Epilepsy Syndromes with Onset at a Variable Age

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Objectives

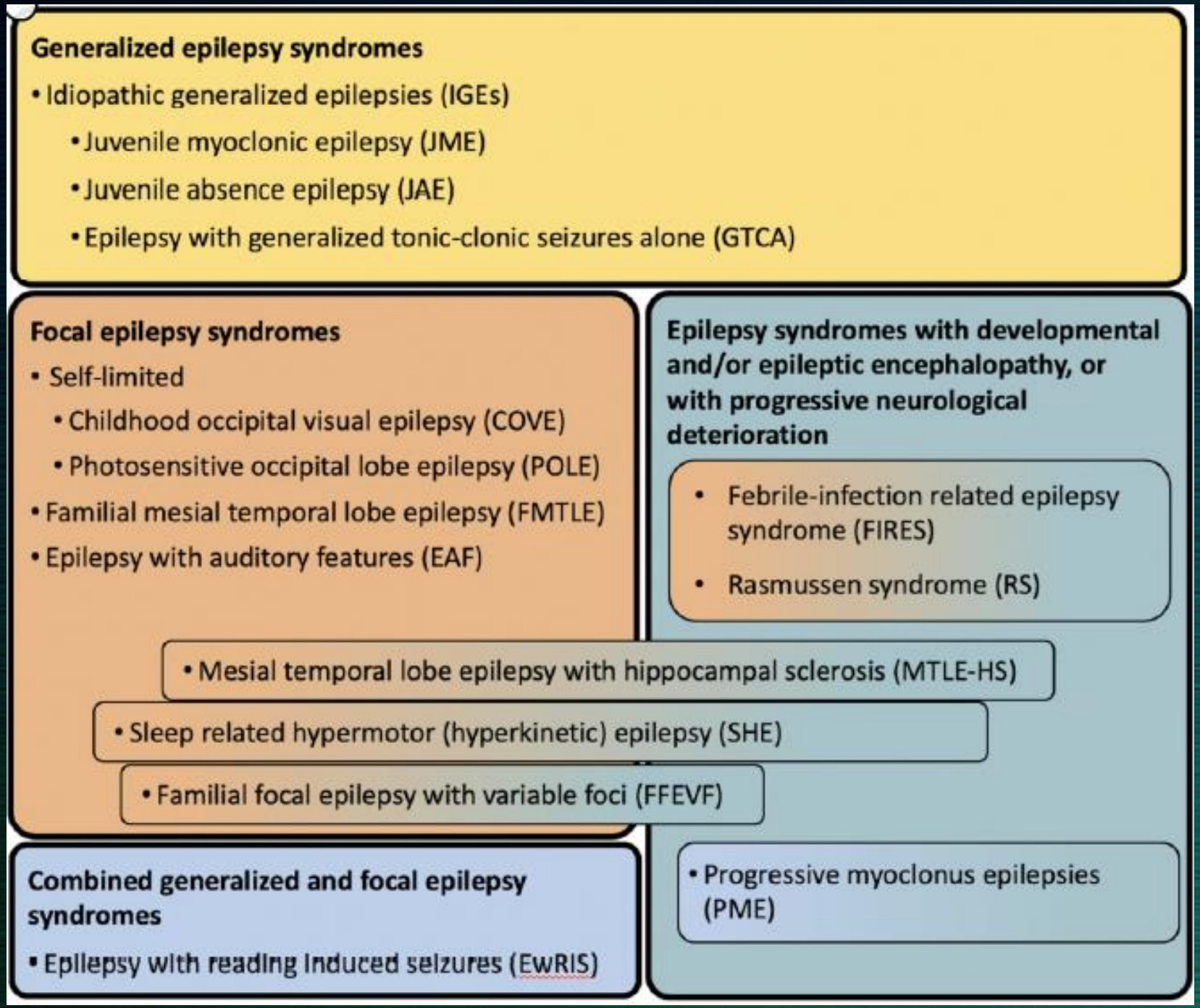
What is meant by “onset at a variable age”?

How do we classify these syndromes?

What are the diagnostic criteria for each syndrome?

At a Variable Age

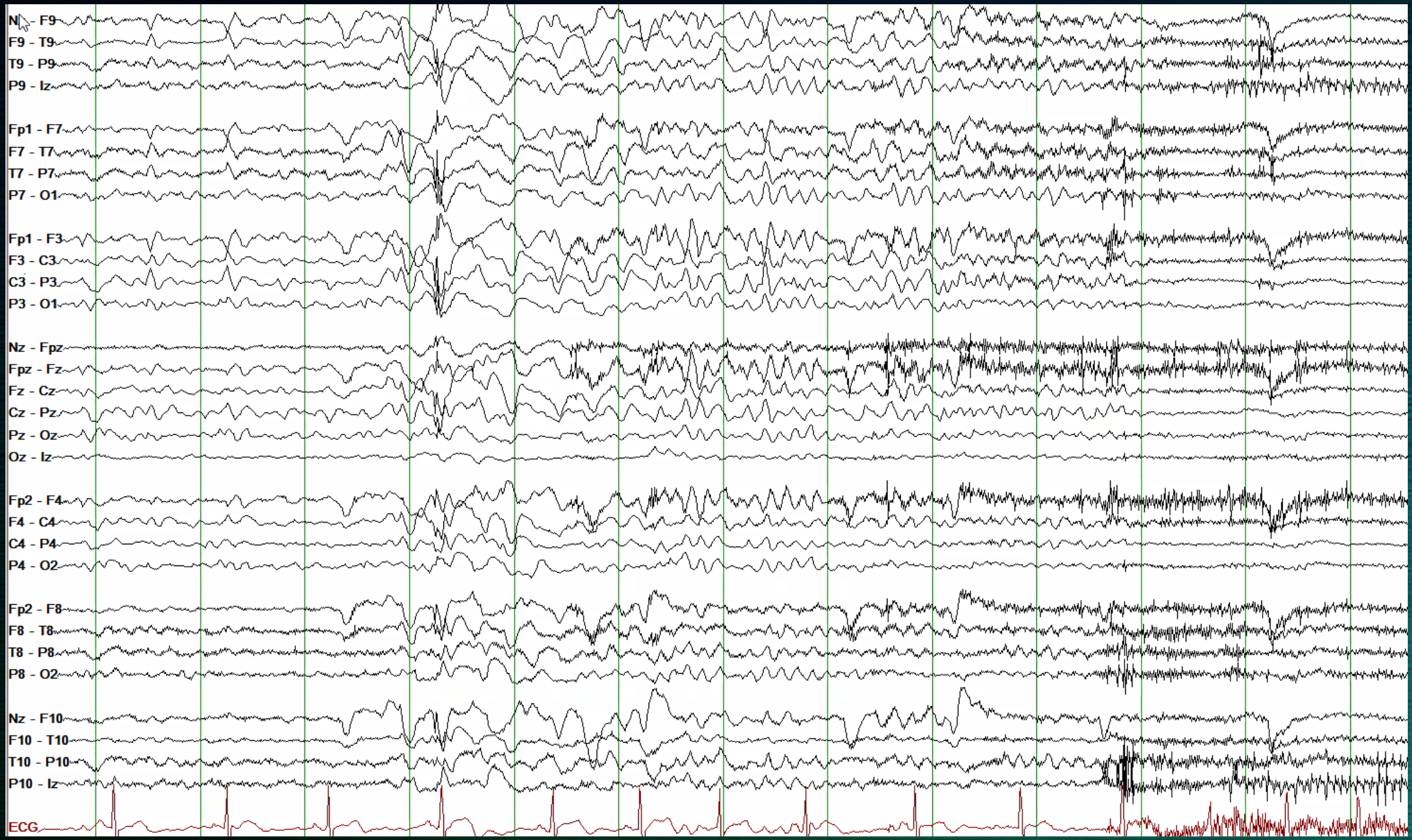
Syndromes that can begin both in pediatrics (≤18 years) and adulthood (≥19 years)


Generalized epilepsy syndromes
• Idiopathic generalized epilepsies (IGEs)
• Juvenile myoclonic epilepsy (JME)
• Juvenile absence epilepsy (JAE)
• Epilepsy with generalized tonic-clonic seizures alone (GTCA)
Focal epilepsy syndromes
• Self-limited
• Childhood occipital visual epilepsy (COVE)
• Photosensitive occipital lobe epilepsy (POLE)
• Familial mesial temporal lobe epilepsy (FMTLE)
• Epilepsy with auditory features (EAF)
• Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS)
• Sleep related hypermotor (hyperkinetic) epilepsy (SHE)
• Familial focal epilepsy with variable foci (FFEVF)
Epilepsy syndromes with developmental and/or epileptic encephalopathy, or with progressive neurological deterioration
• Febrile-infection related epilepsy syndrome (FIRES)
• Rasmussen syndrome (RS)
• Progressive myoclonus epilepsies (PME)
Combined generalized and focal epilepsy syndromes
• Epilepsy with reading induced seizures (EwRIS)

Focal Epilepsy Syndromes

Sleep-related hypermotor (hyperkinetic) epilepsy (SHE)

	Mandatory	**Alert**	**Exclusionary**
Seizures	Brief, focal motor seizures with hyperkinetic or asymmetric tonic/dystonic features seen mostly in sleep	Seizures predominantly from the awake state	Seizures ONLY during wakefulness Generalized onset seizures
EEG		Frequent discharges outside of frontal regions Generalized discharges	
Age at onset		<10 years or >20 years	<2 months or >64 years
Development at onset		Moderate to severe ID	
Exam		Focal abnormalities on neuro exam	
An MRI is not required for diagnosis of the syndrome but should be done to evaluate underlying etiology			
An ictal EEG is not required for diagnosis			


N - F9
F9 - T9
T9 - P9
P9 - Iz
Fp1 - F7
F7 - T7
T7 - P7
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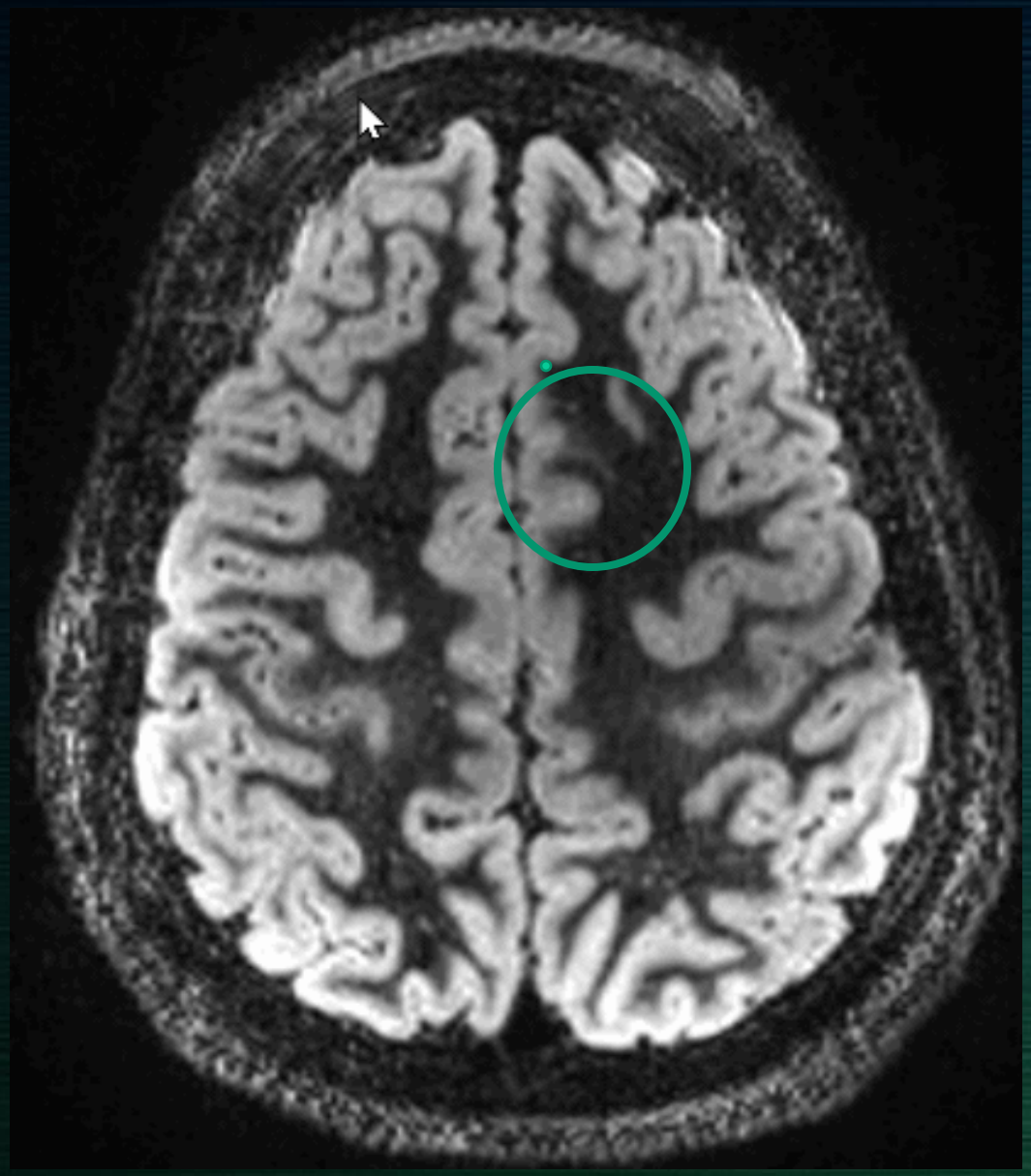
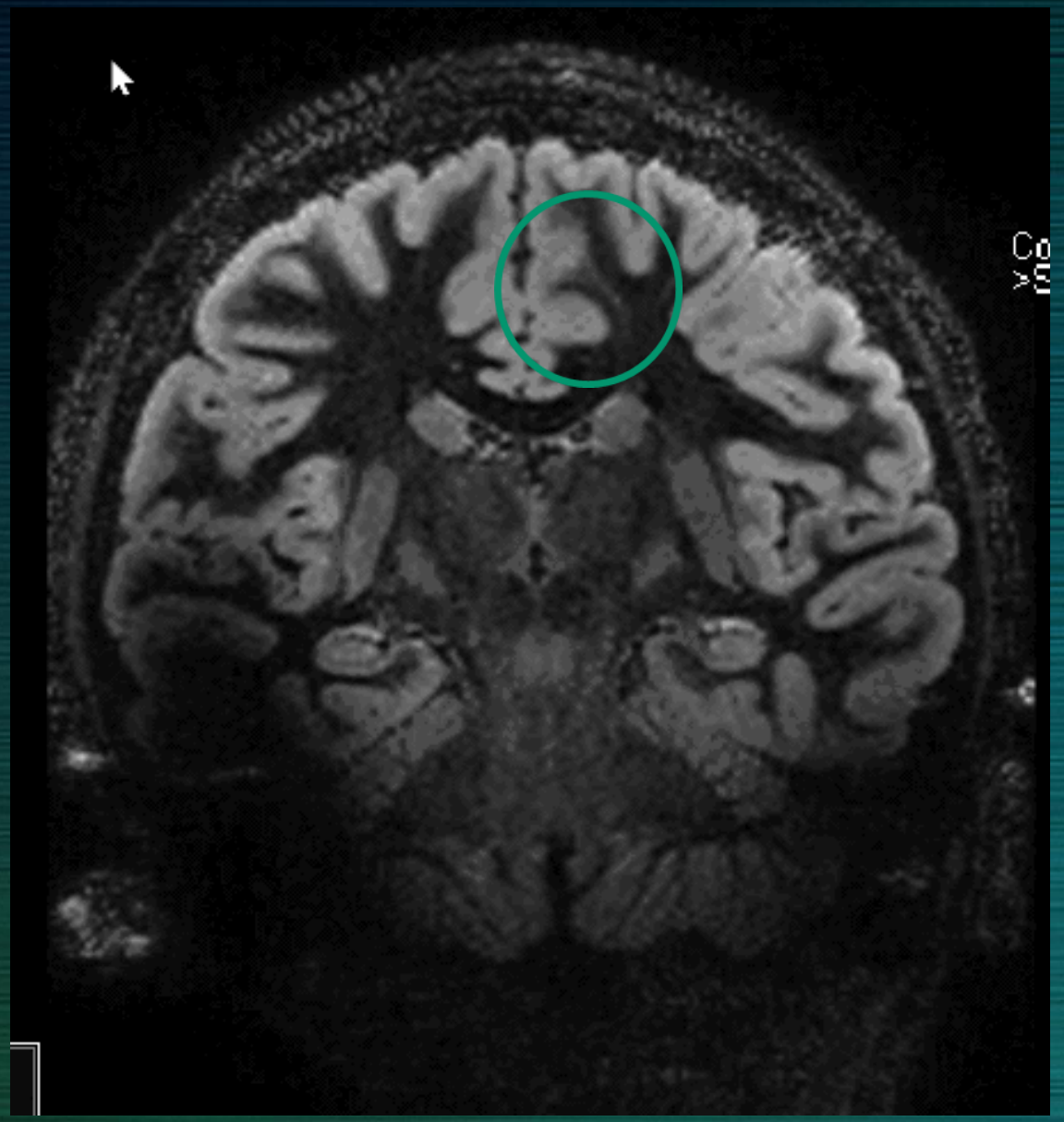
Fp1 - F3
F3 - C3
C3 - P3
P3 - O1
Nz - Fpz
Fpz - Fz
Fz - Cz
Cz - Pz
Pz - Oz
Oz - Iz
Fp2 - F4
F4 - C4
C4 - P4
P4 - O2
Fp2 - F8
F8 - T8
T8 - P8
P8 - O2
Nz - F10
F10 - T10
T10 - P10
P10 - Iz
ECG





Familial Mesial Temporal Lobe Epilepsy

	Mandatory	**Alert**	**Exclusionary**
Seizures	Focal cognitive (esp déjà vu), sensory or autonomic seizures		Generalized onset seizures
EEG		Generalized discharges	
Development at onset		ID	
Exam		Focal abnormalities on neuro exam	
Imaging	Normal or hippocampal atrophy/sclerosis		
Family history	Family history of individuals with focal seizures that arise from the mesial temporal lobe		
An MRI is required for diagnosis to exclude other causes			
An ictal EEG is not required for diagnosis			

Familial Focal Epilepsy with Variable Foci

	Mandatory	**Alert**	**Exclusionary**
Seizures	Focal onset seizures		Generalized onset seizures
EEG		Generalized discharges	
Age at onset		Neonatal onset	
Development at onset			Moderate to profound ID
Neurological exam		Focal neurological abnormalities	
Imaging	Normal or focal cortical dysplasia		
Family history	Family history of persons with focal seizures that arise from cortical regions that differ between family members		Family history of focal seizures that occur exclusively before 20 months of age
An MRI is required for diagnosis, as family history of focal seizures may be incidental, due to an acquired cause			
An ictal EEG is not required for diagnosis			

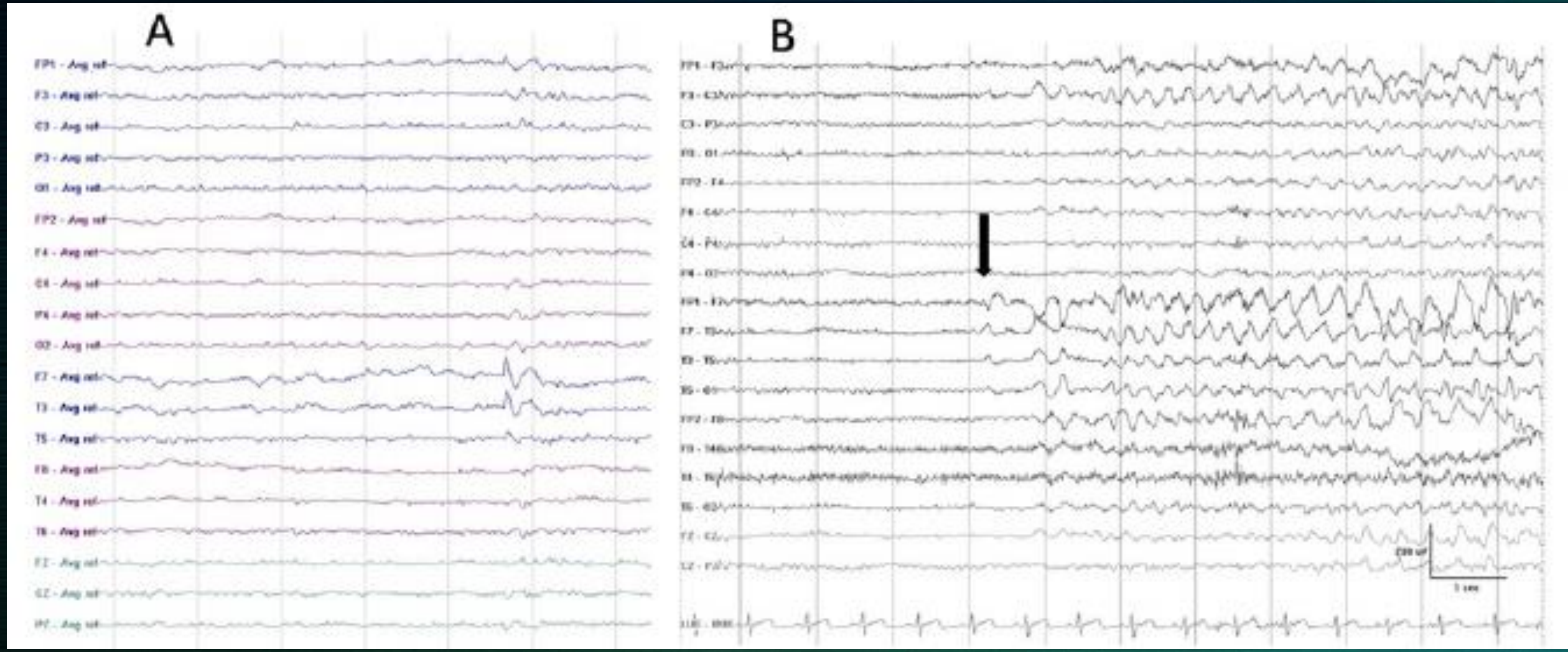
Look carefully for genetic variant that may also result in FCD – DEPDC5, NPRL2, NPRL3, TSC1 or 2

Epilepsy with Auditory Features

	Mandatory	**Alert**	**Exclusionary**
Seizures	Focal sensory auditory seizures and/or focal cognitive seizures with receptive aphasia		Generalized onset seizures Other focal onset seizures
EEG		Generalized discharge	
Development at onset			Moderate to severe ID
Neurological exam		Focal neurological abnormalities	
Imaging	Normal or focal cortical dysplasia		
An MRI is required for diagnosis to exclude other causes			
An ictal EEG is not required for diagnosis			

Mesial Temporal Lobe Epilepsy with HS

	Mandatory	**Alert**	**Exclusionary**
Seizures	Focal aware or impaired awareness seizures with initial semiology referable to mesial temporal lobe networks	Initial semiology refereable to networks other than mesial temporal	Generalized onset seizures
EEG		Consistent absence of temporal discharge despite repeated EEG Generalized discharge High amplitude centrotemporal spikes Discharges or focal slowing outside the temporal region	Recorded seizures with generalized onset Recorded seizures with onset outside of temporal lobe
Age at onset		<2 years	
Development at onset		Moderate to severe ID	
Neurological exam		Focal findings such as hemiparesis	
Imaging	Hippocampal sclerosis on MRI		
An MRI with hippocampal sclerosis is mandatory for diagnosis			
An ictal EEG is not required for diagnosis			


A
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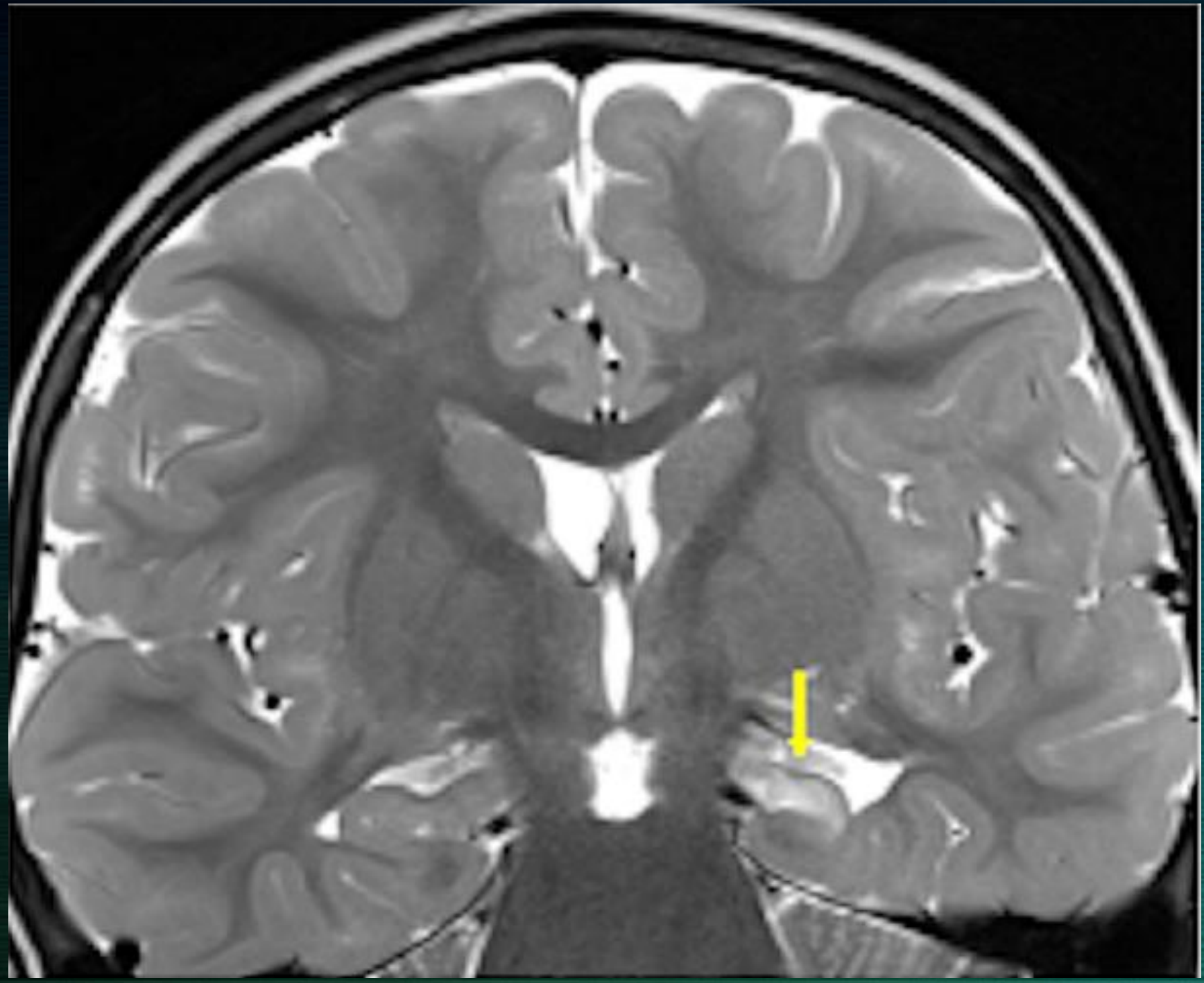
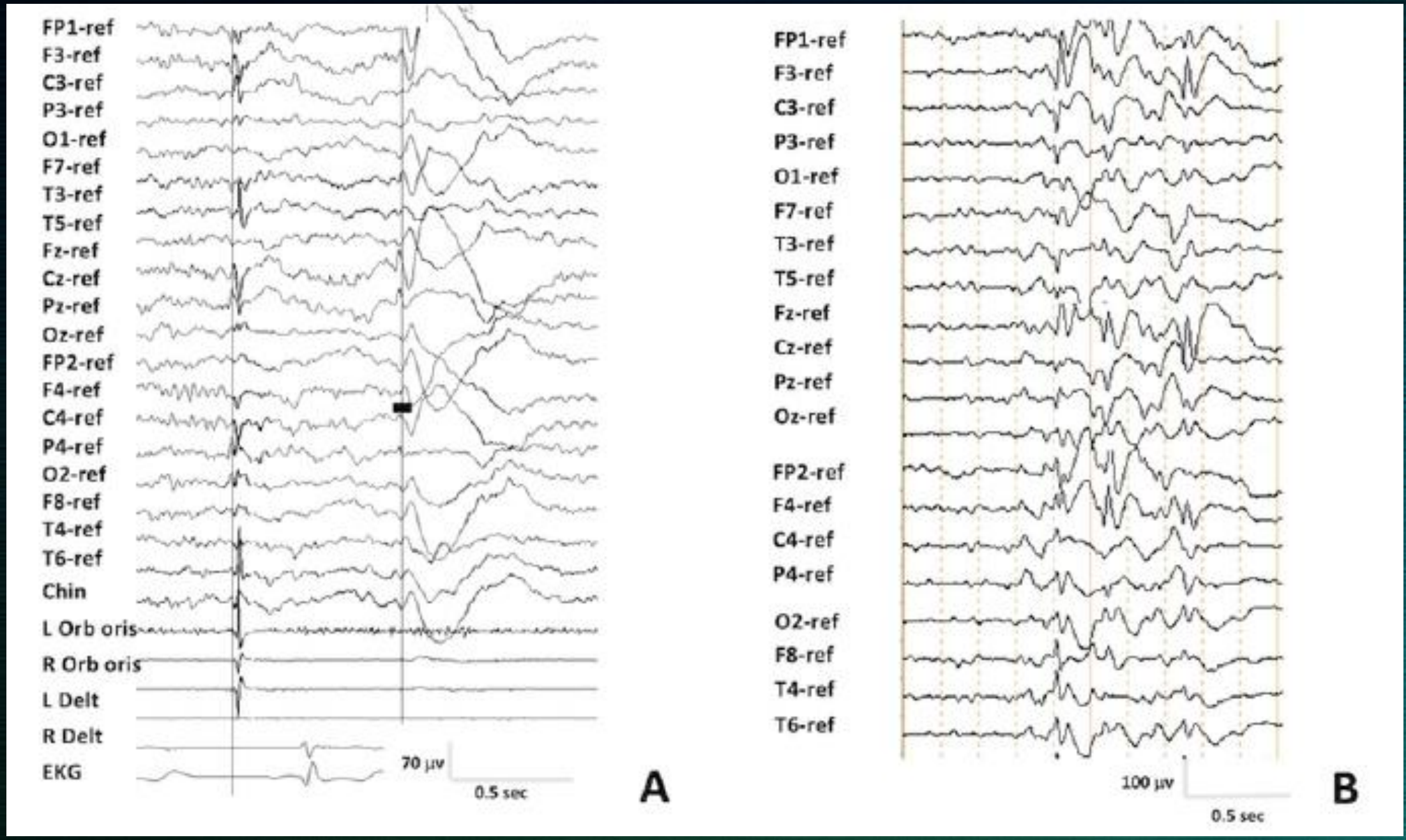


Combined Focal and Generalized

Epilepsy with Reading-Induced Seizures

	Mandatory	**Alert**	**Exclusionary**
Seizures	Reflex myoclonic seizures affecting orofacial muscles, triggered by reading or language-related tasks	Prominent myoclonic jerks affecting upper limbs	All other seizure types except GTCS
EEG			Background slowing excluding the postictal phase of a GTCS
Age at onset		>20 years	
Development at onset	Normal		
Neurological exam	Normal		
Imaging	Normal		
An MRI is required for diagnosis to exclude a structural cause			
An ictal EEG is not required, however observation during reading is highly recommended as it shows the characteristic myoclonus affecting orofacial muscles			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C3-ref
P3-ref
O1-ref
F7-ref
T3-ref
T5-ref
Fz-ref
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Oz-ref
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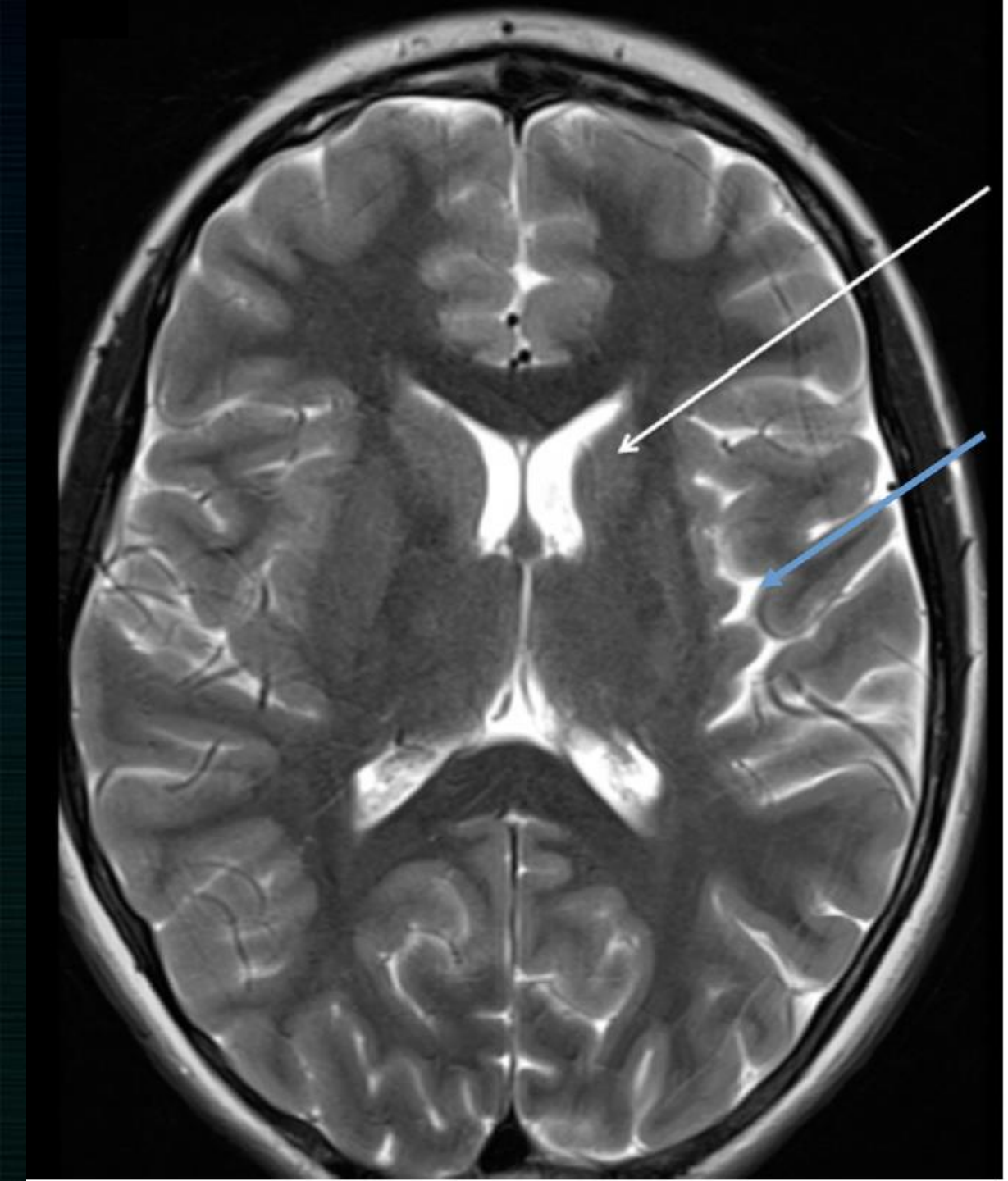
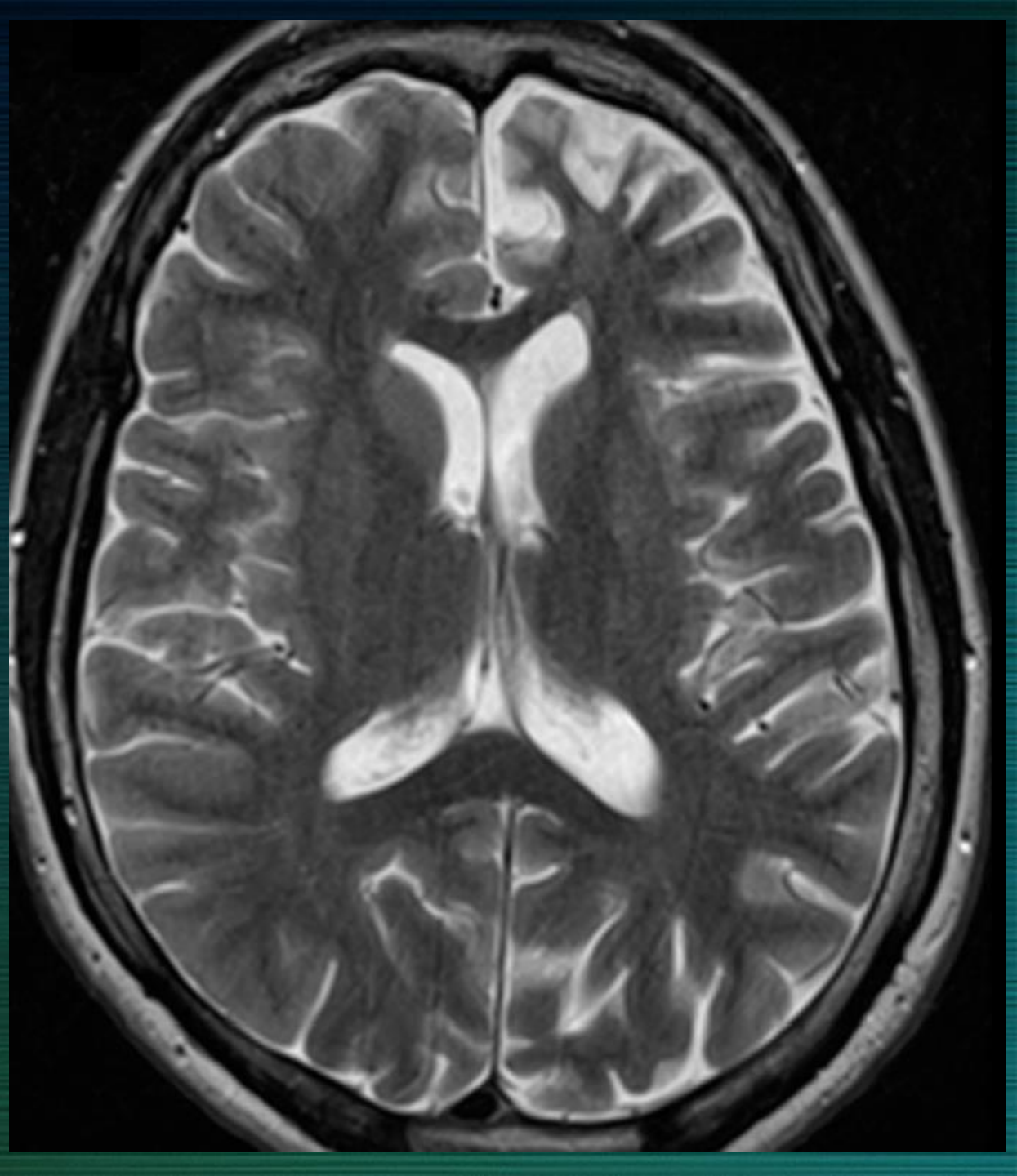
Oz-ref
FP2-ref
F4-ref
C4-ref
P4-ref
O2-ref
F8-ref
T4-ref
T6-ref
100 µv
0.5 sec
B

DEEs or Epilepsies with Progressive Neurological Deterioration

Rasmussen Syndrome

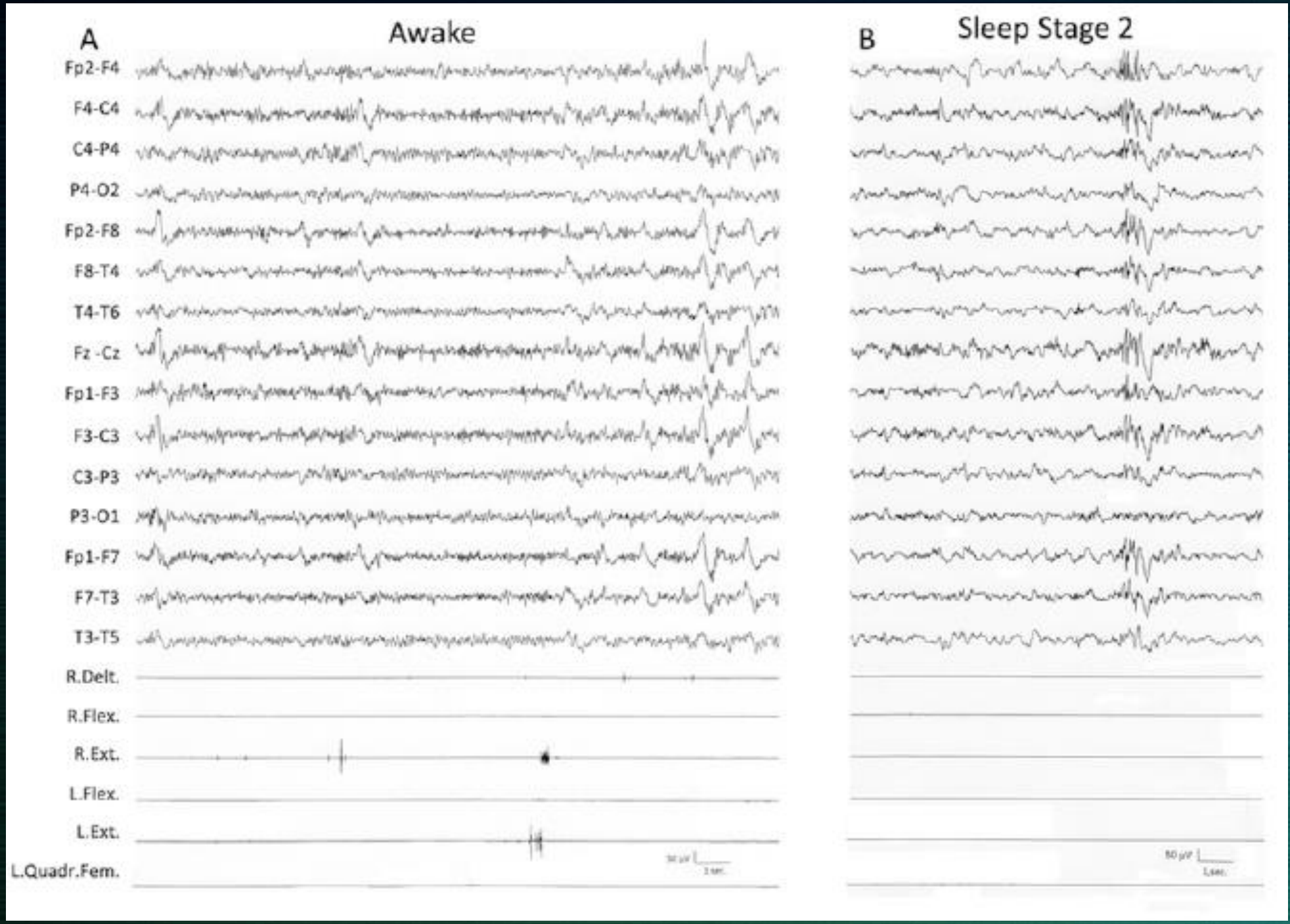
	Mandatory	**Alert**	**Exclusionary**
Seizures	Focal/hemispheric seizures which often increase in frequency over weeks to months	Focal onset indcpendently in both hemispheres	Generalized onset seizures
EEG	Hemispheric slowing and discharges	Generalized spike-wave	
Age at onset		Onset in adolescence or adulthood	
Development at onset		Delayed development prior to seizure onset	
Neurological exam			Hemiparesis present at seizure onset
Imaging	Progressive hemiatrophy (early insula and caudate head)	Lack of hyperintense signal and/or atrophy of ipsilateral caudate head and/or lack of hyperintense signal of grey or white matter	Imaging shows Sturge-Weber syndrome
Other			Metabolic cause of EPC Specific antibody-mediated encephalitis
Longterm outcome	DRE, progressive neuro deficits		
An MRI is required for diagnosis but an ictal EEG is not required			

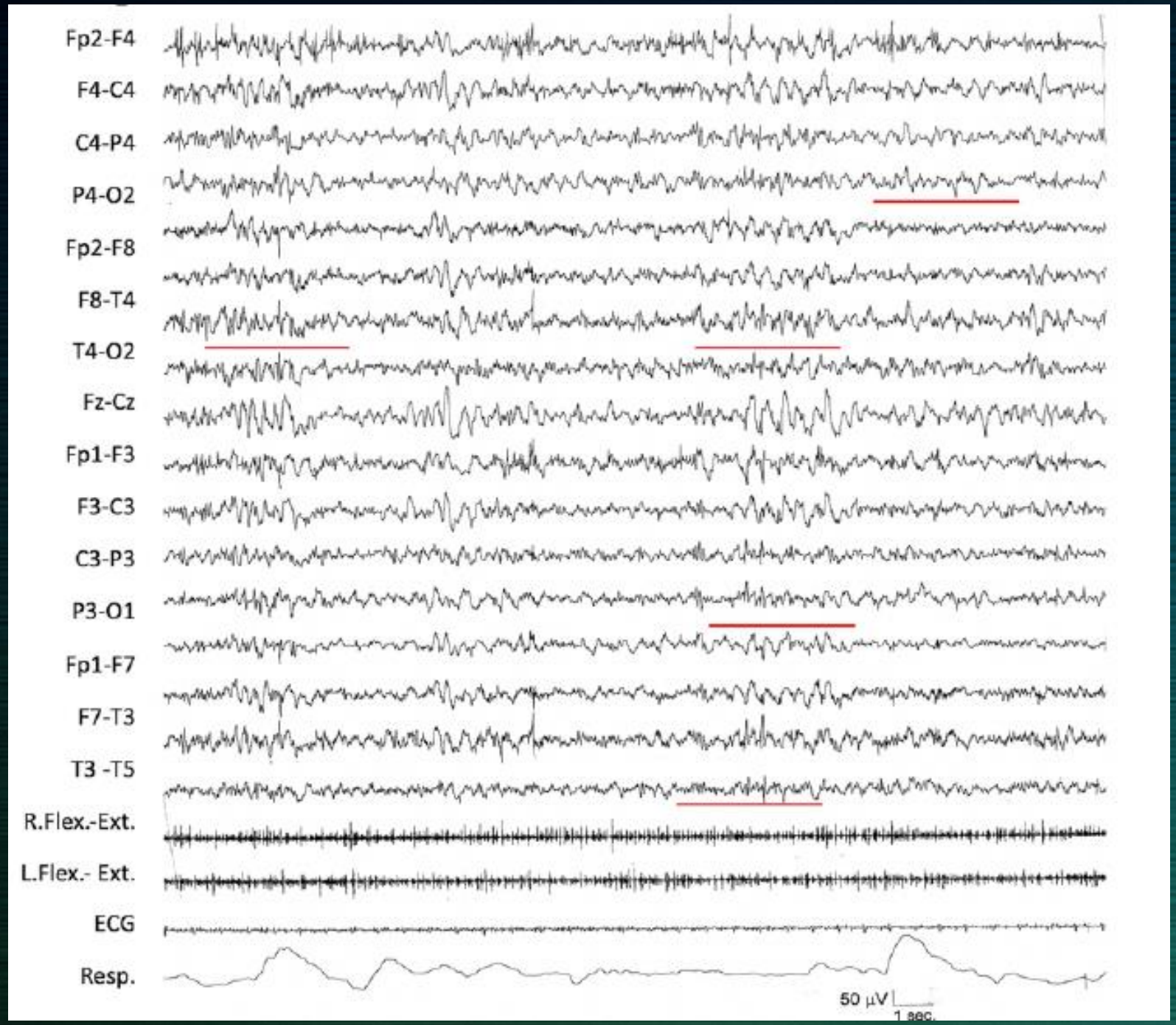




Progressive Myoclonus Epilepsy

	Mandatory	**Alert**	**Exclusionary**
Seizures	Myoclonic seizures		
EEG	Generalized spike and polyspike-wave		Persistent focal abnormalities, other than occipital
Age at onset	2-50 years	>20 years	
Development	Normal at onset		
Neurological exam	Normal at onset		
Comorbidities	Progressive neurocognitive deterioration over time		
Imaging	Normal at onset		
Course of illness	Progressive worsening of myoclonus, myoclonic and GTC seizures, cognitive decline, progressive cerebellar signs EEG deterioration with progressive slowing and/or increased discharges		


A
Awake
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp2-F8
F8-T4
T4-T6
Fz -Cz
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp1-F7
F7-T3
T3-T5
R.Delt.
R.Flex.
R.Ext.
L.Flex.
L.Ext.
L.Quadr.Fem.
B
Sleep Stage 2


Fp2-F4
F4-C4
C4-P4
P4-O2
Fp2-F8
F8-T4
T4-O2
Fz-Cz
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp1-F7
F7-T3
T3 -T5
R.Flex.-Ext.
L.Flex.- Ext.
ECG
Resp.
50 µV
1 sec.

Summary

- Syndrome identification helps to hone diagnostic investigations, select best therapeutic options and provide more accurate prognosis regarding seizure outcome and risk of comorbidities

- Some syndromes onset at a variable age

- Most of these are focal epilepsies, some of which may be associated with DEE/progressive neurological deterioration