EEG Course 2010: Generalized Epileptiforms

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Childhood absence epilepsy
- 10% prevalence, incidence 7/100,000/yr
- frequent absence seizures with abrupt onset and termination
- onset 3-10 yrs; peak 5-7 years, female > male
- neurologically normal subject
- 3Hz Spike and wave complexes is the typical EEG abnormality
- generalized tonic clonic seizures- infrequent (<10%) seen only after onset of absence
- some develop GTC in adolescence or early adulthood

Juvenile absence epilepsy
- absences tend to occur in clusters
- age of onset 8-18 years, peak 13 years
- more likely to present with GTCS
- more likely to have myoclonic seizures
- uncertain whether this is a distinct entity from CAE

Childhood Absence Epilepsy - video
small-spike-high-delta complex
Rhythmic notched-delta

HYPERVENTILATION EFFECT

FP1-F7
F7 - T7
T7 - FT
P7 - O1
FPFP-F8
F8 - T8
T8 - P8
P8 - O2
FP1-F3
F3 - C3
C3 - P3
P3 - C1
FPFP2-F4
F4 - O4
C4 - P4
P4 - O2

100 µV
1 SEC
Juvenile myoclonic epilepsy (JME)

- **Prevalence**: 8% to 10% among patients with epilepsies.
- **Age at onset**
  - Absences: 5 to 16 years (peak at 10 years); myoclonic jerks: 8 to 26 years (peak at 14 to 15 years);
  - generalized tonic-clonic seizures (GTCS): months after onset of myoclonic jerks.
- **Sex**: Males = females.
- **Neurological and mental state**: Normal.
- **Genetics**: Probably complex and polygenic inheritance. Susceptibility loci in chromosome 6p11-12 (EJM1) and 15q14 (EJM2). Genes C6orf33 or BRD2 (RING3) in the EJM1 region. Genetic heterogeneity is common.

EEG Findings - JME

- **Inter-ictal EEG**
  - In untreated patients, EEG is usually abnormal, with generalized discharges of irregular 3 to 6 Hz spike/polyspike waves.
  - Focal abnormalities occur in 1/3. Also 1/3 show photoparoxysmal responses. A normal EEG in a patient suspected of having JME should prompt an EEG on sleep and awakening.
- **Ictal EEG**
  - Myoclonic jerks = generalized multiple spikes. Absences = generalized 3 to 6 Hz multiple spike waves.

Juvenile myoclonic epilepsy: 3.5-4.5 Hz SWC

Myoclonic jerk - JME
West's syndrome (Infantile Spasms)
- applied to the triad of hypsarrhythmia, mental retardation and infantile spasms
- IS refers to brief atonia followed by tonic contraction of the axial and proximal limb muscles
- onset before the age of 1 year (mean 4-7 months)
- divided into symptomatic, cryptogenic and idiopathic groups

Infantile spasms
- Infantile spasms with (classical or typical) Hypsarrhythmia
  - 63 % of Infantile spasms (Gastaut 1964)
- Infantile spasms without (typical) Hypsarrhythmia or with atypical Hypsarrhythmia
- 24 hr video-EEG studies of Infantile spasms yield varieties of hypsarrhythmia EEG patterns

Classical (typical) Hypsarrhythmia
Gibbs and Gibbs (1952):
"...random high voltage slow waves and spikes. These spikes vary from moment to moment, both in duration and location ...At times they appear to be focal, and a few seconds later they seem to originate from multiple foci. Occasionally the spike discharge becomes generalized, but it never appears as a rhythmically repetitive and highly organized pattern that could be confused with a discharge of the petit mal or petit mal variant type. The abnormality is almost continuous..."
EEG patterns versus Stage of Sleep

- Awake
- Sleep-1
- Sleep-2-3
- Arousal
- REMs


Hypsarrhythmia

- Hrachovy et al (1984) described 5 types
  - Hypsarrhythmia with burst of generalized SWC and synchronous background
  - Asymmetric Hypsarrhythmia
  - Hypsarrhythmia with a persistent focus of spikes or sharp waves
  - Hypsarrhythmia with episodes (2-10 seconds) of (generalized or regional) flattening
  - Hypsarrhythmia with relative high voltage asynchronous slows and relatively little epileptiform activity

Electrodecremental in Hypsarrhythmia

Infantile Spasms

Seizure
Asymmetric Hypsarrhythmia: Rt hemimegalencephaly

Asymmetric Hypsarrhythmia: Lt Cortical Tubers in Tuberous sclerosis

Hypsarrhythmia with persistent right temporal foci
Lennox Gastaut syndrome
- Electroclinical syndrome often used loosely for intractable epilepsy in childhood
- Key components: difficult to control seizure types, specific interictal and ictal EEG abnormalities and diffuse cognitive dysfunction
- Mixed & multiple seizure types
  - Tonic
  - Tonic-clonic
  - Myoclonic
  - Atypical absences
  - "Drop attacks" - a form of atonic, tonic, or myoclonic seizures

Lennox Gastaut syndrome
- Atonic seizures are rare but the label is abused for seizures where falls occur
- Clinical seizures begin at about the age of 2 yrs
- Typical EEG pattern may not be seen till 3-4 y/o
- Slow spike and wave complexes or multifocal independent sharp waves
- Mental retardation may evolve with time, not all patients are mentally retarded
- Rigorous classification of this syndrome is difficult
Lennox-Gastaut Syndrome: Multifocal spikes

- Classical hypersynchrony evolves into Lennox-Gastaut syndrome:
  - 1.5 y/o with hx of Infantile spasms at 3 mo: generalized spikes and multifocal spikes, background organized

Lennox-Gastaut syndrome: 11 y/o with refractory epilepsy post encephalitis at 2y/o

SSWC with Multifocal spikes

LENNOX-GASTAUT SYNDROME
GENERALIZED SHARP AND SLOW WAVE COMPLEXES

LENNOX-GASTAUT SYNDROME
ATONIC SEIZURES
LGS – Atonic seizure

Myoclonic Astatic Epilepsy (Doose syndrome)

- Onset: 2 and 5 y/o. M:F- 3:1
- Premorbid: Normal (84%) or mild-mod delayed (speech) (Doose and Baier 1987)
- Gen SWC; may have SSWC
- Development decline if sz uncontrolled
- 1st generalized tonic-clonic seizure as initial symptom in more than half of the cases (Doose and Baier 1987a), rarely a myoclonic, astatic, myoclonic-astatic, or absence seizure.
- GTC usu prolonged, recurring frequently and during the daytime.

After a period of GTCs → ‘minor motor seizures’ : myoclonic seizures, absences, and drop attacks. This period of frequent seizures lasts 1 to 3 years
- Drop attacks: pure astatic, myoclonic-astatic, or atypical absence sz

EEG
- Regular and irregular bilaterally synchronous 2- to 3-Hz spike-waves and polyspike patterns with a 4- to 7-Hz background
Myoclonic Astatic Epilepsy (Doose syndrome)

**DDx:**
- Late-onset infantile spasms
- Lennox-Gastaut syndrome, and
- Continuous spike waves in slow sleep (or ESES) or Landau-Kleffner syndrome

**Prognosis:**
- Complete seizure control ~50% (Doose & Baier 1987; Dulac et al 1990)
- Uncontrolled cases: IQ↓ severely retarded. Other neurologic abn: ataxia, poor motor function, dysarthria, and poor language development
- If GTC or tonic seizures appear, prognosis is poor

**Drug of choices:** VPA+LTG (Panayiotopoulos et al 1993).
- VPA, ETX, & BZD (clobazam>clonazepam), have been used successfully (Doose & Baier 1987)
- CBZ, PHT, and VGB aggravate sz, PB should be avoided with VPA (Perucca et al 1998)

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**Epilepsy with Myoclonic Absences (Tassinari's syndrome)**

- Onset: few months – early teen (mean 7 yo)
- Prevalence 0.5-1%, male > female
- Premorbid: normal development
- Myoclonic absences: impaired consciousness with myoclonic jerks of UEs, head, body
- No eyelids twitching, ± perioral myoclonia
- Tonic contracture UEs-> elevation UEs
- Other sz 2/3: GTC(poor prognosis)
- EEG: brief gen discharges 3Hz

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**Lennox-Gastaut syndrome versus EM-AS of Doose**

<table>
<thead>
<tr>
<th>Lennox-Gastaut syndrome</th>
<th>EM-AS of Doose</th>
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<tbody>
<tr>
<td>Main seizures</td>
<td>Tonic, atomic and atypical absences</td>
</tr>
<tr>
<td></td>
<td>Myoclonic, atomic and myoclonic-atomic</td>
</tr>
<tr>
<td>Tonic seizures</td>
<td>Common and characteristic: diurnal and nocturnal</td>
</tr>
<tr>
<td></td>
<td>Probable exclusion criteria: Incidental tonic seizures are accepted by some authorities</td>
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<tr>
<td>Tonic drop attacks</td>
<td>Common</td>
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<tr>
<td></td>
<td>Uncommon; they occur independently of other seizures</td>
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<tr>
<td>Atypical absences</td>
<td>Common</td>
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<td></td>
<td>Uncommon; they usually accompany myoclonic or tonic episodes</td>
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<tr>
<td>Developmental abnormalities before onset of seizures</td>
<td>Symptomatic or possibly symptomatic idiopathic cases (accepted by some authorities)</td>
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<tr>
<td></td>
<td>Idiopathic* (though symptomatic or possibly symptomatic cases are included in the 1989 ILAE classification*)</td>
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<tr>
<td>Autopsy</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Common</td>
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<tr>
<td>Genetic predisposition</td>
<td>Common</td>
</tr>
<tr>
<td></td>
<td>Incompatible</td>
</tr>
<tr>
<td>Development from West syndrome</td>
<td>Abnormal by rule</td>
</tr>
<tr>
<td></td>
<td>Usually normal, particularly at onset</td>
</tr>
<tr>
<td>EEG background</td>
<td>Abnormal by rule</td>
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<tr>
<td></td>
<td>Common and characteristic</td>
</tr>
<tr>
<td></td>
<td>Exceptional and mainly in sleep</td>
</tr>
<tr>
<td>EEG isoelectric fast activity and rapid spikes</td>
<td>Usually &lt;3-0.5 Hz</td>
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<tr>
<td></td>
<td>Usually 3-9 Hz</td>
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<tr>
<td>EEG 0.5-3Hz</td>
<td>Commonly bad</td>
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<td>Commonly relatively good</td>
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**Myoclonic Astatic Epilepsy (Doose syndrome)**

VPA, ETX, & BZD (clobazam>clonazepam), have been used successfully (Doose & Baier 1987)
CBZ, PHT, and VGB aggravate sz, PB should be avoided with VPA (Perucca et al 1998)
Myoclonic Absences (Tassinari’s syndrome)

- Half pts resistant to treatments -> cognitive deterioration
- Treatments: VPA high doses with ESM or LTG.
  - TPM, LEV, Clonazepam and Acetazolamide should be tried.

Epilepsy with Myoclonic Absences

Ohtahara Syndrome

- Onset in early infancy
- Main seizure pattern: brief tonic seizures
- Other sz types: clonic sz, erratic myoclonic jerks, partial seizures. Later in the course, GTC (both in awake and in sleep) usually when the infant is disturbed or awakened.
- After onset of sz, pt inactive and hypotonic

CLINICAL MANIFESTATIONS (cont.)

- Severe psychomotor retardation
- Intractable seizures
- Poor prognosis, 50% reported die in infancy or childhood
- Polyetiology: cortical dysgenesis, hyperglycinemia, HIE
- Progression to West syndrome between 2 and 6 months of age -> LGS or -> severe partial epilepsy

EEG in Ohtahara’s

- Interictal EEG: suppression-burst with high-voltage paroxysmal discharges separated by nearly flat tracing that last for up to 18 seconds
- S-B pattern: predominant or asynchronous and may increase during sleep.
- S-B may gradually -> hypersynchrony (WS) between 3-6 mo, then to SSWC (LGS) (Ohtahara et al 1987)

Early myoclonic encephalopathy

- Aicardi and Goutieres (1978)
- Onset of erratic or fragmentary myoclonus, as early as a few hours after birth.
- Other sz types: simple partial szs, massive myoclonia, and tonic spasms
- Erratic, partial myoclonus usu. involves the face or extremities and may be restricted to an eyebrow, a single limb, or a finger, shift typically from one part of the body to another in a random, asynchronous fashion
EME - CLINICAL MANIFESTATIONS:

- Partial szs are frequent and occur shortly after erratic myoclonus.
- Semiology of partial szs: subtle, consisting, for instance, of eye deviation, autonomic Δ such as apnea, or flushing of the face (Dalla Bernardina et al 1983).
- Tonic szs are reported frequently, and can occur as early as in 1st mo life or after.
- Real epileptic spasms are rare and generally appear later.

EME - Etiology:

- Nonketotic hyperglycinemia (Dalla Bernardina et al 1979)
- D-glyceric acidemia (Grandgeorge et al 1980)
- Propionic acidemia (Vigevano et al 1982)
- Molybdenum cofactor deficiency (Aukett et al 1988)
- Methylmalonic acidemia (Lombroso 1990)

<table>
<thead>
<tr>
<th>Ohtahara</th>
<th>EME</th>
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<tr>
<td>Main seizures</td>
<td>Tonic spasm</td>
</tr>
<tr>
<td>Main etiology</td>
<td>CNS malformations</td>
</tr>
<tr>
<td>Suppression-Burst</td>
<td>Sleep and awake</td>
</tr>
<tr>
<td>Paroxysmal burst</td>
<td>Longer</td>
</tr>
<tr>
<td>Suppression</td>
<td>Shorter</td>
</tr>
<tr>
<td>Transformation to West syndrome</td>
<td>As a rule</td>
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Severe Myoclonic Epilepsy in Infancy (Dravet syndrome)

- Described by Dravet in 1978
- 1/20,000-40,000 (Hurst 1990, Dravet et al 1992)
- Polymorphic epilepsy of infants (Aicardi 1986)
- Onset within 1st yr of life
- Usually triggered by fever, begins with unilateral clonic sz, often alternating, or generalized
- Sz may be brief or long in duration
- It often recurs in 6 to 8 wks, may be prolonged, -> febrile status
- Later in the course-> afebrile seizures

Dravet syndrome (SMEI)

- Pre-seismic period: early onset febrile clonic sz, unilateral or generalized,brief or prolonged, freq FBS, freq->convulsive status
- Seismic period: other sz types; myoclonic, atypical absence, complex partial sz ->2nd gen. Myoclonic -> myoclonic status
- Post-seismic period: sz improved but serious & residual mental/abn neuro remain forever

SMEI - Clinical manifestations:

- Psychomotor retard- 2nd yr after onset of sz
- Progressive neurologic deficits: ataxia & corticospinal tract signs
- All are cognitively impaired (severely in 50%) but without deterioration after the age of 4 years (Guerrini and Dravet 1998)
- Mortality: 15.9% - 18% (Dravet et al 2002). The cause of death is variable, including drowning, accident, seizure, SE, infection, and sudden unexpected death
EEG in SMEI

- Interictal EEGs: generalized and focal and multifocal anomalies
- Photosensitivity in ≥ 40% (Dravet et al 2002)
- Background is variable, often with an either transitory or permanent
- EEG: a diffuse dysrhythmia of slow waves, intermixed with focal and diffuse spikes

PATHOGENESIS & PATHOPHYSIOLOGY

- 15% to 25% of cases +ve family history of either epilepsy or FBC, suggesting genetic
- 4 series of sporadic SMEI (137 patients), 35–100% of patients had SCN1A mutations (Claes et al 2001, Sugawara et al 2001, Ohmori et al 2002 and Nabbout et al 2003)
- Mutations in SCN1A-33% (Wallace RH et al. Neurology. 2003 Sep 23; 61(6): 765-9)

Treatment - SMEI

- Very refractory
- VPA & BZD (clonazepam, lorazepam) the most useful drugs.
- PB, KBr (convulsive seizures), and ETX (myoclonic szs and absences) can help some children.
- CBZ and LTG often have an aggravating effect (Guerrini et al 1998; Wallace 1998)

Clinical spectrum of Epileptic spasms assoc with cortical malformation

- Ohtahara synd
- West Syndrome
- LGS and Symptomatic Gen epilepsies
- WS with Partial sz
- Localized-related Epilepsies
- Localized-related Epilepsies

Kobayashi. Neuropediatrics 2001:236-244
PLEDs in Children - (based on 7 patients)

- Often in context of chronic rather than acute lesion (immature animal preparation only displays PLED’s in chronic phase)
- Often diffuse CNS dysfunction-often metabolic factors
- Often continue to have seizures after PLED’s
- Often do not have decreased level of alertness with PLED’s

**SSPE**

- Period 4-20 sec with mean 5-8 sec
- complex complexes of slow waves
- last 1-3 sec
- may begin focally but usually generalized and synchronous
- have myoclonic jerks associated with discharges
- Complexes may only be seen during sleep

**PERIODIC LATERALIZED EPILEPTIFORM DISCHARGES (PLEDS)**

14 y/o with fever, left hemiconvulsion and acute right hemispheric infarction

10 y/o with SSPE: Periodic complexes occurring every 0.5-3 sec

5 y/o with SSPE presented with Progressive myoclonic epilepsy and cognitive decline

Markand ON., Panszi JG. The Electroencephalogram in Subacute Sclerosing Panencephalitis Arch Neurol 1975 :32:719-26

Period 4-20 sec with mean 5-8 sec

complex complexes of slow waves

last 1-3 sec

may begin focally but usually generalized and synchronous

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Complexes may only be seen during sleep