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INVITED REVIEW

# Pediatric epilepsy syndromes with associated developmental impairment

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**Abstract**

In 2022, the International League Against Epilepsy revised their classification of epilepsy syndromes for clinicians to better understand the relationships between different epilepsy syndromes, their underlying causes, and their associated developmental and behavioral features. This review highlights portions of the current classification with an emphasis on epilepsy syndromes that readily present with developmental challenges and provides a unique framework, based on electroencephalography, to easily identify and understand these syndromes. Included in this review are a helpful categorization scheme with visual aid, descriptions of updated epilepsy syndromes, figures of relevant identifiers of syndrome and information regarding future directions toward treatment and research. Covered syndromes include developmental and epileptic encephalopathy, Dravet syndrome, Rasmussen syndrome, and infantile epileptic spasm syndrome, among others.

Epilepsy syndromes, defined as 'a characteristic cluster of clinical and electroencephalography (EEG) features, often supported by specific etiological findings' have well-established associations with developmental comorbidities.[1] Epilepsy syndrome classification is an important tool to accurately diagnose and prognosticate patients. In 2022, the International League Against Epilepsy revised their classification of epilepsy syndromes for clinicians to better understand the relationships between different epilepsy syndromes, their underlying causes, and their associated developmental and behavioral features.[1] The new terminology and definitions aim to clarify diagnoses, optimize management strategies, and improve outcomes for children with epilepsy. This review highlights portions of the 2022 International League Against Epilepsy revision with an emphasis on epilepsy syndromes that readily present with developmental impairments. The EEG features within epilepsy syndromes are grouped based on a categorization scheme that allows clinicians to understand overlapping phenotypes based on a patient's EEG. This simple categorization enables providers to appropriately identify and aid patients with epilepsy associated with developmental disability, all from the EEG.[2] The categorization model (Figure 1) outlined in this article has been used in clinical practice for more than two decades. The model allows for a quick and easy categorization of the EEG. EEG can prognosticate the patient's outcome even before a diagnosis of a recognized syndrome is reached and is thus an extremely powerful and valuable tool. An overview is provided in Table 1.

## CATEGORY 1

Epilepsy syndromes within category 1 are familial.[2] The EEG is normal.[2] Patients have preserved cognitive

**Abbreviations:** DEE-SWAS, developmental epileptic encephalopathy with spike–wave activation in sleep; EEM, epilepsy with eyelid myoclonia; EE-SWAS, epileptic encephalopathy with spike–wave activation in sleep; EIDEE, early infantile developmental epileptic encephalopathy; EMAtS, epilepsy with myoclonic-atonic seizures; FIRES, febrile infection-related epilepsy syndrome; IESS, infantile epileptic spasm syndrome; LGS, Lennox–Gastaut syndrome; SeLECTS, self-limited epilepsy with centrotemporal spikes.

outcomes and respond to medications well. There are no syndromes highly associated with poor developmental outcomes.

## CATEGORY 2

Epilepsy syndromes in this category are termed 'idiopathic generalized epilepsies'.[2] They have a strong predilection to run in families.[2] These epilepsy syndromes are caused by polygenic pathogenic variants rather than monogenic pathogenic variants. Most of these epilepsy syndromes have good cognitive outcomes and are controlled with medications. The EEG has a normal background for age and generalized discharges.[2] Table 2 outlines the expected speed of the posterior dominant rhythm according to age. Two syndromes within this category more highly associated with developmental disability are epilepsy with myoclonic-atonic seizures (EMAtS) and epilepsy with eyelid myoclonia (EEM).[1]

### Epilepsy with myoclonic-atonic seizures

EMAtS, formerly called Doose syndrome or myoclonic-atonic epilepsy, is a syndrome that occurs between the ages of 2 years and 6 years.[1] Common seizure types include myoclonic seizures, atonic (drop) seizures, and generalized convulsions.[1] Patients often have a history of febrile seizures. Seizures can be frequent and hard to control at the onset. Males are more commonly affected than females.[1] The EEG in EMAtS reveals a normal background with generalized spike and wave discharges.[2]

Developmental problems in patients with EMAtS are common.[3] Notably, developmental problems do not precede seizure onset. Harder-to-control seizures generally indicate a higher likelihood of developmental regression or stagnation. Hyperactivity, aggression, and sleep disturbance are common if seizures are poorly controlled.[3] Patients with multiple seizure types and developmental impairments are often mistakenly diagnosed with Lennox–Gastaut syndrome (LGS). A key feature to consider in this distinction is whether the developmental impairment preceded seizure onset, which would be more suggestive of LGS.

**What this paper adds**

- The revised epilepsy syndrome classification by the International League Against Epilepsy aims to improve the outcomes for children with epilepsy.
- The electroencephalography features of epilepsy syndromes are grouped based on a categorization model.
- This model allows clinicians to understand overlapping phenotypes and aid with both identification and diagnosis.

### Epilepsy with eyelid myoclonia

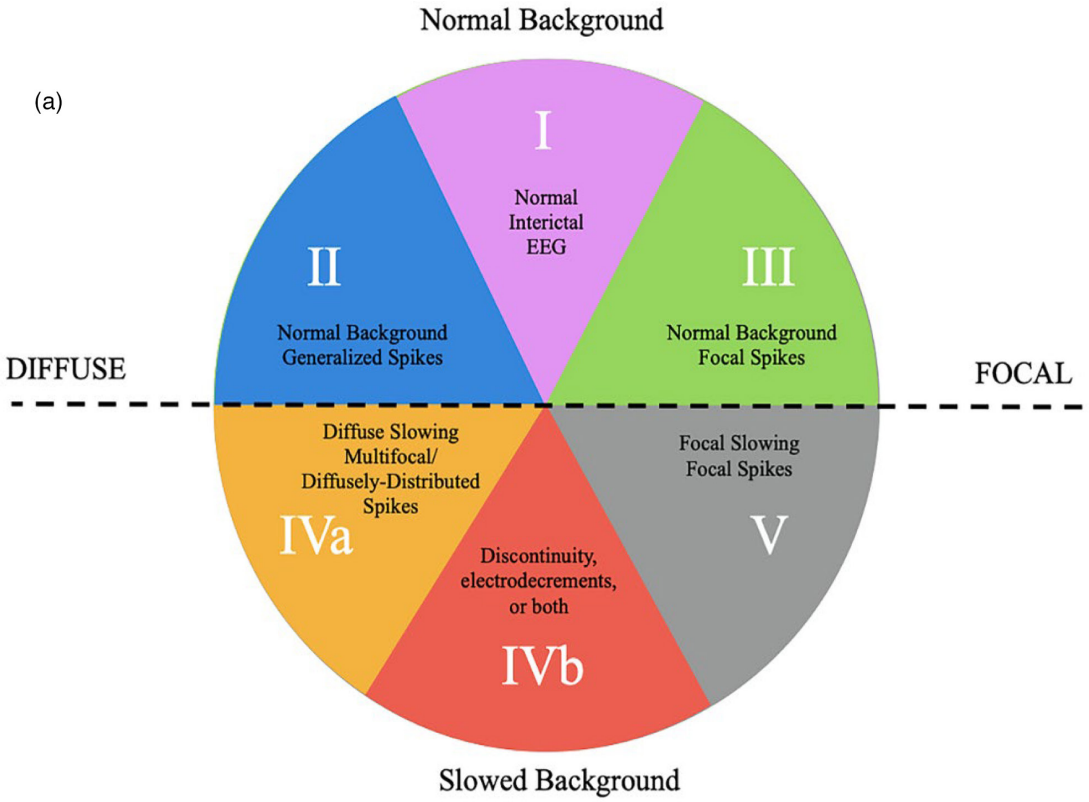
EEM, previously called Jeavons syndrome, is an epilepsy syndrome characterized by eyelid myoclonia with or without absence seizures, epileptic discharges on EEG with eye closure, and photosensitivity (seizures are induced by flashing lights).[1] This syndrome presents between the ages of 6 and 8 years and has a 2:1 female to male predominance.[1]

Seizures consist of staring spells with very fast eye blinks (absence with eyelid myoclonia) and isolated eyelid myoclonia.[1] These seizures occur frequently throughout the day and are easily triggered by light and hyperventilation.[1] Generalized convulsions are prevalent in patients with EEM, although they occur infrequently.

Characteristic EEG findings include a normal background with irregular polyspike–wave complexes.[2] There is marked photosensitivity.

Cognitive deterioration occurs with frequent seizures.[4] The degree of generalized cognitive impairment ranges from borderline-impaired to extremely low intellectual functioning. Discrepancies in intellectual ability across studies of EEM may reflect methodological differences in how intellectual functioning is documented and measured. Alternatively, patient samples may vary in genomic and environmental risk for neurobehavioral comorbidities, contributing to differences in intellectual outcomes across studies of EEM.[5] Because of the rarity of EEM, a detailed neurocognitive profile for the syndrome has not been well defined. Patients may show selective deficits in processing

**FIGURE 1** (a) Visual schematic of epilepsy syndrome categories and EEG features. (b) Comprehensive list of epilepsy syndromes in each category. Abbreviations: CAE, childhood absence epilepsy; COVE, childhood occipital visual epilepsy; DEE-SWAS, developmental epileptic encephalopathy with spike–wave activation in sleep; EAF, epilepsy with auditory features; EEM, epilepsy with eyelid myoclonia; EE-SWAS, encephalopathy with spike–wave activation in sleep; EIDEE, early infantile developmental epileptic encephalopathy; EIMFS, epilepsy of infancy with migrating focal seizures; EMA, epilepsy with myoclonic absences; EMAtS, epilepsy with myoclonic-atonic seizures; EwRIS, epilepsy with reading-induced seizures; FFEVF, familial focal epilepsy with variable foci; FIRES, febrile infection-related epilepsy syndrome; FMTLE, familial mesial temporal lobe epilepsy; GEFS+, genetic epilepsy with febrile seizures plus; GTCA, epilepsy with generalized tonic–clonic seizures alone; HHE, hemiconvulsion-hemiplegia epilepsy syndrome; IESS, infantile epileptic spasm syndrome; JAE, juvenile absence epilepsy; JME, juvenile myoclonic epilepsy; LGS, Lennox–Gastaut syndrome; MEI, myoclonic epilepsy in infancy; MTLE-HS, mesial temporal lobe epilepsy with hippocampal sclerosis; PME, progressive myoclonic epilepsy; POLE, photosensitive occipital lobe epilepsy; SeLEAS, self-limited epilepsy with autonomic seizures; SeLECTS, self-limited epilepsy with centrotemporal spikes; SeLFIE, self-limited familial neonatal-infantile epilepsy; SeLIE, self-limited infantile epilepsy; SeLNE, self-limited neonatal epilepsy; SHE, sleep-related hypermotor epilepsy.



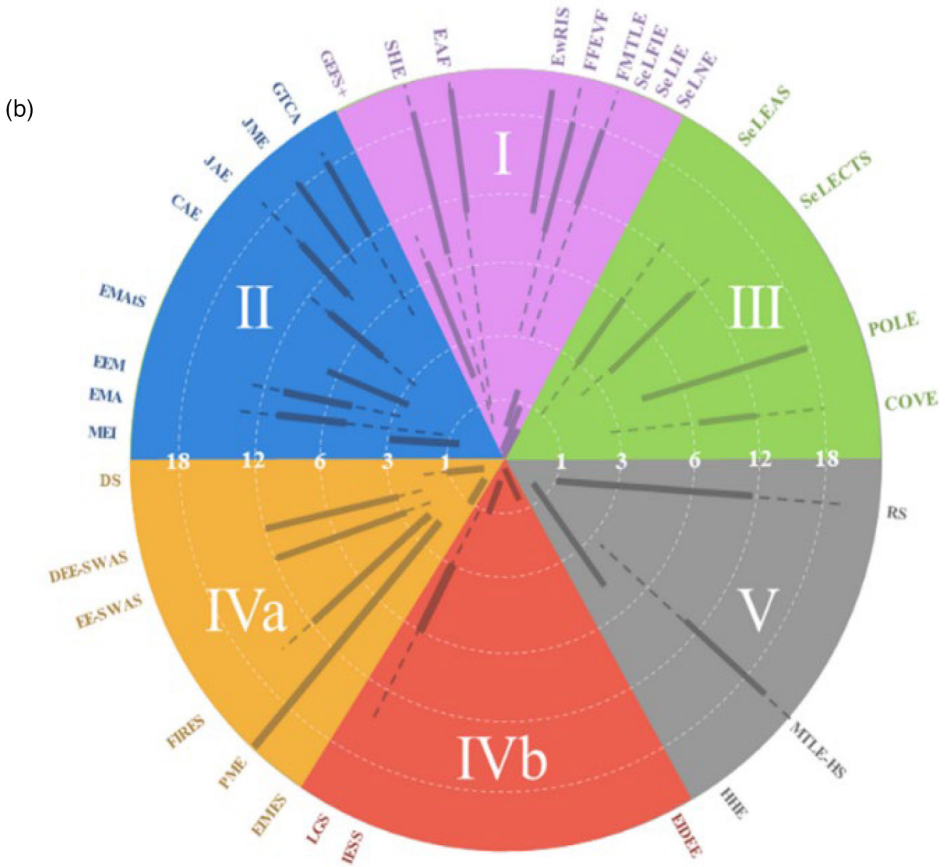



**TABLE 1** Epilepsy syndromes with high developmental relevance classified according to electroencephalography category.

| Category | Syndrome | Medication responsiveness | General developmental outcomes | Probable cause |
|---|---|---|---|---|
| 1 | – | – | – | – |
| 2 | EEM<br>EMAtS | Good | Variable | Polygenic |
| 3 | SeLECTS | Excellent | Generally excellent | Polygenic |
| 4a | Dravet syndrome | Seizures can be controlled with targeted therapy | | |
| | DEE-SWAS | | Poor, especially with inadequate seizure control | Monogenic |
| | EE-SWAS | Conventional therapy is ineffective | | |
| 4b | EIDEE<br>IESS | Poor; consider surgical intervention early in appropriate cases | | Monogenic, but often rare mutations |
| | LGS | | Poor | |
| 5 | Rasmussen syndrome<br>FIRES | Poor | Poor | Structural |

Categories 2 and 3 indicate developmentally favorable outcomes; categories 4b and 5 indicate greatly affected development outcomes.

Abbreviations: DEE-SWAS, developmental epileptic encephalopathy with spike–wave activation in sleep; EEM, epilepsy with eyelid myoclonia; EE-SWAS, epileptic encephalopathy with spike–wave activation in sleep; EIDEE, early infantile developmental epileptic encephalopathy; EMAtS, epilepsy with myoclonic-atonic seizures; FIRES, febrile infection-related epilepsy syndrome; IESS, infantile epileptic spasm syndrome; LGS, Lennox–Gastaut syndrome; SeLECTS, self-limited epilepsy with centrotemporal spikes.

**TABLE 2** Posterior dominant rhythm according to age.

| Age | Minimum posterior dominant rhythm |
|---|---|
| 6 months | 4 Hz |
| 12 months | 6 Hz |
| 3+ years | 8 Hz |

speed, and in some aspects of verbal learning and memory.[4] Many children will not outgrow EEM and seizures may be difficult to treat. Children with EEM may miss school because of uncontrolled seizures, which can negatively impact cognitive and academic skill development.

## CATEGORY 3

The epilepsy syndromes in category 3 are relatively benign. The EEG reveals a normal background for age with focal discharges.[2] While most children outgrow these epilepsy syndromes, there can be associated attention-deficit/hyperactivity disorder (ADHD) and anxiety or depression, which can contribute to challenges in school. The most well-known epilepsy syndrome within category 3 that may be associated with developmental challenges is self-limited epilepsy with centrotemporal spikes (SeLECTS).[1]

### Self-limited epilepsy with centrotemporal spikes

SeLECTS, previously called Rolandic epilepsy, is a type of epilepsy that typically affects school-age children and usually resolves by adolescence.[1] Seizures classically cluster near falling asleep or waking up. Semiology is characterized by facial twitching with guttural noises, speech arrest, and hypersalivation.[1] Between 33% and 66% of patients may experience secondary generalization after focal onset seizure.[6] The EEG classically shows centrotemporal sharp waves with a horizontal dipole (Figure 2). These discharges are typically seen bilaterally, although not in all cases.

Treatment is often not classically indicated due to infrequent seizures.[6] However, increased frequency or family preference may warrant treatment, in which case antiseizure medications may be used with high efficacy.[6]

Although seizures in SeLECTS carry a relatively self-limited prognosis in most cases, neuropsychological dysfunction may be evident in children with this syndrome. Deficits in language processing, memory, and attention are commonly observed.[6] Children with SeLECTS may also show ADHD symptoms and externalizing behavior problems. General intellectual ability and other aspects of neuropsychological functioning (e.g. visuospatial skills, processing speed) are likely to be within the normal range,[6] although subtle weaknesses may be evident in these areas relative to peers without SeLECTS.[7] Rarely, SeLECTS can transform into epileptic encephalopathy with spike–wave activation in sleep (EE-SWAS). Overall, social skills as an adult are not impaired and most children will go on to be fully functioning members of society.[8] Most patients are seizure-free by adolescence.[1]

## CATEGORY 4A

Category 4a epilepsy syndromes are associated with difficult-to-control seizures and poor developmental outcomes. These

epilepsy syndromes are often surprising to parents because the child will have typical development before seizure onset. These epilepsy syndromes are highly associated with single-gene pathogenic variants.[9]

The role of the pathogenic variants (through the lens of epilepsy and development) can be, as we now understand it, twofold. The pathogenic variant itself can cause developmental problems. The pathogenic variant can also result in epilepsy which, in turn, can lead to associated impairments.[1] Importantly, seizure control decreases associated morbidity and mortality but does not always impact developmental outcomes.

The EEG in category 4a epilepsy syndromes reveals a slowed background and multifocal epileptiform discharges (Figure 3).[9] One of the hallmark epilepsy syndromes in category 4a that begins in infancy is Dravet syndrome.[9]

## Dravet syndrome

Dravet syndrome is a developmental and epileptic encephalopathy that presents in infancy.[10] Its hallmark features are prolonged febrile seizures, hemiconvulsive seizures, and developmental stagnation or impairment.[10] Often, children with Dravet syndrome have first-degree relatives with febrile seizures, generalized epilepsy, or migraines. Seizures are typically very difficult to control in patients with Dravet syndrome.

The EEG reveals background slowing with multifocal discharges.[9] Dravet syndrome is caused by a pathogenic variant in the *SCN1A* gene.[9]

Cognitive and behavioral impairments are most evident after the age of 2 years.[11] Most individuals with Dravet syndrome eventually display generalized cognitive impairment.[11] In less impaired individuals, a discernible pattern of strengths and weaknesses, involving visual-perceptual and visual-motor skills may be apparent.[11] Dravet syndrome has thus been conceptualized as a 'dorsal stream vulnerability' syndrome, in which there may be more impairment in (dorsal stream) visual-motor skills than (ventral stream) visual-perceptual processing.[11] Clumsiness and unsteady gait typically emerge later in development. Fine motor skills are similarly affected. From a social and emotional perspective, attention problems, hyperactivity, and autism spectrum disorder are common.[11]

Treatment of Dravet syndrome is directed toward seizure control because there are high rates of status epilepticus and sudden unexpected death in epilepsy.[1] Approximately 10% to 20% of children with Dravet syndrome pass away before reaching adulthood. Despite new and effective medications, the impact on seizure control has not resulted in improved developmental outcomes for children with Dravet syndrome.

## Developmental epileptic encephalopathy with spike–wave activation in sleep and epileptic encephalopathy with spike–wave activation in sleep

Developmental epileptic encephalopathy with spike–wave activation in sleep (DEE-SWAS) and EE-SWAS are disorders that cause marked impairment in cognition and development

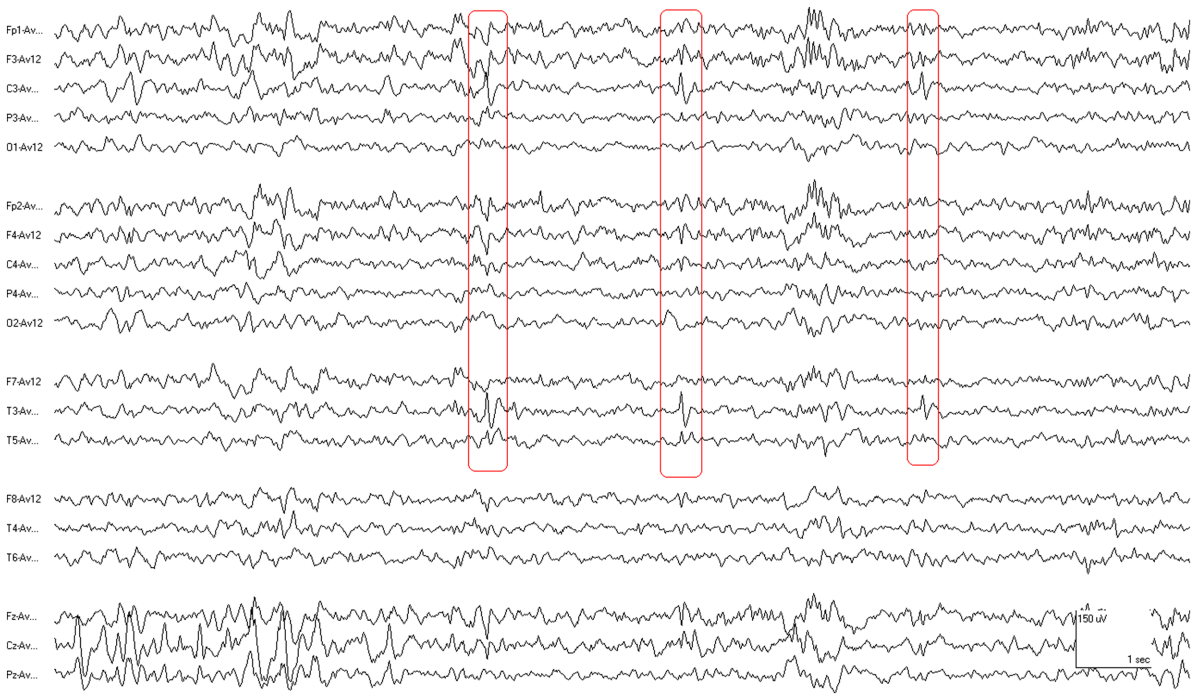



**FIGURE 2** Stereotyped centrotemporal spikes with a horizontal dipole are evident on this referential montage. These features are consistent with the clinical diagnosis of self-limited epilepsy with centrotemporal spikes.

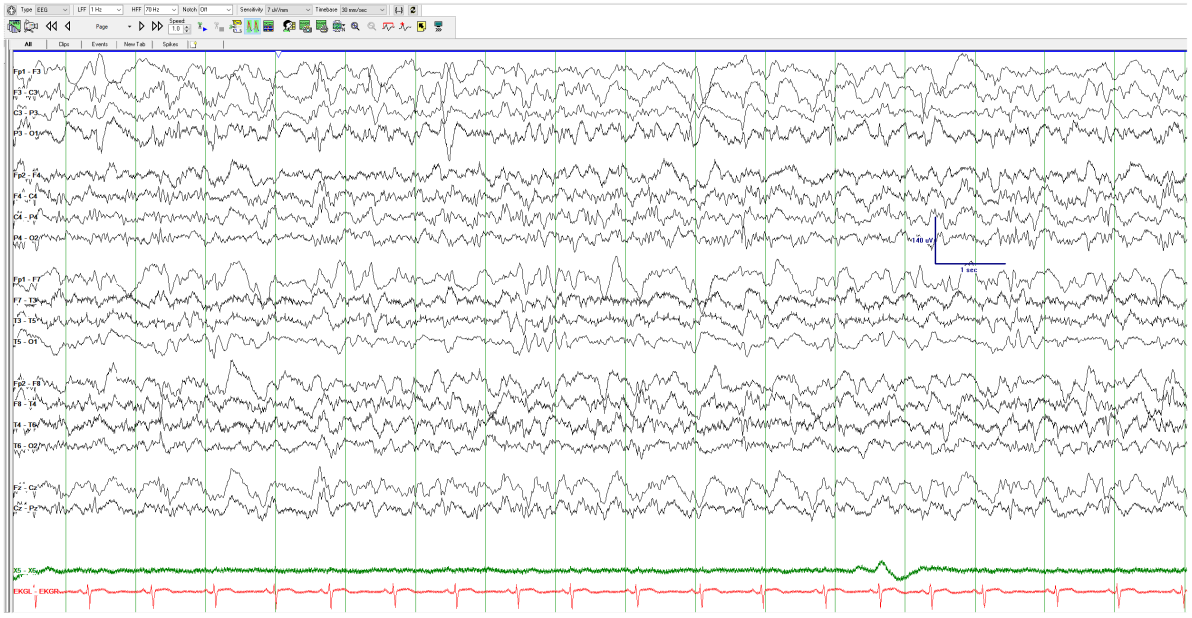


**FIGURE 3** Electroencephalography in category 4a epilepsies reveals a slowed background and multifocal epileptiform discharges.

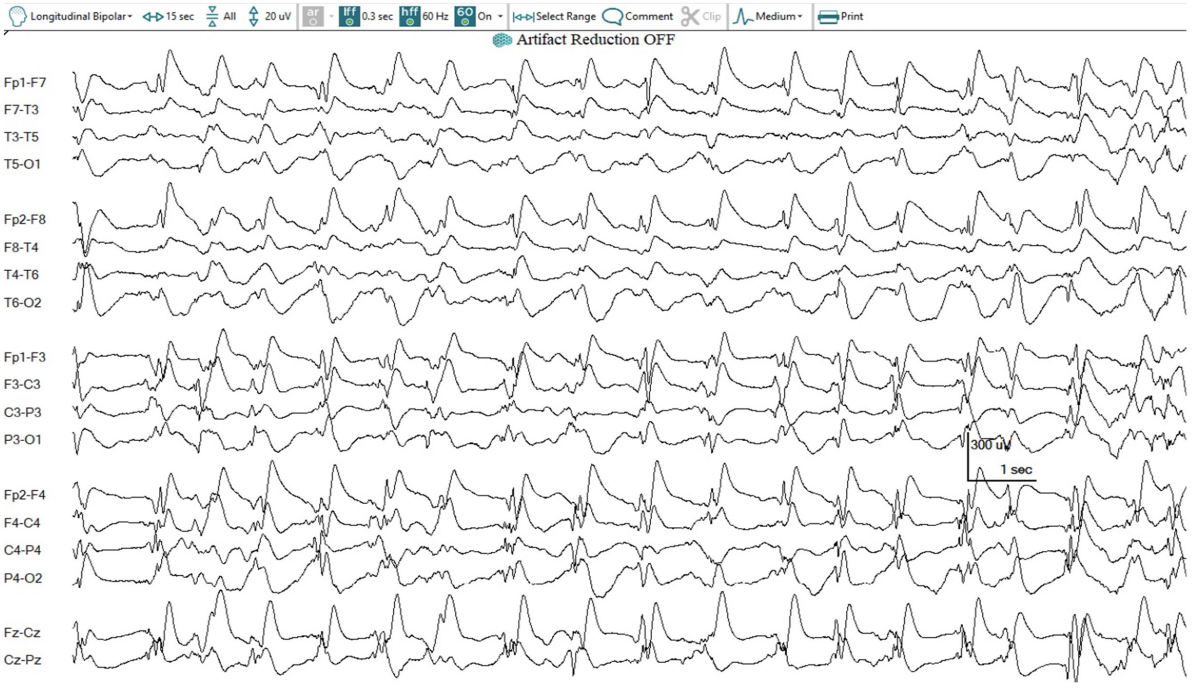



**FIGURE 4** Longitudinal bipolar electroencephalography with spike–wave activation in non-rapid eye movement sleep.

due to abnormal brain waves that occur during sleep.[1] The term DEE-SWAS applies to patients who have baseline developmental delay and then further deteriorate due to spike–wave activation in sleep.[1] EE-SWAS refers to patients who deteriorate in the setting of having previous typical development due to spike–wave activation in sleep.[1] Children who develop DEE-SWAS or EE-SWAS typically present between the ages of 4 years and 5 years.[1]

Most patients have a history of seizures before developing spike–wave activation in sleep. The EEG shows diffuse slow spike and wave in non-rapid eye movement sleep (Figure 4).

Developmental problems are significant and include a variable pattern of deterioration across cognitive and intellectual functioning, language, and motor skills.[11] Cases may present with profound developmental milestone loss and florid encephalopathy.[11] Patients also often

develop behavioral abnormalities, including aggression, poor emotional control and interpersonal skills, and ADHD symptoms.[12]

A family history is present in up to 50% of cases.[13] A common single-gene pathogenic variant includes *GRIN2A*, which results in a drastic form of DEE-SWAS or EE-SWAS that is difficult to treat.[13]

Outcomes are worse in younger children with DEE-SWAS or EE-SWAS.[10] Residual deficits often occur after resolution of spike–wave activation in sleep. Residual deficits are most apparent in verbal skills, attention, and behavior (e.g. social disturbances, hyperactivity).[12] Premorbid development impairments and severity of regression after the onset of epileptic activity are also important predictors of long-term outcomes.[12]

## CATEGORY 4B

Similar to category 4a epilepsy syndromes, category 4b syndromes are associated with drug-resistant epilepsy and significant developmental disability.[2] The hallmark feature that differentiates category 4a from category 4b is discontinuity on the EEG.[2] EEG discontinuity reflects a disruption in the speed of the background, with diffuse attenuation (Figure 5).[2] Both categories 4a and 4b reveal a universally slowed background with multifocal epileptiform discharges.[2] The spectrum of age-related category 4b epilepsy syndromes ranging from birth to late childhood are covered in the following sections.

### Early infantile developmental epileptic encephalopathy

Early infantile developmental epileptic encephalopathy (EIDEE) formerly consisted of two syndromes called Ohtahara syndrome and early myoclonic encephalopathy. It is a severe DEE that occurs in the neonatal or infantile period. Seizures are typically frequent and difficult to control.[10] Seizure types may include clonic, myoclonic, tonic, or epileptic spasm.[10] Generalized convulsive seizures are uncommon given the early onset and incomplete myelination patterns related to age.

The EEG in EIDEE typically reveals burst suppression (Figure 6).[10] In cases that do not show burst suppression, the background is universally slow.[2] There are often multifocal epileptiform discharges.

Patients with EIDEE have poor outcomes, with a shortened lifespan and significant developmental delays.[14] Many patients are fully dependent on caregivers for support. Over 75% of cases eventually transform into LGS.[15]

Recent research indicated that prompt seizure treatment with medications or surgery can impact the lifespan and developmental outcomes.[15] A thorough workup with magnetic resonance imaging and genetic testing is indicated in patients with EIDEE. It is important to consider etiologies that may be responsive to vitamins, such as pyridoxine-dependent epilepsy, which may present in a similar fashion.

### Infantile epileptic spasm syndrome

Infantile epileptic spasm syndrome (IESS) presents with characteristic epileptic spasms in infancy. Epileptic spasms are movements that consist of a quick head nod and bilateral arm extension.[10] These episodes cluster, are uncomfortable for the patient, and tend to occur more after waking from sleep.[10] The typical onset of spasms is between the ages of 3 months and 12 months, with a peak at the age of 5 months.[10]

The EEG in IESS shows a hallmark feature known as hypsarhythmia (Figure 7).[9,16] Hypsarhythmia is an EEG

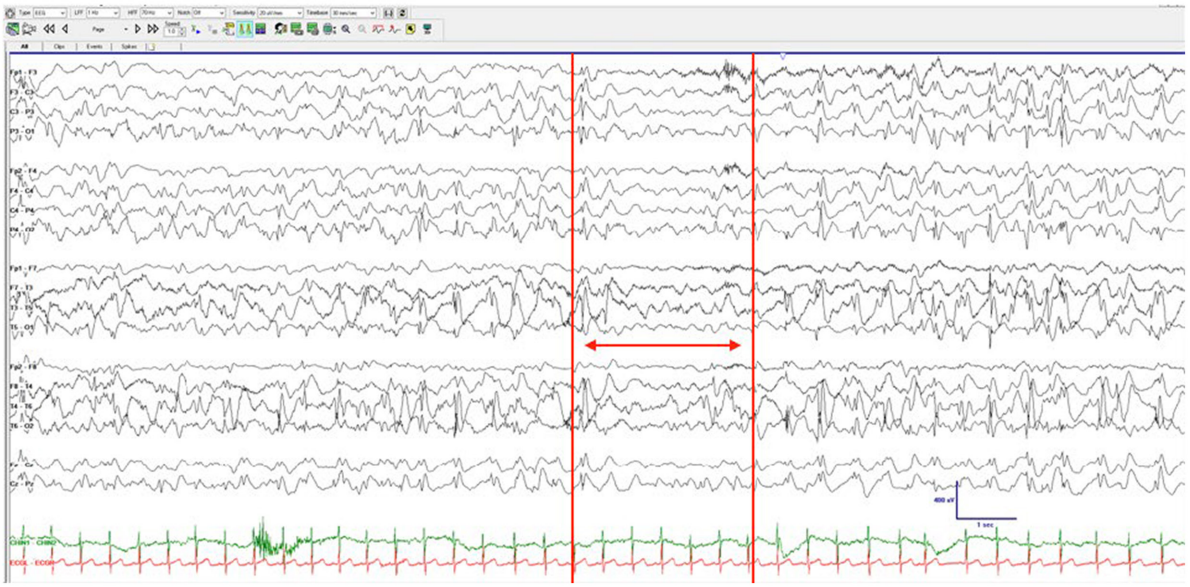


**FIGURE 5** Longitudinal bipolar electroencephalography showcasing discontinuity (the period between the red markers).

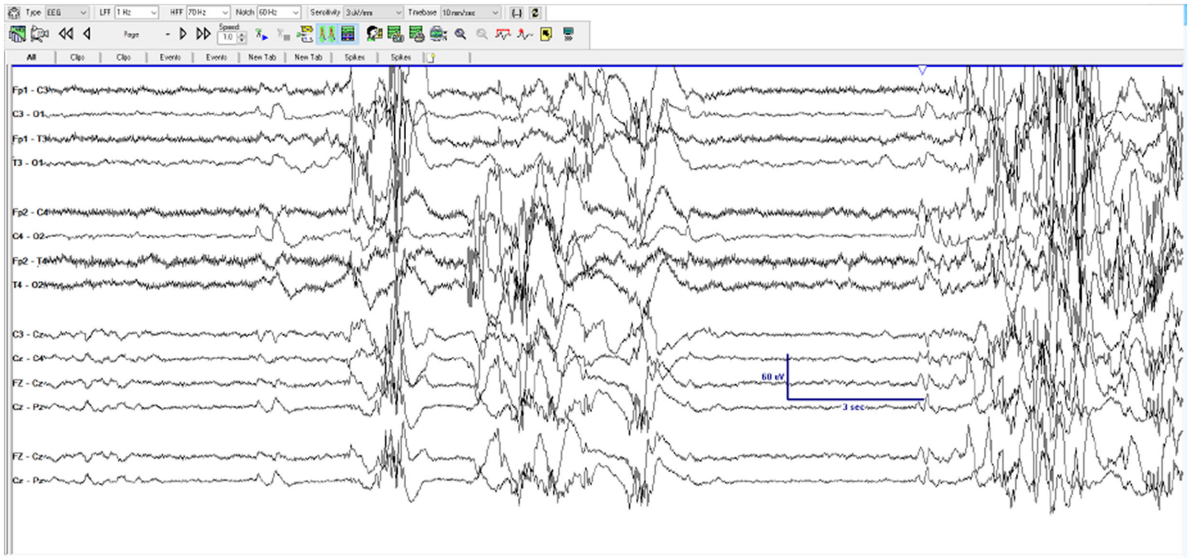


**FIGURE 6** Longitudinal bipolar montage showcasing periods of diffuse suppression followed by high-amplitude bursts indicative of early infantile developmental epileptic encephalopathy.

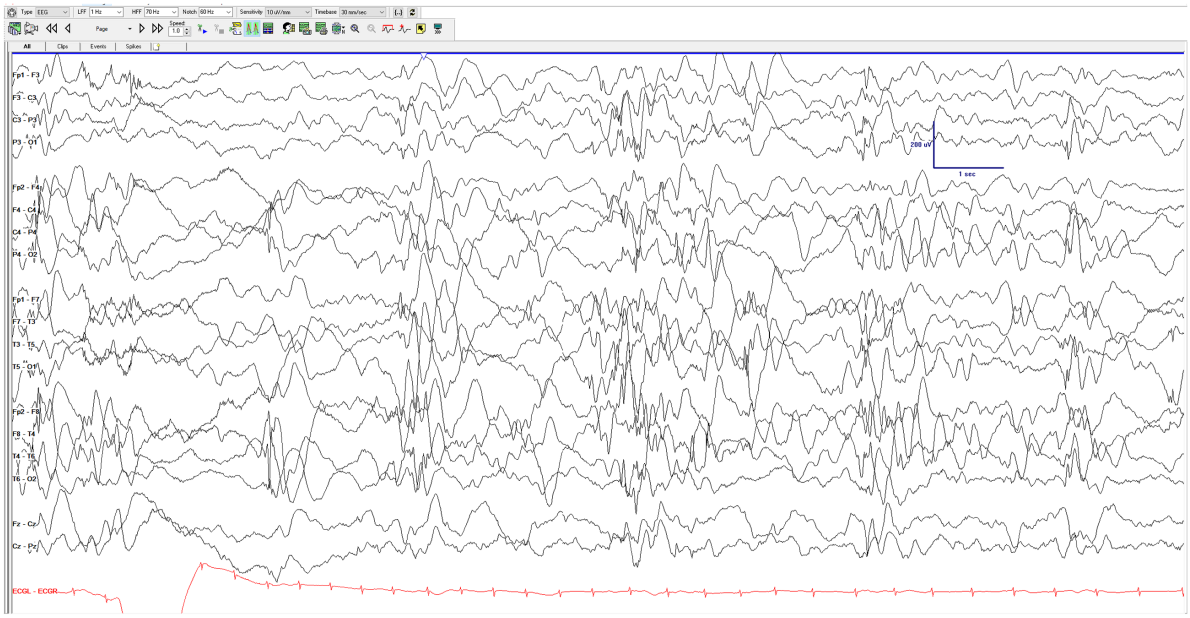


**FIGURE 7** Electroencephalography with hypsarhythmia.

pattern that consists of high-amplitude (typically greater than 300 μV) waveforms.[17] The EEG background in hypsarhythmia is discontinuous and chaotic. When clinicians suspect that a patient may have IESS, it is imperative to record the patient on EEG long enough to capture a full sleep–wake cycle.[17] An awake-only EEG may miss hypsarhythmia.

IESS is associated with structural brain abnormalities including, but not limited to: trisomy 21; tuberous sclerosis; Aicardi syndrome; Sturge–Weber syndrome; incontinentia pigmenti; CDKL5 deficiency disorder; and *KCTN1* pathogenic variations.[18] Some patients with IESS may not have an identifiable cause despite extensive workup. Over time, this cohort of patients, called cryptogenic, has decreased with whole-exome sequencing.

Treatment of IESS is evolving. Options include adrenocorticotropic hormone, prednisolone, vigabatrin, or a ketogenic diet.

IESS has historically been associated with a high degree of morbidity and mortality.[17] Approximately one-third of children diagnosed with IESS may die because of the disorder.[18] The remainder readily go on to develop LGS. Studies showed that in promptly treated patients who do not have an etiology of their spasms, spasms may resolve with relatively spared development. Historically, somewhere between

15% and 20% of cases have good developmental outcomes (defined as an IQ >85) after treatment.[18] The remainder of patients may continue to have seizures and face significant long-term disability.[18]

## Lennox–Gastaut syndrome

LGS is a severe type of childhood-onset epilepsy. Etiologies include structural brain deficits, metabolic disorders, and genetic disorders.[1] The workup of LGS typically includes EEG, brain magnetic resonance imaging, and genetic testing.

LGS is defined by a triad of symptoms. Multiple seizure types, intellectual disability, and slow spike–wave discharges seen on EEG are the features that make up the triad.[1] LGS typically presents between the ages of 3 years and 5 years, although it can occur as young as age 18 months or as old as age 8 years.[1] Tonic and atonic seizures are common. Additional seizure types include myoclonic, focal, generalized, and atypical absence.[1]

The EEG is patients with LGS consists of a diffusely slow and discontinuous background, with abundant interictal slow spike–wave discharges and generalized paroxysmal fast activity.[2]

Seizures are difficult to treat in LGS.[1] Most patients with refractory epilepsy do not benefit from the use of more than two antiseizure medications. Antiseizure medication polypharmacy can contribute significantly to behavioral problems, cognition, and sleepiness.

Development in LGS is impaired globally and precedes seizure onset.[19] Children with LGS have high rates of hyperactivity, aggression, autism spectrum disorder, and sleep disturbances.[19] Children with LGS continue to have seizures into adulthood. Severe intellectual disability occurs in more than 90% of patients.[19] Continued long-term care is critical.

# CATEGORY 5

Category 5 epilepsy syndromes most often relate to structural insults that affect the brain. Children are previously typically developing. These epilepsy syndromes present with seizures and markedly abnormal neurological examinations during the active phase of these syndromes. These syndromes have EEGs with focal or generalized slowing and focal or multifocal discharges.[2] EEG abnormalities correspond with the structural insults to the brain. Two hallmark disorders to be aware of are Rasmussen syndrome and febrile infection-related epilepsy syndrome (FIRES).

## Rasmussen syndrome

Rasmussen syndrome is an epilepsy syndrome characterized by unilateral inflammation of the cerebral cortex resulting in drug-resistant epilepsy, developmental regression, and hemiparesis.[20] The mechanisms underlying the cause of this sudden inflammation are poorly understood. Immunotherapy is historically ineffective. Typically, age at onset is 6 years although it can range from infancy to adulthood.[20]

As the inflammation progresses, the brain is damaged and atrophies (Figure 8). Cognitive and motor dysfunction follow accordingly.[20]

Nearly all patients with Rasmussen syndrome show typical cognitive development before seizure onset. Patients with left hemispheric involvement initially show selective deficits in verbal abilities, whereas patients with right hemispheric involvement show more impairment in nonverbal and perceptual reasoning skills.[21] Children also develop hemiparesis.[21] Importantly, ongoing seizures may eventually compromise the function of the unaffected hemisphere.[21] Longitudinal research showed deterioration in both verbal and nonverbal abilities as Rasmussen syndrome progresses.[21]

The EEG in Rasmussen syndrome shows an asymmetric, slow background with epileptiform discharges on the affected side of the brain.[2]

In young patients, surgery on the affected brain hemisphere may be an option to stop the inflammation process as neuromodulation is ineffective.[21] The outcomes of patients with Rasmussen syndrome who undergo surgery versus those who do not undergo surgery do not greatly differ given the extent of inflammation and damage to the hemisphere of the brain.[21] Outcomes after hemispherectomy are related to the affected cerebral hemisphere and side of surgery. Children who have left hemispherectomy show more

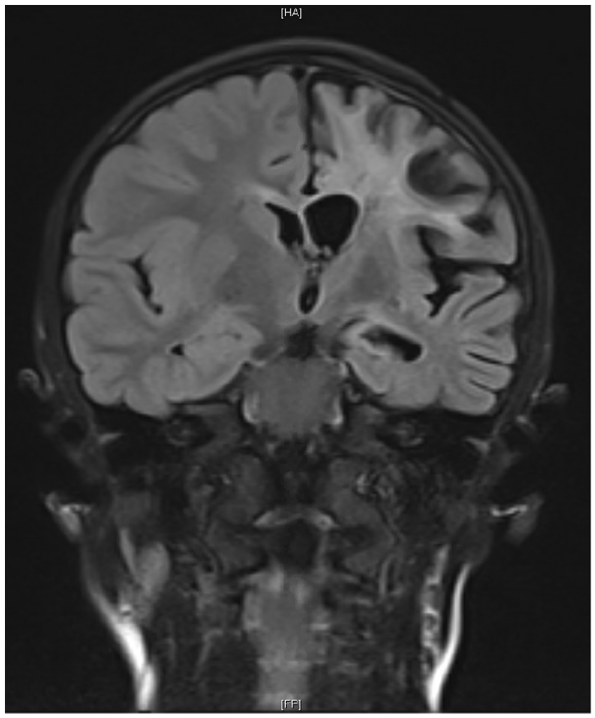



**FIGURE 8** Magnetic resonance imaging fluid-attenuated inversion recovery sequence showcasing signal change and atrophy in the affected left hemisphere in a patient with Rasmussen syndrome.

widespread neurocognitive deficits, with ongoing deterioration in verbal ability postoperatively.[21] The persistence of seizures postoperatively also negatively impacts cognitive outcomes, regardless of the side of surgery.

## Febrile infection-related epilepsy syndrome

FIRES is a severe outcome of a routine febrile illness that results in refractory status epilepticus. FIRES can occur anywhere between 24 hours and 2 weeks after a febrile illness.[22] The pathogenesis of FIRES is poorly understood.[22]

EEG features include status epilepticus at onset followed by diffuse slowing with multifocal discharges.[2] After resolution of status epilepticus, a static encephalopathy with a slowed background and multifocal epileptiform discharges may continue in patients with FIRES.

The mortality of FIRES is high. Survivors are left with drug-resistant epilepsy and intellectual disability.[22] Approximately 33% of survivors have borderline cognitive functioning. Another 33% have moderate intellectual disability and the remainder of patients have profound disability or are left in a vegetative state.[22]

Anakinra, a recombinant interleukin-1 receptor antagonist, has been effective in stopping status epilepticus in cases of FIRES.[22]

# DISCUSSION

The updated 2022 classification has strived to better classify epilepsy syndromes. Epilepsy syndrome categorization through EEG, as outlined earlier, is a powerful methodology that allows epilepsy syndrome phenotypes to be quickly recognized. Through quick recognition of syndrome categorization, streamlined diagnostic workup, targeted treatment, and needed developmental therapies can be planned.

Importantly, while epilepsy syndrome classification is a cornerstone for clinical management and prediction of comorbidities, emerging research suggests that there are factors outside of epilepsy syndromes that contribute to cognitive and behavioral outcomes in individual patients. These factors may include the integrity of brain structure, connectivity, and function, as well as several risk and resilience factors, such as socioeconomic disadvantage, social support, genetic and environmental differences, lifestyle practices, and cognitive reserve. Such factors may help to explain variability in neurobehavioral phenotypes within individual syndromes, as well as overlap in phenotypes across syndromes, especially in the less severe childhood epilepsies. Future research is needed to clarify the extent to which these factors influence neurobehavioral phenotypes in the more severe childhood epilepsies.

The degree to which successful treatment of seizures impacts development in several epilepsy syndromes, and by how much, is critical to understand going forward. Along with better understanding and consideration of individual patient factors, we can continue to work to better treat epilepsy and significantly improve quality of life and developmental outcomes for individuals with epilepsy.

## DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study

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