Comprehensive ILAE teaching course with a combination of lectures and expert-led practical sessions

Clare College, Cambridge, UK
30th March – 2nd April 2026

EEG in the First Year of Life

- from newborn to toddler

Course directors

Dr Ronit Pressler
Great Ormond Street Hospital for Children, London, UK

Dr Monika Eisermann
Dr. von Haunersches Kinderspital, München, Germany

Timetable

Monday, 30th March 2026		
09:00-10:20	***Registration* and refreshments**	**Garden Room**
10:20-10:30	***Welcome***	**Riley Auditorium**
10:30-11:00	**Rachel Thornton (UK)** Technical aspects, challenges, and pitfalls	**Riley Auditorium**
11:00-11:30	**Fabrice Wallois (France):** Normal EEG in preterm and term infants	**Riley Auditorium**
11:30-12:00	**Emilie Bourel-Ponchel (France)** Normal EEG in Infancy	**Riley Auditorium**
12:00-13:00	***Lunch***	**Garden Room**
13:00-13:30	**Monika Eisermann (Germany):** Abnormal EEG in newborns and infants	**Riley Auditorium**
13:30-14:00	**Alexandre Datta (Switzerland)** Sleep in infancy – normal and abnormal	**Riley Auditorium**
14:00-15:30	Workshop I - Normal EEG in newborns & infants	**Seminar rooms**
15:30-16:00	***Coffee break***	**Garden Room**
16:00-17:30	Workshop I - Abnormal EEG in newborns & infants	**Seminar rooms**
18:30-19:30	***Dinner***	**The Buttery**

Tuesday, 31st March 2026		
09:00-09:30	**Sushma Goyal (UK):** EEG in preterm brain injury	**Riley Auditorium**
09:30-10:00	**Geraldine Boylan (Ireland)** EEG in HIE & neonatal stroke	**Riley Auditorium**
10:00-10:30	***Coffee break***	**Garden Room**
10:30-12:30	Workshop III - Brain injury in term & preterm infants	**Seminar rooms**
12:30-13:30	***Lunch***	**Garden Room**
13:30-14:00	**Ronit Pressler (UK):** EEG in neonatal seizures	**Riley Auditorium**
14:00-14:30	**Ronit Pressler (UK):** Classification of neonatal seizure & epilepsies	**Riley Auditorium**
14:30-15:00	**Topun Austin (UK):** Neonatologists view of EEG and aEEG	**Riley Auditorium**
15:00-15:30	***Coffee break***	**Garden Room**
15:30-17:30	Workshop IV - Neonatal seizures	**Seminar rooms**
	Free evening	

Wednesday, 1st April 2026		
09:00-09:30	**Monika Eisermann (Germany):** Early onset developmental & epileptic encephalopathies	**Riley Auditorium**
09:30-10:00	**Christian Korff (Switzerland)** Hypsarrhythmia and epileptic spasms	**Riley Auditorium**
10:00-10:30	***Coffee break***	**Garden Room**
10:30-12:30	Workshop V – DEEs in Infancy	**Seminar rooms**
12:30-13:30	***Lunch***	**Garden Room**
13:30-14:00	**Nicola Specchio (Italy):** EEG abnormalities in genetic disorders	**Riley Auditorium**
14:00-14:30	**Federico Vigevano (Italy):** EEG abnormalities in inborn error of metabolism	**Riley Auditorium**
14:30-15:00	**Nicola Specchio (Italy):** EEG in self-limiting epilepsy syndromes	**Riley Auditorium**
15:00-15:30	***Coffee break***	**Garden Room**
15:30-17:30	Workshop VI – Epilepsy syndromes in infancy	**Seminar rooms**
19:00-22:30	***Drinks Reception and Gala Dinner***	**Grand Hall**

Thursday, 2nd April 2026		
09:00-09:30	**Rachel Thornton (UK)** Cortical malformations in infancy	**Riley Auditorium**
09:30-10:00	**María Ángeles Pérez-Jiménez (Spain):** Non-epileptic events in infancy	**Riley Auditorium**
10:00-10:30	***Coffee break***	**Garden Room**
10:30-12:15	Workshop VII – Mixed cases	**Seminar rooms**
12:20-13:00	**Ronit Pressler & Monika Eisermann** Quiz	**Riley Auditorium**
13:00-13:30	***Lunch***	**Garden Room**
13:30	***END OF COURSE***	

Course director and admin

Ronit M Pressler, PhD, MD, FRCP, MRCPCH, London, UK

Ronit Pressler is Head of the Department of Clinical Neurophysiology and Consultant in Clinical Neurophysiology at Great Ormond Street Hospital for Children. She is Associate Professor at the UCL Great Ormond Street Institute of Child Health, London, and Visiting Professor at the Medical University of Vienna.

She serves as Secretary of the ILAE Europe Commission. Since 2015, she has served on the Council of the British Society for Clinical Neurophysiology (BSCN) and currently serves as President. She chairs and has chaired several ILAE task forces and neonatal working groups, including the ILAE Neonatal Seizure Task Force and the ILAE Acute Symptomatic Seizure Task Force. She is Associate Editor of Epilepsia Open.

Her research focuses on neonatal and paediatric EEG, the diagnosis and treatment of neonatal seizures, and epilepsy in early childhood.

Monika Eisermann, MD, MD, Munich, Germany

Dr Monika Eisermann is Consultant Pediatric Epileptologist and Clinical Neurophysiologist at the Munich University Center for Children with Medical and Developmental Complexity in Germany. After medical studies, fellowship in Pediatrics, Neuropediatrics and Epileptology, and doctorate in Germany, she trained in Clinical Neurophysiology at Saint Vincent de Paul Hospital in Paris with Perrine Plouin. Until 2025, she worked at the Pediatric University Hospital Necker Enfants Malades Hospital in Paris.

She served as member of the executive committee of the French Society of Clinical Neurophysiology Society, acting as delegate and liaison officer to the International Societies. Her research interests are neonatal epilepsies and early onset developmental and epileptic encephalopathies. She has a vast teaching experience resulting from lectures given at French universities, by organizing national seminaries and workshops in pediatric clinical neurophysiology, and by lecturing at national and international congresses and courses. Since 2011, she is director of the Pediatric Virepa EEG course of the ILAE Academy, in 2018, she co-founded the ILAE school of EEG in the first year of life.

Louise Jones, London, UK

Louise Jones is the Course Administrator. She also works as Administrator to The British Society for Clinical Neurology and has previously worked as Research PA to both Dr Ronit Pressler & Professor Helen Cross. With over 35 years' experience as a PA / Medical Conferencing Coordinator, working both for the private sector & the NHS across various medical specialties.

Faculty

Alexandre N. Datta, MD, Basel, Switzerland

Professor Dr. Alexandre Datta is head of Paediatric Neurology and Developmental Medicine Department at the University Children's Hospital Basel, co-head of the Center of Epileptology, Sleep and Chronobiology of Basel University Hospitals and Head of the Research Group "Paediatric epilepsy and sleep" at the Department of Clinical Research of the University of Basel, Switzerland. He trained in Paediatrics and Paediatric Neurology at University Children's Hospitals Basel and Geneva, Switzerland and undertook a fellowship in Pediatric Epileptology at Hôpital Necker-Enfants Malades and INSERM unity U663 CEA in Paris, France. He has a particular clinical and scientific interest in childhood epilepsy and sleep and is involved in many national and international research projects, in particular in brain plasticity and nocturnal regeneration epilepsy (in particular SeLECTS), sleep and circadian rhythm in preterm and term babies and narcolepsy and other central disorders of hypersomnolence. He is in the executive board of the Swiss Society of Clinical Neurophysiology (SGKN), the Swiss Federation of Clinical Neuro-Societies (SFCNS), the Swiss Narcolepsy Network (SNANE). He gives talks in national and international congresses, is co-organizer of the Swiss EEG Academy and of FAMOSES Switzerland as well as teacher at VIREPA.

Christian Korff, MD, Geneva, Switzerland

Prof Christian Korff is head of the Pediatric Neurology Unit at Children's University Hospitals, Geneva, Switzerland. He graduated from the University of Geneva Medical School in 1996, and his post-graduate training included residencies in various Pediatric and Neurology centers in Switzerland. From 2003 to 2005, he completed a clinical and research fellowship in Pediatric Neurology and Epileptology at Children's Memorial Hospital, Chicago, Illinois, where he developed a specific expertise in pediatric seizure semiology and epilepsy syndrome classification. Christian served the International League against Epilepsy (ILaE) as member of the Task Force that developed the online epilepsy diagnosis manual (epilepsydiagnosis.org) from 2009 - 2013. He has long been an active member of various international networks involved in epilepsy genetics research, such as Euroepinomics, and has co-led a swiss-french regional group of interest in the field since 2017. He has been involved in various clinical, teaching and research projects in emerging countries, and is the principal investigator of a Swiss-Vietnamese joint research project on genetic investigations in children with Developmental and Epileptic Encephalopathies. His current clinical and research interests include in particular various aspects of pediatric epilepsy (semiology, genetics, inflammation) and EEG analysis.

Emilie Bourel-Ponchel, PhD, France

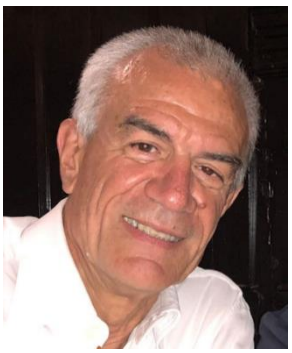
Emilie is Professor of Clinical Neurophysiology (PU-PH) at Amiens University Hospital and the University of Picardie Jules Verne (France). I work in the Department of Paediatric Functional Explorations of the Nervous System and serve as associate Director of the Inserm research unit UMR 1105 GRAMFC (Group for Research on Multimodal Analysis of Brain Function). My clinical and research activities focus on paediatric neurophysiology, with a particular interest in neonatal and paediatric electroencephalography (EEG). My research aims to develop multimodal functional biomarkers, combining EEG with other neurophysiological and clinical data, to improve the early prognostic assessment of neurological disorders in newborns and children, particularly in conditions such as prematurity and hypoxic–ischemic encephalopathy. I am also actively involved in academic training in clinical neurophysiology and neuroscience in France, through university teaching and national training programs for physicians and neurophysiology technologists.

Fabrice Wallois, MD, PhD, PU-PH, Amiens, France

Professor Fabrice Wallois is a specialist of clinical neurophysiological investigations in children and premature infants. He is the head of the department of functional explorations of the pediatric nervous system In Amiens University Hospital.

His research relates to the analysis and the maturation of the neural networks, physiological or pathological, in the child and in the animal. More recently, the development of acquisition and analysis tools allowing the characterization of the electric (EEG), magnetic (MEG) and metabolic (NIRS) activities and their modulations in certain pathological situations as well as the localization of their sources in the epileptic child and in premature infants are in the centre of the research To meet this goal he aims for development of tools allowing simultaneous analysis of modification in electric and local hemodynamic cerebral activity, under physiological (cerebral maturation) and pathological conditions (anoxic ischemia of the premature baby, neurological suffering of the preborn, convulsion and epilepsy of the child). He developed the GRAMFC in 2004 as a multidisciplinary group and unifies since then a team of neuropsychologists, intensive care paediatricians and specialists in signal processing. It is recognized by the minister and by the Inserm (French National Institute of Health and Research in Medicine) (Inserm U 1105) since 2008.

Federico Vigevano, MD, Rome, Italy



Professor Federico Vigevano is Head of Developmental Disabilities DPT – IRCCS San Raffaele – Rome. He has a Postgraduate Diploma in Neurology and Psychiatry achieved in Rome; Training in Pediatric Epilepsy at Saint Paul Center of Marseilles in 1977; Since 1978 to 2024 Pediatric neurologist at Children's Hospital Bambino Gesù where he held the position of head of Neuroscience DPT. Since February 2024 he holds the position of Developmental Disabilities DPT at San Raffaele Research Institute in Rome. He identified a clinical entity that is currently called Self-Limited Infantile Epilepsy. He has published as first author or co-author more than 300 papers in the most important international journals dedicated prevalently to epilepsy and paediatric neurology.

Geraldine Boylan, PhD, Cork, Ireland

Geraldine Boylan is Professor of Neonatal Physiology, Department of Paediatrics & Child Health, University College Cork and Director of the INFANT Research Centre (www.infantcentre.ie).

She is an expert in neonatal neurophysiology and leads the Neonatal Brain Research Group at the INFANT centre - a multidisciplinary research team focused on neuromonitoring for infants in the neonatal intensive care unit, particularly for seizure detection and the early diagnosis of brain injury. Her team uses AI to develop automated systems for newborn seizure detection and brain health assessment. She has developed a number of patents in this area, licenced technologies to industry and is co-founder of UCC spinout company CergenX.

María Ángeles Pérez-Jiménez, MD, PhD, Madrid, Spain

Dr María Ángeles Pérez-Jiménez is a Clinical Neurophysiologist and pediatric epileptologist. She is responsible for the Paediatric Epilepsy Monitoring Unit, Niño Jesús Paediatric University Hospital in Madrid. She coordinates the comprehensive presurgical multimodal evaluation of children and adolescents (epilepsy surgery program), mainly conducting non-invasive and invasive video-EEG monitoring studies. She is a researcher associated to clinical and translational projects regarding epilepsy surgery and neurodevelopment. She actively collaborates in ILAE sponsored educational activities on pediatric epilepsy, and she is a board member of the Spanish Epilepsy Society (SEEP).

Nicola Specchio, MD, PhD, Rome, Italy

Nicola Specchio is a paediatric neurologist and epileptologist in the Department of Neuroscience at Bambino Gesù Children's Hospital (IRCCS) in Rome, Italy, where he leads the Neurology, Epilepsy and Movement Disorders Unit. His clinical activity focuses on the diagnosis and treatment of children with epilepsy, with particular interest in seizure semiology and the classification of epileptic seizures and syndromes. He is involved in the presurgical evaluation of patients with drug-resistant epilepsy and in the management of genetic epilepsies.

He has published widely in international journals including Epilepsia, Epilepsy Research, and Epilepsy & Behavior, and is involved in several clinical research projects on invasive monitoring and the genetic causes of early-onset epileptic encephalopathies. He currently serves as Chair of the ILAE Europe Commission and Secretary-General of the Italian Chapter of the International League Against Epilepsy (ILAE).

Rachel Thornton PhD, Cambridge, UK

Dr Rachel Thornton is Consultant Clinical Neurophysiologist at Cambridge University Hospitals NHS Trust. Her main clinical interests are pre-surgical evaluation in children with Complex Epilepsy and EEG monitoring in paediatric and neonatal intensive care settings. Her research focuses on the evaluation of brain networks using EEG in focal epilepsy as well as seizure semiology in children in collaboration with groups at UCL and Kings College London. She sits on the Enabling Technologies task force for the UK Epilepsy Research Institute. She has a keen interest in education and training, having co-founded an annual paediatric sEEG workshop and as well as developing the UK ILAE EEG and semiology course

Sushma Goyal, MD MRCPCH, London, UK

Sushma is the Lead Consultant Paediatric Clinical Neurophysiologist at Evelina London Children's Hospital and an Honorary Consultant at King's College Hospital, London. Her specialist interests include diagnosis of seizures and epilepsy in neonates and children and evaluation of children for epilepsy surgery. She was a part of the King's team that won the NHS Innovation Challenge Prize for developing Home video EEG telemetry in the UK. She teaches on the British Neurophysiology and Paediatric Neurology training programmes and is also a faculty on neonatal and paediatric EEG courses conducted by the ILAE. She is the International Secretary of the British Society of Clinical Neurophysiology and was a member of ILAE Neurophysiology taskforce set up for the role of EEG in the diagnosis and classification of epilepsy syndromes.

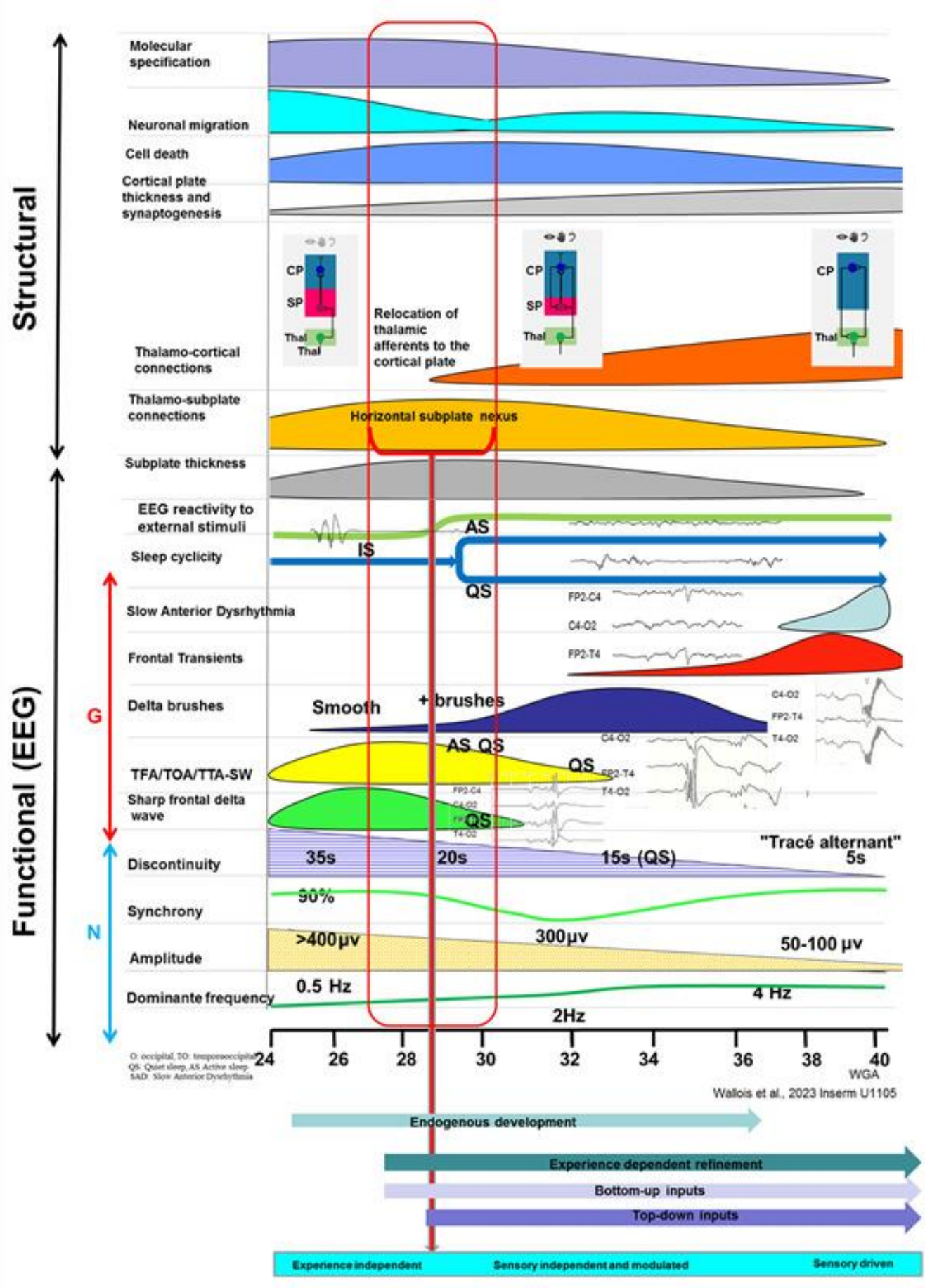
Syed Shah, MD MRCP, Sheffield, UK

Dr Syed Shah is a Consultant Clinical Neurophysiologist at Sheffield Teaching Hospitals NHS Foundation Trust. He trained in Leeds and has worked in neurology and neurophysiology in different regions across the world. He was elected to the BSCN Council in 2022 and currently serves as Webmaster. Alongside his clinical and academic interests in EEG, nerve conduction studies and electromyography, he has been actively involved in organising various national and international neurophysiology meetings

Topun Austin, PhD, MD, MRCP, MRCPCH, Cambridge, UK

Prof Topun Austin is Consultant Neonatologist and Affiliate Associate Professor at the University of Cambridge and Honorary Professor of Neurophotonics at University College London. He has a broad range of interests in neonatal neuroscience from cerebrovascular physiology to sleep, consciousness and cognition in the developing brain. He has a longstanding collaboration with the Biomedical Optics Research Laboratory at University College London and together have pioneered a number of new optical technologies to monitor and image the newborn brain. He is also a visiting fellow at Nanyang Technology University in Singapore, where he is collaborating on studies investigating mother-infant neural synchrony, early infant development and improving cognitive flexibility in school-aged children. Clinically he is the lead for neonatal neurocritical care in Cambridge, providing brain-orientated care for preterm and sick newborn infants.

Maturation of EEG in neonate and infants



Wallois et al in press.

Neonatal Seizure Detector

New in Persyst 15 is a neonatal-specific seizure detector. The Neonatal Seizure Detector is the latest cutting-edge technology from Persyst that leverages deep learning and AI. The detector operates on reduced electrode arrays from double-distance down to just three electrodes. Combined with an optimized trend panel, Persyst 15 significantly reduces the workload when analyzing neonatal recordings.

Even though it has only been available for a short time, two recent papers have highlighted the effectiveness of the neonatal-specific detector. [1,2]

[1] Duckworth E., Motan D., Howse K., Boyd S., Pressler R., Chalia M. Diagnostic Accuracy of the Persyst Automated Seizure Detector in the Neonatal Population. J. Integr. Neurosci. (2024) 23(8), 150. https://doi.org/10.31083/j.jin2308150

[2] Keene J., Benedetti G., Tomko S., Guerriero R. Quantitative EEG in the neonatal intensive care unit: Current application and future promise. Annals of the Child Neurology Society. (2023) 1(4), 289-298.

FOR MORE INFORMATION, CONTACT sales@persyst.com US: 928.708.0705 UK & EU: +44 (0) 2045405597

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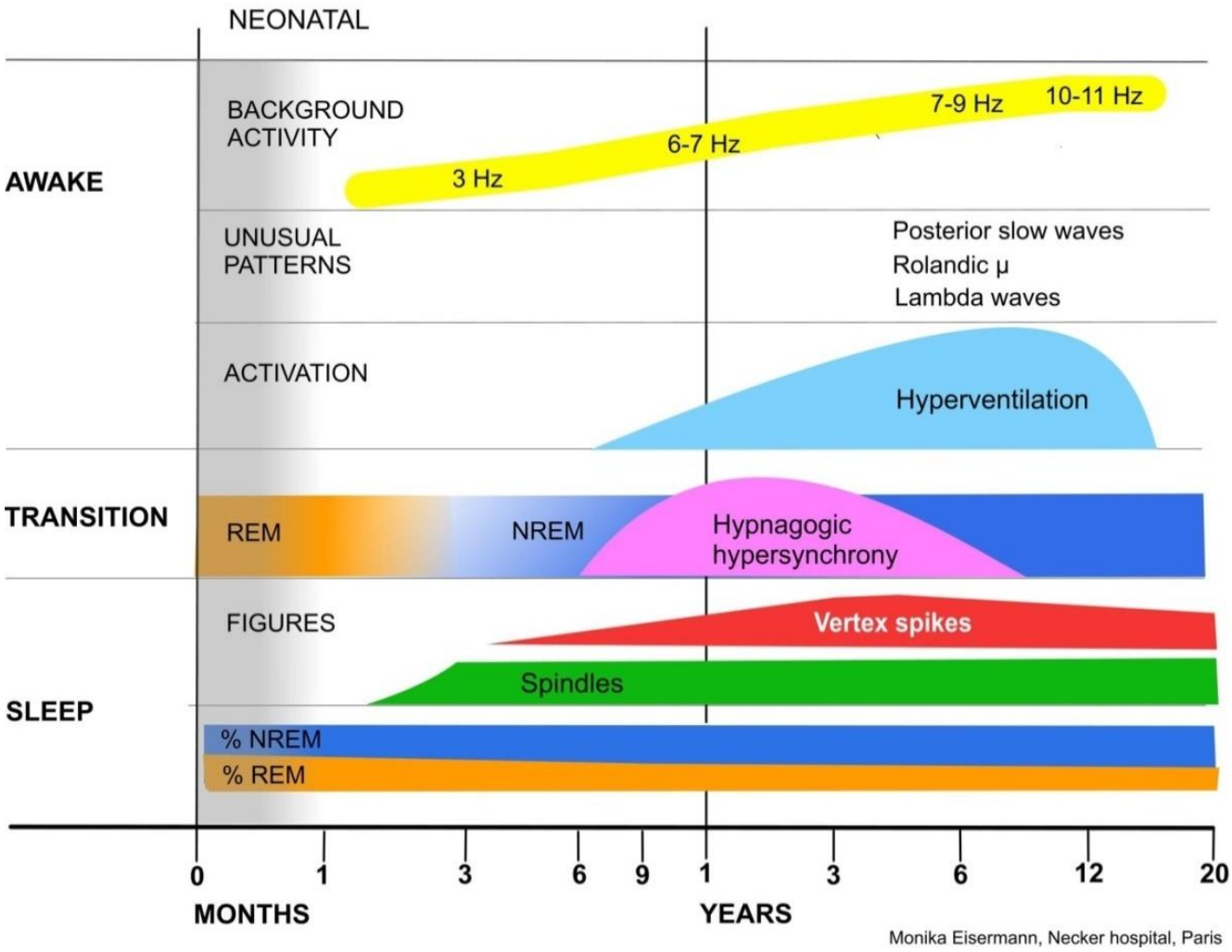
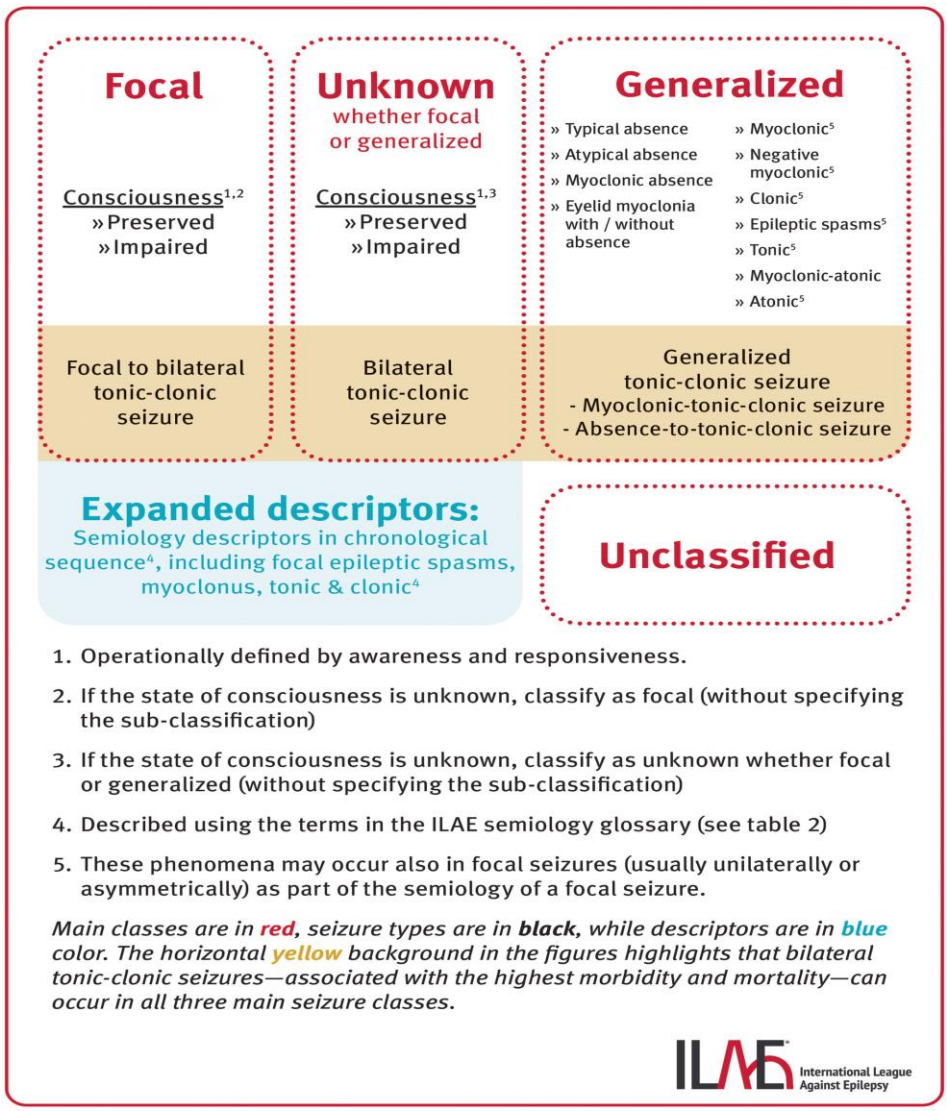
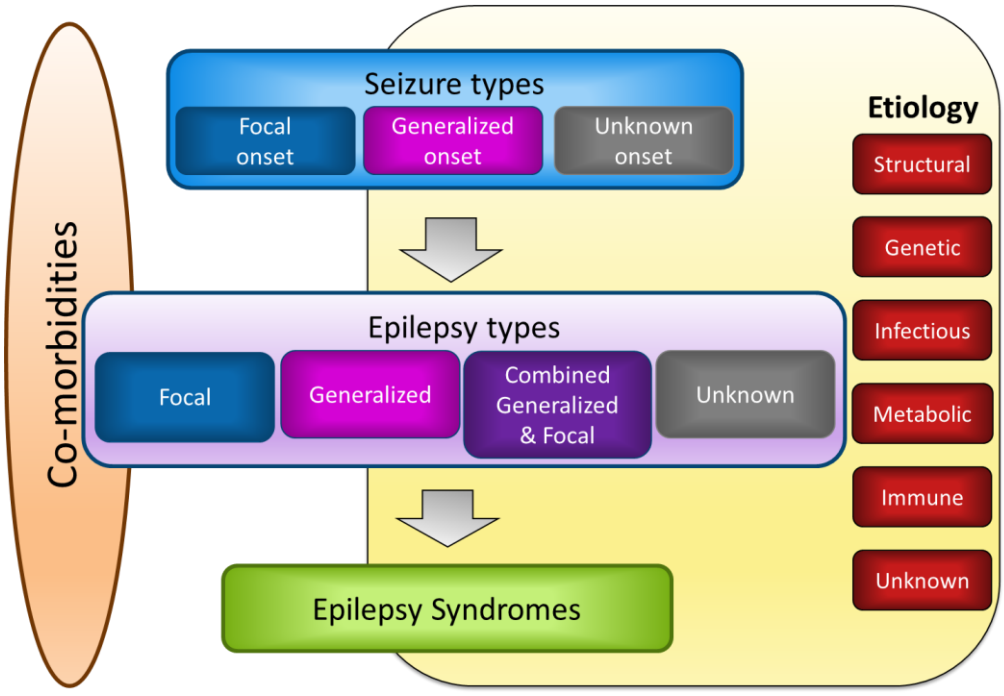


Monika Eisermann, Necker hospital, Paris

ILAE classification of seizure and syndromes



Beniczky et al Epilepsia 2025



Scheffer et al Epilepsia 2017

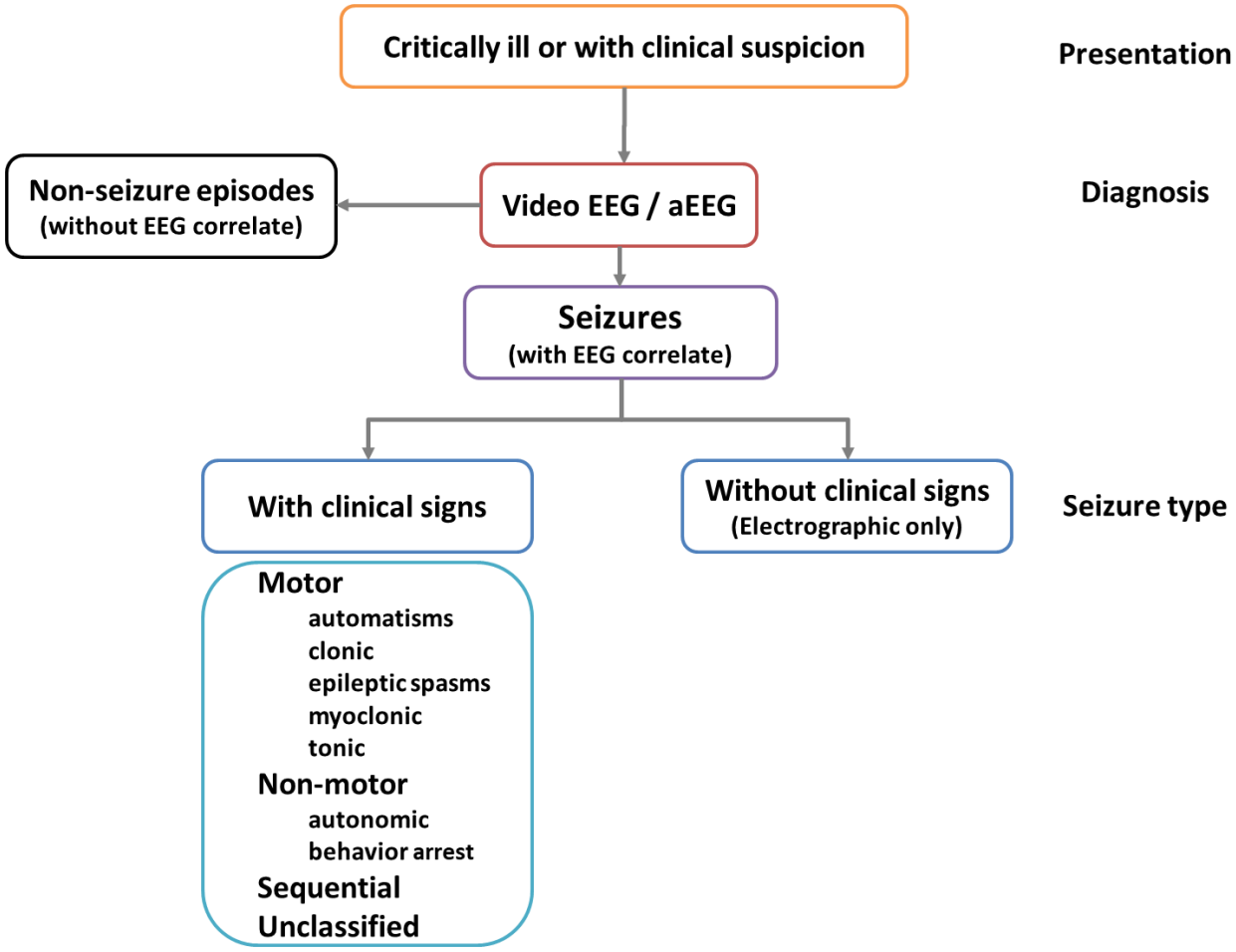
Angelini
Pharma

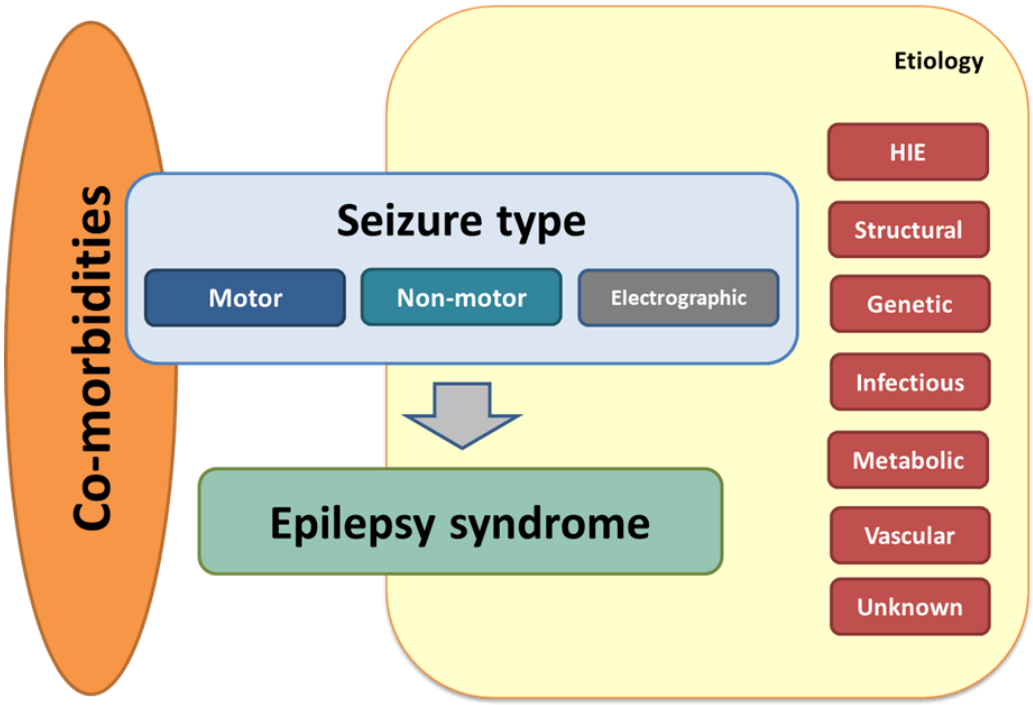
Every day we Care for People´s Health, embracing Science with Passion.

For over 50 years, we have been dedicated to improving the lives of people living with **mental health** disorders and, more recently, neurological conditions such as **epilepsy**.

We consistently invest in **research** to develop new products and ensure their effectiveness, while also standing up against the **stigma** that still surrounds these conditions.

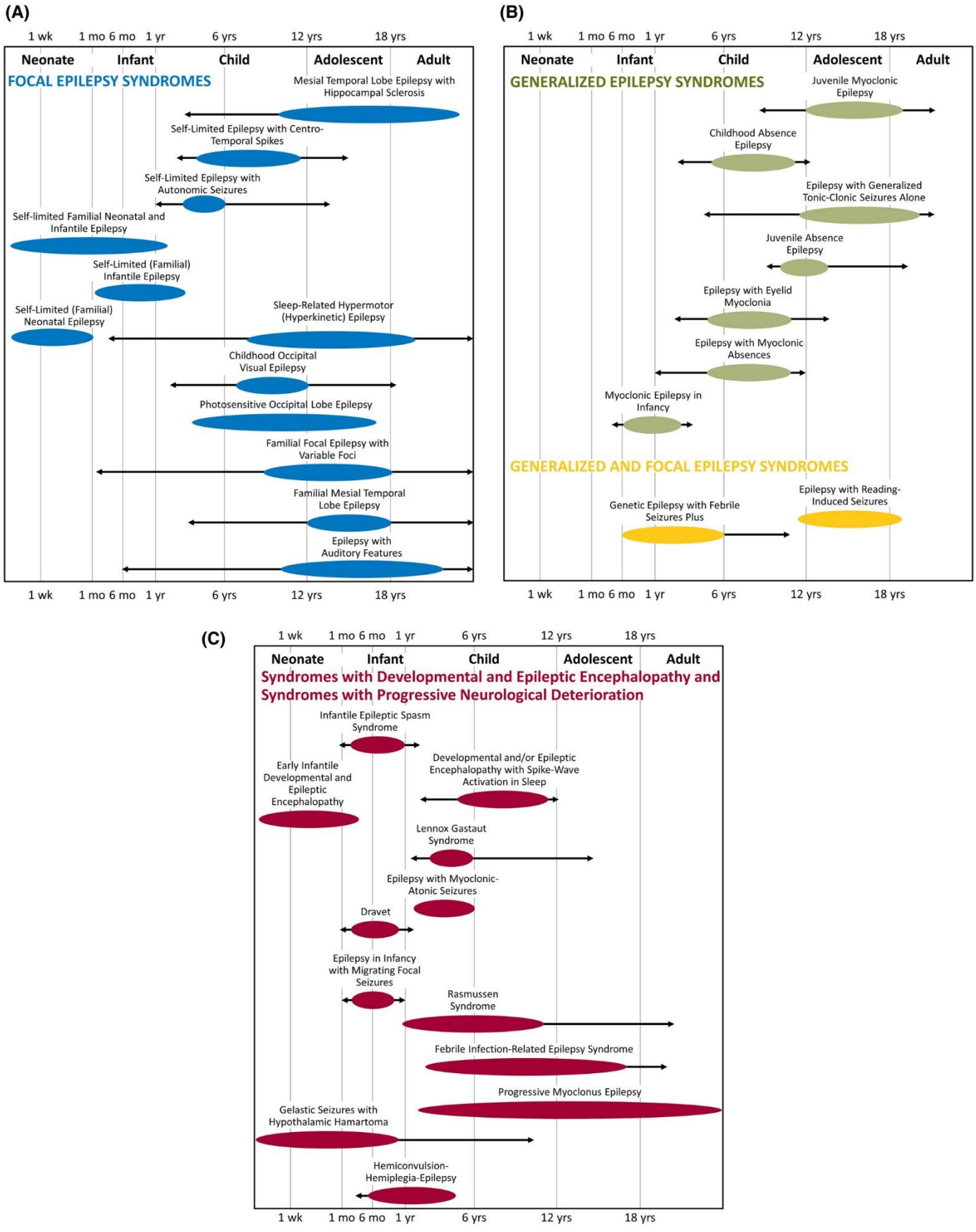
Classification of seizure and syndromes in neonates





Pressler et al Epilepsia 2021

Classification of epilepsy syndromes, based on age at presentation



Wirrell et al Epilepsia 2022

R Thornton (UK): Technical aspects and pitfalls

EEG in the First Year of Life
- from newborn to toddler

EEG in neonates: How do I record a better EEG?

Dr Rachel Thornton
Cambridge University Hospitals NHS Trust

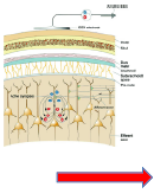
1

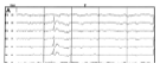
Learning objectives

1. Understand
   1. Why EEG is different in babies
   2. How to optimise a recording for neonates and factors which may affect interpretation
   3. Indications for EEG in babies
   4. How to modify testing in seizures for infants
2. Recognise
   1. Common artefacts

2

Introduction



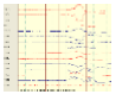


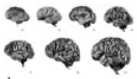
- Why is it different in babies?
- How can I optimise my recording?
  - Montages
  - Timing: how long is long enough?
  - Video
  - Polygraphy
- Environment
  - Artefacts
  - Sedation
- Considerations for interpretation

3

Why are babies different?

- Not just a small adult!
- Size
- The Brain and skull
  - Myelination and Sulcation
  - Maturation of behaviour
  - Skull thickness and heterogeneity
- Endogenous influences
  - State: ultradian and circadian rhythms are different
- Exogenous influences
  - Medication/ Sedation



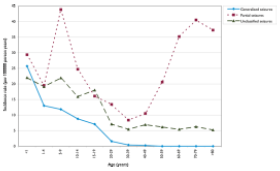


4

Indications for EEG <2 years

- Paroxysmal events: what are these?
  - Non-seizure episodes
  - Clinical Seizures: including localisation
  - Electrographic seizures: (detected on CFM)
  - Clinical/ electrographic uncoupling
- Monitoring and prognostication
  - HIE
  - Early onset epilepsies/ encephalopathies
- Assessment of development/ maturation
- Assessment of impact of therapy
- Coma: Why is the baby not waking? Prognosis?

New Diagnoses of seizures and epilepsy



Adelow et al 2009

5

How do I optimise my recording?

Number of electrodes

- **Fewer electrodes:** Limited information

- **More electrodes:** more disturbance to the baby and risk of 'bridging' (hot cot + hot baby)

- Too much information to process quickly (too many lines = sweating doctor)

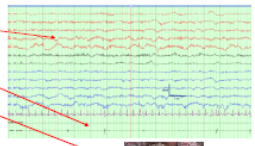
Limit Artefacts

- **The Environment**
  - Leads: keep them still
  - 50/60 Hz
  - Surrounding electrical equipment: move it!
- **Patients**
  - Won't stay still...
  - Blink
  - Sweat
  - Have a heart...

6

Artefacts: Tips to identify the culprit…

- Is this extracranial?
  - Check other equipment and monitors
  - Check polygraphic channels
  - Check video
- YOU MAY NEED TO CHECK MORE THAN ONE!
- Distribution on the EEG
  - Eye movements
  - Temporal channels: sucking, muscle
  - Central: tongue, tapping -> potential on a low amplitude recording

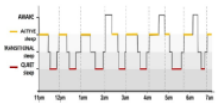


BE EXTRA CAUTIOUS IF PROGNOSTICATING: CHECK GAIN AND DISTRIBUTION

7

How long do I need to record for?

- It depends on your question
- Consider pattern of circadian rhythm
- Neonates (preterm to 3 months post term)
  - Capture sleep and wake (60 minutes)
- Older children (>3 months)
  - Yield is higher with sleep: time your record with feed to facilitate this
- Monitoring: Consider aEEG or other quantitative approach
- Telemetry (long term video EEG monitoring)
  - As long as is needed for the events
  - Brief often sufficient in babies BUT check you have the right thing!



8

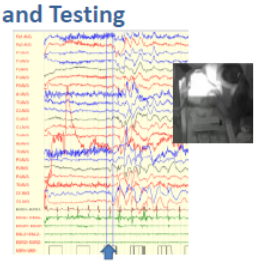
A word on Stimulus and Testing

Stimulus

- Assessment of reactivity recommended in literature
- NICU: Standardise for your units: auditory + tactile
- >8 weeks: intermittent photic stimulus
- Should include LOW frequency

Testing

- Assessment of responsiveness
- Information about where a seizure starts (Yes even in babies!)



12 weeks, 3 seizures. SCN1A

9

TESTING IN BABIES AND TODDLERS

Remember **'Say what you see!!'**

Uncover & Describe

Stimulus: Noise? Tactile?

Check limbs

Squeeze my hand (both sides)

Stick out your tongue

Point to mummy/TV/teddy etc

After the Seizure, Record Obs and Description of Seizure.

10

What do I need to report…

- Post menstrual age (more on why in the next talk)..
- The Environment
  - Is there an oscillator, ECMO, anything else which could not be moved?
  - Interventions during the recording
- Why is the EEG being done? Have the events been captured
- State of patient: sleep, wake, cooled?
- Sedation
- Developmental considerations
- Family History

11

Summary

- NICU, children's wards and children are challenging, but not impossible
  - Optimise the environment and ensure good and EQUAL impedance
  - Use multiple sources to identify and eliminate artefact
- Train your team to record, describe, stimulate and test
- Consider the mode of recording most suitable for the question
- Record for an adequate duration
- Consider gestational age and circumstances (sedation, state etc)

12

F Wallois (FR): Normal EEG in newborns

EEG in the First Year of Life
- from newborn to toddler

Physiology of EEG maturation and normal neonatal EEG

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Overview

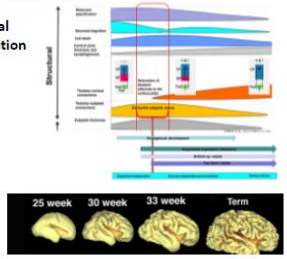
- Introduction
- The immature cortex
- EEG-biomarkers of functional maturation
  - Theta temporal and slow wave
  - Delta brushes
  - Frontal sharp transients

2

Introduction

The basic mechanisms of structural neuronal development in the third trimester of gestation

- Cellular proliferation
- Cellular Migration
- Cellular differentiation
- Synaptic selection/reorganisation
- Gyration
- Myelinisation
- The subplate



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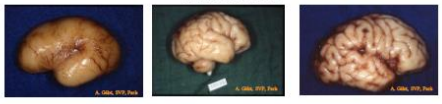
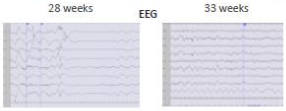
The immaturity of the cortex

Macroscopic level



20 weeks 28 weeks 33 weeks

EEG



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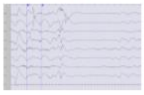
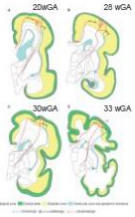
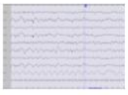
The immaturity of the cortex

A transient circuitry:
The subplate



28 wGA





33wGA

20-26wk GA the subplate receives thalamocortical afferents
26-28wk GA the first afferents reach the cortical plate
28-30wk GA the first synapses occur in the cortical plate

Kostovic, 2010

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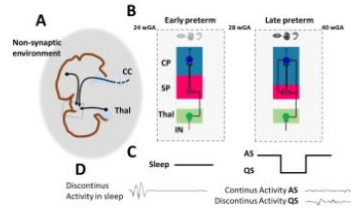
The immaturity of the cortex

The subplate



Complex structural and functional relationship?

Wallois et al., 2021, 2023

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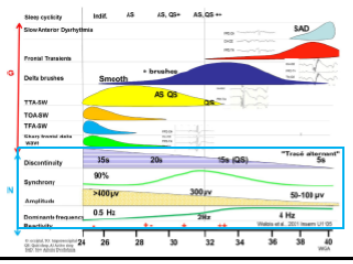
The synopsis of functional electrical activities of the immature brain



Wallois et al., 2021

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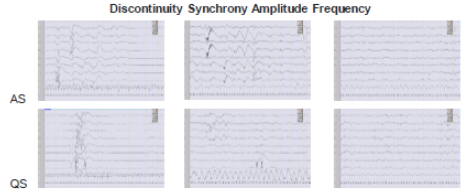
EEG-biomarkers of functional maturation: generators



The discontinuity suggests that some generators of bursts are modified during the development
The synchrony suggests that both hemispheres are synchronized by deep mechanisms or metabolic oscillatory activity
The occurrence of sleep stages suggests functional input from the reticula and thalami

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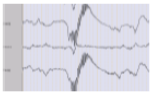
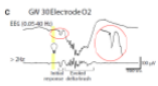
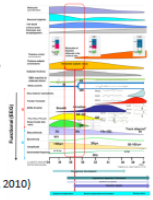
EEG-biomarkers of functional maturation: generators



Delta brushes





- they occur at mostly 28 WGA
- they might be triggered by different sensory modalities from 30 wGA
- they are diffuse and can be recorded in different cortical areas
- their source is unknown but they are recorded all over the different cortical layers
- In the visual system, in rat, they might occur before visual experience (Colonese et al., 2010)
- In the auditory cortices they occur together with auditory experience
- Their shapes are modified by sleep IVH and PVL
- Their connectivity is unknown

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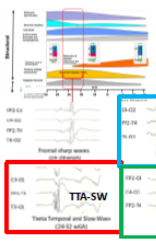
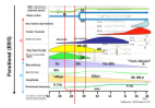
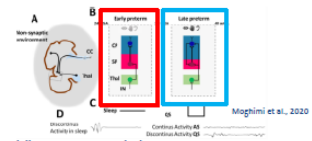
EEG-biomarkers of functional maturation: generators



The internal world

The frontal sharp transient





Moghimi et al., 2020

Specific coupled or coalescent oscillators appear and disappear or are masked

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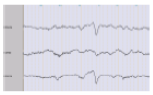
EEG-biomarkers of functional maturation: generators

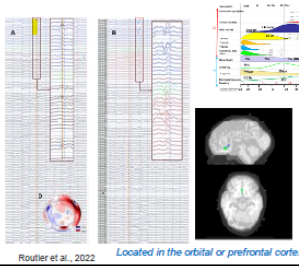
The transition from in to ex utéro

The frontal sharp transients



Frontal transient (34-41w)

Functional hypothesis:
The coding of odours and mother attachment



Routier et al., 2022

Located in the orbital or prefrontal cortex

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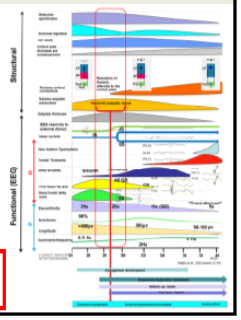
Summary

In very premature neonates, activities are inked to spontaneous endogenous oscillators and network-based activities

Then in premature neonates when thalamic afferents are relocated to the cortical plate activities are linked to spontaneous endogenous oscillators that are modulated by afferent sensory inputs and network-based activities

Spontaneous and/or modulated oscillators participate to
- Synaptogenesis
- Myelinisation
- Neuronal migration
- Neuronal guidance
- Cellular differentiation
- Establishment of neuronal functionalities

A grain of sand in this well-oiled horology might impact the life span of the structural and functional neuronal organisation leading to Neurodevelopmental disorders and epilepsy



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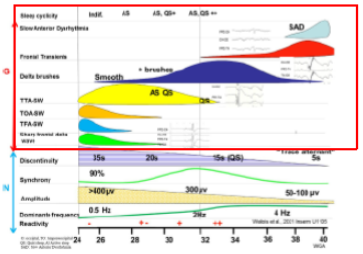

Wallois et al., 2021

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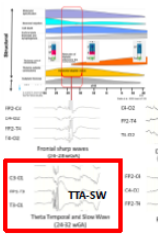
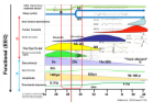
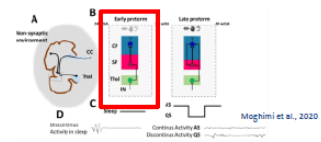
EEG-biomarkers of functional maturation: generators



The internal world

The TTA-SW





Moghimi et al., 2020

Specific coupled or coalescent oscillators appear and disappear or are masked

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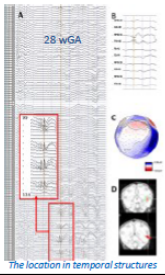
EEG-biomarkers of functional maturation: generators



TTA-SW participate to
- Synaptogenesis
- Myelinisation
- Neuronal migration
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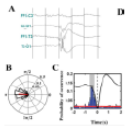
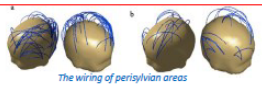
- Cellular differentiation
- Establishment of neuronal functionalities

A grain of sand in this well-oiled horology might impact the life span of the structural and functional neuronal organisation of language and communication.



Coupling of fast and slow oscillators

The location in temporal structures



The wiring of perisylvian areas

Moghimi et al., 2020; Routier et al., 2017, Adebimpe et al., 2018, Wallois et al., 2021

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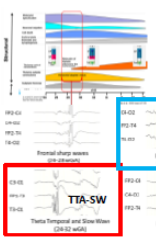
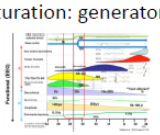
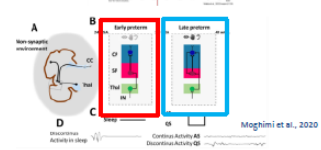
EEG-biomarkers of functional maturation: generators



The internal world

The delta brush



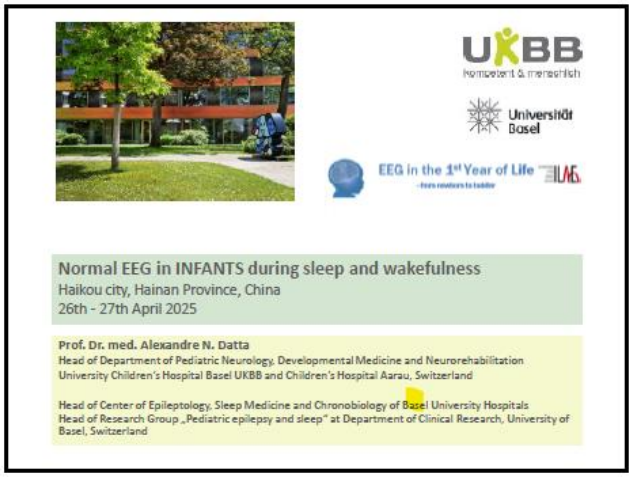


Moghimi et al., 2020

Specific coupled or coalescent oscillators appear and disappear or are masked

12

A Datta (CH): Normal EEG in infants



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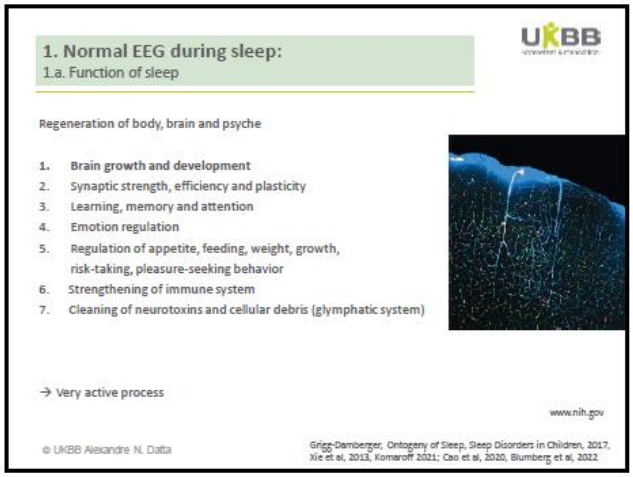

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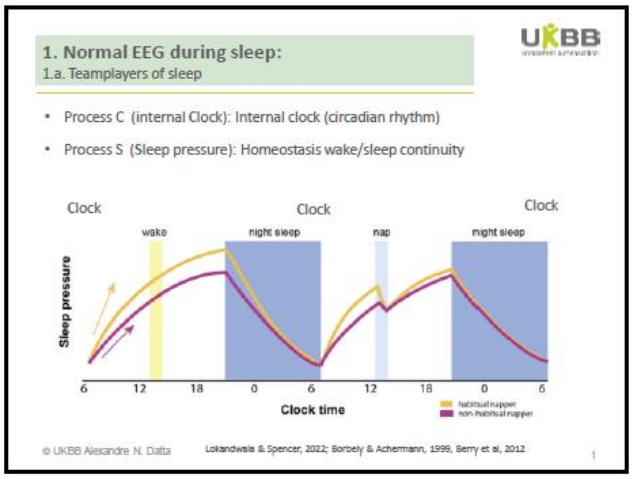

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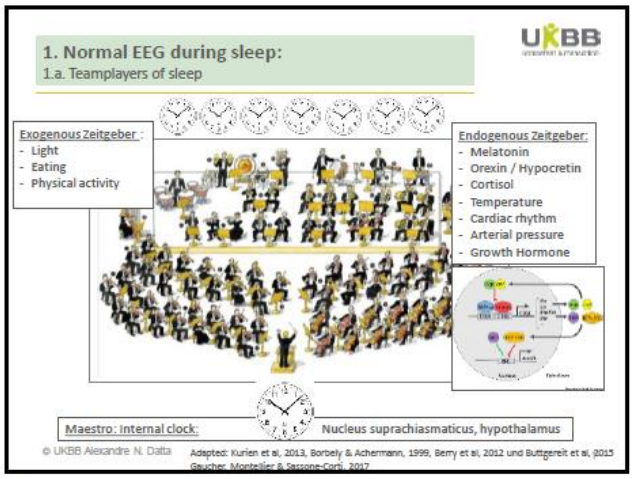

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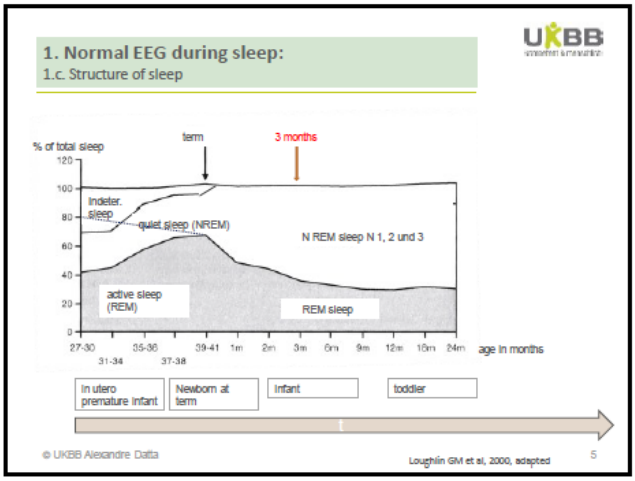

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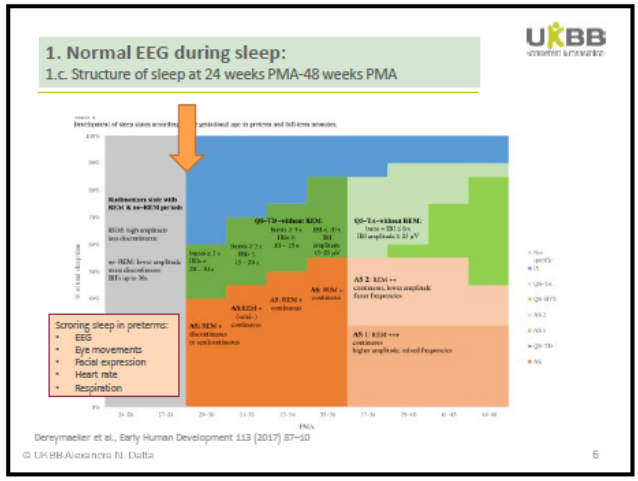
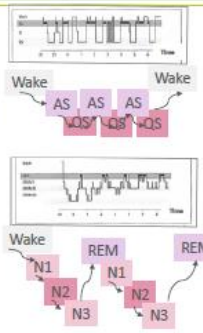


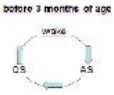
6

1. Normal EEG during sleep:
1.c. Sleep structure first 3 months, after 3 months

1-3 months

- Wake
- Active sleep (AS, REM)
- Quiet sleep (QS, NREM)





after 3 months:

- W
- NREM N1
- NREM N2
- NREM N3
- REM

adapted from Grigg-Damberger, 2016

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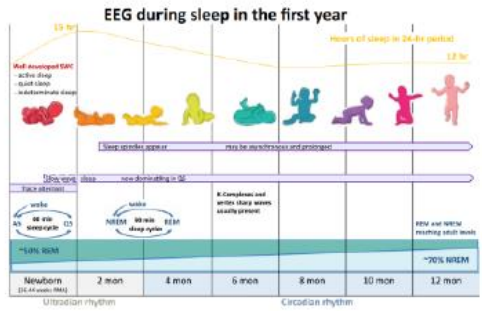
1. Normal EEG during sleep:
1.c. Sleep structure first 3 months, after 3 months

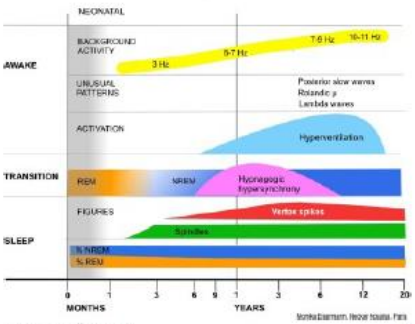


Lenehan et al, 2023

8

1. Normal EEG during sleep:
1.c. Sleep structure first 3 months, after 3 months

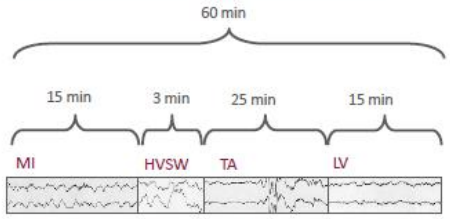
EEG maturational stages



Eisermann et al, 2013

9

1. Normal EEG during sleep:
1.c. Sleep structure 0-3 months, one cycle



active sleep 1 (REM) quiet sleep (NREM) active sleep 2 (REM)

LV	=	Low Voltage
MI	=	Mixed intermittent, „activité moyenne"
HVSW	=	High Voltage Slow Wave
TA	=	Tracé alternant

Andre et al, 2010
Grigg-Damberger et al., 2016
Dereymaeker et al,

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1. Normal EEG during sleep:
1.d. Normal sleep patterns

	Infancy (2–12 mo)
Sleep onset	REM sleep onset lessoning after 3 mo, uncommon after 6 mo
Dominant posterior rhythm (DPR)	DPR first seen 3–5 mo as irregular 50–100 µV 3–5 mo; 5–6 Hz by 5–6 mo; 7 Hz by 12 mo; DPR < 5 Hz by 1 y abnormal, reactivity of DPR to eye opening first seen 3–6 mo
Drowsiness and NREM 1	Hypnagogic hypersynchrony (4–6 Hz first seen age 6–8 mo maximum frontocentral regions

Sleep spindles	If no sleep spindles, score all NREM sleep as NREM (N); once sleep spindles are present, score N1, N2 and N3. 12–14 Hz sleep spindles first seen 44–46 w CA over midline central; sleep spindles often last 8 up to 10 –15 sec especially around 3–4 mo
Vertex waves and K-complexes	K-complexes first appear 5 – 6 m o maximal frontal Rare broad vertex waves maximal central first seen 6 mo
REM (R) sleep	4–5 Hz with bursts of saw tooth waves 5 mo

Grigg-Damberger, 2016

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3. Normal EEG 1. year of life dring wakefulness
3.a. Background activity during wakefulness

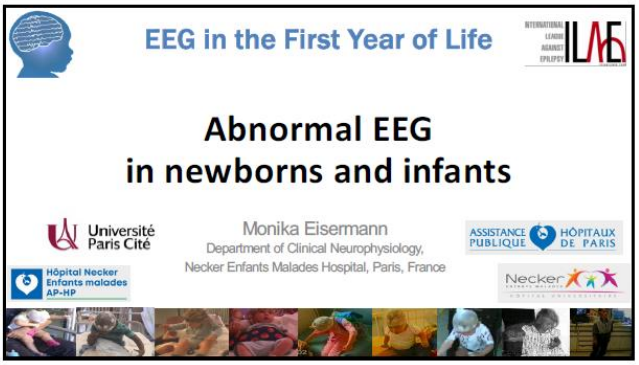
Background activity – closed eyes

< 3 months:	2-3 Hz, max centro-parietal
3-6 months:	3-4 Hz, max occipital
6-9 months:	5 (-6) Hz, max occipital
9-18 months:	mostly 6-7 Hz (70%), rarely 7-8 Hz
	amplitude: 30-100 µV (passive eye closure), 200 µV at 12 mo
> 2 y:	7-8 Hz (82%)

Schmitt & Wohlrab, Zschokke, Springer,

12

M Eisermann (D): Abnormal EEG in newborns and infants



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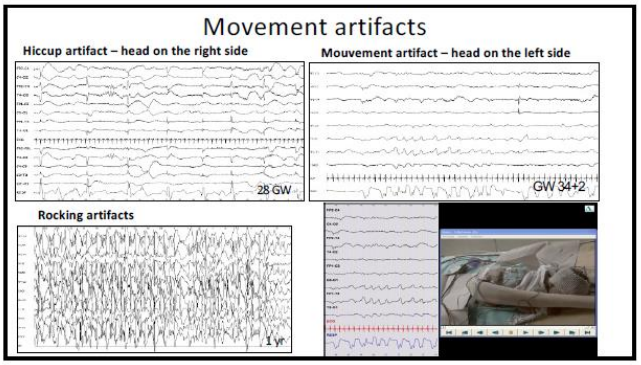

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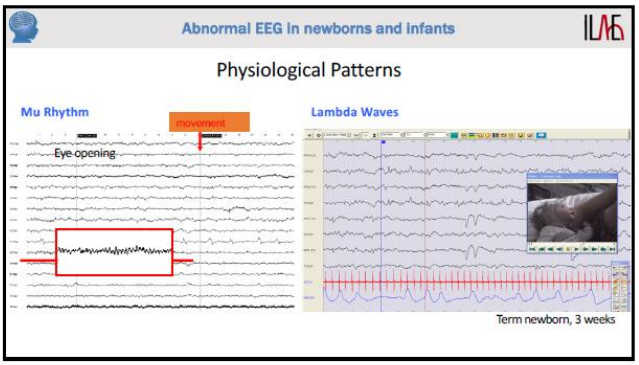

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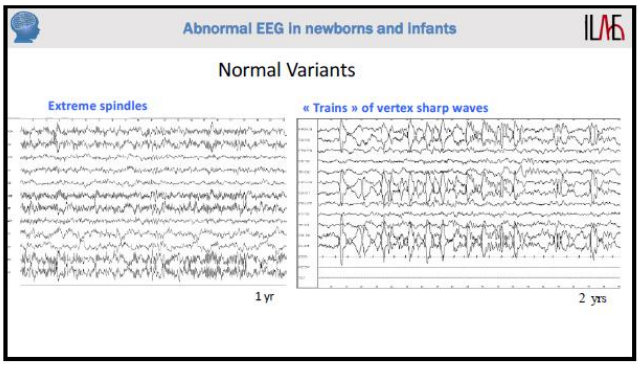

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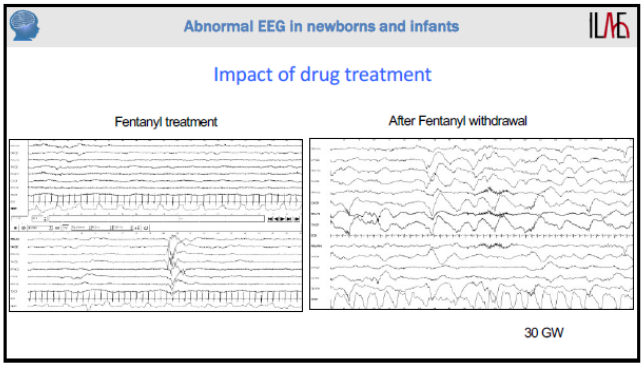

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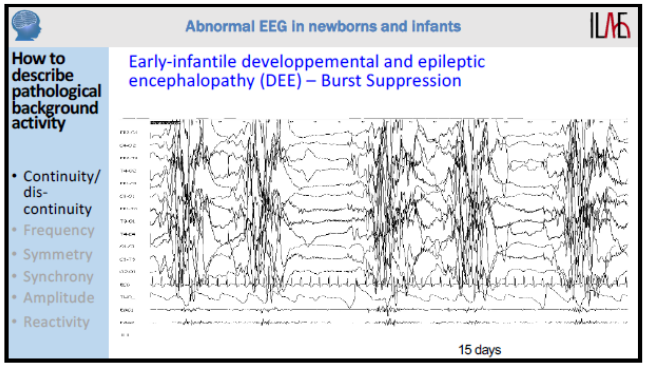

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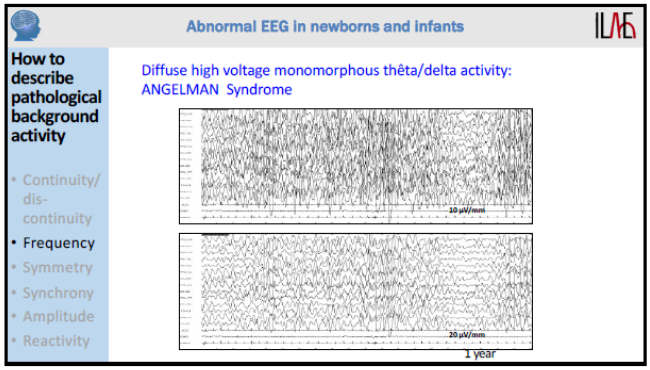

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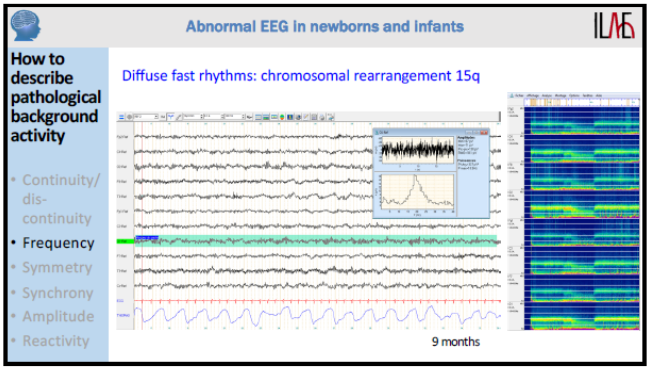
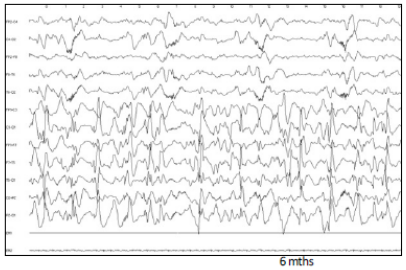


8

How to describe pathological background activity

- Continuity/ dis-continuity
- Frequency
- Symmetry
- Synchrony
- Amplitude
- Reactivity

Aicardi Syndrome – Corpus Callosum Agenesis

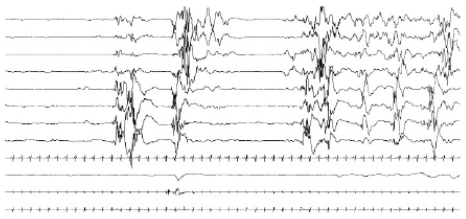


9

How to describe pathological background activity

- Continuity/ dis-continuity
- Frequency
- Symmetry
- Synchrony
- Amplitude
- Reactivity

Pathologically asynchronous background



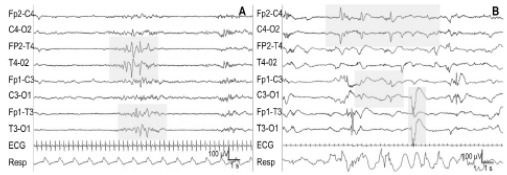
2-day-old full-term neonate. Discontinous intermittently asynchronous BS pattern.

10

How to describe pathologic al grapho-elements

- Morphology
- Amplitude
- Repetition
- Spatial distribution
- Temporal distribution
- Reactivity

Positive temporal sharp waves
Positive rolandic sharp waves
Deformed/dysmorphous high amplitude occipital waves

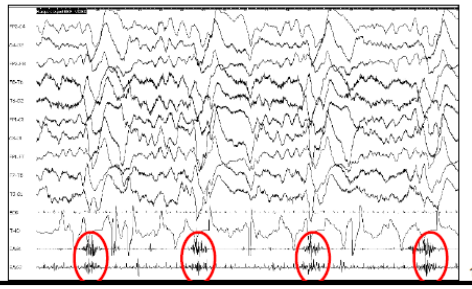


11

How to describe pathologic al grapho-elements

- Morphology
- Amplitude
- Repetition
- Spatial distribution
- Temporal distribution
- Reactivity

Diffuse high voltage slow wave complexes – cluster of epileptic spasms

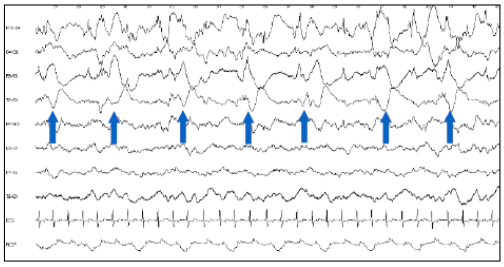


12

How to describe pathologic al grapho-elements

- Morphology
- Amplitude
- Repetition
- Spatial distribution
- Temporal distribution
- Reactivity

Periodic slow complexes



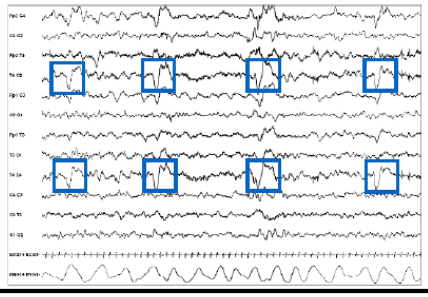
20 mths, Herpes Simplex Encephalitis

13

How to describe pathologic al grapho-elements

- Morphology
- Amplitude
- Repetition
- Spatial distribution
- Temporal distribution
- Reactivity

Focal **Tuberous Sclerosis Complex**

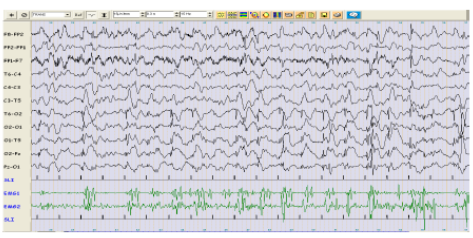


14

How to describe pathological grapho-elements

- Morphology
- Repetition
- Amplitude
- Spatial distribution
- Temporal distribution
- Reproduction on time scale
- Reactivity

Occipital spikes and myoclonia triggered by low frequency IPS: ceroidlipofuscinosis



15

Summary

- Make sure that the EEG pattern you qualify as « abnormal » is really abnormal (artifacts, unusual patterns, normal variants, medication, maturational aspects, vigilance state)
- **Keep in mind that it maybe more dangerous to conclude on a "pathological EEG tracing" facing a normal one, than missing light abnormal transients**

16

A Datta (CH) Sleep in the first year of life

UKBB kompetent & menschlich

Sleep in the first 2 years of life

PD Dr. med. **Alexandre N. Datta**
Head of Epileptology, EEG and Sleep Lab
Pediatric Neurology and Developmental Medicine Department
University Children's Hospital Basel, Switzerland

1. Function of sleep

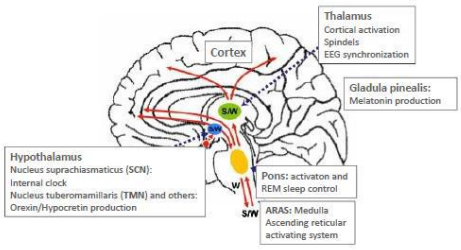
Regeneration of body, brain and psyche

1. Brain growth and development
2. Synaptic strength, efficiency and plasticity
3. Learning, memory and attention
4. Emotion regulation
5. Regulation of appetite, feeding, weight, growth, risk-taking, pleasure-seeking behavior
6. Strenghtening of immune system
7. Cleaning of neurotoxins and cellular debris

→ Very active process

 Adapted from Grigg-Damberger, Ontogeny of Sleep, Sleep Disorders in Children, 2017

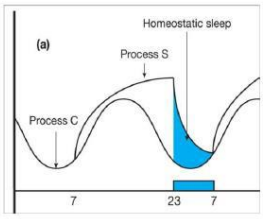
2. Neuronal structures of sleep?



 Out of Neurobiology of Sleep, National Sleep Foundation 3

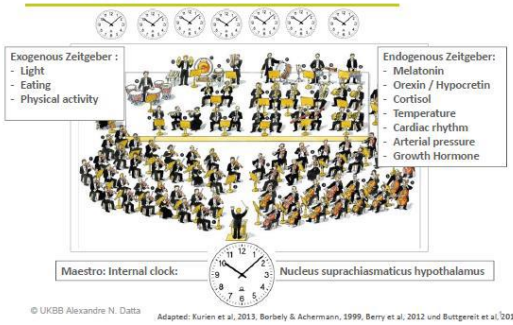
3. Team players of sleep

- Process C (internal Clock): Internal clock (circadian rhythm)
- Process S (Sleep pressure): Homeostasis wake/sleep continuity



 Adapted: Kurien et al, 2013, Borbely & Achermann, 1999, Berry et al, 2012 und Buttgereit et al, 2015 1

3. Team players of sleep

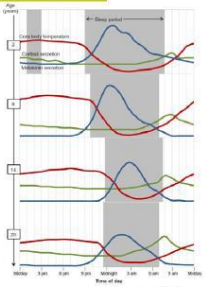


 Adapted: Kurien et al, 2013, Borbely & Achermann, 1999, Berry et al, 2012 und Buttgereit et al, 2015

4. Development of the circadian rhythm

age	rhythm	Zeitgeber
fetus	ultradian	- Interal clock mother
premature 26-37 weeks	ultradian	- Internal clock
neonate Up to 3 months	ultradian	- Internal clock, eat - After 4 weeks: light, Melatonin
infant after 3 months	circadian	- Endogenous: Melatonin, Cortisol, temperature, FC, PA - Exogenous: light, meals, activity/ inactivity
toddler	circadian	
School child	circadian	
adolescent	circadian	

t



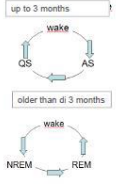
Adapted Mirmiran et al, 2003
Cremer et al, 2017
Koch et al, under review.

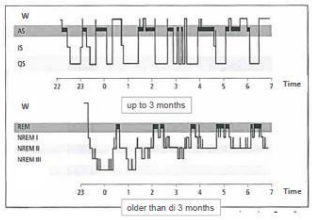
Carpenter et al, 2014

 6

5. Sleep structure
a. Sleep phases, cycles and stages

1. Sleep phases
2. Sleep cycles
3. Sleep rhythm

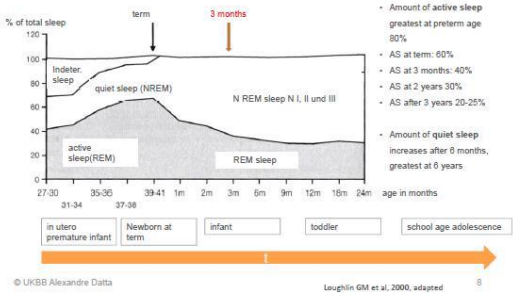




Hypnogram

 7

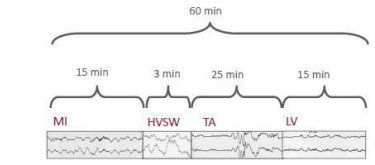
5. Sleep structure
a. Sleep phases, cycles and stages



- Amount of **active sleep** greatest at preterm age 80%
- AS at term: 60%
- AS at 3 months: 40%
- AS at 2 years 30%
- AS after 3 years 20-25%
- Amount of **quiet sleep** increases after 6 months, greatest at 6 years

 Loughlin GM et al, 2000, adapted 8

5. Sleep structure
a. Sleep phases, cycles and stages



LV	=	Low Voltage
MI	=	Mixed intermittent, „activité moyenne"
HVSW	=	High Voltage Slow Wave
TA	=	Tracé alternant

Dreyfus-Brisac C + Monod N, 1965
Parmalelee AH et al, 1968
Dreyfus-Brisac C, 1970
Curzi-Dalcacova L et al, 1988
Andre et al, 2010
Grigg-Damberger, 2016

5. Sleep structure
a. Sleep phases, cycles and stages

American Academy of Sleep Medicine Scoring Manual definitions of electroencephalogram patterns of sleep and wake in infants 0–2 months

EEG Pattern	AASM Manual Definition	Sleep Stages Seen	Representative Electroencephalogram Sample and Comments
Trace alternant (TA)	≥ 3 alternating runs of bilaterally symmetrical synchronous high voltage (50–150 μV) bursts of 1–3 Hz delta activity lasting 3–5 sec (range 3–8 sec) alternating with periods of lower amplitude (25–50 μV) 4–7 Hz theta activity (range 4–12 sec).	Nonrapid eye movement (NREM)	• Permissive to look at preceding and following epochs to see TA pattern. • TA first appears 37 w CA, prominent pattern at 40 w CA, disappears after 44 w CA, often 46 w CA replaced by HVS. • Interburst intervals (IBIs) last 4–6 sec 35–36 w CA, 2–4 sec 37–44 w. Amplitude of IBIs increases with increasing CA.
High voltage slow (HVS)	Continuous synchronous symmetrical predominantly high voltage (100–150 μV) 1–3 Hz delta activity, which often has an occipital or central predominance.	NREM, rarely rapid eye movement (REM)	• HVS precedes TA when 2 patterns present during same NREM period. • HVS is the more mature EEG pattern of stage N sleep at term. • May see low voltage 12–14 Hz sleep spindles over C4, C3 and/or C4 in HV as early as 43–48 weeks CA.
Mixed (M)	Both HVS and low voltage polyrhythmic components intermingled with little periodicity; lower amplitude than seen in HVS.	Wake, REM, rarely NREM	
Low voltage irregular (LVI)	Continuous low voltage mixed-frequency activity with delta and predominantly theta activity.	REM, Wake	• Continuous irregular centrally predominant 25–50 μV 4–7 Hz activity intermixed with occasional 1–3 Hz delta of similarly low amplitude. • LVI seen in NREM sleep typically after a period of NREM sleep.

TA, quiet sleep (NREM)

HVSW, quiet sleep (NREM)

MI, active sleep (REM)

LV (REM)

Grigg-Damberger, 2016

5. Sleep structure
b. Sleep patterns in preterm infants

Table 1 Normal maturation in neonates

CCA	Background activity	Synchrony	Characteristic transients	Wake/sleep cycle	Reactivity
24–26	D with IBI 10–60 s	+++	STDPS	–	–
27–29	D with IBI 10–40 s polymorphic 0.1–14 Hz hypersynchronous	–	PTT, most prominent at 29 weeks; diffuse ↓B; occipital slow activity	–	–
30–32	D with IBI 5–20 s; occipital α and mix of α, σ and θ in centro-temporal regions; AS: C starts to appear	+/–	Abundance of occipital delta activity; central ↓B; PTT; FST may be seen	+/– poorly differentiated	–
33–34	Aw: predominantly C; QS: D with IBI 5–15 s; AS: TC	+ (– in QS)	↓B over rolandic and occipital areas; temporal ⍺ bursts may be seen; BFD and FST start to appear	AS, QS, AS predominates	+/–
35–37	Aw: C low-voltage mixed activity; QS: D, but TA starts to appear; AS: C max. in occipital regions	+++ (+/– in QS)	FST; BFD may be present; ↓B less frequent	Aw, QS and AS	+
38–44	Aw: C low-voltage mixed activity; QS: TA (disappears by 46 weeks); AS: C low voltage irregular activity	+++	FST and BFD dominant; sharp transients in temporal areas; ↓B rarely seen	Fully developed sleep cycles	+

Sleep

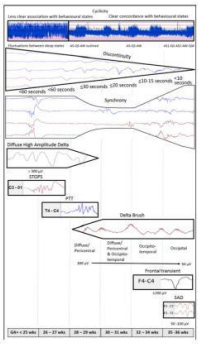
Sleep stages AS, QS, IS only distinguishable after 30 (-32) weeks on EEG, scoring on behavioral observation after 24 weeks

Pitt M, Pressler R. Early Human Development 2005

5. Sleep structure
b. Sleep patterns in preterm infants

When do these patterns appear in sleep?

- Delta brushes: NREM > REM.
- Frontal sharp transients (encoches frontales): NREM, especially at onset, but also W and REM.
- Slow anterior dysrhythmias (SAD) AS1 REM.
- Sharp transients central and temporal, sharp theta or alpha bursts: frequently in QS, esp. tracé alternant, persist during R and W.



Pavlidis E et al, 2017

5. Sleep structure
d. Sleep patterns infants after term in NREM

Hypnagogic hypersynchrony

Drowsiness: **Hypnagogic hypersynchrony**, first appears at 3 months, most prominent between 3-11 months, in 95% of all infants and children up to 4 years, gruadually disappearing , 10% in 11-year olds and rare after 12 y.

initially continuous, then in bursts, initially fronto-central, then diffuse. Rhythmic high amplitude 75-350 mikroV, 3-5 Hz waves

Gradual alpha dropout after the age of 6 years

At / after arousal: **Post arousal hypersynchrony:** first appears at 3 months, peak at 1-2 years, gruadually disappearing after 4 years

central, fronto-central. Spontaneous or when attempting to arouse, also called hypnopomic hypersynchrony.

5. Sleep structure
d. Sleep patterns after term in NREM

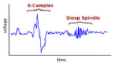
Vertex waves:

- appear beween 3 and 6 months, mostly at 4 months, after 16 months with a shape resembling older children and adults.
- in NREM N1 and NREM N2, with maximum over central, predominantly electronegative. At young age often in runs.
- Around 3 years often with high amplitude (>250 mikroV) and sharply peaked, occasionaly misidentified as epileptiform.

5. Sleep structure
d. Sleep patterns after term in NREM

K complexes:

- appear at 5-6 months, well established after 18 months,
- in NREM N2, in response to external stimuli such as sounds, touches on the skin and internal ones such as inspiratory interruptions
- Surface negative, 50-100 mikroV, lasting 200 ms, followed by a surface positive 30-50 mikoV 300-500 ms wave max. over prefrontal and frontal, often combined with spindels



- suppressing cortical arousal in response to stimuli that the sleeping brain evaluates not to signal danger
- aiding sleep-based memory consolidation.

5. Sleep structure
d. Sleep patterns after term

Spindels

- „pre" spindels at neonatal age, first spindels at 44-46 weeks CA (4-6 weeks).
- 12-14 Hz, over midline central, often last 8 up to 10-15 s around 3-4 months, can be asynchronous in the first year, then synchronous in 70%. Often sharply contoured.
- Max central and parietal in the first 3 years, then vertex, independent 11-12 Hz frontal spindels.

Geiger et al, 2011, Astill et al, 2014, Lustenberger et al, 2012 Naders et al, 2015

- sustained and relayed to the cortex by thalamo-thalamic and thalamo-cortical feedback loops.
- essential role in both sensory processing, long term memory consolidation, fluid intelligence, motor task accuracy.

5. Sleep structure
d. Sleep patterns after term of NREM

- **Slow wave activity of NREM 3 sleep**

  NREM N3 is scored when =/> then 20% of 30 s epoch contanins SWA, usually > 150 microV, in young children often > 300 microV. Often scored after 3 months of age as soon as N1, N2 and N3 can be distinguished.

- **Bioccipital delta slowing in NREM sleep**

  Runs of high voltage 1-2 delta slowing over occipital regions bilaterally. Often seen between 6 months and 4 years. Uncommona fetr 6 years.

- **Fast activity of early NREM sleep**

  20-25 Hz Beta activity maximal over central and postcentral EEG derivations, appears at drowsiness and persists into NREM N1 and sometimes N2. Appears at 5-6 months and reaches max at 18 months, rarely seen after 7 years.

Grigg-Damberger, 2016 and 2017

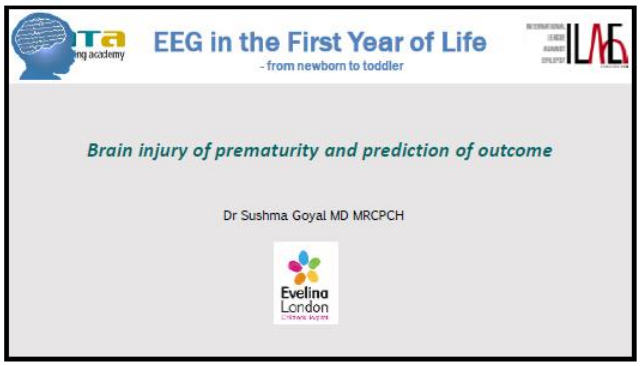
5. Sleep structure
d. Sleep patterns after term for REM sleep

REM sleep

- In infancy REM sleep resembels that of adult but with slower dominant EEG frequency and higher voltage.
  - At 7-8 weeks: 3 Hz,
  - at 5 months 4-5 Hz with saw tooth waves,
  - at 9 months 4-6 Hz,
  - at 1-5 years runs of 5-7 Hz.
  - After 5-10 years background activity of REM resembels adults with mixed frequency activity, saw tooth waves midline central, REM.

Sheldon SH et al, Principles and Practice of pediatric sleep medicine, 2014

S Goyal (UK): EEG in brain injury of prematurity



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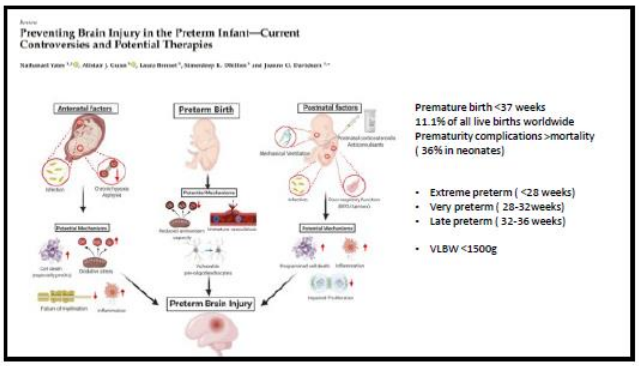

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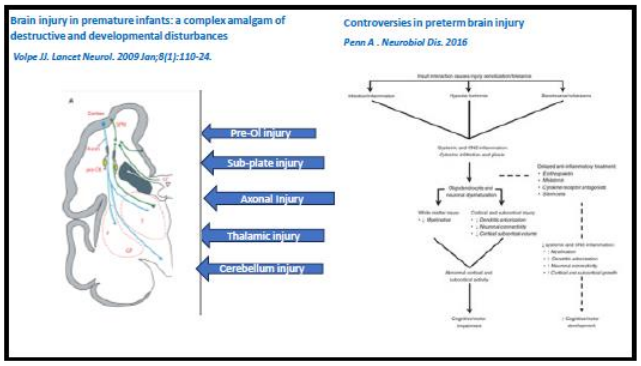

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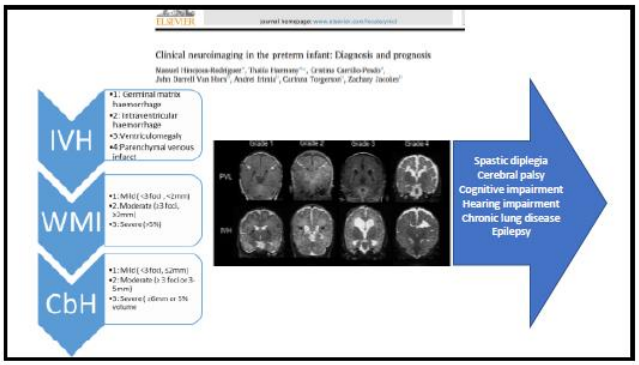

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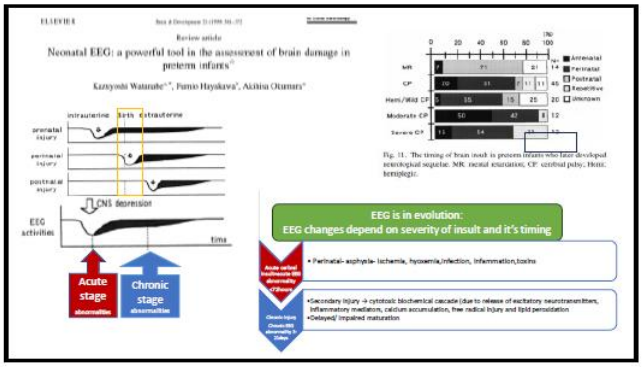

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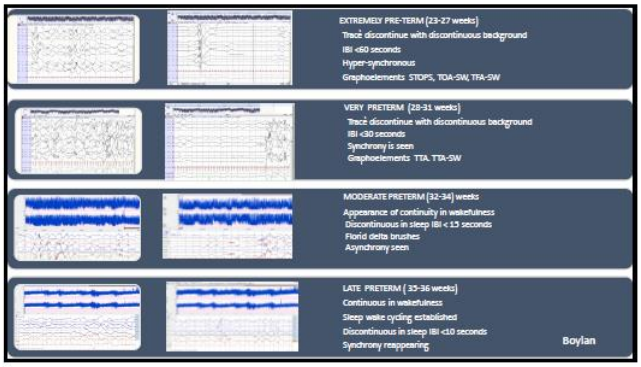

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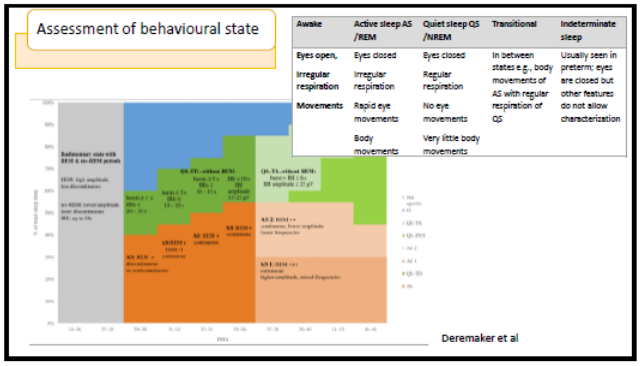

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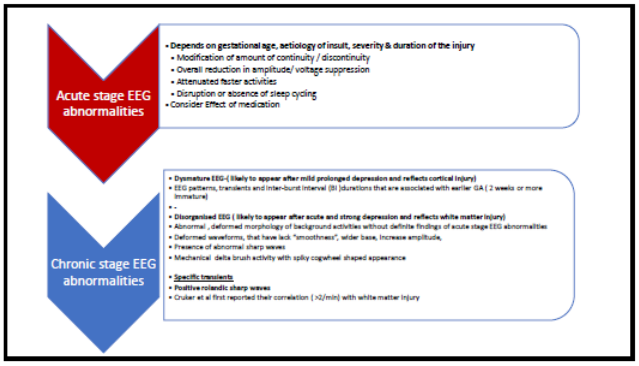
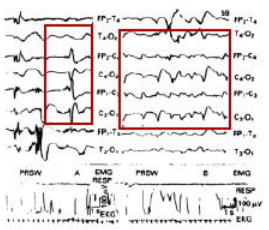


8

Positive rolandic sharp waves in the EEG of the premature newborn: a five year prospective study

Stéphane Marret, Dominique Parain, Emmanuel Jeannot, Danielle Rieu, Claude Fessart



PRSW were classified as type A (isolated and sharply differentiated from the background activity)

B (occurring in bundles and less well differentiated from background activity) according to Blume and Dreyfus-Brisac

Incidence PRSW (38%) 301 <33 weeks

- Absence of PRSW on the neonatal EEG is correlated with unimpaired motor development (98-2%)
- Presence impaired development is more frequent (68%)

Okumura reported their correlation (0.1/min) with white matter injury

9

Aetiology: Hypoxic-ischemic encephalopathy (33%) and intracranial haemorrhage (27%)

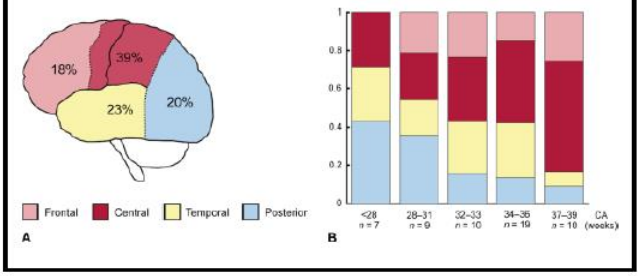
First seizure : Pe preterm median(six days) vs Term (median 27 hours)

Seizure characteristics							
Any subclinical seizures	61 (96%)	12 (67%)	9 (56%)	40 (71%)	0.2	331 (94%)	0.6
Only subclinical seizure	22 (24%)	5 (28%)	2 (13%)	15 (27%)	0.4	72 (14%)	0.01
Death	32 (35%)	7 (39%)	6 (33%)	19 (33%)	0.9	78 (15%)	<0.0005

10

Location of onset of seizures in premature infants with corrected age. (A) Onset location for all infants in preterm group. (B) Age-related changes in location of seizure onset.

Janackova, S., Boyd, S., Yrzavikis, E., et al., 2016. Electroencephalographic characteristics of epileptic seizures in preterm neonates. Clin Neurophysiol 127.



11

Background EEG features and prediction of cognitive outcomes in very preterm infants: A systematic review

Annice H.T. Kong[a,b,*], Melissa M. Lai[a,b], Simon Finnigan[a,b], Robert S. Ware[c], Roslyn N. Boyd[a,b], Paul B. Colditz[a,b]

Dysmature/disorganised EEG pattern

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Biagioni et al. 1996	2	7	1	53	0.67 (0.09, 0.99)	0.88 (0.77, 0.95)		
La Bhanonic et al. 2012	20	3	16	22	0.56 (0.39, 0.72)	0.88 (0.69, 0.97)		
Selton et al. 2010	21	7	14	14	0.60 (0.42, 0.76)	0.67 (0.43, 0.85)		
Selton et al. 2013	20	6	6	20	0.77 (0.56, 0.91)	0.80 (0.59, 0.93)		

12

Can EEG accurately predict 2-year neurodevelopmental outcome for preterm infants?

Table 2 Confusion matrix, sensitivity, specificity, positive and negative predictive value (PPV and NPV) of EEG at three different time points and the relationship with neurodevelopmental outcome in all available infants

	EEG	Outcome: Normal	Outcome: Abnormal	P value*	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
EEG-1 (n=57)	All infants	Normal (n=18)	17	1	0.011	0.68 (0.55 to 0.80)	94 (71 to 100)	43 (27 to 59)	41 (26 to 58)	94 (73 to 100)
		Abnormal (n=39)	23	16						
EEG-12 (n=50)	All infants	Normal (n=27)	27	0	<0.001	0.84 (0.70 to 0.92)	100 (75 to 100)	68 (51 to 81)	50 (30 to 70)	100 (87 to 100)
		Abnormal (n=23)	13	13						
EEG-36 (n=45)	All infants	Normal (n=29)	29	0	<0.001	0.91 (0.80 to 1.00)	100 (89 to 100)	88 (66 to 93)	63 (35 to 85)	100 (88 to 100)
		Abnormal (n=16)	6	10						

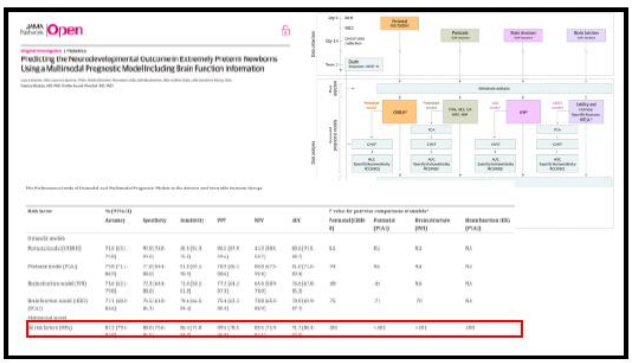
13

A standardised assessment scheme for conventional EEG in preterm infants

Elena Parlidis[a,*], Rhodri O. Lloyd[a,b], Vicki Livingstone[a,b], John M. O'Toole[a,b], Peter M. Filan[a,b,c], Francesca Pisani[d], Geraldine B. Boylan[a,b,e]

Fig. 1. EEG assessment scheme with 6 groups of PMA and the relevant EEG features divided in 4 categories.

14



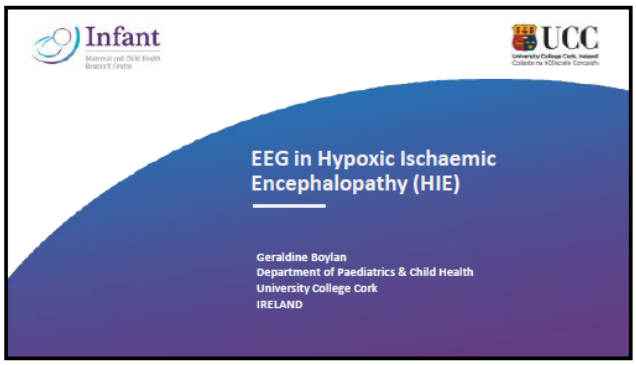
15

Summary

- The cause, pattern and outcome of brain injury is complex and challenging in pre-terms
- There is preliminary evidence that background EEG features can predict cognitive outcomes in very preterm neonates
- EEG is a useful adjunct to diagnose and prognosticate outcome of pre-term brain injury
- Standardisation is needed with respect to terminology
- Timing of first and serial EEGs is paramount

16

G Boylan (Ireland): EEG in Hypoxic ischemic encephalopathy



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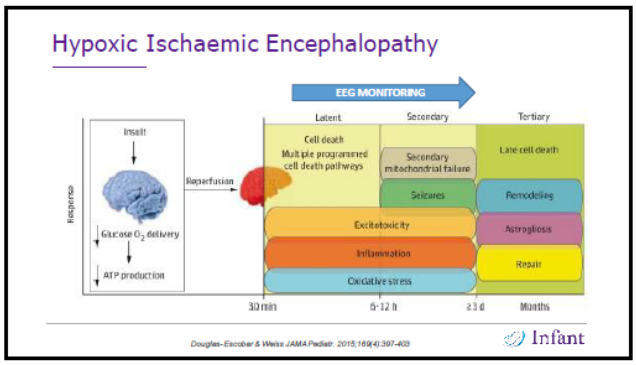

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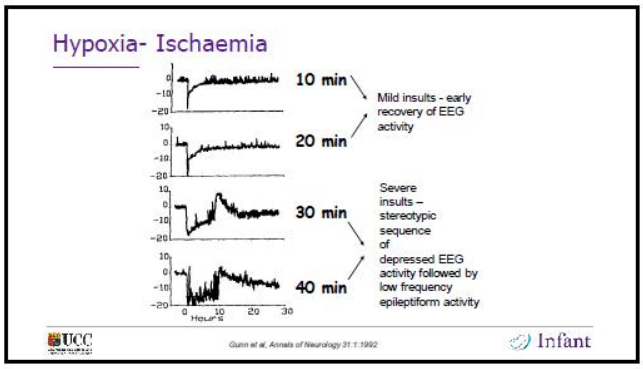

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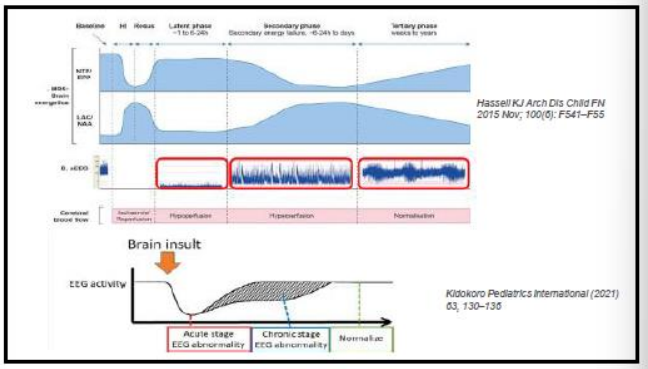

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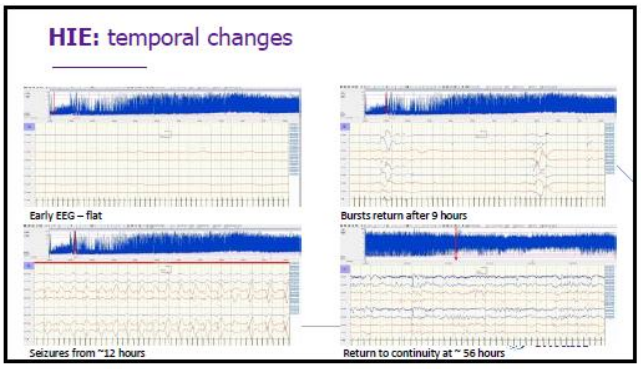

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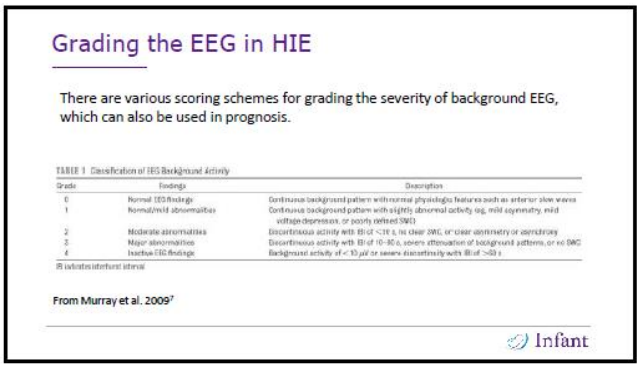

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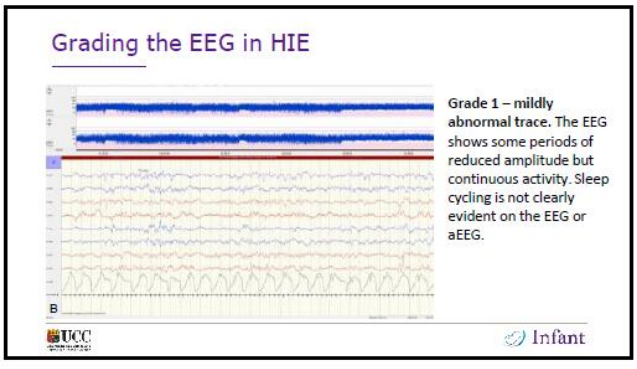

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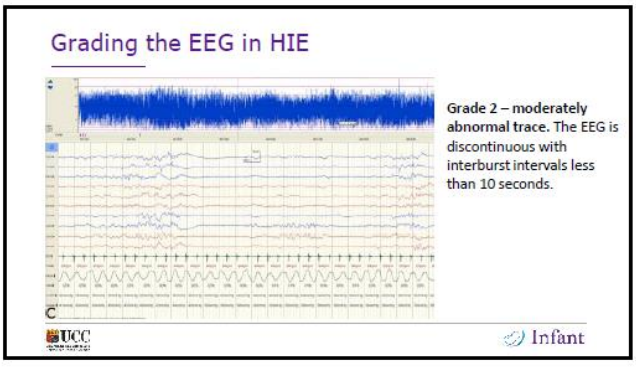
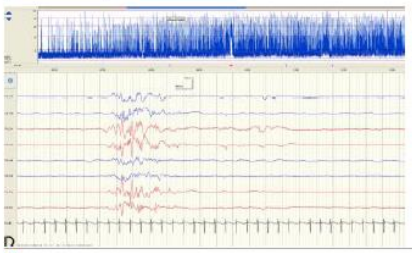


8

Grading the EEG in HIE

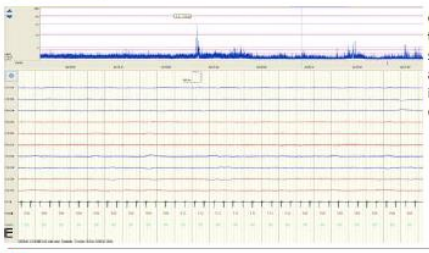


Grade 3 – severely abnormal trace. The EEG is highly discontinuous with interburst intervals of 10-60 seconds.

UCC Infant

9

Grading the EEG in HIE



Grade 4 – Isoelectric trace. EEG is fully suppressed with no activity above 10μV or interburst intervals in excess of 60 seconds.

UCC Infant

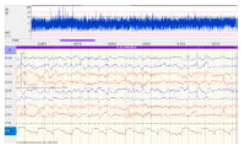
10

Pediatric RESEARCH

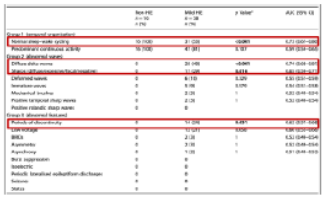
CLINICAL RESEARCH ARTICLE

Multichannel EEG abnormalities during the first 6 hours in infants with mild hypoxic–ischaemic encephalopathy

- 58 infants with mild HIE; 15 controls
- 1-hour of EEG at 6 hours



Mild HIE

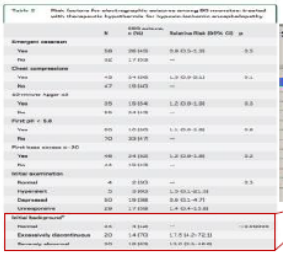


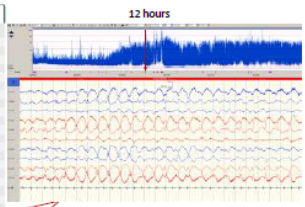
UCC Infant

Garvey et al. Pediatric Research (2021) 90:117–124

11

Seizure Prediction in HIE



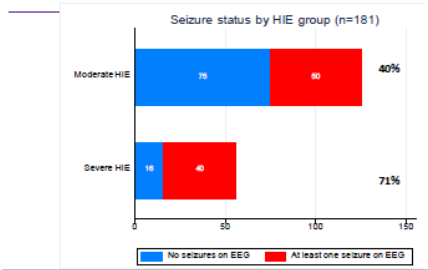


UCC Infant

Glass et al. Neurology 2014; Comet et al.Pediatric Research (2018) 84:399 – 402

12

Seizures & HIE



Rennie et al. Arch Dis Child Fetal Neonatal Ed. 2019 Sep;104(5):F493-F501
Pavel et al. Lancet Child Adolesc Health. 2020 Oct;4(10):740-749

Infant

13

Seizure characteristics HIE (n=55 with early EEG monitoring)

	All infants n=55	Moderate HIE n=31	Severe HIE n=24	p-value
	Median (IQR)	*Median (IQR)*	*Median (IQR)*	
Age at start of EEG monitoring (hours)	4.2 (2.9-7.3)	4.3 (3.3-6.9)	4.1 (2.4-7.8)	0.635
Age at first seizure (hours)	14.4 (10.7-19.4)	13.1 (8.6-19.1)	14.8 (13.5-19.7)	0.191
Total seizure burden (min)	70 (30-133)	58.5 (23.2-75.2)	119.5 (42.8-212)	0.005
Hour after birth max SB reached	23 (14-36)	15 (12-31)	27 (20-53)	0.003

Rennie et al. Arch Dis Child Fetal Neonatal Ed. 2019 Sep;104(5):F493-F501
Pavel et al. Lancet Child Adolesc Health. 2020 Oct;4(10):740-749

Infant

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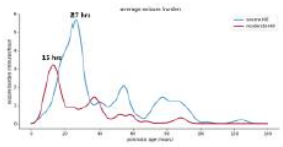
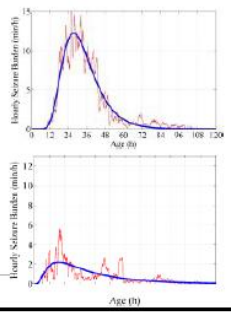
Seizure burden in HIE

Temporal evolution



Courtesy J.O'Toole, UCC

Effect of TH



Wusthoff et al J Child Neurol 2011; Low et al ADC 2012; Lynch et al Epilepsia 2012; Srinivasakumar et al J Pediatr 2013; Guidetti et al. Dev Med Child Neuro 2016

15

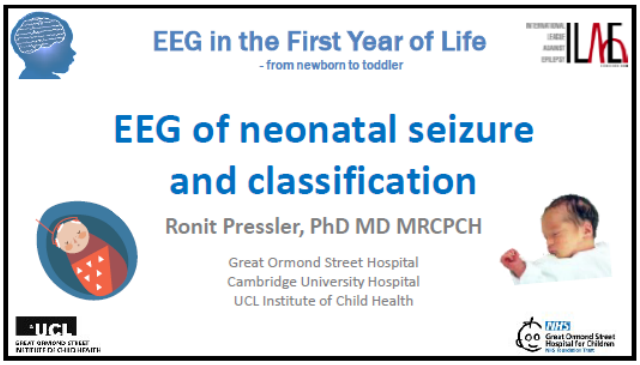
Conclusion

- EEG is a powerful marker of the severity of encephalopathy
- EEG evolves over first few days
- Seizures are common in moderate and severe HIE with onset generally in first 24 hours

UCC Infant

16

R Pressler (UK): Neonatal seizures and classification



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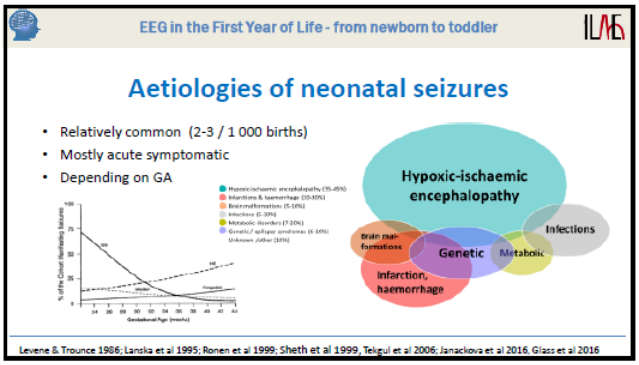

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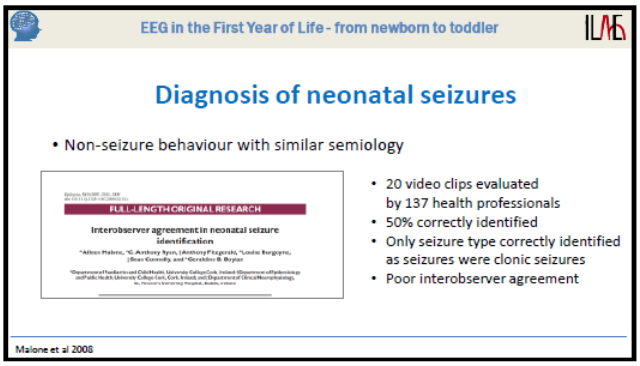

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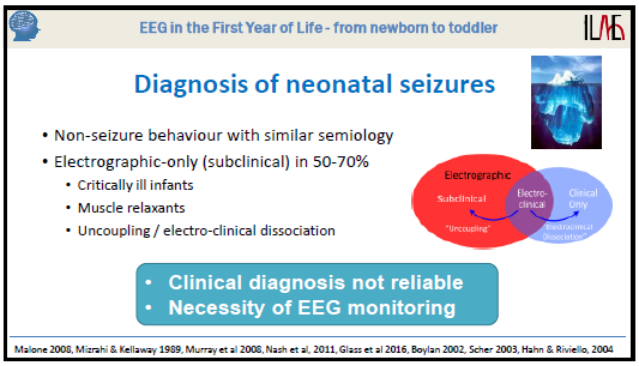

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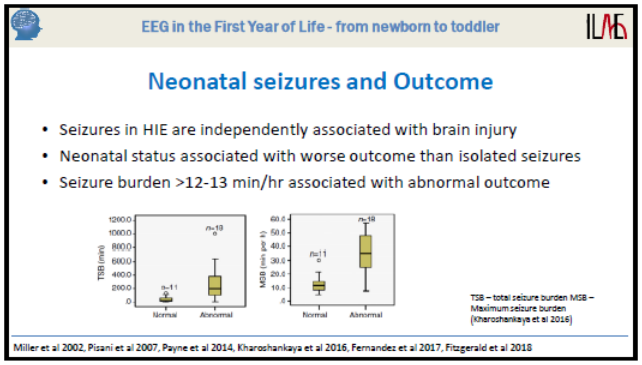

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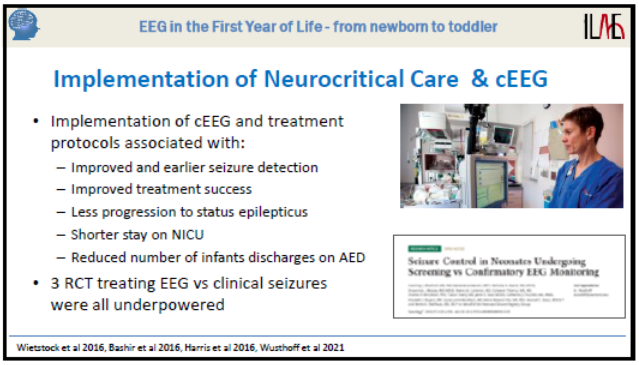


6

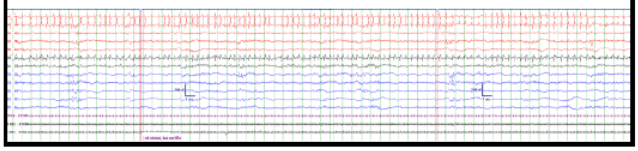
Definition of seizures

- **ILAE, Fisher et al 2005/2014**
  - A seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain
  - Does not including electrographic seizures
- **ACNS, 2013: Definition of electrographic seizure**
  - A paroxysmal abnormal, sustained change in the EEG
  - repetitive and evolving pattern with a minimum 2 µV voltage (peak to peak) and duration of at least 10 seconds

7

Definition of Neonatal Status

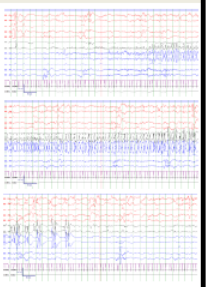
- **ILAE:** no definition specifically for neonates (Nunes et al 2024)
- **American Clinical Neurophysiology Society**
  Status epilepticus as present when the summed duration of electrographic seizures comprises >50% of an arbitrarily defined 1-hour epoch (Tsuchida et al 2013).



8

EEG features

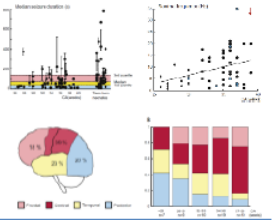
- Any rhythmic activity is suspicious
- Sudden, distinct beginning & end
- Focal origin with spread
- Evolution of amplitude & morphology
- Minimum duration ≥10 sec



Ref: Tsuchida et al ACNS guidleines 2013

EEG characteristics of neonatal seizures

- Duration: mean ~ 2-3 min
- Frequency: increasing with PMA
- Localisation: central & temporal most common
- Propagation: mostly focal and regional



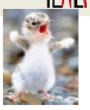
Clancy 1987, Scher 1993, Patrizi 1993, Okumura 2008, Janáckova 2010

Ictal EEG pattern

- Repetitive sharp waves or spikes
- Spike-and-wave / sharp-and-slow wave complexes
- Rhythmic, often sinusoidal slow waves
- Recruiting faster activities
- Zip like pattern
- Electrodecremental event
- Simultaneous independent seizures

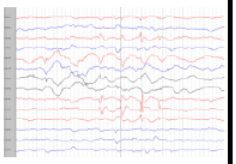
11

Brief Inter/ictal Rhythmic Discharges (BIRDs)



Discharges <10 s of uncertain significance ?

- Rhythmic discharges - with recruitment
- Occur in premature and sick neonates
  (Associated with seizures in same/other EEG and poor outcome
- Also described in adults
- If with clinical manifestation => seizures ?

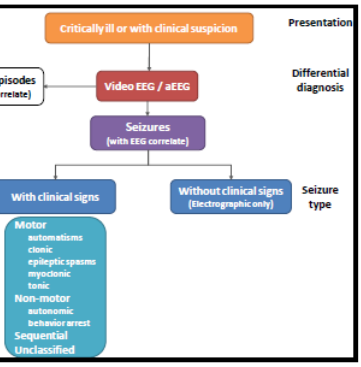


Shewmon 1990;, Nagarajanet at al 2011, Oliveira et al 2000, Yoo et al 2014, 2017

12

ILAE Neonatal Seizure Classification

Pressler et al, Epilepsia 2021
https://www.ilae.org/guidelines/definition-and-classification

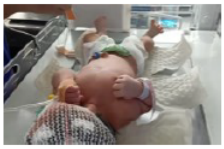


13

EEG in the First Year of Life - from newborn to toddler

Motor
Clonic

Definition:
- Involuntary contractions of muscles or muscle groups
- Regularly repetitive jerking at 2–3 c/s, prolonged



Clinical context:
- Easy to diagnose clinically
- Common in stroke (unilateral)
- Multifocal seen in other aetiologies

Mizrahi & Kellaway 1989, Tharp 2002, Low et al 2014; Spagnoli et al 2015; Nunes et al 2008 & 2018

14

EEG in the First Year of Life - from newborn to toddler

Motor
Tonic

Definition:
- A sustained increase in muscle contraction,
- Lasts longer than spasms (> 2 sec)

Clinical context:
- Focal / asymmetric in neonates
- Typically for early onset developmental epileptic encephalopathy
- Also in other epileptic encephalopathies and genetic neonatal epilepsies

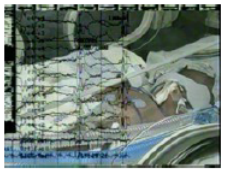
Aicardi and Ohtahara, S., 2002; Nabbout & Dulac 2003, Kato et al 2013; Mihl et al 2013; Pisano et al 2015; Nunes et al 2018, Cornet et al 2021

15

EEG in the First Year of Life - from newborn to toddler

Motor
Myoclonic

Definition:
- Sudden & brief (<100 ms) involuntary contraction(s) of muscles
- Single or multiple with variable topography (axial, limb, distal)



Clinical context:
- Clinically difficult to differentiate from non-epileptic myoclonus
- Typical for early infantile DEE, inborn error of metabolism and in preterms

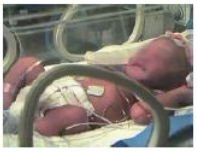
Plouin & Kaminska 2013; Ohtahara & Yamatogi 2006; Ronen et al 2007; Lloyde et al 2017, Nunes et al 2018

16

EEG in the First Year of Life - from newborn to toddler

Motor
Automatisms

Definition:
- A more or less coordinated, repetitive motor activity
- Often resembles a voluntary movement / action
- Often oral or manual



Clinical context:
- Normal / abnormal behaviour mimic automatisms (EEG confirmation)
- Often a component of seizures in self-limited neonatal seizures, or temporal lobe seizures

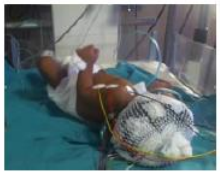
Mizrahi & Kellaway 1989; Sand et al 2016

17

EEG in the First Year of Life - from newborn to toddler

Motor
Spasms

Definition:
- A sudden flexion, extension, or mixed extension–flexion of proximal and truncal muscles
- More sustained than a myoclonic but < 2 s



Clinical context:
- Rare in neonates
- May be seen in pyridoxine dependent seizures and other metabolic disorders, also genetic

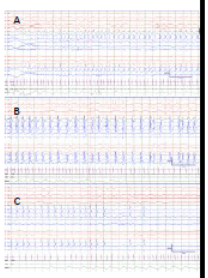
Plouin & Kaminska 2013; Porri et al 2014; Ohtahara et al., 1992; Ohtahara and Yamatogi, 2003

18

Non-motor
autonomic

- **Definition:**
- A distinct alteration of autonomic nervous system function such as respiratory, cardiovascular, pupillary and other functions

- **Clinical context**
- Rare in isolation, often part of sequential
- May be seen in intraventricular haemorrhage or temporal lobe lesions



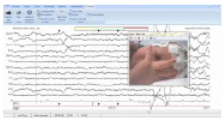
Nunes et al 2018

19

Non-motor
Behavioural arrest

Definition:
- Arrest (pause) of activities, freezing, immobilization.

Clinical context:
- Only seen in wakefulness and therefore rare / difficult to capture in neonates
- Requires video EEG
- May be seen in HIE or as part of sequential seizures



By courtesy of Dr Magda Nunes, Brazil

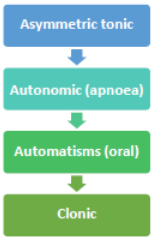
Sands et al 2016; Nunes et al 2019; Santarone et al 2020

20

Motor
Sequential

Definition:
- Variety of clinical signs during a given seizure
- Sequence of heterogeneous components
- Often with tonic phase

Clinical context:
- Possibly associated with genetic or metabolic causes
- Often seen in self-limited neonatal seizures and KCNQ2 encephalopathy

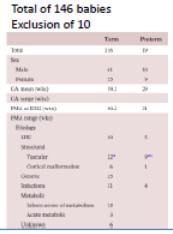


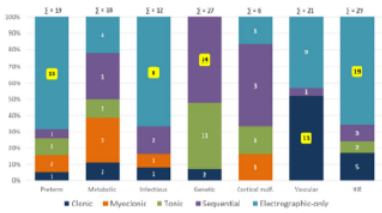
Simoneti et al 2012; Mihl et al 2013; Weckhuysen et al 2013; Fong et al 2014; Sand et al 2016, Nunes et al 2018; Cornet et al 2021

21

Validation of neonatal seizure classification

- Total of 146 babies
- Exclusion of 10



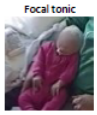


Pressler et al 2021, Yosawitz et al 2022, 2024

22

Brighton Collaboration Case Definition defining diagnostic certain

Focal clonic



Focal tonic

Pellegrin et al, 2019, Pressler et al 2021

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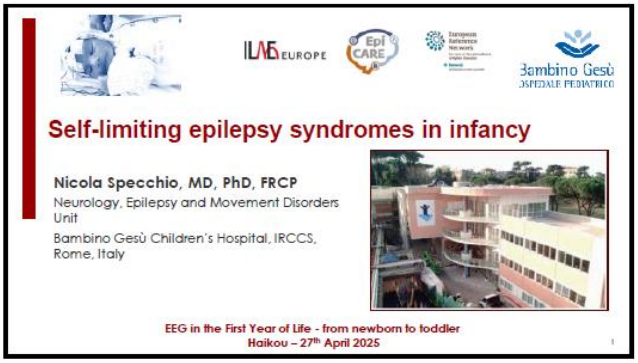
Summary

- EEG is the gold standard in the diagnosis of neonatal seizure
- Availability of EEG / aEEG affects diagnostic certainty
- High seizure burden associated with poor outcome
- Classification of seizures can aid diagnosis and management
- New classification of epilepsy syndrome

24

N Specchio (IT): Self-limiting epilepsy syndromes in infancy



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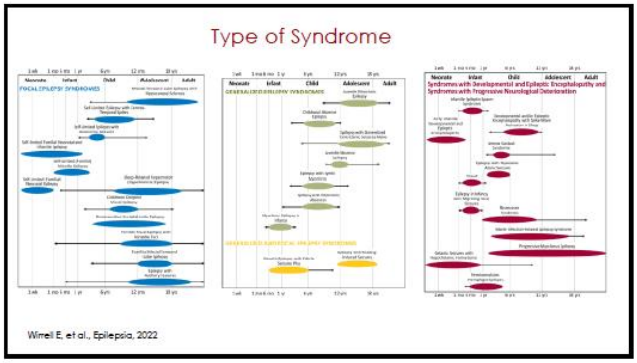

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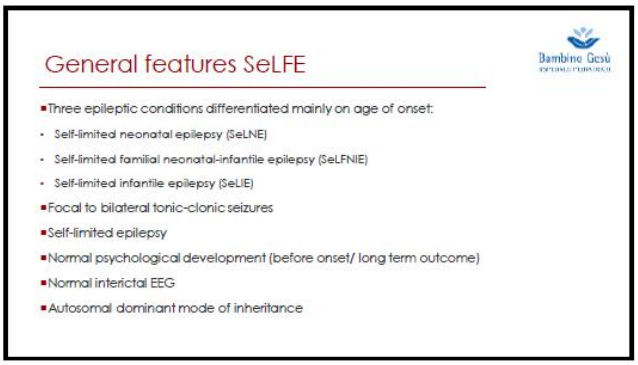

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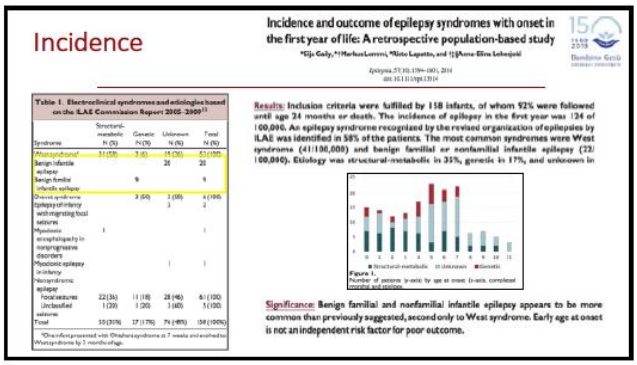

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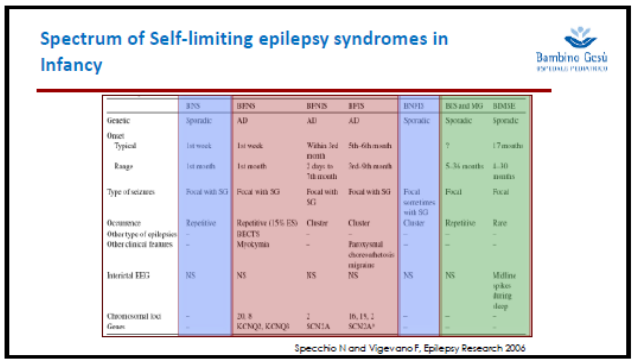

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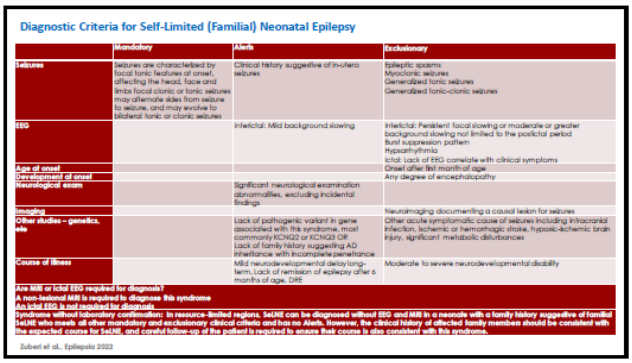

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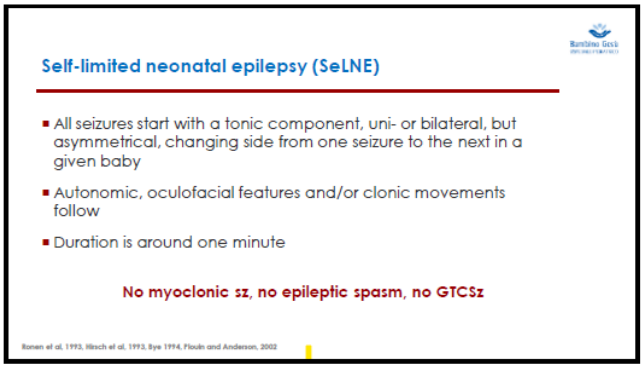

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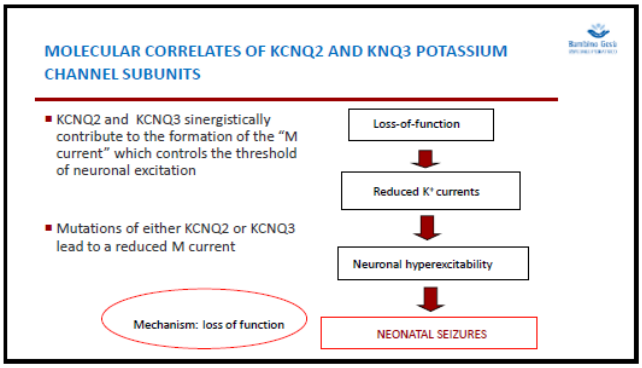

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Diagnostic Criteria for Self-Limited Familial Neonatal-Infantile Epilepsy

	Mandatory	Alerts	Exclusionary
Seizures	Focal tonic seizures with head and eye deviation, followed by other tonic and clonic features and may evolve to bilateral tonic clonic seizures	Sequential seizures	Epileptic spasms Myoclonic seizures
EEG		Interictal: Mild background slowing	Interictal: Persistent focal slowing or moderate or greater background slowing not limited to the postictal period Burst suppression pattern Hypsarrhythmia Ictal: Lack of EEG correlate with clinical symptoms
Age of onset	1 day to 23 months		
Development at onset		A history of prior acute symptomatic seizures including intracranial infection, ischemic or hemorrhagic stroke, hypoxic-ischemic brain injury, significant metabolic disturbances	Encephalopathy
Neurological exam		Significant neurological examination abnormalities excluding incidental findings	
Imaging			Neuroimaging documenting a causal lesion for seizures
Other studies – genetics, etc		Lack of pathogenic variant in genes associated with this syndrome (usually SCN2A)	
Course of illness		Mild neurodevelopmental delay long-term Lack of remission of epilepsy by age 2 years Drug resistant epilepsy	Moderate to severe neurodevelopmental disability

Are MRI or Ictal EEG required for diagnosis?
A non-lesional MRI is required to diagnose this syndrome.
An ictal EEG is not required for diagnosis.

Syndrome without laboratory confirmation: In resource-limited regions, Self-limited neonatal-infantile epilepsy can be diagnosed without EEG and MRI in a neonate with a family history suggestive of familial self-limited neonatal-infantile epilepsy who meets all other mandatory and exclusionary clinical criteria and has no Alerts. However, the clinical history of affected family members should be consistent with the expected course for SeLNE, and careful follow-up of the patient is required to ensure their course is also consistent with this syndrome.

Zuberi et al., Epilepsia 2022

9

Diagnostic Criteria for Self-Limited (Familial) Infantile Epilepsy

	Mandatory	Alerts	Exclusionary
Seizures	Focal seizures occur with behavioural arrest, impaired awareness, automatisms, head/eye version, and clonic movements (often alternating from one side to the other and progressing to a hemiclonic or focal to bilateral tonic-clonic seizure). Seizures are usually brief (<3 minutes).	Prolonged or focal clonic (hemiclonic) seizures (>10 minutes)	Epileptic spasms Myoclonic seizures Sequential seizures Tonic seizures
EEG		Interictal: Mild background slowing	Interictal: Persistent focal slowing or moderate or greater background slowing not limited to the postictal period Hypsarrhythmia
Age of onset		Onset 18-36 months of age	Age at onset <1 month or >36 months
Development at onset		Mild developmental delay	Moderate to profound delay Neurocognitive regression
Neurological exam		Significant neurological examination abnormalities, excluding incidental findings	
Imaging			Causal lesion on brain MRI
Other studies – genetics, etc		Lack of pathogenic variants found in PRRT2, SCN2A, KCNQ2 or KCNQ3 OR Lack of family history suggesting autosomal dominant inheritance with incomplete penetrance	
Course of illness		Lack of remission by late childhood	Neurocognitive regression with myoclonic seizures, ataxia, spasticity

Are MRI or Ictal EEG required for diagnosis?
A non-lesional MRI is required to diagnose this syndrome.
An ictal EEG is not required for diagnosis.

Syndrome without laboratory confirmation: In resource-limited regions, SeLIE can be diagnosed without EEG and MRI in an infant with a family history suggestive of familial SeLIE who meets all other mandatory and exclusionary clinical criteria and has no Alerts. However, the clinical history of affected family members should be consistent with the expected course for SeLIE, and careful follow-up of the patient is required to ensure their course is also consistent with this syndrome.

Zuberi et al., Epilepsia 2022

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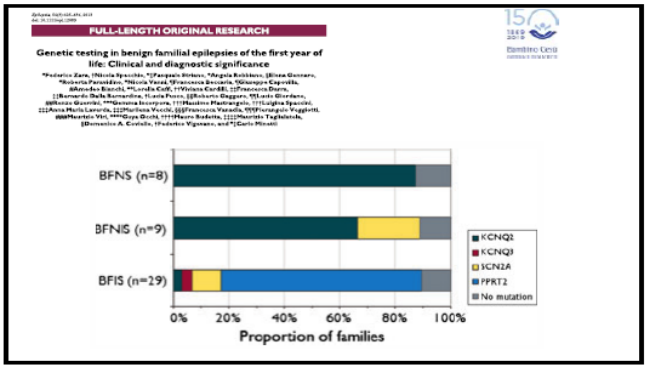

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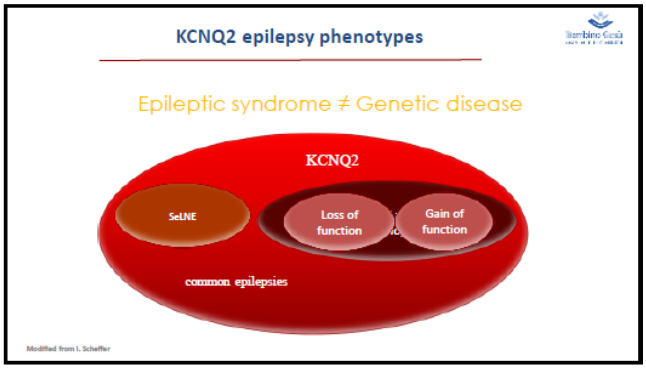

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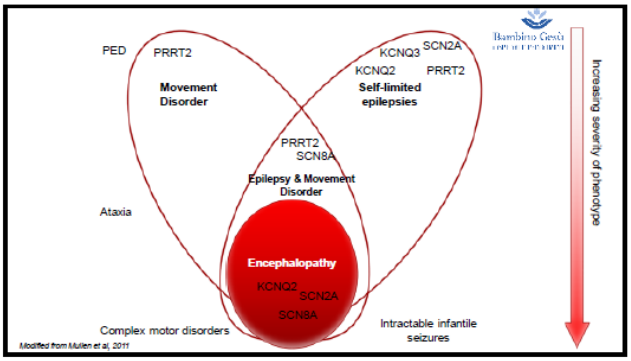

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Summary

- Self-limited epilepsies in the first year of life have peculiar clinical and EEG manifestations; some features overlap.
- The three entities could be included in a unique "spectrum" with variable genetic mutations: KCNQ2 genetic variants are the major cause of Neonatal and Neonatal Infantile Seizures, PRRT2 of Infantile Seizures, but this is not exclusive. SCN2A and PRRT2 not found in the neonatal form.
- Spectrum of self-limiting epilepsies with onset in the neonatal or neonatal-infantile period
  - KCNQ2-3, SCN2A, PRRT2, SCN8A
- KCNQ2, SCN2A, SCN8A encephalopathy or other neurological symptoms associated
- Interictal EEG findings not very informative
- Consider seizure semiology and ictal EEG
- It is important to recognize all the self-limiting entities, to avoid useless and harmful ASMs treatment.
- Peculiar association with paroxysmal movement disorders
- The same genes can provoke severe epileptic encephalopathy, but the localization of the mutation and the functional impairment of the protein are different.
- Long-term evolution is variable

14

M Eisermann (D): EEG in early onset developmental & epileptic encephalopathies

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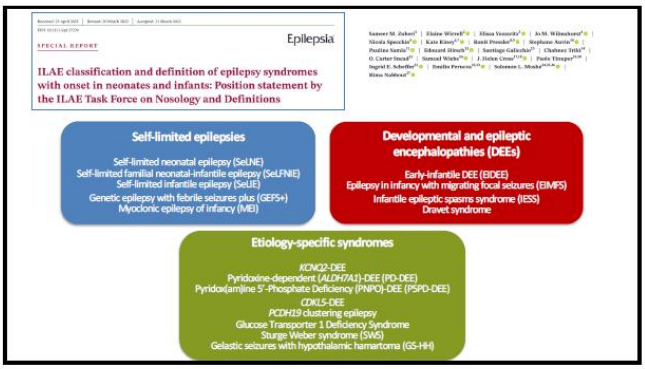

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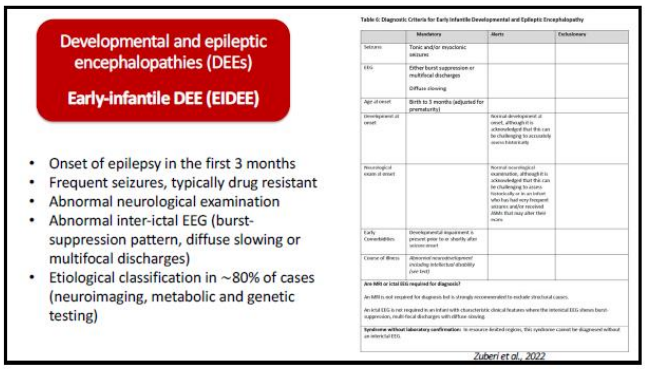

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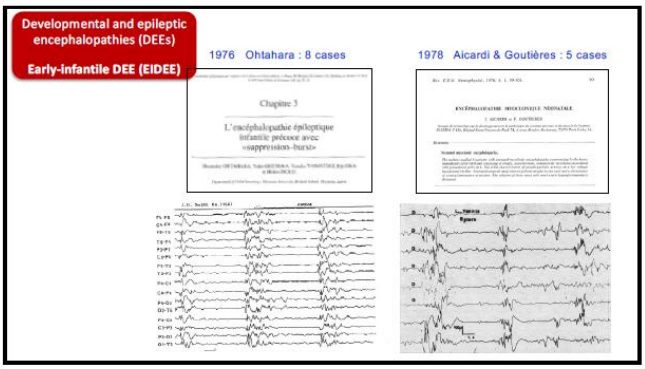

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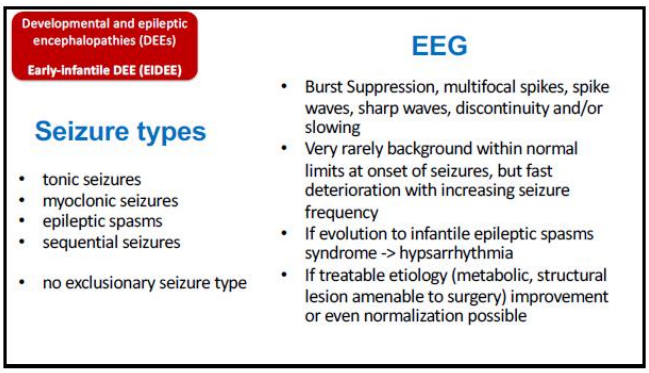

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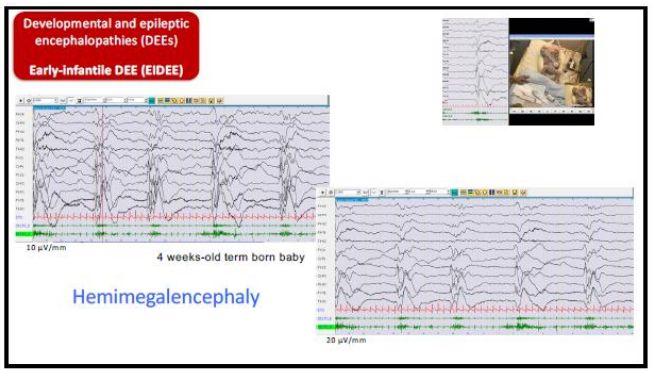

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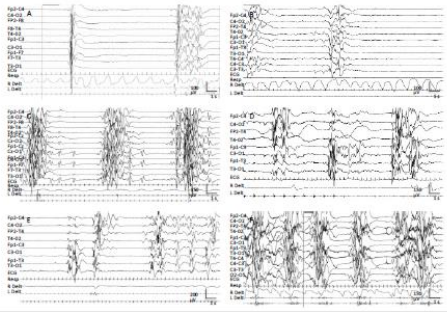
Burst suppression in full-term neonates - different aspects



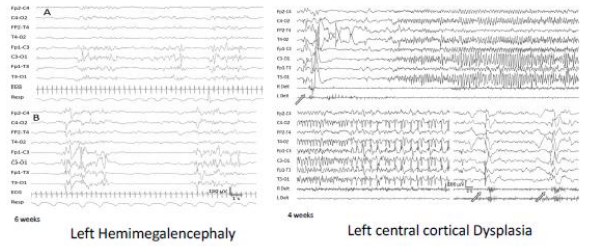
7

Developmental and epileptic encephalopathies (DEEs)

Early-infantile DEE (EIDEE)

Focal cortical malformations

- Stereotyped seizures with lateralizing / focal signs, often epileptic spasms
- Constant asymmetry ou focalisation of background and interictal anomalies



Left Hemimegalencephaly

Left central cortical Dysplasia

8

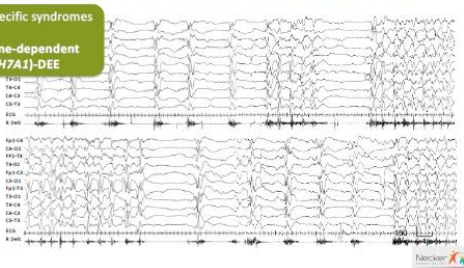
Developmental and epileptic encephalopathies (DEEs)

Early-infantile DEE (EIDEE)

Metabolic diseases
Pyridoxine-dépendant DEE

Etiology-specific syndromes

Pyridoxine-dependent (*ALDH7A1*)-DEE



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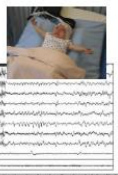
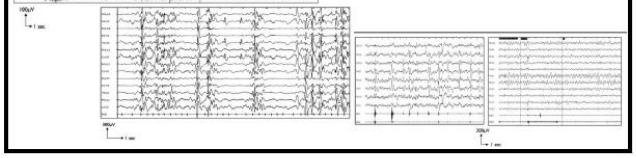
Etiology-specific syndromes

***CDKL5*-DEE**





FULL-LENGTH ORIGINAL RESEARCH

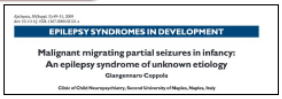
The three stages of epilepsy in patients with *CDKL5* mutations

*†Nadia Bahi-Buisson, ‡‡Anna Kaminska, §¶Nathalie Boddaert, ‖Mariana Rio, **Alexandra Afenjar, ¶Marlen Gérard, ††Fabienne Giuliano, ‡‡‡Jacques Motte, ⁂Delphine Héron, ¶¶Marie Ange N'Guyen Morel, ††Perrine Plouin, ###Christian Richelme, ***Vincent des Portes, *†‖Olivier Dulac, †††Christophe Philippe, *†‖Catherine Chiron, *†‖Rima Nabbout, and ‡‡‡Thierry Bienvenu

10

Developmental and epileptic encephalopathies (DEEs)

Epilepsie of infancy with migrating focal seizures



EPILEPSY SYNDROMES IN DEVELOPMENT

Malignant migrating partial seizures in infancy: An epilepsy syndrome of unknown etiology

Giangennaro Coppola

Clinic of Child Neuropsychiatry, Second University of Naples, Naples, Italy

- Seizure onset within the first six to seven months of life (M3; D13-M7)
- Drug-resistant focal seizures associated with severe encephalopathy
- Seizures initially rare, often undiscovered during 45 d (1 wk/3 mths)
- Autonomic manifestations: apnoe, facial erythrosis, cyanosis, hypersalivation
- Correlation between topography of dicharges and semiology
  - Occipital : oculoclonia and head and eye deviation
  - Rolandic: contro-lateral clonies
  - Temporal: staring, other oral automatisms
  - Frontal: contralateral hypertonia
- In the beginning of the disease seizures can stay for a long time localized → erroneous surgical indication!

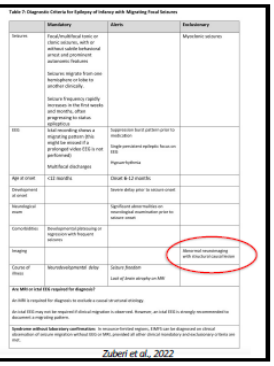


Table 7: Diagnostic Criteria for Epilepsy of Infancy with Migrating Focal Seizures

	Mandatory	Alerts	Exclusionary
Seizures	Focal/multifocal tonic or clonic seizures, with or without subtle behavioral arrest and prominent autonomic features Seizures migrate from one hemisphere or lobe to another clinically. Seizure frequency rapidly increases in the first weeks and months, often progressing to status epilepticus		Myoclonic seizures
EEG	Ictal recording shows a migrating pattern (this might be missed if a prolonged video EEG is not performed) Multifocal discharges	Suppression burst pattern prior to medication Single persistent epileptic focus on EEG Pigeon hydrenia	
Age at onset	<12 months	Onset 6-12 months	
Development at onset		Severe delay prior to seizure onset	
Neurological exam		Significant abnormalities on neurological examination prior to seizure onset	
Comorbidities	Developmental plateauing or regression with frequent seizures		
Imaging			Abnormal neuroimaging with structural causal lesion
Course of illness	Monotherapeutic delay	Seizure freedom Lack of brain atrophy on MRI	
Are MRI or ictal EEG required for diagnosis?			
An MRI is required for diagnosis to exclude a causal structural etiology. An ictal EEG may not be required if clinical migration is observed. However, an ictal EEG is strongly recommended to document a migrating pattern.			
Syndrome without laboratory confirmation: In resource-limited regions, EMFS can be diagnosed on clinical observation of seizure migration without EEG or MRI, provided all other clinical mandatory and exclusionary criteria are met.			

Zuberi et al., 2022

11

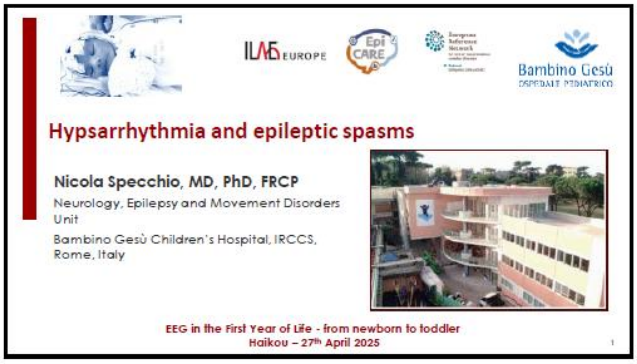
Developmental and epileptic encephalopathies (DEEs)

Epilepsie of infancy with migrating focal seizures

4 months-old infant

12

N Specchio (CH)): Hypsarrhythmia and epileptic spasms



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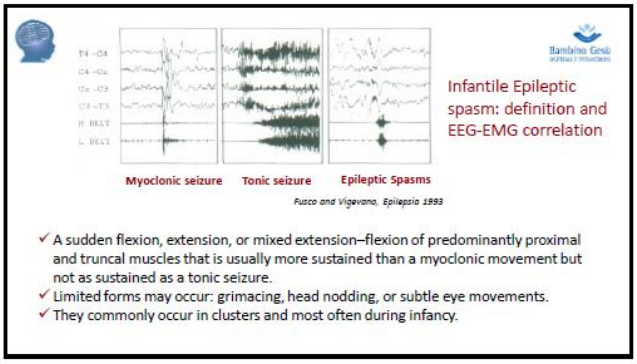

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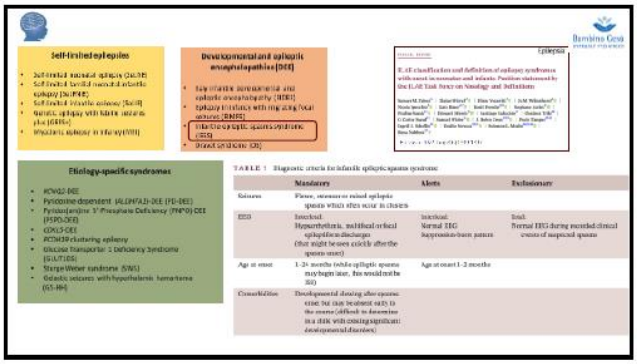

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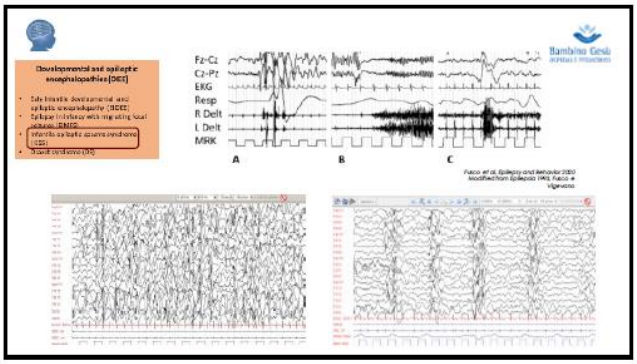

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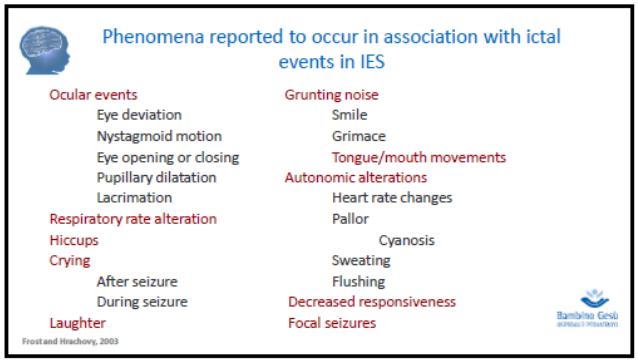

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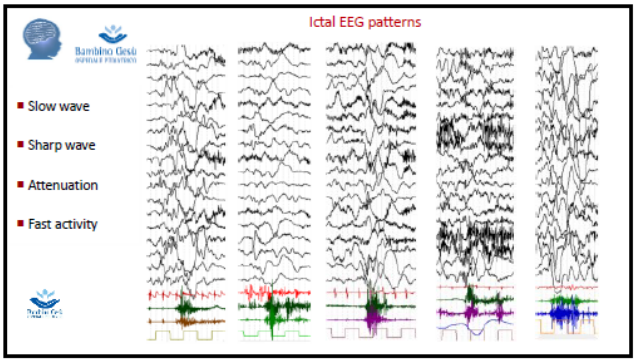

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SUBTLE SPASMS

- Isolated signs of spasms
- Beginning of a cluster of spasms
- If we observe a cluster of spasms we see that there are some ictal events in which the movement of the limbs and trunk is very slight or almost absent and the ictal signs are limited to yawning, gasping, facial grimacing and staring
- These minimal clinical events are called "subtle spasms"

Lux and Osborne, 2004

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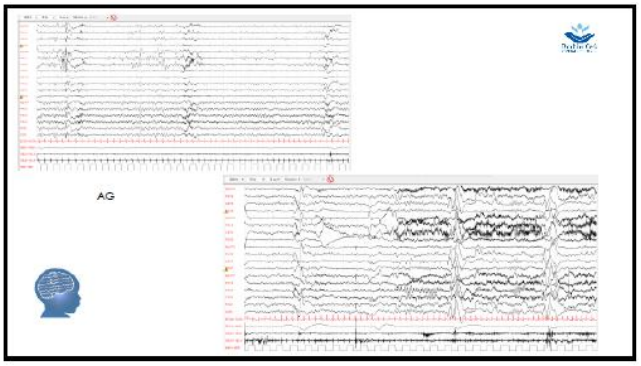

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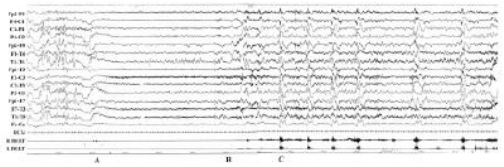
Focal Seizure triggers Spasms



Pap.Val. 5m Right temporal dysplasia

Vigevano F, Specchio N et al., 2007

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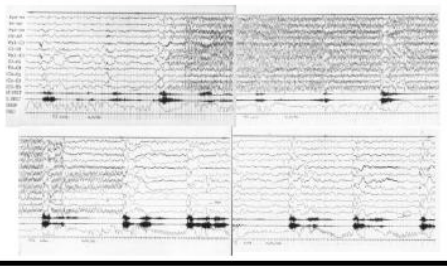
O.F. 3 m – Left frontal focal cortical dysplasia
Focal seizure during a cluster of spasms



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Focal seizures and epileptic spasms as a single ictal event

Pachatz C, Fusco L, Vigevano F, Epilepsia 2003

- Usually a focal seizure precedes and triggers the cluster of spasm, but epileptic spasms could be intermingled with the focal seizure.
- More rarely the spasms trigger focal seizure
- Etiology could be multivarious, mainly malformation of cortical development (focal, unilateral or diffuse)

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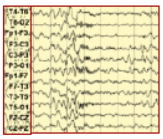
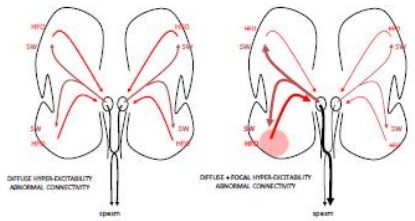


- The cortex probably plays a major role in generating activity associated with spasms.
- The occurrence of spasms likely is related to a complex and abnormal interaction between the cortex and the subcortical structures.
- The ictal gamma rhythm might reflect neocortical dysfunction involved in this abnormal interaction.

12

NEUROPHYSIOLOGY OF SPASMS



Akiyama 2005
Bisulli 2002

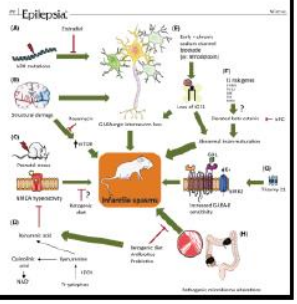
Chugani 2015
Asano 2005
De la Vassiere 2014

13

Mechanisms of infantile epileptic spasms syndrome: What have we learned from animal models? 2023

Key points

- Animal models have been invaluable in our understanding of infantile epileptic spasms syndrome (IESS).
- Multiple etiologies with independent mechanisms are likely important for IESS.
- Understanding the mechanistic underpinnings of IESS may allow for more targeted and rational drug design.



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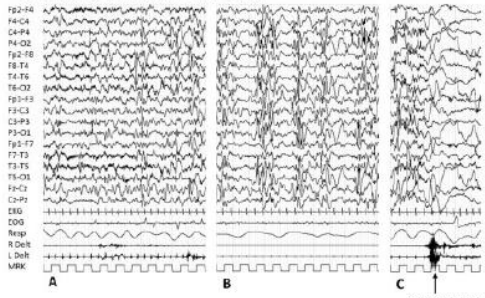
Three different scenarios for epileptic spasms

Lucia Fusco[a,d], Domenico Serino [b], Marta Elena Santarcone[a]

« IESS»



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BASED SCORE FOR HYPSARRHYTHMYA

BASED = Burden of AmplitudeS and Epileptiform Disharges

BASED score 2015	Description
0	Normal
1	Any definite nonepileptiform abnormality
2	<3 spike foci AND no common background slow waves ≥200 μv[AV]
3	MFS <50% of one second bins[a] AND no common background slow waves ≥160 μv[AV], OR No MFS but common background slow waves ≥200 μv[AV]
4 (Hyps[+])	MFS >50% of one second bins[a] AND common background slow waves ≥200 μv[AV]
5 (Hyps[++])	MFS ≥50% of one second bins[a], OR Common background slow waves ≥300 μv[AV] in 2 or more bilateral head regions

John R. Mytinger

Epilepsy Research 116 (2015) 93–98

The BASED score appears to be a reliable, accurate and feasible EEG grading scale for the assessment of children with infantile spasms. Future infantile spasms clinical trials require clarification of hypsarrhythmia criteria to improve inter-rater agreement and thus improve the validity of electrographic outcomes.

Table 4
The 2021 BASED score.

BASED score	Description
0	Normal
1	Any definite nonepileptiform abnormality
2	<3 spike foci AND no channel with abnormal high amplitude
3	≥3 spike foci – <50% of one second bins AND no channel with abnormal high amplitude, OR No MFS but common background slow waves ≥200 μv[AV]
4 (Probable HE)	<3 spike foci ≥3 channel with abnormal high amplitude ≥3 spike foci – <50% of one second bins AND ≥3 channel with abnormal high amplitude, OR Not meetign criteria for 5 but includes GMFS or paroxysmal voltage abnormalities
5 (Definite HE)	≥3 spike foci that are ≥50% of one second bins

John R. Mytinger

Epilepsy Research 173 (2021) 106631

The 2021 Based score includes elements with high levels of Inter-Rater Reliability and correlates well with the presence or absence of infantile Spasms

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Conclusions

- ✓ Multiple etiologies can provoke spasms
- ✓ There are some variables in the ictal clinical and EEG pattern
- ✓ The spasm can appear alone or as a part of a more complex ictal event
- ✓ Spasms are a subcortical event: difficult to apply the category of "focal" or "generalized"
- ✓ IESS can present different scenarios
- ✓ Hypsarrhythmia plays the most relevant role on cognitive outcome and neuropsychiatric comorbidities
- ✓ To score the burden of Hypsarrhythmia it can be useful for predicting patient outcome.

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Acknowledgments

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18

M Eisermann (D): Inborn error of metabolism

EEG in the First Year of Life
Haikou city, 26th and 27th April 2025

Seizures and EEG abnormalities in Inborn Error of Metabolism

Monika Eisermann
Service de Neurophysiologie Clinique
Necker Enfants Malades Hospital, Paris, France

Metabolic diseases presenting with seizures

Neonatal Period–Early Infancy	Late Infancy–Childhood	Adolescence–Adulthood
Pyridoxine-dependent epilepsy		
PNPO deficiency	Creatine synthesis defects	Juvenile NCL
Folinic-acid responsive seizures	Late infantile NCL	Lafora body disease and
Biotinidase deficiency	Mitochondrial disorders	Unverricht–Lundborg disease
Holocarboxylase synthetase deficiency	Organic acidurias	Mitochondrial disorders: MELAS
GLUT-1 (Glucose transporter-1) deficiency	Sialidosis	(Mitochondrial
Serine biosynthesis defects	Gangliosidosis	encephalomyopathy, lactic
Molybdenum cofactor and	GLUT-1 deficiency	acidosis and stroke-like episodes),
Sulfite oxidase deficiency	Congenital disorders of	MERRF (Myoclonic epilepsy with
Menkes disease	glycosylation	ragged red fibers)
Non-ketotic hyperglycinemia	Purine metabolism defects	Lysosomal storage diseases: Late
Organic acidemias	Uridine responsive epilepsy	onset gangliosidosis,
Urea cycle defects	caused by CAD mutations	Niemann–Pick type C, Gaucher
Peroxisomal disorders	Disorders of methylation and	type III
Congenital disorder of glycosylation	folate metabolism	GLUT-1 deficiency
Congenital and early infantile Neuronal	Neurotransmitter defects	Porphyria
ceroid lipofuscinosis (NCL)	Congenital disorders of autophagy	Wilson's disease
Mitochondrial disorders		

Sharma & Prasad, 2017

Neonatal seizures
Inborn Error of Metabolism ?

Clues to the presence of IEM in the neonatal period:

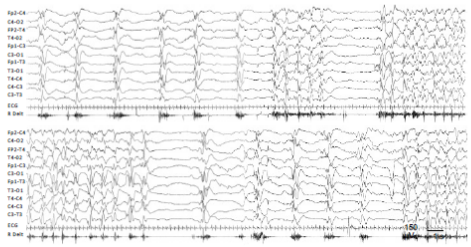
- Family history: parental consanguinity, family h/o neonatal deaths, neurological illnesses
- Pregnancy: abnormal / excessive fetal movements (intrauterine seizures), HELLP syndrome
- Rapidly progressive encephalopathy
- Deterioration after a period of apparent normalcy
- Severe metabolic acidosis
- Hiccups (fluttering or hiccoughs)
- Excitability, pedaling, boxing, myoclonias, tremulations of high amplitude
- Unusual odors of urine, cerumen (rare)

Pyrixodine-dependent DEE
Pyridox(am)ine 5'-Phosphate Deficiency DEE

- Symptoms usually very early, within hours or days after birth
- Intrauterine seizures reported with onset at the end of the last trimester (mothers perceiving excessive fetal jerks)
- Irritability, hyperexcitability
- Sleeplessness, features of hyperalertness, hyperacusis
- Paroxysmal facial grimacing
- Abnormal eye movements
- Emesis, abdominal distention, presenting as sepsis

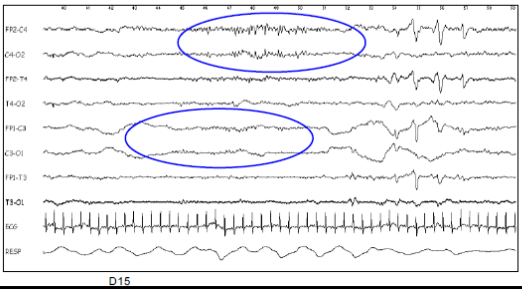
Etiology-specific syndromes

Pyridoxine-dependent (*ALDH7A1*)-DEE



Maple Syrup Urine Disease

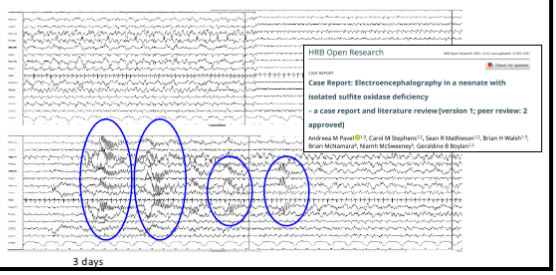
Comb-like pattern



D15

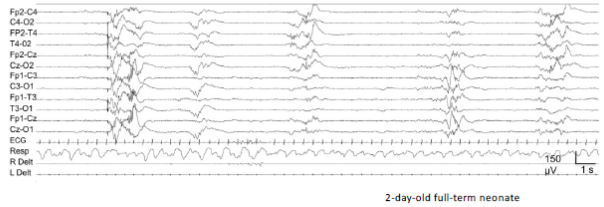
Isolated Sulfite Oxidase Deficiency

Seizures
Delta-beta complexes



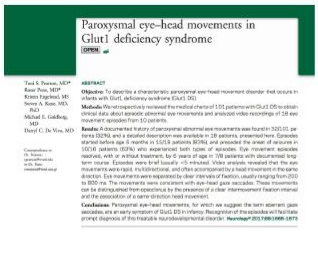
Glycine encephalopathy (nonketotic hyperglycinemia)

discontinous, intermittently **asynchronous** background activity with **dysmature** features



2-day-old full-term neonate

Glut1 deficiency



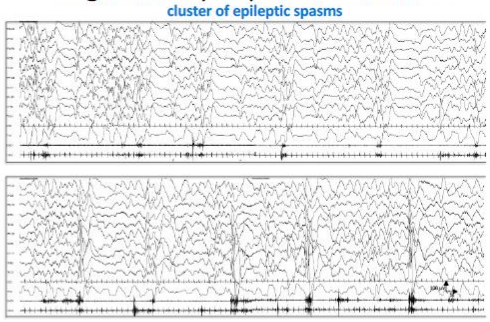
2 mths

5 mths

3 mths

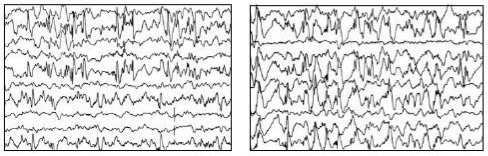
Congenital Glycolysation disorders

cluster of epileptic spasms

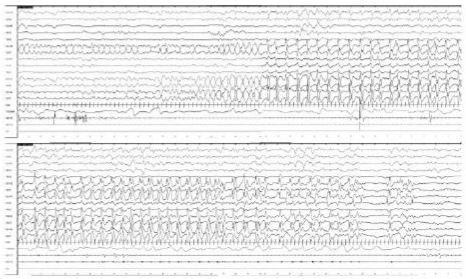


Congenital Glycolysation disorders

- Group of rare metabolic diseases, with multisystemic involvement and frequent neurological impairment, particularly epilepsy
- **Epileptic spasms were observed in ALG1-, ALG6, ALG11-CDG and CDG-Ix**
- Epileptic spasms of early onset, showing possibly focal aspects, and possibly associated with myoclonus
- EEG: poorly organized background activity, abundant posterior spike and fast rhythm activity, but **no hypsarrhythmia**

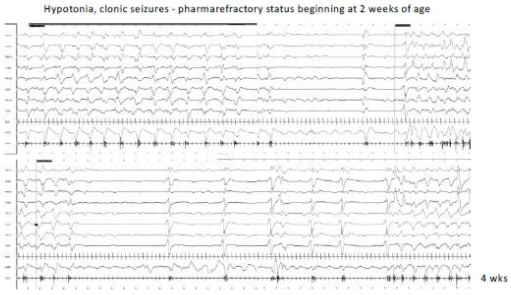


Peroxisomal Disorder mutation HMZ gene *HSD17B4*



Mitochondrial diseases

Hypotonia, clonic seizures - pharmarefractory status beginning at 2 weeks of age



4 wks

Summary

- Numerous entities
- Non-specific but few distinctive EEG pattern that should be identified
- In several IEM in infancy **causative treatment is available**
- **Diagnosis as early as possible to avoid further damage!**
- Seizure semiology and EEG aspect can give important clues to the differential diagnosis
- EEG helpful in assessing severity, treatment response and prognosis

Rachel Thornton (UK): Malformation of Cortical Development

Great Ormond Street Hospital for Children NHS Foundation Trust

UCL

Malformations of Cortical Development

Dr Rachel Thornton
Consultant Clinical Neurophysiologist

Great Ormond Street Hospital, London
Addenbrookes Hospital, Cambridge
Honorary Senior Lecturer Institute of Child Health, UCL

EEG in the First Year of Life
- from newborn to toddler

ILAE

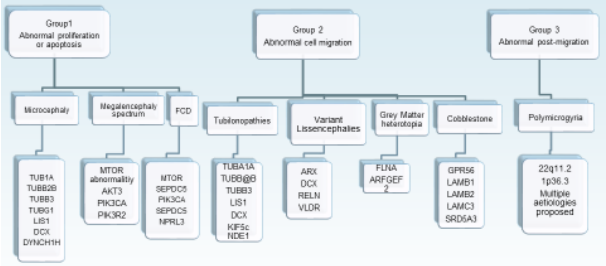
Introduction

- MCD commonly associated with intellectual disability and intractable epilepsy
- >100 genes identified as causative
- Somatic mutations are common, but most probably still not detected[1]
- Focal cortical dysplasia: commonest cause of intractable structural epilepsy in children
- Delay in identification -> inappropriate counselling and delay in treatment

Age at presentation depends on severity of malformation

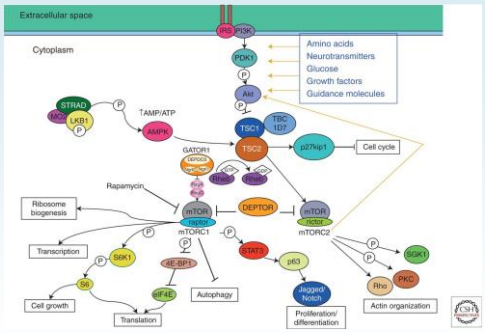
[1]Jamuar et al NEJM, 2014, [2]Guerrini and Dobyns, Lancet Neurol 2014

Classification of MCD



- Classification based on proposed cellular mechanism
- Overlap between histological and clinical phenotype and genotype/ aetiology
- Electroclinical syndrome varies by severity and distribution of abnormality
- Reality is complex and a pathway based classification considering phenotype may be helpful

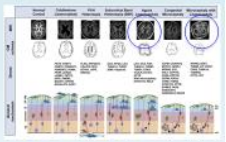
mTOR pathway: mechanism of MCD

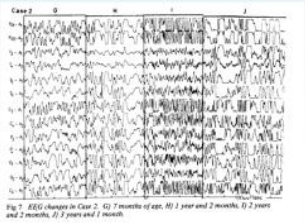


Barkovich et al. Cold Spring Harb Perspect Med 2015

Lissencephaly

'Classic' Lissencephaly:
- 11.7 per 1,000,000 live births
- Pachy/agyria on MRI
- LIS1 or DCX gene
- 90% have seizures (<6 months in 75%)
- 80% spasms
- EEG depends on severity of malformation
- Evolves to diffuse fast in 1st year of life



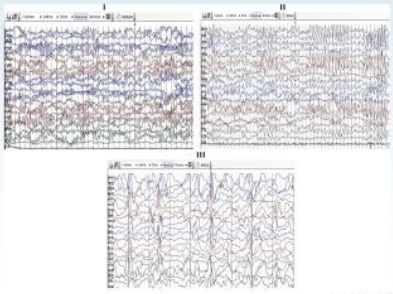


The Evolution of Electroencephalographic Features in Lissencephaly Syndrome

Hakamada et al, Brain and Development 1979

Relation of EEG to Pattern of involvement

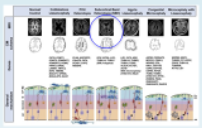
- 14 patients with lissencephaly restricted to cortex
- 9/14 infantile spasms
- 7/14 type 1 EEG, anterior > posterior agyria on MRI
- 4/14 type 2 EEG, posterior > anterior on MRI
- 3/14 type 3 EEG, diffuse on MRI



Menascu et al, Seizure 2013

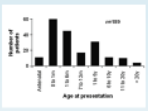
Double cortex syndrome

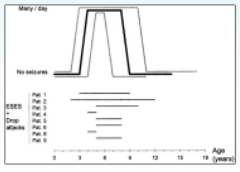
X-linked: 90% affected are female
- Epilepsy onset later than Lissencephaly
- DCX mutation
- EEG shows spasms evolving to Lennox-Gastaut Syndrome
- Multiple seizure types including drop attacks and focal seizures
- Callosotomy may benefit drops

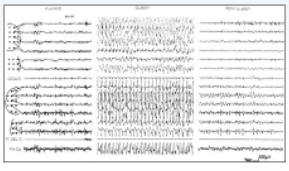


Polymicrogyria (+/- PNH)

- Highly heterogeneous disorder
- Several chromosomal deletion/duplication syndromes
- Ischaemic or infective insult in utero
- Age of presentation relates to extent of abnormality
- Most severe bilateral, generalised
- Highly variable EEG depending location and extent of PMG
- Focal motor -> ESES & atonic seizures reported in a small group of bilateral PMG, with better outcome

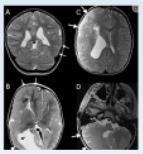






Leventer et al, Brain, 2010, Guerrini et al, Neurology 1998

Dysplastic megalencephalies



DMEG (formerly Hemimegalencephaly)

- mTOR pathway gene mutation associated
- Most are somatic
- In DMEG, 8-35% of cells may carry the mutation
- Morphology variable
- Early onset encephalopathy with seizures in first days 85%

Several small series in young children

- EEG: suppression burst, hemi-hypsarrythmia or repetitive spikes/ spike and wave
- Progressive contralateral involvement[1]
- Bilateral synchronous epileptiform discharges are not associated with poor outcome after hemispherotomy[2]
- Care with electrode position in relation to malformation

[1]Di Rocco, et al., 2006, [2]Bulteau et al., 2013

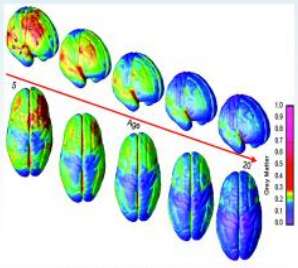
Epilepsy surgery in infants: The role of EEG

- Resective epilepsy surgery is technically challenging with higher risk in infants
- Localisation is challenging: semiology may appear generalised when focal[1]
- Small series report good outcomes in focal seizures
- Intractable seizures -> poor neurocognitive outcomes
- Recent review of 20 papers with 465 patients < 3 years of age, seizure freedom 45-90%
  - Most resections were multilobar or hemispherotomy
  - Highlighted semiology is difficult to interpret in this age group
  - Interictal EEG may be focal, multifocal or generalised even with a focal lesion
  - Ictal EEG is usually focal
- Intracranial EEG may be successful where data is discordant
  - sEEG not suitable in <2 years

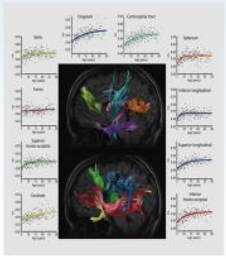
Dravet et al 1989, Dorfmuller et al, 2014.

Why is EEG and Semiology so challenging?

- Infants unable to report symptoms
- Behaviour is difficult to interpret (see infant semiology lecture)
- Grey and white matter maturation is earlier in visual, motor and somatosensory cortices-> less complex behaviours or autonomic features
- MRI less helpful: appearing and disappearing lesions



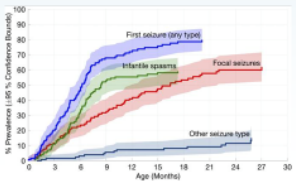
Nitin Gogtay et al. PNAS 2004



Lebel et al, NeuroImage, 2008

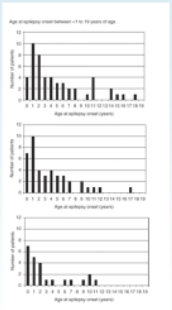
Tuberous Sclerosis

- mTOR pathway mutation: TSC 1 or 2
- Multiple FCD2b like lesions
- Biomarkers in TS study: 74% of infants had EEG change before seizures
- Both interictal and ictal changes may be challenging to localise
- Patterns include focal sharp waves, diffuse slowing and hysarrythmia
- Prospective 130 patient study: Seizures in 76%, often refractory
  - EEG and clinical data collected in all
  - First seizure most frequent <12 months, 55% focal seizures, 57% spasms
  - 32% infants had 1 seizure type, 41 %, 2 seizure types, 3% 3 seizure types

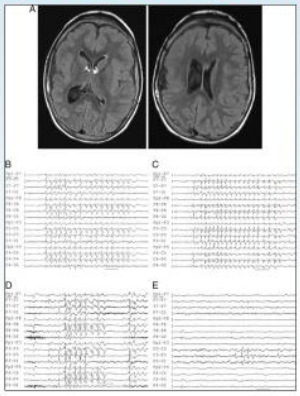


Focal Cortical Dysplasia type 2b

- Commonest underlying abnormality in refractory focal epilepsy in children
- Seizure onset usually <5 years, varies with location
- Large or multi-lobar abnormalities most common in <1 year
- Presentation with unilateral or bilateral epileptiform features and focal ictal EEG change
- Focal fast activity prior to onset of spasms suggests underlying structural pathology



Widespread EEG change does not preclude



Successful surgery for epilepsy due to early brain lesions despite generalized EEG findings.
Wyllie, E; Lachhwani, D; MBBS, MD; Gupta, A; Chirla, A; Cosmo, G; Worley, S; Kotagal, P; Ruggieri, P; Bingaman, W
Neurology: 69(4):389-397, July 24, 2007.
DOI: 10.1212/01.wnl.0000266586.55715.3f

Invasive EEG for young children

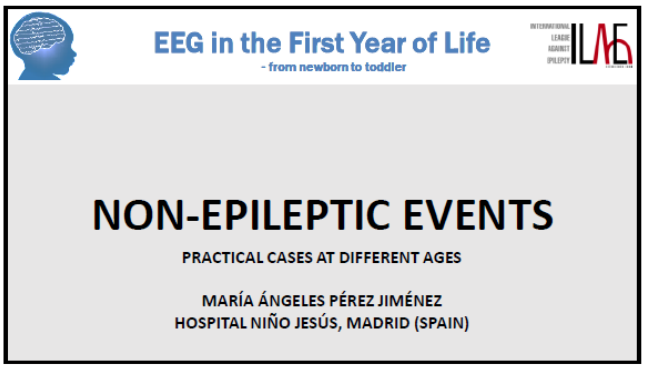
- 26 children with drug refractory epilepsy
- Mean seizure onset 5.2 months
- 15 focal seizures, 11 focal seizures + spasms
- 3 had tuberous sclerosis
- Invasive EEG allowed delineation of the epileptogenic region when MRI lesion was not defined
- 21/26 had FCD on histology
- FCD on invasive EEG is defined by continuous spiking on the interictal record with low voltage fast at onset

Invasive explorations in children younger than 3 years
Delphine Taussig *, Georg Dorfmüller, Martine Fohlen, Claude Jalin, Christine Bulteau, Sarah Ferrand-Sorbets, Mathilde Chipaux, Olivier Delalande

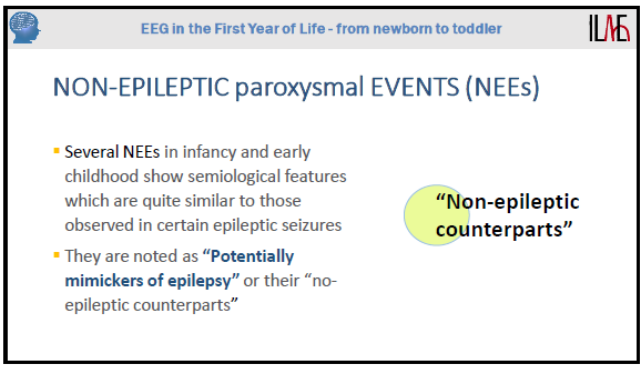
Summary

- Malformations of cortical development commonest structural pathology with intractable focal epilepsy in children
- Larger, more diffuse malformations -> onset of seizures in early life
- Specific EEG features in Lissencephaly
- Multifocal, focal and apparently generalised abnormalities may seen in focal malformations in <1 year olds
- Role of EEG:
  - May indicate diagnosis
  - Localisation of focal malformations and identification of surgical candidates (particularly ictal EEG)
  - Potential role as a biomarker (e.g. in tuberous sclerosis)

MA Pérez Jiménez (S): Non-epileptic events in infancy



1



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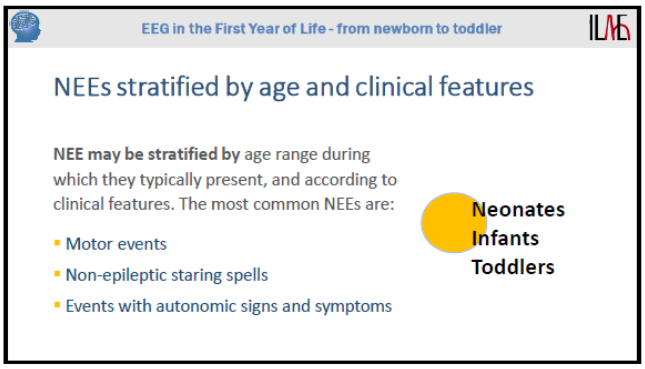

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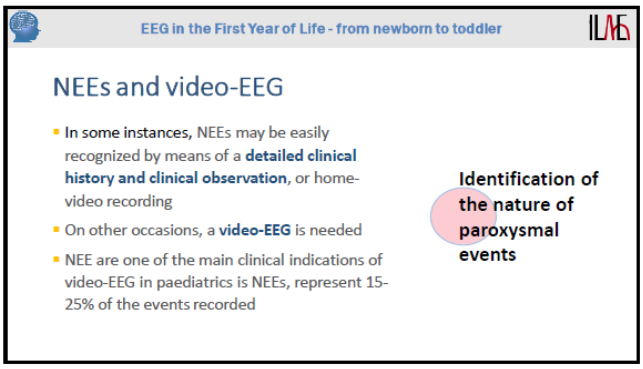

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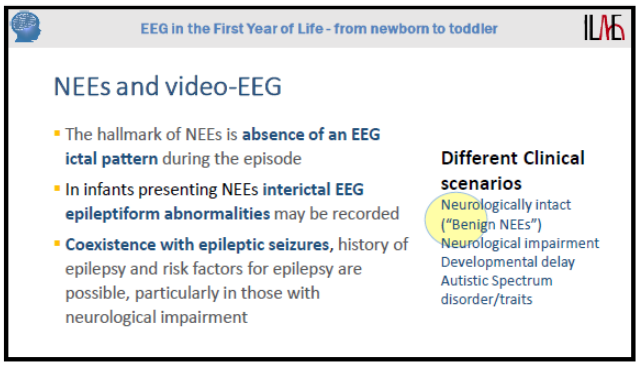

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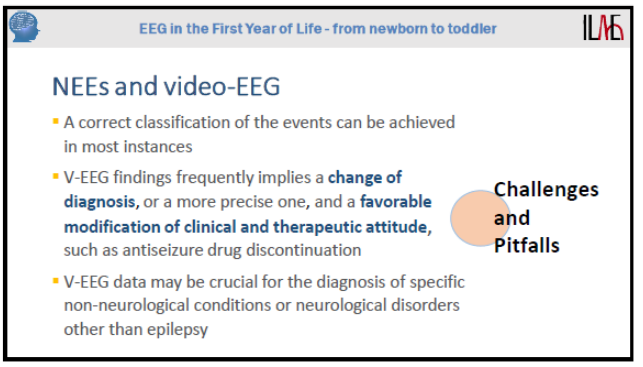


6

Difficult to classify events

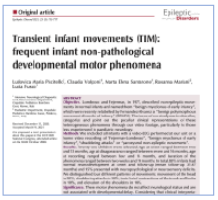
- Some episodes may remain as "difficult-to-classify events", or of **uncertain nature**
- NEEs and epileptic seizures **may appear intermingled**
- Epileptic seizures may show mild or bizarre semiology and no ictal scalp EEG changes during the episodes, or unclear ones

Epileptic or non epileptic?
Repeated studies and follow-up may ultimately clarify the diagnosis

7

Infants with non-epileptic MOTOR spells (1)

- Bilateral axoryzomelic motor spells
  - Bilateral brief axial contractions
  - Shuddering
  - Head nods
- Sandifer syndrome
- Reflex tonic/dystonic spells in neurologically impaired infants
- Hyperekplexia


Original article
Epileptic Disorders
Transient infant movements (TIM): frequent infant non-pathological developmental motor phenomena

8

Infants with non-epileptic MOTOR spells (2)

- Focal of multifocal limb jerks
  - Benign neonatal myoclonus
  - Clonus
  - Erratic myoclonus
  - Trembling
- Oculomotor phenomena
  - "Benign" Tonic upgaze
  - Nystagmus / Erratic movements
  - Oculomotor apraxia


Seizure
Extremely sustained startle-induced clonus: Non-epileptic motor attacks mimicking clonic seizures in children with encephalopathy

9

Infants with repetitive motor behaviours

- Dyskinesias
  - Anti-NMDA encephalitis
  - Glut-1 Deficiency
  - Developmental and epileptic Encephalopathies
  - Drug-induced
- Sleep rhythmic movement disorders


Movement Disorders in Patients With Genetic Developmental and Epileptic Encephalopathies

10

"Staring spells" / motionless episodes / Autonomic and mixed phenomena

- Self-gratification behaviour (Infantile masturbation)
- Breath holding spells
- Alternating Hemiplegia of childhood
- Benign paroxysmal vertigo
- Cyclic vomiting


Handbook of Clinical Neurology
Chapter 16 - Alternating hemiplegia of childhood

11

TAKE-HOME MESSAGE

- NEEs can be differentiated from epileptic seizures by means of video-EEG recording
- Video-EEG allows for early identification of clear-cut "benign pictures", avoiding iatrogenic clinical management
- It also prevents overestimation of seizure incidence in neurologically impaired infants and in those with previous epilepsy history
- Differential diagnosis may be challenging in some cases, particularly in those having abnormal neurological status and epilepsy

12

Recommended reading

- Bourel-Ponchel E, Gueden S, Hasaerts D, Héberlé C, Malfilâtre G, Mony L, Vignolo-Diard P, Lamblin MD. Normal EEG during the neonatal period: maturational aspects from premature to full-term newborns. Neurophysiol Clin. 2021 51(1):61-88.
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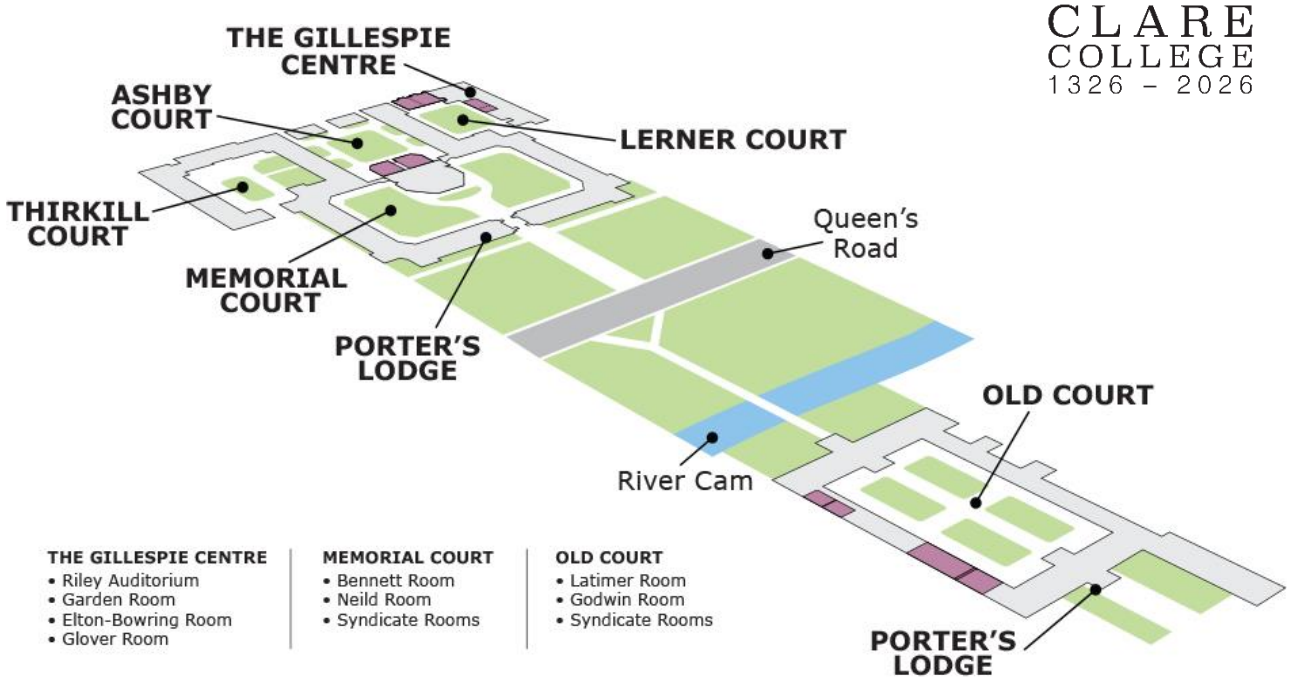
Venue

Gillespie Conference Centre, Memorial Court, Queens Road, Cambridge CB3 9AJ

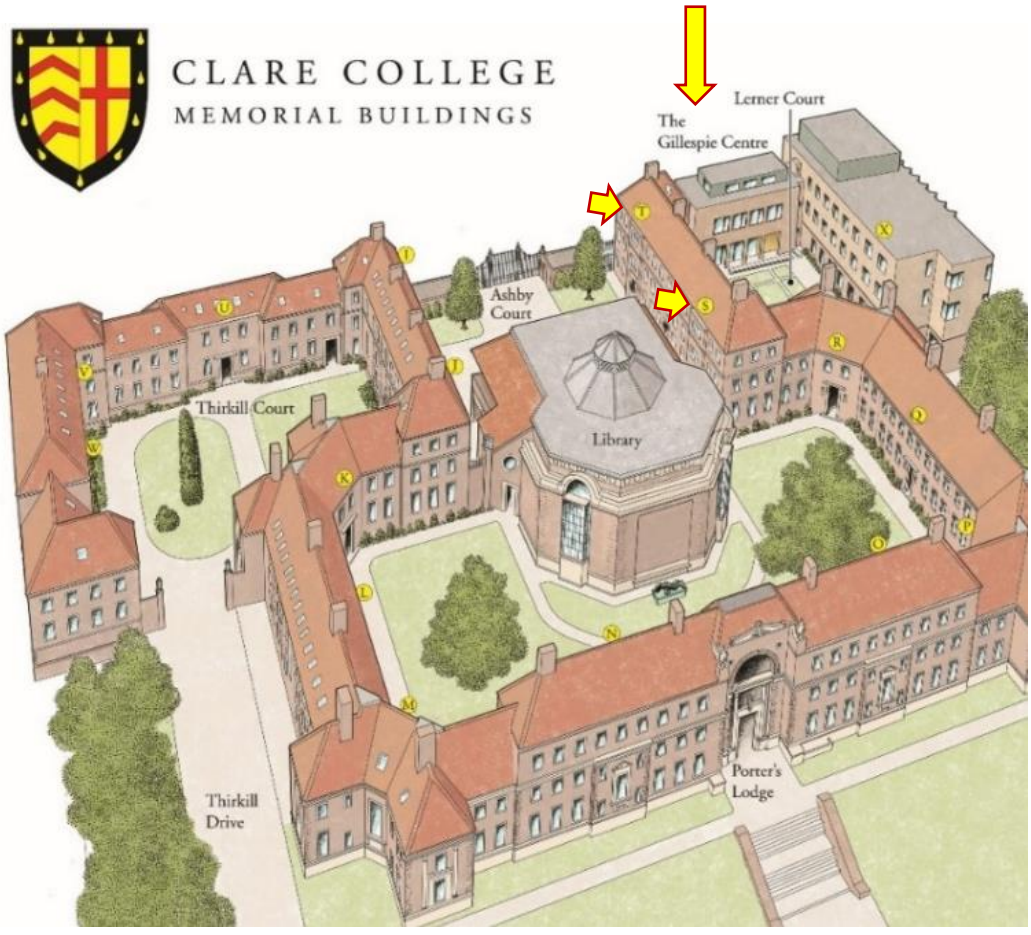


Room finder

Riley Auditorium	Gillespie Centre, lower ground
Elton Room	Gillespie Centre, ground floor
Bowring Room	Gillespie Centre, 1st floor
Glover Room	Gillespie Centre, 1st floor

T4, T9, T14 — entrance T

S2 — entrance S



ILAE Curriculum Learning Objectives addressed by this course

1.4.10 Recognize & describe ictal patterns (L2)
1.4.7 Recognize & describe background activity & sleep patterns in infancy (L2)
1.4.9 Recognize & describe interictal abnormalities (L2)
1.7.5 Correctly diagnose & classify combined focal & generalized epilepsies including epileptic encephalopathy (L2)
1.8.2 Recognize the semiology of PNES and the use of video-EEG procedures and suggestion techniques in the diagnosis of suspected PNES in infants (L2)

Please complete course feedback via this link:

- In-person: https://www.surveymonkey.com/r/EEG2026
- Virtual: https://www.surveymonkey.com/r/EEG2026virtual

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