Neonatal Electroencephalography: Maturational Changes of the Preterm Brain

Eli M. Mizrahi, MD
Chair, Department of Neurology
Professor of Neurology and Pediatrics
James A. Quigley Endowed Chair in Pediatric Neurology
Baylor College of Medicine
Houston, TX

ACNS Annual Course
February 11, 2021

Disclosures

- Royalties
  - Wolthers Kluwer/Demos Medical Publishers
- Consulting
  - UCB Biopharma

Learning Objectives

- Recognize normal age-dependent developmental features of neonatal EEG
- Recognize abnormal age-dependent features of neonatal EEG and their clinical implications
- Understand the clinical utility of neonatal electroencephalography

ACNS Guidelines and Neonatal EEG

- Guideline 5: Minimal Technical Standards for Pediatric Electroencephalography
  - August 2016
- Guideline 13: Continuous EEG Monitoring in Neonates
  - January 2012
- Guideline 16: Standardized EEG Terminology and Categorization for the Description of Continuous EEG Monitoring in Neonates
  - December 2012

http://www.acns.org/practice/guidelines

Basis for Interpretation

- The normal neonatal EEG undergoes rapid and predictable changes as a consequence of brain growth and development.
- Abnormalities may be characterized by altered developmental characteristics as well as specific patterns or wave-forms.
- Patterns that are normal at one development stage may be abnormal at another.

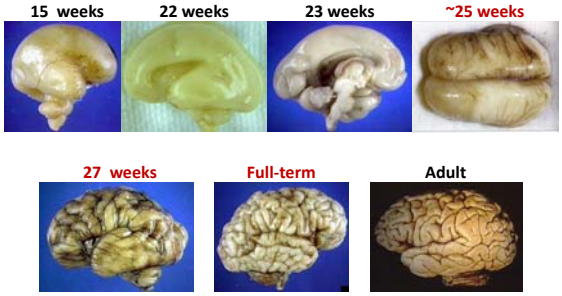
Challenges in Interpretation

- The significance of some features of the neonatal EEG have not been determined.
- Certain abnormal EEG findings in the period immediately following brain injury may be transient.
  - Their significance is related to change over time
  - Underscores the need for serial recordings

Neonatal EEG and Brain Development

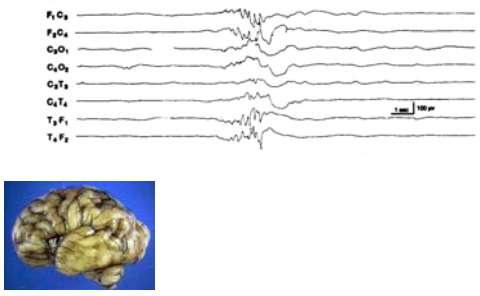
- Basic assumption
  - Brain development proceeds at the same rate whether the infant is in the nursery or *in utero*
- Caution ⚠
  - No intercurrent CNS injuries

An Accelerated Anatomic View of Brain Development

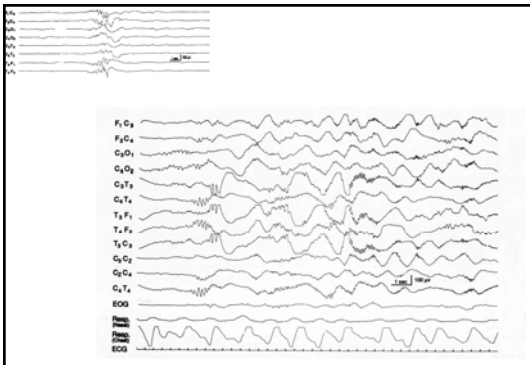


http://medstat.med.utah.edu

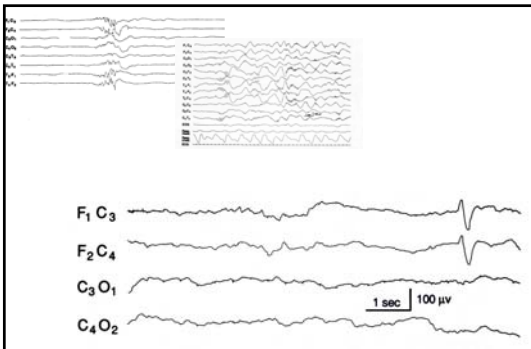
Neonatal Electroencephalography Marker of Rapid Brain Growth



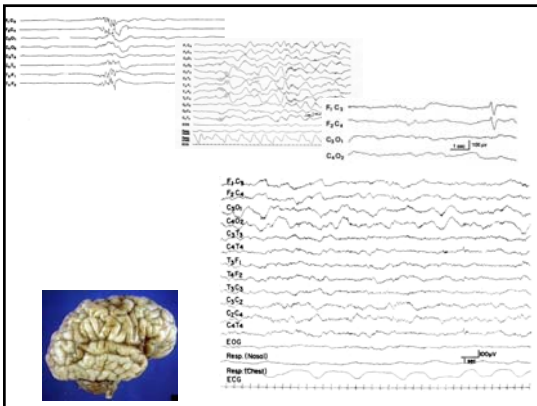
27-28 wks CA



30-32 weeks CA



36 weeks CA



40 weeks CA

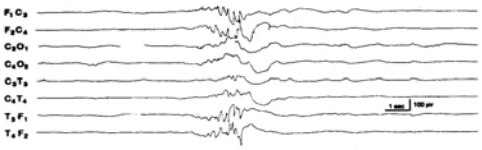
Trends in Appearance of Neonatal EEG Parallel Brain Development:

Orderly Approach to Visual Analysis

- Continuity
- Synchrony
- Waveforms
- Wake/sleep cycles

Continuity

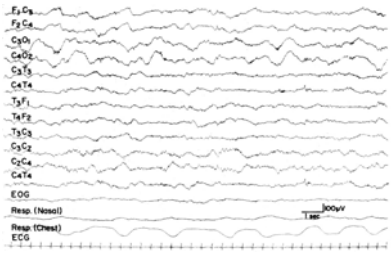
- There is a gradual change from a discontinuous pattern to a continuous pattern



27-28 weeks CA

Continuity

- Continuity first appears in wakefulness
- Residual discontinuity in sleep, even at term

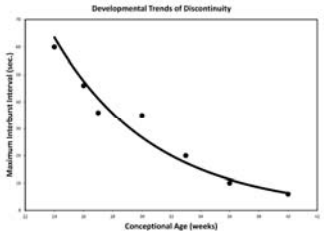


40 weeks CA

Developmental Trends of Discontinuity

Postmenstrual Age	Maximum interburst interval	Voltage of interburst
< 30 weeks	35 seconds	<25μV
30-33 weeks	20 seconds	<25μV
34-36 weeks	10 seconds	~25μV
37-40 weeks	6 seconds	>25μV

ACNS Guideline 16



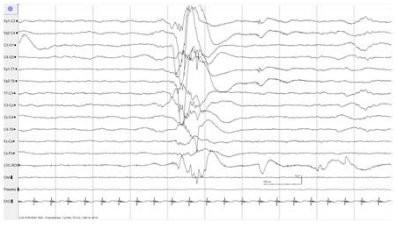
Mizrahi and Hrachovy, 2016

Synchrony

- Initial period of synchrony
  - "Hypersynchrony"
  - May be variable
- Followed by asynchrony
- Then gradual return to synchrony on the two sides
  - Degree of synchrony increases with conceptional age

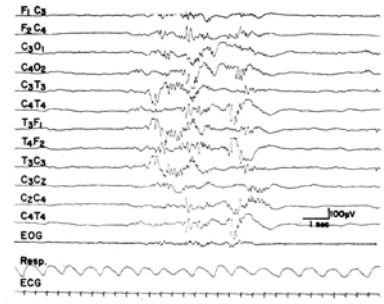
Synchrony

- Initial period of "hypersynchrony"
- Associated with discontinuity



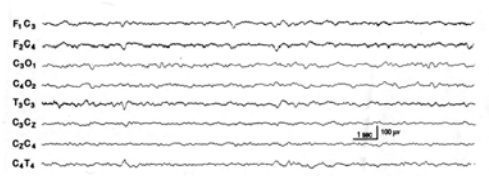
27-28 weeks CA

Synchrony



29-30 weeks CA

Synchrony

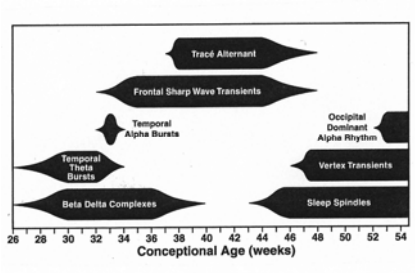


40 weeks CA

Specific Waveforms

- Emergence and disappearance of specific waveforms
  - Specific character and location
  - Orderly progression
- "Grapho-elements"
- Markers of conceptional age
  - Beta-delta complexes: "brushes"
  - Temporal bursts: theta and alpha frequencies
  - Frontal sharp waves: "encoches frontales"

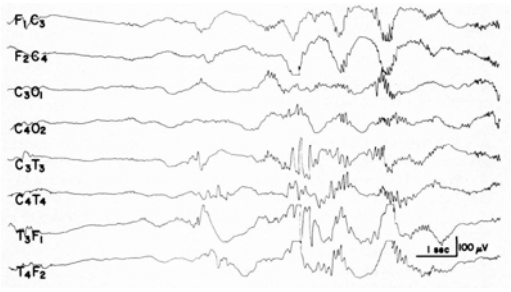
Grapho-elements



Beta-delta Complexes

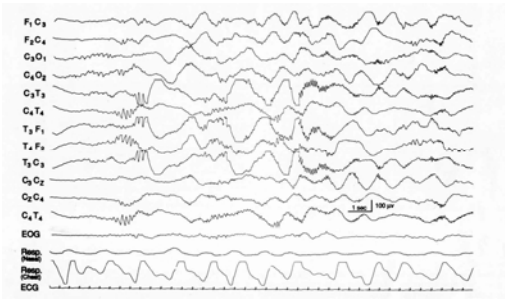
- Hallmark of prematurity
  - Slow-wave with superimposed fast activity
- Initially central
- Eventually posterior
- Onset: 29 weeks C.A.
- Disappearance: 38 weeks

Beta-delta Complexes



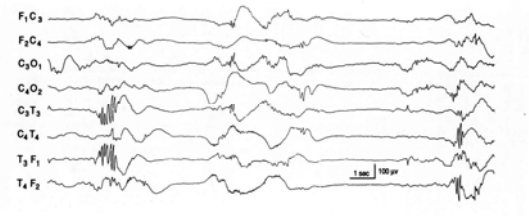
29-30 weeks CA

Temporal Theta Bursts



30-32 weeks CA

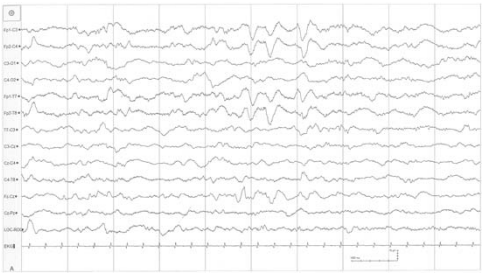
Temporal Alpha Bursts



32-33 weeks CA

Frontal Sharp Transients

Synchronous, symmetrical; Onset at 34- 35 weeks C.A.; Persist through term



38 to 40 weeks CA

Development of Reactivity and Wake/Sleep Cycles

- Changes in EEG activity in response to stimuli emerge at about 33-34 weeks C.A.
  - State-dependent
- Clear EEG differences between wakefulness and sleep emerge at about 36-37 weeks C.A.

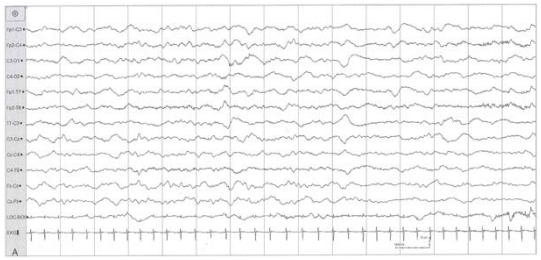
Sleep

- Classification
  - Active
  - Quiet
  - Transitional
  - Indeterminant
- Wake-Sleep Cycling
  - Pattern of alterations of behavioral states

	Preterm	Term
Active	Behavioral: eyes closed, intermittent REM, limb and body movements (segmental or generalized myoclonous and tonic posturing). EEG: Discontinuous, increasing continuity with increasing CA	Behavioral: eyes closed, intermittent REM, irregular respirations, small and large body movements EEG: Indistinguishable from normal wakefulness
Quiet	Behavioral: eyes closed, absent REM, limited body movements EEG: Discontinuous, increasing continuity with increasing CA	Behavioral: eyes closed, absent REM, limited body movements EEG: Alternates between higher and lower voltage slow activity (tracé alternant) until post-term

Wake/Sleep Cycle

Awake

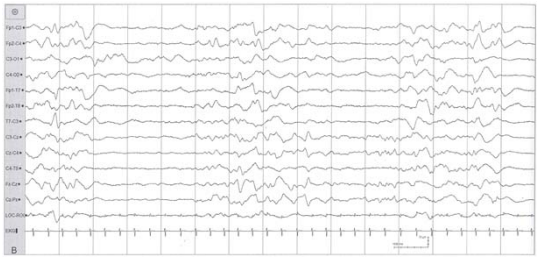


38 to 40 week CA

Wake/Sleep Cycle

NREM Sleep

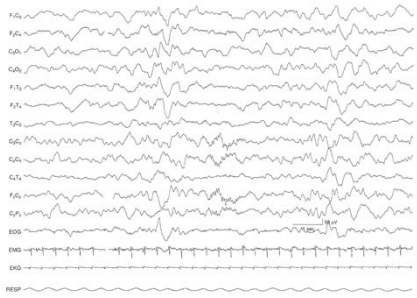
Tracé Alternant



38 to 40 week CA

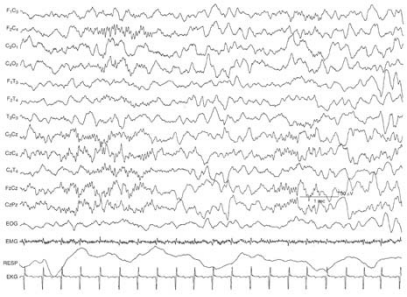
Wake/Sleep Cycle

Rudimentary Sleep Spindles



41 to 44 week CA

Sleep Spindles

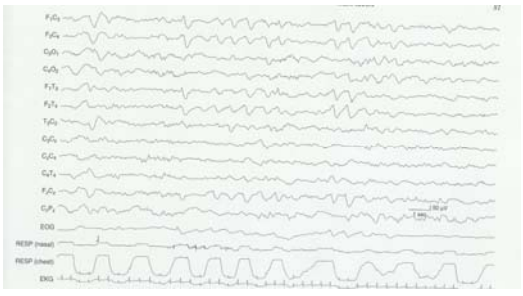


45 to 48 week CA

Additional Normal Waveforms

- There are some waveforms that are considered normal but not specifically considered age-dependent grapho-elements
  - Bifrontal delta in near-term and term infants
  - "Anterior Dysrhythmia"
    - Although not abnormal

Bifrontal Delta



38 – 40 weeks CA

Normal → Abnormal

Age-Dependent Expectations

Age-dependent EEG Abnormalities
Suggesting Diffuse and Focal Injury

- EEG abnormalities are dependent upon the range of possible normal activity at a given epoch of age
  - 25-26 weeks C.A.
  - 27-28 weeks C.A.
  - 29-30 weeks C.A.
  - 31-33 weeks C.A.
  - 34-35 weeks C.A.
  - 36-37 weeks C.A.
  - 38-40 weeks C.A.
  - 41-44 weeks C.A.

Age-dependent Patterns of Diffuse Brain Injury

• Prolonged interburst duration	25-28 wks C.A.
• Depressed voltage	25-28 wks C.A.
• Dyschronism	29-30 wks C.A.
• Prolonged generalized voltage attenuation	34-35 wks C.A.
• Absence of sleep cycling	36-37 wks C.A.
• Depressed and undifferentiated background	36-37 wks C.A.
• Suppression-burst activity	36-37 wks C.A.
• Hypsarrhythmia	41-44 wks C.A.

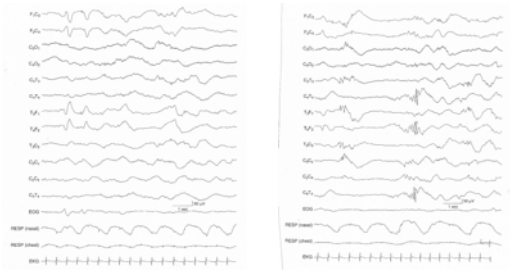
Dyschronism

- Determination of conceptional age depends upon the presence or absence of specific established developmental milestones characterized by specific EEG features.
- Dyschronism
  - The finding of developmental features that are inconsistent with age
    - Other EEG features
    - Infant's actual age

Dyschronism

- Internal
  - Mixture of developmental features present in different physiologic states
  - Precise determination of conceptional age cannot be made
  - Suggests diffuse dysfunction
- External
  - Developmental features in all wake/sleep states are immature for stated age
    - EEG-age determination correct?
    - Clinical-age determination correct?
  - Immature EEG features evidence of delayed maturation

Internal Dyschronism

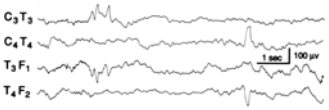


Age-dependent Patterns of Focal Brain Injury

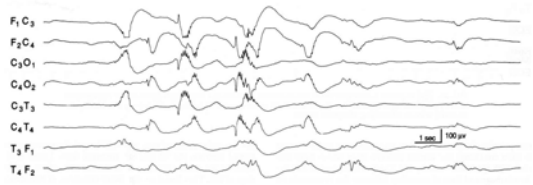
- Voltage depression over one hemisphere — 25-28 wks C.A.
- Central positive sharp waves — 29-30 wks C.A.
- Persistent focal sharp waves — 31-33 wks C.A.
- Electrical seizure activity — 34-35 wks C.A.

Central Positive Sharp Waves

- Positive rolandic sharp waves
- Initially associated with intraventricular hemorrhage
- Now more clearly associated with related abnormalities
  - Periventricular leukomalacia

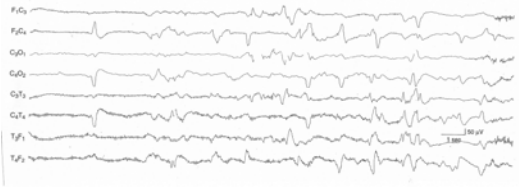


Central Positive Sharp Waves



29-30 weeks CA

Central Positive Sharp Waves

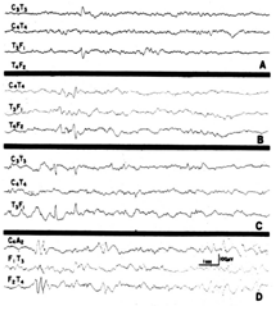


36 weeks CA - IVH

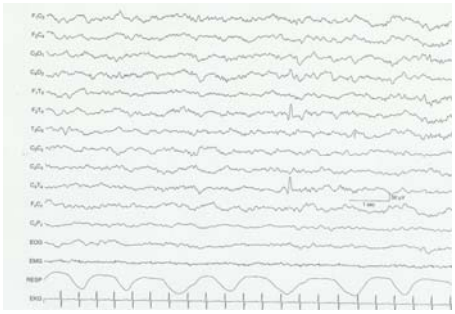
Temporal Sharp Waves

- May be present as normal activity
- No clear criteria to differentiate normal from abnormal temporal sharp waves
- Consider
  - Amplitude and duration
  - Occurrence
  - Complexity of waveform
  - Polarity
  - Changing states

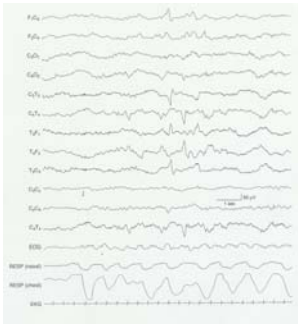
Temporal Sharp Waves



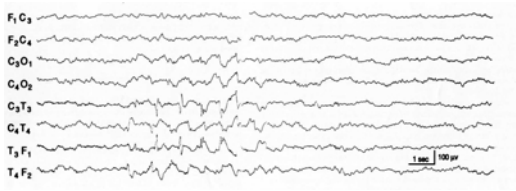
Temporal Sharp Waves



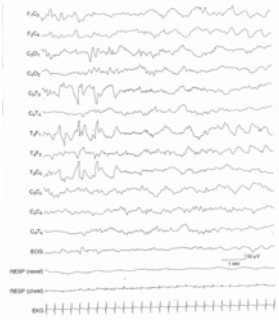
Temporal Sharp Waves



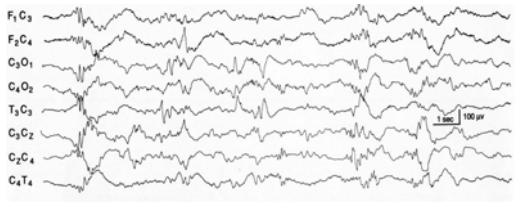
Temporal Sharp Waves



Temporal Sharp Waves

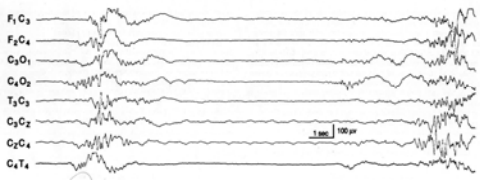


Multifocal Sharp Waves
Focal vs Diffuse Injury



Timing of EEG and Rationale for Serial Recordings

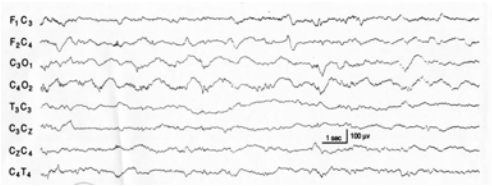
Understanding the timing of the EEG in relationship to injury is important in the interpretation of the findings.



40 weeks CA – day 1 of life

Timing of EEG and Rationale for Serial Recordings

Understanding the timing of the EEG in relationship to injury is important in the interpretation of the findings.



4 days later

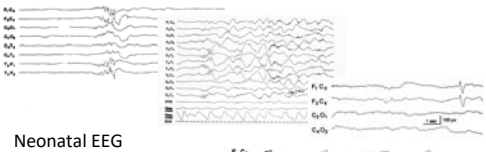
Learning Objectives

- Recognize normal age-dependent developmental features of neonatal EEG
- Recognize abnormal age-dependent features of neonatal EEG and their clinical implications
- Understand the clinical utility of neonatal electroencephalography

Clinical Utility of Neonatal EEG

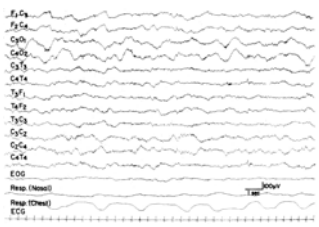
Age-dependent interpretation of EEG is best utilized in the context of a clinical question:

- What is the infant's conceptional age?
- Has the infant suffered a diffuse brain injury?
- Is there evidence of a focal brain injury?
- What is the prognosis?
- Has the infant experienced a seizure?



Neonatal EEG interpretation based upon and orderly approach

- Continuity
- Synchrony
- Waveforms
- Wake/sleep cycles



40 weeks CA

Acknowledgements

James D. Frost, Jr., M.D.
Richard A. Hrachovy, M.D.
Peter Kellaway, Ph.D. (1920-2003)

Peter Kellaway Section of Neurophysiology
Department of Neurology
Baylor College of Medicine

Section of Neurology and Developmental Neuroscience
Department of Pediatrics
Baylor College of Medicine

Section of Epilepsy, Neurophysiology and Neurocritical Care

Neurophysiology Laboratories
Texas Children's Hospital

Anne Anderson, MD
James Riviello, MD
Elaine Seto, MD, PhD

Kelvin Dillard, R.EEG T.
Lisa Rhodes, R. EEG T.
Anita Thompson, R. EEG T.