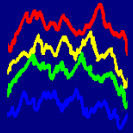


EPILEPTIC ENCEPHALOPATHIES

Marina Nikanorova

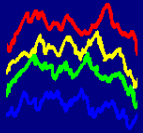
Danish Epilepsy Center, Dianalund



Definition

(ILAE Task Force on Classification and Terminology, 2001)

Epileptic encephalopathy is a pathologic condition in which the epileptic process is believed to contribute to the progressive disturbance in the cortical functions



Epileptic encephalopathies

Neonates

- Early myoclonic encephalopathy
- Ohtahara syndrome
CSWS

Early infancy

- Migrating partial epilepsy
of infancy

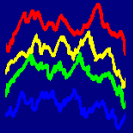
Infancy

- West syndrome

• Dravet syndrome

Childhood

- Myoclonic astatic epilepsy
- Epileptic encephalopathy with
including Landau-Kleffner syndrome
- Lennox – Gastaut syndrome
- Rasmussen syndrome



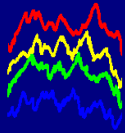
Cognitive, motor and sensory deterioration in epileptic encephalopathies

II. Due to the very frequent or severe seizures

(e.g. early myoclonic encephalopathy, Dravet syndrome, migrating partial epilepsy of infancy, Lennox-Gastaut syndrome)

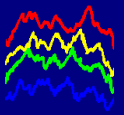
II. Due to the subcontinuous paroxysmal interictal activity

(e.g. Ohtahara syndrome, West syndrome, encephalopathy with CSWS)



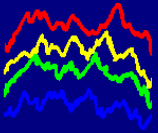
Early myoclonic encephalopathy

- neonatal onset
- persistent partial /fragmentary erratic myoclonia associated with partial motor seizures
- at the age of 3-4 months occur repetitive tonic spasms
- EEG - suppression-burst pattern
- severe psychomotor delay, marked hypotonia, disturbed alertness
- poor prognosis (> 50 % cases - death before age 1-2 years or vegetative state)



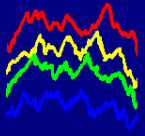
Early myoclonic encephalopathy: ictal event





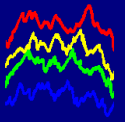
Lennox – Gastaut syndrome

- onset – 3 – 10 years (peak 3 – 5 years)
- seizure types – tonic axial, atonic, atypical absences, episodes of non-convulsive status epilepticus
- EEG – bursts of diffuse slow spike-waves, 1 -2 Hz, during wakefulness and slow polyspikes and generalized fast rhythms, 10 Hz, during sleep
- intellectual deterioration associated with diffuse personality disorder
- seizure intractability



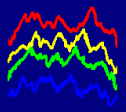
Lennox-Gastaut syndrome: tonic seizure





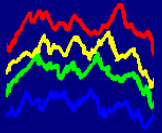
Lennox-Gastaut syndrome: atonic seizure





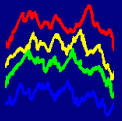
Ohtahara syndrome

- onset – early infancy, 75 % before age 1 month
- etiology – lissencephaly, Aicardi syndrome, cortical dysplasia, hemimegalencephaly
- tonic spasms, symmetric or lateralized, single or clusters
- other seizure types – partial seizures, rare myoclonic
- EEG – suppression – burst pattern
- arrest of psychomotor development, spastic bi-, hemi- / tetraparesis, ataxia, dystonia
- seizure intractability
- poor prognosis – severe psychomotor retardation, often death in early infancy

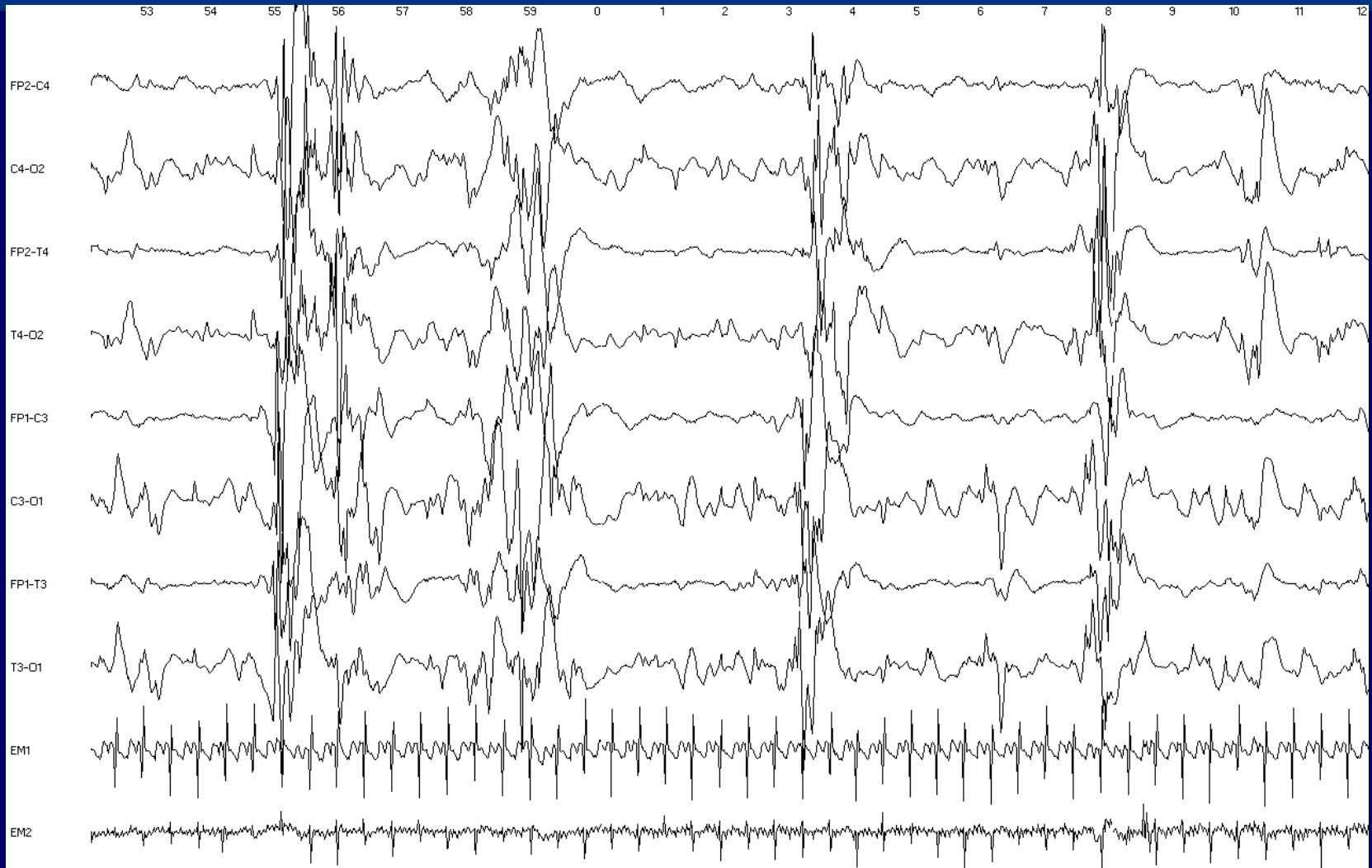


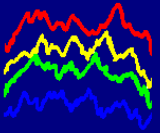
Ohtahara syndrome: ictal event





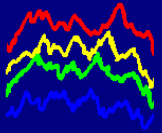
Ohtahara syndrome: suppression – burst pattern





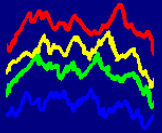
West syndrome

- onset – 3 – 10 months
- infantile spasms
- EEG – hypsarrhythmia
- mental retardation
- visual and/or auditory agnosia, autism, hyperkinetic behaviour
- 6 – 15 % spontaneous remission, 25 – 30 % multifocal epilepsy, 40 – 50 % Lennox-Gastaut syndrome



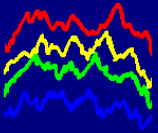
West syndrome: ictal event





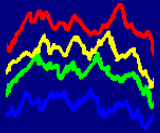
West syndrome: hypsarrhythmia





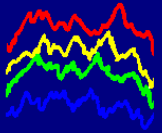
Encephalopathy with CSWS

- age-related, self-limited disorder
- typical EEG-pattern – CSWS (continuous spike-waves during slow sleep)
- epilepsy with focal / apparently generalized seizures
(uni- or bilateral clonic, tonic-clonic, absences, partial motor, atonic)
- neuropsychological impairment (global or selective regression of cognitive functions, apart from acquired aphasia)
- motor impairment (ataxia, dyspraxia, dystonia)



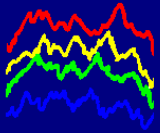
Encephalopathy with CSWS





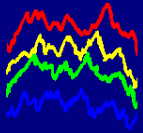
Specific features of childhood epileptic encephalopathies

- heterogeneity
- severity
- cognitive impact
- pharmacoresistance
- syndrome – specific efficacy profile of AEDs



Factors of epilepsy intractability in children different to those in adults

- many epileptic syndromes are unique pediatric conditions
- seizures are more frequent
- negative influence of seizures on the development
- negative impact of AEDs on the development
- developmental plasticity



Evolution of epileptic encephalopathies

Unique pediatric

Transitional

Adult

0 – 6 years

4 – 10 years

> 10 years

Early myoclonic encephalopathy

Migrating partial epilepsy of infancy

Ohtahara syndrome

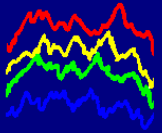
West syndrome

Myoclonic astatic epilepsy

Lennox – Gastaut syndrome

Rasmussen syndrome

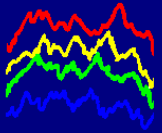
Encephalopathy with CSWS



More frequent seizures in children compared to those in adults

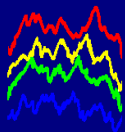
Especially in the very young children with unique pediatric disorders

- in adults seizures often occur on a weekly or monthly basis, in young children – up to 50 seizures per day
- unsuccessful medication can be determined in a few days or weeks
- combinations of AEDs can be evaluated in a few months



Negative influence of seizures on the development

- Compared to adults, epilepsies with frequent seizures in children are catastrophic in relation to the psychomotor development
- Seizures themselves may cause developmental delay and mental retardation
- Control of seizures in children can ameliorate the developmental delay



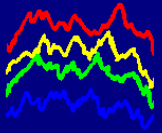
Negative impact of AEDs on the development

- AEDs may cause in children the decrease in awareness, activity and learning
- High AED doses are often required to maintain the seizure control



Seizure control

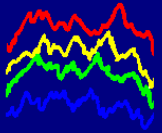
**AED impact on ability to learn
and develop**



Developmental plasticity

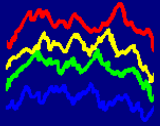
The opportunity of brain reorganization is present in early childhood but not in adults

Example: the child with left hemispherectomy at the age < 5-7 years can develop functional language presumably by transfer of the language area to the non-dominant hemisphere



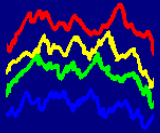
Treatment of epileptic encephalopathies: main approaches

- AED treatment
- epilepsy surgery of epileptogenic lesional zones
- ketogenic diet
- vagal nerve stimulation



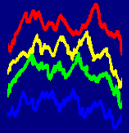
Treatment protocols in epileptic encephalopathies

- **Dravet syndrome** – Stiripentol + Frisium
- **West syndrome** – Vigabatrin, ACTH, Hydrocortison
- **Myoclonic astatic epilepsy** } Valproate + Lamotrigine
- **Lennox-Gastaut syndrome** }
- **Encephalopathy with CSWS** – steroids, Ospolot, Valproate, Clobazam



New AEDs in treatment of epileptic encephalopathies

- deficit in therapeutic trials for childhood epilepsy syndromes
- trials are performed mainly in children with focal epilepsy, while epileptic encephalopathies are neglected
- infantile epilepsies remain “therapeutic orphans”
- epileptic encephalopathies require specific trials

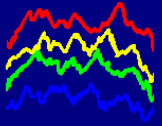


Epileptic encephalopathies: from child to adult

- Connection between childhood and adult epileptologists is still somewhat of a gap
- Epileptic encephalopathies are simplified in adults into a vague and broad conception of “Lennox-Gastaut” syndrome → specific etiologies and treatment protocols are often ignored

HOWEVER:

- Increase in life expectancy and social integration of patients with childhood epileptic encephalopathies



LET'S BRIDGE THE GAP!