Epilepsy Syndromes of Adolescence and Adulthood

Suda Jirasakuldej, MD

King Chulalongkorn Memorial Hospital

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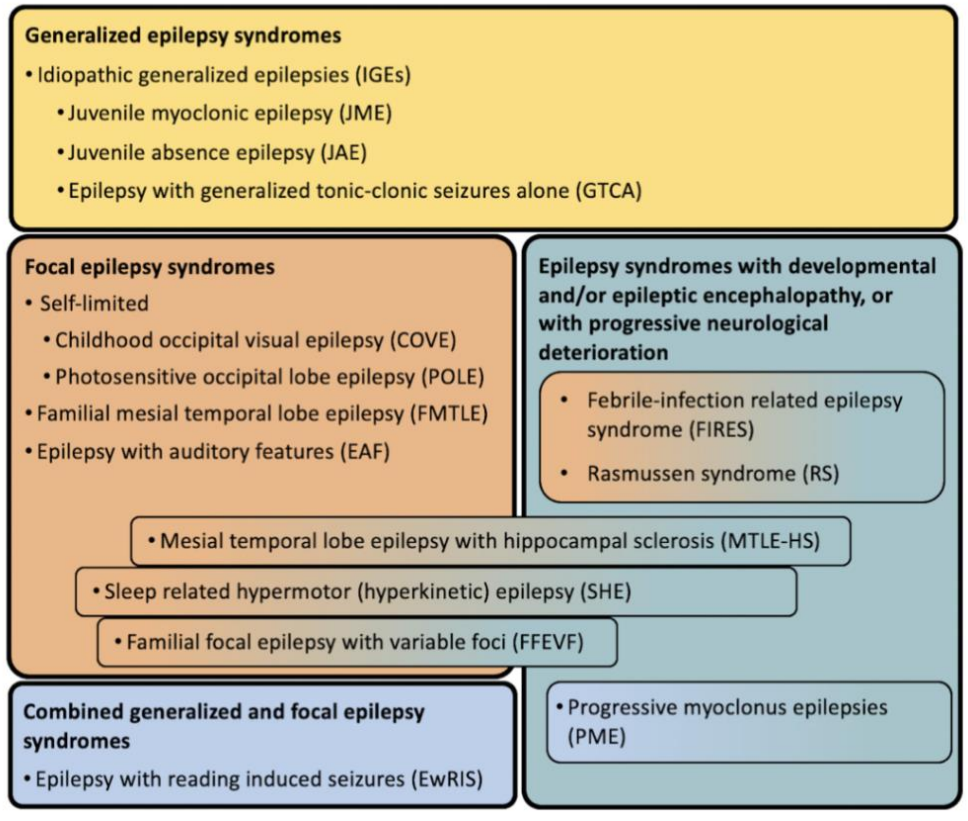
Epilepsy syndrome classification

- Age of onset
- Epilepsy type: focal, generalized, combined
- Associated with developmental and/or epileptic encephalopathy (D and/or EE) or progressive neurological deterioration

Table 1
Epilepsy syndrome classification based on age

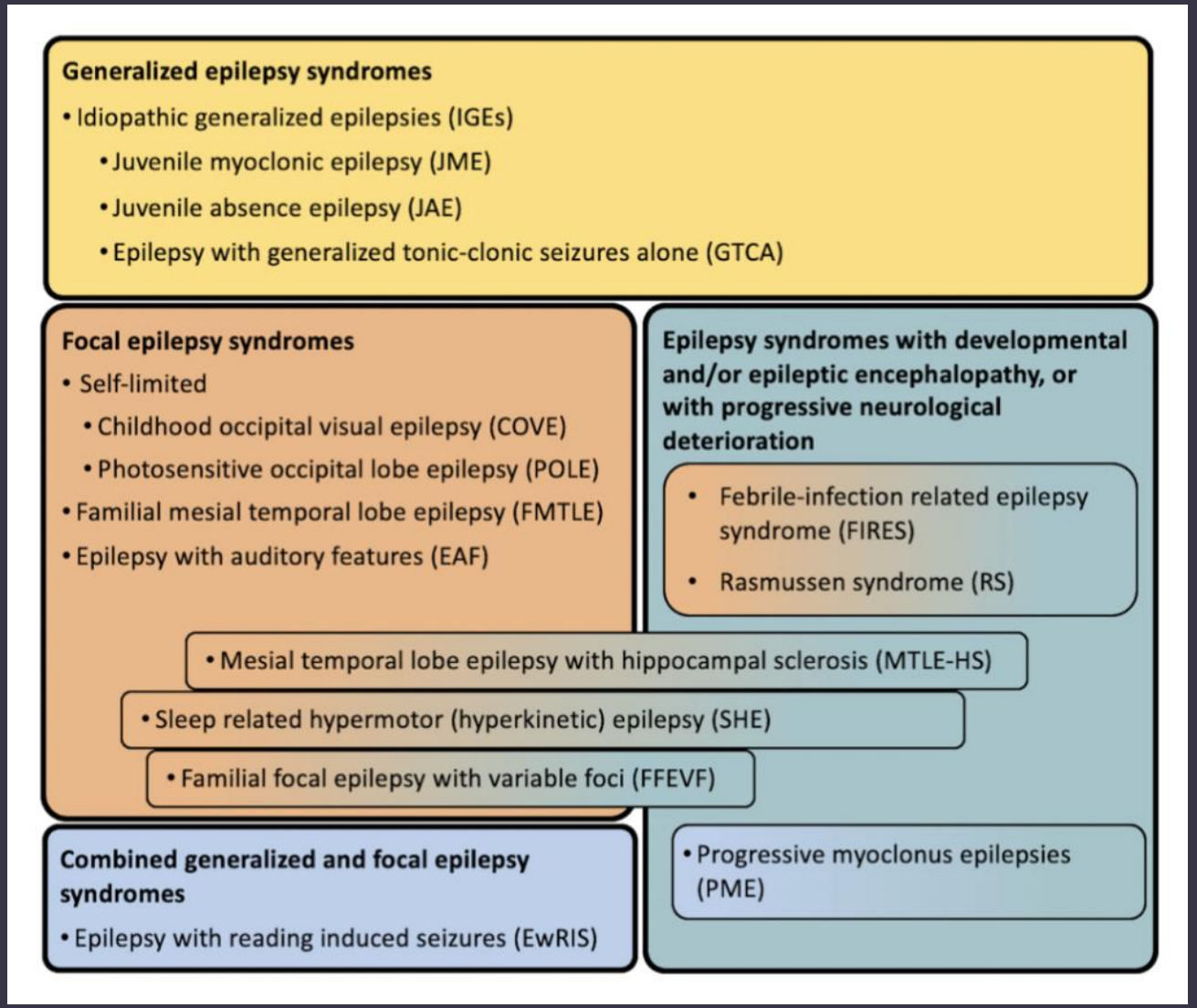
Neonatal/Infantile Onset	Childhood Onset	Adolescent/Adult Onset	Any Age
Self-limited neonatal seizures and self-limited familial neonatal epilepsy	Epilepsy with myoclonic atonic seizures	Juvenile absence epilepsy	Familial focal epilepsy with variable foci
Self-limited familial and nonfamilial infantile epilepsy	Epilepsy with eyelid myoclonia	Juvenile myoclonic epilepsy	Reflex epilepsies
Early myoclonic encephalopathy	Lennox-Gastaut syndrome	Epilepsy with generalized tonic-clonic seizures alone	Progressive myoclonic epilepsies
Ohtahara syndrome	Childhood absence epilepsy	Autosomal dominant epilepsy with auditory features	
West syndrome	Epilepsy with myoclonic absences	Other familial temporal lobe epilepsies	
Dravet syndrome	Panayiotopoulos syndrome		
Myoclonic epilepsy in infancy	Childhood occipital epilepsy		
Epilepsy of infancy with migrating focal seizures	Photosensitive occipital lobe epilepsy		
Myoclonic encephalopathy in nonprogressive disorders	Childhood epilepsy with centrotemporal spikes		
Febrile seizures plus, genetic epilepsy with febrile seizures plus	Atypical childhood epilepsy with centrotemporal spikes		
	Epileptic encephalopathy with continuous spike and wave during sleep		
	Landau-Kleffner syndrome		
	Autosomal dominant nocturnal frontal lobe epilepsy		

Neurol Clin. 2021;39(3):779–95.



Epilepsia. 2022;63:1443–74.

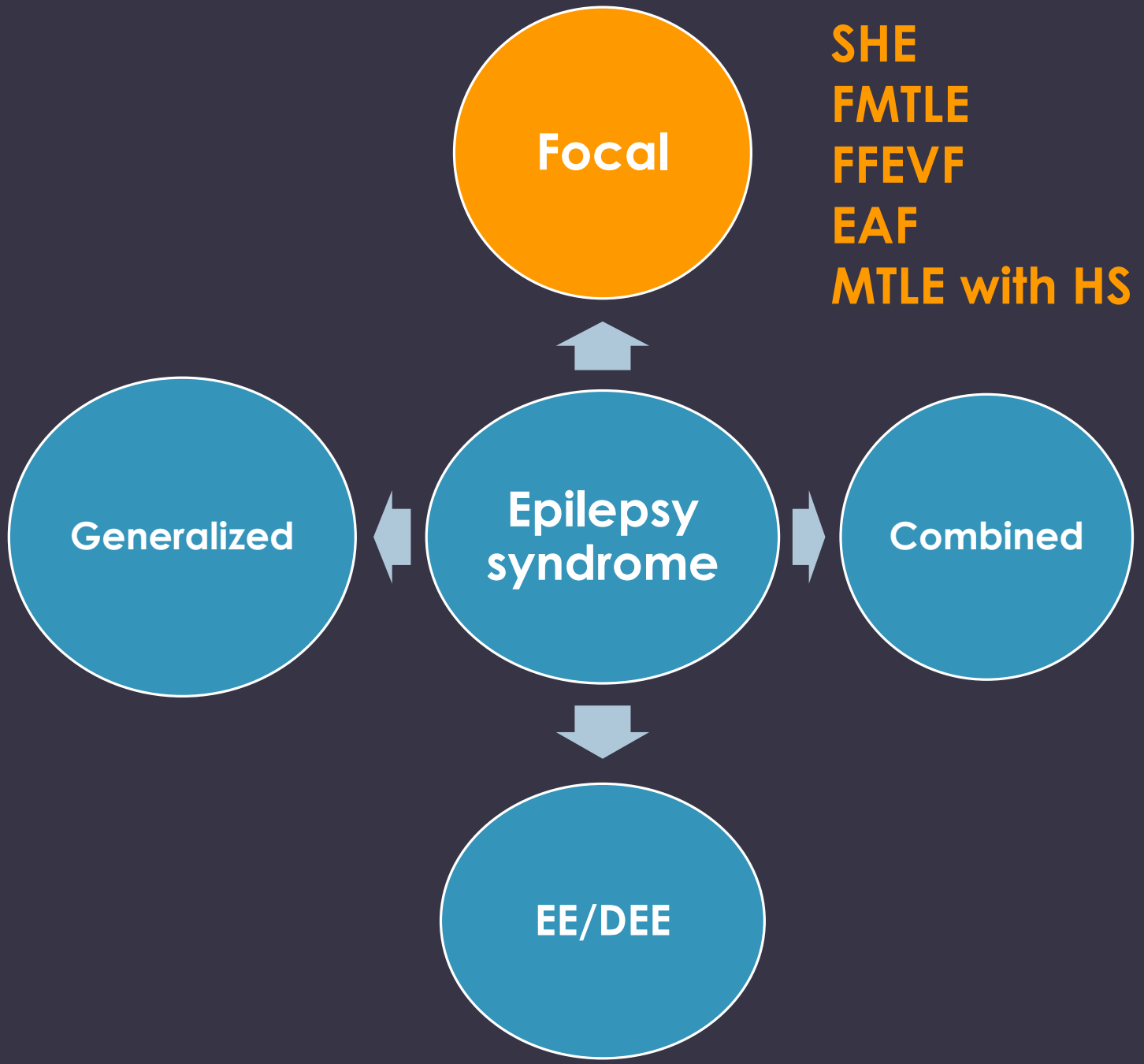
Epilepsy syndromes begin at a variable age



Epilepsia. 2022;63:1443–74.

Outline: Epilepsy syndrome of adolescence and adult

- **Focal epilepsy syndrome**
  - Sleep related hypermotor epilepsy (SHE)
  - Familial mesial temporal lobe epilepsy (FMTLE)
  - Familial focal epilepsy with variable foci (FFEVF)
  - Epilepsy with auditory feature (EAF)
  - MTLE-HS
- **Generalized epilepsy syndrome**
  - IGE: JAE, JME, GTCA
- **Combined generalized and focal epilepsy**
  - Epilepsy with reading induced seizure (EwRIS)
- **Epilepsy syndrome with DE and/or EE or with progressive neurological deterioration**
  - NORSE & Febrile infection related epilepsy syndrome (FIRES)
  - Rasmussen syndrome (RS)
  - Progressive myoclonic epilepsy (PME)


Focal
SHE
FMTLE
FFEVF
EAF
MTLE with HS
Generalized
Epilepsy syndrome
Combined
EE/DEE

Sleep related hypermotor epilepsy (SHE)

Sleep related hypermotor (hyperkinetic) epilepsy

- Previously known as AD nocturnal frontal lobe epilepsy
- Age at seizure onset mostly in first 2 decades of life
  - Typically in adolescence (11–14 yrs), range 2 months to 64 years
- Etiology: Structural (FCD), genetic (CHRNA4, CHRNA2, CHRNB2, KCNT1, DEPDC5, NPRL2, NPRL3, PRIMA1), acquired
- Course of illness: related to underlying etiology

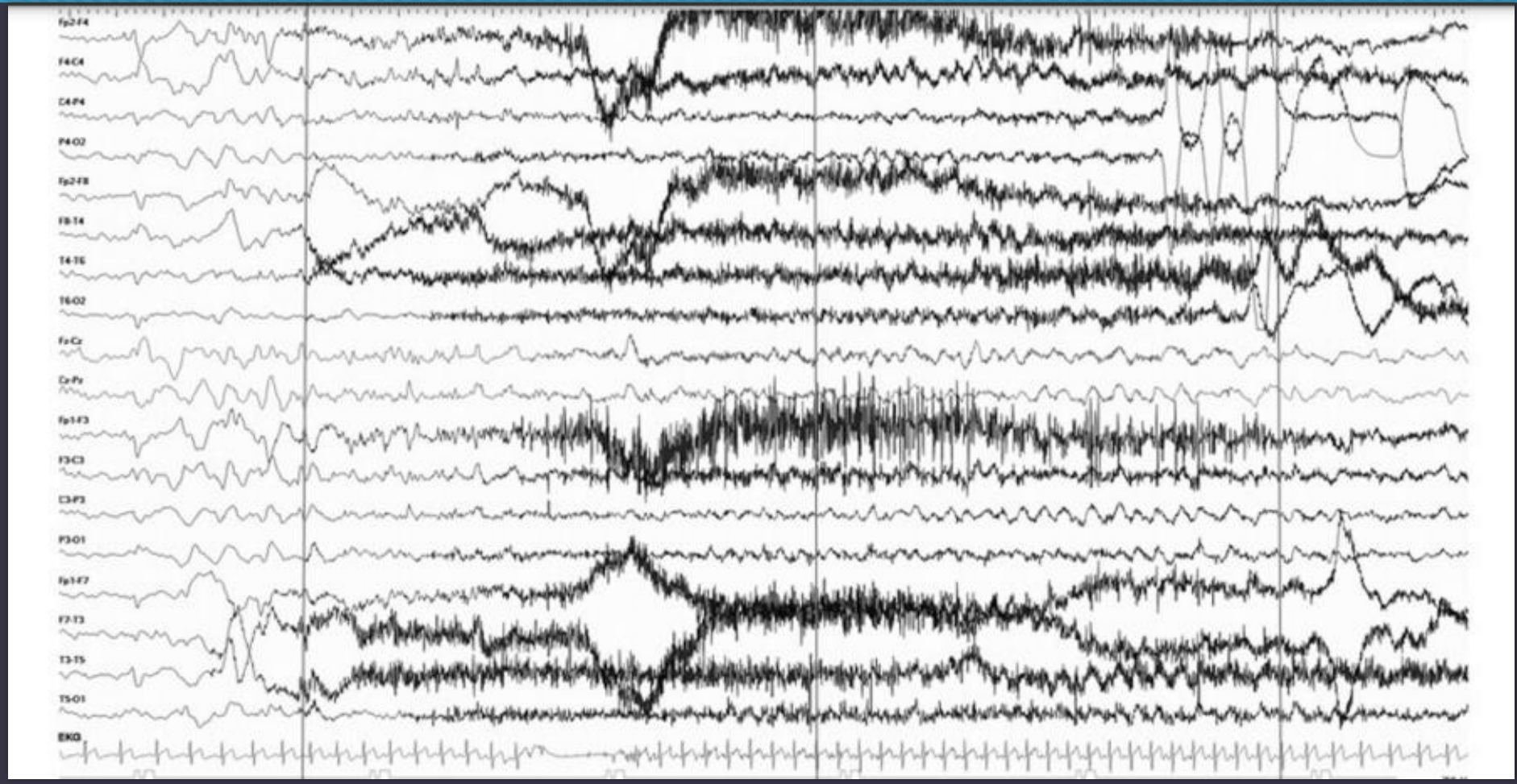
SHE: Characteristic seizures

- Clusters of stereotyped hyperkinetic or asymmetric dystonic/tonic motor pattern
- Predominant from sleep
- Abrupt onset and offset
- Typically brief (< 2 min)
- Preserved awareness

EEG

- Interictal EEG
  - Awake: Normal BG, non-epileptiform in most (50%–90%) patients
  - Sleep: 50% IEDs over frontal areas
- Ictal EEG
  - May not show definitive ictal patterns, obscured by movement artifact
  - Show evolving sharp or spike-and-wave discharges, rhythmic slow activity
  - Diffuse background flattening over frontal areas
  - Postictal focal slowing
- **Prolonged video EEG:** best diagnostic test to **identify events with stereotyped semiology from sleep** to confirm diagnosis

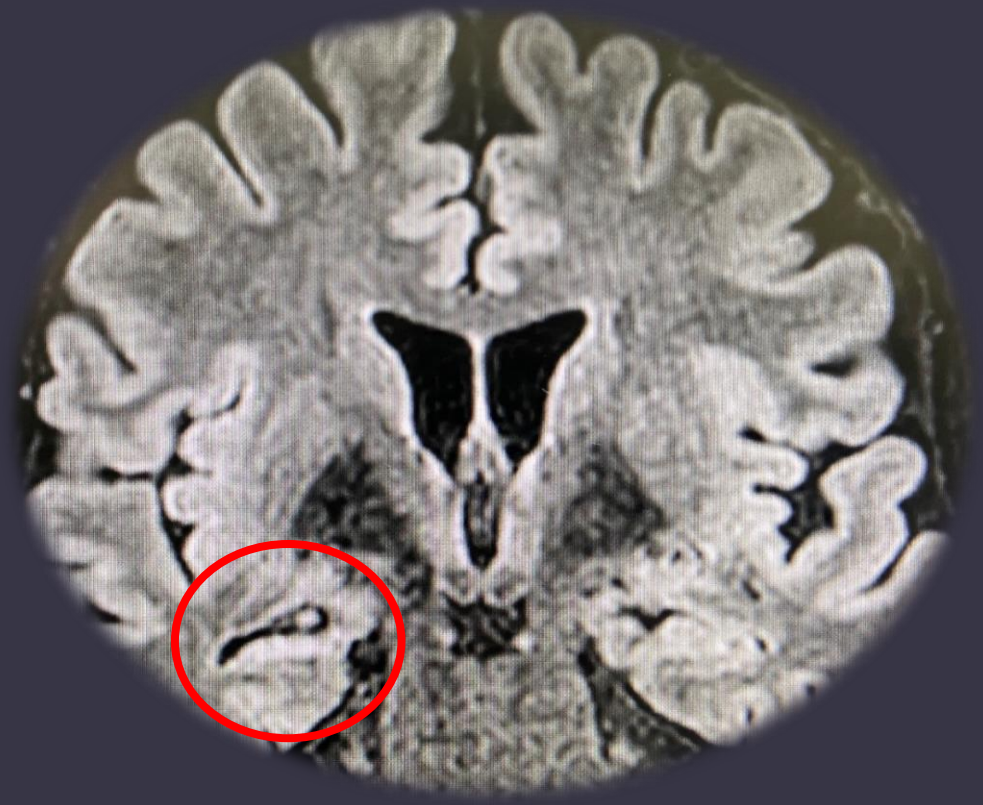
ICTAL EEG



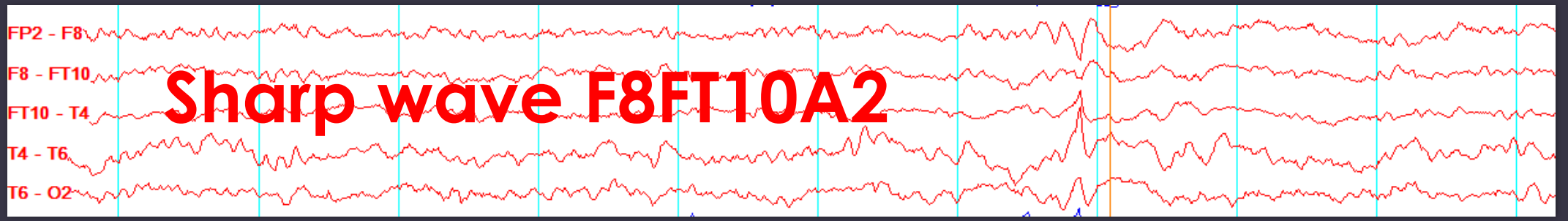
Curr Treat Options Neurol. 2020;22(1):1.

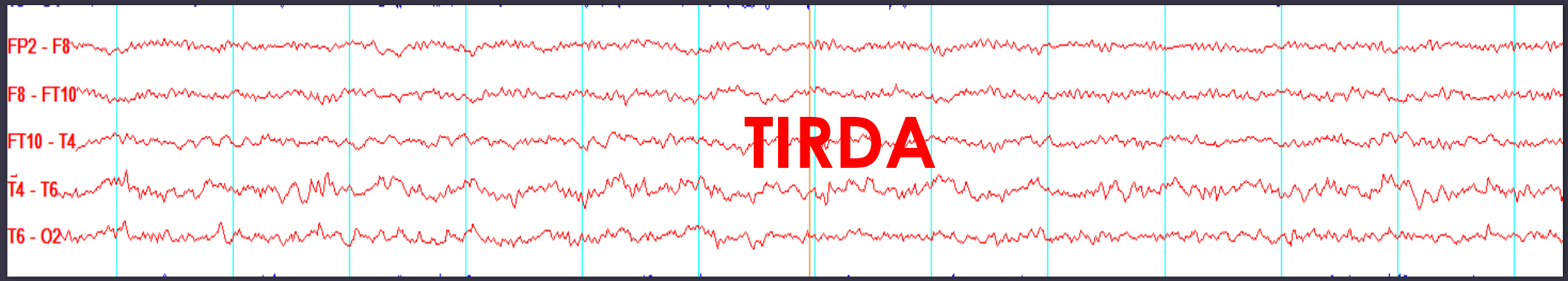
Case 47 y/o man refractory focal epilepsy

- Seizure onset 18 y/o
- Seizure type
  - GTC
  - Aura with focal impaired awareness several minutes and postictal confusion
  - Autonomic aura: palpitation for several seconds

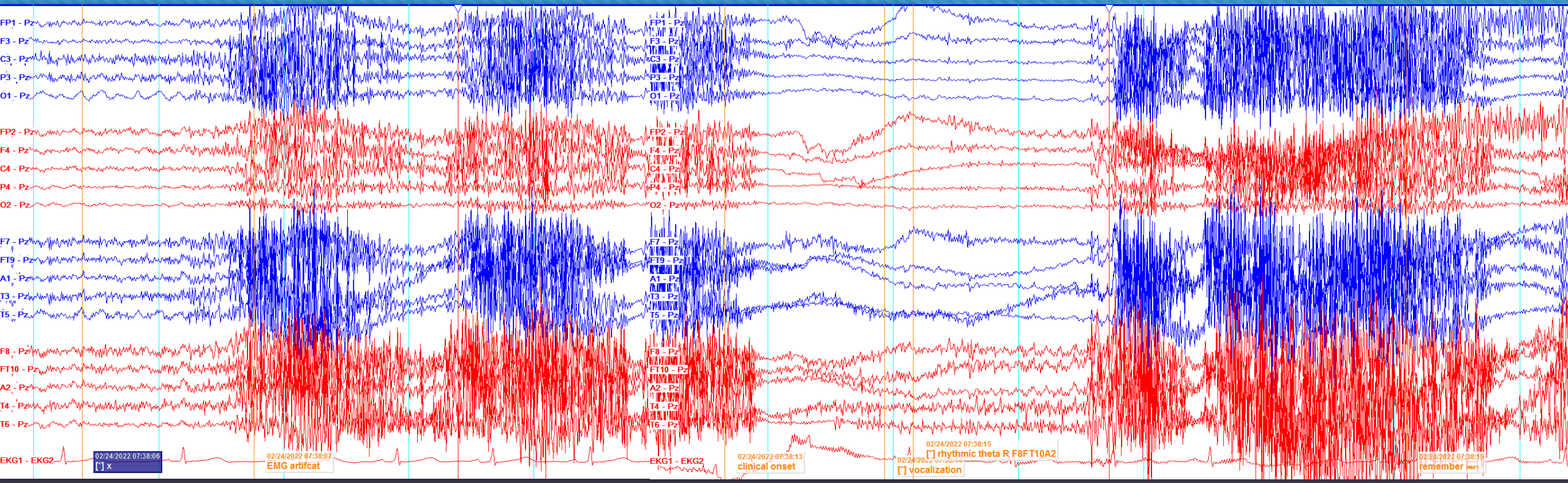


Interictal EEG



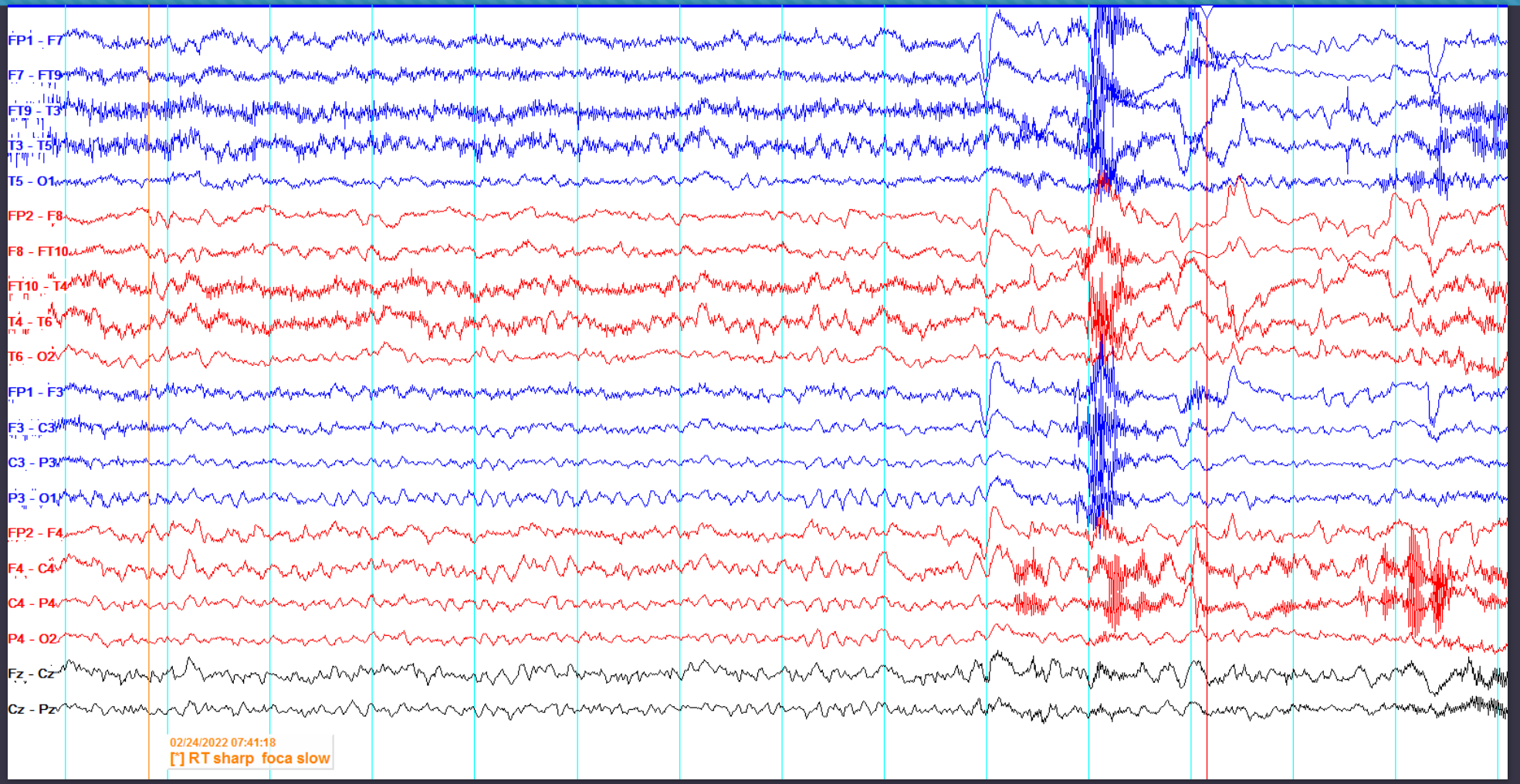


Ictal EEG: rhythmic theta F8FT10A2



Increased heart rate → Vocalization → Impaired awareness, oral automatism → No postictal aphasia

Postictal right temporal sharp and slow



Progression

- Standard right anteromedial temporal lobectomy
- Seizure free since surgery

Mesial temporal lobe epilepsy with hippocampal sclerosis

MTLE with HS

- Age at seizure onset is typically in adolescent and young adult
- Focal aware or impaired awareness seizures with semiological features referable to medial temporal lobe networks
- Imaging: hippocampal sclerosis
- Often drug resistance

Familial mesial temporal lobe epilepsy

FMTLE

- Typically onset in adolescence or adulthood (3-63 yr)
- Focal aware seizures with mTLE semiology
- Normal MRI or HS/atrophy
- FH of individuals with focal seizures arise from mesial temporal lobe
- Normal intellectual development, no neurological abnormalities
- Related gene: DEPDC5
- Favorable prognosis

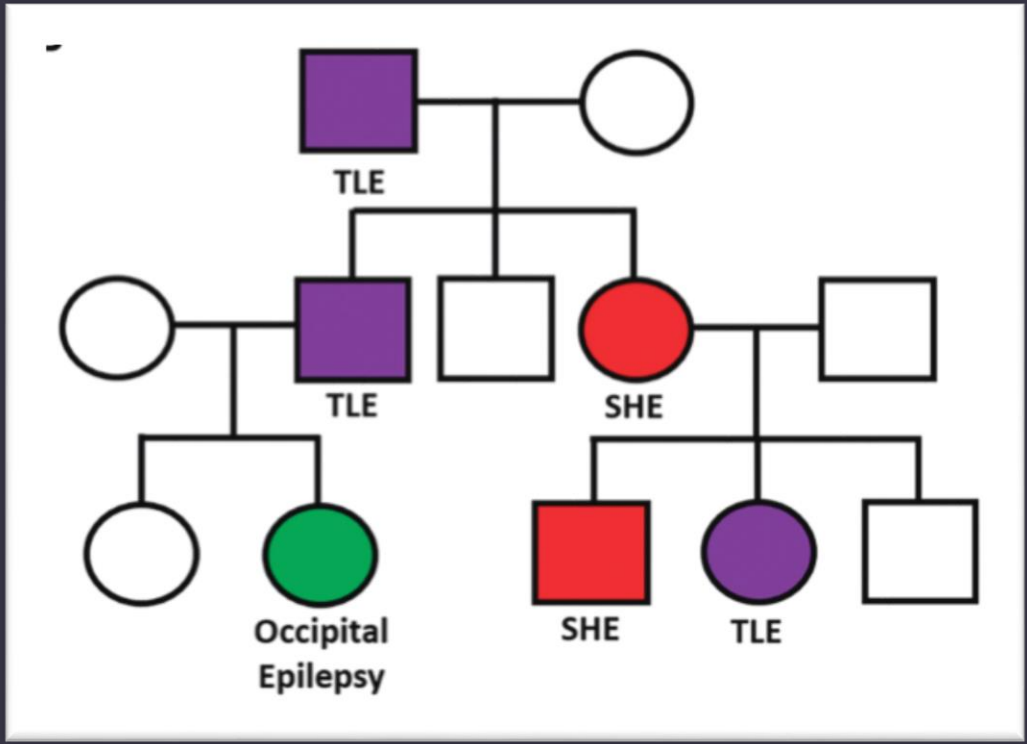
Epilepsy with auditory features

EAF

- Onset adolescence/adulthood
- Mostly sporadic, also ADEAF (related gene LGI1, RELN, MICAL1)
- Focal aware seizures with auditory symptoms and/or receptive aphasia
- Some patients have seizures precipitated by specific sounds
- Rarely may have focal to bilateral tonic–clonic seizures
- 1/3 are drug resistant
- MRI: normal or FCD

Familial focal epilepsy with variable foci

FFEVF



- Rare AD familial focal epilepsy syndrome
- **Focal seizures arising from different cortical regions (most common frontal or temporal) in different family members with variable severity**
- Related gene: TSC1, TSC2, DEPDC5, NPRL2, NPRL3
- Most cases are responsive to ASMs
- Patients with DRE and FCDII, epilepsy surgery may result in full remission

Continuum (Minneap Minn). 2022;28(2):339-362.

Syndrome	Onset (usual)	Clinical	Interictal EEG	Imaging
SHE	Second decade of life	From sleep, brief hyperkinetic or asymmetric tonic/dystonic motor seizures	Background interictal EEG is usually normal; focal (usually frontal) epileptiform abnormality can be seen	Normal, FCD, or acquired structural abnormality
FMTLE	Adolescence or adulthood	Typically, focal aware seizures with intense déjà vu and associated features, e.g., dreamy perceptions, fear or panic, slow motion, visual or auditory illusions, and autonomic manifestations	Background interictal EEG is usually normal or may show mild temporal slowing; temporal epileptiform abnormality can occasionally be seen	Normal, rarely hippocampal atrophy or increased T2 signal
FFEVF	First or second decade of life	Focal seizures, semiology dependent on focal cortical area involved in an individual, but constant in that individual	Background interictal EEG is usually normal; focal epileptiform abnormality can be seen	Normal or FCD
EAF	Second or third decade of life	Sensory seizures (auditory), cognitive seizures with receptive aphasia	Background interictal EEG is usually normal; focal (usually temporal) epileptiform abnormality can be seen	Usually normal, although posterior temporal FCD reported

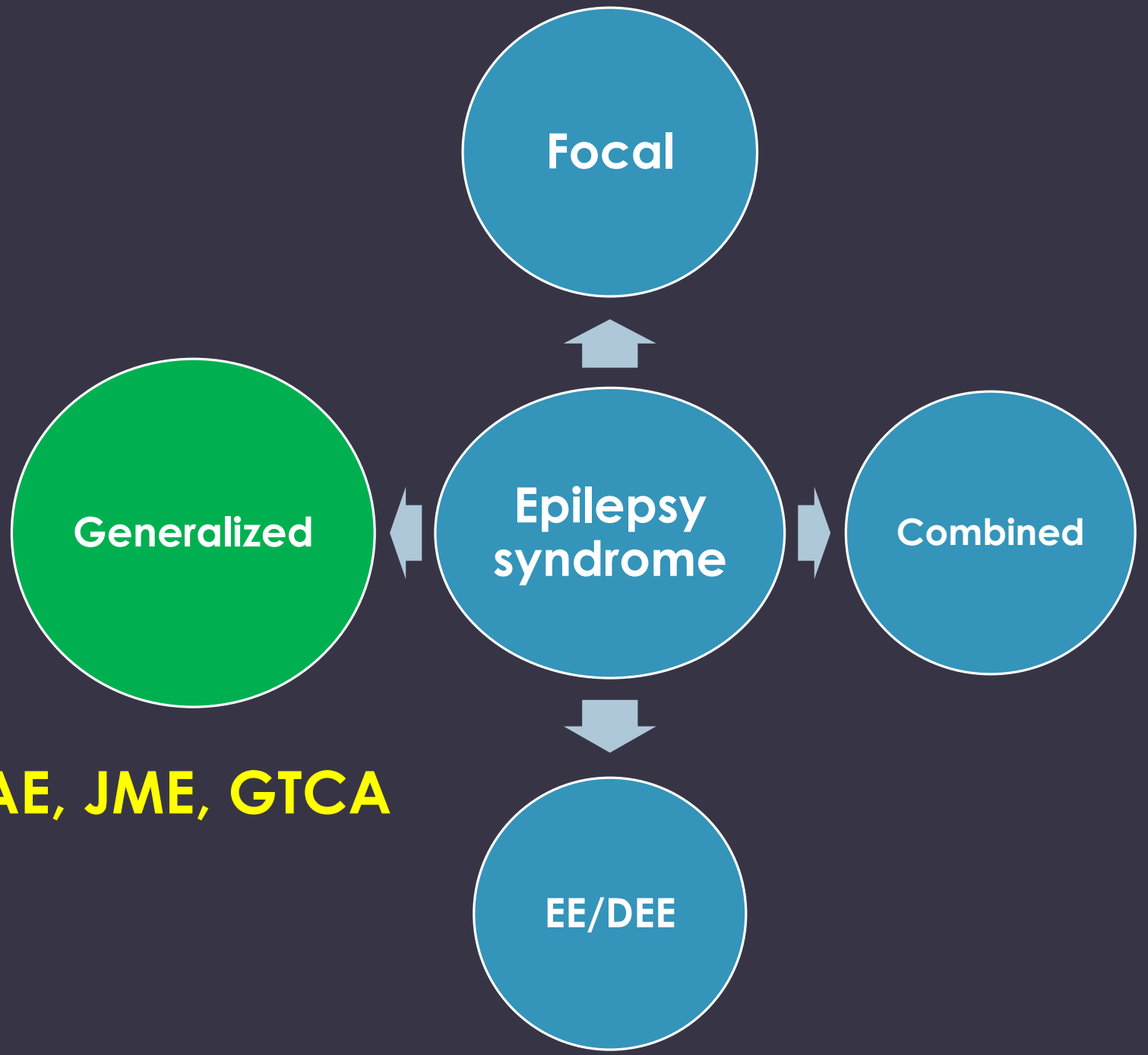
Abbreviations: EAF, epilepsy with auditory features; EEG, electroencephalogram; FCD, focal cortical dysplasia; FFEVF, familial focal epilepsy with variable foci; FMTLE, familial mesial temporal lobe epilepsy; SHE, sleep-related hypermotor (hyperkinetic) epilepsy.

Epilepsia. 2022;63:1443–74.

Focal epilepsy syndrome	Related genes
SHE	*CHRNA4, CHRNA2, CHRNB2, DEPDC5, KCNT1, NPRL2, NPRL3, PRIMA1*
FMTLE	*DEPDC5* (Mendelian inheritance is rare, FMTLE typically displays complex inheritance)
FFEVF	*TSC1, TSC2, DEPDC5, NPRL2, NPRL3*
EAF	*LGI1, RELN, MICAL1*

Abbreviations: EAF, epilepsy with auditory features; FFEVF, familial focal epilepsy with variable foci; FMTLE, familial mesial temporal lobe epilepsy; SHE, sleep-related hypermotor (hyperkinetic) epilepsy.

Epilepsia. 2022;63:1443–74.



JAE, JME, GTCA

Generalized epilepsy syndrome

GGE in adolescent and adult

Childhood absence epilepsy

Juvenile absence epilepsy

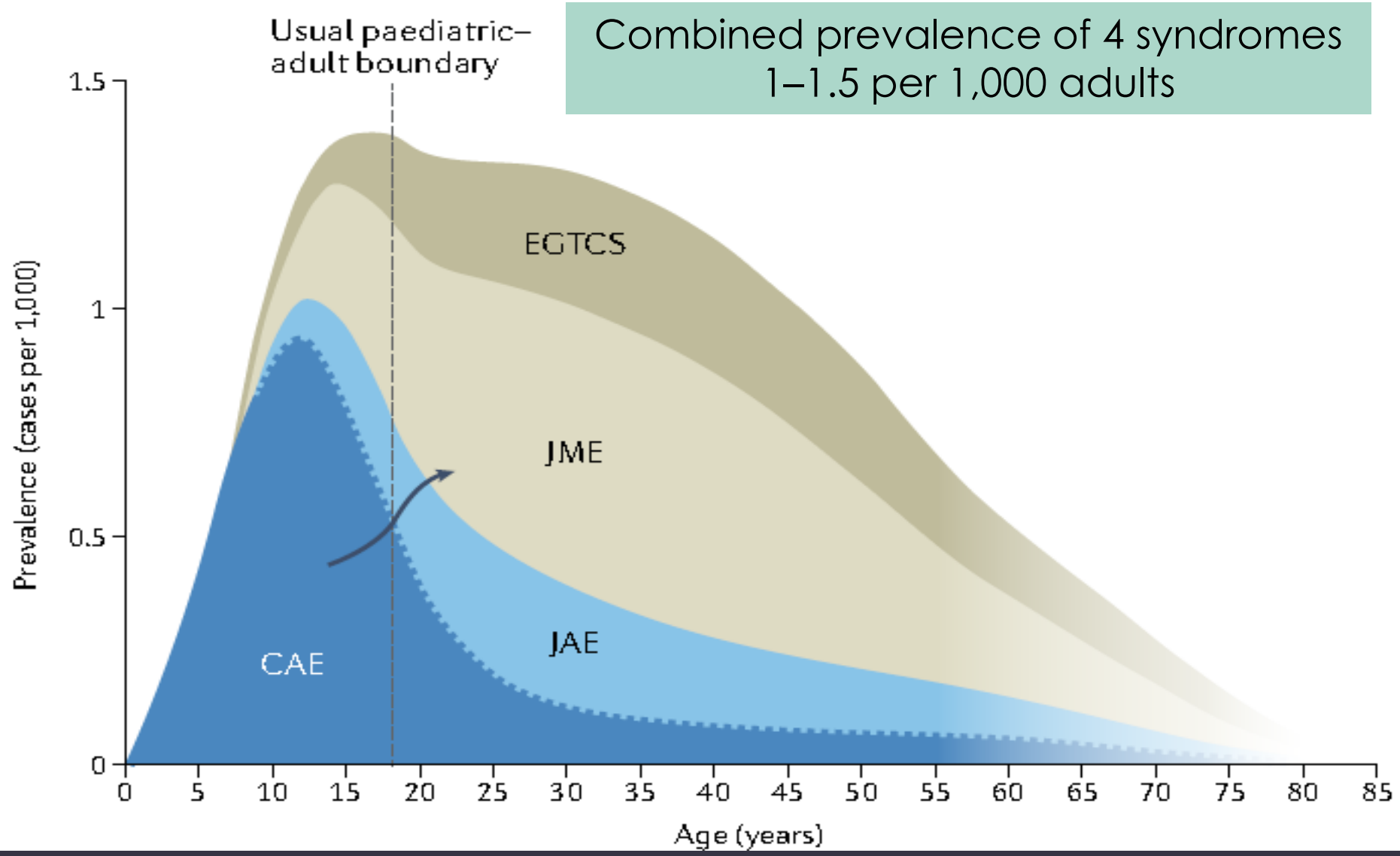
Juvenile Myoclonic Epilepsy

Epilepsy with Generalized Tonic-Clonic Seizures Alone

- **Clinical**: age at onset, seizure types, relationship of seizures to sleep–wake cycle, family history
- **EEG**: Normal background, interictal generalized epileptiform discharges

Prevalence of active GGE syndromes across the lifespan

Combined prevalence of 4 syndromes
1–1.5 per 1,000 adults



Nat Rev Neurol. 2022;18(2):71–83.

GGE

- Functional imbalance of bilateral frontothalamocortical networks → seizure & cognitive impairment
- Neuropsychological deficits and psychiatric traits
  - Poorer academic performance
  - Dysfunctional social cognition
  - Personality disorder: impulsivity, emotional instability
  - Affective & anxiety disorder
- Genetic
  - Polygenic modes of inheritance (combinations of multiple gene alterations)

    ** esp. GABA receptor subunit **

Genetic defect in some GGE

Gene	Locus	Protein	Phenotype
GABRG2	5q31–33	$GABA_A$ receptor γ_2-subunit	CAE and FS
GABRA1	5q34–35	$GABA_A$ receptor α_1-subunit	JME, CAE
CLCN2	3q26	ClC-2 voltage-gated Cl channel	CAE, JAE, JME, EMA
EFHC1	6p11–12	Myoclonin1	JME
CACNA1H	16p13.3	T-type Ca^{2+} channel α_{1H}-subunit	CAE
CACNB4	2q22–23	Ca^{2+} channel β_4-subunit	JME, JAE
CACNA1A	19p13	P/Q-type Ca^{2+} channel α_{1A}-subunit	CAE with ataxia
RORB	9q21.13	Transcriptional factors	Eyelid myoclonia with Ab
List of loci from genome-wide linkage analyses of small multiplex families			
1p, 2q36, 3q26, 5q12-q14, 5q34, 6p21, 8q24, 8p, 9q32–33; 10q25–26, 10p11, 11q13, 13q22–31, 14q23, 15q14, 18q21, 19q13			IGE, CAE, JME
List of CNVs, risk factors of IGE			
Microdeletions: 15q13.3, 15q11.2, 16p13.11			IGE, JME
Duplication: 1q21.3			Early onset CAE

CAE, childhood absence epilepsy; *EMA*, myoclonic–astatic epilepsy; *FS*, febrile seizures; *IGE*, idiopathic generalized epilepsy; *JAE*, juvenile absence epilepsy; *JME*, juvenile myoclonic epilepsy.

Guerrini R. Handb Clin Neurol. 2019;161:3-15.

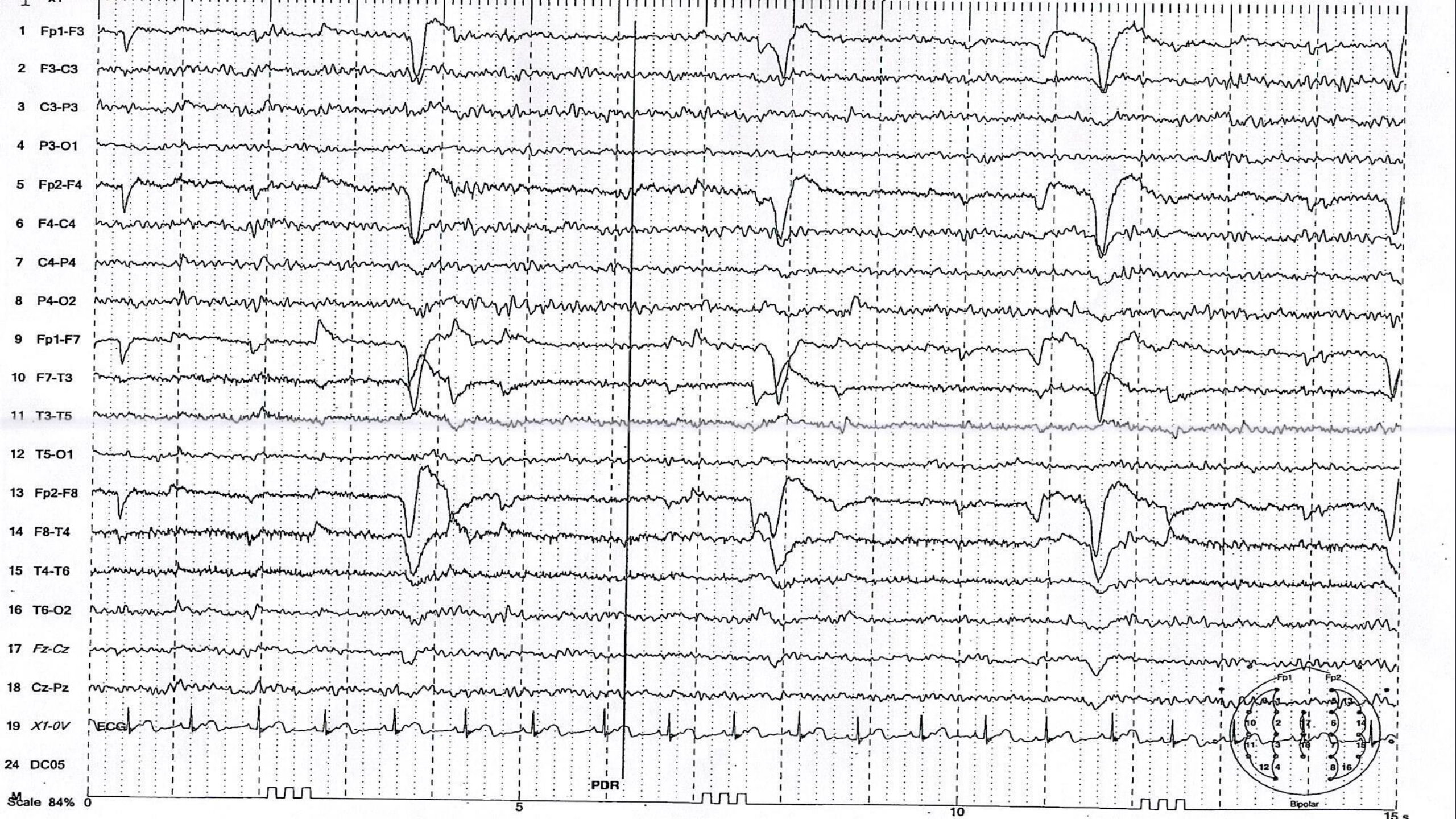
Juvenile Absence Epilepsy

JAE

- Age of onset 9-13, arnge 8-20 years
- Absence seizure, less than daily
- GTCs > 90% shortly after absence seizure
- Triggers: sleep deprivation, alcohol, HV
- Normal development and cognition (+/-ADHD, LD)

JAE EEG

- Interictal
  - Generalized spike/polyspike, may show focal abnormality, asymmetrical burst of spike/polyspike waves
  - SW: less organized, more fragmented than CAE
- Ictal
  - Generalized 3-4 Hz spike/polyspike waves elicit by hyperventilation
  - Absences may have a faster rhythm of GSW at 4–5Hz, esp. at onset
- Photoparoxysmal response 25%


1 Fp1-F3
2 F3-C3
3 C3-P3
4 P3-O1
5 Fp2-F4
6 F4-C4
7 C4-P4
8 P4-O2
9 Fp1-F7
10 F7-T3
11 T3-T5
12 T5-O1
13 Fp2-F8
14 F8-T4
15 T4-T6
16 T6-O2
17 Fz-Cz
18 Cz-Pz
19 X1-0V
ECG
24 DC05
M
Scale 84%
0
5
10
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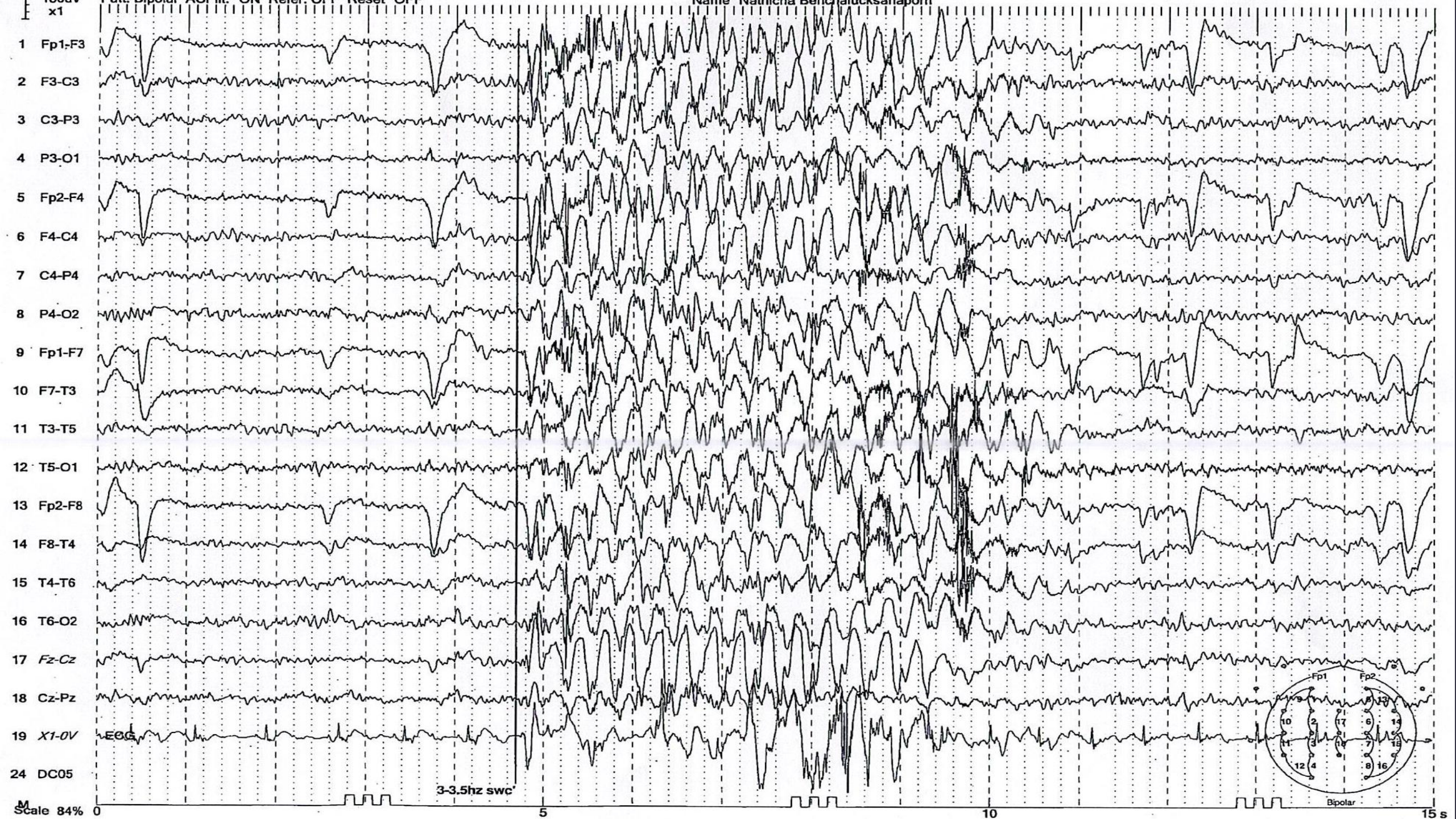
PDR
Fp1
Fp2
Bipolar


Name: Nathicha Benchalucksanaporn
1 Fp1-F3
2 F3-C3
3 C3-P3
4 P3-O1
5 Fp2-F4
6 F4-C4
7 C4-P4
8 P4-O2
9 Fp1-F7
10 F7-T3
11 T3-T5
12 T5-O1
13 Fp2-F8
14 F8-T4
15 T4-T6
16 T6-O2
17 Fz-Cz
18 Cz-Pz
19 X1-0V
ECG
24 DC05
3-3.5hz swc'
Scale 84%
0
5
10
15 s
Fp1
Fp2
Bipolar

	CAE	JAE
Age at onset	2 to 13 years (4-10)	8-20 years (9-13)
Absence seizure	More frequent (10s-100s/day) Cluster Shorter duration 3-20s Severe loss of awareness	Less frequent (1-10/day) Sporadic Longer duration 5-30s Less complete impaired awareness
GTCs	Less common	More common
EEG	Bilateral, 3Hz(2.5-4) synchronous, symmetrical SW Irregular generalized SW uncommon OIRDA 21%	Generalized spike/PSW 3-5.5 Hz Irregular generalized SW more common

JAE

- Typically pharmacoresponsive syndrome
  - ETX, VPA, LTG
- Avoided PHT, CBZ, GBP, pregabalin, vigabatrin
- Lifelong requirement for medication expected

Juvenile Myoclonic Epilepsy

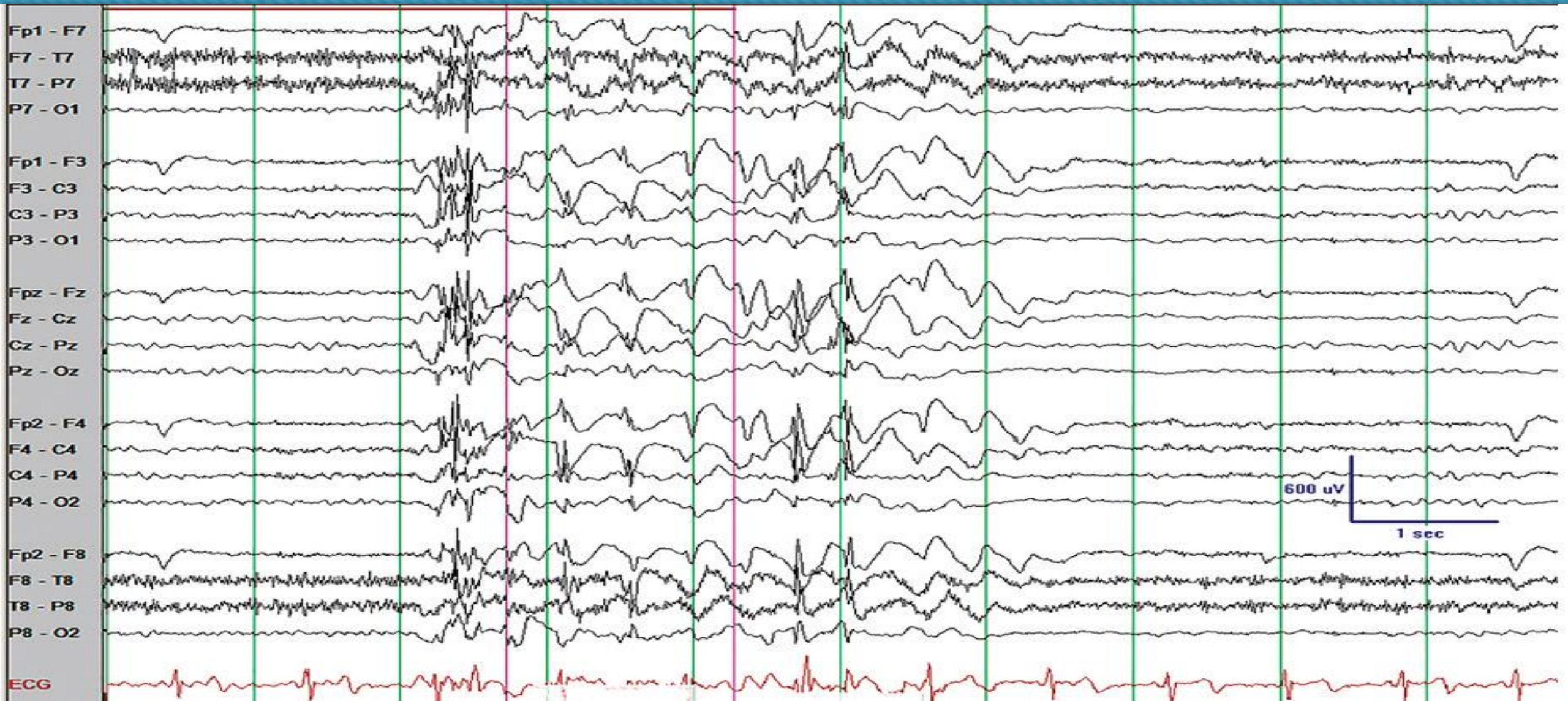
JME

- **5% to 10% of all epilepsy**, onset 10-24 years (8-40)
- Most constant clinical feature is **myoclonic seizures**
  - Predominantly involving upper extremities
  - Generally bilateral
  - Esp. upon awakening, within 2 hour after awakening
  - 25% asymmetrical
- Majority develop **GTCs**, usually shortly after awakening
  - Often preceded by series of myoclonic seizures → **myoclonic-tonic-clonic seizure**
- At least 1/3 experience **absence seizures**

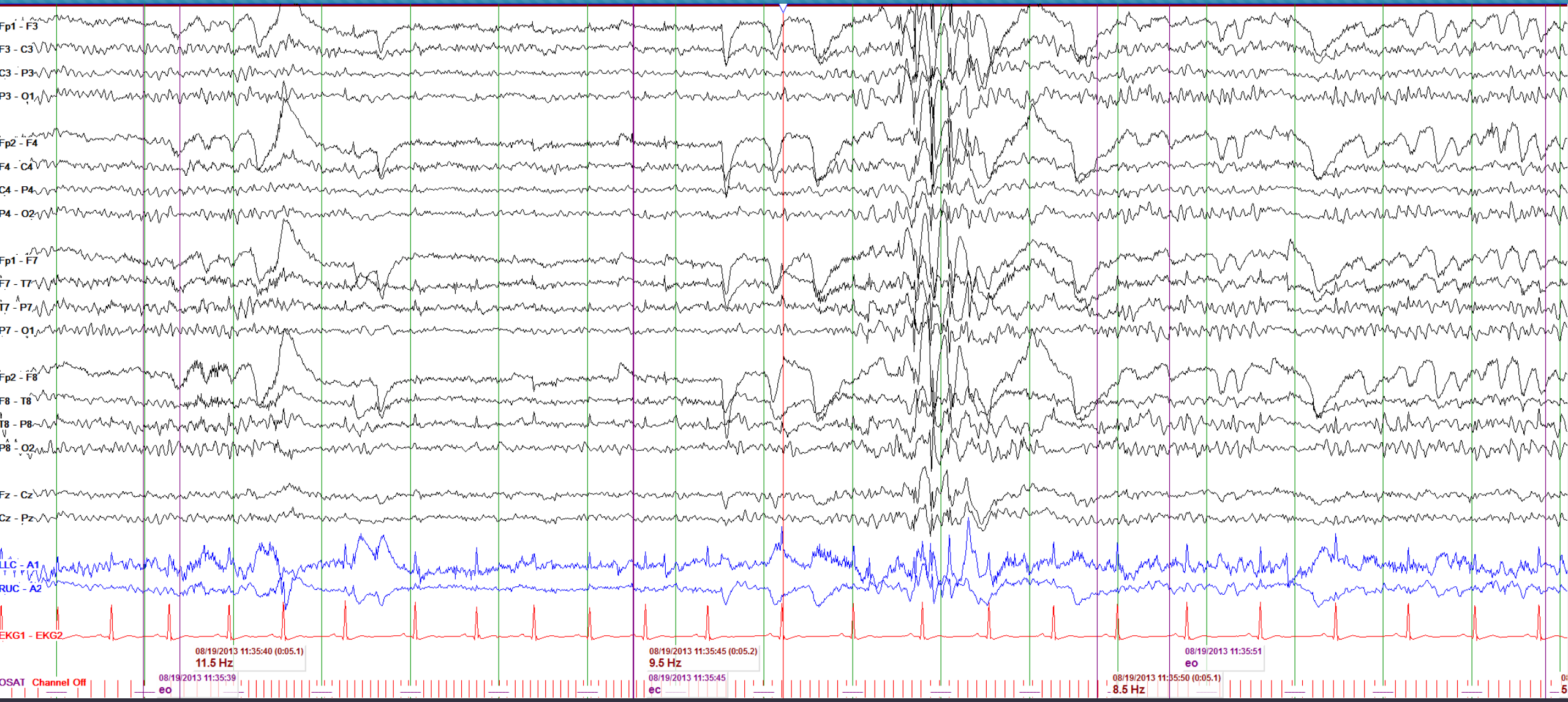
JME: EEG

- Normal EEG background
- Abrupt paroxysmal generalized 4-6 Hz spike or PSW (fast spike and wave)
- +/- Focal spike
- Potentiated by sleep/sleep deprivation, alcohol use, menses, photic stimulation (>1/3 PPR, typically at 10-30Hz PS)

Developmentally normal 16-year-old boy who presented with single early morning GTCs
History of myoclonus, exacerbated by sleep deprivation
EEG showed generalized polyspike and spike-wave discharge



Photoparoxysmal response



JME management

ASMs

- VPA is efficacious
  - Avoid in women of child-bearing age
- LEV, LTG may be effective
- Myoclonic seizure worsened by CBZ,OXC, PHT, GBP, VGB

Counselling

- Lifestyle modification
- Medication compliance
- Avoid alcohol & illicit drug
- Avoid sleep deprivation
- Avoid flashing lights (40-90% photosensitive)

JME prognosis

- Seizure freedom is achievable: Life long treatment?
  - 35% ongoing seizure despite in ASMs
  - **22% seizure free after discontinuation ASMs**
  - With advancing age → increased number of patient remain seizure free

Eur. J. Neurol 2018;26:856-64.

Epilepsia 2017;58,1244–50. Seizure 2014;23,344–8.

Epilepsy with Generalized Tonic-Clonic Seizures alone

Epilepsy With GTCs Alone

- Typical age of onset of 16 years (6-28)
- GTCs peak in early morning
- Small peak upon falling sleep/naps or in the evening
- Triggers: sleep deprivation, photic stimulation, stress, alcohol
- EEG: 4-5 Hz generalized spike/polyspike-and-slow-wave
- Pharmacoresponsive, but lifelong predisposition to seizure expected

Summary clinical presentation of GGE

Table 1 | **Typical clinical presentations of GGE syndromes**

Syndrome	Approximate proportion of adults with GGE (%)	Seizure types	Typical age at onset (peak) (years)	Sex ratio
Childhood absence epilepsy	15	Absence (100%)[a] Tonic–clonic (20%)	4–12 (6)	F > M
Juvenile absence epilepsy	15	Absence (100%)[b] Tonic–clonic (90%)[c]	8–20 (14)	F = M
Juvenile myoclonic epilepsy	45	Myoclonic (100%) Absence (30%)[b] Tonic–clonic (90%)[d]	6–25 (14)	F ≥ M
Epilepsy with generalized tonic–clonic seizures alone	25	Tonic–clonic (100%)	5–40 (17)	F = M

Overlaps:
CAE & JAE

Phonotypic inconclusive in about 1/5

Evolving:
CAE → JME

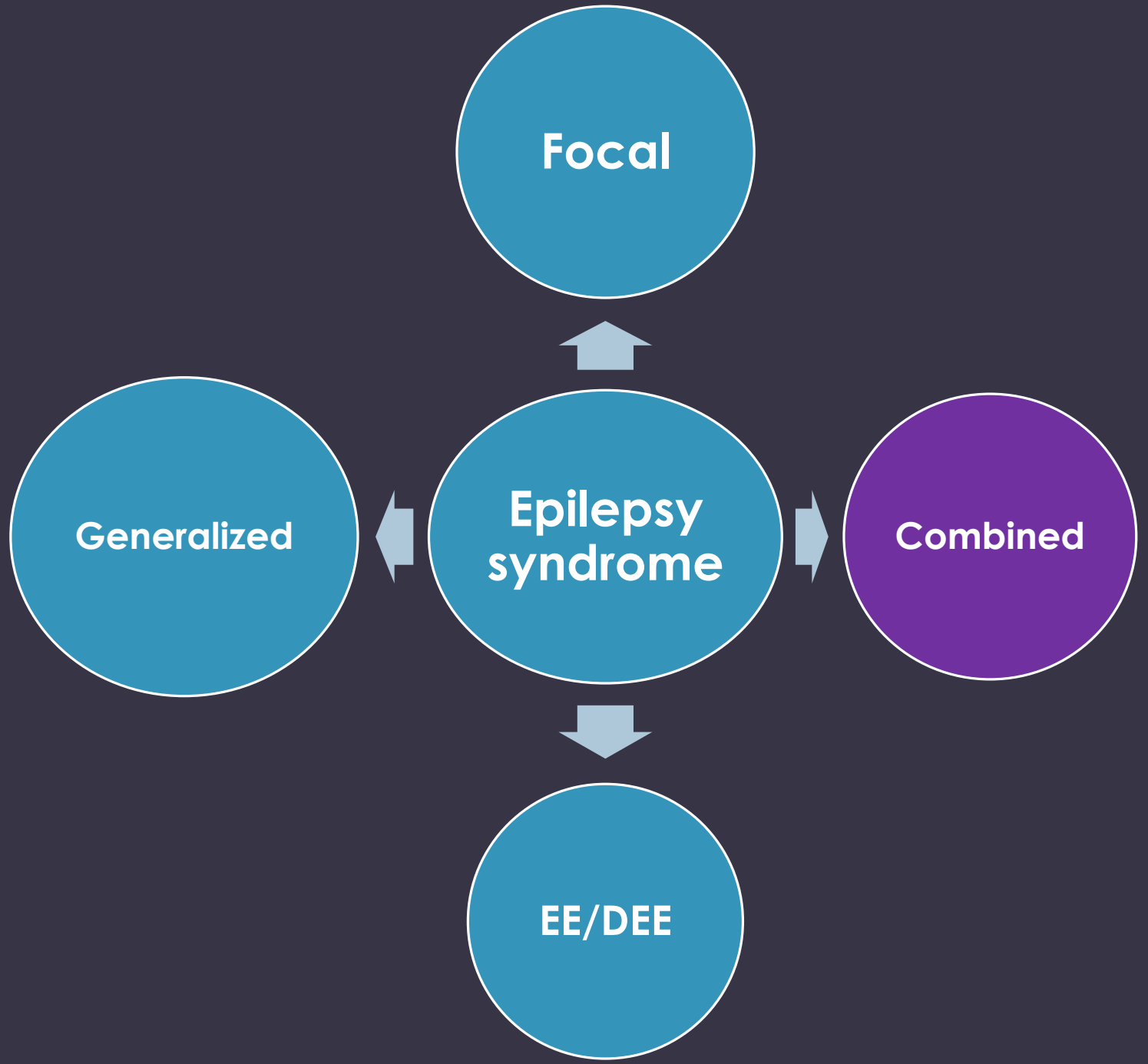
Nat Rev Neurol. 2022;18(2):71–83.

Prognosis GGE

- CAE
  - Very good prognosis, 80-90% remission by age 12
  - Less favorable prognosis: early and late onset (<4 and >10 years), initial drug resistance, photosensitivity
- JAE
  - Achieve seizure freedom (>80%) with appropriate treatment
  - Epilepsy is usually lifelong
  - 1/5 frequent, sometimes refractory absence and GTCs
- JME
  - Controllable with appropriate therapy in 90%
  - Considered lifelong epilepsy, tendency for relapse after drug withdrawal

GGE prognosis update

- Successful pharmacological treatment without AEs are less likely than previously thought
  - Seizure freedom → VPA 70%, LTG or LEV 40-50%
- CAE can persist until older age in 20%
- JME can resolve after adolescence

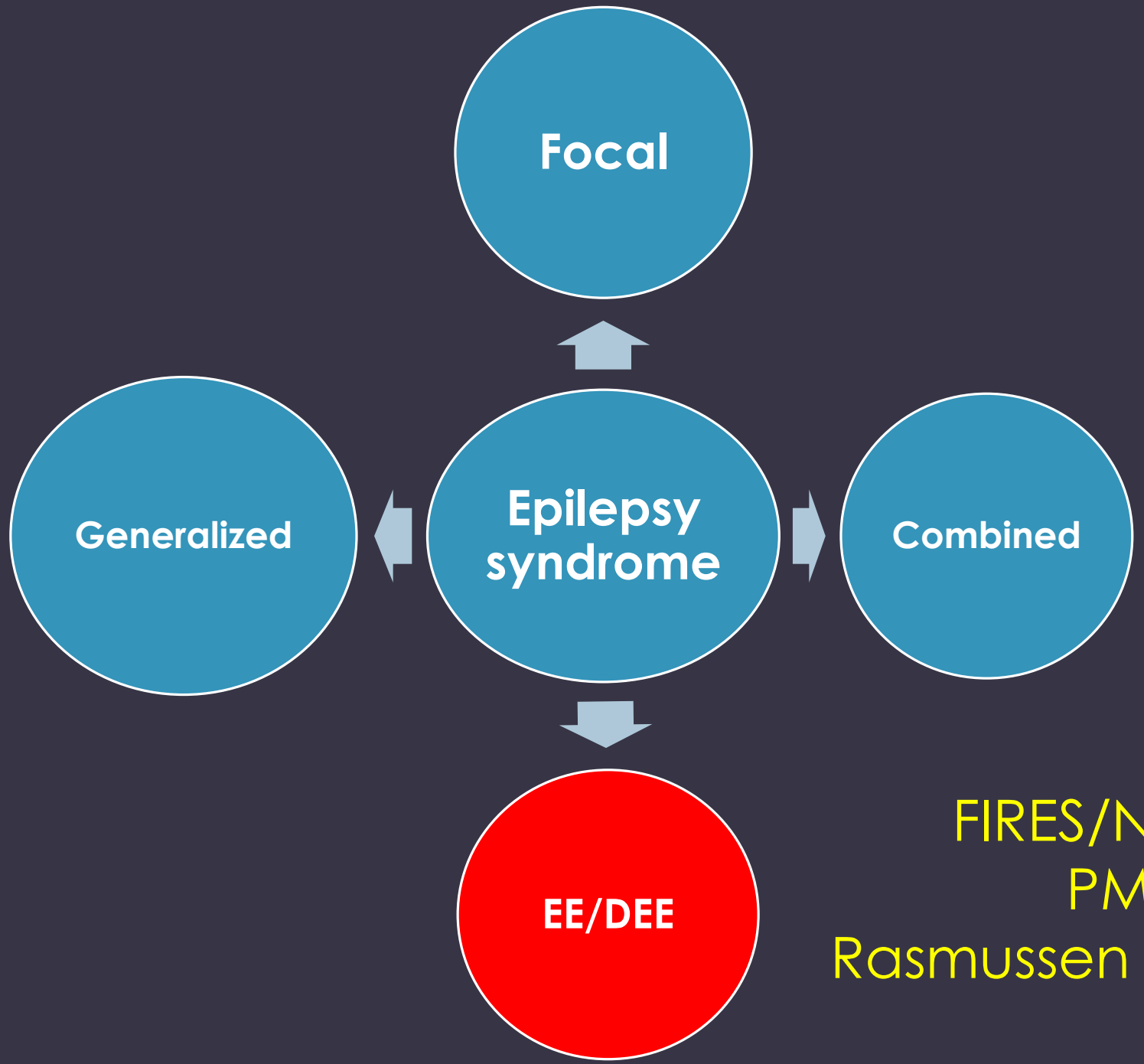


EwRIS

Epilepsy with reading induced seizure

EwRIS

- Rare combined generalized and focal epilepsy syndrome
- Typically in late teens(median=17.5 years, range = 10–46 years)
- Reflex myoclonic seizures affecting orofacial muscles triggered by reading +/- → GTC
- Triggers: reading, language related task (talk, writing, making complex decision)
- Developmental, neuro exam, MRI: normal
- Favorable prognosis



FIRES/NORSE
PME
Rasmussen syndrome

New onset refractory status epilepticus (NORSE)
&
Febrile infection related epilepsy syndrome (FIRES)

New-onset refractory status epilepticus

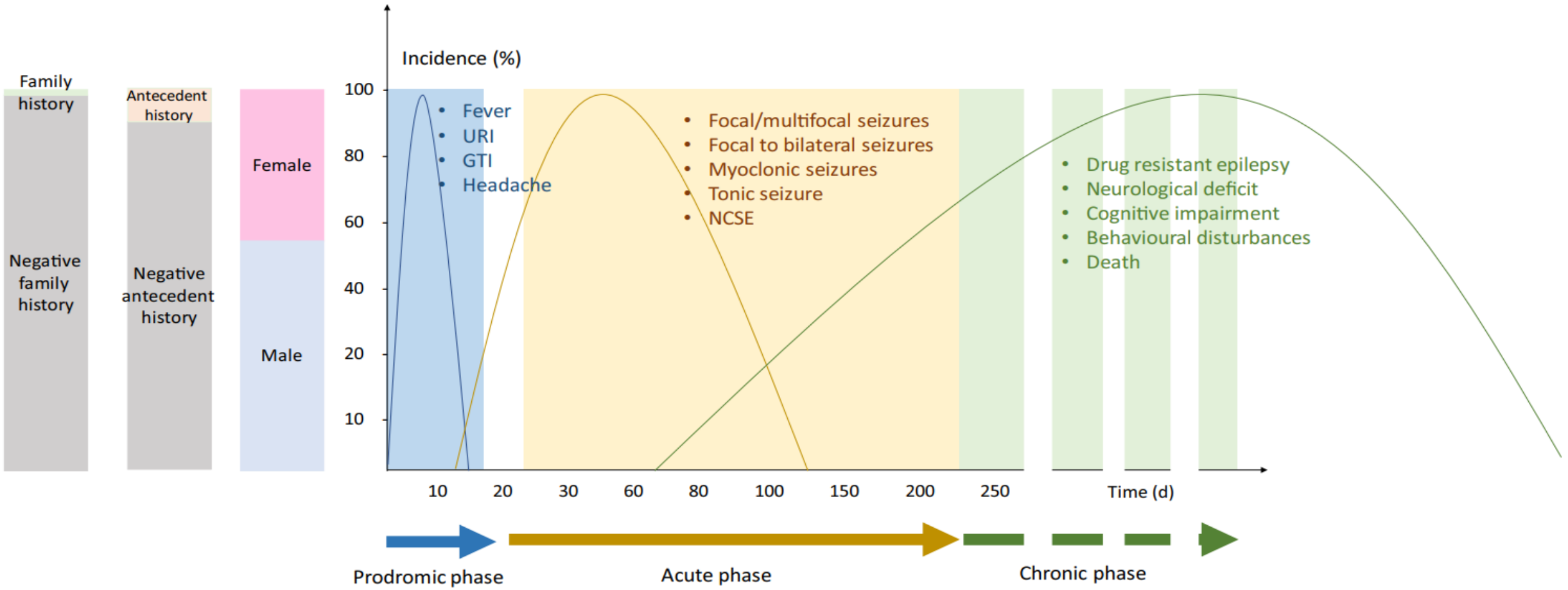
- Rare **clinical presentations** characterized by **de novo onset of RSE** in patient without active epilepsy and without clearly identifiable acute or active structural, toxic, or metabolic cause
  - *Diagnosis after initial workup rules out obvious causes of RSE, usually takes 48–72 h*

- FIRES is considered a subcategory of NORSE, diagnosis requires prior **febrile infection starting between 2 weeks and 24 hours** before onset of RSE

NORSE & FIRES

- Mainly affect school-age children and young adults
- **Acute phase**: high seizure burden, lasts 1–12 weeks
- **Chronic phase**: drug-resistant multifocal epilepsy and intellectual disability or learning difficulties

Clinical findings of FIRES & NORSE



Developmental Medicine & Child Neurology 2020,62: 897–905.

Etiology assessment

Etiology

Unknown 50%

Infection 10%

Inflammatory, autoimmune 40%

Genetic: rare
Mitochondrial, POLG1, SCN1A, PCDH19, CADASIL

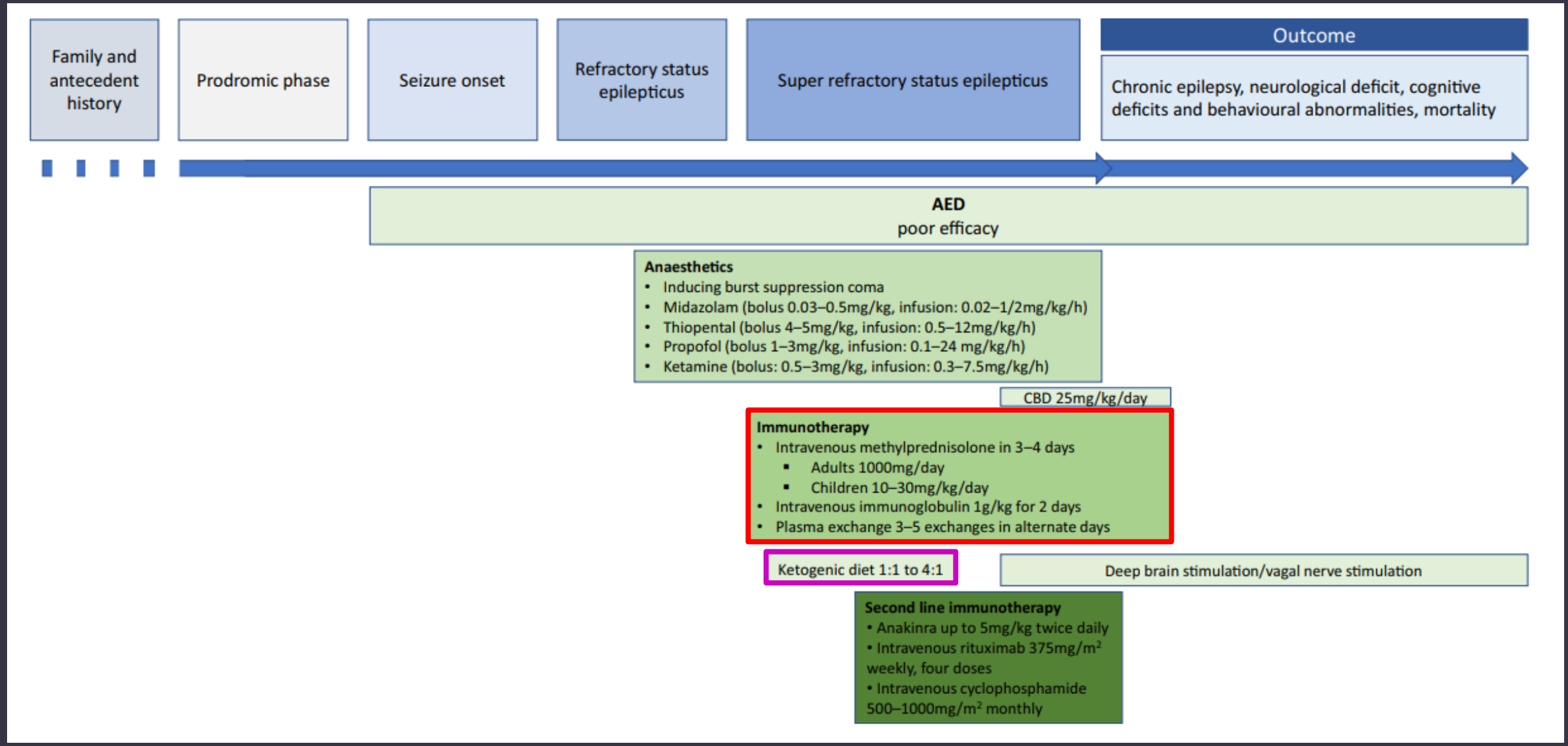
Seizure 2019;68:72-8.

Table 1 – Aetiological assessment. Adapted from [14,40].

Recommended in all patients	
MRI brain with contrast angiography and venography	
Blood and serum analysis	Standard biological assessment
	Autoimmune antibody panel: ANA, ANCA, anti-thyroid, anti-neuronal surface antigens, onconeuronal antibody panel
	VDRL, HIV 1-2, bacterial and fungal cultures
	Bacterial serologies: Chlamydia pneumoniae, Bartonella henselae, Mycoplasma pneumonia, Coxiella burnetii, Shigella sp. and Chlamydia psittaci
Nasopharyngeal swab	Respiratory viral DFA panel; SARS-CoV2 PCR
Gastrointestinal pathogens	Multiplex PCR
CSF	Cell counts, protein, and glucose, immunoelectrophoresis
	Bacterial and fungal stains and cultures including *Mycobacterium tuberculosis*
	RT-PCR for HIV, PCR for HSV1-2, VZV, EBV
	PCR for *Chlamydia pneumoniae*, *Bartonella henselae*, *Mycoplasma pneumonia*, *Coxiella burnetii*, *Shigella* sp.
	VDRL, Lyme
	Paraneoplastic and autoimmune epilepsy antibody panel
EEG	
Immunocompromised patients	
Serum analysis	Serology for cryptococcus species, *Histoplasma capsulatum*, *Toxoplasma gondii*
CSF	Stain for fungi, PCR for *Toxoplasma gondii*, JC Virus, CMV, HHV6, parvovirus ± West Nile Virus
Risk of exposure to specific pathogens according to geographical factors	
Oncological screening	
Serum analysis	Cancer serum markers
CSF	CSF cytology and flow cytometry
CT chest-abdomen-pelvis, pelvic or scrotal ultrasound, pelvic MRI, mammogram whole body PET CT	
Screening for inborn error of metabolism and mitochondrial disorders	
Ammonia, acute porphyria screen, LDH, urine analysis	
Plasma and CSF lactate, pyruvate, muscle biopsy	
Genetic screening	
Panel, whole exome, CGH array, mitochondrial genome sequencing	
Brain biopsy	

Rev neurol (Paris). 2022;178:74 – 83.

Treatment of FIRES & NORSE



Developmental Medicine & Child Neurology 2020,62: 897–905.

Rasmussen syndrome

Rasmussen syndrome

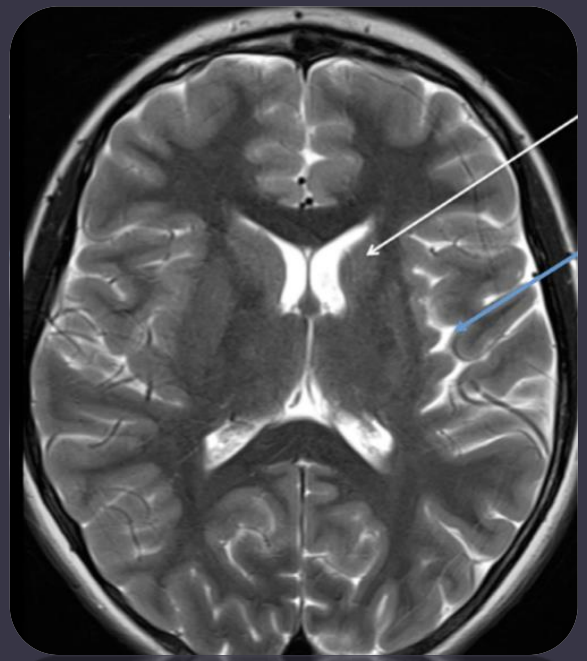
- Rare chronic neurological disorder, characterized by unilateral inflammation of cerebral cortex, drug-resistant epilepsy, and progressive neurological and cognitive deterioration
- Typical age of onset at 1–10 years (median 6 yrs)
- 10% adolescent and young adult
  - Clinical course in adolescent and adult usually slower and less severe final deficits

Rasmussen syndrome: Three stages

- **Initial prodromal phase (lasting months to years)**
  - Infrequent seizures and mild hemiparesis
- **Acute phase (lasting months to years)**
  - Increasingly frequent seizures, at times with EPC, progressive hemiparesis, hemianopia, cognitive, and language deterioration
- **Chronic phase**
  - Permanent stable hemiparesis and other neurological disabilities, continued seizures (less frequent)

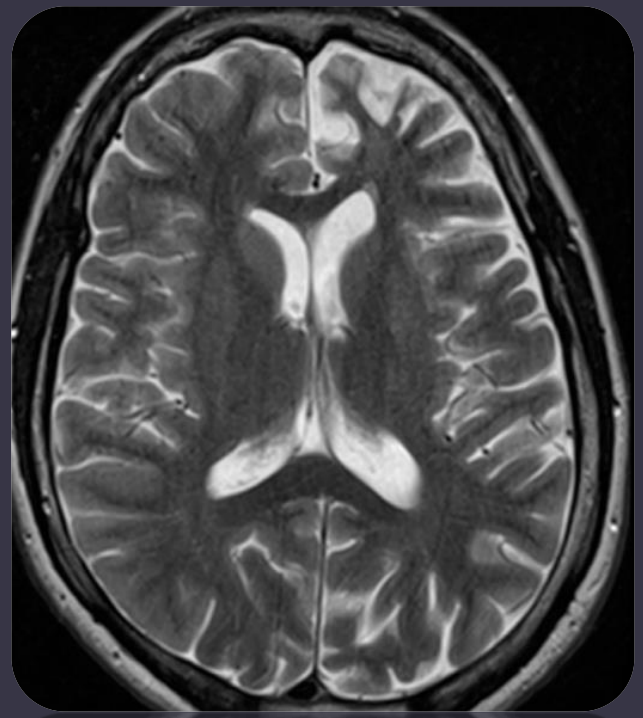
Progressive hemispheric atrophy ‘Fronto-insular predilection’

Atrophy of head of caudate with subtle loss of volume of left insular region



Interval 8 years

Increased atrophy of left hemisphere



Epilepsia. 2022;63:1443–74.

Rasmussen syndrome

- CSF: normal, mild pleocytosis, mild elevated protein, oligoclonal band
- EEG: Unihemispheric slowing w/w/o epileptiform activity and unilateral seizure onset
- Treatment: Medical therapy → Hemispheric disconnection surgery or hemispherectomy (only cure for seizure)

Progressive myoclonus epilepsy

Key features

(1) Myoclonic seizure
(2) Progressive motor and cognitive impairment
(3) Sensory and cerebellar signs
(4) Abnormal background slowing on EEG, generalized spike/polyspike
(5) Prior normal development and cognition

Photosensitivity is common feature

Other features: ataxia, dysarthria, vision loss, hearing loss, neuropathy, myopathy

May be family history, AR inheritance in most cases, but can be sporadic

Severity and prognosis depend upon etiology

PME (common)

- Unverricht–Lundborg disease (ULD)
- Lafora disease
- Neuronal ceroid lipofuscinosis (NCL)
- Mitochondrial disorders (myoclonic epilepsy with ragged red fibers, POLG-related disorders, MELAS)
- Sialidosis

Key characteristic of etiologies of PME

PME type	Age at onset	Progression	Diagnosis
ULD	7–13 years	Slow cognitive and motor deterioration with stabilization in adulthood	Cystatin B (*EMP1*) expansion variations account for ~90% of cases worldwide
LD	6–19 years	Early rapid cognitive, vision, and motor deterioration; fatal approximately a decade after onset; focal seizures with visual symptoms are an early feature	Laforin (*EMP2A*) pathogenic gene variant in 70%, malin (*EMP2B*) pathogenic gene variant in 27%, no pathogenic variant found in 3%; Lafora bodies are seen in sweat duct cells or other tissues
CLN2	2–4 years	Initial speech delay and seizures, subsequently deterioration in cognition and motor skills, and then vision loss emerges at 4–6 years of age	*CLN2/TPP1* pathogenic gene variants; TPP1 enzyme activity is reduced; EEG can show a photoparoxysmal response at low (1–3 Hz) frequency; curvilinear bodies profile of lipofuscin accumulation in tissues (e.g., skin) or lymphocytes
CLN3	4–10 years	Rapidly progressing vision loss, with macular degeneration, optic atrophy ± retinitis pigmentosa; survival: late teens—30 years	*CLN3* pathogenic gene variants; fingerprint profile of lipofuscin accumulation in tissue (e.g., skin) or lymphocytes; lymphocytes are vacuolated
Adult onset NCL (type A)	11–50 years	Slow development of dementia and ataxia; visual impairment is not expected	*CLN6* pathogenic gene variants (pathogenic variants in *CTSD*, *PPT1*, *CLN3*, *CLN5*, *CTSF*, and *GRN* also reported); mixed type inclusions (fingerprint, curvilinear, rectilinear) in tissue (e.g., skin) or lymphocytes

Abbreviations: TPP1, tripeptidyl-peptidase 1; PME, progressive myoclonus epilepsies; MRI, magnetic resonance imaging; ULD, Unverricht–Lundborg disease; LD, Lafora disease; CLN, ceroid lipofuscinosis; NCL, neuronal ceroid lipofuscinosis; EEG, electroencephalogram.

Epilepsia. 2022;63:1443–1474.

Summary : Epilepsy syndrome of adolescence and adult

- Focal epilepsy syndrome
  - SHE, FMTLE, FFEVF, EAF, MTLE-HS
- Generalized epilepsy syndrome
  - IGE: JAE, JME, GTCA
- Combined generalized and focal epilepsy
  - EwRIS
- Epilepsy syndrome with DE and/or EE or with progressive neurological deterioration
  - NORSE & FIRES, RS, PME

- Detailed electro-clinical approach is a key to reach syndrome diagnosis
  - (Age at onset, seizure types, relationship of seizures to sleep–wake cycle, family history, EEG)
- Provide guidance on management and prognosis