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Review Article

Early Life Seizures: A Narrative Review and a Scheme to Recognize Them

Salvatore Michele Carnazzo[1], Giovanni Cacciaguerra[1]*, Giusi Maria Caltabiano[1], Desireè Balconara[1], Mattia Comella[1], Germana Lena[1], Claudia Oliva[1] and Piero Pavone[2]

[1]Postgraduate Training Program in Pediatrics, Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy

[2]Department of Clinical and Experimental Medicine, University Hospital "Policlinico-San Marco", Catania, Italy

***Corresponding Author:** Giovanni Cacciaguerra, Postgraduate Training Program in Pediatrics, Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy.

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Abstract

Seizures are a very frequent acute neurological event in children, caused by abnormal and excessive discharges of neurons.

The recurrence of two or more unprovoked seizures characterizes the condition of epilepsy.

The most recent classification of seizures distinguishes epilepsies into focal, generalized, and unknown.

Seizures occurring in the first year of life might have an evolution ranging from benign to severe; in particular, febrile seizures simplexes are a group of seizures that occur with greater frequency in pediatric age and only 1 - 1,5% evolve into epilepsy, likewise Benign Familial Neonatal Epilepsy which tends to gradually disappear within the first months of life.

Febrile Seizure complex (FSc) might have a variable prognosis not always predictable. Severe seizures presenting at an early age include epileptic encephalopathies a group of disorders defined based on "the notion that epileptic activity may contribute to severe neurocognitive and behavioral dysfunction above and beyond what would be expected from the underlying pathology alone".

Seizures are a frequent occurrence in the first year of life, this report aims to present the clinical manifestation of each of these disorders and provide an updated review of the conditions associated with seizures in the first year of life.

Keywords: Seizures; Benign Familial Neonatal Epilepsy; Febrile Seizure Complex (FSc)

Early life seizure with a usually benign course

Benign familial neonatal epilepsy

Mutation of Several potassium channel genes have been implicated in different forms of genetic and acquired epilepsy, among them KCNQ2 and KCNQ3, which code for KV7.2 and KV7.3 voltage-gated potassium channels [1]; the mutation of these genes is implicated in the genesis of benign neonatal familiar epilepsy (BFNE). The clinical features of this disorder are relatively typical: the seizures begin in the first days of life in otherwise healthy looking babies and are typically associated with a family history of neonatal seizures [2]. Usually, onset occurs between the second and eighth day of life, in otherwise healthy infants. Seizures, mostly focal, affect both sides of the body alternately and are often associated with apnea [3]. Crises are isolated or grouped; they are

usually short, 1 to 2 minutes. However, they can be very frequent, up to 20 times a day, the prognosis is favorable. Seizures usually disappear in the first year of life and patients have no neurologic sequelae. Cases have been described in which seizures continued beyond the year, in the form of occasional febrile seizures and childhood idiopathic epileptic disease, particularly rolandic epilepsy [4].

Acute symptomatic seizures

Acute symptomatic and provoked seizures refer to seizures that occur within the first 7 days of an event or after a well-documented brain insult. These terms are often used interchangeably [5].

Provoked seizures are classified as resulting from transient derangements that involve metabolic, toxic, medication side-effects, electrolytic dysregulation, acute hypoglycemia, hypocalcemia, and hyponatremia. The occurrence of the ASS is particularly high in the infantile period since at this age, the brain seems to be more susceptible to such insults. The most common etiologies of provoked neonatal crises are some acute neurological diseases, namely ischemic/hemorrhagic brain disorders of hypoxic-ischemic encephalopathy (HIE; 38%), ischemic stroke (18%) and intracranial haemorrhage (12%).

Other etiologies of acute symptomatic neonatal seizures include transient metabolic derangements (4%) and central nervous system (CNS) infections (4%) [7]. The proportion of seizures caused by these etiologies has not changed much in the last decade, although acute meningitis and/or encephalitis are much less common in developed countries now compared with earlier decades. Currently, acute CNS infections are a relatively uncommon cause of neonatal seizures, on par with many other congenital causes, such as brain malformations (4%), inborn metabolic disorders (3%), and other genetic causes of benign (3%) or severe neonatal-onset epilepsies (6%) [6]. Epileptic events manifest themselves clinically as generalized tonic-clonic seizures, while focal or unilateral types are uncommon.

Febrile seizures simplex (FS)

Convulsive seizures affect 2% to 5% of children representing one of the most frequent causes of visits to the pediatric emergency room.

FSs are defined as short (< 15 min.) generalized seizures, not recurring within 24h which occur during a febrile illness not resulting from an acute disease of the nervous system, in a child aged between 6 months and 60 months, with no neurologic deficits and no previous afebrile seizures [8]. Fever is a normal response to infection, characterized by a large release of high levels of cytokines and can alter normal brain activity, triggering seizures. Risk factors for FS are male gender, a family history of FS, an elevated peak body temperature, neonatal asphyxia, low serum calcium, sodium or blood sugar.

The highest incidence of convulsive seizures has been reported in children younger than 3 years, with declining rates in older children [9].

In according to guidelines of the American Academy of Pediatrics, the management of the fs provides lumbar puncture for any child who presents with a seizure and fever and has meningeal signs and symptoms (eg, neck stiffness, Kernig and/or Brudzinski signs) or in any child whose history or examination suggests the presence of meningitis or intracranial infection (level evidence A) [8]; In any infant between 6 and 12 months of age who presents with a seizure and fever, a lumbar puncture is an option when the child is considered deficient in Haemophilus influenzae type b (Hib) or Streptococcus pneumoniae immunization or when immunization status cannot be determined because of an increased risk of bacterial meningitis [10]. This underlines the importance of a differential diagnosis m the conditions that can occur with seizures and fever, or persisting loss of consciousness, and post-ictal drowsiness.

The evolution in epileptic seizures is rare and almost similar to that of the general population, and no persistent residual signs of the motor, behavioral, and cognitive disturbances are reported.

This underlines the importance of a differential diagnosis m the conditions that can occur with seizures and fever, or persisting loss of consciousness, and post-ictal drowsiness.

Early life seizure with prognosis not predictable

Febrile seizures complex

Complex febrile seizures represent 20% to 30% of all febrile seizures, and there is still little knowledge about their etiology or susceptibility.

Febrile seizures to be defined complex must have characteristics that differentiate them from simple febrile convulsions such as focal features, prolonged duration (> 15 minutes), and recurrent episodes within 24 hours [11].

In the National Collaborative Perinatal Project, 1706 children with febrile seizures were identified from a total of 54,000 and followed from birth until 7 years of age. The initial febrile seizure was defined as complex in approximately 28%. Focal features were present in 4%, with prolonged duration (>15 minutes) in 7.6% and recurrent episodes within 24 hours in 16.2% [5,8,12].

The mechanism by which fever provokes a febrile seizure remains unclear; the main theories suggest that febrile seizures are caused by a mutation temperature-induced change of susceptible GABAA receptors or genetic and environmental factors, resulting in an inflammatory process that influences neuronal excitement and predisposing one to a febrile seizure.

Mutations in some genes have been associated with febrile seizures, in particular the SCN1A gene mutation, associated with Dravet syndrome and other variety of mutations including SCN1A, SCN1B, and GABGR2, with the latter having an association with absence seizures.

The association between febrile seizures and mesial temporal sclerosis is still a matter of debate. Retrospective studies have reported an association between prolonged or atypical febrile seizures and intractable temporal lobe epilepsy; however, epidemiological studies failed to show a causal relationship between febrile seizures and temporal lobe epilepsy [13]. This suggests that febrile seizures are a marker of susceptibility to seizures and future epilepsy (in some cases) rather than a direct cause. A minority of cases of mesial temporal sclerosis or focal seizures are associated with prior febrile.

Early life seizures with usually severe course

Neonatal seizures

Enormous progress has been made in recent years in understanding the etiological mechanisms, diagnostics and neuroimaging of neonatal seizures.

Hypoxic-ischemic encephalopathy (HIE) in term neonates and intraventricular hemorrhage (IVH) in premature neonates are the most prevalent etiology. Other common causes are cerebral infarction, central nervous system (CNS) infection, brain malformation, or metabolic disorders [13].

The latest task force recently proposed a classification that considers four domains: clinical presentation (suspected or high-risk clinical events), diagnosis (with EEG), manifestation (with or without clinic manifestation) and types of seizures with clinical signs (motor: automatisms, clonic spasms, epileptic, myoclonic, sequential, and tonic; non-motor: autonomous and behavioral stopping; is not classified) or without clinical signs (electrographic only).

This new classification, yet to be defined, should increase the diagnostic value of crisis semiology concerning the etiology and outcome of neonatal crises.

The timing of the onset of crises provides the first indication etiology of crises.

The acute seizures that occur on the first day of life are typically associated with neonatal Hypoxic-Ischemic Encephalopathy is generally characterized by a low APGAR score.

Neonatal crises that occur up to 72 hours after birth are related to a secondary condition and may be associated with stroke or brain malformations, bacterial meningitis, intrauterine infection, IVH in preterm infants, medication withdrawal and metabolic disorders.

Some inborn errors metabolism (IEM), are characterized by an early manifestation of seizures; among these errors of the metabolism of pyridoxine, pyridox (am) ine deficiency of 5′-phosphate oxidase (PNPO), GLUT-1 (glucose transporter deficiency 1), nonketotic hyperglycinemia, Maple syrup urine diseases are the most cited examples [14].

According to the greater susceptibility of the brain during the early stages of development and in the neonatal period and during childhood, the prognosis of neonatal seizures is in most cases it is severe. For a long time, neonatal seizures were treated with phenobarbital and phenytoin as first-line drugs. Recently, phenobarbital and phenytoin treatment in neonatal seizures has been questioned because of doubtful seizure control and for the consequence of long term alterations in brain structures.

Epileptic encephalopathies

The term epileptic encephalopathy refers to a heterogeneous group of early-onset epileptic disorders, in which epileptic activity impairs cognitive and behavioral function.

Epileptic encephalopathies include severe epileptic disorders that share similar characteristics: onset in early life, persistent electroencephalographic abnormalities, drug resistant seizures of various types, and cognitive involvement [15]. The epileptic encephalopathy manifesting in the first months of life include Early

Infantile Epileptic Encephalopathy (EIEE) (also known as Ohtahara syndrome), Early Myoclonic Encephalopathy (EME), Epilepsy of Infancy with Migrating Focal Seizures (EIMFS), Infantile Spams Syndrome (ISS) (also known as West syndrome), Severe Myoclonic Epilepsy in infancy or Dravet Syndrome (DS) and Myoclonic Encephalopathies in non-progressive disorder [16].

Early infantile epileptic encephalopathy-Early myoclonic encephalopathy

Early myoclonic epileptic encephalopathy, also known as Ohtahara syndrome, usually has onset from 2 weeks of age. Clinical manifestations associated with this type of crisis are very variable and typically manifest with tonic spasm, a paroxysmal jerk (usually with a duration greater than 250 milliseconds) followed by a prolonged tonic posture of the upper extensor and/or lower limbs, which lasts several seconds [17].

The electrographic characteristic of these seizures is heterogeneous and generally manifested with an explosion of chaotic, generalized, high-amplitude, mixed-frequency activity (often with overlapping peaks, polyspikes or rapid paroxysmal activity) followed by generalized tension attenuation and often with the subsequent appearance of fast diffuse low voltage activity Interictal EEG is characterized in early childhood epileptic encephalopathy from a blast suppression pattern. (bursts of high-amplitude spikes and polyspikes that alternate with periods of electrographic suppression [18].

The etiology is extremely varied and not completely clear; structural brain abnormalities such as hemimegalencephaly and cortical dysplasia have been described and are evidenced on MRI. Mutations in several genes have been implicated, including ARX, STXBP1, KCNQ2, SLC25A22, and CDKL5 and mutation in SLC25A22, which encodes the mitochondrial glutamate/H^+ symporter, has been associated with this encephalopathy.

Treatment of epileptic encephalopathy is extremely challenging and the prognosis is often severe with limited data indicating modest efficacy for a variety of antiepileptic drugs and the ketogenic diet. Long-term most patients suffer from adverse neurocognitive outcomes, early death and transition to something else forms of epileptic encephalopathy such as infantile spasms and Lennox-Gastaut syndrome [19].

However, in a minority of patients for which specific etiology treatment is available and promptly given (eg, hemispherectomy for hemimegalencephaly or pyridoxine for pyridoxine addiction), excellent neurodevelopmental outcomes are possible.

Epilepsy of infancy with migrating focal seizures

Epilepsy of childhood with focal migratory seizures (EIMFS) is a rare encephalopathy (DEE) characterized by seizures migration between cerebral hemispheres, alteration of cognitive development and in some cases regression of acquired skills.

Onset occurs in the first 6 months of life, with convulsions that often-increased frequency in the first few months and are refractory to antiepileptic drugs [20].

The etiology is still unknown, pathogenic variants have been identified in 24 genes, most of the cases are dominant heterozygous de novo variants, although homozygous and compound heterozygous variants in recessive disorders have also been defined. Gene more frequently associated with EIMFS is KCNT1, found in 6 out of 12 cases, by Barcia., *et al.* in 2012. It was also the sodium channel genes involved, including SCN1A, SCN2A and SCN8A.

A cohort of 135 patients was described by Rosemary Burgess, Shuyu Wang., *et al*. to define the genetic characteristics of this devastating syndrome.

The study of these authors showed interhemispheric crisis migration, clinically and/or via EEG; patient age ranged from 1 month to 16 years (median = 3 years 5 months).

A total of 117 patients were singletons; 14 had brothers or half-siblings with EIMFS and 4 had siblings with other DEEs. Twelve patients were from 9 consanguineous families (3 brothers, 6 singles). Thirty-six of 124 patients had a first or second degree relative with epilepsy or febrile seizures, including the above 18 brothers and half-sisters. The median age of onset of seizures was 4 weeks.

Onset in the first week of life has been observed in patients with the following genes: SCN2A, KCNQ2 and BRAT1, while seizure type at onset included focal seizures, tonic seizures and epileptic spasms, with additional seizure types.

Epileptic spasms occurred in 22% of patients. All patients had refractory epilepsy in the course of their disease; however, 3 with SCN2A variants and 2 with KCNQ2 variants were seizure-free for 1 year or more.

Seizure migration was observed clinically and on at least 1 EEG in 112 patients, with 88 patients displaying both clinical

and electrical migration. In addition to focal seizures and ictal interhemispheric migration, interictal EEG findings for the 134 patients for whom data were available included focal/multifocal spikes in all patients.

Hypsarrhythmia (classic or modified) was seen in 13 patients, an electrodecremental pattern without hypsarrhythmia in 11, and a burst-suppression pattern in 19, with some patients displaying different patterns at different times.

Pharmacological treatment attempts have been carried out with several, known anticonvulsant drugs including vigabatrin, stiripentol, valproic acid and clobazam, but with poor results; Robertino Dilena, Jacopo C., *et al*. described two patients with KCNT1-related EIMFS, focusing on some of the criticality of personalized therapy with quinidine other authors have described the cannabidiol response in childhood epilepsy with focal migrant seizures associated with KCNT1 mutations [21].

Infantile spasms syndrome

West's syndrome, or infantile spasms, is an epileptic syndrome, quite specific for childhood, frequently with a poor prognosis.

The incidence of West syndrome has been estimated to be 2 - 3.5 per 10000 live birth. It strikes half of the children with severe epilepsy, 60% boys. It affects half the infants with severe epilepsy, 60% being boys and convulsions appear between the ages of 4 and 6 months [22].

The disease is characterized by a characteristic triad: sudden axial muscle contraction that occurs in a cluster, psychomotor retardation or deterioration, and increased prevalence of paroxysmal activity on the electroencephalogram (EEG).

The spasm attacks are characterized by a series of sudden muscle movement contractions with which the head is flexed, the arms are extended and the legs are pulled up. Less commonly, your attack includes nodal extensor spasms characterized by extension rather than flexing the arms, legs and trunk. Rarely, the attacks end with a brief clonic seizure.

The etiology of West's syndrome is varied and includes hypoxic-ischemic encephalopathy, perinatal strokes, metabolic errors, brain tumors, usually benign, neurocutaneous syndromes including Sturge-Weber syndrome, and Tuberous Sclerosis Complex, structural brain disorders, malformation syndromes, inborn errors of metabolism and as recently shown immunologic factors [23]. In more than 20% of cases the cause cannot be identified.

More than 25 inborn errors of metabolism were considered etiological or predisposing factors. Of the innate errors of metabolism; Menkes disease is the condition that causes the higher incidence of infantile spasms; West's syndrome occurs in other pathological conditions, in particular spasms attributable to the syndrome have been observed in some inherited metabolic diseases such as phenylketonuria.

The intercritical EEG of West Syndrome presents with a high voltage arrhythmia and asynchronous, slow, and sharp waves, in a chaotic distribution with multifocal spikes and poly-spikes. Critical EEG might show a pattern of synchronous and symmetric spike-wave discharges. Atypical modified hypsarrhythmia might be observed at the intercritical EEG with a pattern of asymmetric features, focal discharges, and semi-periodic burst-suppression.

Treatment of west syndrome does not include conventional antiepileptic drugs. Current guidelines and reviews recommend treatment with hormones such as adrenocorticotropic hormone (ACTH) or vigabatrin. However, the spasms persist in 33% to 56% of patients despite the use of these effective treatments.

A recent meta-analysis has compared the use of low-dose ACTH as an alternative to high-dose ACTH for the short-term treatment of infantile spasms. The meta-analysis concluded that low dose ACTH is more effective and with fewer side effects than high doses. Previous evidence of the efficacy of corticosteroids for the treatment of infantile spasms is not recommended e their use as an alternative to ACTH not to be recommended [24].

The results of these recent studies and the benefits associated with corticosteroids suggest that high-dose prednisolone may be recommended. as an alternative to ACTH, especially in countries where ACTH is not available.

Severe myoclonic epilepsy in infancy-Dravet syndrome

Dravet syndrome, once known as Severe myoclonic epilepsy in infancy, was first described by Dravet in 1978.

It is considered a rare disease, with an incidence of less than 1 in 40 000. Despite knowledge of this epilepsy increases, the number of diagnoses patients is probably higher, but it remains a rare disease. Recently, (Dura` -Trave., *et al*. 2007) found a rate of 1.4% in epilepsies of children aged < 15 years [25].

Dravet syndrome can be divided into three stages. The first stage is the "fever stage". The debut happens in the first year of life, usually between 4 and 8 months, in an normal presenting

baby with a seizure, related or not (about 35%) fever (infection, vaccination, etc). Typically, it is a file clonic seizure, initially generalized or beginning in a part of the body and invading an entire side (hemiclonic seizures), or become generalized. Its duration is variable, often long, more than 15 minutes at times evolving into a state epilepticus. It can be focal, motor seizures, or an outbreak of myoclonic spasms that are not immediately recognized as epileptic in nature. EEG is usually normal as well as other investigations and this first attack is considered to be a complicated febrile attack [26].

Shortly after (2 weeks - 2 months) other crises occur, feverish or not, and are repeated, even in the states, despite the anticonvulsant drug that was established.

The second phase involves a "worsening phase" characterized by Different types of seizures that appear between 1 and 4 years: short myoclonic convulsions, atypical absences, with mild myoclonia and the head nodding, more or less prolonged "dulling" status "(a state with impairment of consciousness of the variable intensity), focal convulsions, with motor (deviation of the head, stiffness or clonic jerks of a limb, hypotonia, etc.) and autonomous (pallor, redness, cyanosis of the lips, etc.) components, with or without loss of contact, and others difficult to classify. Psychomotor development becomes slower from the second year onwards (tongue, fine and gross motor skills).

Disturbance in attention, hyperactivity, and sometimes autistic features (stereotypies, also poor eye contact).

Finally "stabilization stage": seizures decrease and occur mainly in sleep, myoclonus and absences may disappear and focal seizures persist or decrease. Psychomotor development and behavior tend to improve, but cognitive impairment persists, which is variable between patients.

The main diagnoses criteria for classical DS are: normal development before the start of the seizure; two or more febrile seizure complexes before 12 months; myoclonic, hemiclonic or generalized tonic-clonic seizures; the latter two during crises and refractory seizures after 2 years of age. A new form of Dravet syndrome has been described as "severe borderline myoclonic epilepsy of childhood "(SMEIB), characterized by patients who they lack some of the key features such as myoclonic seizures o generalized activity of peaks and waves [27].

Genes that have been reported to cause DS phenotypes include SCN1A, SCN2A, SCN8A, SCN9A, SCN1B, PCDH19, GABRA1, GABRG2, STXBP1, HCN1, CHD2, and KCNA2. Many of these genes, appear to be associated to a different clinical picture, for example, the SCN1A mutation is associated with a range of alterations that include not only the brain but also cardiac, hearing, vision, movement issues, urinary, bowel, and endocrine functions.

Myoclonic encephalopathies in nonprogressive disorder (MSNE)

MSNE is a condition characterized by the recurrence of a long-lasting myoclonic state that appears in infants and young people children with non-progressive encephalopathy and with a poor prognosis [28].

This encephalopathy was associated with a spectrum of conditions as Angelman syndrome and in some children with 4p-syndrome, but few of them have stressed how, in some of these cases, the electroclinical picture was typically that of a myoclonic status is nonprogressive [29].

A recent study described a cohort of 29 patients with the diagnosis of MSNE.

Cohort described was composed: 18 were females and 11 males with a male-female ratio of 1:1.5. Their current ages range between 4 and 15 years (mean age 6 yr). The mean time of follow-up was 7 yr (range 2 - 13 yr). Familial antecedents of epilepsy were reported in four (13%) and febrile seizures in two patients [30] (6.5%).

The etiology was genetic in 18 patients: a deficit in chromosome 15q11-q13 (Angelman syndrome) in 15 patients, deletion of the short arm of chromosome 4 (WolfHirschhorn syndrome or 4p-syndrome) in two cases, and Rett syndrome in the remaining one. Prenatal or perinatal anoxic insults were found in five cases and the etiology was unknown in six patients.

The main EEG features of this encephalopathy can be divided into 3 groups: theta-delta periodic predominant activity in the central regions or may appear like short runs of slow delta pace in the back regions in the first group; in the second group electrical activity of the brain manifests with shows a diffuse slow background with status epilepticus or theta-delta rhythm prevalent in the frontal regions, in patient with myoclonic jerks or relevant abnormal movements. In the third group, the developmental delay is mild, and focal motor seizures involve mainly the face; the EEG displays generalized spike-wave paroxysms.

Conclusion

Early life seizures are a frequent condition that the pediatrician assists during the clinical activity; the correct differential clinical and electroencephalographic diagnosis is essential for correct classification, optimal therapy to establish prognosis.

With our narrative review we tried, following a logical scheme, to describe in a methodical way and with the most up-to-date findings on the early life seizures.

Concluding, a scheme including the main characteristics of this pathologies is proposed to better orient the diagnosis of the various forms of early epilepsy.

Febrile seizures simplex -Short (< 15 min.) generalized seizures -Not recurring within 24 h which occur during - Febrile illness not resulting from an acute disease of the nervous system - Aged between 6 months and 60 month, with no neurologic deficits and no previous afebrile seizures.	**Acute symptomatic seizures** **-** 7 days of an event or after well-documented brain insult - Ischemic/hemorrhagic brain disorders of hypoxic-ischemic encephalopathy (HIE; 38%), ischemic stroke (18%) intracranial haemorrhage (12%).	**Epileptic encephalopathies** Early life, persistent electroencephalographic abnormalities, drugresistant seizures of various types, and cognitive involvement onset from 2 weeks of age. Tonic spasm, a paroxysmal jerk (usually with a duration greater than 250 milliseconds) followed by prolonged tonic posture of the upper extensor and/or lower limbs, which lasts several seconds EEG blast suppression pattern
Febrile seizures complex -Febrile seizures convulsions with focal features -Prolonged duration (> 15 minutes) -Recurrent episodes within 24 hours	Main features for a quick classification of early life seizures	**Epilepsy of infancy with migrating focal seizures** -Migration between cerebral hemispheres -Alteration of cognitive development and in some cases -Regression of acquired skills. -During first 6 months of life, often increased frequency in the first few months and are refractory to antiepileptic drugs.
Severe myoclonic epilepsy in infancy- Dravet syndrome -Fever stage: clonic seizure, initially generalized or beginning in a part of the body and invading an entire side (hemiclonic seizures), or become generalized. -Worsening phase: Different types of seizures that appear between 1 and 4 years. short myoclonic convulsions, atypical absences. -Stabilization stage: seizures decrease and occur mainly in sleep, myoclonus and absences may disappear and focal seizures persist or decrease. Psychomotor development and behavior tends to improve, but cognitive impairment persists, which is variable between patients.	**MSNE** -Recurrence of a long-lasting myoclonic state that appears in infants and young people children with non-progressive encephalopathy and with a poor prognosis associated to a spectrum of contition as Angelman syndrome and in some children with 4p-syndrome -EEG features 3 groups: -Theta-delta periodic predominant activity in the central regions or may appear like short runs of slow delta pace in the back regions; -Electrical activity of the brain manifests with shows a diffuse slow background with status epilepticus or theta-delta rhythm prevalent in the frontal regions, in patient with myoclonic jerks or relevant abnormal movements. -the developmental ones	**Infantile spasms syndrome** -Sudden axial muscle contraction that occurs in cluster -Psychomotor retardation or deterioration, increased prevalence paroxysmal activity on the electroencephalogram. -Etiology varied: hypoxic-ischemic encephalopathy, perinatal strokes, metabolic errors, brain tumors, benign, neurocutaneous,Sturge-Weber syndrome, and Tuberous Sclerosis Complex, structural brain disorders, malformative syndromes, inborn errors of metabolism and as recently shown immunologic factors

Table 1: A diagram with the main and most recognizable characteristics of early life seizures.

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Conflicts of Interest

There are no conflicts of interest.

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is coherent with these guidelines.

Author Contributions

P.P., G.C., S.M.C. and G.M.C. reviewed the literature, critically discussed various aspects of classification, and read the manuscript; D.B., G.L., M.C. and C.O. wrote the manuscript.

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