Epilepsy Syndromes with Onset in Neonates & Infants

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Disclosures relevant to this presentation

Chair ILAE Commission on Classification & Terminology 2013-17

Member ILAE Task Force on Neonatal Seizures 2013-17

Member ILAE Task Force on Nosology & Definitions 2017-21

Member ILAE Task Force on Etiology Specific Syndromes 2021-25

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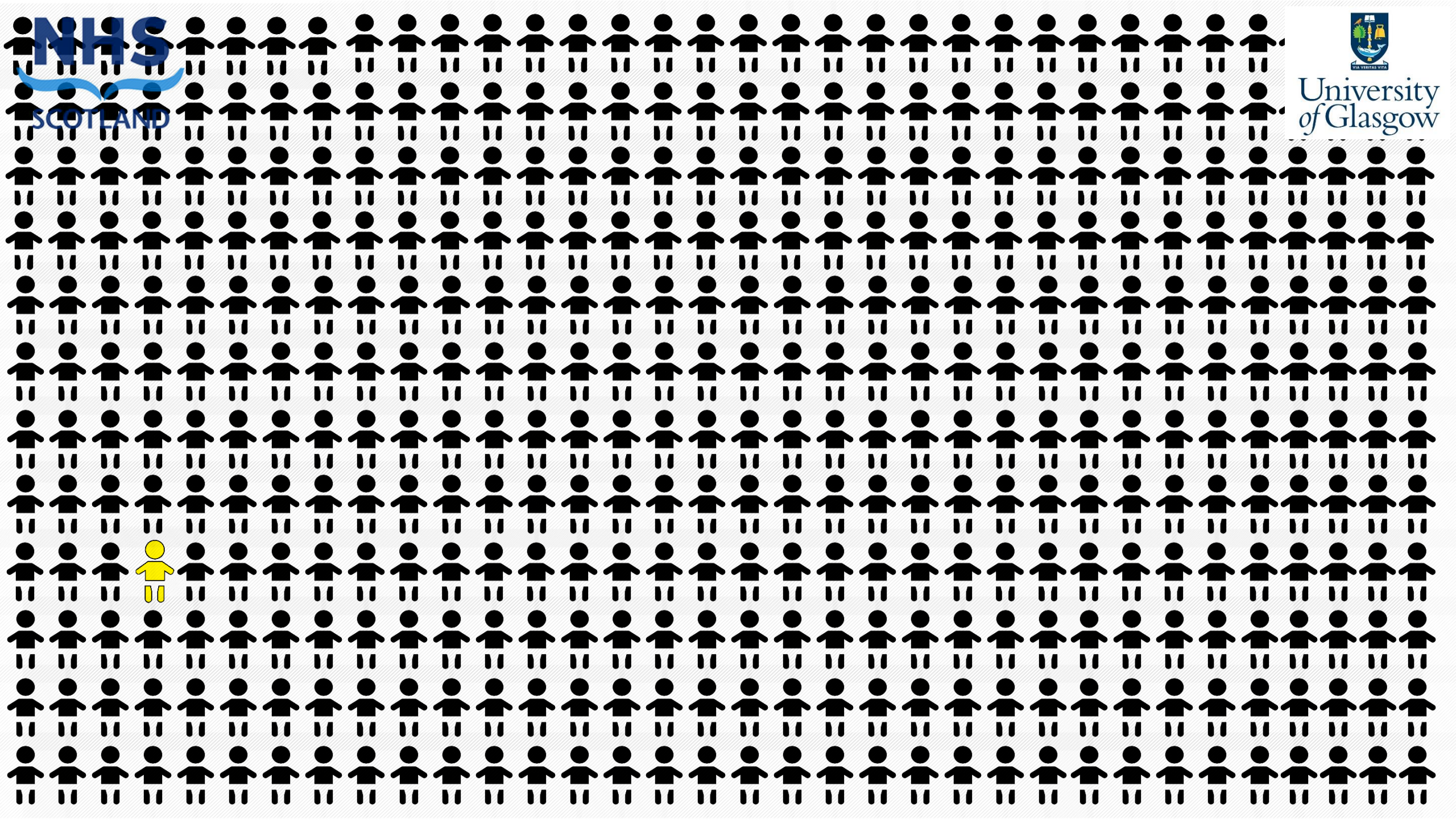
SPECIAL REPORT

ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: Position statement by the ILAE Task Force on Nosology and Definitions

Sameer M. Zuberi[1] | Elaine Wirrell[2] | Elissa Yozawitz[3] | Jo M. Wilmshurst[4] | Nicola Specchio[5] | Kate Riney[6,7] | Ronit Pressler[8,9] | Stephane Auvin[10] | Pauline Samia[11] | Edouard Hirsch[12] | Santiago Galicchio[13] | Chahnez Triki[14] | O. Carter Snead[15] | Samuel Wiebe[16] | J. Helen Cross[17,18] | Paolo Tinuper[19,20] | Ingrid E. Scheffer[21] | Emilio Perucca[22,23] | Solomon L. Moshé[24,25,26] | Rima Nabbout[27]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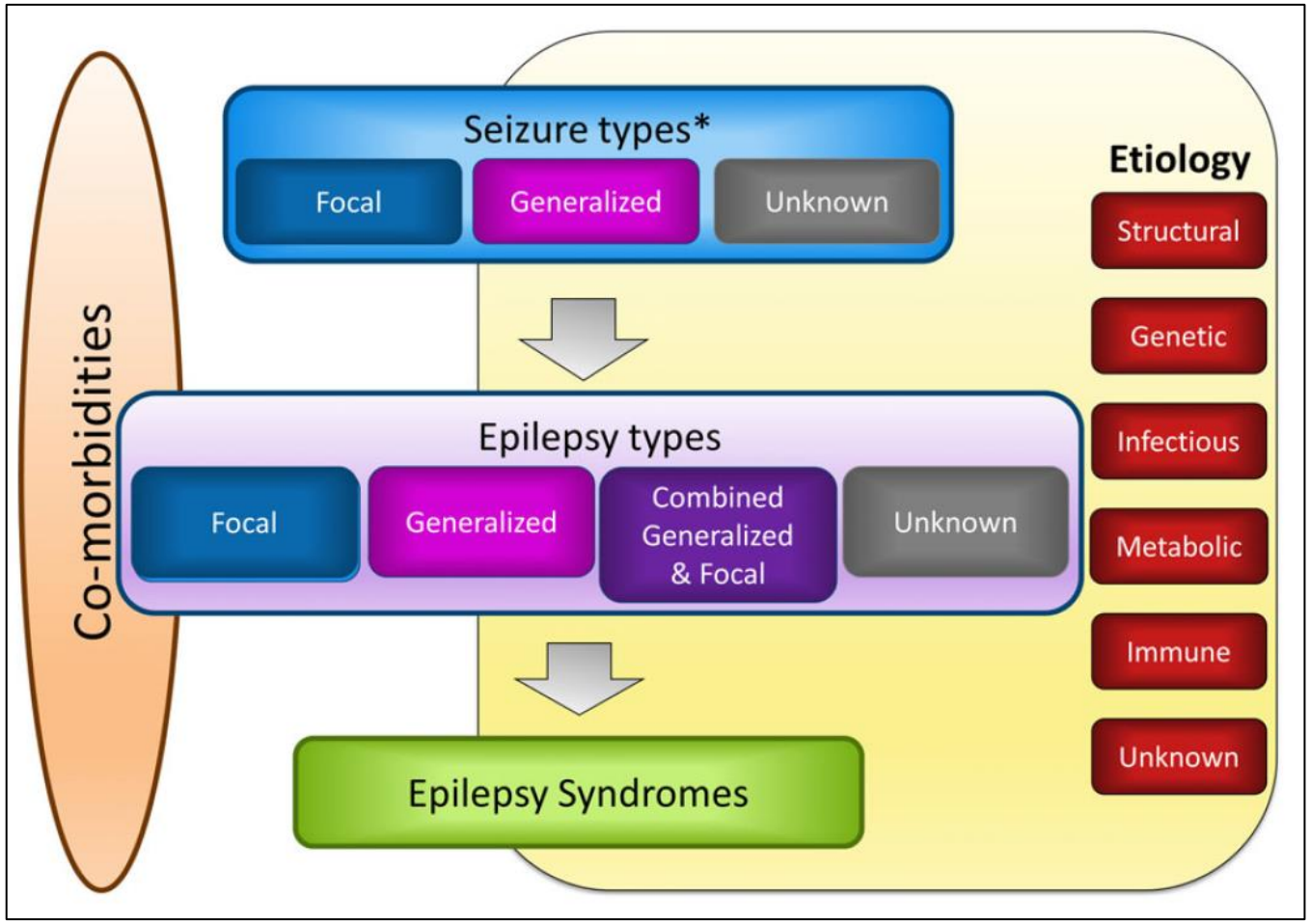

ILAE POSITION PAPER

ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology

[1,2,3]Ingrid E. Scheffer, [1]Samuel Berkovic, [4]Giuseppe Capovilla, [5]Mary B. Connolly, [6]Jacqueline French, [7]Laura Guilhoto, [8,9]Edouard Hirsch, [10]Satish Jain, [11]Gary W. Mathern, [12]Solomon L. Moshé, [13]Douglas R. Nordli, [14]Emilio Perucca, [15]Torbjörn Tomson, [16]Samuel Wiebe, [17]Yue-Hua Zhang, and [18,19]Sameer M. Zuberi

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An epilepsy syndrome is a characteristic cluster of clinical and EEG features often supported by specific etiological findings (structural, genetic, immune and infectious

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Epilepsia

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The ILAE classification of seizures and the epilepsies: Modification for seizures in the neonate. Position paper by the ILAE Task Force on Neonatal Seizures

Ronit M. Pressler[1,2] | Maria Roberta Cilio[3] | Eli M. Mizrahi[4] | Solomon L. Moshé[5,6] | Magda L. Nunes[7] | Perrine Plouin[8] | Sampsa Vanhatalo[9] | Elissa Yozawitz[5,6] | Linda S. de Vries[10] | Kollencheri Puthenveettil Vinayan[11] | Chahnez C. Triki[12] | Jo M. Wilmshurst[13] | Hitoshi Yamatomo[14] | Sameer M. Zuberi[15]

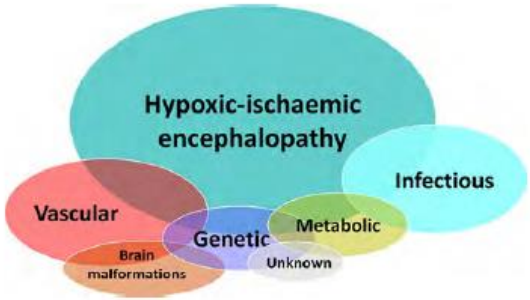
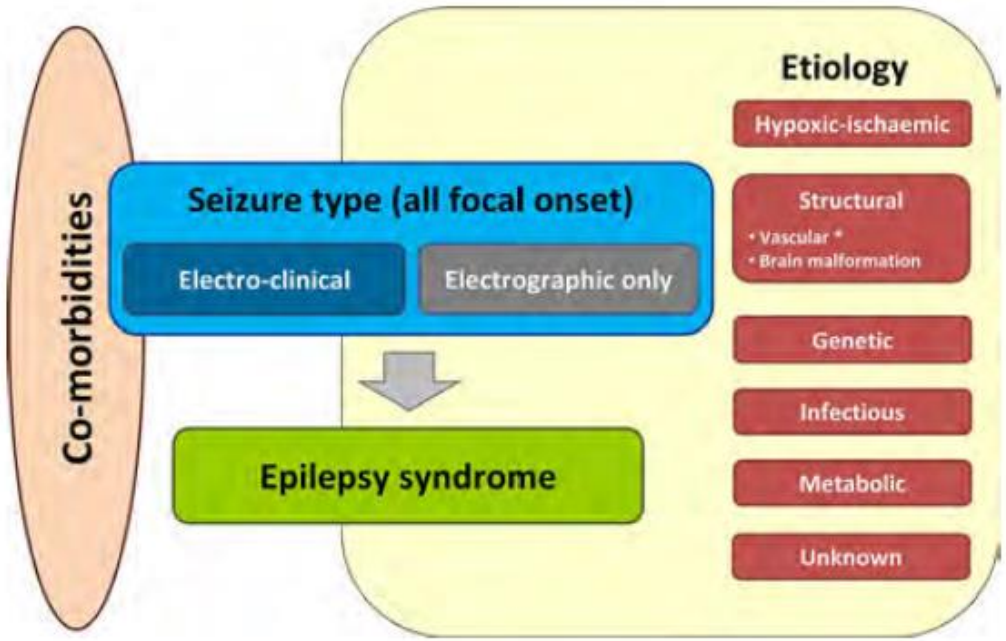
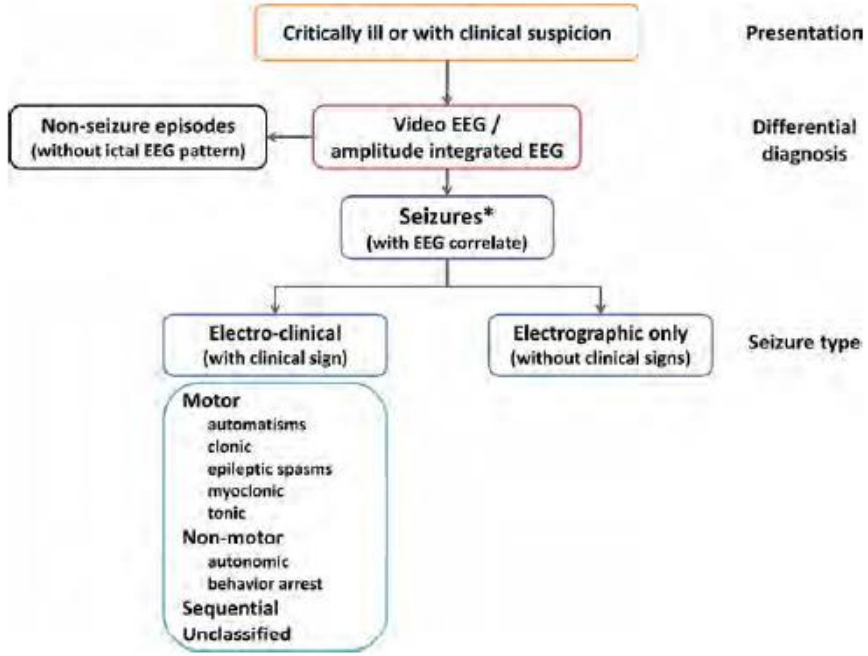


FIGURE 1 Relative occurrences of common etiologies of neonatal seizures in term infants. Adapted from [3–5,8,81,82]





Classification should guide clinical management

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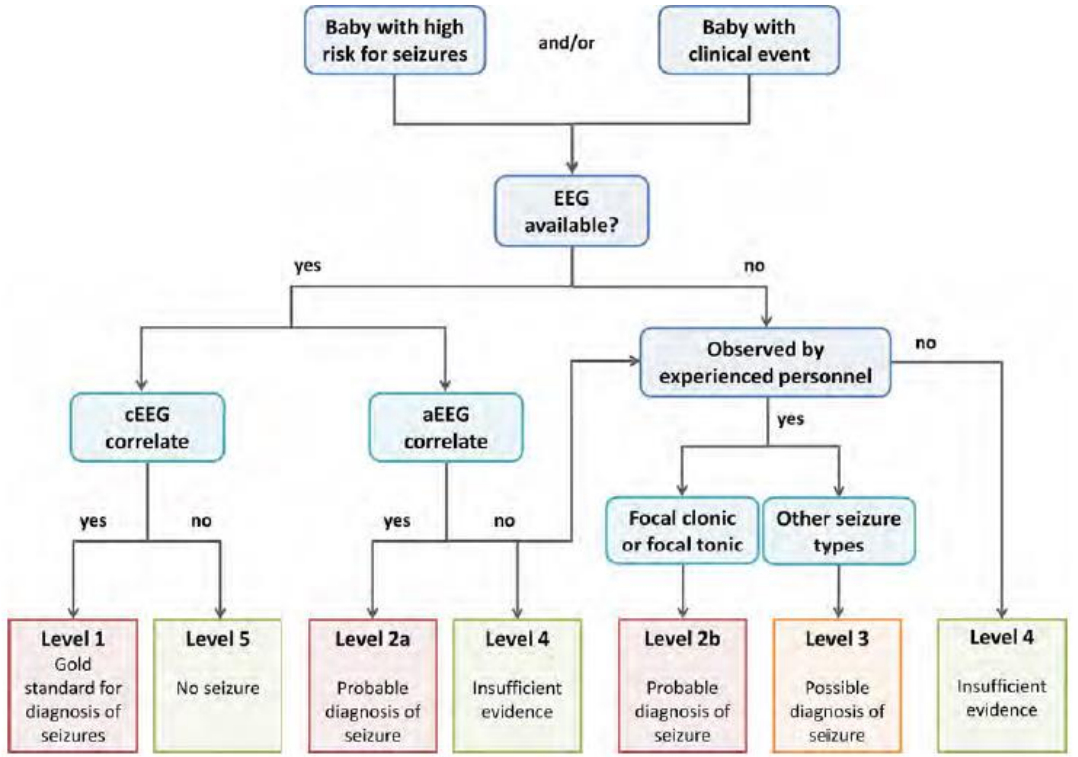

FIGURE 5 Algorithm to determine degrees of diagnostic certainties for neonatal seizures. This flow chart will help to determine the diagnostic certainty of neonatal seizures depending on the available diagnostic method (EEG, aEEG or observation by experienced personnel) and seizure type. Developed by the Brighton collaboration (adapted from[4]). cEEG conventional EEG; aEEG; amplitude-integrated EEG

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Self-limited epilepsies

- Self-limited neonatal epilepsy (SeLNE)
- Self-limited familial neonatal-infantile epilepsy (SeLFNIE)
- Self-limited infantile epilepsy (SeLIE)
- Genetic epilepsy with febrile seizures plus (GEFS+)
- Myoclonic epilepsy in infancy (MEI)

Developmental and epileptic encephalopathies (DEE)

- Ealy infantile developmental and epileptic encephalopathy (EIDEE)
- Epilepsy in infancy with migrating focal seizures (EIMFS)
- Infantile epileptic spasms syndrome (IESS)
- Dravet syndrome (DS)

Etiology-specific syndromes

- *KCNQ2*-DEE
- Pyridoxine-dependent (*ALDH7A1*)-DEE (PD-DEE)
- Pyridox(am)ine 5'-Phosphate Deficiency (PNPO)-DEE (P5PD-DEE)
- *CDKL5*-DEE
- *PCDH19* clustering epilepsy
- Glucose Transporter 1 Deficiency Syndrome (GLUT1DS)
- Sturge Weber syndrome (SWS)
- Gelastic seizures with hypothalamic hamartoma (GS-HH)

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Epilepsies where there is likely to be spontaneous remission

Developmental and epileptic encephalopathies (DEE)

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- Epilepsy in infancy with migrating focal seizures (EIMFS)
- Infantile epileptic spasms syndrome (IESS)
- Dravet syndrome (DS)

Epilepsies where developmental impairment is related to both the underlying etiology independent of epileptiform activity and the epileptic encephalopathy

Etiology-specific syndromes

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- Pyridoxine-dependent (*ALDH7A1*)-DEE (PD-DEE)
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Syndromes due to specific genetic, structural, immune and infectious etiologies where there are consistent electroclinical features, management and prognostic implications

Self-limited neonatal epilepsy

TABLE 1 Diagnostic criteria for self-limited (familial) neonatal epilepsy

	Mandatory	Alerts	Exclusionary
Seizures	Seizures are characterized by focal tonic features at onset, affecting the head, face, and limbs. Focal clonic or tonic seizures may alternate sides from seizure to seizure, and may evolve to bilateral tonic or clonic seizures	Clinical history suggestive of in utero seizures	Epileptic spasms Myoclonic seizures Generalized tonic seizures Generalized tonic-clonic seizures
EEG		Interictal: Mild background slowing	Interictal: Persistent focal slowing or moderate or greater background slowing not limited to the postictal period Burst suppression pattern Hypsarrhythmia Ictal: Lack of EEG correlate with clinical symptoms
Age at onset			Onset after first month of age
Development at onset			Any degree of encephalopathy
Neurological exam		Significant neurological examination abnormalities, excluding incidental findings	
Imaging			Neuroimaging documenting a causal lesion for seizures
Other studies – genetics		Lack of pathogenic variant in gene associated with this syndrome, most commonly *KCNQ2* or *KCNQ3* OR Lack of family history suggesting AD inheritance with incomplete penetrance	Other acute symptomatic cause of seizures including intracranial infection, ischemic or hemorrhagic stroke, hypoxic-ischemic brain injury, significant metabolic disturbances
Course of illness		Mild neurodevelopmental delay long-term Lack of remission of epilepsy after 6 months of age Drug-resistant epilepsy	Moderate to severe neurodevelopmental disability
Are MRI or ictal EEG required for diagnosis? A nonlesional MRI is required to diagnose this syndrome An ictal EEG is not required for diagnosis			
Syndrome without laboratory confirmation: In resource-limited regions, SeLNE can be diagnosed without EEG and MRI in a neonate with a family history suggestive of familial SeLNE who meets all other mandatory and exclusionary clinical criteria and has no Alerts. However, the clinical history of affected family members should be consistent with the expected course for SeLNE, and careful follow-up of the patient is required to ensure their course is also consistent with this syndrome			

Abbreviations: EEG, electroencephalogram; MRI, magnetic resonance imaging; SelNE, self-limited neonatal epilepsy.

Early Infantile Developmental &Epileptic Encephalopathy replaces the terms Ohtahara syndrome and Early Myoclonic Encephalopathy

TABLE 5 Diagnostic criteria for early infantile developmental and epileptic encephalopathy

	Mandatory	Alerts	Exclusionary
Seizures	Tonic and/or myoclonic seizures		
EEG	Interictal: Either burst suppression or multifocal discharges Diffuse slowing		
Age at onset	Birth to 3 months (adjusted for prematurity)		
Development at onset		Normal development at onset, although it is acknowledged that this can be challenging to accurately assess historically	
Neurological exam at onset		Normal neurological examination, although it is acknowledged that this can be challenging to assess historically or in an infant who has had very frequent seizures and/or received ASMs that may alter their exam	
Early Comorbidities	Developmental impairment is present prior to or shortly after seizure onset		
Course of illness	Abnormal neurodevelopment including intellectual disability		
Are MRI or ictal EEG required for diagnosis? An MRI is not required for diagnosis but is strongly recommended to exclude structural causes An ictal EEG is not required in an infant with characteristic clinical features where the interictal EEG shows burst-suppression, multi-focal discharges with diffuse slowing			
Syndrome without laboratory confirmation: In resource-limited regions, this syndrome cannot be diagnosed without an interictal EEG			

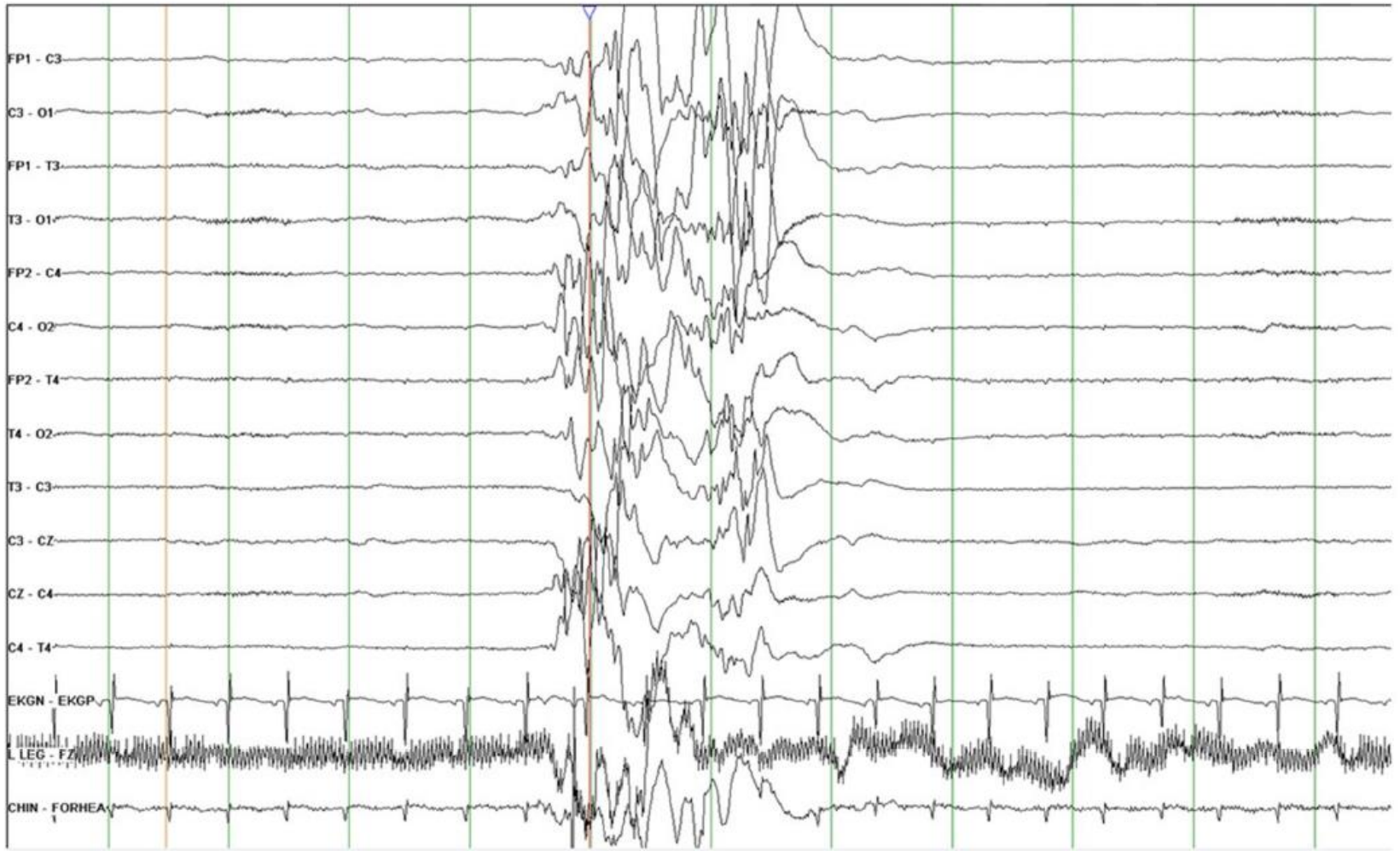

FIGURE 5 A 4-week-old boy with Early Infantile DEE. He presented on day 2 of life with sequential seizures with a prominent tonic component and severe encephalopathy. The EEG (20 microvolt/mm, 30 mm/s) shows a burst-suppression pattern. Genetic testing showed a *KCNQ2* pathogenic variant. The patient showed a marked reduction in seizures with carbamazepine but remained profoundly delayed

Dravet syndrome

TABLE 8 Diagnostic criteria for Dravet syndrome

	Mandatory	Alerts	Exclusionary
Seizures	Recurrent focal clonic (hemiclonic) febrile and afebrile seizures (which often alternate sides from seizure to seizure), focal to bilateral tonic-clonic, and/or generalized clonic seizures	No history of prolonged seizures (>10 min) Lack of fever sensitivity as a seizure trigger	Epileptic spasms Early infantile *SCN1A* DEE
EEG		Normal EEG background without interictal discharges after age 2 years	
Age at onset	1–20 months	1–2 months or 15–20 months	
Development at onset		Developmental delay at seizure onset	
Neurological exam		Focal neurological findings (other than Todd's paresis)	
Imaging			MRI showing a causal focal lesion
Other testing: ie, genetics, and so on		Lack of pathogenic *SCN1A* or other causal variant	
Course of illness	Drug-resistant epilepsy Intellectual disability	Good efficacy with prophylactic sodium-channel agents including carbamazepine, oxcarbazepine, and phenytoin	
Is MRI or ictal EEG required for diagnosis? An MRI is not required for diagnosis but is highly recommended to exclude other causes. An ictal EEG is not required for diagnosis			
Possible evolving syndrome: In a child <12 months who presents with a prolonged hemiclonic or bilateral tonic-clonic seizure with fever, and no other underlying cause, the possibility of Dravet syndrome should be considered. Further convulsive seizures (often with fever, and if prolonged or hemiclonic) would allow more definitive diagnosis of Dravet syndrome. A diagnosis would be further supported by the finding of a pathogenic *SCN1A* variant			
Syndrome without laboratory confirmation: In resource-limited regions, Dravet syndrome can be diagnosed in children without Alerts who meet all other clinical mandatory and exclusionary criteria, without EEG, MRI, and genetic testing			

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Epilepsia

FULL-LENGTH ORIGINAL RESEARCH

Defining Dravet syndrome: An essential pre-requisite for precision medicine trials

Wenhui Li[1,2] | Amy L. Schneider[2] | Ingrid E. Scheffer[2,3,4]

Syndrome papers provide overviews. Review the literature for finer details of each syndrome

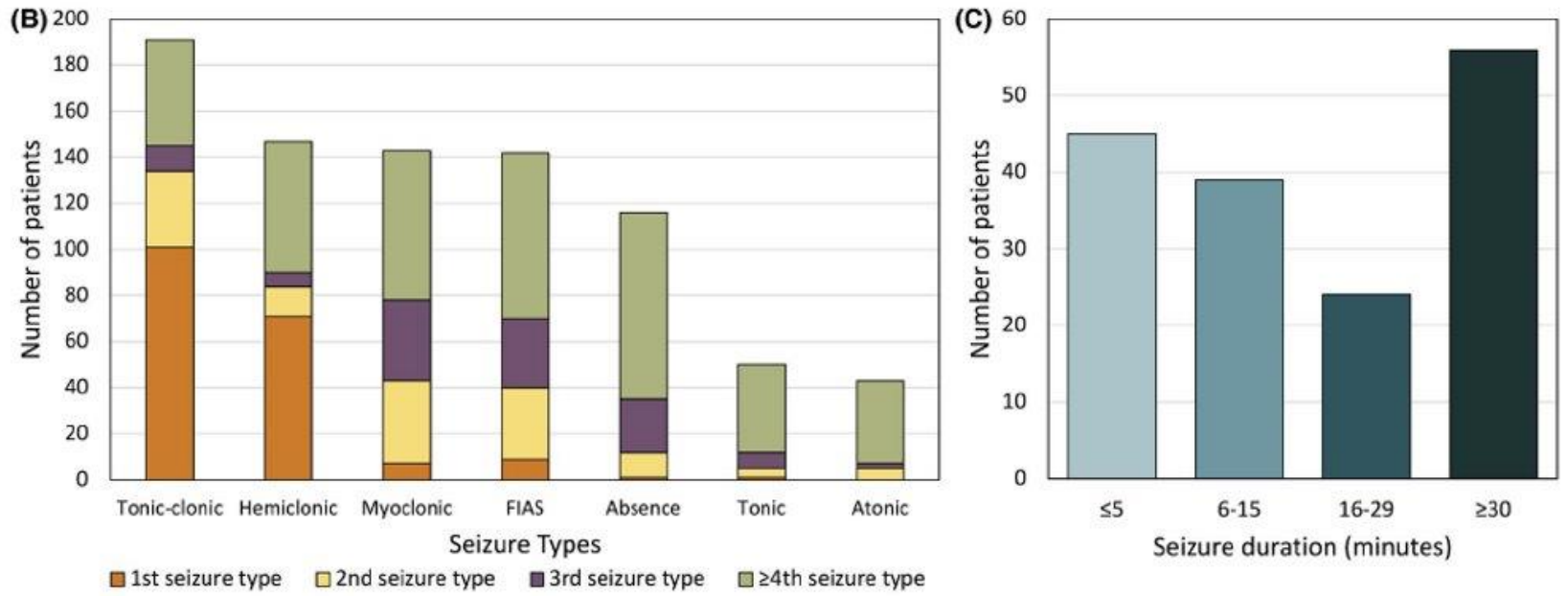


FIGURE 1 (A) Age at seizure onset in our cohort of 205 patients with *SCN1A*-Dravet syndrome together with published patients with onset after 12 months or with pathogenic mosaic *SCN1A* variants. (B) First, second, third, and fourth or more seizure type to develop in patients. (C) Duration of first seizure in 164 patients with *SCN1A*-Dravet syndrome

Infantile epileptic spasms syndrome

TABLE 7 Diagnostic criteria for infantile epileptic spasms syndrome

	Mandatory	Alerts	Exclusionary
Seizures	Flexor, extensor or mixed epileptic spasms which often occur in clusters		
EEG	Interictal: Hypsarrhythmia, multifocal or focal epileptiform discharges (that might be seen quickly after the spasms onset)	Interictal: Normal EEG Suppression-burst pattern	Ictal: Normal EEG during recorded clinical events of suspected spasms
Age at onset	1–24 months (while epileptic spasms may begin later, this would not be ISS)	Age at onset 1–2 months	
Comorbidities	Developmental slowing after spasms onset but may be absent early in the course (difficult to determine in a child with existing significant developmental disorders)		

Is MRI or ictal EEG required for diagnosis?

An MRI is not required for diagnosis but is highly recommended to evaluate for underlying cause.

An ictal EEG is not required for diagnosis provided the interictal study shows hypsarrhythmia or epileptiform abnormalities or developmental delay. In the absence of hypsarrhythmia or epileptiform anomalies, an ictal recording is required

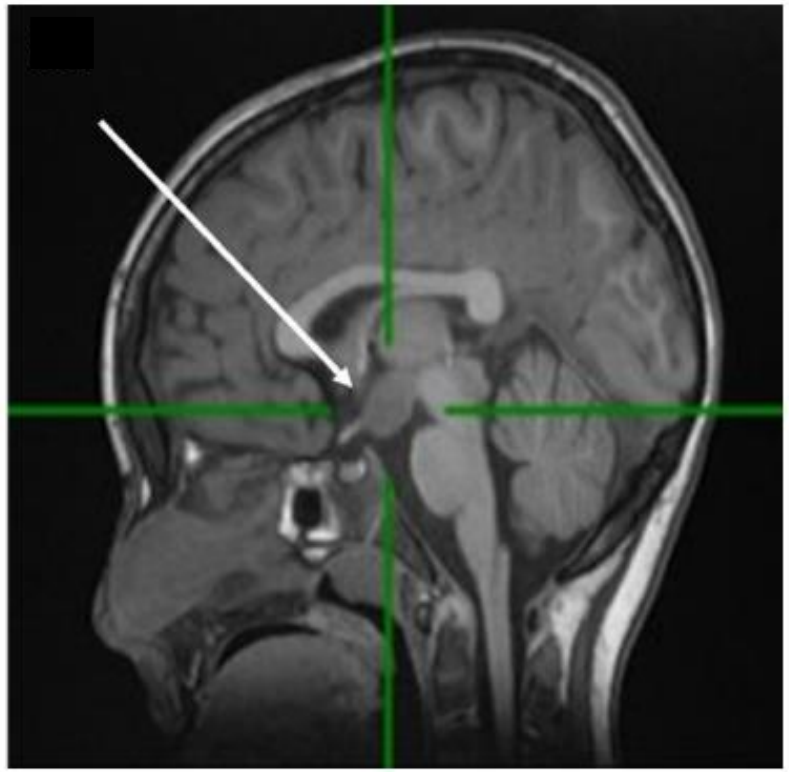
Possible evolving syndrome: Infants with preceding brain injury, developmental brain malformations, or specific genetic conditions, including early-infantile DEE, who show significant interictal EEG abnormalities (high amplitude, background slowing, and/or multifocal discharges) should be watched carefully for the development of clinical epileptic spasms. However, the syndrome of ISS cannot be diagnosed prior to onset of the mandatory seizure type

Syndrome without laboratory confirmation: In resource-limited regions, an interictal EEG is highly recommended. However, if EEG is unavailable, if clear clusters of typical epileptic spasms are witnessed by an experienced clinician (in person or on video recording), with the other clinical mandatory and exclusionary criteria, ISS can be diagnosed

Etiology specific syndrome - Gelastic seizures with hypothalamic hamartoma

TABLE 15 Diagnostic criteria for gelastic seizures with hypothalamic hamartoma

	Mandatory	Alerts	Exclusionary
Seizures	Gelastic seizures with mechanical, mirthless laughter, inappropriate to context	Seizure frequency less than daily	
EEG		Interictal: Generalized or focal background slowing (excluding immediate postictal period) Ictal: Gelastic seizures may lack ictal EEG correlate	
Age at onset		Onset >5 years of age	
Development at onset		Clear developmental delay at seizure onset	
Neurological exam		Focal neurological findings (other than Todd's paresis) or generalized hypotonia	
Imaging	Hypothalamic hamartoma (may require thin slices through the hypothalamic region to confirm)		
Course of illness	Drug-resistant epilepsy	Lack of behavioral problems including aggression, impulsivity, and hyperactivity	
Is MRI or ictal EEG required for diagnosis? An MRI is required for diagnosis An ictal EEG is not required for diagnosis. Furthermore, gelastic seizures may lack ictal correlate on EEG			
Syndrome without laboratory confirmation: In resource-limited regions, HH-GS cannot be diagnosed in the absence of an MRI, as gelastic seizures may arise from other brain regions			



Precision medicine drives classification in the epilepsies

"A treatment approach in which disease treatment and prevention is tailored to individual variability in genes, environment and lifestyle for each person"

Medical therapy, surgical treatment, metabolic therapy, gene related therapy

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Epilepsy Syndromes with Onset in Childhood

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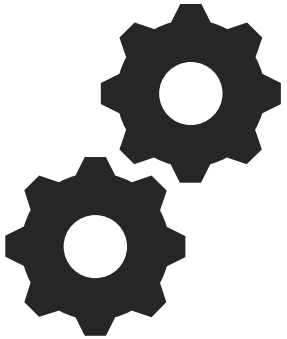
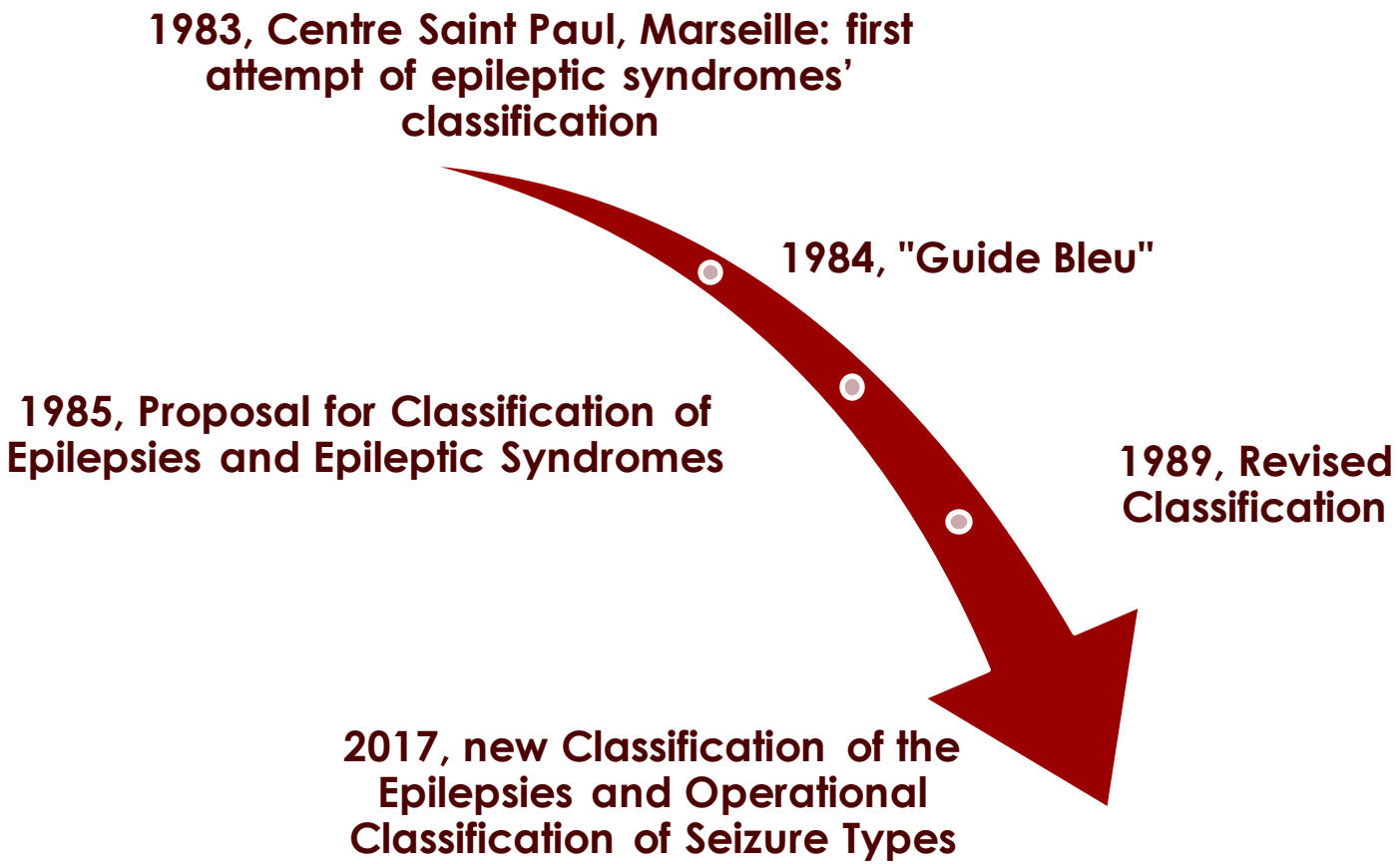
Outline

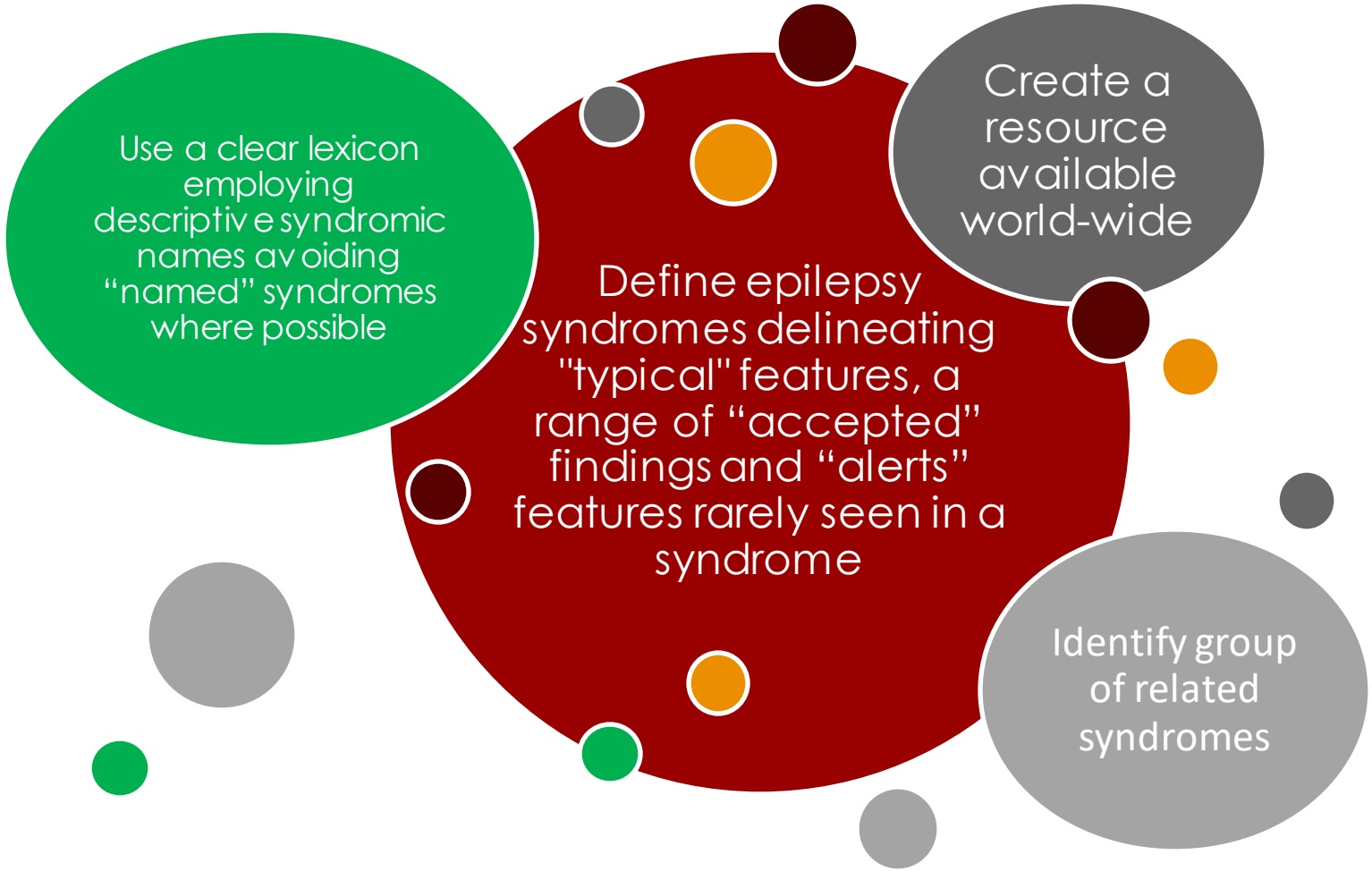
- Historical overview
- Purposes of the ILAE Task Force for Nosology
- Process of defining syndromes
- Definition and Classification of syndromes
- Core criteria and related Delphi process
- Further definitions
- Conclusions



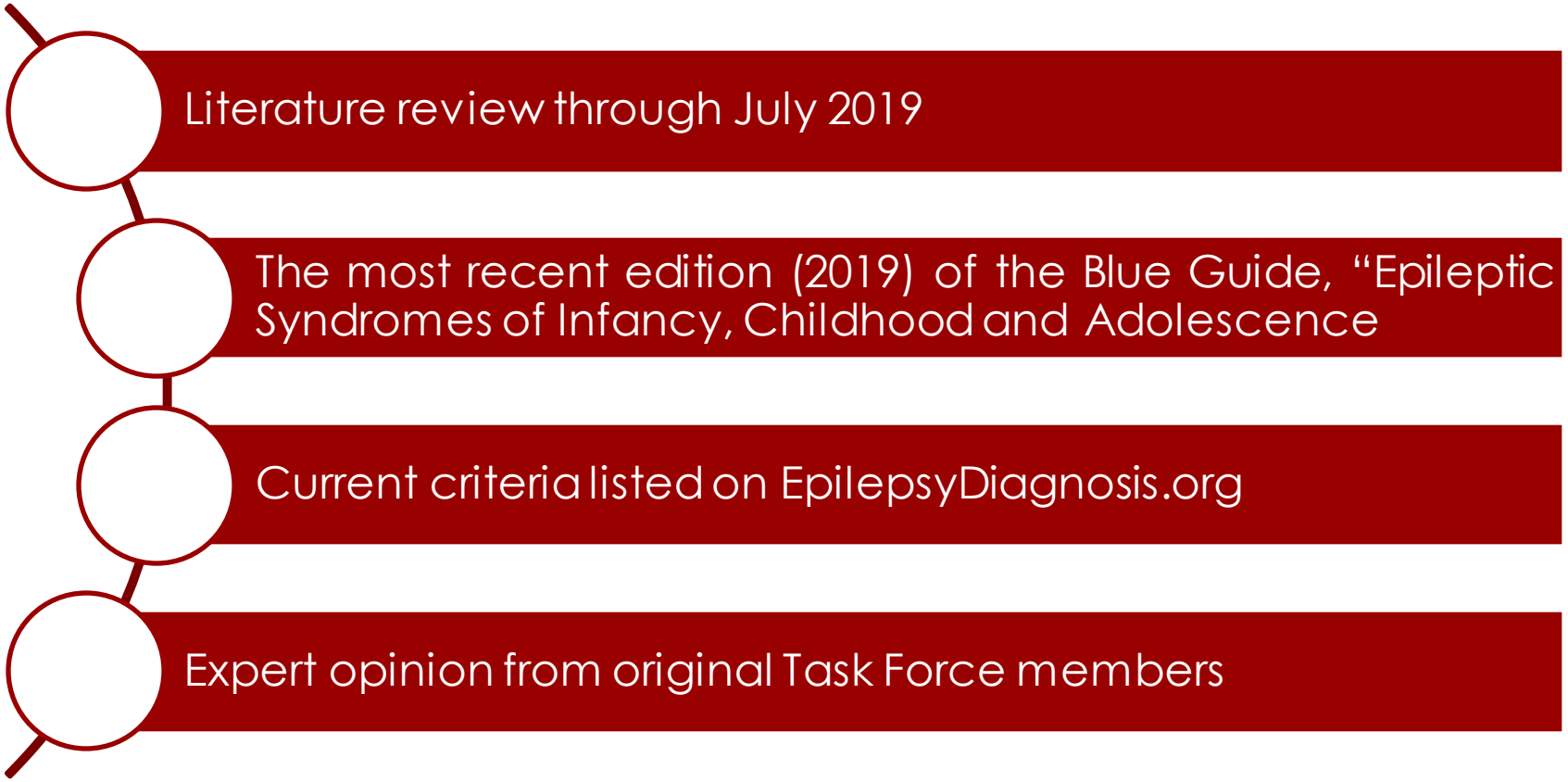
Historical overview



Purposes of the ILAE Task Force on Nosology



Process of defining syndromes



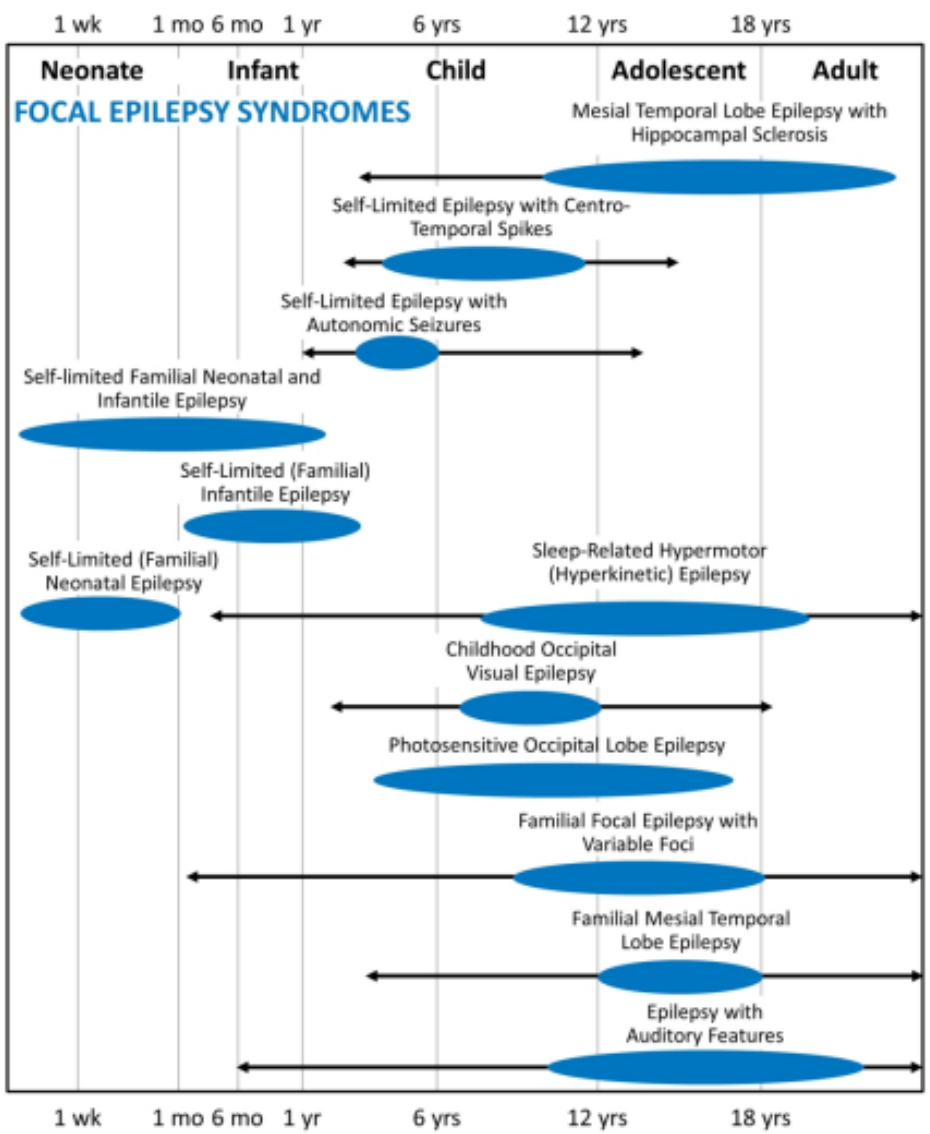
Definition and Classification

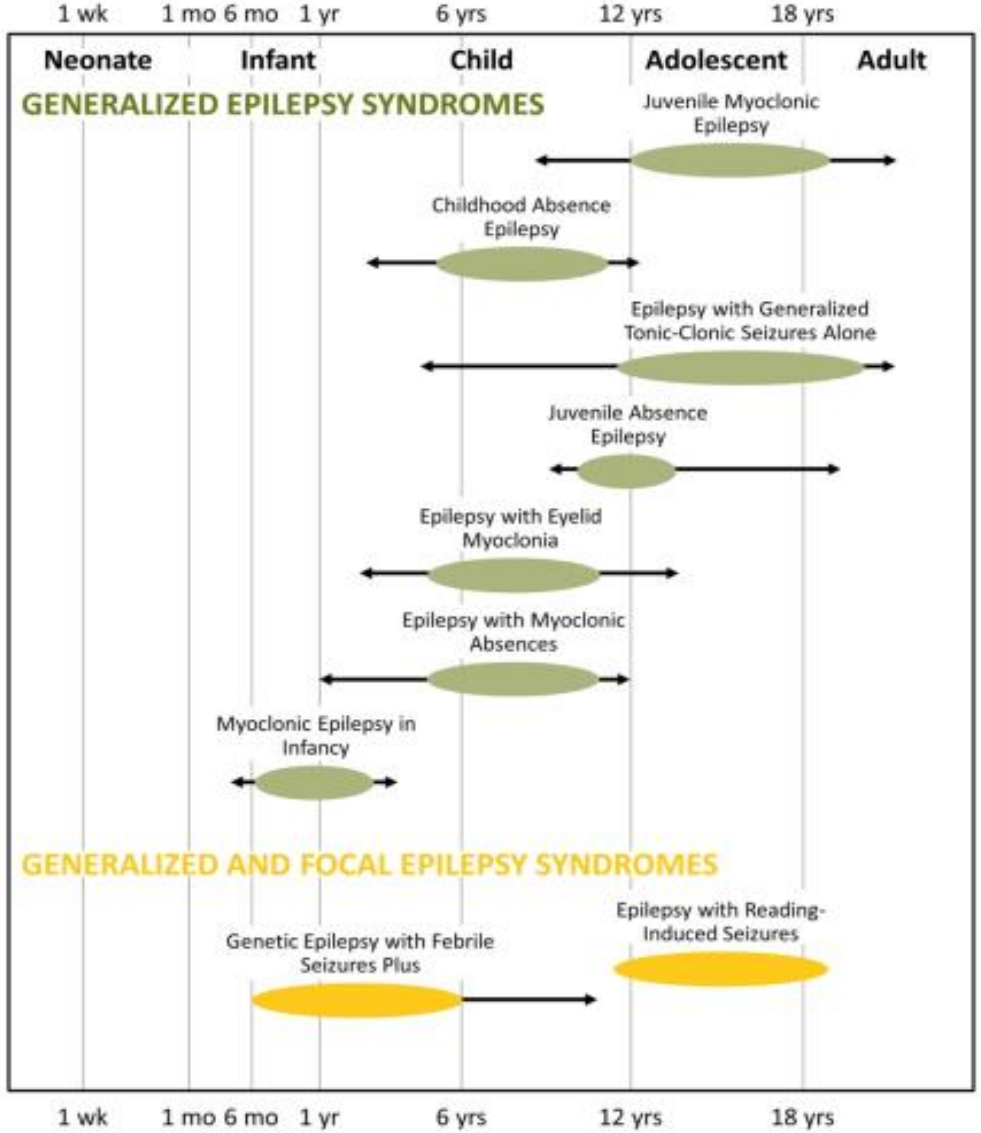
Epileptic syndrome: a characteristic cluster of clinical and EEG features, often supported by specific etiological findings (structural, genetic, metabolic, immune and infectious).

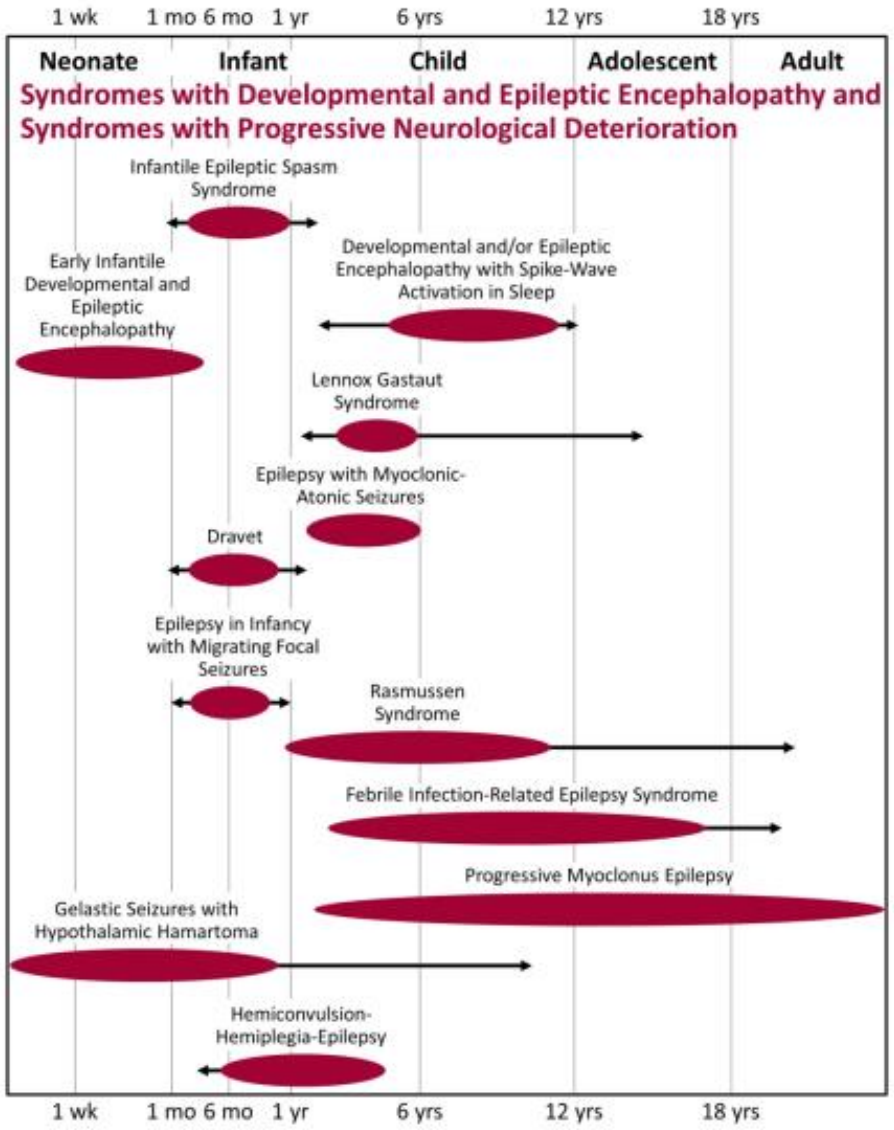
Syndromes are divided based on age at onset and on syndrome type (generalized epilepsy syndromes, focal epilepsy syndromes, focal and generalized epilepsy syndromes and syndromes associated with Developmental and/or Epileptic Encephalopathy (DEE) or Progressive Neurological Deterioration).

4 groups:

1. Neonatal and Infantile onset (for the purpose of the proposed classification infancy was defined as the period up to age 24 months
2. Childhood onset
3. Variable age at onset
4. Idiopathic Generalized Epilepsies.

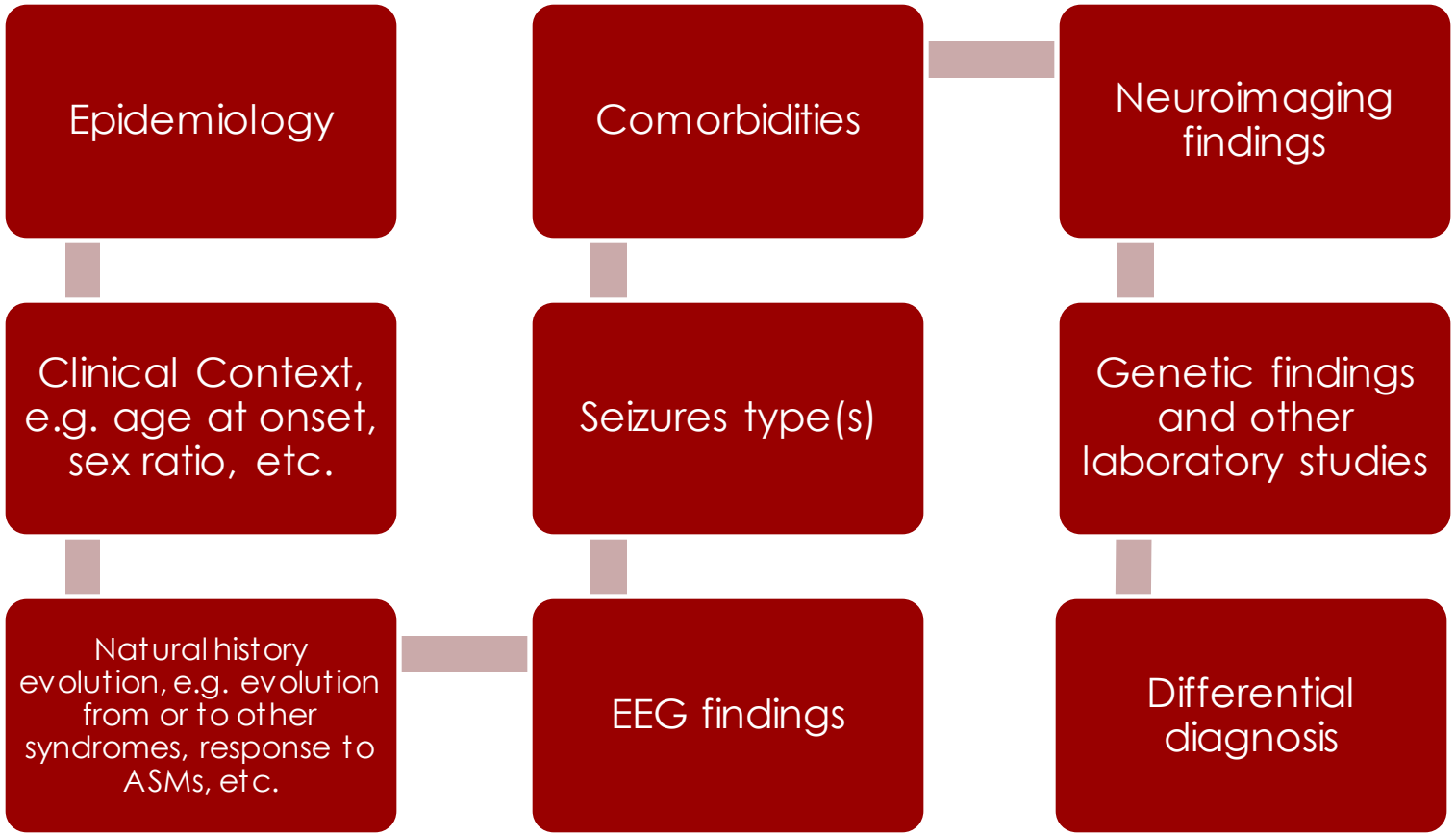

1 wk
1 mo 6 mo
1 yr
6 yrs
12 yrs
18 yrs
Neonate
Infant
Child
Adolescent
Adult
FOCAL EPILEPSY SYNDROMES
Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis
Self-Limited Epilepsy with Centro-Temporal Spikes
Self-Limited Epilepsy with Autonomic Seizures
Self-limited Familial Neonatal and Infantile Epilepsy
Self-Limited (Familial) Infantile Epilepsy
Self-Limited (Familial) Neonatal Epilepsy
Sleep-Related Hypermotor (Hyperkinetic) Epilepsy
Childhood Occipital Visual Epilepsy
Photosensitive Occipital Lobe Epilepsy
Familial Focal Epilepsy with Variable Foci
Familial Mesial Temporal Lobe Epilepsy
Epilepsy with Auditory Features


1 wk
1 mo 6 mo
1 yr
6 yrs
12 yrs
18 yrs
Neonate
Infant
Child
Adolescent
Adult
GENERALIZED EPILEPSY SYNDROMES
Juvenile Myoclonic Epilepsy
Childhood Absence Epilepsy
Epilepsy with Generalized Tonic-Clonic Seizures Alone
Juvenile Absence Epilepsy
Epilepsy with Eyelid Myoclonia
Epilepsy with Myoclonic Absences
Myoclonic Epilepsy in Infancy
GENERALIZED AND FOCAL EPILEPSY SYNDROMES
Epilepsy with Reading-Induced Seizures
Genetic Epilepsy with Febrile Seizures Plus



- DEE: an epilepsy associated with developmental impairment due to either the underlying etiology, the superimposed epileptic activity or both.
- The term DEE is more challenging to apply when epilepsy begins later in life, following a normal development, e.g. in Rasmussen Syndrome.
- Thus, the concepts of Epilepsy Syndromes with DEE and Epilepsy Syndromes with Progressive Neurological Deterioration to encompass the group of syndromes associated with cognitive impairment with or without other neurological deterioration and recognize that this impairment may be due to the underlying etiology, superimposed epileptic activity, or both.

Template for clinical data for syndromes



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SPECIAL REPORT

International League Against Epilepsy classification and definition of epilepsy syndromes with onset in childhood: Position paper by the ILAE Task Force on Nosology and Definitions

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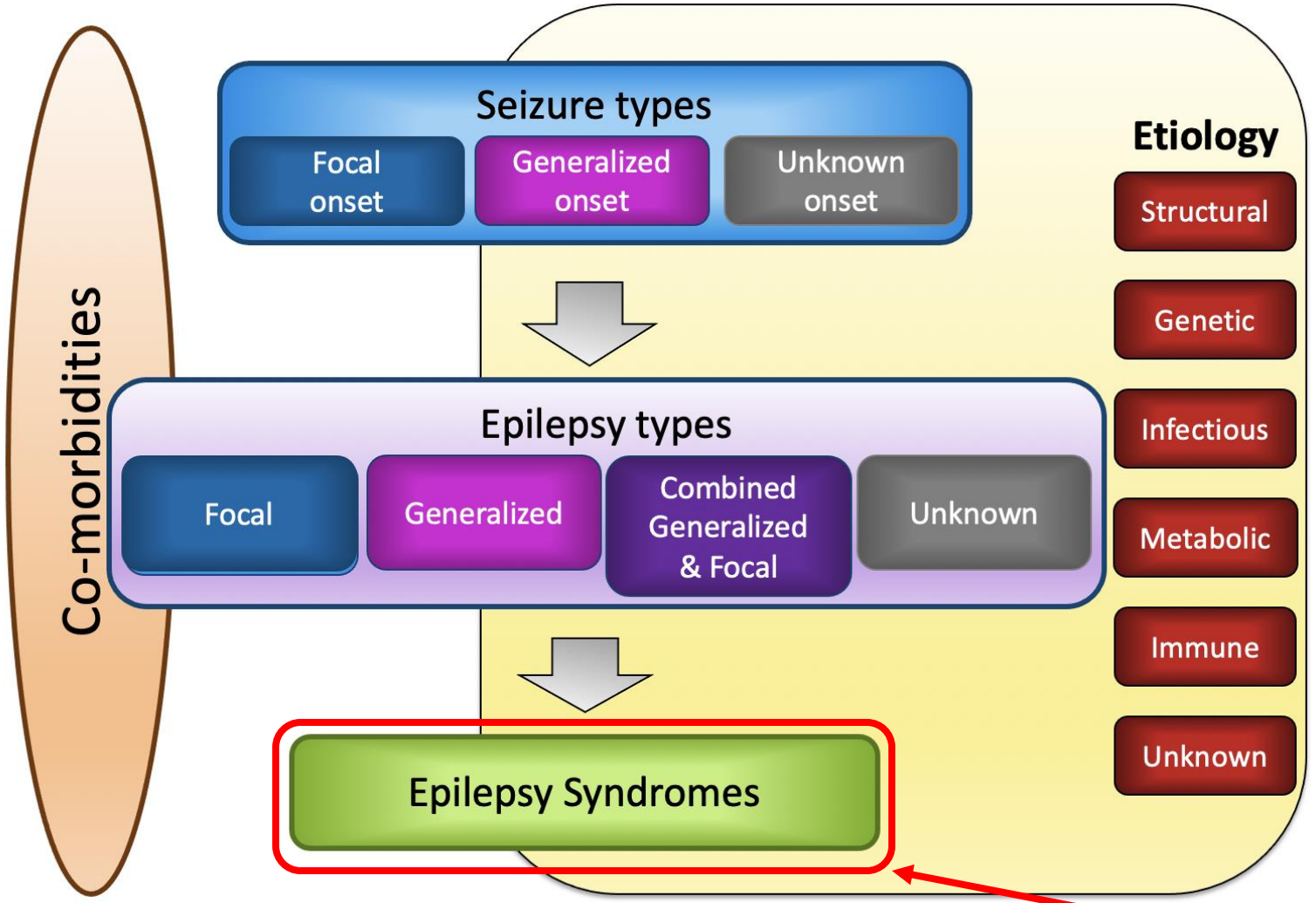

ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology

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- Not for all patients
- Syndrome diagnosis

→ management

→ prognosis

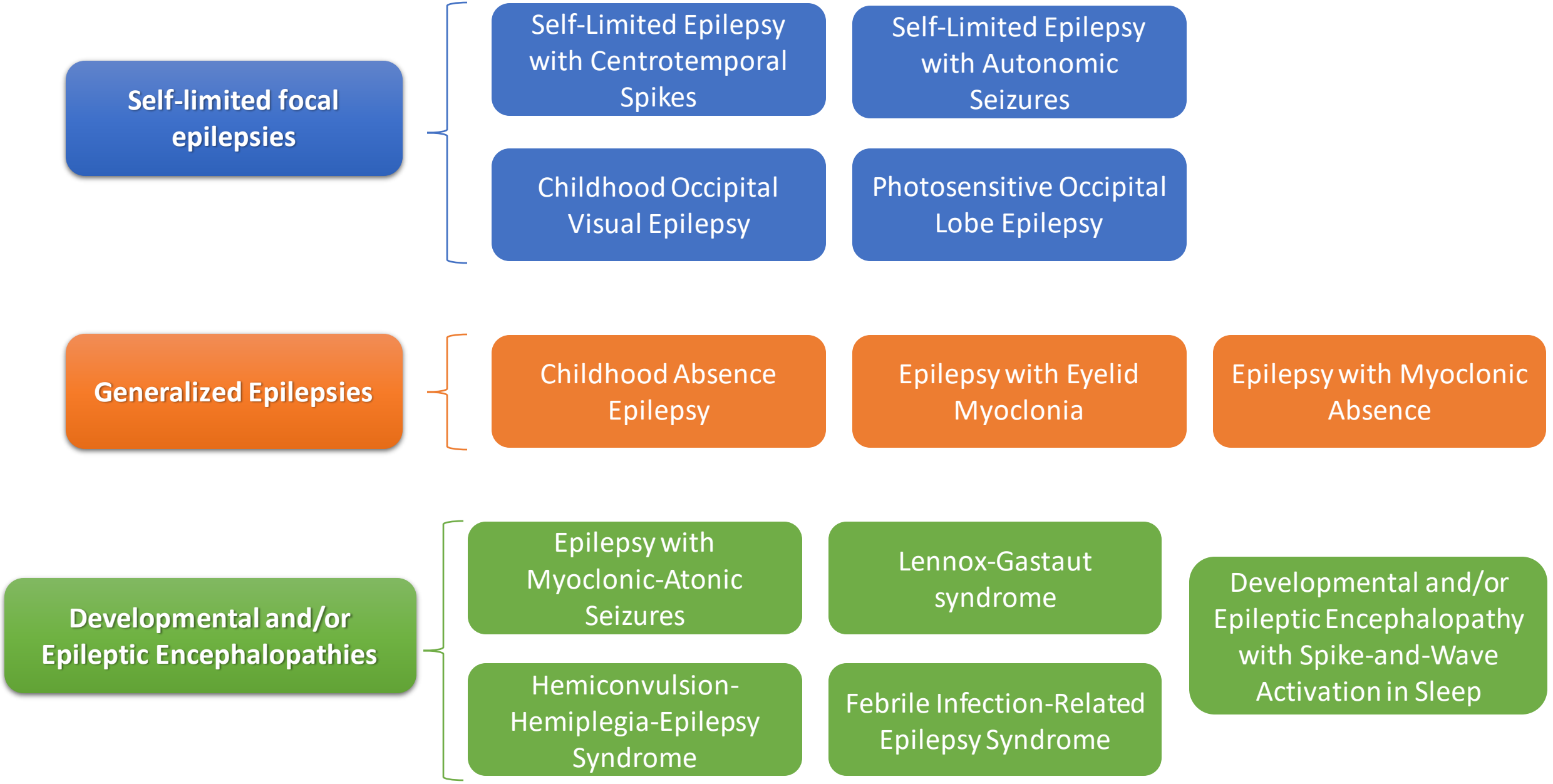
What's new?

New names for Epilepsy Syndromes with Onset in Childhood and new classification

Self-limited focal epilepsies

Generalized Epilepsies

Developmental and/or Epileptic Encephalopathies


Self-limited focal epilepsies
Self-Limited Epilepsy with Centrotemporal Spikes
Self-Limited Epilepsy with Autonomic Seizures
Childhood Occipital Visual Epilepsy
Photosensitive Occipital Lobe Epilepsy
Generalized Epilepsies
Childhood Absence Epilepsy
Epilepsy with Eyelid Myoclonia
Epilepsy with Myoclonic Absence
Developmental and/or Epileptic Encephalopathies
Epilepsy with Myoclonic-Atonic Seizures
Lennox-Gastaut syndrome
Developmental and/or Epileptic Encephalopathy with Spike-and-Wave Activation in Sleep
Hemiconvulsion-Hemiplegia-Epilepsy Syndrome
Febrile Infection-Related Epilepsy Syndrome

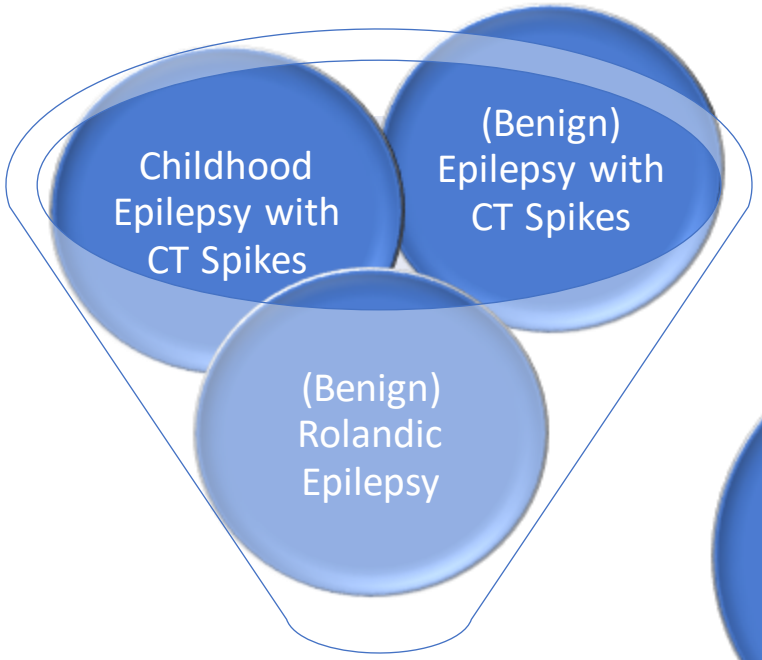
Updated 2022 ILAE guidance

- Epidemiology
- Clinical: age at onset, history, neurological exam
- Natural history: drug responsiveness, likelihood of remission, comorbidities, evolution
- Seizure type(s)
- EEG features: typical findings, if ictal EEG is needed
- Neuroimaging
- Genetics
- Other lab findings, if relevant
- Differential diagnosis

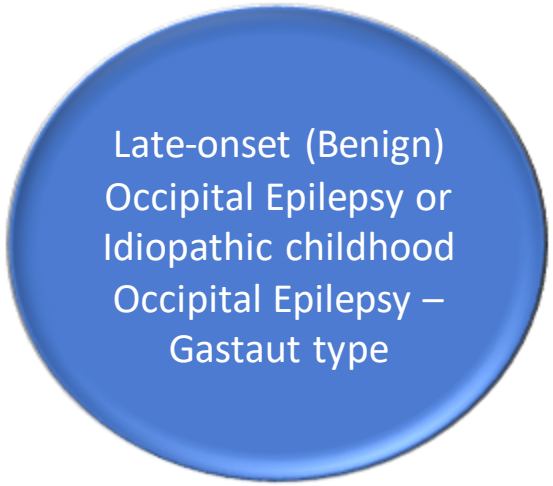
EEG, electroencephalography; ILAE, International League Against Epilepsy; LGS, Lennox-Gastaut syndrome

Wirrell EC, et al. Methodology for classification and definition of epilepsy syndromes: report of the ILAE task force on nosology and definitions. 2022. Available from: https://www.ilae.org/files/dmfile/Syndrome-MethodologyFINALMARCH29.pdf (Accessed 20 April 2022)

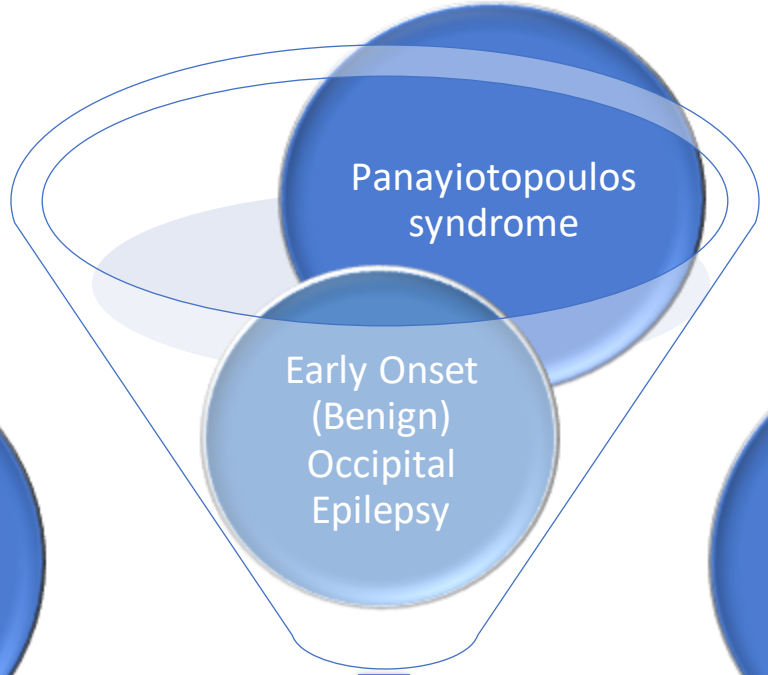
Self-limited focal epilepsies



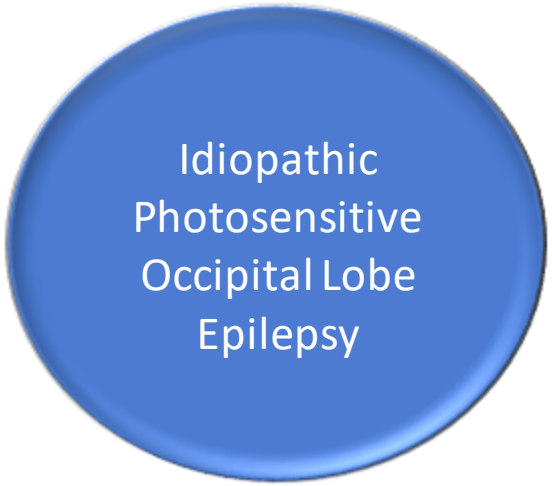
Self-Limited Epilepsy with Centrotemporal Spikes



Childhood Occipital Visual Epilepsy

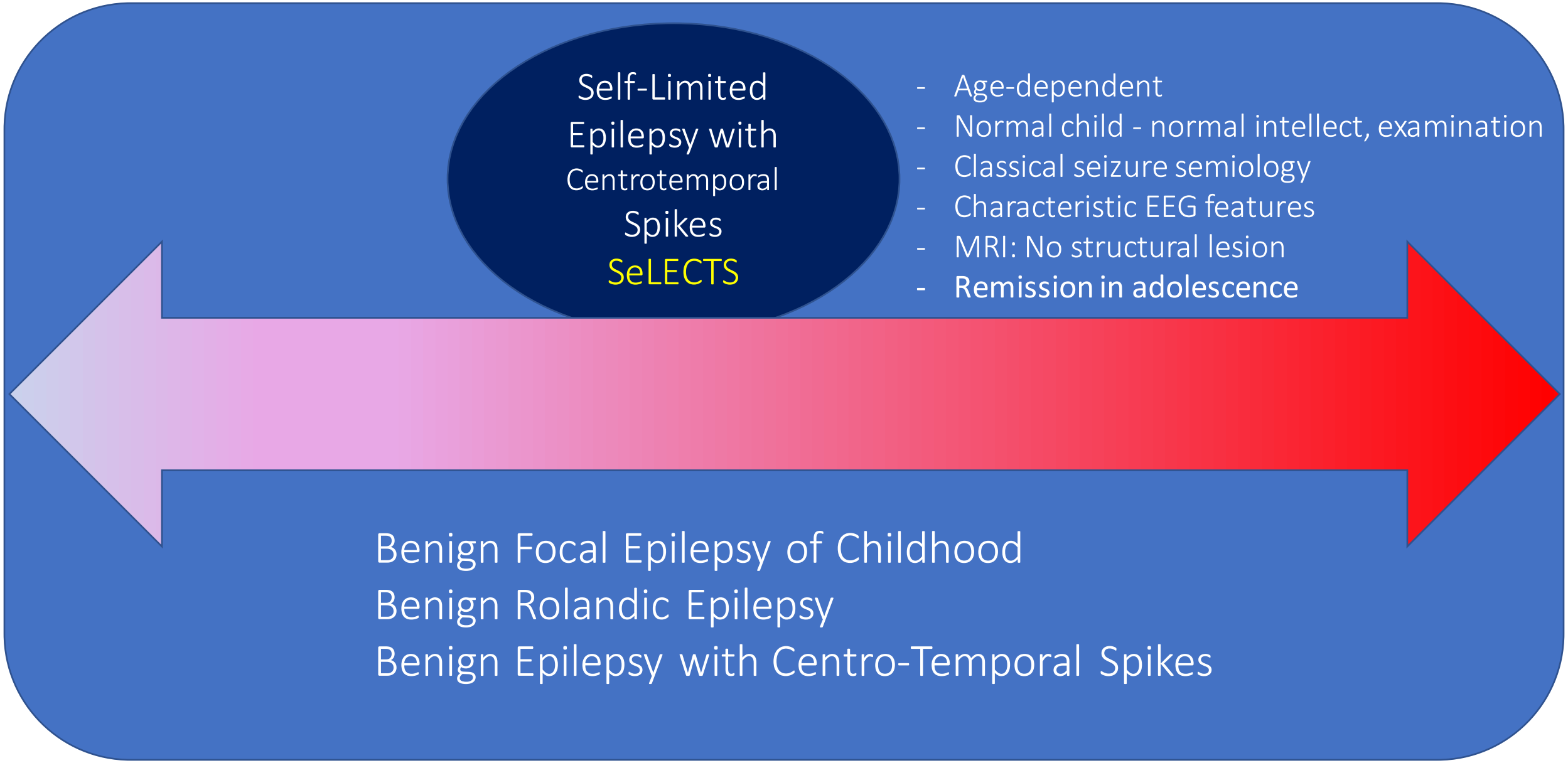


Self-Limited Epilepsy with Autonomic Seizures

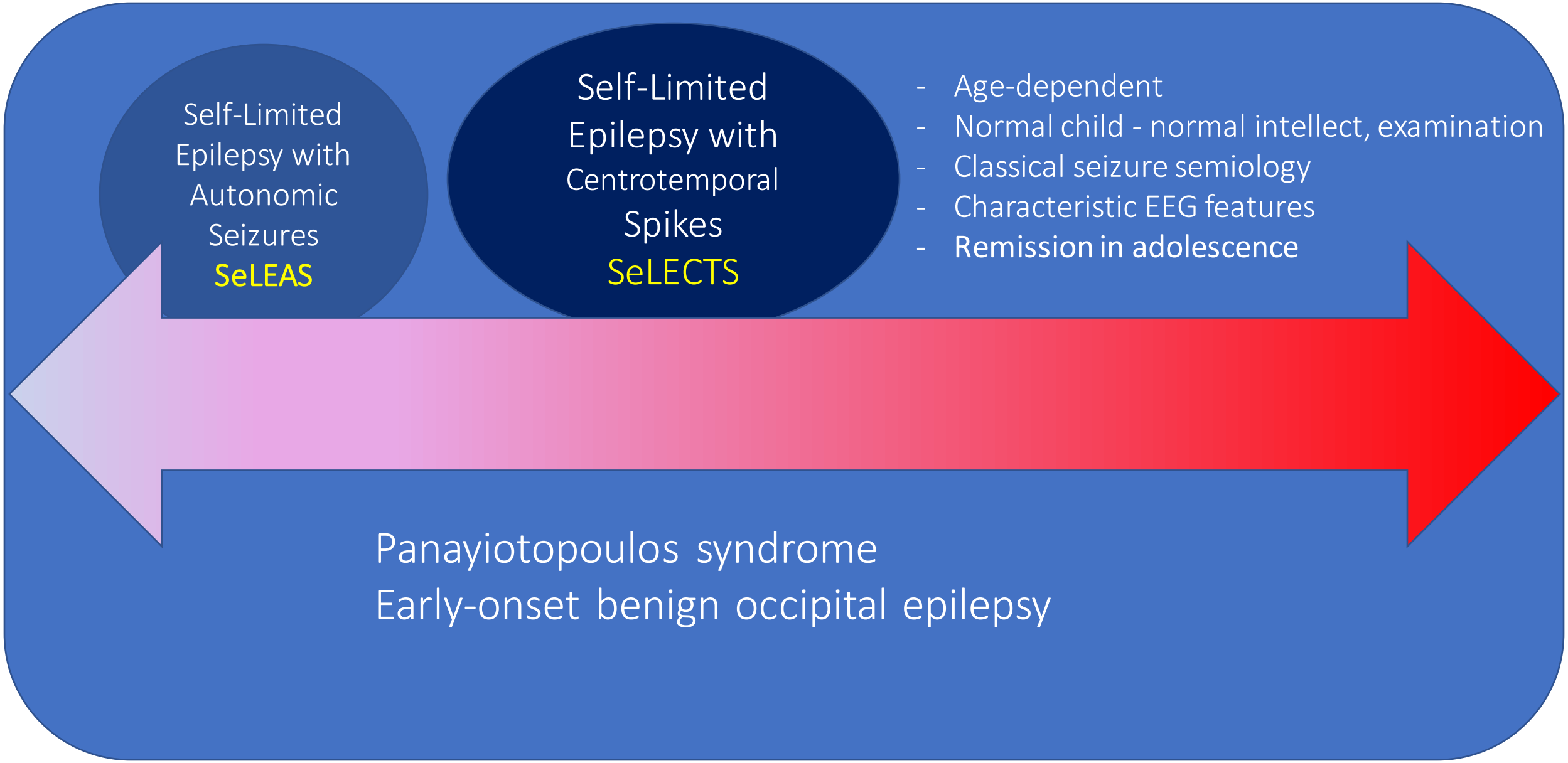


Photosensitive Occipital Lobe Epilepsy

Self-Limited Focal Epilepsies (SeLFE) of Childhood



Self-Limited Focal Epilepsies (SeLFE) of Childhood



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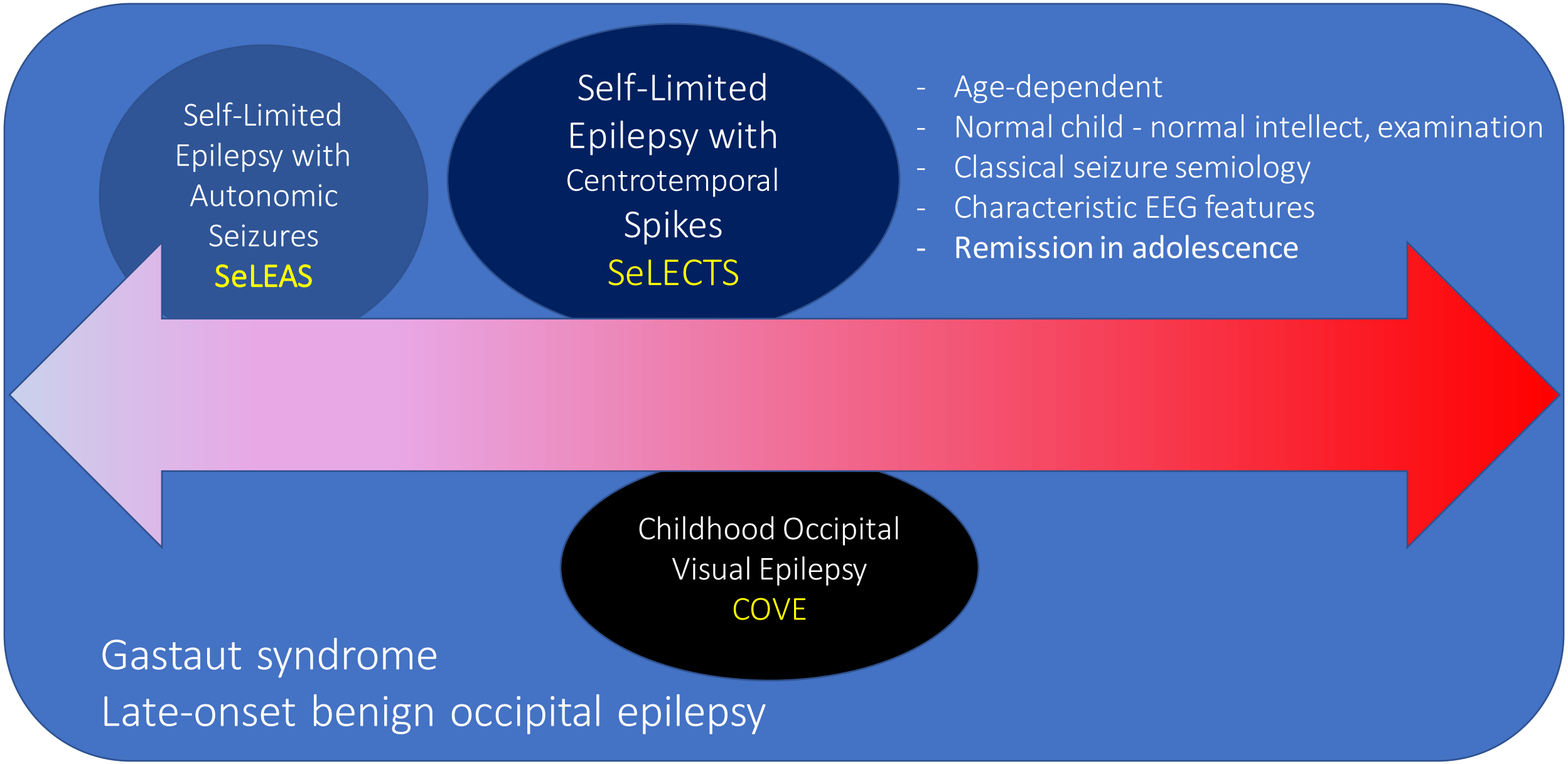

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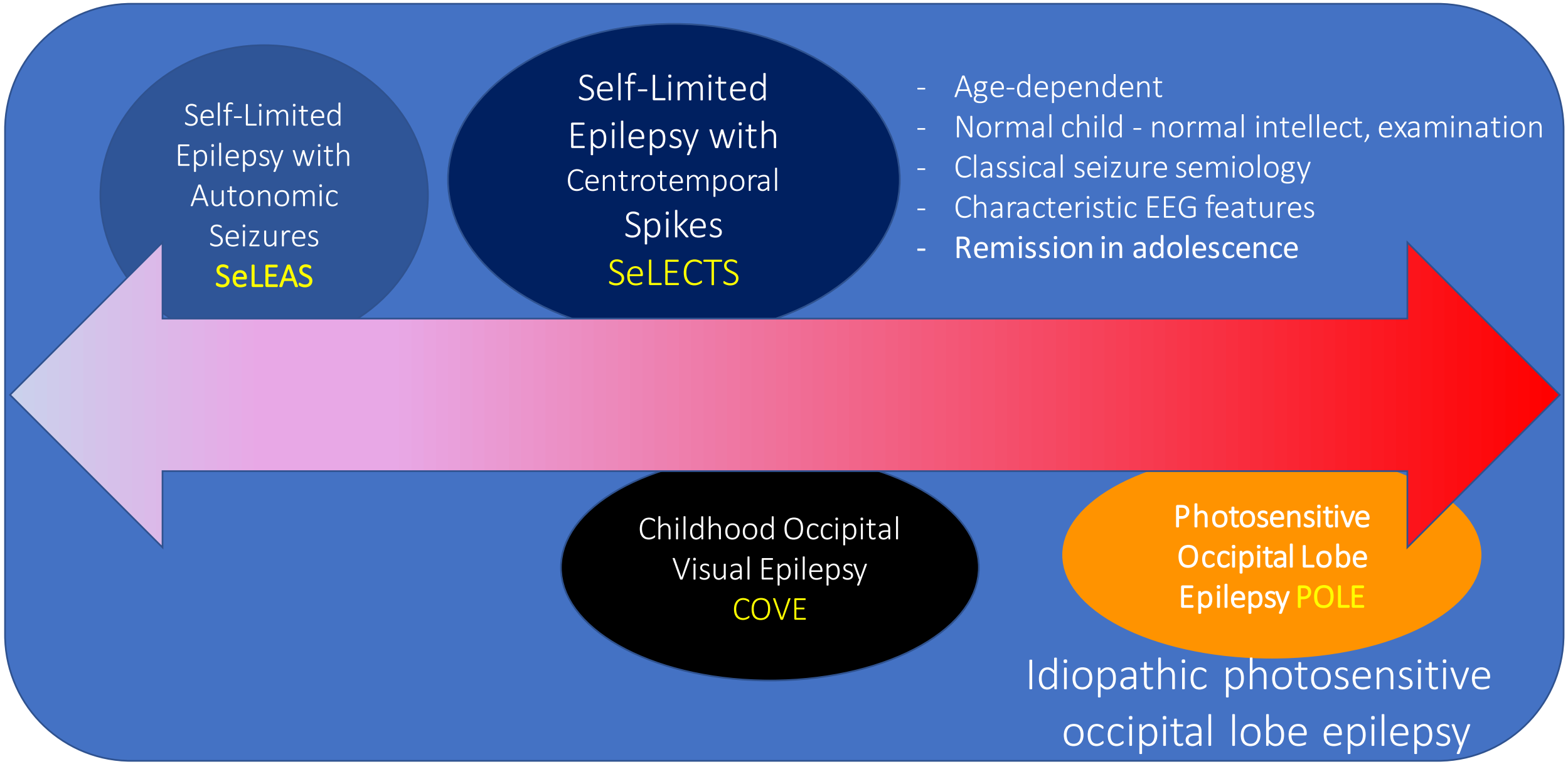
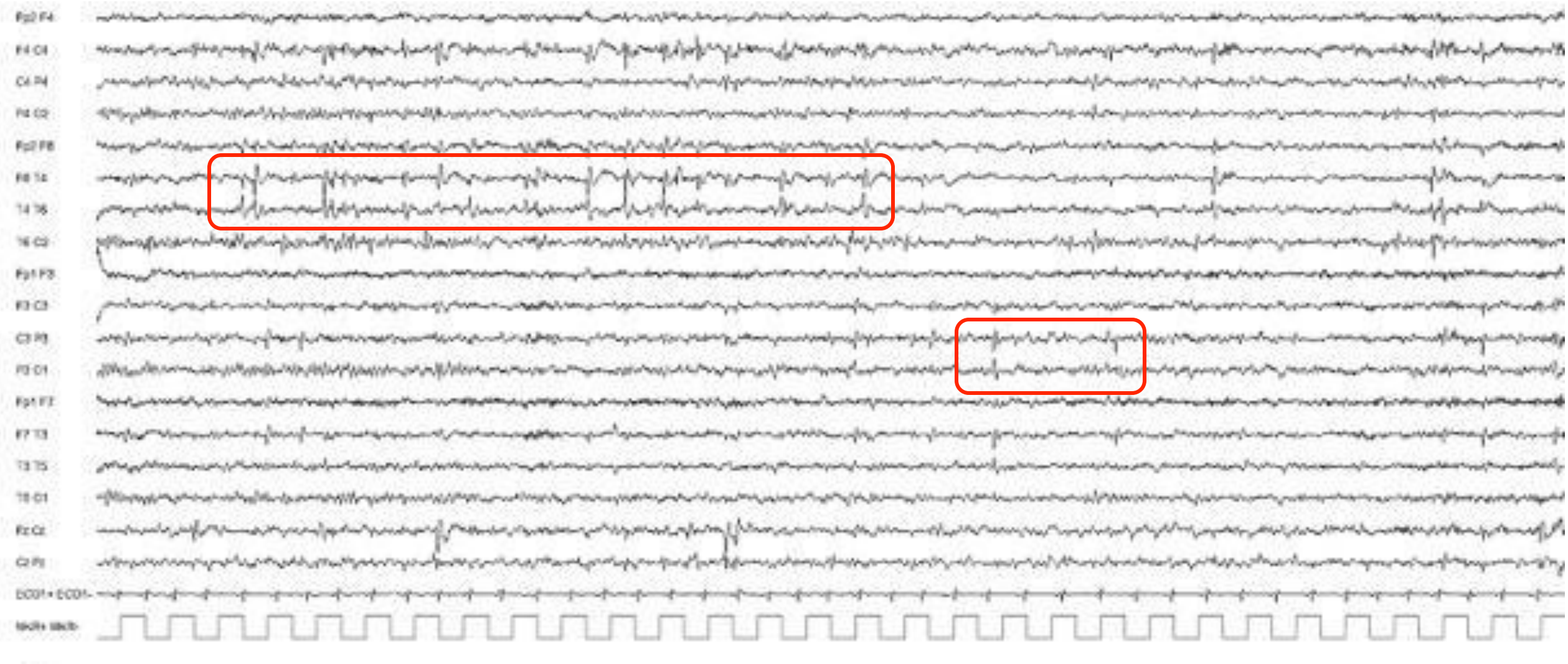


Self-Limited Focal Epilepsies (SeLFE) of Childhood

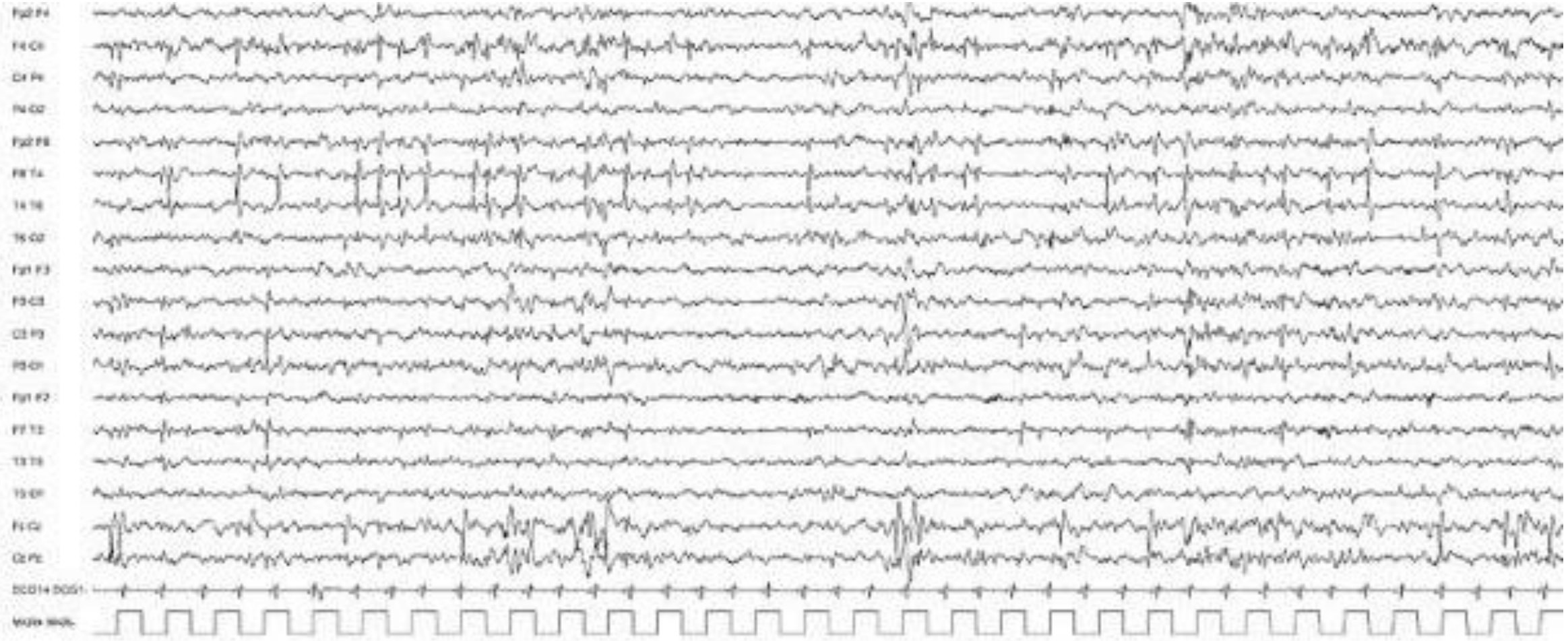
Self-Limited Epilepsy with Centrotemporal Spikes
SeLECTS

- Onset median 7 yrs (range 4-10 yrs)
- Aura: Buccal paraesthesia
- Hemifacial tonic or clonic features
- Drooling, speech arrest – dysarthria, dysphasia
- Focal to bilateral tonic-clonic (FBTC)
- Within 1-2 hrs of falling asleep or prior to awakening
- Remit mid to late adolescence

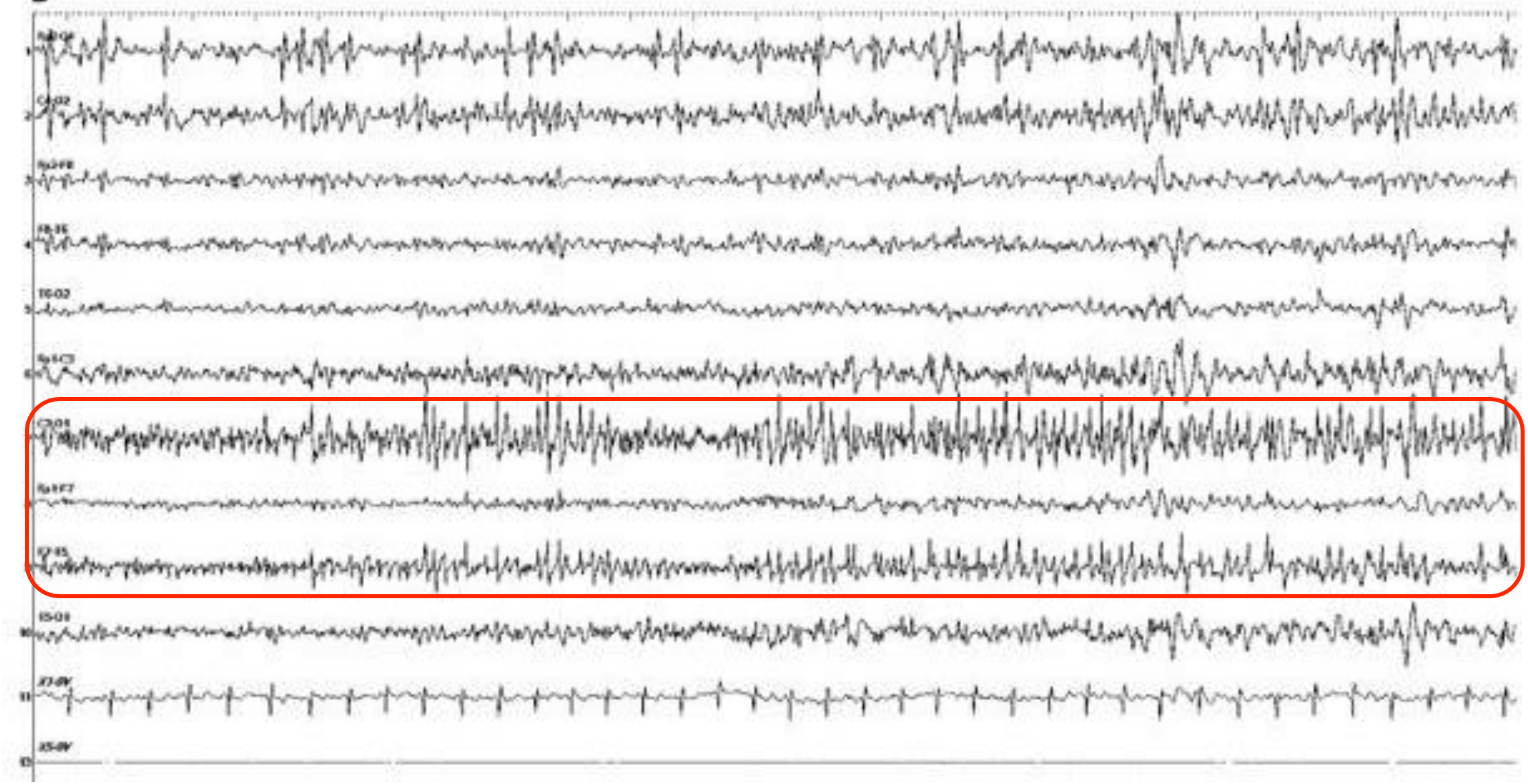


9 yr boy with SeLECTS

Awake EEG: high amplitude right centrotemporal discharges



9 yr boy with SeLECTS
Asleep EEG: increased and higher amplitude discharges



9 yr boy with SeLECTS

Ictal rhythm: L centrotemporal rhythmic spikes ↑ amplitude, ↓frequency

Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS)

Mandatory

- **Seizures**: Focal seizures with dysarthria, sialorrhea, dysphasia
- **EEG**: High amplitude, centrotemporal biphasic epileptiform abnormalities
- **Course of illness**: Remission by mid to late adolescence. No developmental regression

Alerts

- **Seizures**: Focal motor or generalized convulsive status epilepticus >30 min.
- **EEG**: Sustained focal slowing not limited to the postictal phase. Lack of sleep activation of centrotemporal abnormalities
- **Age at onset**: >12 years at onset
- **Development at onset**: Moderate to profound intellectual disability
- **Neurological exam**: Hemiparesis or focal neurological findings, other than Todds paresis

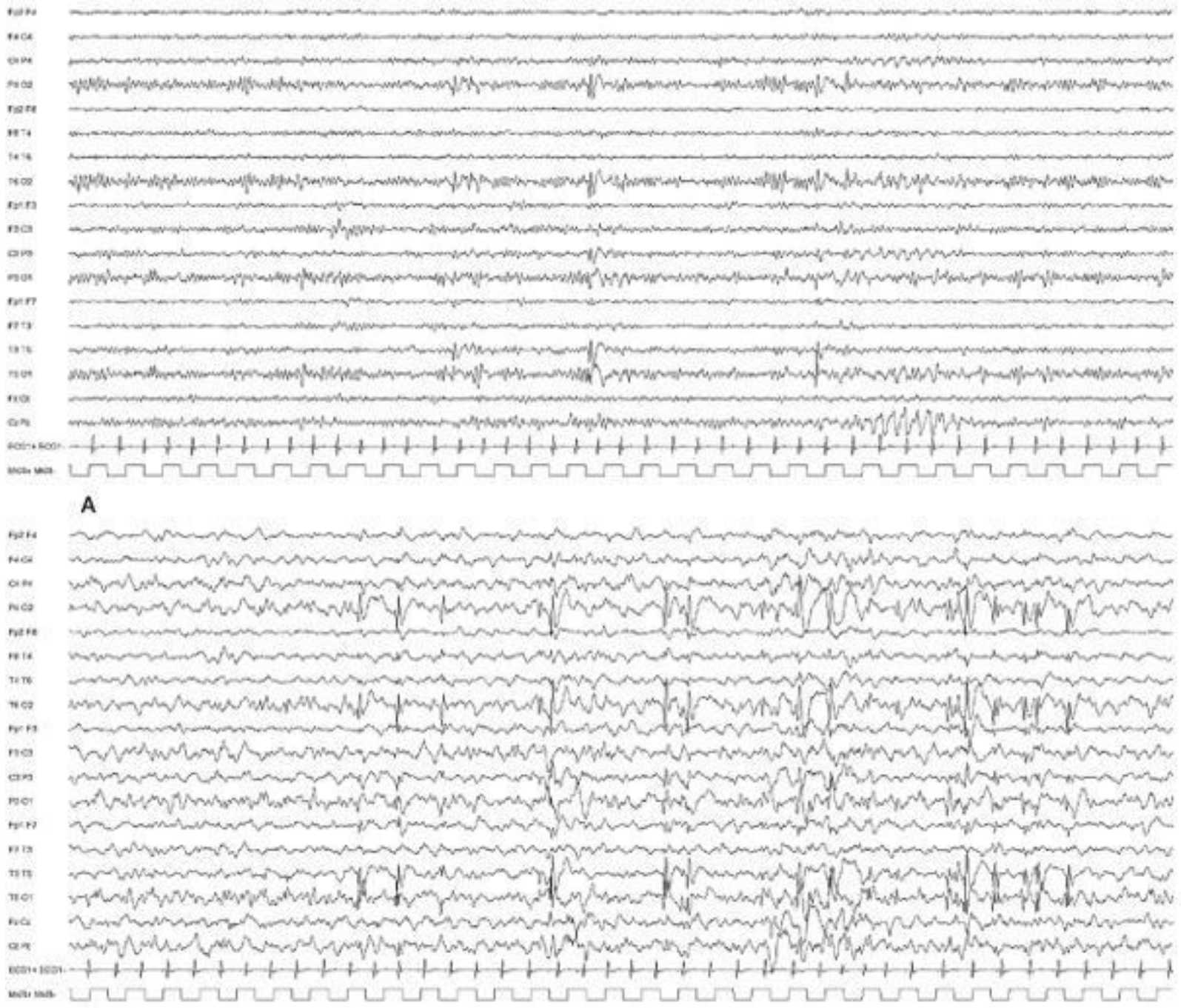
Exclusionary

- **Seizures**: Generalized tonic-clonic seizures during wakefulness.
- **Age at onset**: <3 years of >14 years at onset
- **Development at onset**: Neurocognitive regression with a continuous spike-and-wave pattern in sleep (suggests EE-SWAS)
- **Imaging**: Causal lesion on brain MRI
- **Course of illness**: Neurocognitive regression with a continuous spike-and-wave pattern in sleep suggests evolution to EE-SWAS

Self-Limited Focal Epilepsies (SeLFE) of Childhood

Self-Limited Epilepsy with Autonomic Seizures **SeLEAS**

- Onset 3-6 y (range 1– 14 y)
- Focal autonomic seizures
  - Prominent vomiting and retching
  - Malaise
  - Pallor or flushing
  - Abdominal pain
  - Cardiorespiratory changes
  - Head and eye deviation
- Remits early – mid adolescence



SeLEAS

Awake: Rare posterior quadrant spikes

Asleep: Increase in frequency and amplitude of bilateral posterior discharges

Self-Limited Epilepsy with Autonomic Seizures (SeLEAS)

Mandatory

- **Seizures**: Focal autonomic seizures, with or without impaired awareness. Autonomic symptoms often involve prominent retching and vomiting, but may also include malaise, pallor, flushing, abdominal pain, pupillary or cardiorespiratory changes
- **EEG**: High amplitude, focal or multifocal epileptiform abnormalities which increase in drowsiness and sleep
- **Course of illness**: Remission by early to mid-adolescence. No developmental regression

Alerts

- **Seizures**: Seizure frequency greater than monthly
- **EEG**: Sustained focal slowing not limited to the postictal phase. Unilateral focal abnormalities in a consistent focal area across serial EEGs
- **Age at onset**: <3 years or >8 years at onset
- **Development at onset**: Moderate to profound intellectual disability
- **Neurological exam**: Hemiparesis or focal neurological findings, other than Todds paresis

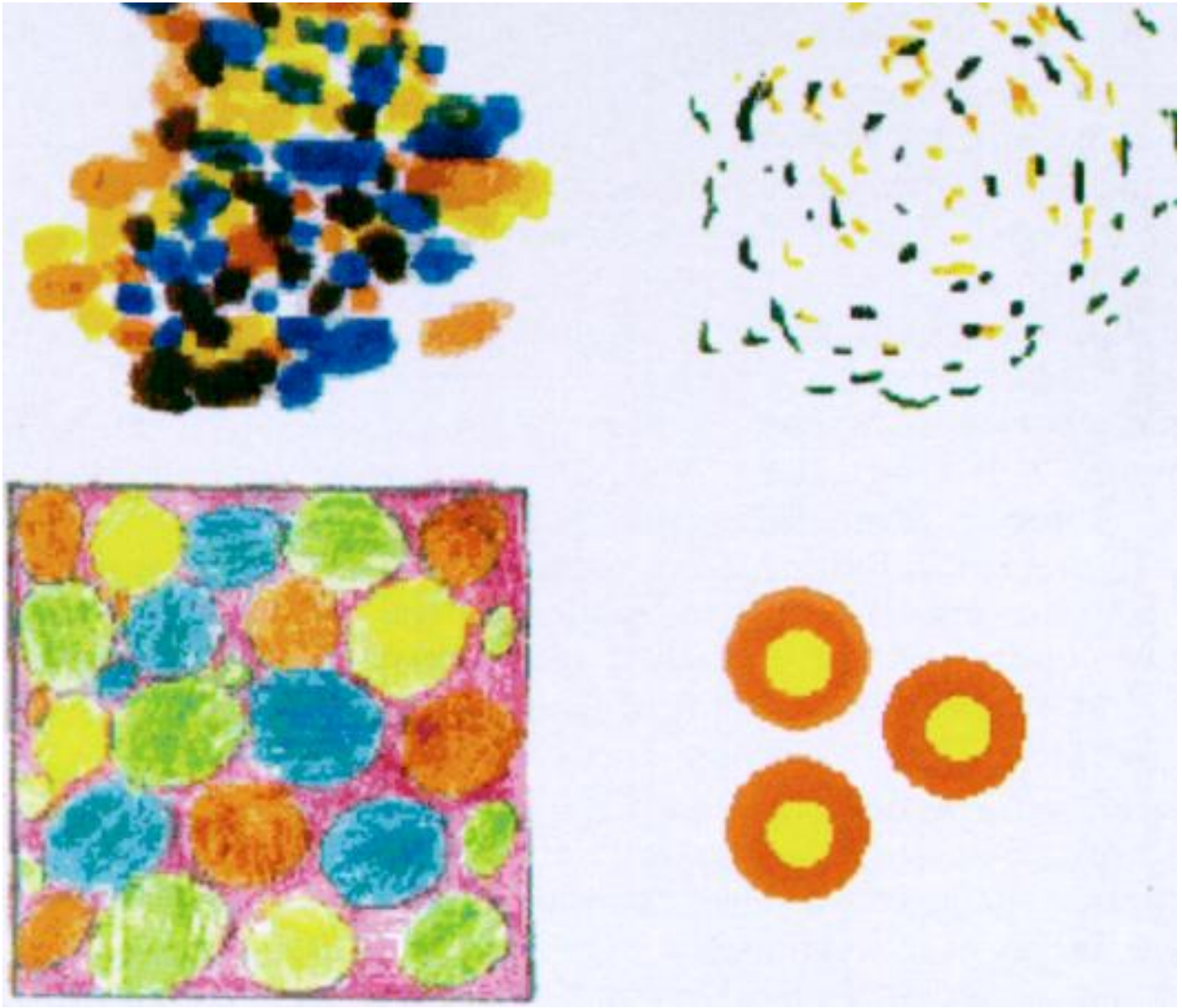
Exclusionary

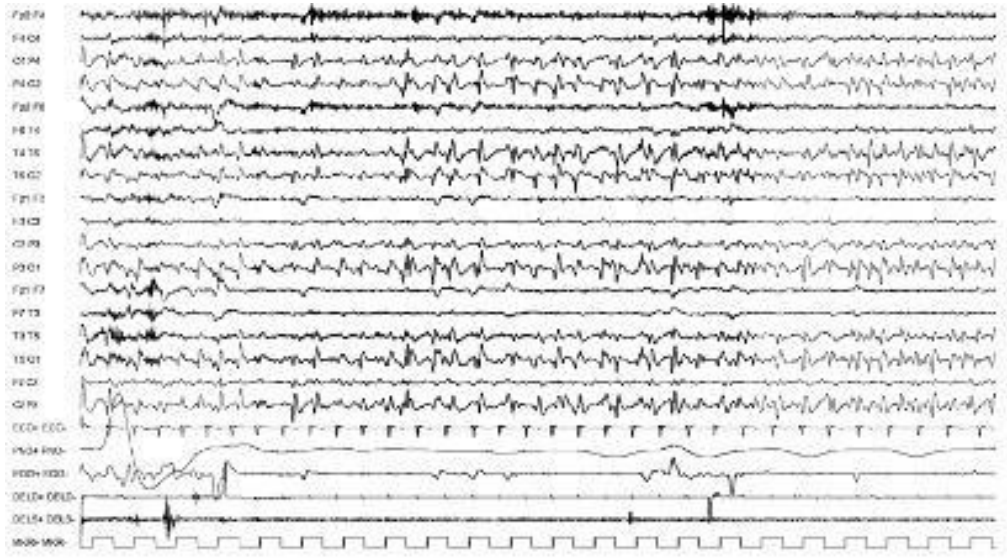
- **Age at onset**: <1 year or >14 years at onset
- **Development at onset**: Neurocognitive regression with a continuous spike-and-wave pattern in sleep (suggests EE-SWAS)
- **Imaging**: Causal lesion on brain MRI
- **Course of illness**: Neurocognitive regression with a continuous spike-and-wave pattern in sleep suggests evolution to EE-SWAS

Self-Limited Focal Epilepsies (SeLFE) of Childhood

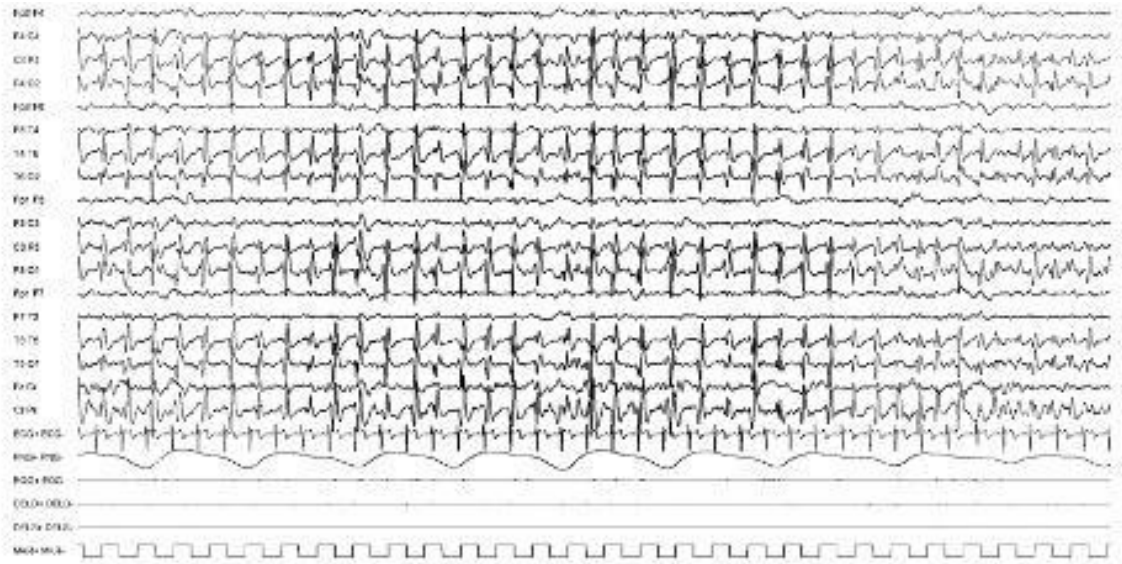
Childhood Occipital Visual Epilepsy
COVE

- Focal sensory visual seizures
  - Elementary visual phenomena
  - Multicoloured circles
  - ± awareness
  - ± head and eye deviation
  - Awake

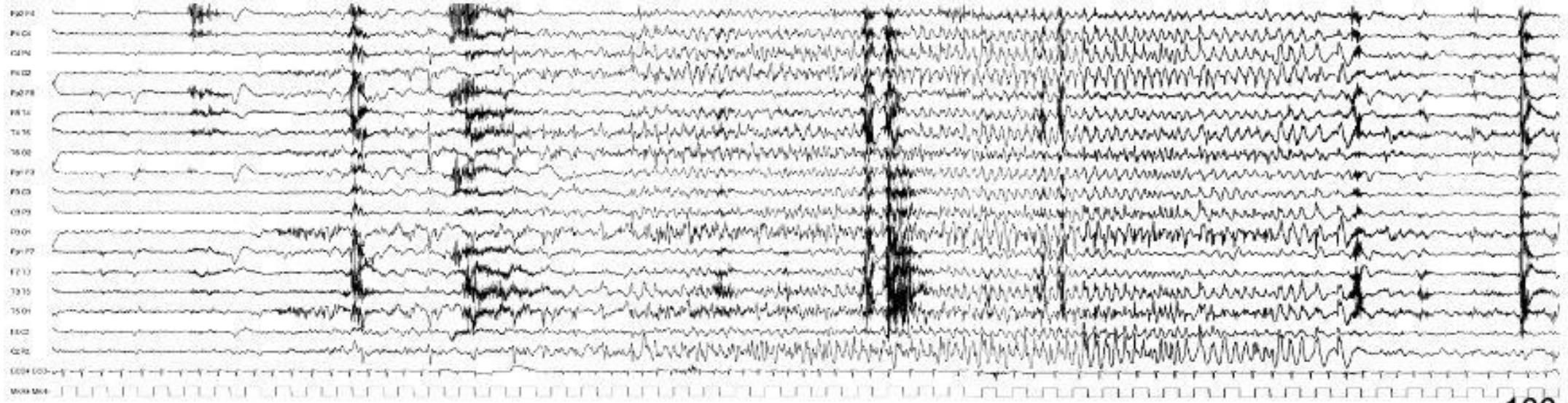




A Awake: posterior spikes



B Sleep: ↑ posterior spikes



C Ictal: bilateral posterior low voltage fast activity
most prominent posterior regions

Childhood Occipital Visual Epilepsy (COVE)

Mandatory

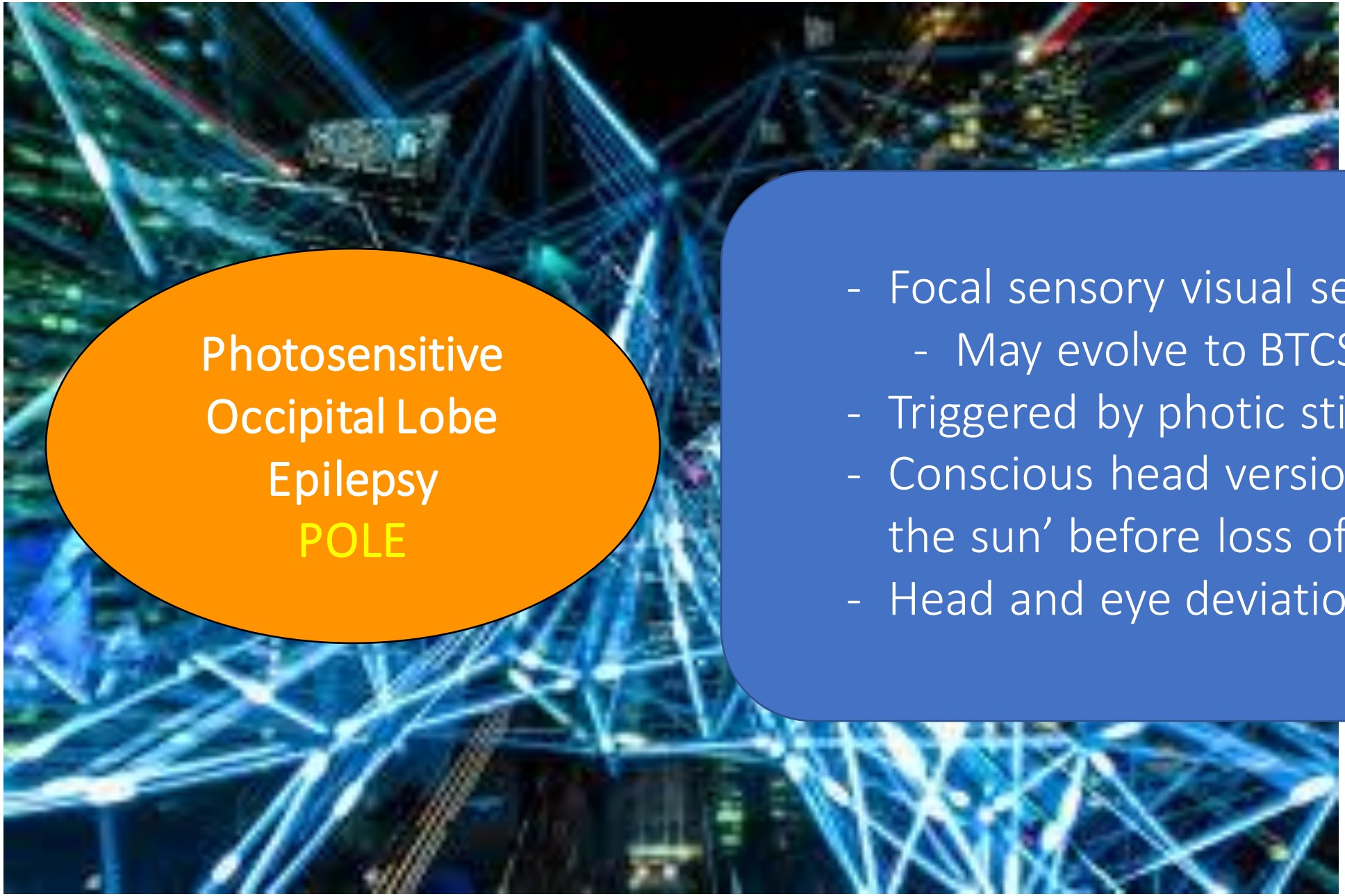
- **Seizures**: Focal sensory visual seizures with elementary visual phenomena (multi-colored circles), with or without impaired awareness, and with or without motor signs (deviation of the eyes or turning of the head. Seizures arise predominantly or exclusively from wakefulness
- **EEG**: Occipital spikes or spikes-and-wave abnormalities (awake or sleep).

Alerts

- **Seizures**: Prolonged seizure lasting >15 minutes. GTCS during wakefulness
- **EEG**: Sustained focal slowing not limited to the postictal phase
- **Age at onset**: <6 years >14 years at onset
- **Development at onset**: Intellectual disability
- **Neurological exam**: Any significant neurological examination abnormality

Exclusionary

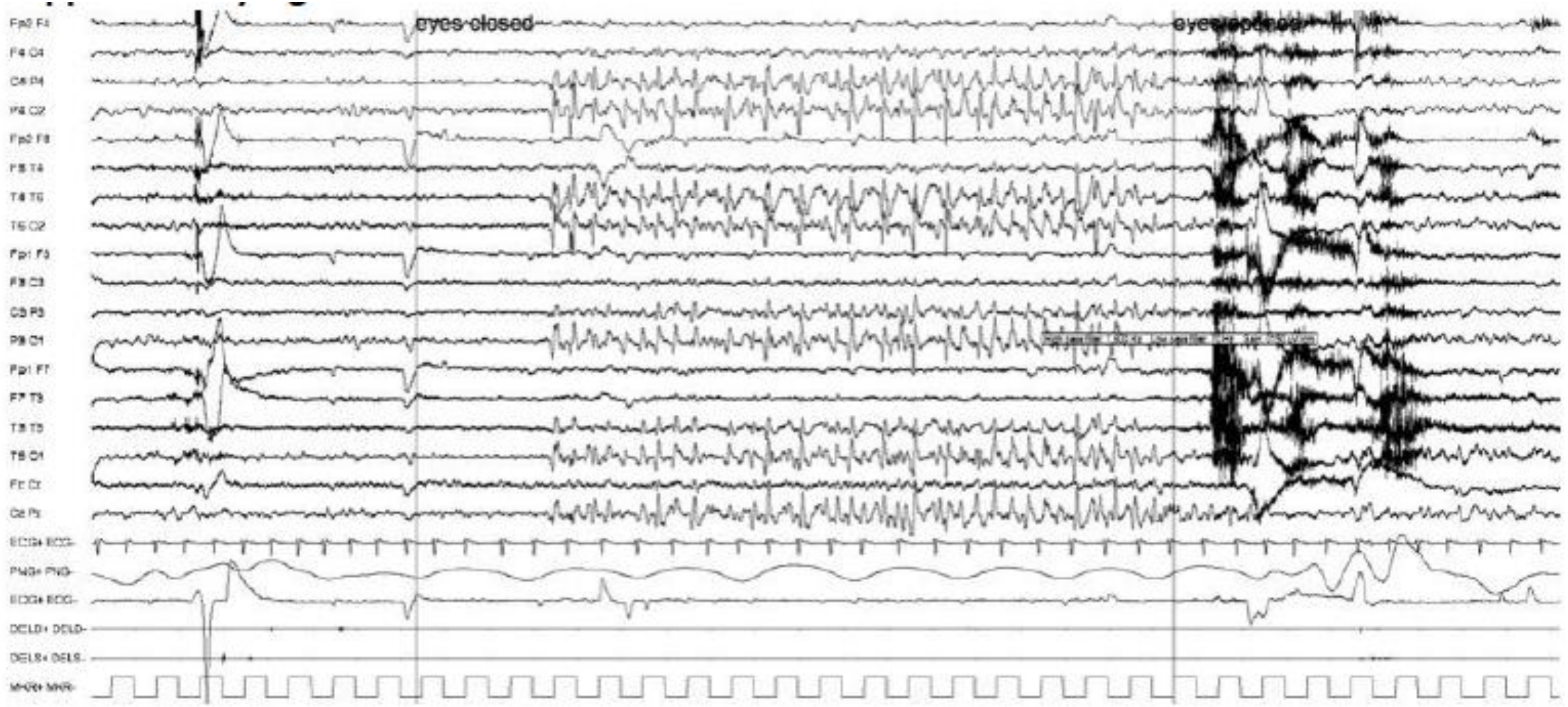
- **Seizures:** Drop (tonic or atonic) seizures. Atypical absences. Progressive myoclonus
- **Age at onset**: <1 year or >19 years at onset
- **Development at onset**: Neurocognitive regression
- **Neurological exam**: Persistent visual field deficit
- **Imaging**: Causal lesion on brain MRI. Cerebral occipital lobe calcifications
- **Course of illness**: Neurocognitive regression. Development of myoclonic seizures, ataxia, spasticity



Photosensitive Occipital Lobe Epilepsy

POLE

- Focal sensory visual seizures
  - May evolve to BTCS
- Triggered by photic stimuli
- Conscious head version ‘chasing the sun’ before loss of awareness
- Head and eye deviation



POLE Interictal: diffuse spike-wave elicited by eye closure
Discharge stops on eye opening

Photosensitive Occipital Lobe Epilepsy (POLE)

Mandatory

- **Seizures**: Focal sensory visual seizures (see text), which may evolve to bilateral tonic-clonic seizures. Seizures are triggered by photic stimuli, such as flickering sunlight
- **EEG**: Occipital epileptiform abnormalities facilitated by eye closure and IPS

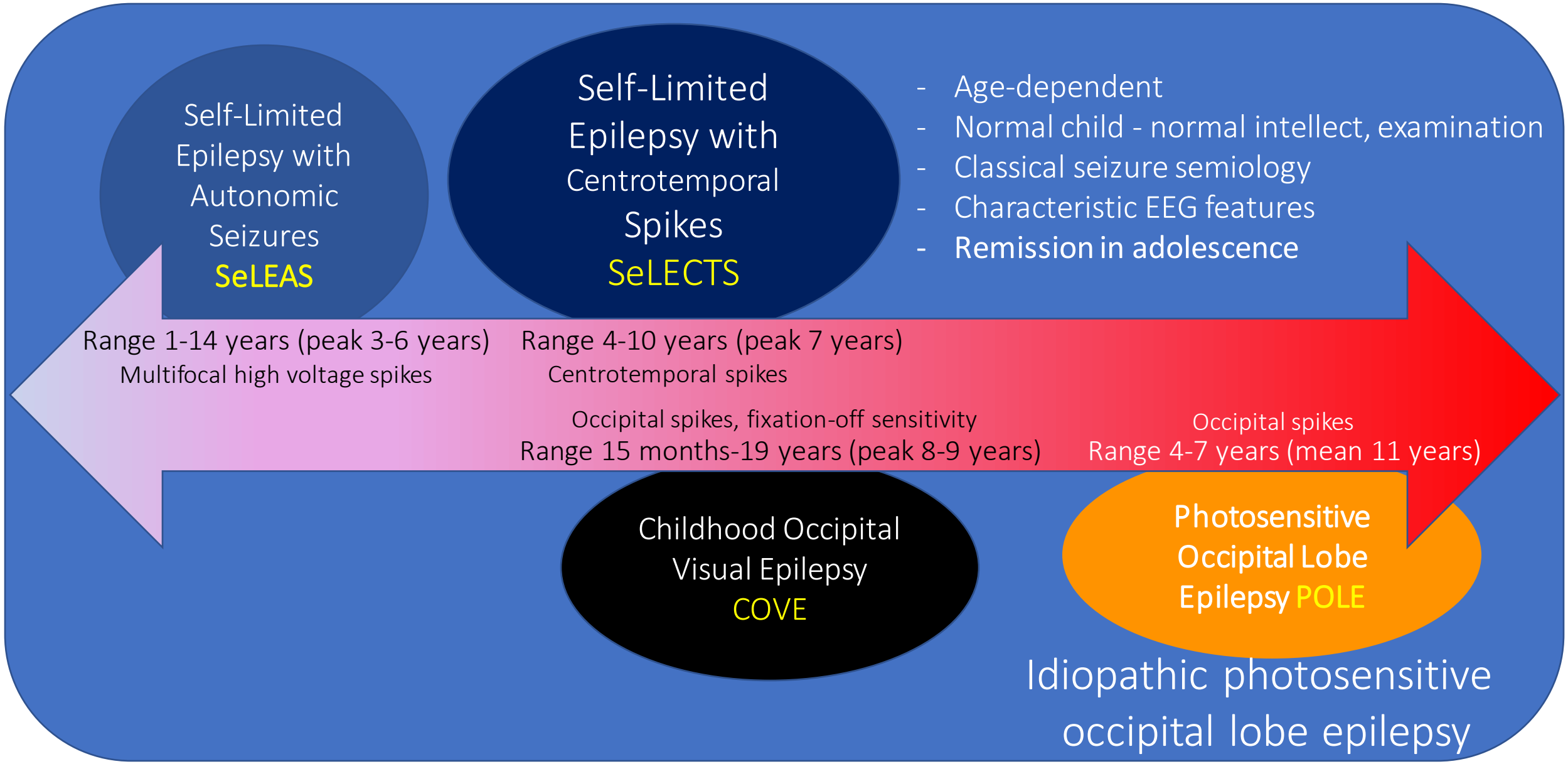
Alerts

- **Seizures**: Prolonged seizures lasting >15 minutes
- **EEG**: Sustained focal slowing not limited to the postictal phase. Photoparoxysmal response at slow photic frequency (1-2 Hz) (suggest CLN2 disease)
- **Age at onset**: <4 years >17 years at onset
- **Development at onset**: Moderate to profound intellectual disability
- **Neurological exam**: Any significant neurological examination abnormality

Exclusionary

- **Seizures:** Eyelid myoclonia. Progressive myoclonus
- **Age at onset**: <1 year or >50 years at onset
- **Development at onset**: Neurocognitive regression
- **Neurological exam**: Permanent visual field deficit
- **Imaging**: Causal lesion on brain MRI

Self-Limited Focal Epilepsies (SeLFE) of Childhood

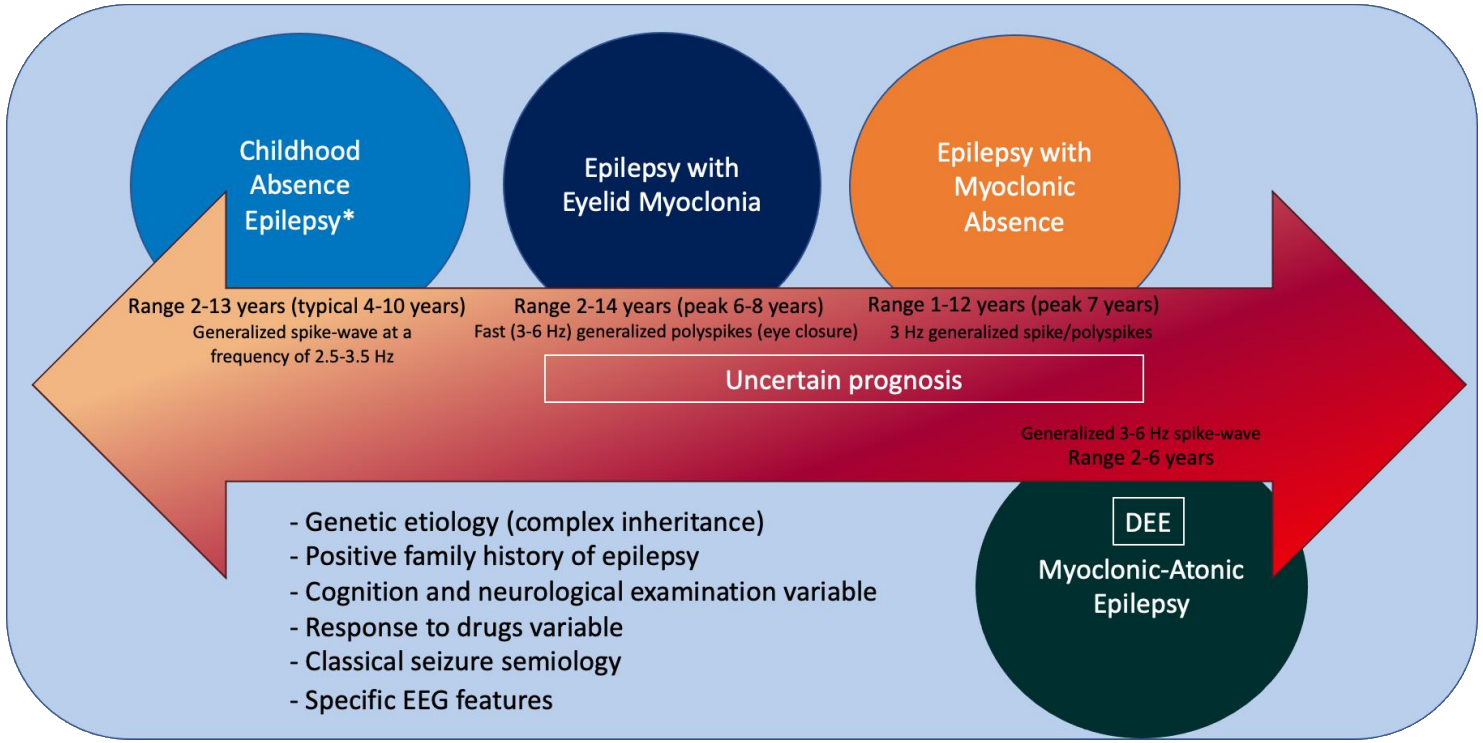


Generalized Epilepsies

Genetic Generalized Epilepsies of Childhood are a group of condition characterized by genetic etiology with complex inheritance, namely with polygenic basis.

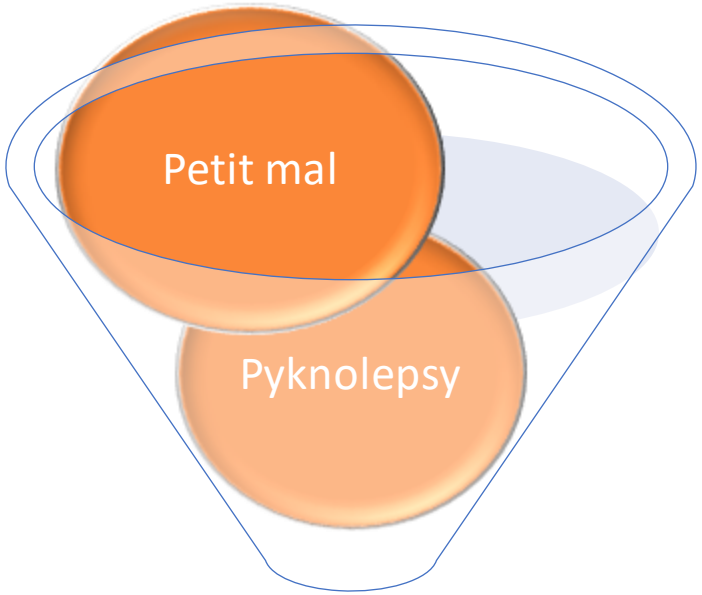
- A positive family history of epilepsy is frequent.
- Cognition, neurological examination and response to drugs are variable.
- Seizure's semiology, and EEG features are specific for each of the syndromes included in this group.

The Genetic Generalized Epilepsy Syndromes of Childhood



*discussed in the paper on IGE syndromes

Generalized Epilepsies



Childhood Absence Epilepsy

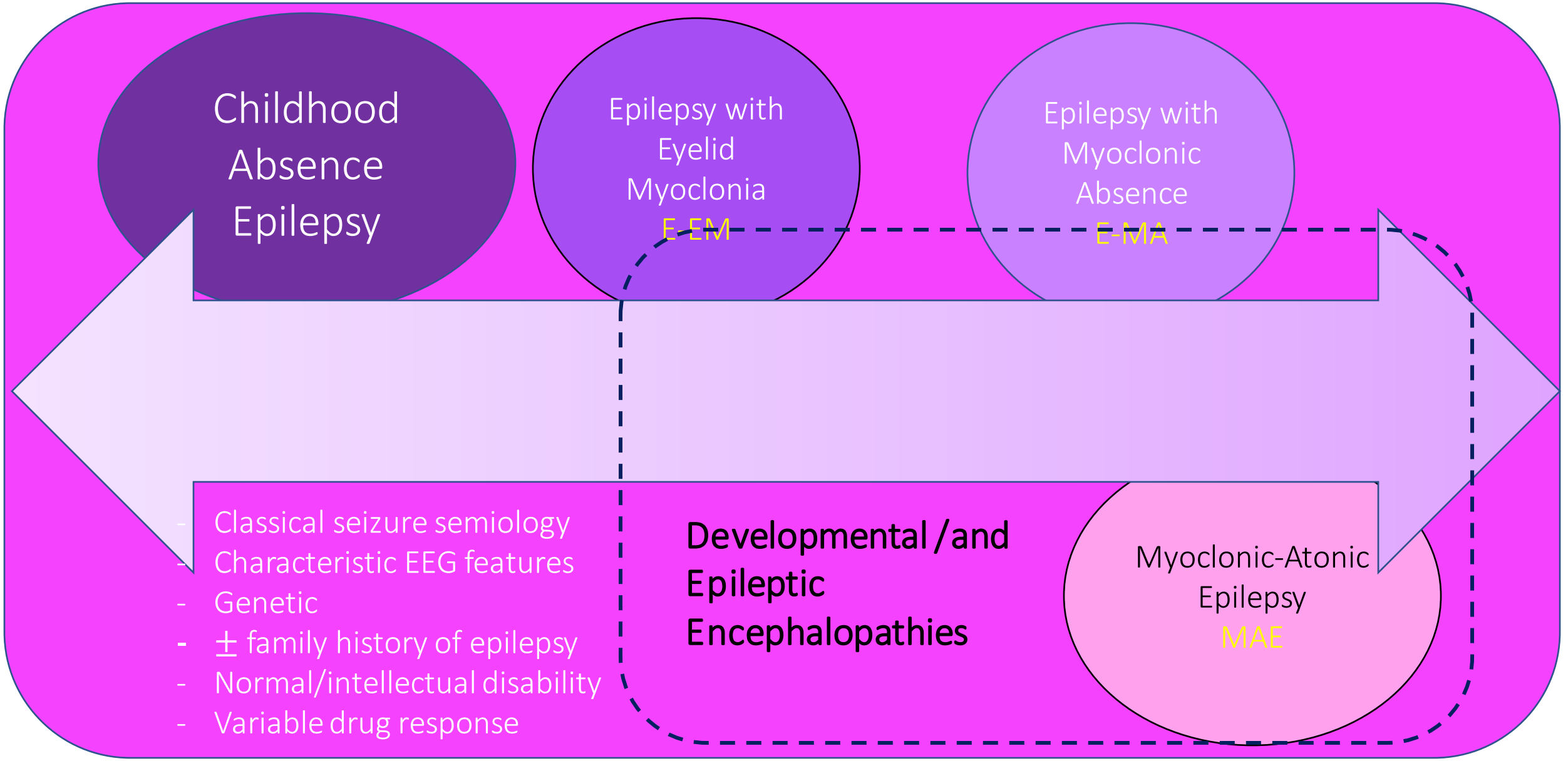
Jeavons Syndrome

Epilepsy with Eyelid Myoclonia

Bureau and Tassinari syndrome

Epilepsy with Myoclonic Absence

Generalized Epilepsy Syndromes of Childhood



Epilepsy with Eyelid Myoclonia (EEM)

Mandatory

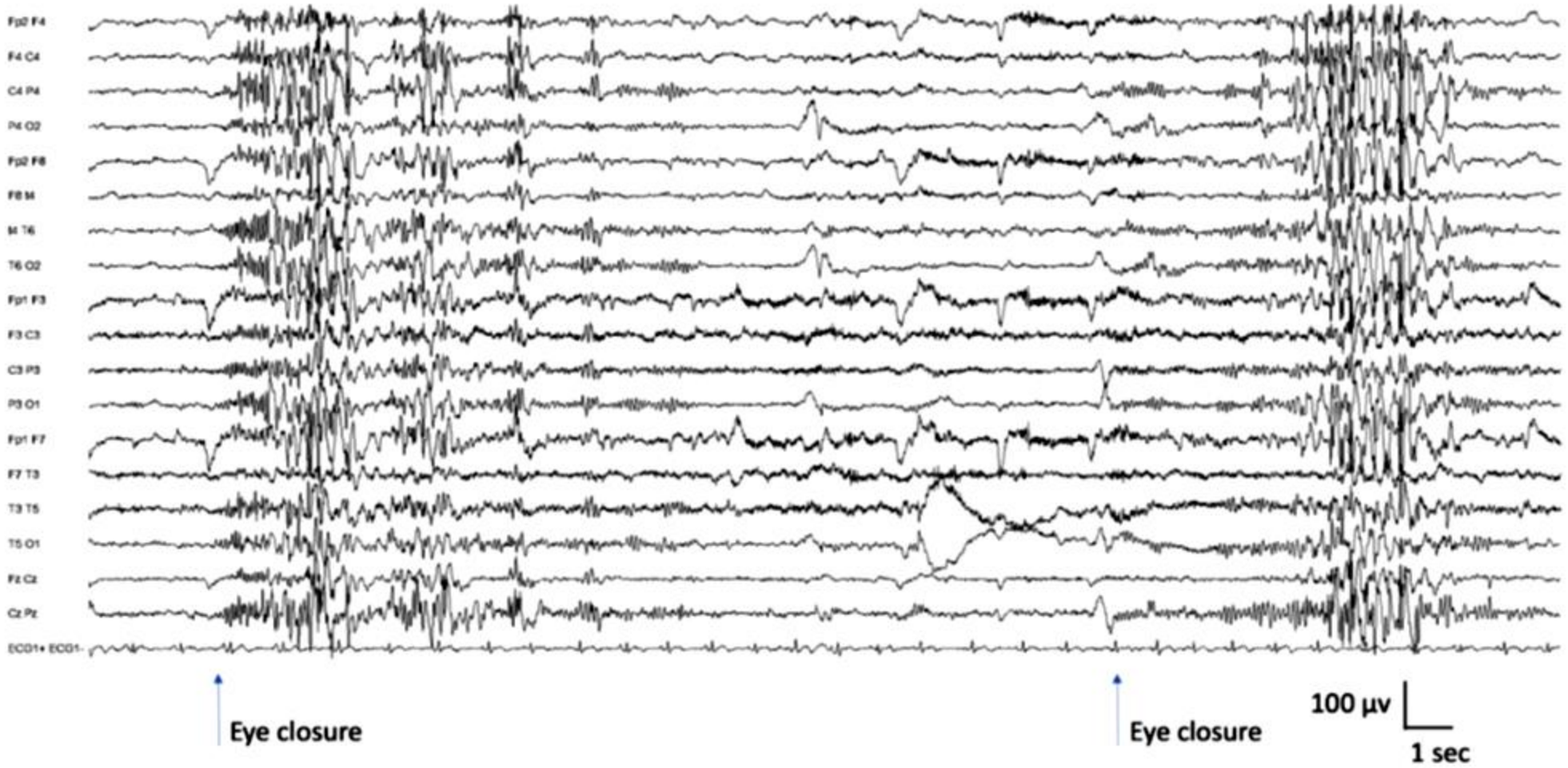
- **Seizures**: Eyelid myoclonia
- **EEG**: Eye closure and intermittent photic stimulation elicits fast (3-6 Hz) generalized polyspikes or polyspike-and-wave

Alerts

- **Seizures**: Inability to induce eyelid myoclonia in the office by slow eye closure during exposure to bright light in an untreated patient. Myoclonic jerks affecting limbs – strongly consider JME
- **Neurological exam**: Focal neurological findings
- **Imaging**: Potentially relevant abnormal neuroimaging, excluding incidental findings

Exclusionary

- **Seizures:** Any of the following seizure types:
  - Myoclonic-absence seizures
  - Focal seizures
- **EEG**: Focal slowing. Consistently unilateral focal spikes. Generalized slow spike-and-wave at frequency <2.5 Hz (unless it is at the end of a higher frequency burst). Diffuse background slowing that is not limited to the postictal period. Lack of EEG correlate with typical clinical event
- **Age at onset**: <2 years or >14 years at onset
- **Imaging**: Abnormal neuroimaging with causative lesion
- **Course of illness**: Progressive cognitive decline over the course of the epilepsy



Epilepsy with Eyelid Myoclonia: Ictal EEG in 14-year-old patient with. Background activity is normal. Each time the patient closes the eyes (eye closure artifact is seen) there is a generalized polyspike-and-wave discharge lasting between 6 and 8 seconds clinically associated with eyelid myoclonia. During the second event, soon after eye closure, there is a fast activity discharge that builds up.

Epilepsy with Myoclonic Absence (EMA)

Mandatory

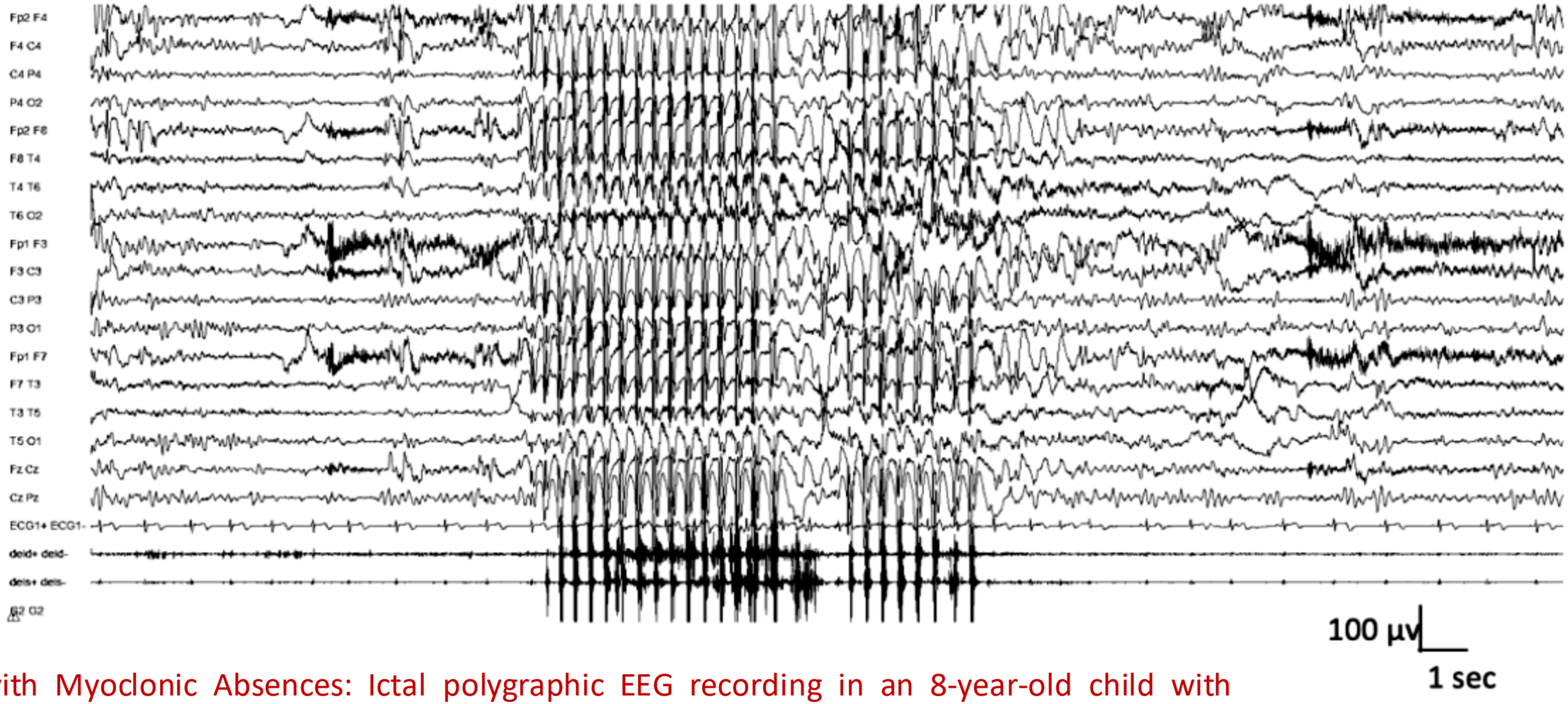
- **Seizures**: Myoclonic absence seizures as predominant type
- **EEG**: Regular 3 Hz generalized spike-and-wave time-locked with the myoclonic jerks

Alerts

- **Neurological exam**: Moderate or greater intellectual disability. Focal neurological findings

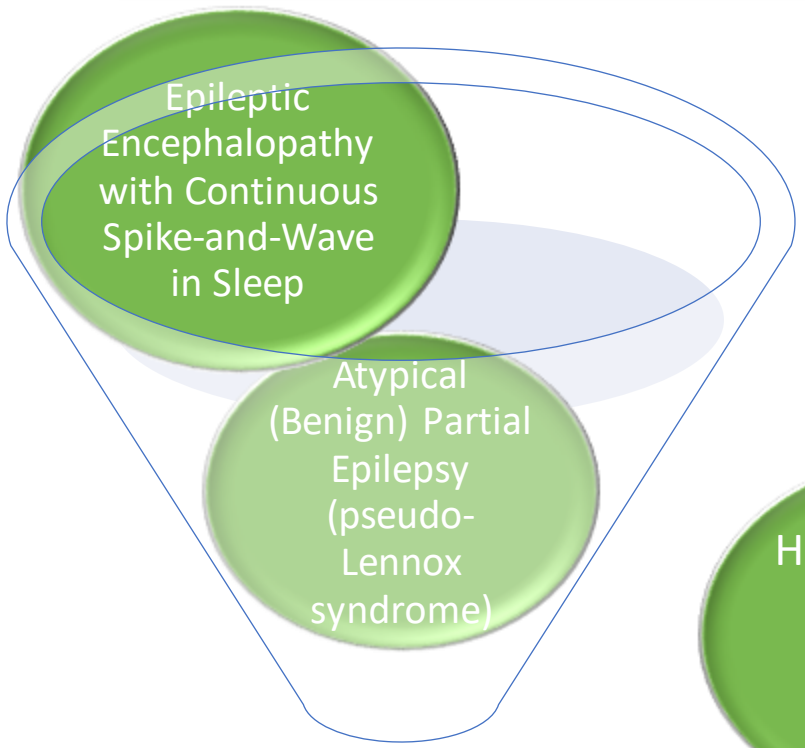
Exclusionary

- **Seizures:** Focal seizures. Atonic, Myoclonic-Atonic or Tonic seizures
- **EEG**: Focal slowing. Consistently unilateral focal spikes. Generalized slow spike-and-wave at frequency <2 Hz (unless it is at the end of a higher frequency burst). Diffuse background slowing that is not limited to the postictal period.
- **Age at onset**: <1 year or >12 years at onset
- **Imaging**: Abnormal neuroimaging with causative lesion
- **Course of illness**: Progressive cognitive decline over the course of epilepsy



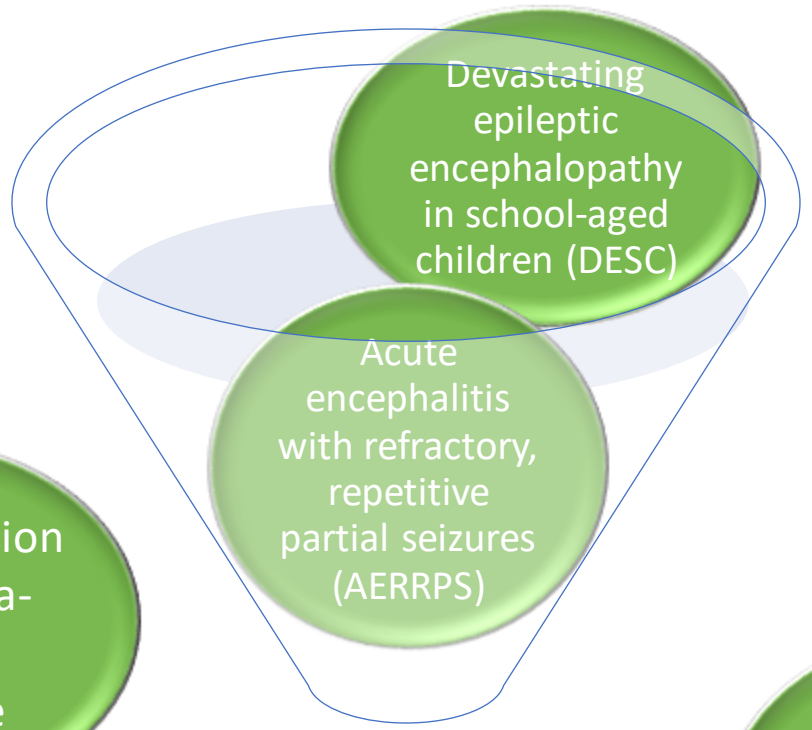
Epilepsy with Myoclonic Absences: Ictal polygraphic EEG recording in an 8-year-old child with showing a paroxysmal generalized 3 Hz spike-and-wave discharge. EMG channels (right and left deltoids) show bilateral myoclonic jerks synchronous with epileptiform abnormalities, and between jerks there is a sustained increase in muscle tone

Developmental and/or Epileptic Encephalopathies



Developmental and/or Epileptic Encephalopathy with Spike-and-Wave Activation in Sleep

Hemiconvulsion -Hemiplegia-Epilepsy Syndrome



Febrile Infection-Related Epilepsy Syndrome

Doose syndrome

Epilepsy with Myoclonic-Atonic Seizures

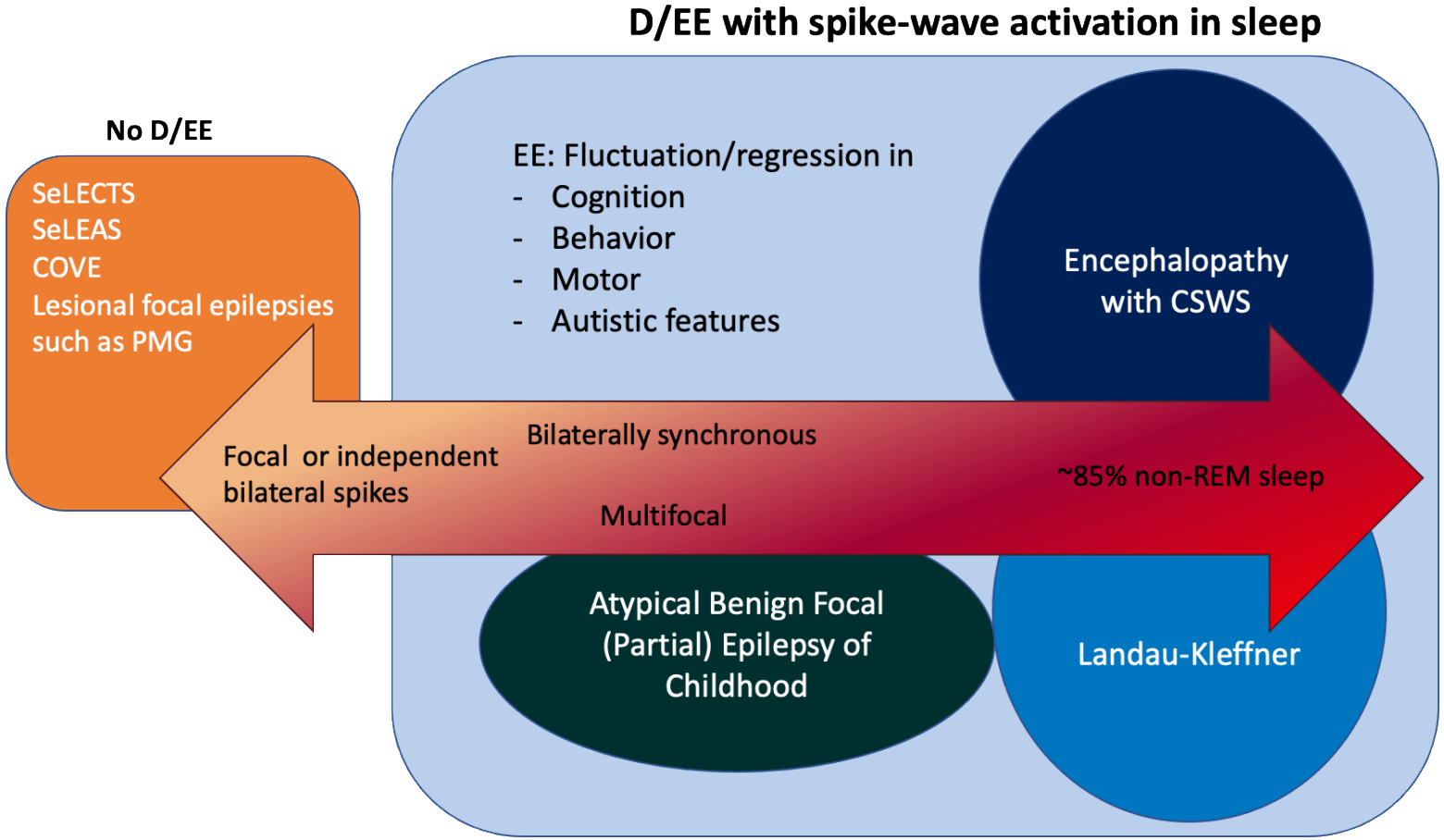
Lennox-Gastaut syndrome

FOCUS ON
Developmental and/or Epileptic Encephalopathy with Spike-and-Wave Activation in Sleep

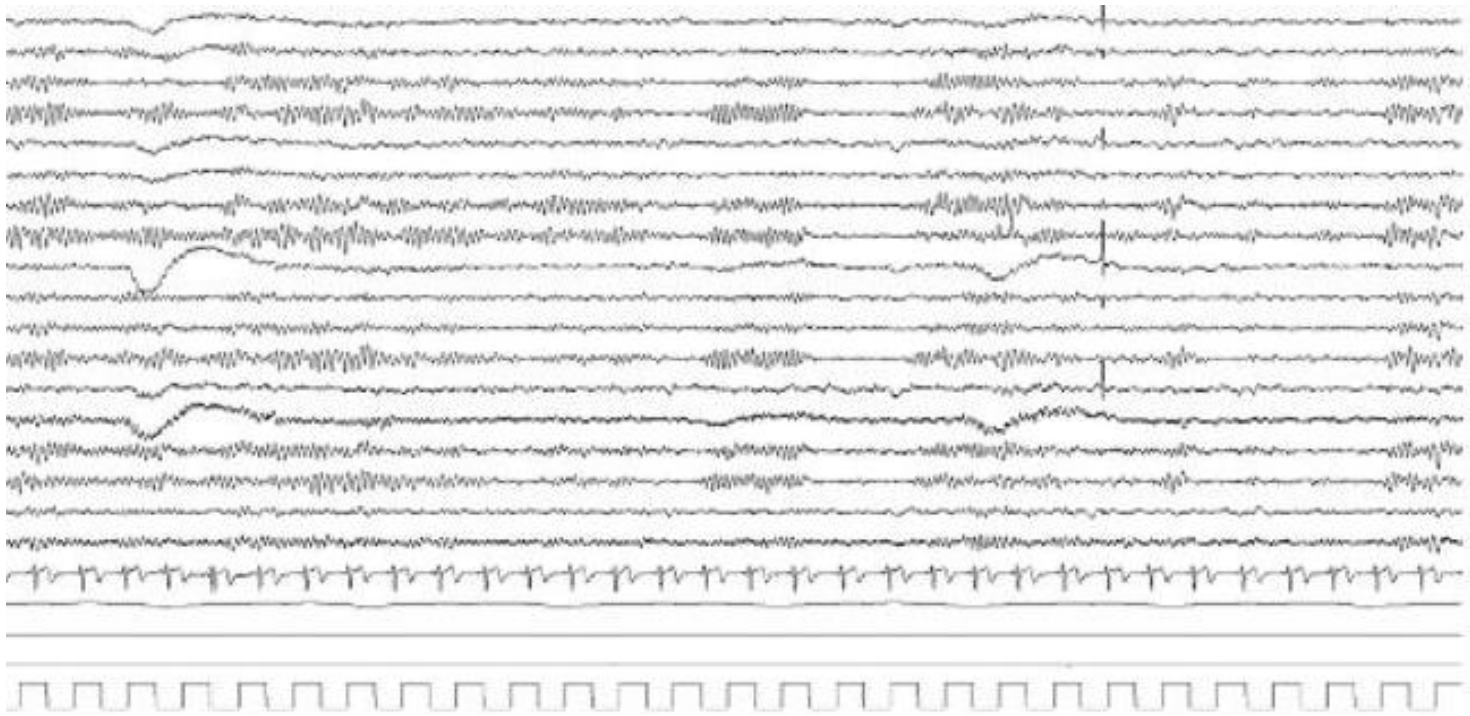
The Developmental and Epileptic Encephalopathies or Epileptic Encephalopathies with Onset in Childhood

Spectrum of conditions:

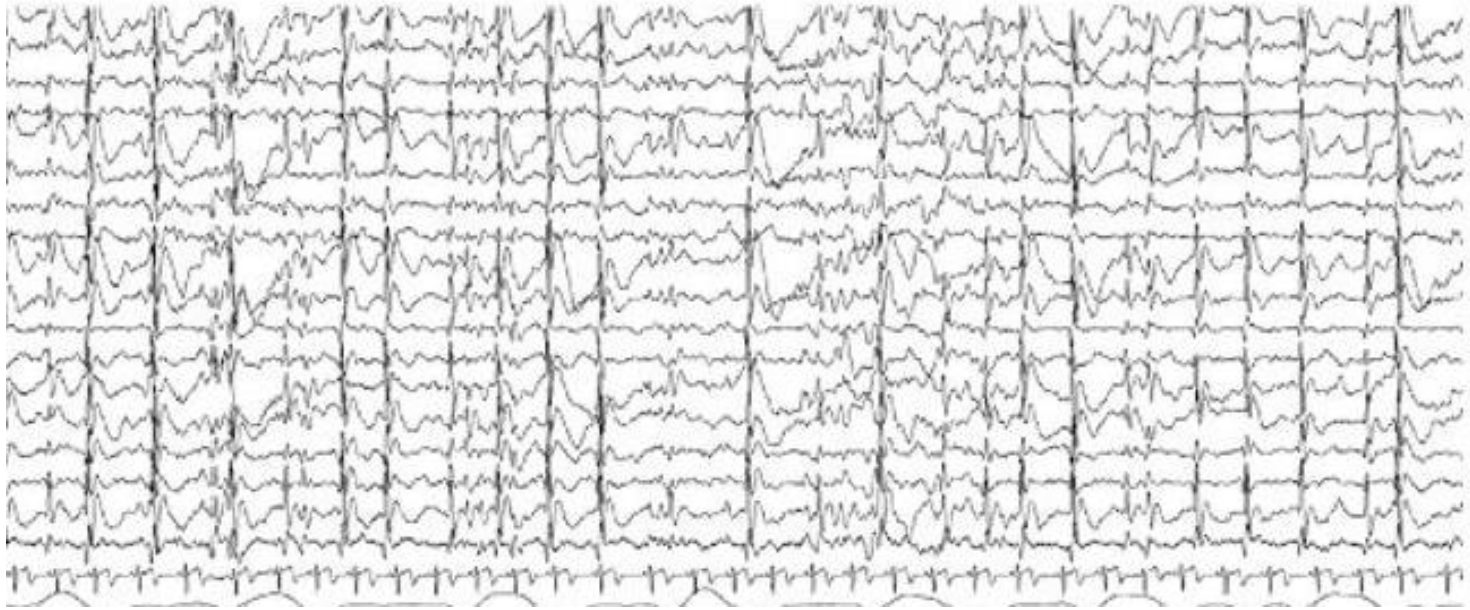
- cognitive, language, behavioral and motor regression associated with marked spike-and-wave activation in sleep.
- Regression is seen within weeks from the EEG pattern.
- Landau-Kleffner syndrome is a specific sub-type of EE-SWAS, where regression affects mainly language with an acquired auditory agnosia.



D/EE-SWAS



Awake



Sleep

Developmental Epileptic Encephalopathy with spike-and-wave activation in sleep (DEE-SWAS) and Epileptic Encephalopathy with spike-and-wave activation in sleep (EE-SWAS)

Mandatory

- **EEG**: Slow (1.5-2Hz) spike-and-wave abnormalities in N-REM sleep. Abnormalities are markedly activated in sleep
- **Development at onset**: Cognitive, behavioral or motor regression or plateauing temporally related to SWAS on EEG
- **Long term outcome**: Remission of SWAS pattern on EEG by mid adolescence, although EEG often remains abnormal

Alerts

- **Seizures**: Tonic seizures during sleep
- **EEG**: Generalized paroxysmal fast activity in sleep (consider Lennox-Gastaut syndrome). Generalized slow spike-and-wave <2.5 Hz in both awake and asleep states (consider Lennox-Gastaut syndrome)
- **Age at onset**: >1 and <2 years at onset

Exclusionary

- **Seizures**: Epileptic spasms
- **Age at onset**: <1 year or >12 years at onset

Epilepsy with Myoclonic Atonic Seizures (EMAtS)

ILAE Classification and Definition of Epilepsy Syndromes with Onset in Childhood: Position Paper by the ILAE Task Force on Nosology and Definitions

- Onset between 2 and 6 years
- Myoclonic–atonic seizures
  - brief myoclonic jerk
  - affecting the proximal muscles, often associated with a slight vocalization, followed by a very brief atonic com- ponent
- Myoclonic, absences, GTC, tonic, non-convulsive SE

Epilepsy with Myoclonic Atonic Seizures (EMAtS)

Mandatory

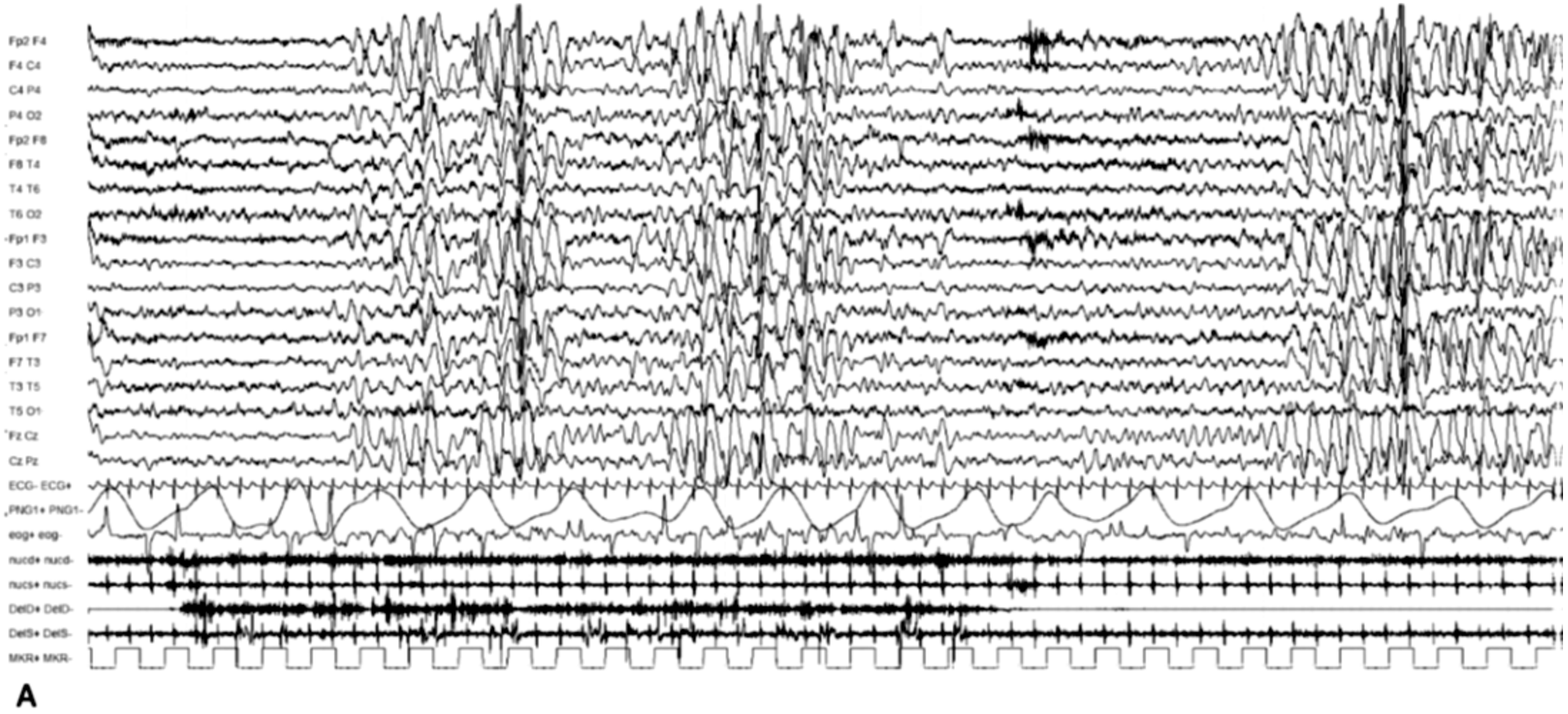
- **Seizures**: Myoclonic-atonic seizures
- **EEG**: Generalized 2-6 Hz spike-wave or polyspike-and-wave abnormalities

Alerts

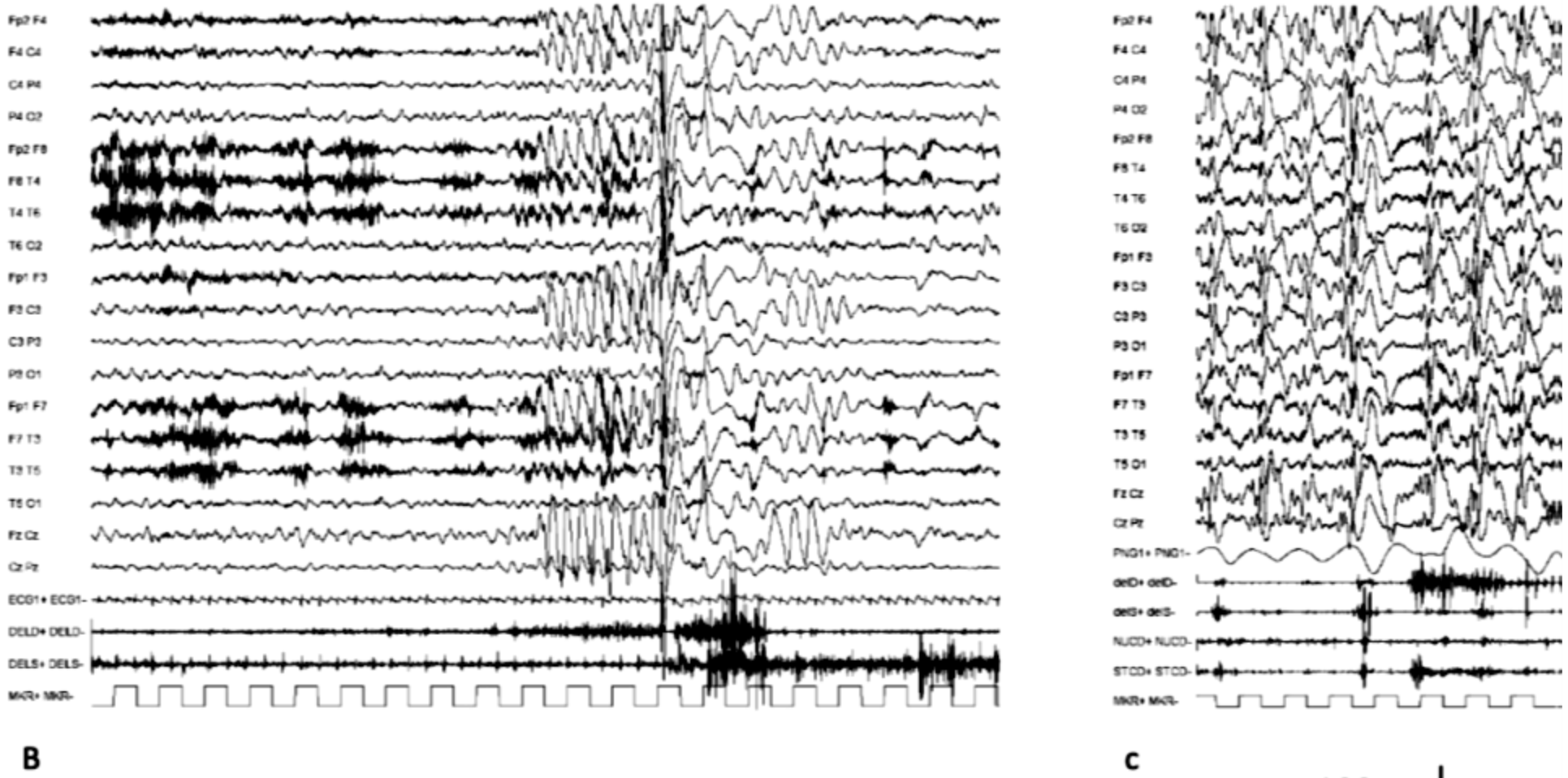
- **Seizures**: Tonic seizures within 12 months of epilepsy onset
- **EEG**: Generalized paroxysmal fast activity in sleep. Generalized slow spike-and-wave <2 Hz. Photoparoxysmal response at low frequencies (suggests CLN2 disease)
- **Development at onset**: Moderate to severe developmental delay preceding seizure onset
- **Neurological exam**: Focal neurological findings

Exclusionary

- **Seizures:** Epileptic spasms or ISS prior to diagnosis. Focal seizures
- **EEG**: Persistent focal abnormalities. Hypsarrhythmia
- **Age at onset**: <6 months or >8 years at onset
- **Imaging**: Causal lesion on MRI



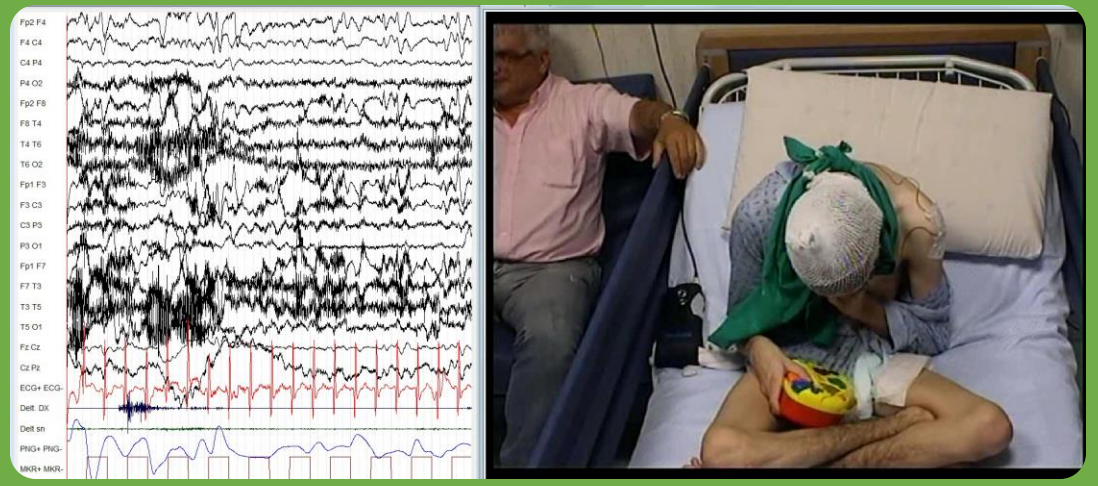
Epilepsy with Myoclonic Atonic Seizures: Interictal and ictal polygraphic EEG recordings in a 3-year-old child.
A. Interictal EEG shows bilateral posterior slow waves (4-6 Hz). There are generalized abnormalities characterized by high amplitude spikes and spike-and-wave abnormalities intermingled with high amplitude delta waves without any clinical changes.

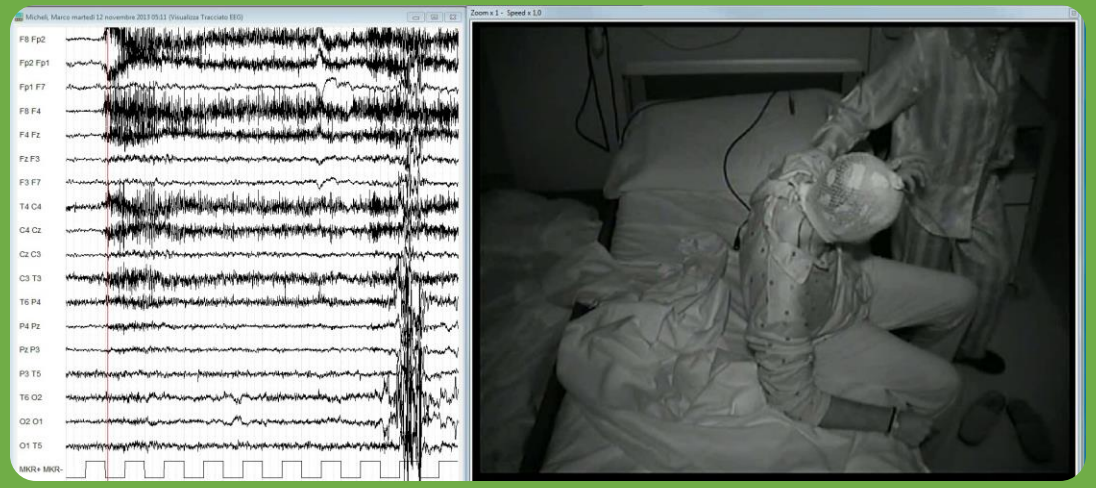


Epilepsy with Myoclonic Atonic Seizures: Interictal and ictal polygraphic EEG recordings in a 3-year-old child. B. and C. Examples of myoclonic atonic seizures associated with a generalized spike-and-wave discharge of brief duration. EMG channels show loss of tone in the deltoids (B) and in nuchal and sternocleidomastoid muscles (C). Clinically, the child experiences abrupt falls with both events.

Lennox-Gastaut syndrome LGS

- 1-2% epilepsies
- Onset 3-7 y (< 18 y)
- 20% evolve from Infantile Spasms
- Multiple seizure types – Tonic seizures
- Cognitive ± behavioral problems
- Developmental slowing or regression

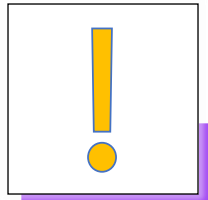




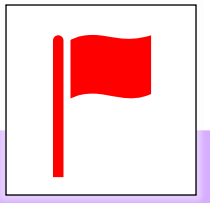
Gastaut et al, 1966, ’75; Camfield et al, 1996

Lennox-Gastaut syndrome (LGS)

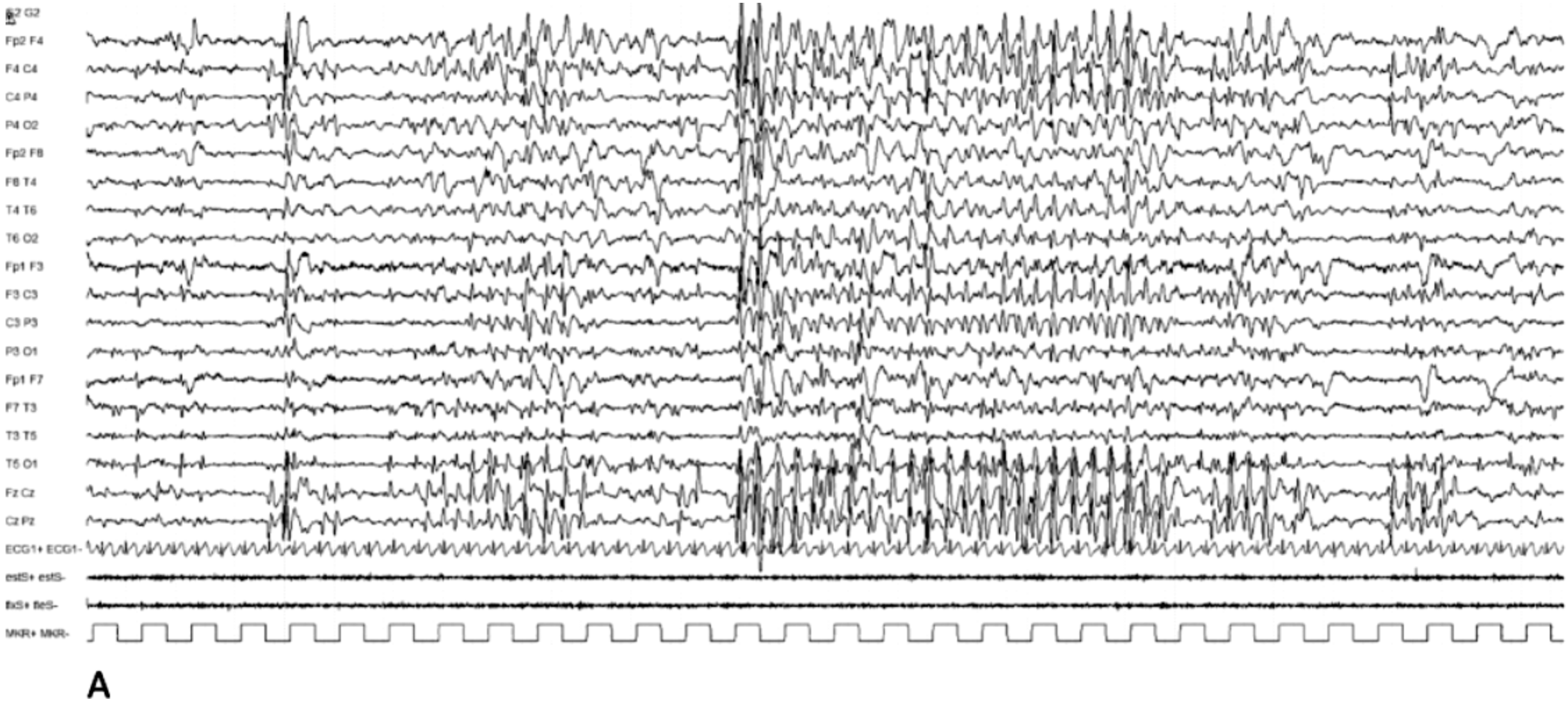
- Tonic seizure
- ± atypical absence, myoclonic, FIAS, GTC, spasms, NCSE
- GSSW, GPFA
- Onset < 18 y
- Mild – profound ID



- Onset > 10 y
- PPR at slow frequency 1-2 Hz (? CLN2 disease)

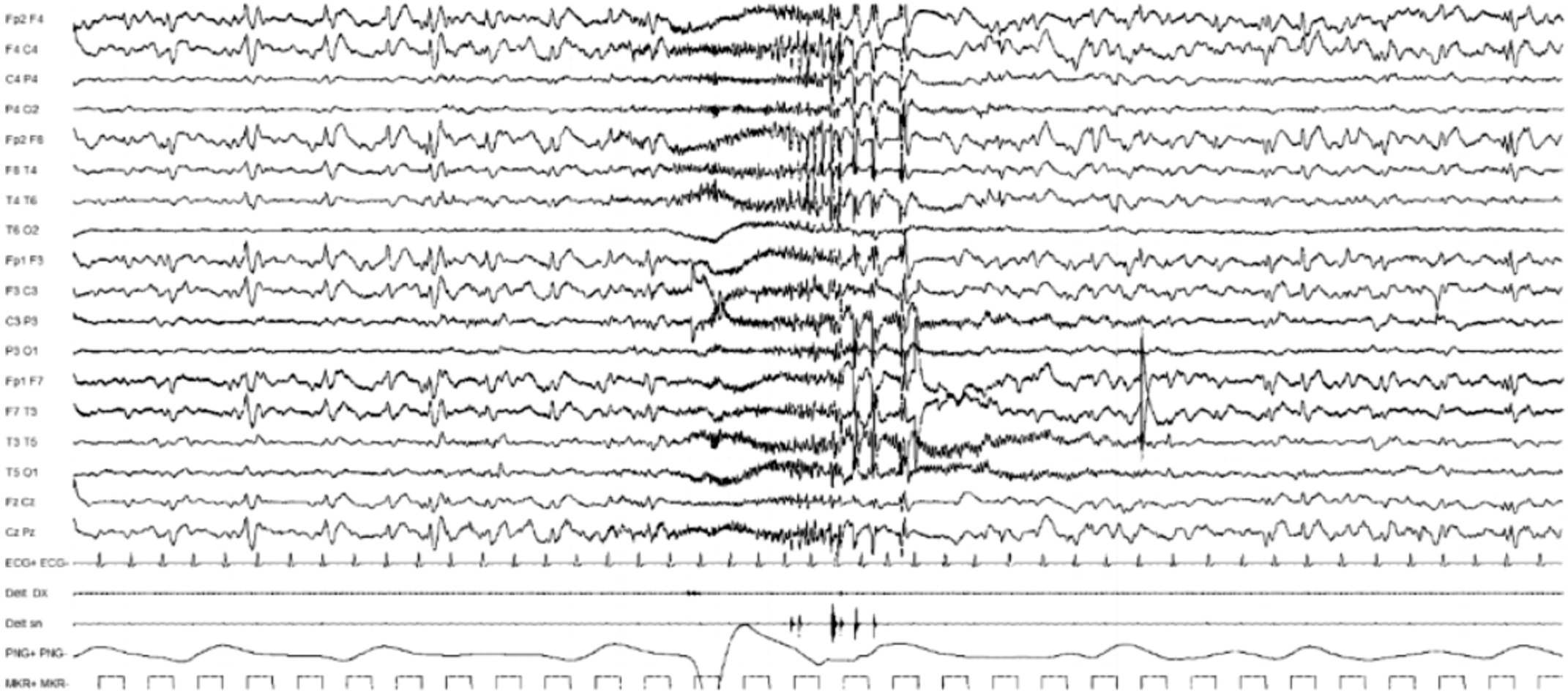


- Persistent focal discharge without generalized spike-wave



A

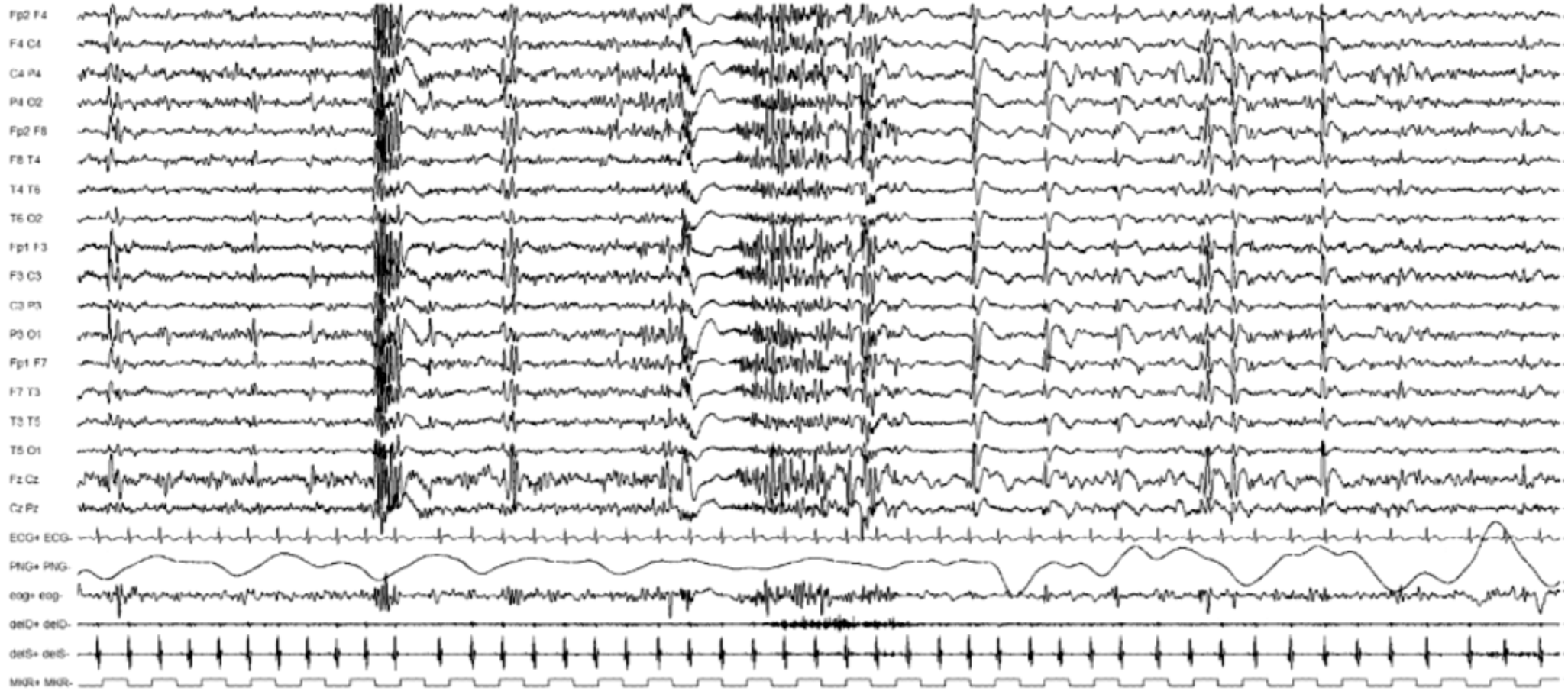
Lennox-Gastaut Syndrome: Interictal and ictal polygraphic EEG recordings.
A. Generalized slow spike-andwave abnormalities (between 2 and 2.5 Hz) are seen, lasting 8 seconds, not associated with any clinical signs.



B

Lennox-Gastaut Syndrome: Interictal and ictal polygraphic EEG recordings

B. Generalized paroxysmal 10 Hz fast activity. The discharge is seen during sleep and is not associated with any clinical signs.



Lennox-Gastaut Syndrome: Interictal and ictal polygraphic EEG recordings

C. Ictal EEG showing a generalized electro-decremental response lasting 4 seconds associated with bilateral tonic contraction of the upper limbs, consistent with a generalized tonic seizure.

Further definitions

Syndrome-in-Evolution	Syndromes that lack all Mandatory diagnostic features at onset but take time to evolve, e.g. Rasmussen Syndrome early in the course, prior to appreciation of imaging findings.
Syndrome Without Laboratory Confirmation	Minimum criteria for diagnosis in resource-limited regions, which have little or no access to EEG, advanced neuroimaging or genetic studies.
Etiology-specific epilepsy syndrome	Syndromes in which there is a specific etiology for the epilepsy associated with a clearly defined, relatively uniform and distinct clinical phenotype as well as consistent EEG, neuroimaging and/or genetic results.

Conclusions

- The major goal of the Task Force was to reach consensus regarding which entities met epilepsy syndrome criteria and then define each one, using a rigorous consensus-gathering process and creating a resource available worldwide.
- Identified Mandatory, Exclusionary and Alerts criteria for each syndrome.
- Used descriptive names of syndromes as opposed to eponyms; retained some terms as ‘Dravet syndrome’, ‘Lennox-Gastaut syndrome’ and ‘Rasmussen syndrome’.
- Introduced the term Syndrome-in-Evolution, Syndrome Without Laboratory Confirmation, “Etiology-Specific Epilepsy Syndromes”.
- Not included specific treatment recommendations.

ILAE Task Force on Nosology and Definitions 2017-2021

















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