathic channelopathy. Treatment is disappointing, but some improvement has been noted with a combination of stiripentol and clonazepam in rare patients (Coppola et al., 1995).

Surgery for epilepsy is often performed late in infants with intractable epilepsy, at the time where seizures might already have caused severe and irreversible developmental consequences (Jonas et al., 2005). Potentially treatable etiologies include focal cortical dysplasia, Sturge–Weber syndrome or tumors, which can all present with catastrophic epilepsies and various seizure types (Wyllie, 1996). The focal characteristics of certain seizures that may easily be misinterpreted as generalized might help early identification of such potential surgical treatment candidates. These seizure types include SFS, DTFC seizures and behavioral arrest seizures, which in great majority were associated with subtle focal clinical features, such as version, asymmetric postures or unilateral jerks that could have been missed on less careful analysis.

“Classic” generalized tonic–clonic seizures were not observed in our group of patients. Four patients
had clinically similar episodes that turned out to be of a different category after careful video-EEG analysis: one had a clonic–tonic–clonic seizure, and three had focal seizures with secondary generalization. This is in accordance with previous reports (Hamer et al., 1999; Nordli et al., 1997).

4.2. Age

In our study, generalized seizures were observed later (median age, spasms excluded: 12.5 months) than focal seizures (median age, spasms excluded: 9 months). More specifically, among the most frequent seizure types, focal clonic and BAV seizures were observed early and were not recorded in patients older than 18 months. Focal tonic seizures were recorded at a slightly later median age (12 months), but at a maximal age of 19 months. On the other hand, generalized clonic and atonic seizures were observed in late infancy, but never before 7 months. A notable exception to this rule was the observation of generalized and partial spasms at almost the same median age. This fact reflects the etiologically non-specific, but age-dependent nature of clinical and electrographic ictal expression.

These data confirm previous reports and show that age and location of ictal discharges are two of the most important determinants of seizure phenotypes and ictal patterns. A decrease with age in certain clinical manifestations (asymmetric clonus and symmetric tonic posturing) and an increase in others (aura, limb automatisms, dystonic posturing, and unresponsiveness) was reported in a study on 123 pediatric patients (Nordli et al., 2001). Other authors noticed similar findings in 29 children with temporal lobe seizures, which clinical presentation markedly differed from that of adults (Brockhaus and Elger, 1995). These changes reflect the cerebral maturational processes that occur early in life, including myelination, development of synapses, and neuronal pruning.

4.3. Duration

The most striking finding, overall, was that infantile seizures were short. Their median clinical and electrographic duration, spasms excluded, was 36 and 49 s, respectively, and only two seizures out of 96 clinically lasted for more than 5 min. There was a strong concordance between clinical and electrographic discharges for ictal onsets and terminations time. Partial seizures showed a tendency to last longer than generalized seizures, in accordance with previous data in children with unprovoked afebrile seizures (Shinnar et al., 2001), with the exception of one generalized clonic–tonic–clonic seizure that lasted for more than 25 min. This child was diagnosed with Dravet syndrome, where prolonged early life seizures are a hallmark.

New-onset unprovoked afebrile seizures have been shown to last longer than 5 min in 50% of an important cohort of children aged 1 month to 19 years (Shinnar et al., 2001). These observations are thought to be due to the increased susceptibility to seizures in immature brains (Shinnar et al., 2001; Moshé, 1987). Our findings contrast with these results, but are in accordance with previous data in adults with refractory epilepsy, which indicate that seizures lasting longer than five minutes are rare (Lowenstein et al., 1999). Secondarily generalized tonic–clonic seizures averaged 109 s in a study on adults with intractable partial seizures (Kramer and Levisohn, 1992). In another report on uncontrolled secondarily generalized tonic–clonic seizures in patients aged 11–56 years, the generalized phase averaged 62 s (Theodore et al., 1994). Our findings, like these in adults, show that the majority of seizures in individuals with poorly controlled seizures are brief, if the seizures are frequent enough to be captured during a video-EEG recording session. In contrast, the findings of Shinnar et al. of longer duration seizures at first onset may be explained by the fact that those children with new-onset seizures represent an entirely different patient population. There are many differences between these patient groups, not the least of which is that nearly all of our patients were treated with one or multiple medications that may conceivably shorten their seizure duration. Also, the mechanisms that initiate seizures and terminate seizures in patients with refractory epilepsy, particularly in those treated with anti-epileptic drugs may be different (Shinnar et al., 2001).

4.4. State of awakening

It is remarkable that almost three out of four seizures were noted while patients were awake. Considered the fact that most children aged less than 2 years spend more time sleeping than awake, these data are not in accordance with simple random chance, and more
probably reflect the reported protective effect of deep sleep, which accounts for a higher percentage of total sleep time in infants than later in life (Ficca et al., 2000), on seizure activity (Bazil and Walczak, 1997).

5. Conclusions

This study highlights the fact that, in a significant number of cases, one cannot rely on clinical observations to predict with enough accuracy the electrographic correlate of infantile seizures. It confirms the usefulness and the necessity to perform V-EEG in infants who present with seizures. Relative exceptions to this statement are generalized spasms, and generalized clonic seizures in which fairly homogeneous electrographic features were noted. On the other hand, certain categories, such as tonic seizures, diffuse tonic–focal clonic seizures, behavioral arrest and spasms with focal seizures require video-EEG recording to be described with sufficient accuracy. In such cases, video-EEG findings may add fundamental information with regards to epilepsy syndrome classification and specific treatment options, including surgery. The study also shows a trend toward an evolution of clinical manifestations with age: generalized seizures were observed later than focal seizures; focal clonic and BAV seizures were not recorded in patients older than 18 months; generalized clonic and atonic seizures were not observed before 7 months; and generalized tonic–clonic seizures were not observed at all. Finally, our findings provide a potential basis for a seizure classification more adapted to infants, an essential tool in the management of their epilepsy.

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