Electroclinical Syndromes
~~Epilepsy Syndromes~~

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Disclosures

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- **Lundbeck**
- **Medtronics**

Outline

Electroclinical syndrome classification

Electroclinical Syndromes:

- **Neonatal**
- **Infancy**
- **Childhood**
- **Adolescence**

ILAE Classification (www.ilae.org)

Electroclinical Syndromes are classified according to:

- **Seizure type:**
  - **Focal (localization-related or partial)**
  - **Generalized**
- **Age of onset**
- **Clinical course**
- **Etiology**
  - **Structural/Metabolic (Symptomatic)**
  - **Unknown cause (Cryptogenic)**
  - **Genetic/presumed genetic (Idiopathic)**
- **Electroencephalogram (EEG) findings**

Electroclinical Syndrome Classification

- **Presumed etiology:**
  - **Structural/Metabolic (Symptomatic):**
    - **25% of cases of epilepsy are due to a lesion/insult to the brain or metabolic derangements: tumors, metabolic, stroke, trauma, brain infection, brain malformations, chromosomal abnormalities, etc.**
  - **Unknown cause (Cryptogenic) and Genetic/presumed genetic (Idiopathic):**
    - **75% unknown cause or genetic.**

Ottman R. Epidemiol Rev 1997;19(1):120-8.

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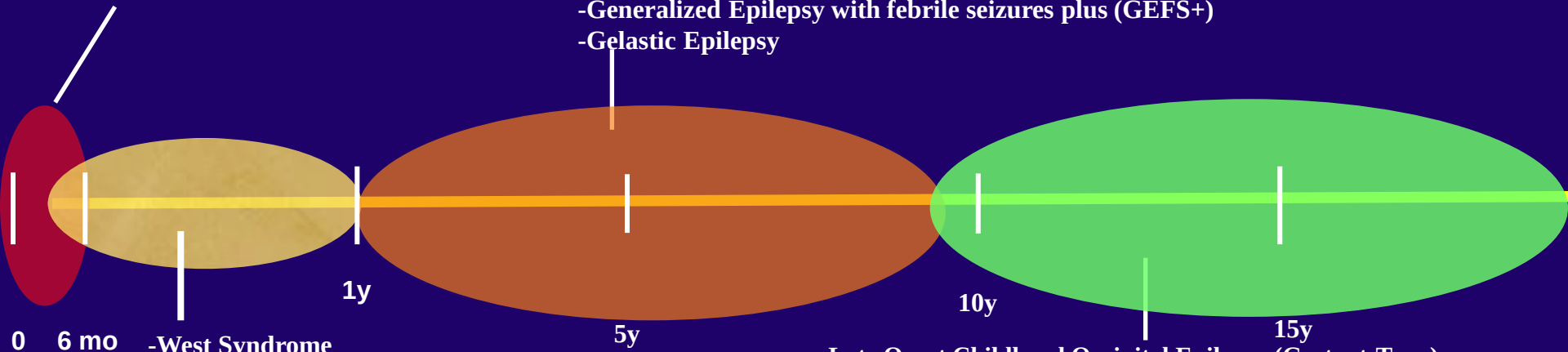
Timeline of the Electroclinical Syndromes

-Benign Familial Neonatal Epilepsy
-Ohtahara syndrome
-Early Myoclonic Encephalopathy

-Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE)
-Lennox-Gastaut Syndrome
-Landau-Kleffner syndrome
-Epilepsy with continuous spike and waves during sleep
-Benign epilepsy with centro-temporal spikes
-Panayiotopoulos syndrome (Early Onset Childhood Occipital Epilepsy
-Epilepsy with Myoclonic Atonic Seizures (Doose syndrome)
-Epilepsy with myoclonic absences
-Childhood Absence Epilepsy
-Absence with perioral myoclonia
-Generalized Epilepsy with febrile seizures plus (GEFS+)
-Gelastic Epilepsy



-West Syndrome
-Dravet Syndrome
-Benign Familial Infantile Epilepsy
-Epilepsy of infancy with migrating focal seizures
-Hemiconvulsion-Hemiplegia Epilepsy Syndrome
-Myoclonic encephalopathy in non-progressive disorders

-Late Onset Childhood Occipital Epilepsy (Gastaut-Type)
-Juvenile Absence Epilepsy
-Juvenile Myoclonic Epilepsy
-Jeavons syndrome
-Epilepsy With Generalized Tonic-Clonic Seizures Alone
-Progressive Myoclonus Epilepsies

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Electroclinical Syndromes in Neonates

Neonatal Electroclinical Syndromes

Syndromes defined by the age of onset:

- **Benign familial neonatal epilepsy:**
  - **Age of onset: 2-7 days; Genes: KCNQ2, KCNQ3; myokymia**
- **Benign familial infantile epilepsy:**
  - **Age of onset: 11-12 weeks; Genes: SCN2A**
- **Benign familial neonatal-infantile epilepsy:**
  - **Age of onset: 6 months; Genes: ATP1A2**

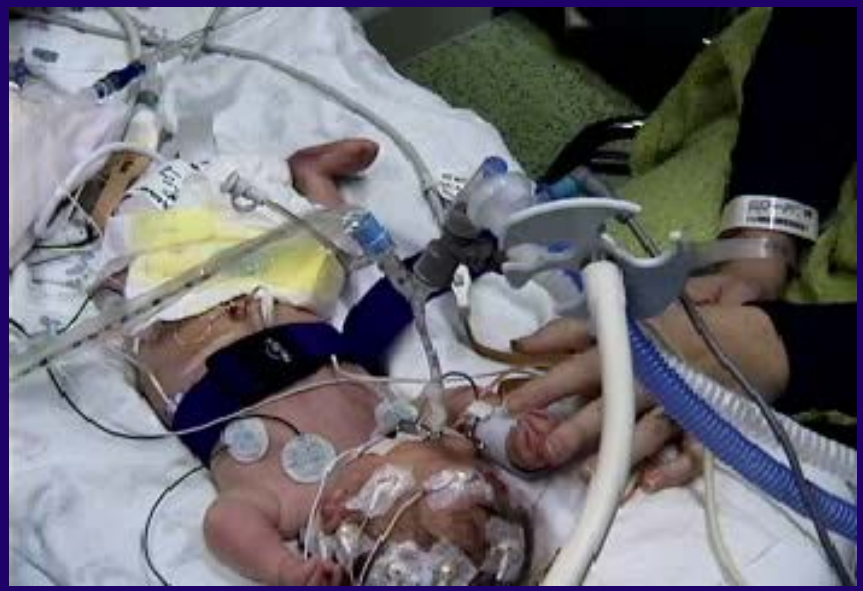
Syndromes are characterized by:

- **Multiple seizures occurring over several days.**
- **Frequently they have focal symptoms with focal EEG abnormalities.**
- **Normal development.**
- **Good prognosis, rarely patients have febrile seizures and rarely develop epilepsy.**

Treatment: Phenobarbital, levetiracetam, topiramate, midazolam.

Early Myoclonic Encephalopathy

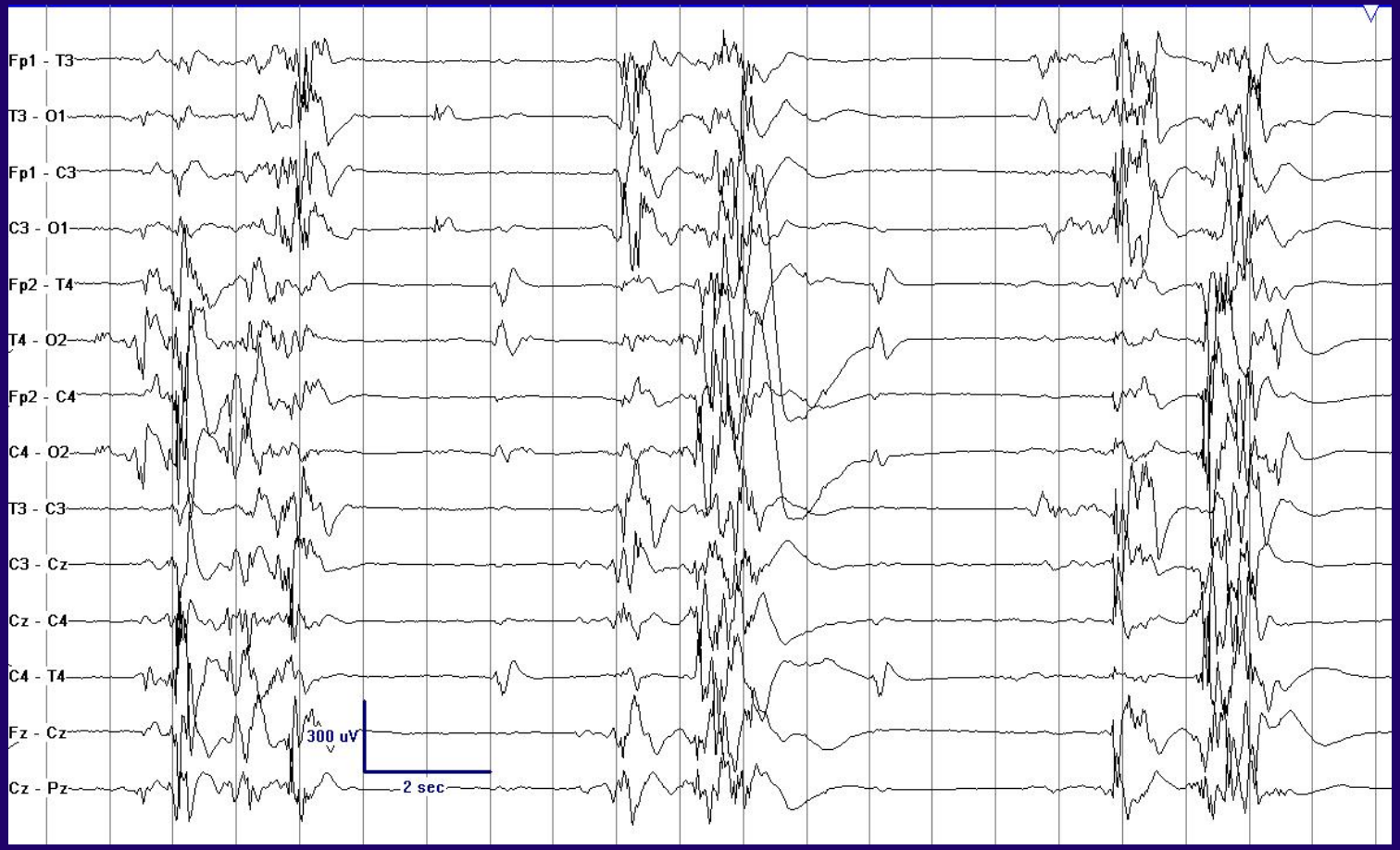
- Age of onset: first few days of life.
- Seizure description: myoclonic seizures with evolution to focal seizures and tonic spasms (2 to 4 months).
- EEG: burst suppression with evolution to hypsarrhythmia and multifocal spike wave.
- Etiology: multifactorial, genetic, brain malformations or metabolic.
- Prognosis: early death. Usually in the first few months of life. Rarely survive, but have profound psychomotor retardation.
- Treatment: Refractory to all treatments.



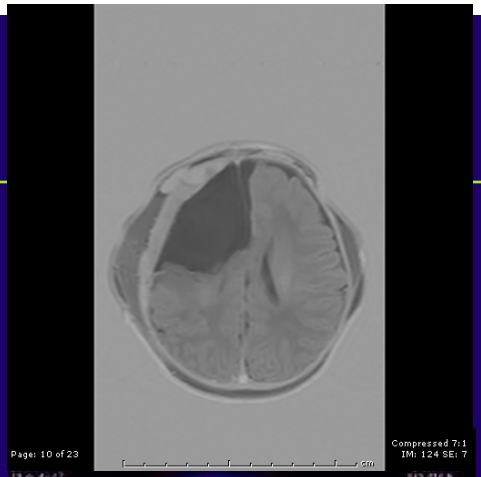
Early Infantile Epileptic Encephalopathy with Burst Suppression (EIEE) (Ohtahara syndrome)

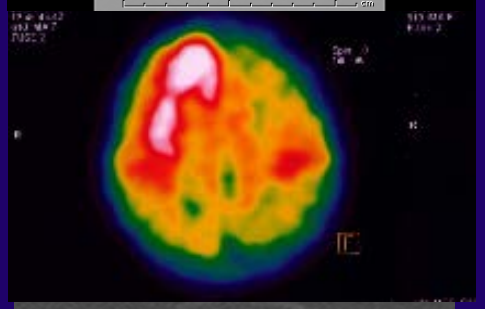
- **Age of onset: first few days of life-3 moths (many mothers report seizures in utero).**
- **Seizure description: tonic spasms, infantile spasms, focal clonic seizures.**
- **EEG: Burst suppression pattern.**
- **Etiology: brain malformation, genetic (ARX) or metabolic conditions (Leigh's disease).**
- **Prognosis: Progress to infantile spasms and Lennox-Gastaut syndrome. If metabolic problem is discovered most die in infancy or early childhood.**
- **Treatment: refractory to all medications. Steroids have been used with little success. Epilepsy surgery may be beneficial with focal brain malformations.**

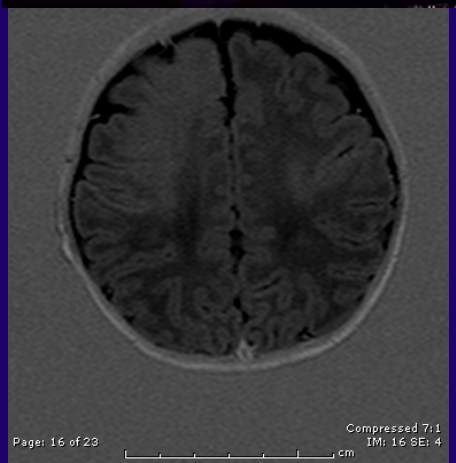
Early Infantile Epileptic Encephalopathy with Burst Suppression (EIEE) (Ohtahara syndrome)

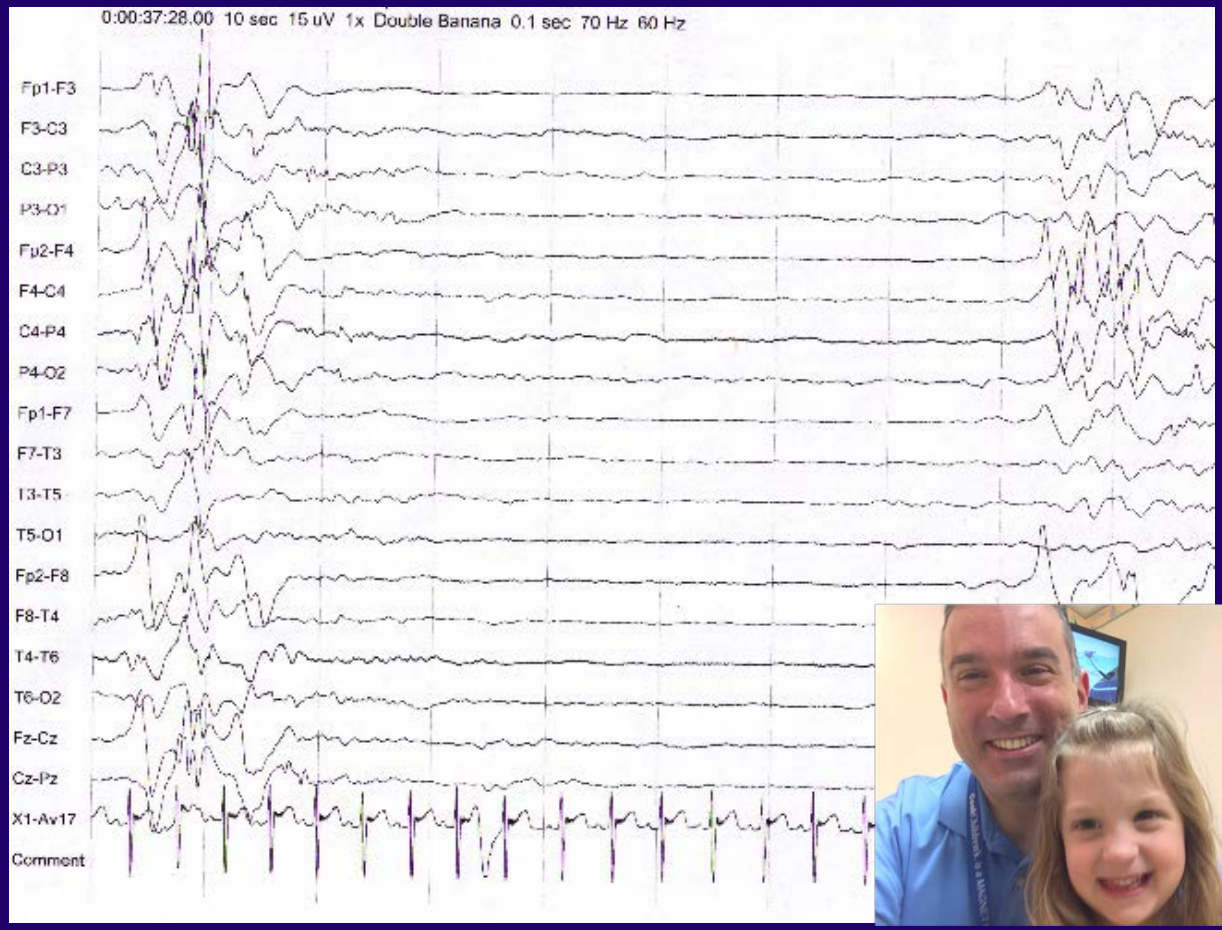


Early Infantile Epileptic Encephalopathy with Burst Suppression (EIEE) (Ohtahara syndrome)









Electroclinical Syndromes in Infancy

Infantile Spasms

Infantile Spasms (West Syndrome)

- **Age of onset: 4-6 months.**
- **Clinical: cluster of flexor, extensor and mixed spasms.**
- **EEG: Hypsarrhythmia**
- **Developmental regression during initial symptoms.**
- **>70% are MR.**
- **>70% will develop other types of seizures.**
- **40% will develop Lennox-Gastaut syndrome.**
- **Treatment: ACTH, prednisone (high dose 4-8 mg/kg), vigabatrin (TSC)**

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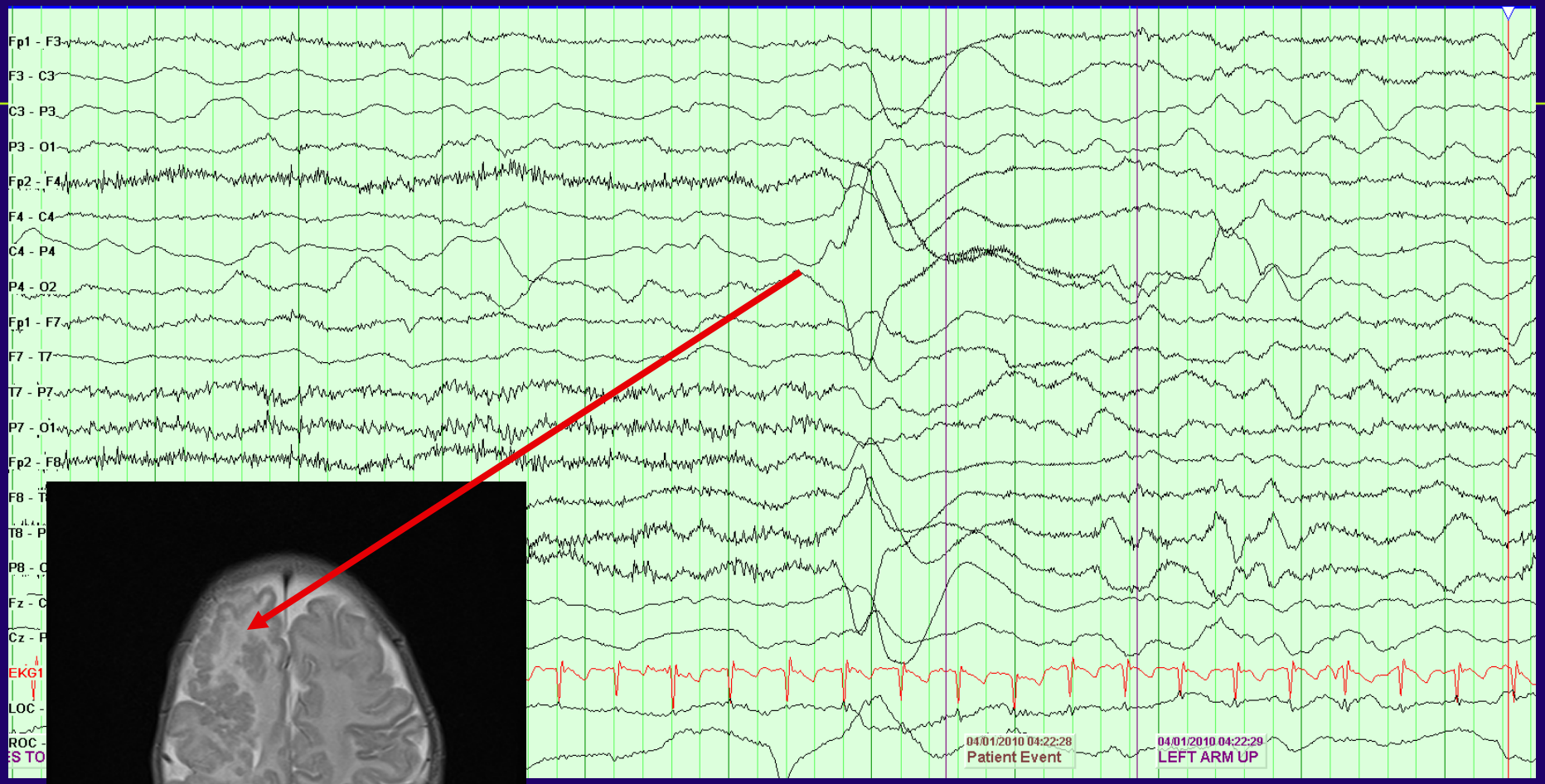

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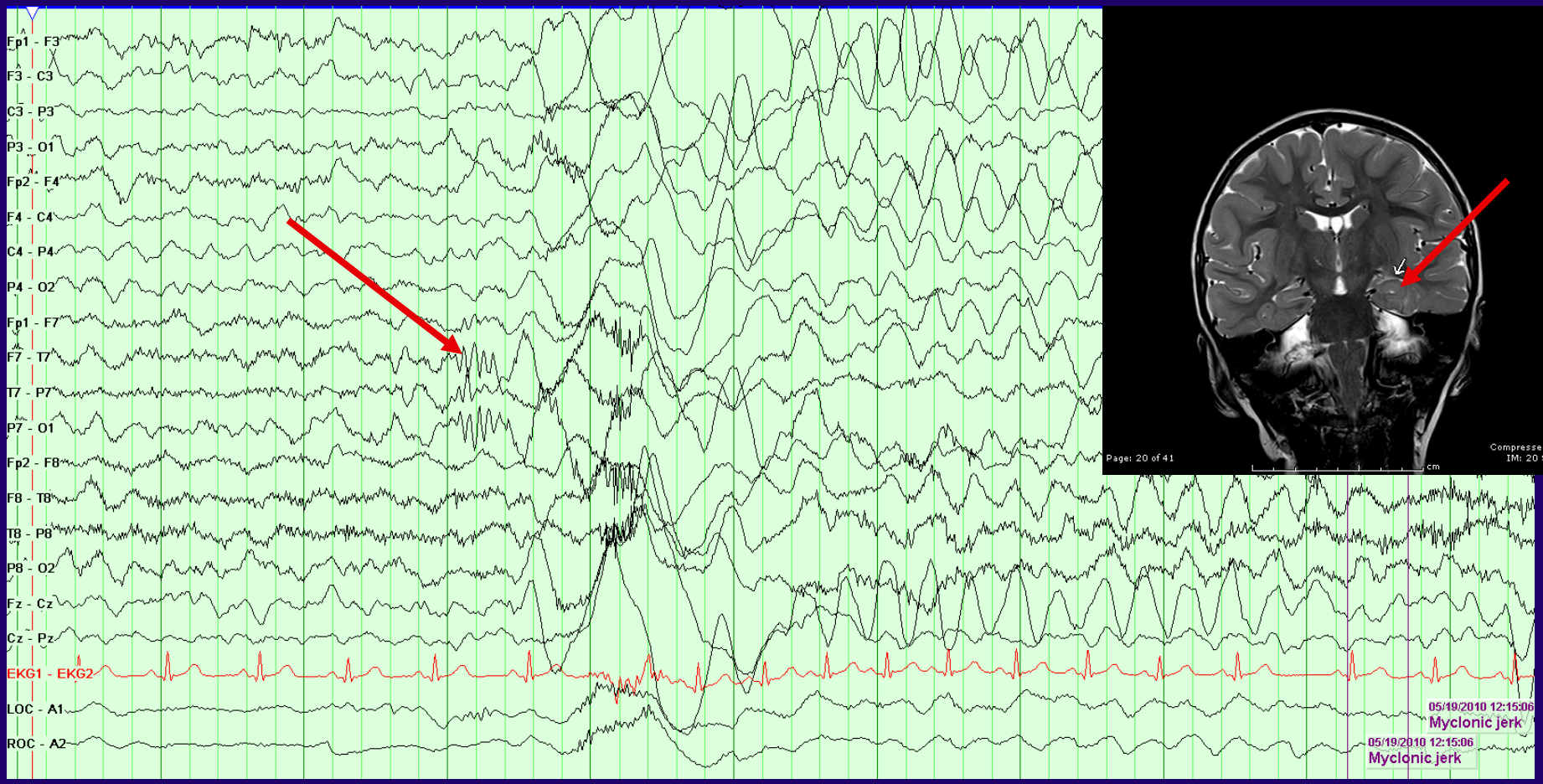
Focal Infantile Spams



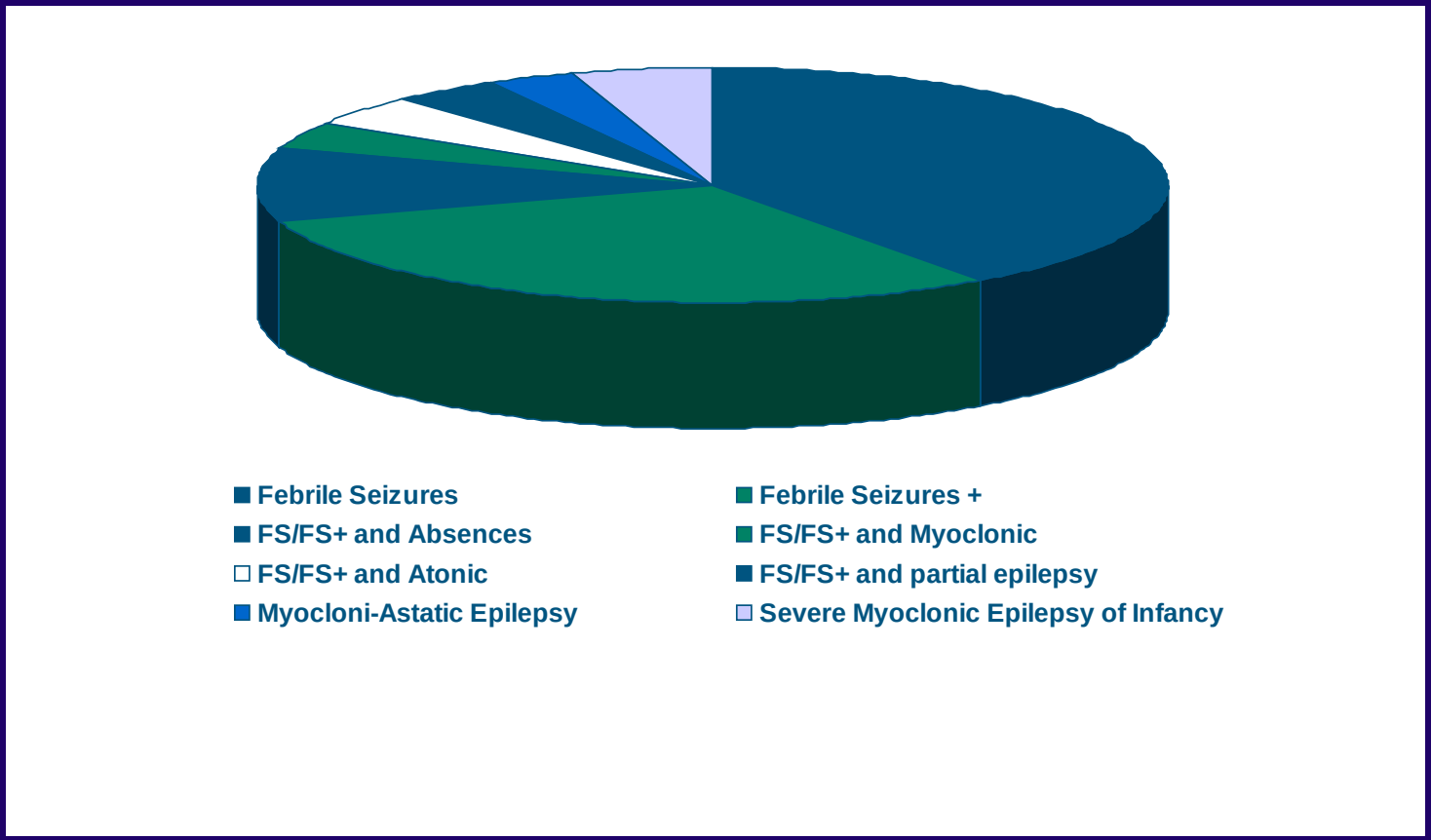
Hemiconvulsion-Hemiplegia Syndrome

- Age of Onset: 5 months-4 years.
- Seizure description: Prolonged focal seizures is the first presentation, followed by focal epilepsy.
- EEG: Initially slow waves, the more focal spike wave activity.
- Prognosis: refractory focal seizures and recurrent bouts of focal SE.
- Etiology: infections and malformations.
- Treatment: Refractory to medication. Hemispherectomy should be considered early in the course.

Generalized Epilepsy with Febrile Seizures Plus (GEFS+)

- Range: 6 months - 6 years
- Seizure description: recurrent febrile seizures that persist longer than 6 years, recurrent status epilepticus, absence, atonic, GTC, focal, multifocal.
- Etiology: SCN1A, SCN2A, SCN1B, GABRG2
- EEG: Generalized spike wave
- Prognosis: depends on epilepsy syndrome
- Treatment: depends on epilepsy syndrome

Generalized Epilepsy with Febrile Seizures Plus (GEFS+)



Severe Myoclonic Epilepsy of Infancy (SMEI)

- Severe myoclonic epilepsy of infancy (Dravet Syndrome)
- Age of onset: First year of life.
- Seizure characteristics: recurrent and prolonged febrile seizures, evolve into myoclonic, atypical absence and focal clonic seizures.
- EEG: Maybe normal at the beginning. Multifocal and/or generalized spike wave.
- Intelligence: Psychomotor regression and gait apraxia.
- Etiology: SCN1A
- Treatment: Refractory to medications (Drugs of choice: valproic acid, clobazam, stiripentol; other medications: felbamate, topiramate, levetiracetam, ketogenic diet, VNS). Fenfluramine. Avoid Na channel medications.

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Electroclinical Syndromes in Childhood

Benign Childhood Epilepsy with Centro-temporal Spikes

- Age range: 3-15yrs
- Clinical: Focal motor seizures with or without secondary generalization. Seen in sleep, rarely in wakefulness
- EEG: centro- temporal spike wave
- Normal intelligence
- Normal imaging
- 30% have ADHD
- Linkage: 15q14; gene: ?
- Treatment: Drug of choice: carbamazepine and oxcarbazepine; Others: levetiracetam, zonisamide.

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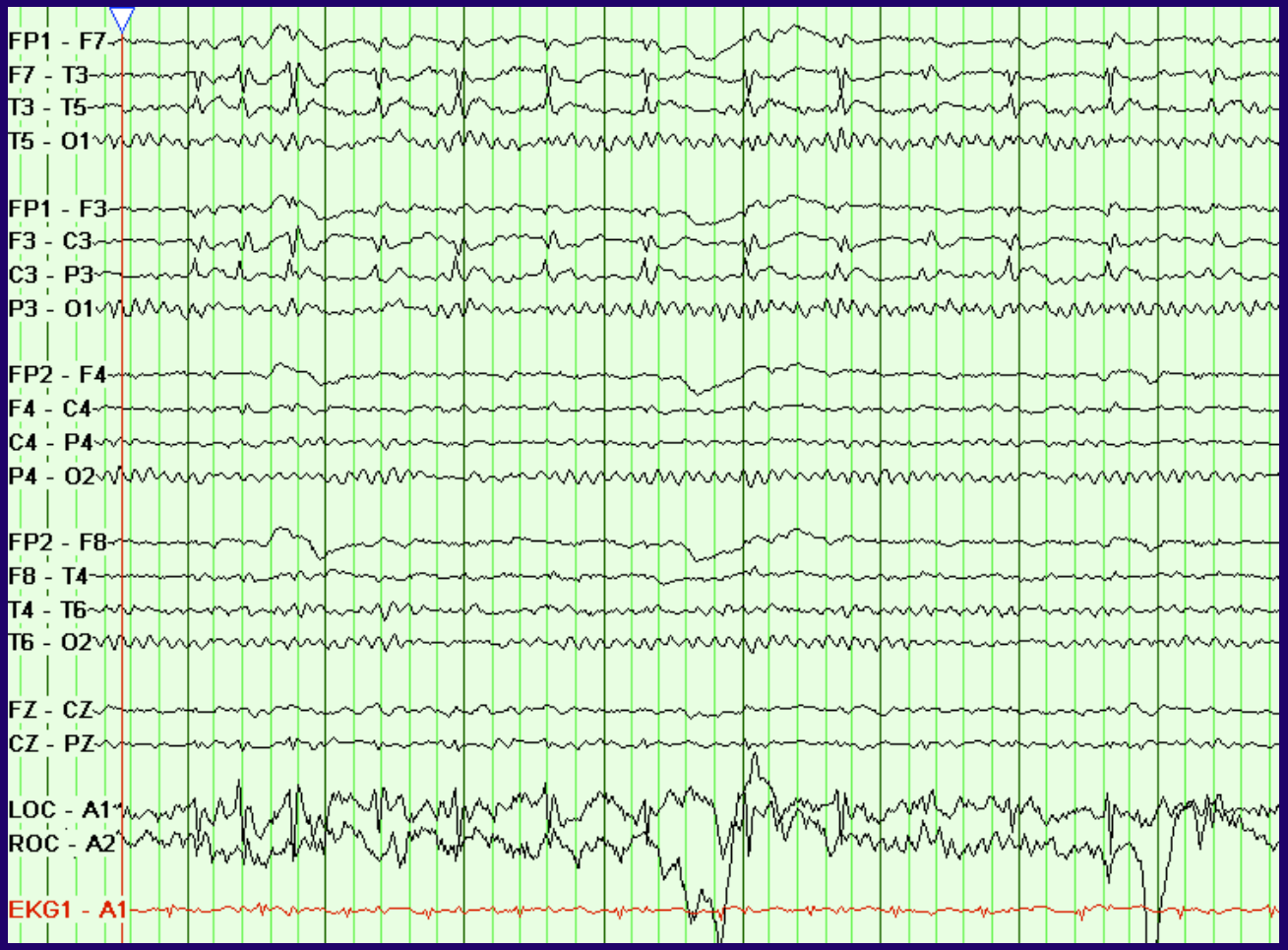
Benign Childhood Epilepsy with Centro-Temporal Spikes



Early Onset Childhood Occipital Epilepsy

- Age range: 3-10 yrs
- Clinical: Panayiotopoulos type early onset eye deviation and ictal vomiting.
- EEG: Unilateral or bilateral occipital spike wave. Some with centro-temporal spike wave.
- Normal intelligence
- Normal imaging
- Linkage: Multifactorial
- Treatment: Drug of choice: carbamazepine and oxcarbazepine; Others: levetiracetam, zonisamide.
- Prognosis: >90% of patients remit after 2-4 years of diagnosis

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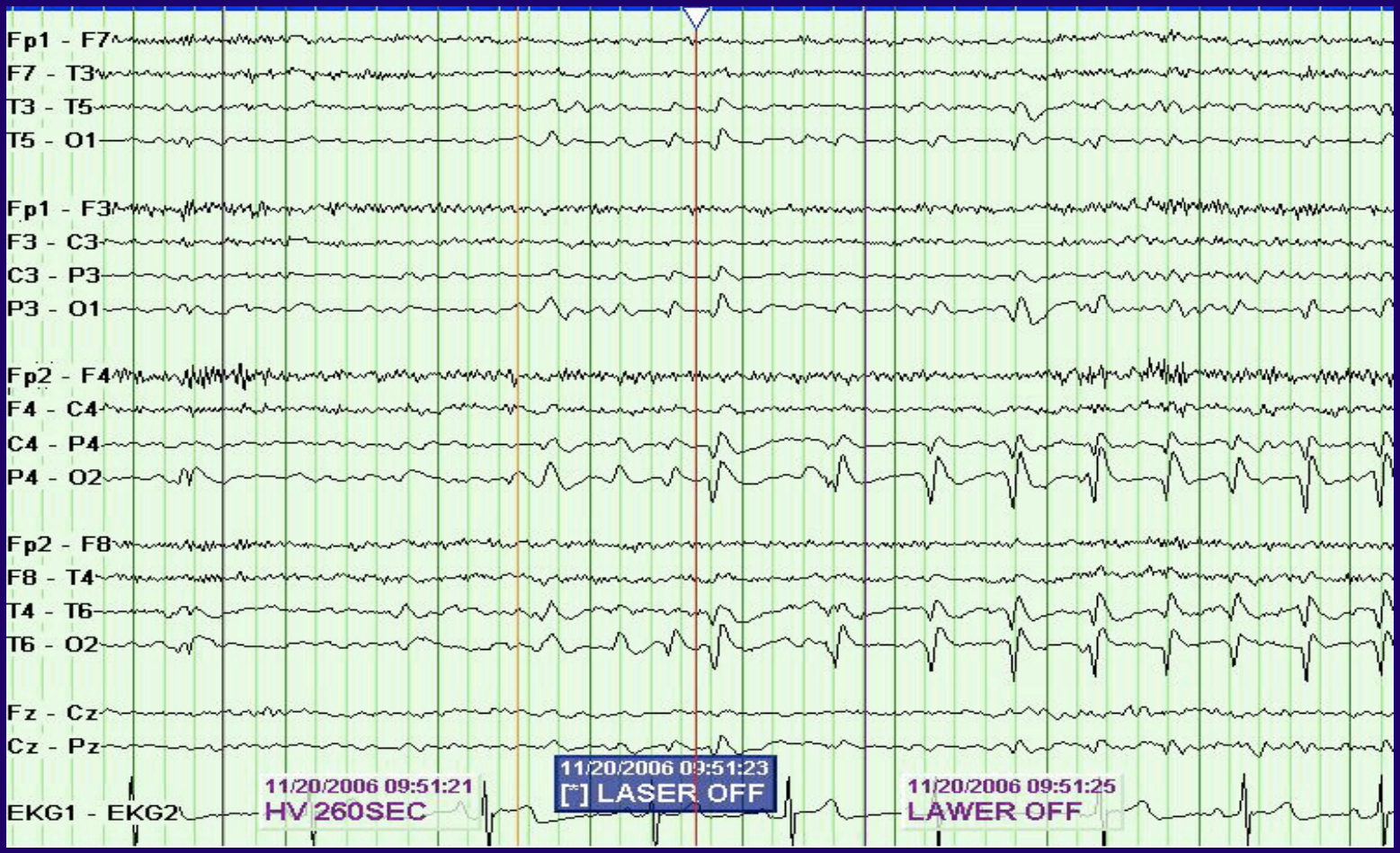
Early Onset Childhood Occipital Epilepsy

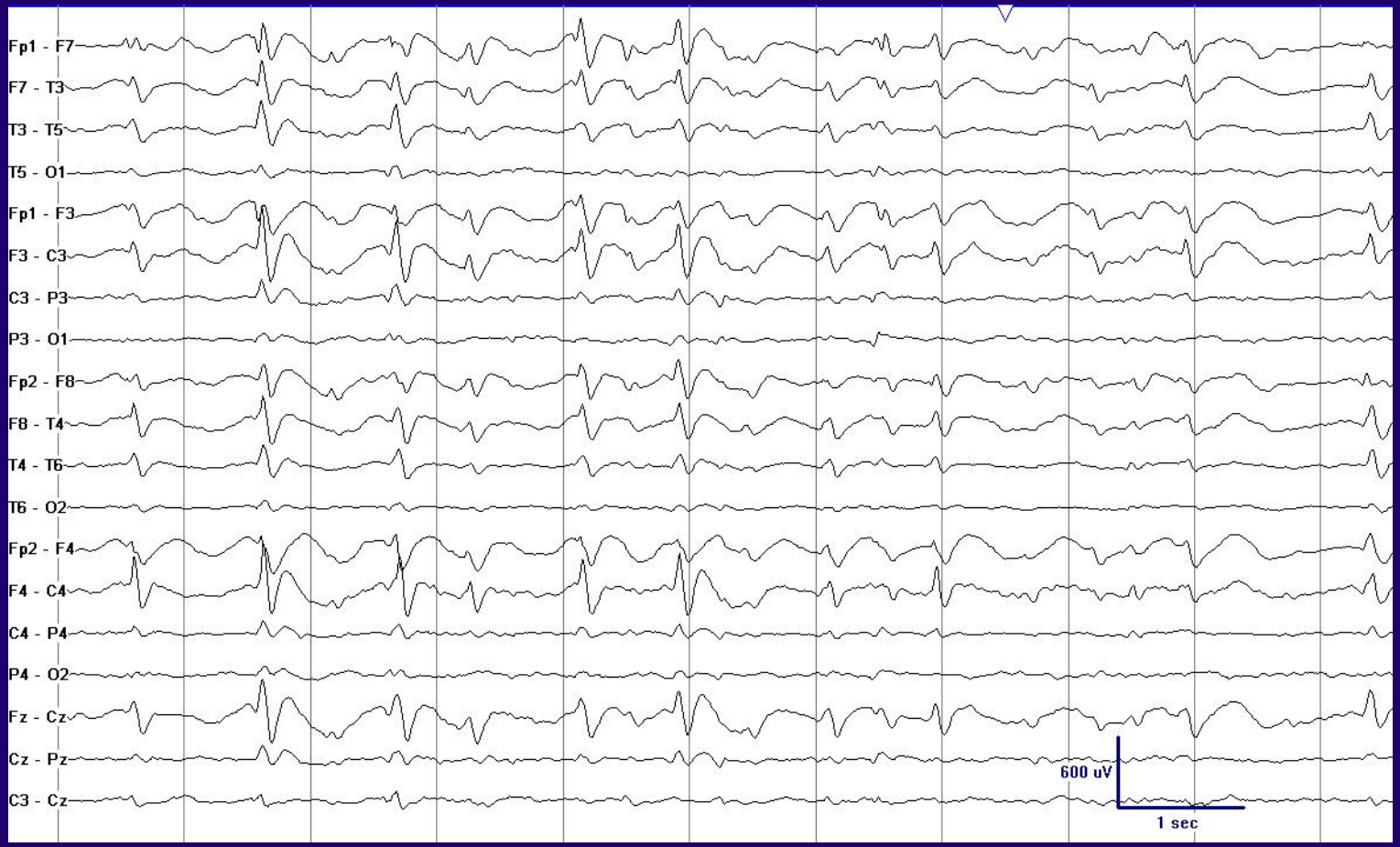


Acquired Epileptic Aphasia (Landau-Kleffner Syndrome)

- **Age of Onset: Usually before 6 years of age.**
- **Clinical: gradual auditory agnosia.**
- **Type of seizures: Rare generalized seizures, focal seizures (up to 75%).**
- **EEG: Centro-temporal and multifocal spike wave (synchronized) exacerbated in stage I-II sleep.**
- **In general the seizures remit and language improves as the EEG improves, although most have long term speech and language disabilities.**
- **Treatment: corticosteroids, valproic acid, benzodiazepines (diazepam or clobazam). Other treatments have included IVIg. In rare cases were seizures are intractable MST has been used.**
  Avoid: carbamazepine, oxcarbazepine, phenytoin, lamotrigine.

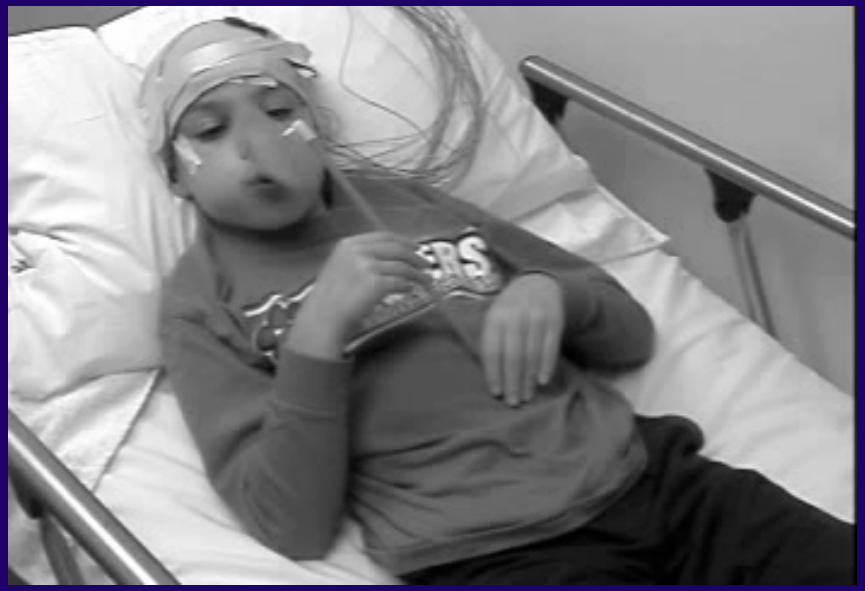
Epileptic Encephalopathy with Continuous Spike and Wave during Sleep

- Age of onset: Usually before age 6 years (4-5 years).
- Types of Seizures: Infrequent focal motor seizures at onset then progresses to multiple seizure types.
- EEG: Continuous bi-frontal and central spike wave in sleep (Stage 1-IV), ESES and disappear in REM stage.
- Prognosis: Seizures may remit, but cognitive deficits persist.
- Treatment: corticosteroids, valproic acid, benzodiazepines (diazepam, clobazam). IVIg rarely used.


Fp1 - F7
F7 - T3
T3 - T5
T5 - O1
Fp1 - F3
F3 - C3
C3 - P3
P3 - O1
Fp2 - F8
F8 - T4
T4 - T6
T6 - O2
Fp2 - F4
F4 - C4
C4 - P4
P4 - O2
Fz - Cz
Cz - Pz
C3 - Cz
600 uV
1 sec

Childhood Absence Epilepsy

- Staring Spells: One of the most common referrals.
- Age range: 3-11yrs
- Clinical: staring spells may or not be associated with automatisms (eye blinking, chewing, head jerks)
- Diagnosis: hyperventilation in the office
- EEG: Generalized 3Hz spike wave
- 36% exhibit attention deficits despite otherwise intact neurocognitive functioning.
- Normal imaging (CAE)
- Linkage: 8q24, gene: CACNA1H, 5q31.1 gene: GABRG2 and 3q26 gene: CLCN2
- Treatment: Drug of choice: ethosuximide; Others: valproic acid and lamotrigine.



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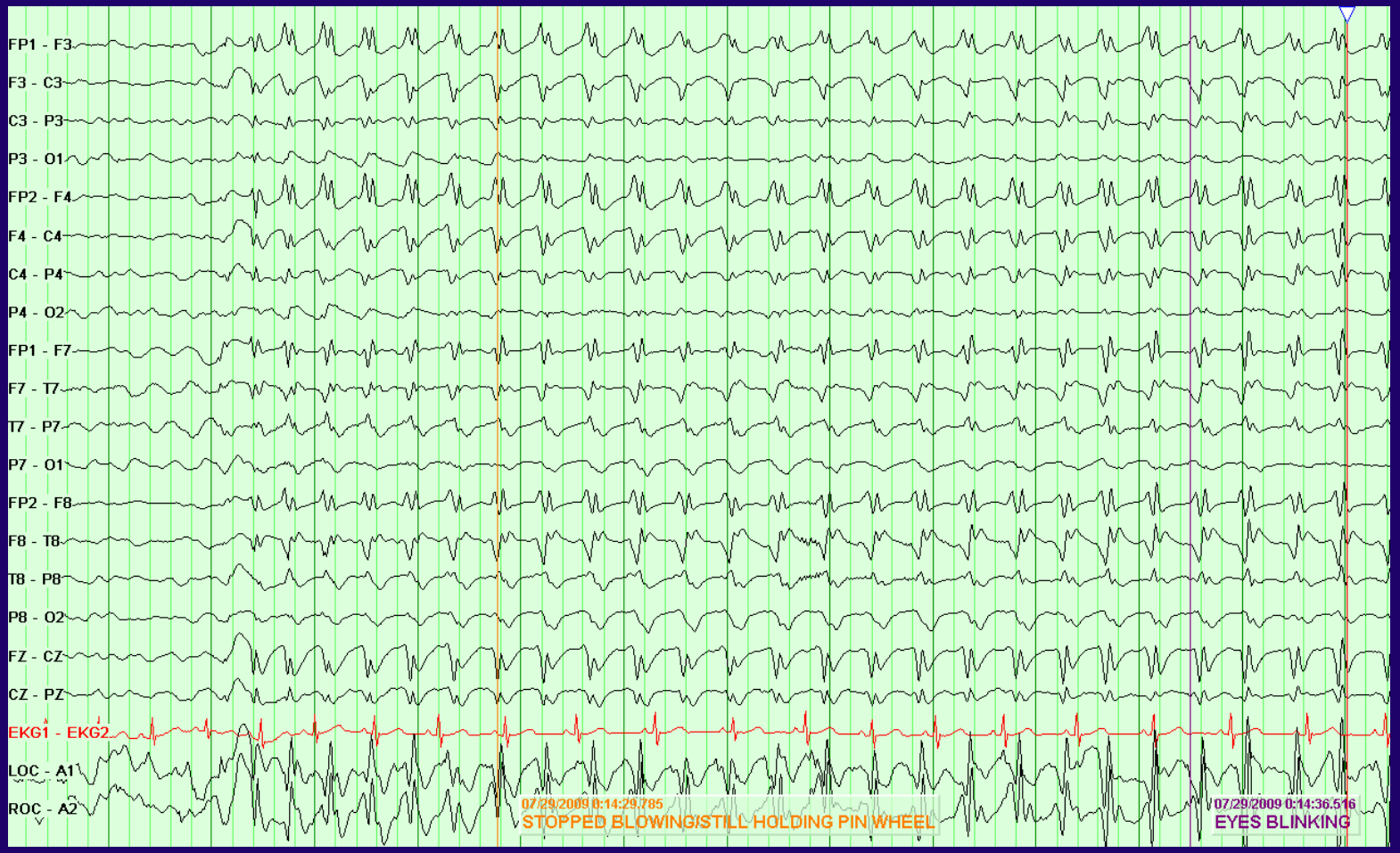
Absence Seizure



Absence with Perioral Myoclonia

- Age of onset: 2-13 yrs
- Seizure description: Absence seizures with perioral myoclonia. Absence status is common. All patients develop GTC seizures.
- EEG: Brief generalize spike/polyspike wave discharges and focal spike-wave. Ictal EEG irregular generalized spike/polyspike wave discharges
- Prognosis: Often treatment resistant and lifelong
- Treatment: valproic acid, ethosuximide, lamotrigine

Eye Lid Myoclonia with or without Absence Seizures (Jeavon Syndrome)

- **Age of onset: 5-8 years**
- **Seizure description: may or may not have absence seizures, eye lid myoclonia, photosensitive seizures and GTC seizures.**
- **EEG: Generalized polyspike wave (3-6 Hz), activated by HV and Photic stimulation.**
- **Prognosis: lifetime condition. Eye lid myoclonia persist and absence seizures improve.**
- **Treatment: valproic acid, ethosuximide, lamotrigine, clobazam dark tinted sunglasses (Zeiss (Z1) lenses).**

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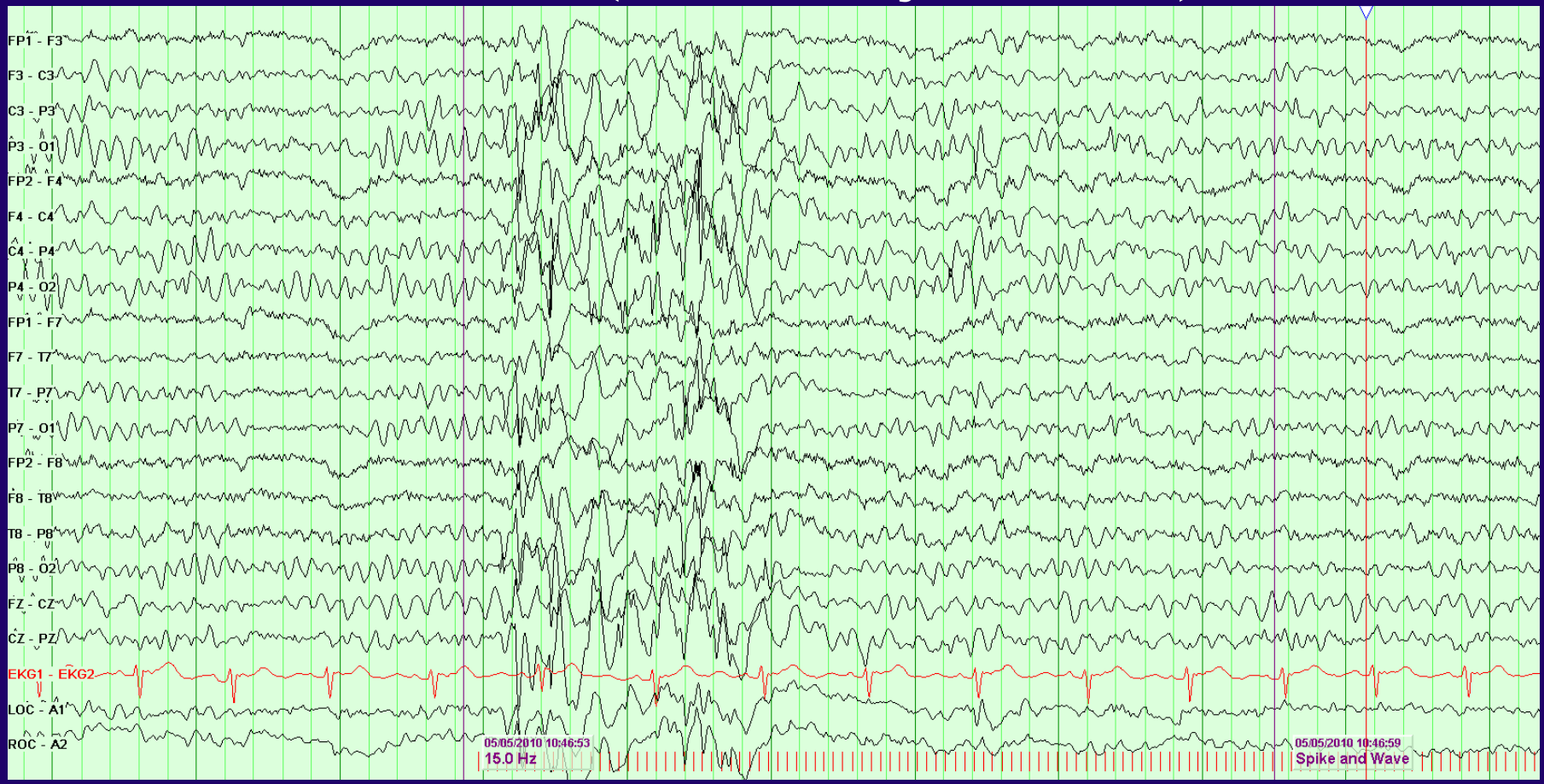
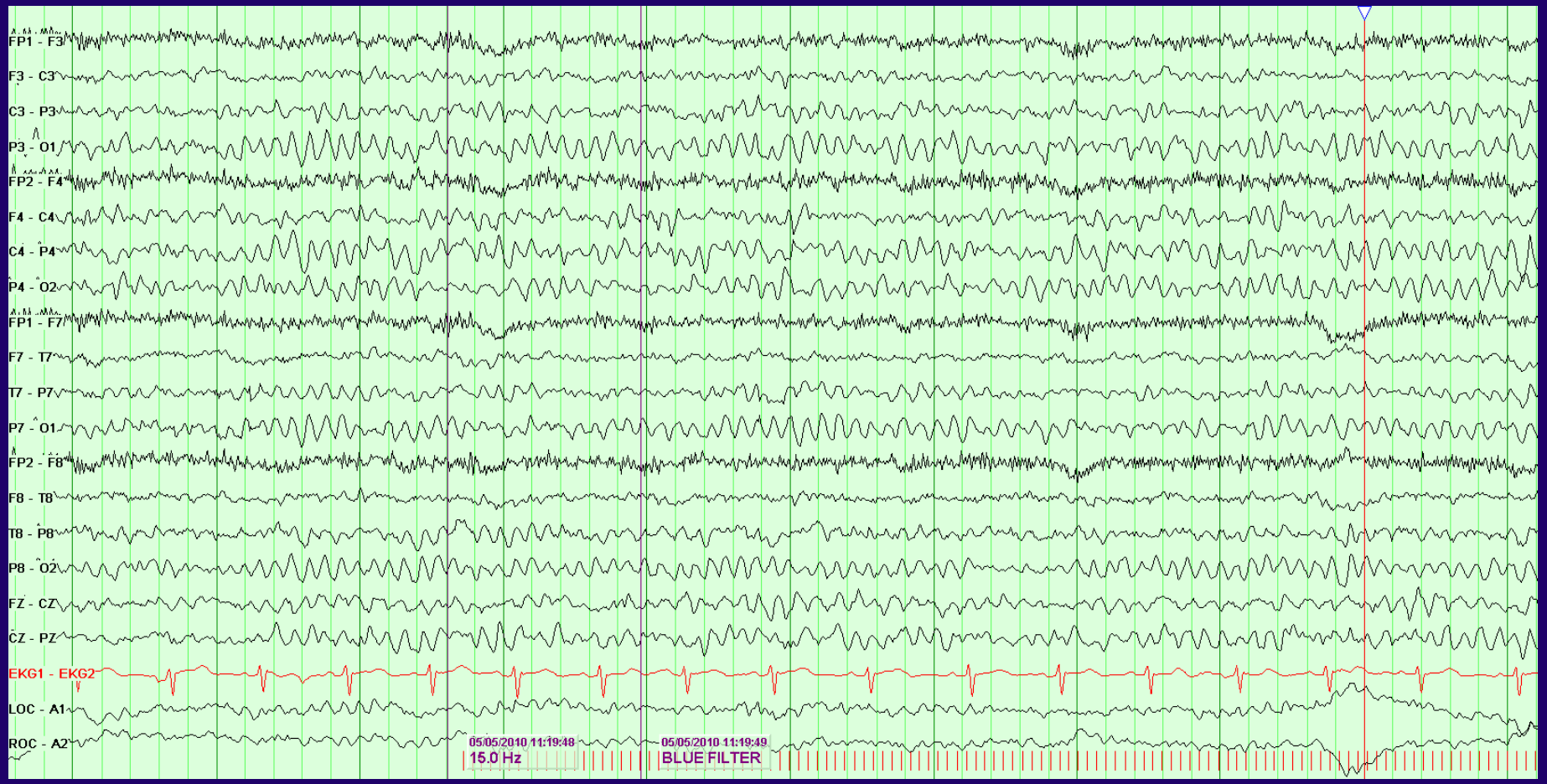
Eye Lid Myoclonia with or without Absence Seizures (Jeavon Syndrome)



Eye Lid Myoclonia with or without Absence Seizures (Jeavon Syndrome)



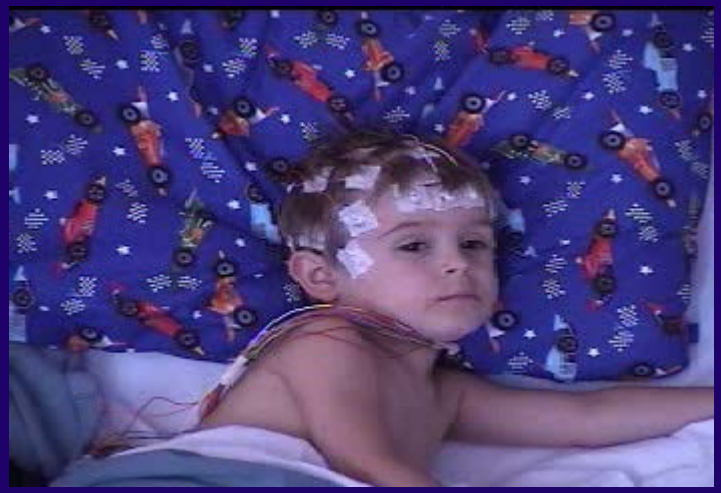
Epilepsy with Myoclonic-Absences

- **Age of onset: 2-12 years (average 7 years)**
- **Male predominance**
- **Etiology: unknown.**
- **Seizure description: abrupt onset of absences accompanied by bilateral rhythmic myoclonic jerks of severe intensity. Each episode of myoclonic absences may last from 10 to 60 seconds.**
- **Other Manifestations: Association with other types of seizures (85%), such as generalized tonic-clonic, pure absence, and falling seizures, occurs in about two thirds of cases reported.**
- **EEG: Generalized 2.5-3 Hz spike wave.**
- **Prognosis: Poor prognosis. May persist into adulthood in about one half of the cases, whereas they disappear in the remaining patients after a mean period of 5.5 years from onset.**
- **Treatment: Refractory to treatment. Valproic acid, ethosuximide (combination of the 2 medications), lamotrigine, topiramate.**

Epilepsy with Myoclonic-Absences

Epilepsy with Myoclonic-Atonic Seizures (Doose Syndrome)

- Sometimes begins with febrile seizures.
- Seizures: myoclonic, atonic, atypical absence, rarely tonic, GTC.
- Onset 7 mo-6 yrs.
- Boys>girls
- Psychomotor retardation is common.
- EEG: generalized spike/polyspike wave.
- 32% of patients have family history of seizures.
- Genetics: complex (multiple genes may be involved)
- Treatment: Valproic Acid, rufinamide, lamotrigine, topiramate, felbamate, clobazam, levetiracetam, ketogenic diet, Steroids, VNS.



Lennox-Gastaut Syndrome

- Age of onset: 2-7yrs
- Infantile spasms (40%)
- Clinical: MR, multiple seizure types (atonic, myoclonic, tonic**, GTC, atypical absence, partial).
- EEG: bi-frontal slow spike wave (1.5-2 Hz).
- Refractory to anti-epileptic medications.
- Genetics: ? (multifactorial)
- Treatment: Drugs of choice: valproic Acid, rufinamide, lamotrigine, topiramate, felbamate, clobazam; Others: levetiracetam; Alternatives: ketogenic diet, VNS, corpus callosotomy.

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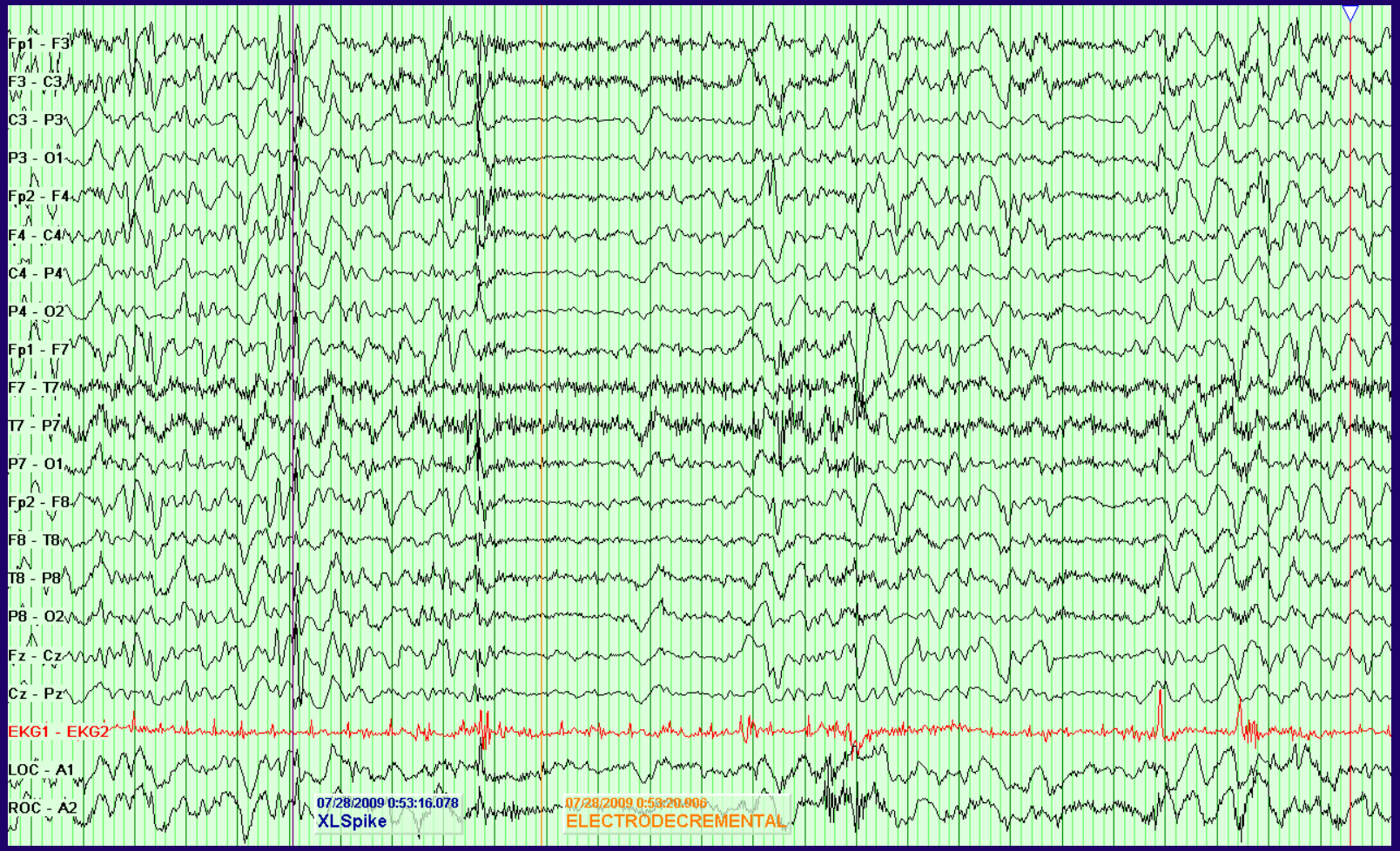
Lennox-Gastaut Syndrome



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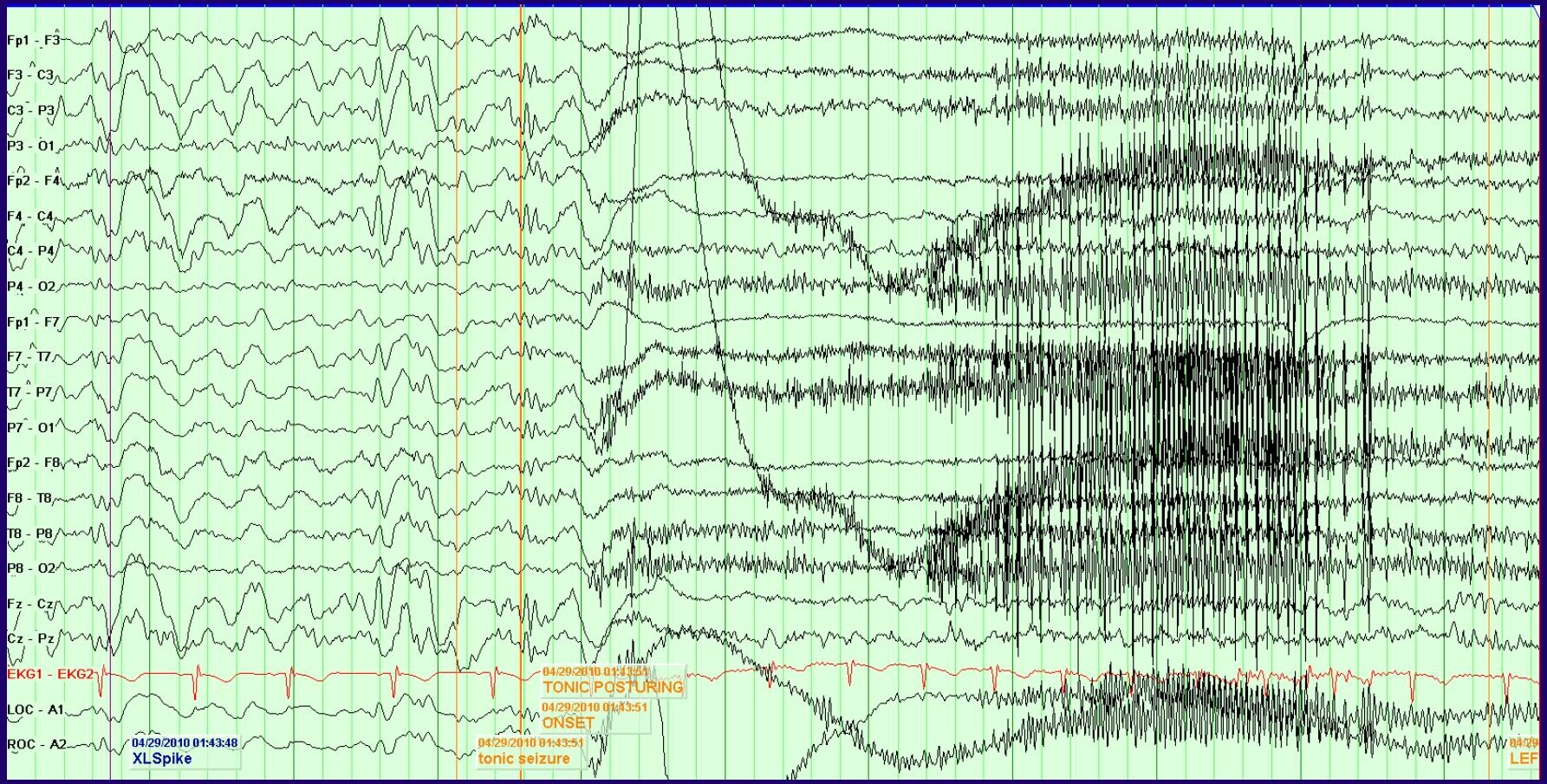
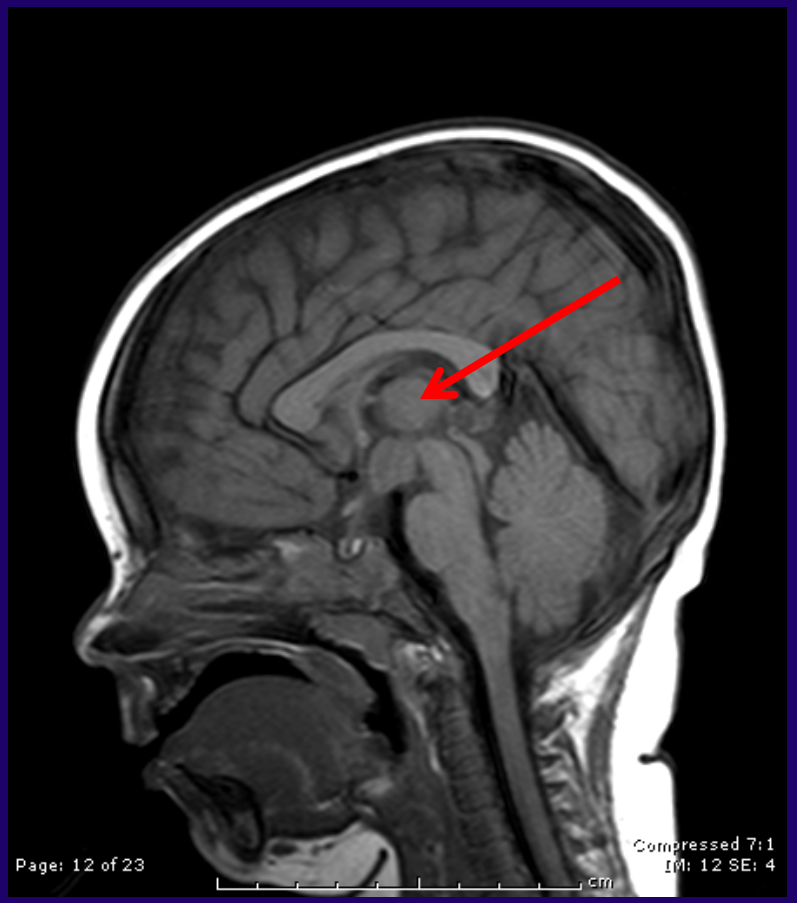
Lennox-Gastaut Syndrome



Gelastic Seizures

- Age of Onset: neonatal-early childhood.
- Seizure types: atypical laughter characterizes the seizures, but they can also have focal, tonic, atonic, TC and absence seizures.
- Etiology: hypothalamic hamartoma is the most frequent finding, though rarely frontal lobe dysplasias or frontal lobe seizures have been associated.
- EEG: ictal diffuse slowing and difficult to localize is the norm, but some have temporal or frontal onset EEG changes.
- Prognosis: early surgery improves long term outcome.
- Treatment: Lesionectomy (thermal ablation) or gamma knife. Refractory to all medications (carbamazepine, oxcarbazepine, lamotrigine, topiramate, levetiracetam and benzodiazepines.



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Gelastic Seizures

Laser Ablation. Monitored in orthogonal slices

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Ablation performed in an intraoperative MR Suite on a 1.5T Siemens Scanner.

3W for 61secs
6W for 79secs
8W for 197secs

Total ablation time ~6 minutes.

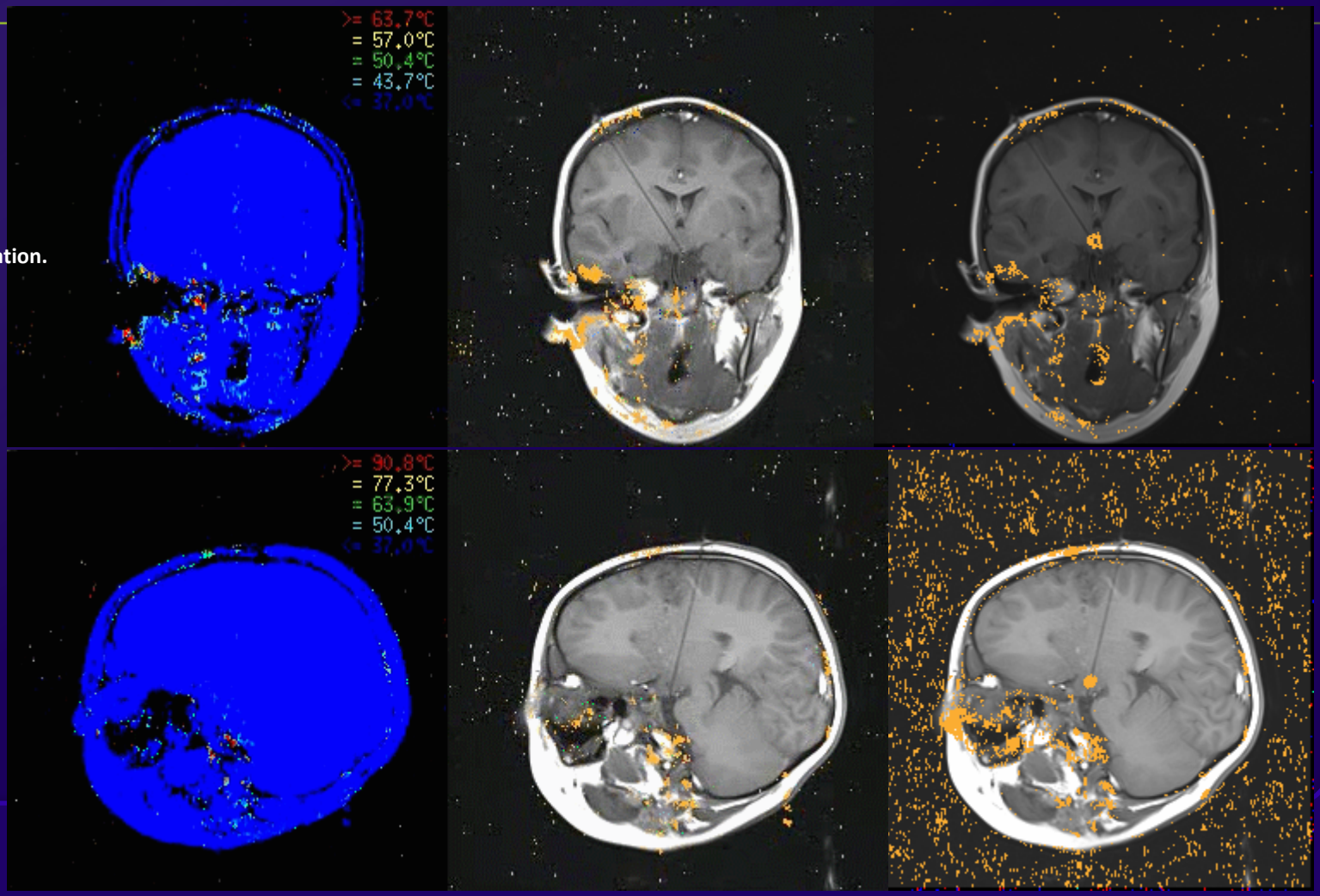
24mm by 12mm ablation.

Animation

Temperature Map

Final Damage Model Image

Damage Model



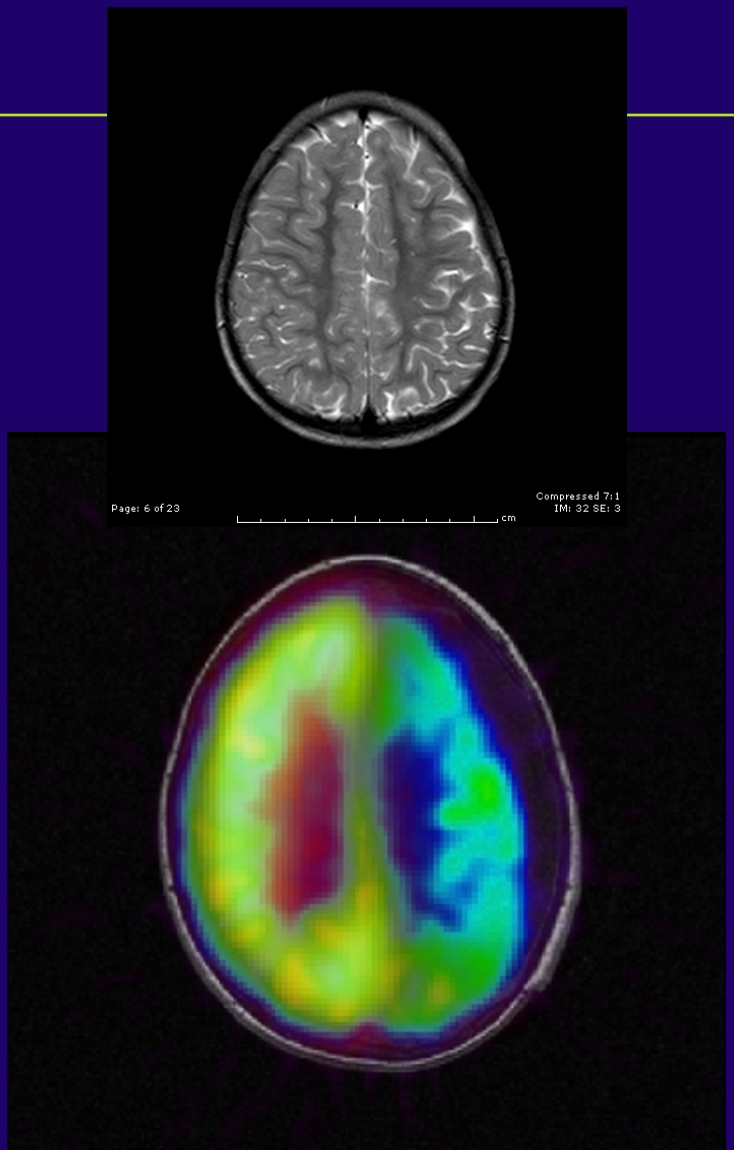
Coronal images

Oblique Images

Visualase Images

Rasmussen Syndrome

- Age of onset: 3-10 years
- Seizure description: focal motor seizures and epilepsia partialis continua.
- EEG: Maybe normal initially, then focal slowing, then spike wave discharges especially in the central areas and multifocal spike wave within a hemisphere.
- Etiology: unknown, suspect encephalitis, immune mediated.
- Treatment: refractory to medication, anatomical>functional hemispherectomy. IVIg, Rituximab and corticosteroids have been used to slow the process.
- Prognosis: unrelenting hemiparesis, memory and speech deficits.



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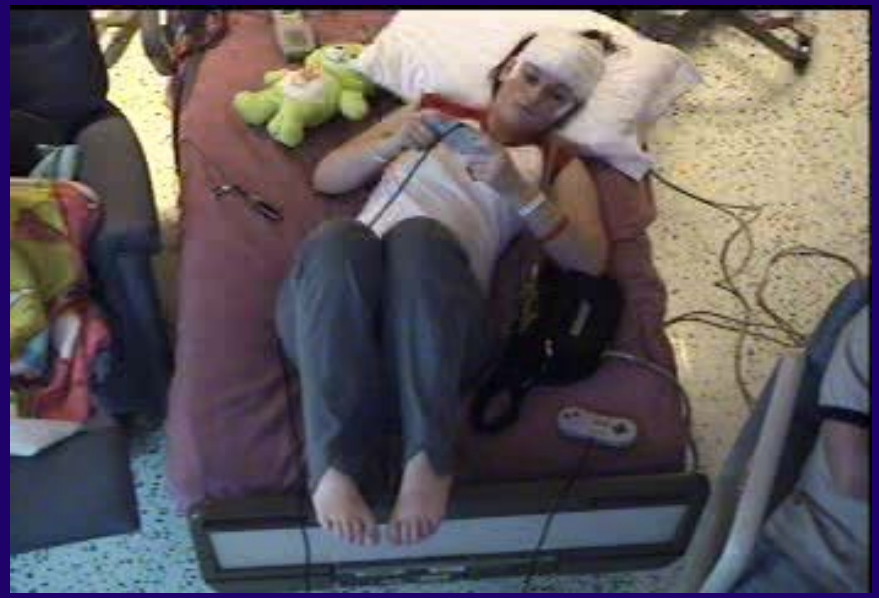
Electroclinical Syndromes in Adolescence

Juvenile Myoclonic Epilepsy

- Age range: 10-17yrs
- Clinical: myoclonic seizures (am), absence seizures and GTC.
- EEG: Generalized spike/polyspike wave, activated with photic and HV.
- Normal intelligence
- Normal imaging
- Linkage: 6p21 (AD), gene: BRD2; 5q14, gene: EFHC1; 5q34, gene: GABRA1
- Treatment: Drugs of choice: lamotrigine, topiramate, valproic acid, levetiracetam; Others: benzodiazepines, felbamate, zonisamide; alternatives: VNS, MAD.



Juvenile Absence Epilepsy

- **Age of onset: 9-13 years**
- **Seizure description: Absence and GTC (20% present in status epilepticus)**
- **EEG: generalized 3-5 Hz spike wave**
- **Intelligence: normal**
- **MRI: normal**
- **Gene: ?**
- **Treatment: valproic acid, lamotrigine, ethosuximide (usually in combination).**

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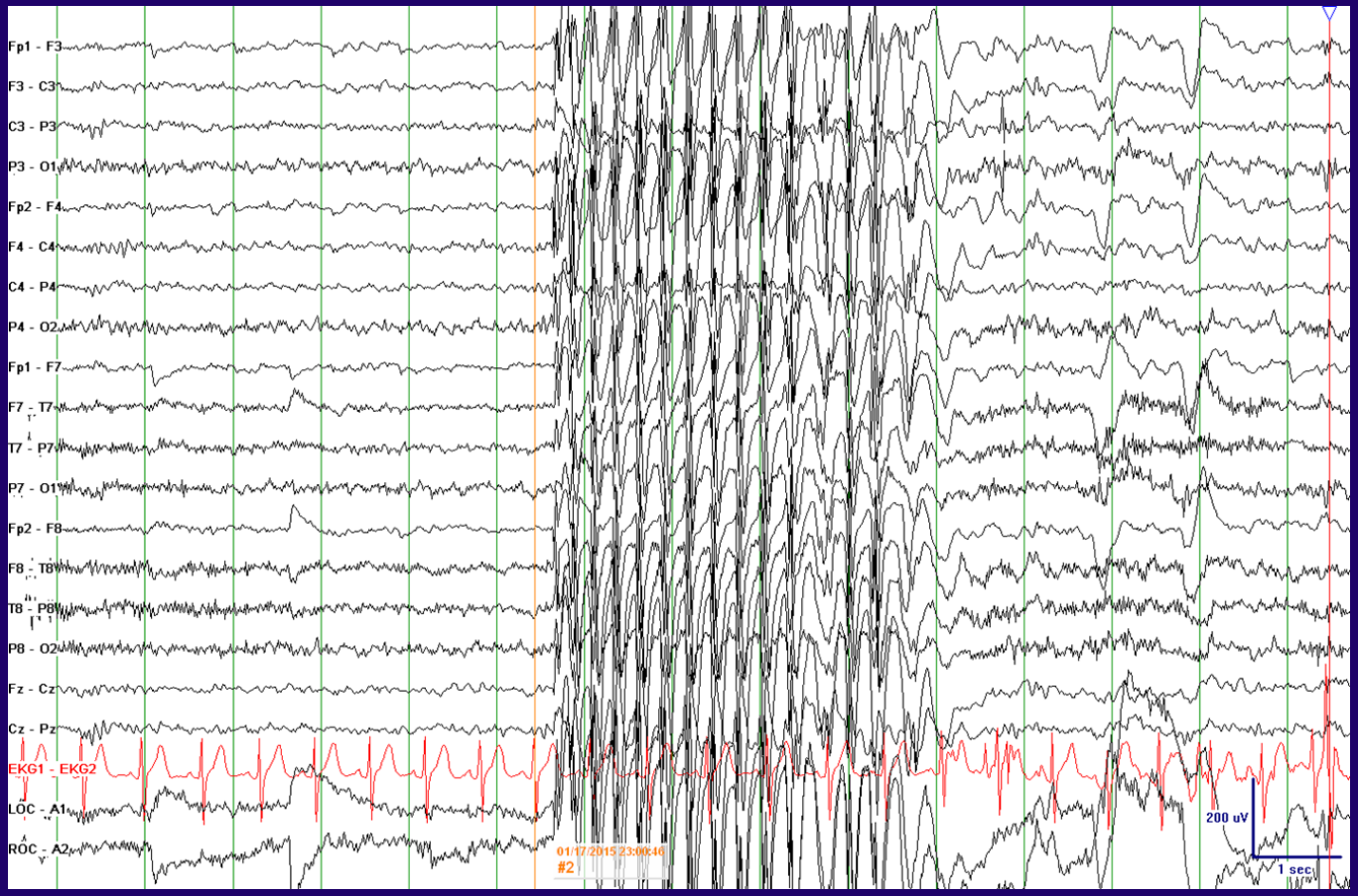
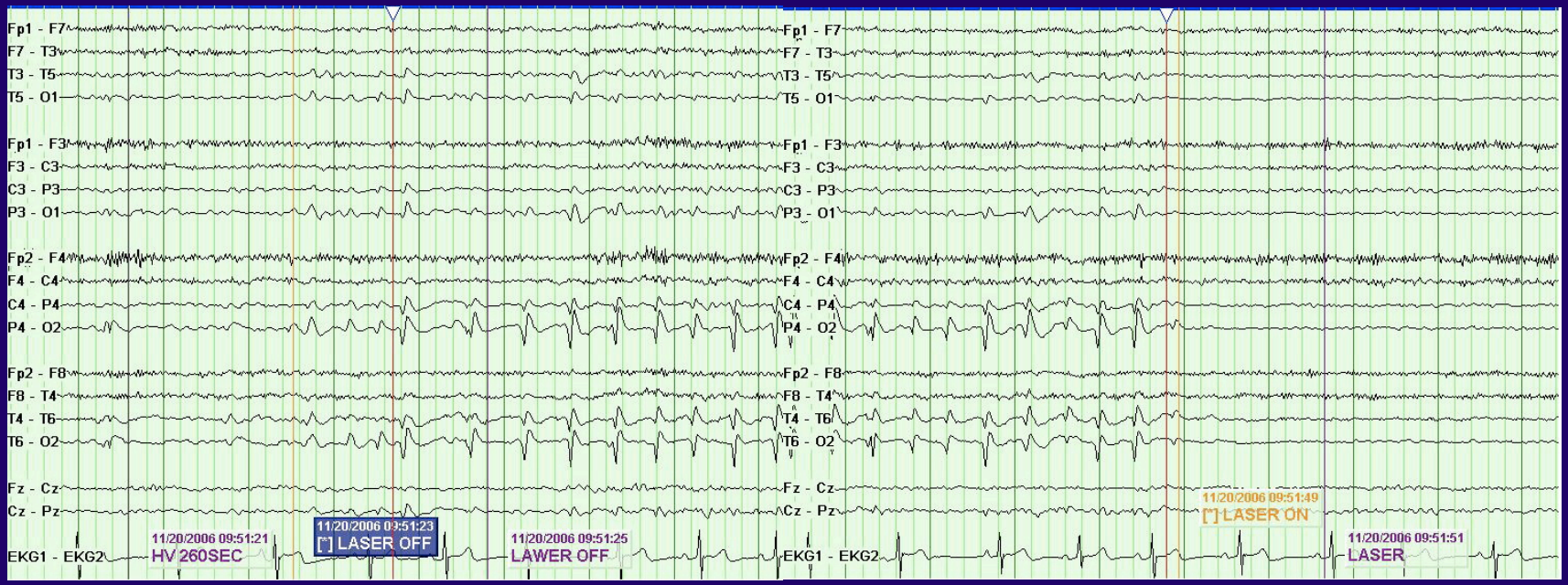
Juvenile Absence Epilepsy



Late Onset Childhood Occipital Epilepsy (Gastaut-Type)

- Age of onset: 8-15 years
- Gastaut type late onset visual disturbances, visual hallucinations. Secondary generalization
- EEG: Unilateral or bilateral occipital spike wave.
- Normal intelligence
- Normal imaging
- Linkage: Multifactorial
- Prognosis: Remission after 2-4 years from diagnosis in 50%.
- Treatment: Drug of choice: carbamazepine and oxcarbazepine; Others: levetiracetam, zonisamide.

Occipital Epilepsy- Fixation-Off Sensitivity EEG



Conclusions

It is important to classify the seizures based on seizure type, age of onset, etiology, EEG, etc. to an electroclinical syndrome.

- **Genetic studies**
- **Educate families on prognosis**
- **Choose the most appropriate anti-seizure medication.**