Cleveland Clinic
Epilepsy Center

EEG Developmental Maturation, Neonatal seizures and Neonatal Encephalopathies

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- Nothing to disclose

Objectives

- 1. Describe the process of EEG maturation in preterm and term babies
- 2. Discuss the epidemiology, etiology and evaluation of neonatal seizures.
- 3. Describe the clinical and EEG characteristics and treatment of the neonatal seizures
- 4. Update the diagnosis and electroclinical characteristics of neonatal encephalopathy

EEG DEVELOPMENTAL MATURATION

Definitions

- Neonate: Newborn infant less than 4 weeks of age
- Preterm: Conceptional age usually 24 to <34
- Near term: Conceptional age 34 to <37 weeks
- Term: Conceptional age 37 weeks and above

Embryogenesis

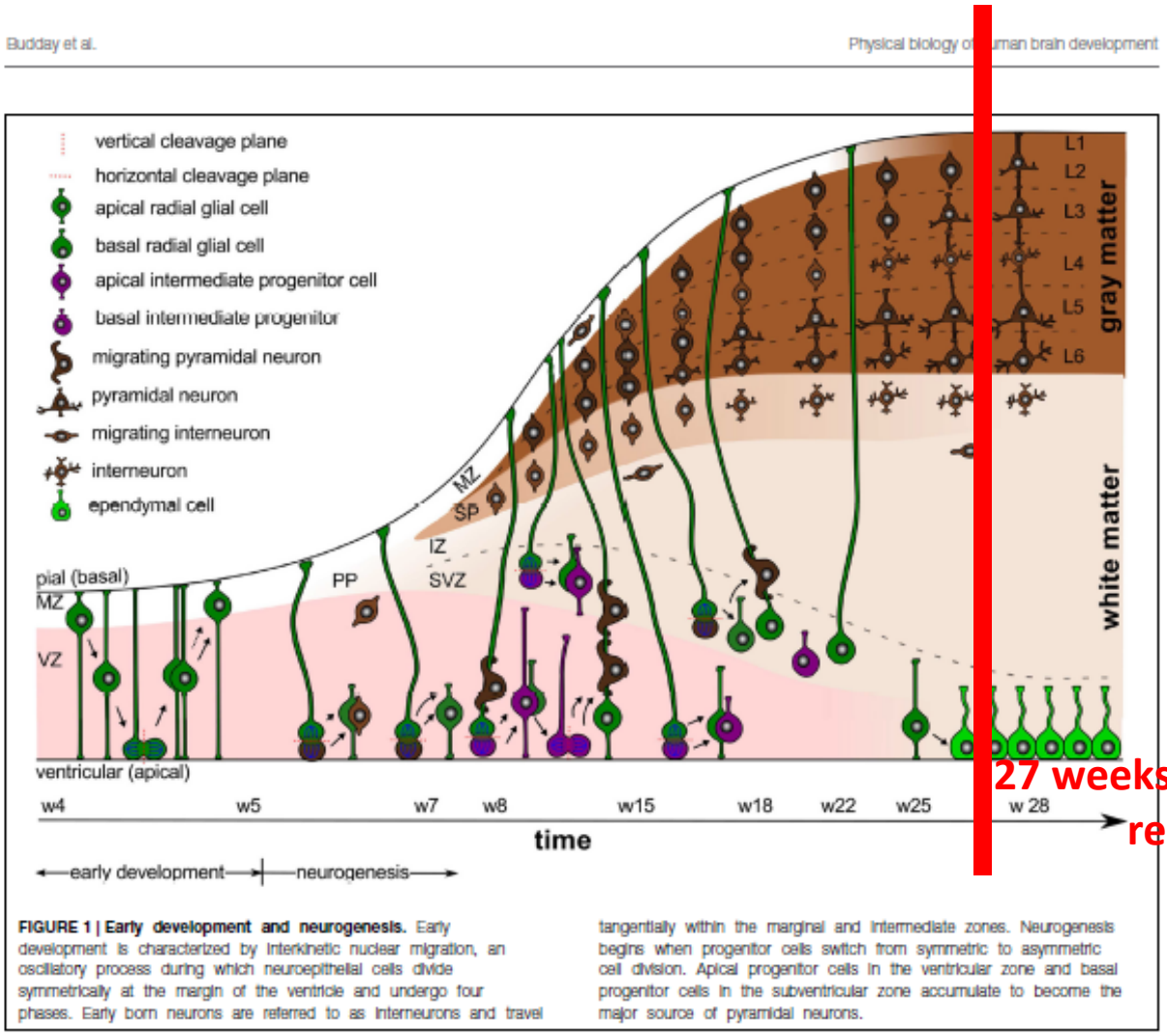


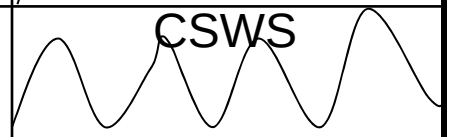
FIGURE 1 | Early development and neurogenesis. Early development is characterized by interkinetic nuclear migration, an oscillatory process during which neuroepithelial cells divide symmetrically at the margin of the ventricle and undergo four phases. Early born neurons are referred to as interneurons and travel tangentially within the marginal and intermediate zones. Neurogenesis begins when progenitor cells switch from symmetric to asymmetric cell division. Apical progenitor cells in the ventricular zone and basal progenitor cells in the subventricular zone accumulate to become the major source of pyramidal neurons.

Budday S et al. Front Cell Neurosci. (2015) Jul 8;9:257.

Basic Organization of the Neonatal EEG Background

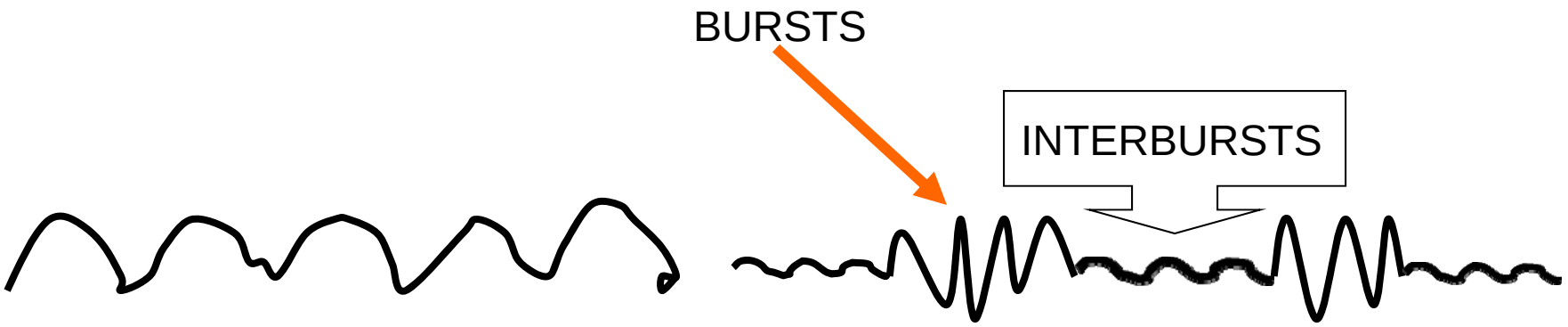
- Continuity and discontinuity
- Symmetry
- Synchrony
- Amplitude
- Reactivity
- Specific composition of the background or grapho-elements

Neonatal EEG Background Evolution in different behavioral states

Conceptional age	Awake (eyes open)	Active Sleep (eyes closed)	Quiet Sleep (eyes closed)
24-29 weeks			
30-34 weeks			 TD
35-36 weeks			 TA
37-40 weeks			 TA & CSWS
40-44 weeks			 CSWS
44-46 weeks			 CSWS & spindle

Modified from Fig 6.23. Ebersole JS & Pedley TA Current Practice of Clinical Electroecephalography. 3rd edition. 2003

Continuity



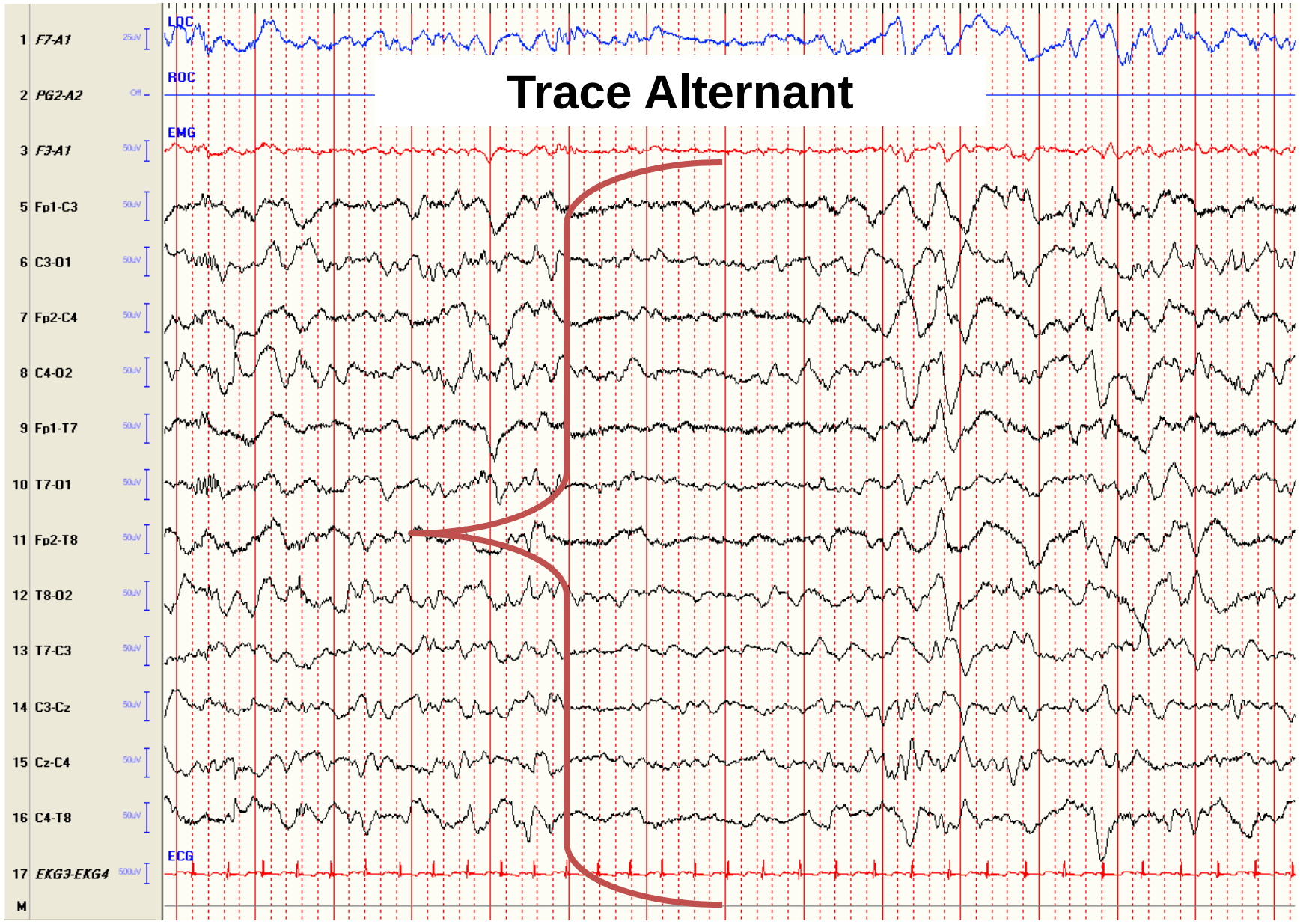
Continuous EEG

Refers to relatively steady amplitude

Discontinuous EEG

Refers to “on periods” (BURST) and “off periods” (INTERBUSRTS)

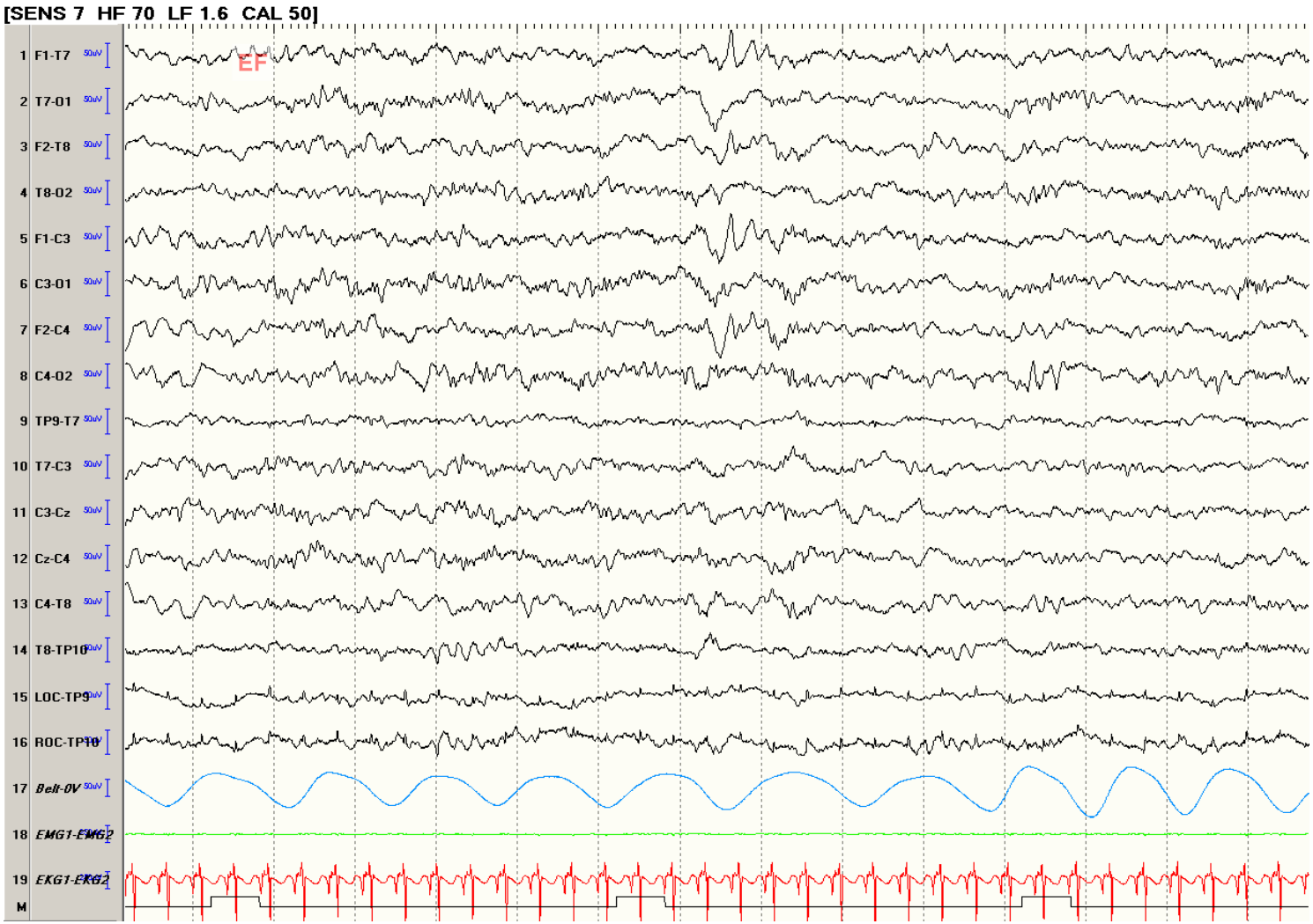
Interburst interval (IBI): discontinuation portion of the EEG



25 day old baby girl born at 39 weeks GA

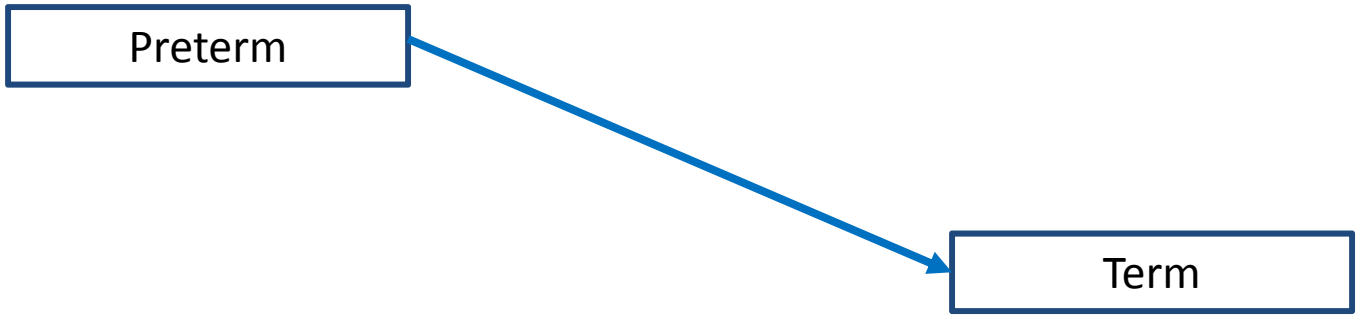
Quiet Sleep

Continuous EEG



Basic Organization of the Neonatal EEG Background

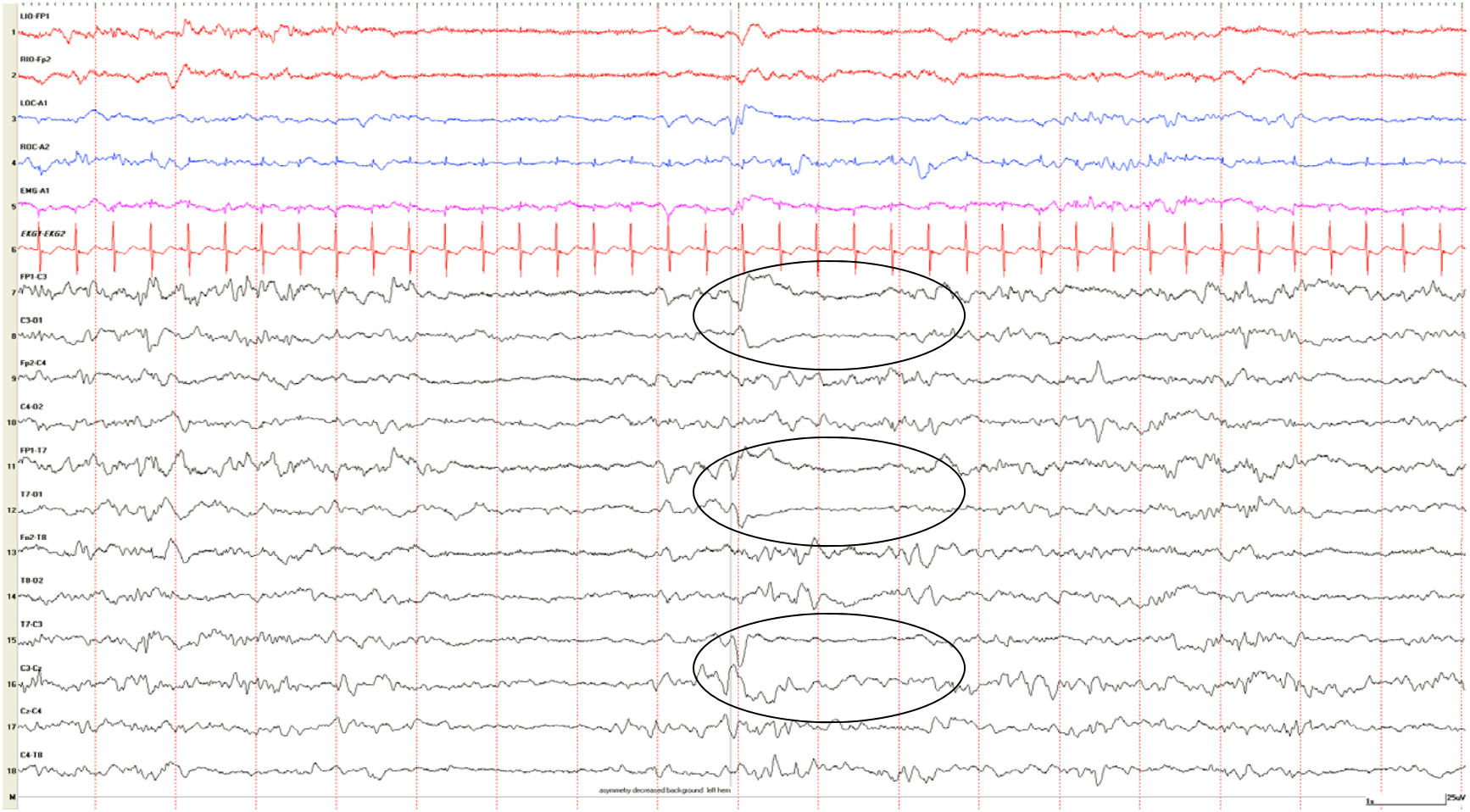
- Amplitude
  - Measured in voltage
  - Voltage: peak to peak value
  - Amplitude of the graphoelements decreased from 24 wks CA to term

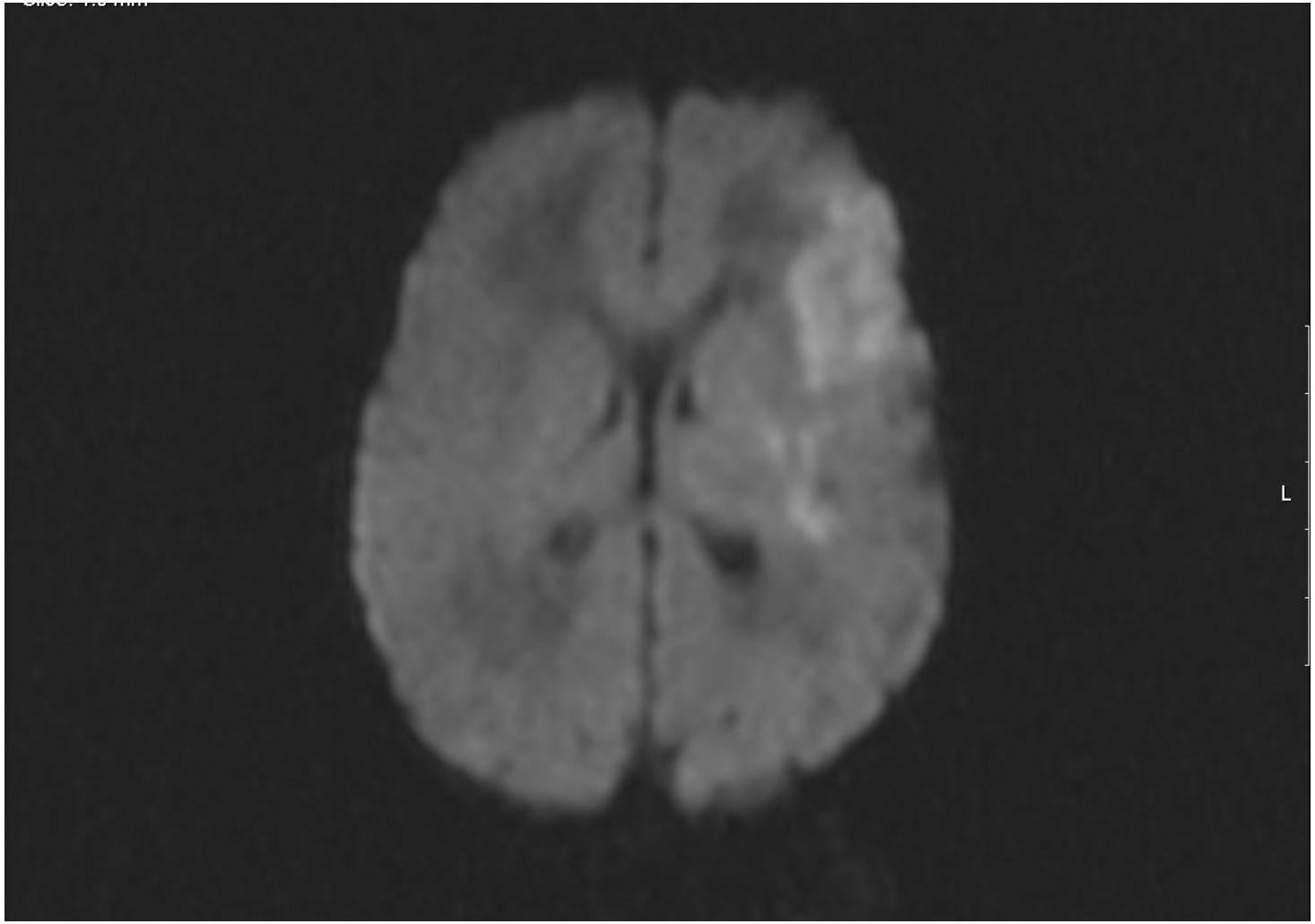


Basic Organization of the Neonatal EEG Background

- Symmetry
  - Amplitude, frequency and waveform elements of the neonatal EEG should be SYMMETRIC

Asymmetric BG

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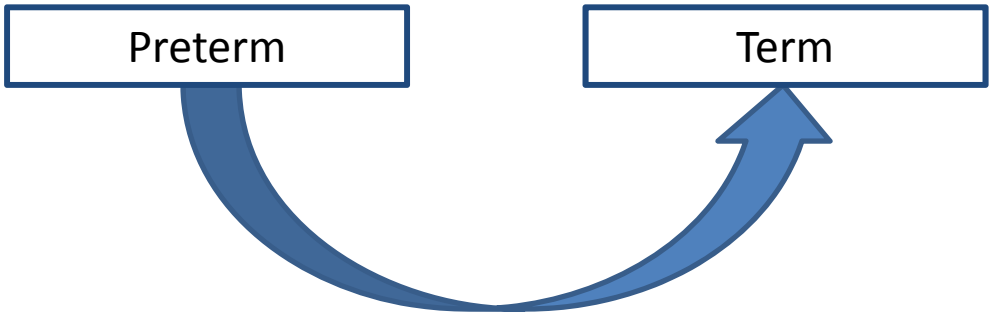
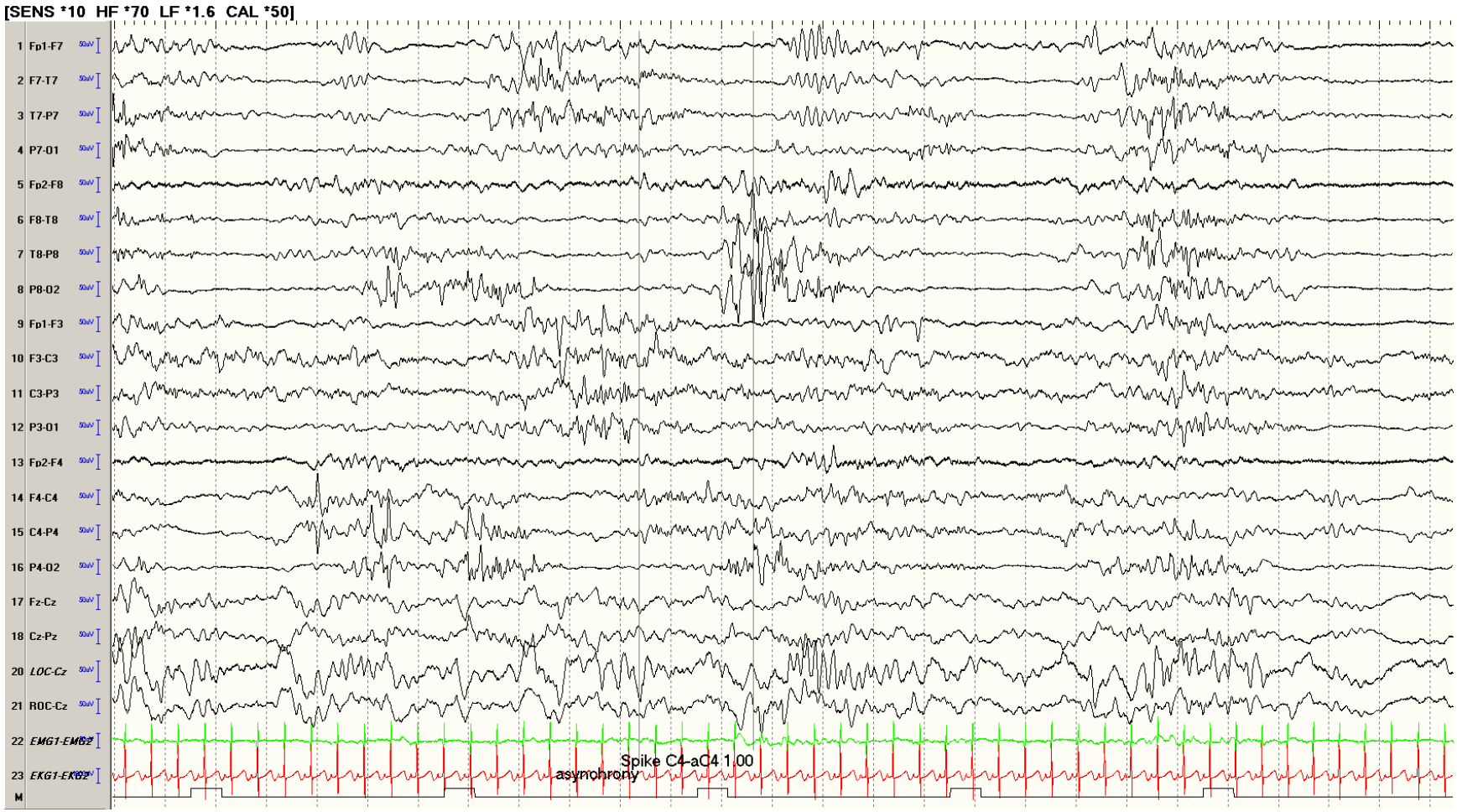
Basic Organization of the Neonatal EEG Background

- Synchrony
  - bursts and graphoelements are synchronized if there is < 1.5 seconds separating the onset of the bursts between the right and left hemisphere
  - Normal synchrony
    - < 29 wks CA: 100%
    - 31-36 wks CA: 70%
    - >37 wks CA: 100%



Asynchrony example



Basic Organization of the Neonatal EEG Background

- Reactivity: Clinical and/or EEG response to external stimulation or internal arousal
- Clinical response:
  - Active movements
  - Respiratory pattern changes
- EEG response:
  - Frequency changes
  - Increased continuity
  - Decreased amplitude
  - Change from sleep to awake pattern

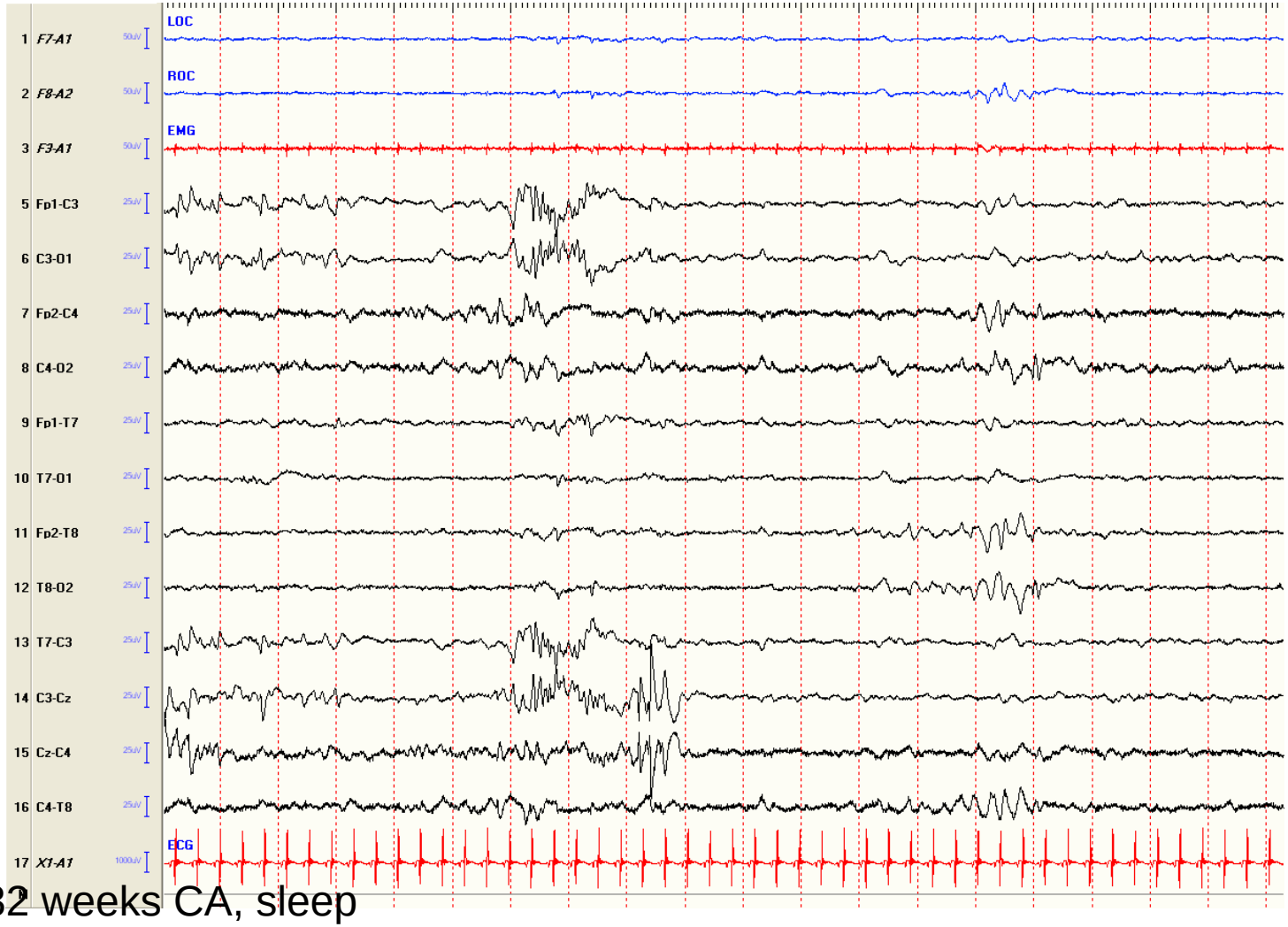
Photic stimulation does not produce photic driving in the term neonate

Basic Organization of the Neonatal EEG Background

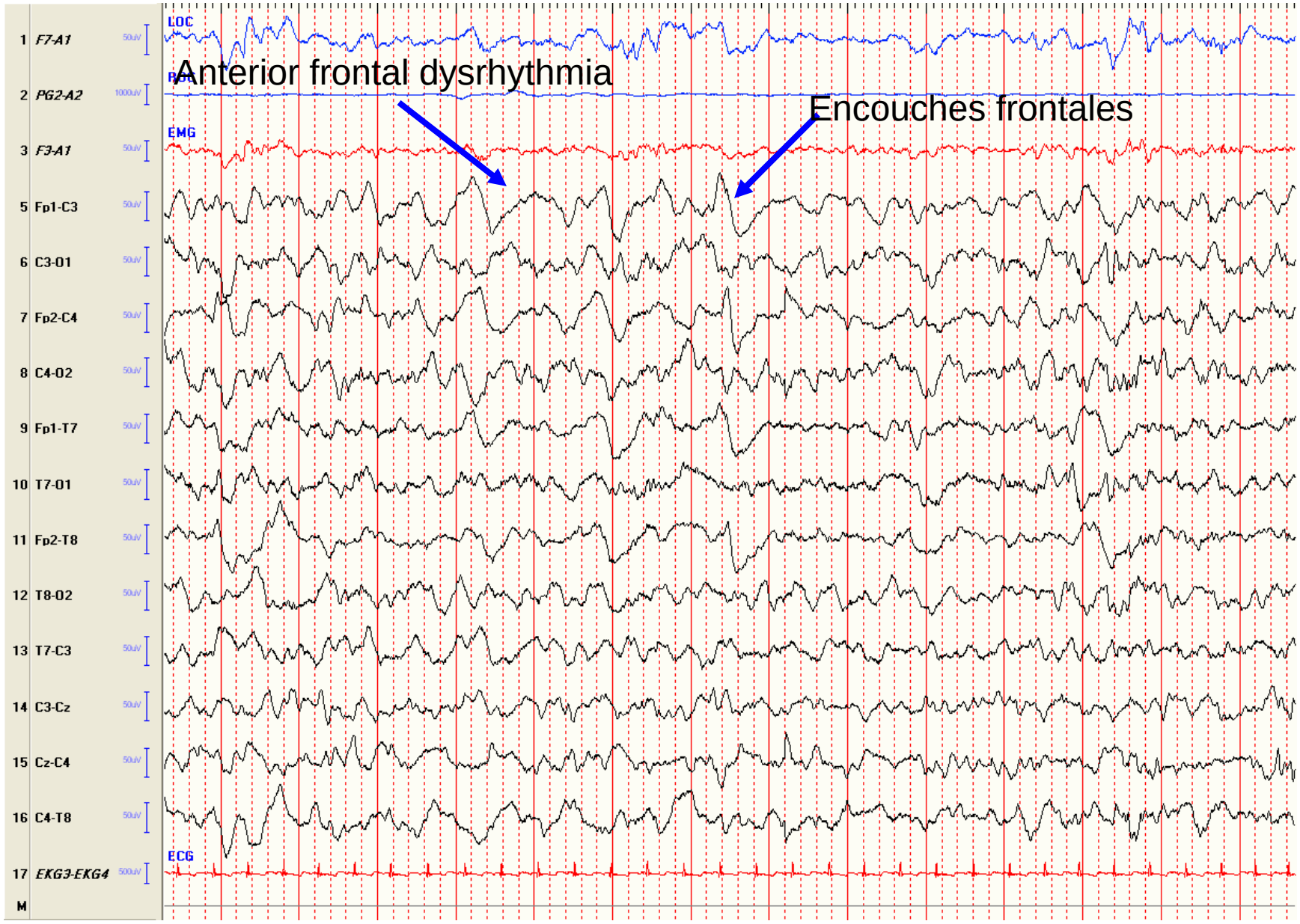
Graphoelements

• Monomorphic occipital delta	• 24-34 weeks
• Delta brushes	• 24-36 weeks, peak 34 weeks, sometimes seen at term during quiet sleep
• Rhythmic temporal theta	• 24-34 weeks
• Anterior dysrhythmia	• 35-44 weeks
• Encouches frontales	• 34-44 weeks

Central delta brushes, right temporo-occipital theta



32 weeks CA, sleep



25 day old baby girl born at 39 weeks GA

Quiet Sleep

The American Clinical Neurophysiology Society's Guideline on Continuous Electroencephalography Monitoring in Neonates

Renée A. Shellhaas, Taeun Chang,† Tammy Tsuchida,† Mark S. Scher,‡ James J. Riviello,§ Nicholas S. Abend,‖ Sylvie Nguyen,¶ Courtney J. Wusthoff,# and Robert R. Clancy‖*

Key Words: Electroencephalography, EEG, Amplitude-integrated EEG, Intensive care, Neonatal seizures, Hypoxic ischemic encephalopathy.

(*J Clin Neurophysiol* 2011;28: 611–617)

et al., 2000; Wyatt et al., 2007), and are potentially treatable by the administration of antiseizure medications (Painter et al., 1999; Rennie and Boylan, 2007; Silverstein and Ferriero, 2008), the largest role of EEG monitoring is the surveillance for and prompt treatment

Who needs continuous EEG?

- Neonates with severe asphyxia and/or on cooling protocol
- Neonates with strong suspicion for seizures (recurrent rhythmic body movements or unexplained apneas)
- Neonates with encephalopathy
- Critically ill neonates on ventilator or with neuromuscular blocking agents
  - Pre and post cardiac surgery
- Neonates with moderate to severe abnormalities on routine EEG

NEONATAL SEIZURES

Epidemiology

- Neonatal seizures occur in 1.5–3.5 per 1000 live term births (Eriksson and Zetterstrom, 1979; Lanska et al.,1995; Ronen et al., 1999).

- 2006-2012 in USA, prevalence of neonatal seizures is 0.04%. (Padiyar S et al 2020)
  - Highest prevalence at 24 week GA = 0.12%
- Mortality rate in infants with seizures is 4%
  - Higher prevalence between 33-36 weeks GA

Epidemiology
Etiology does matters!

- Neonatal seizures occur in up to 26% of neonates with **HIE** (Shellhaas et al. 2011; Tsuchida et al. 2013; Massaro et al 2015)

- Electrographic neonatal seizures is seen in 11.5% of neonates undergoing heart surgery (Clancy RR et al. 2005)

Epidemiology

- The incidence of neonatal seizures is:
  - higher rates in preterm neonates
  - increased with decreasing gestational age and
  - Increased with decreasing birth weight
    - ≥2500 g:1.19/1000,
    - <1000 g: 127.57/1000)

(Pisani F eta l. 2017)

Etiology of Neonatal Seizures

- **Hypoxia Ischemic Encephalopathy**
- **Intraventricular Hemorrage**
- **Stroke**
- **Metabolic disorders and transient alteration of Glycemic and electrolytes**
- -Hypoglycemia
- -hypo or hypernatremia
- -hypocalcemia
- **CNS infections and sepsis**
- **Trauma**
- **Intoxication**

- **Genetic causes**
- *-Malformations of cortical development*
- ---Neuronal Migration Disorder
- ------Polymicrogyria (e.g. TUBA1A)
- ------Pachygyria-lissencephaly spectrum 9e.g. LIS1, ARX)
- ---Overgrown spectrum
- ------Hemimegalencephaly (e.g. PIK3CA)
- ------Focal cortical dysplasia (e.g. DEPDC5)
- ---Tuberous Sclerosis complex (TSC1, TSC2)
- ---Microcephaly (e.g . PNKP, CASK)
- *-Genetic Cellular*
- ---Genetic syndromes
- ------Chromosomal disorders
- ------Neurocutaneous syndrome
- ------Pseudo-TORCH Syndromes
- ---Channelopathies
- ---Synaptic vesicle docking and release
- ---Cell signaling
- *-Vascular Malformations of genetic etiology*
- ---COL4A1-related poroencephaly, schizencephaly or prenatal hemorrhage or prenatal hemorrhage
- ---Vascular malformations with genetic etiology (cavernous malformations, AVMs)
- ---Genetic risk factors for genetic stroke
- *-Genetic metabolic or inborn error of the metabolism*

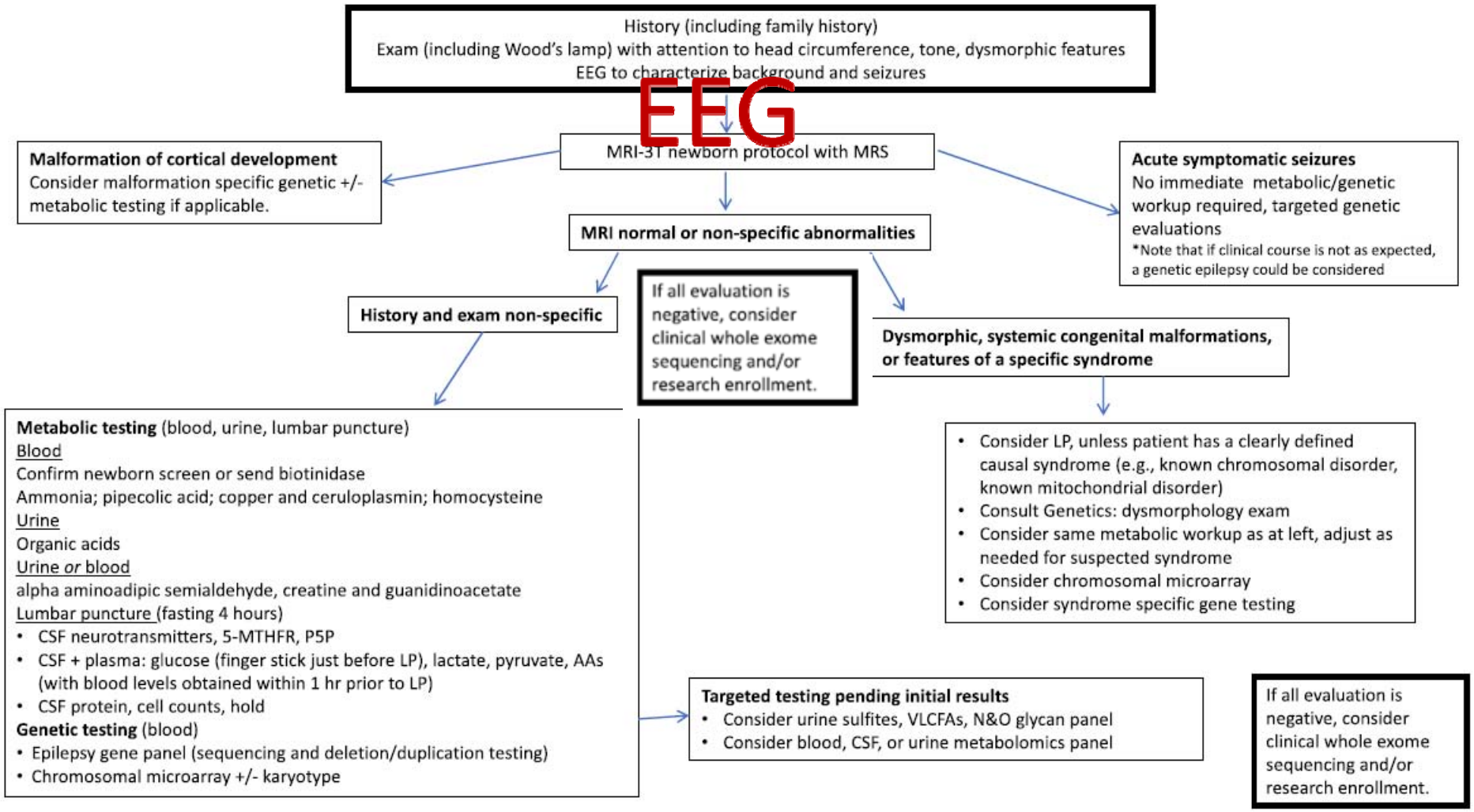


Fig. 2. Diagnostic approach to neonatal seizures. EEG, electroencephalogram; 3 T magnetic resonance imaging; MRS, magnetic resonance spectroscopy; CSF, cerebrospinal fluid; 5-MTHFR, methylenetetrahydrofolate reductase; LP, lumbar puncture; 5P5, pyridoxal-5′-phosphate; AA, amino acid; VLCFA, very long chain fatty acid.

Olson H et al.

Contemporary Profile of Seizures in Neonates: A Prospective Cohort Study

Hannah C. Glass, MDCM, MAS[1,2], Renée A. Shellhaas, MD, MS[3], Courtney J. Wusthoff, MD[4], Taeun Chang, MD[5], Nicholas S. Abend, MD[6], Catherine J. Chu, MD[7], M. Roberta Cilio, MD, PhD[1], David V. Glidden, PhD[2], Sonia L. Bonifacio, MD, MAS[8], Shavonne Massey, MD[6], Tammy N. Tsuchida, MD, PhD[5], Faye S. Silverstein, MD[3], and Janet S. Soul, MDCM[9], on behalf of the Neonatal Seizure Registry Study Group*

Objective To dete ures in neonates monitored with cont

Study design W ale, 88% term) ≤44 weeks' postme ubjects were assessed between Jar guidelines of the American Clinical N n, management, and outcome were (ly onset.

Results The most c mic stroke (18%), and intracranial hem eizures and 16% having status epilepticus; 52% received ≥2 antiseizure medications. During the neonatal admission, 17% died; 49% of survivors had abnormal neurologic examination at hospital discharge. In an adjusted analysis, high seizure burden was a significant risk factor for mortality, length of hospital stay, and abnormal neurological examination at discharge.

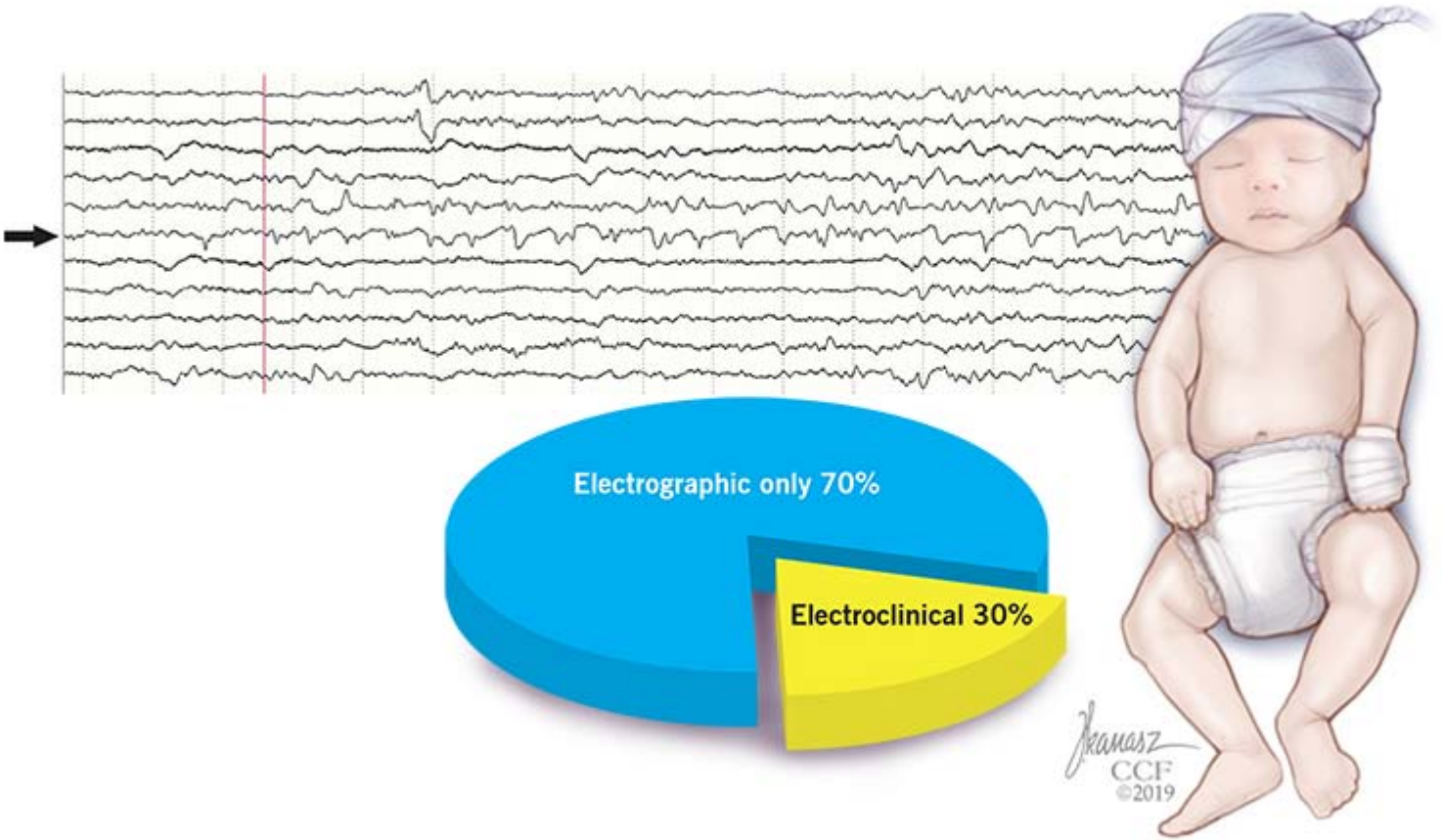
Conclusions In this large contemporary profile of consecutively enrolled newborns with seizures treated at centers that use cEEG per the guidelines of the American Clinical Neurophysiology Society, about one-half had high seizure burden, received ≥2 antiseizure medications, and/or died or had abnormal examination at discharge. Greater seizure burden was associated with increased morbidity and mortality. These findings underscore the importance of accurate determination of neonatal seizure frequency and etiology and a potential for improved outcome if seizure burden is reduced. *(J Pediatr 2016;174:98-103)*.

Etiology

- Hypoxic ischemic encephalopathy 38%
- Ischemic stroke 18%
- Intracranial Hemorrhage 11%

Definition of neonatal seizures

- Electrographic and Electro-Clinical Seizures



Neonatal seizures

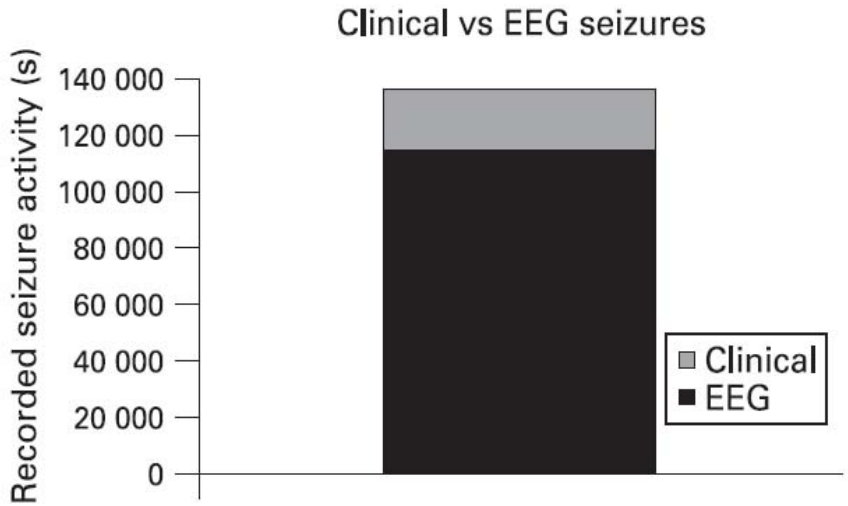
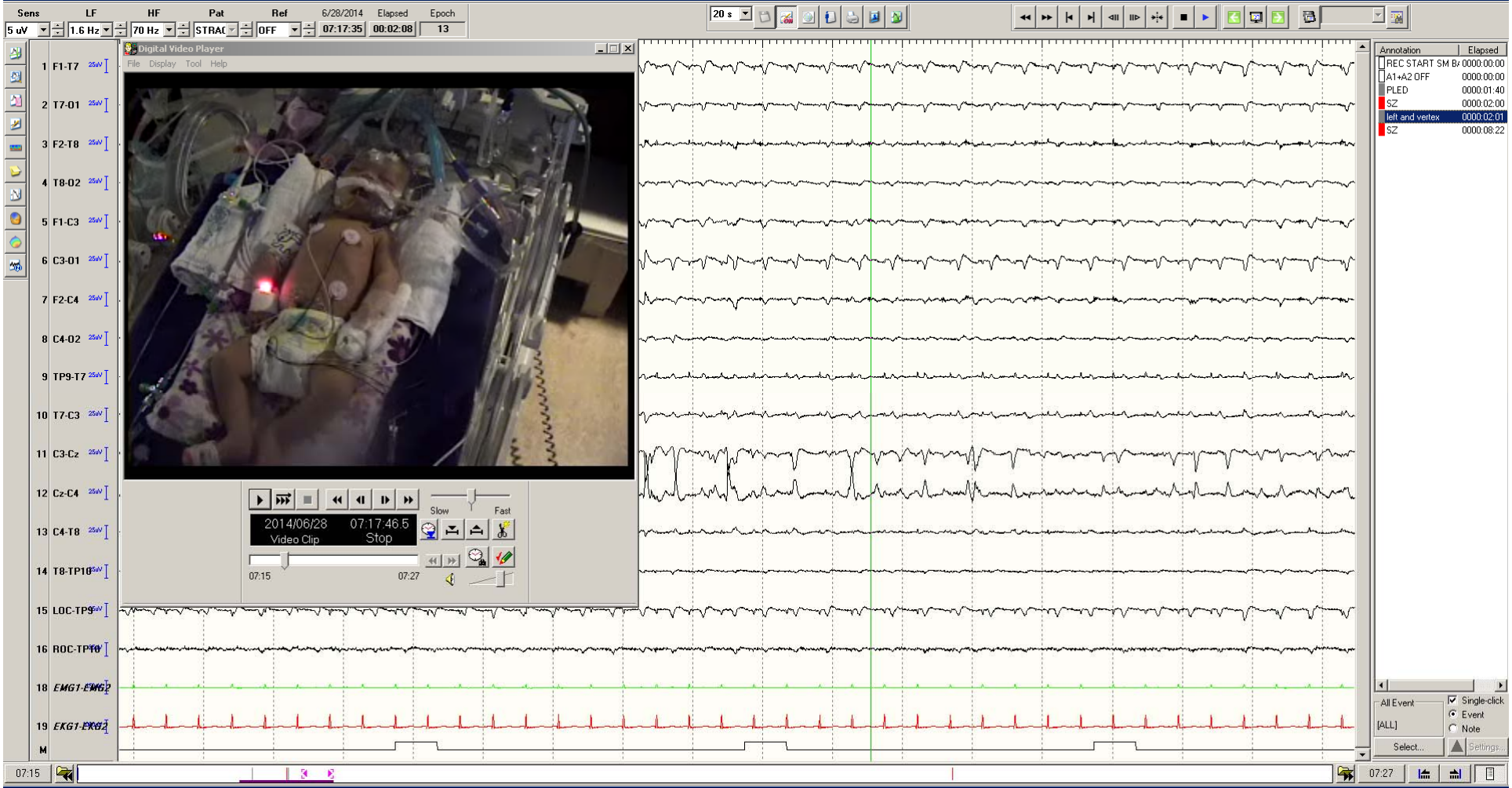


Figure 1 Total recorded electrographic seizure activity measured in seconds, versus total clinical seizure manifestations in nine patients with electrographic seizures recorded on continuous video-EEG during the first 72 hours of life.

Arch Dis Child Fetal Neonatal Ed 2008;**93**:F187–F191. doi:10.1136/adc.2005.086314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4 T8-O2
5 F1-C3
6 C3-O1
7 F2-C4
8 C4-O2
9 TP9-T7
10 T7-C3
11 C3-Cz
12 Cz-C4
13 C4-T8
14 T8-TP10
15 LOC-TP9
16 ROC-TP10
18 EMG1-EMG2
19 EKG1-EKG2
M
Slow
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left and vertex
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All Event
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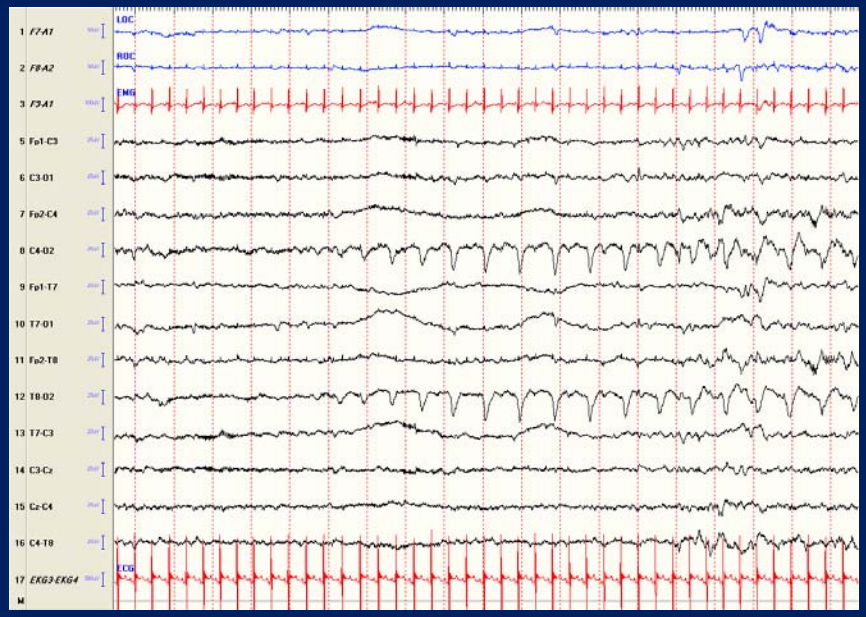
Event
Note
Settings...
07:15
07:27

Neonatal EEG seizures

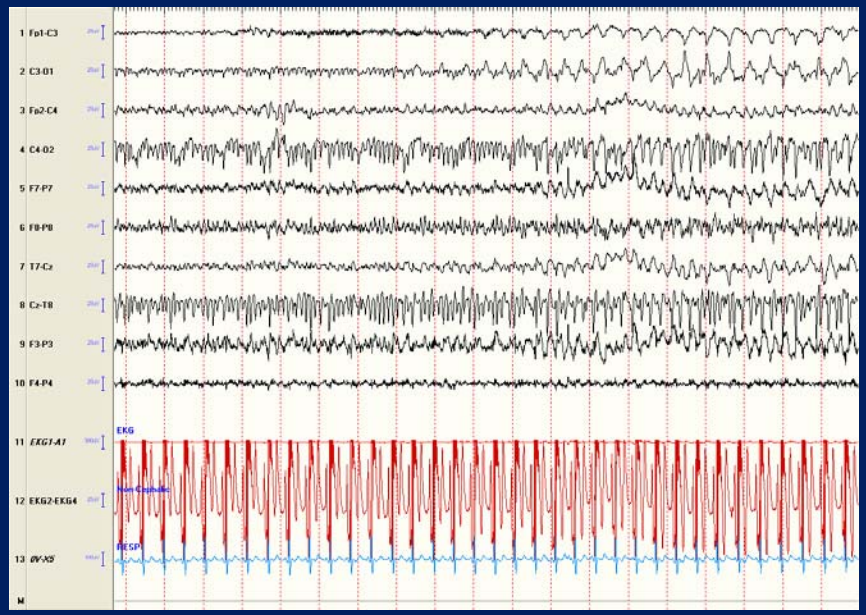
- Sudden
- Repetitive
- Evolving
- Clear onset, middle and end
- Stereotyped ictal pattern
- Amplitude at least 2uV

Common patterns for neonatal seizures

1-2 Hz seizure pattern



Fast frequency seizure pattern



Neonatal EEG seizures
Electrographic characteristics

- Neonates have a high seizure burden (~7 seizures per hour)
- Often seizures are surface positive
- Minimal duration of the seizures is 10 seconds
  - Mean duration of seizures is around 90 seconds
  - Minimal duration between 2 seizure patterns has to be ≥10 seconds to be consider independent seizures
- Background pattern can be present during the seizure and often is abnormal

Seizure burden in neonates

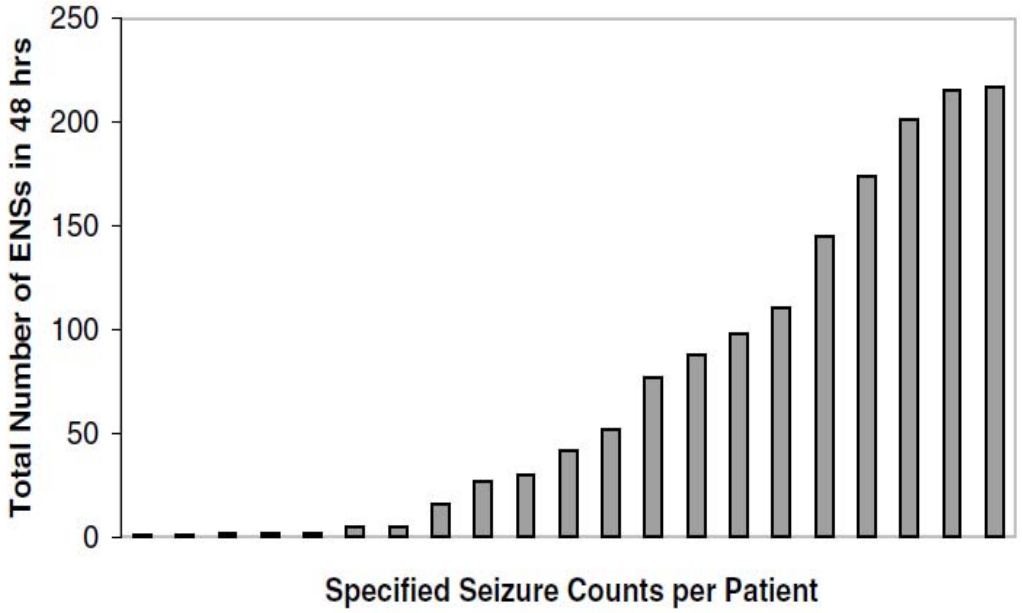


FIG. 3. The distribution of the total electrographic neonatal seizure counts during the 48-h monitoring period.

Out of 21 neonates,
14 had more than 10 szs in 48 hours

Clancy RR et al. Epilepsia 2005; 46: 84-90

Contemporary Profile of Seizures in Neonates: A Prospective Cohort Study

Hannah C. Glass, MDCM, MAS[1,2], Renée A. Shellhaas, MD, MS[3], Courtney J. Wusthoff, MD[4], Taeun Chang, MD[5], Nicholas S. Abend, MD[6], Catherine J. Chu, MD[7], M. Roberta Cilio, MD, PhD[1], David V. Glidden, PhD[2], Sonia L. Bonifacio, MD, MAS[8], Shavonne Massey, MD[6], Tammy N. Tsuchida, MD, PhD[5], Faye S. Silverstein, MD[3], and Janet S. Soul, MDCM[9], on behalf of the Neonatal Seizure Registry Study Group*

Objective To determine the contemporary etiology, burden, and short-term outcomes of seizures in neonates monitored with continuous vid

Study design We prospec s (56% male, 88% term) ≤44 weeks' postmenstrual age seizures. Subjects were assessed between January 2013 lowing the guidelines of the American Clinical Neurophysic ogy, burden, management, and outcome were determinec ned at study onset.

Results The most common se 8%), ischemic stroke (18%), and intracranial hemorrhage (1 %). Seizure burden was high, with 59% having ≥7 electrographic seizures and 16% having status epilepticus; 52% received ≥2 antiseizure medications. During the neonatal admission, 17% died; 49% of survivors had abnormal neurologic examination at hospital discharge. In an adjusted analysis, high seizure burden was a significant risk factor for mortality, length of hospital stay, and abnormal neurological examination at discharge.

Conclusions In this large contemporary profile of consecutively enrolled newborns with seizures treated at centers that use cEEG per the guidelines of the American Clinical Neurophysiology Society, about one-half had high seizure burden, received ≥2 antiseizure medications, and/or died or had abnormal examination at discharge. Greater seizure burden was associated with increased morbidity and mortality. These findings underscore the importance of accurate determination of neonatal seizure frequency and etiology and a potential for improved outcome if seizure burden is reduced. *(J Pediatr 2016;174:98-103)*.

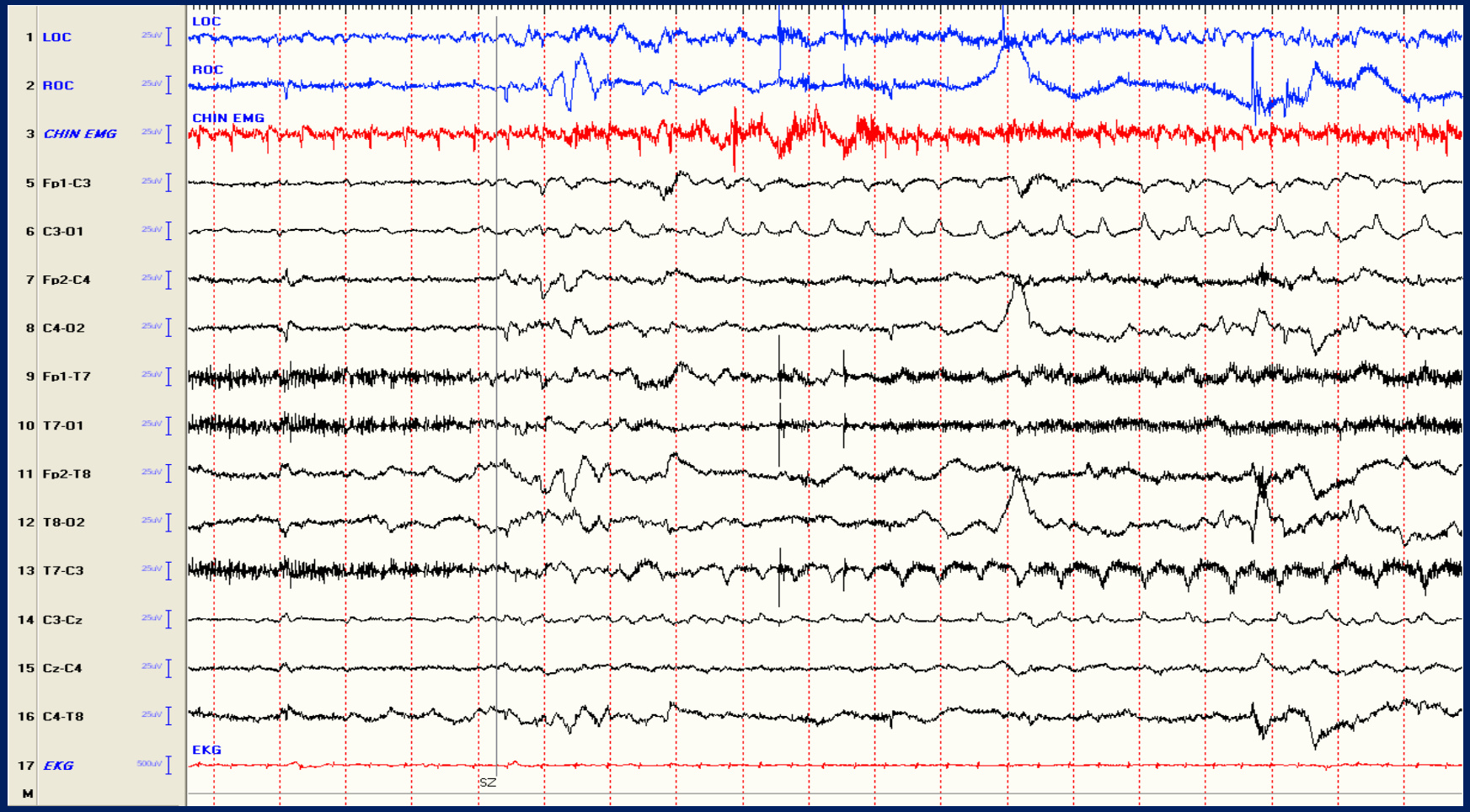
- **Seizure burden**
  - => 7 EEG sz/ hour 59%
  - Status epilepticus 16%
- Treatment => 2 AED 52%

Seizures can involve a single electrode

Often the seizures are multifocal

Often the seizures are simultaneous multifocal

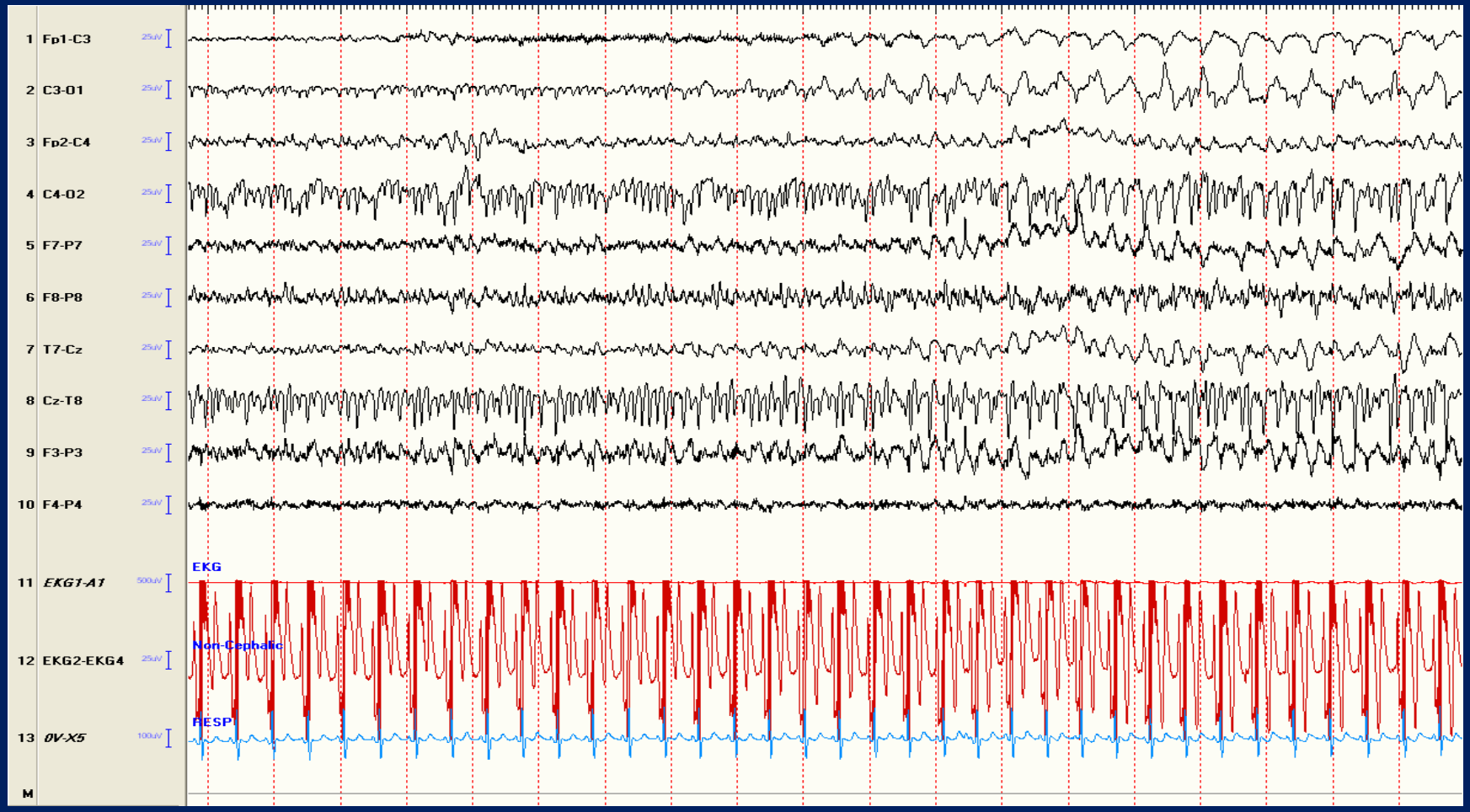
C3 seizure, no clinical signs



78% of neonatal seizures appeared in the C3 -> C4 channel.

Shellhaas R et al. Clin Neurophysiology 2007; 118:2156-2167

Sz with independent rhythms



Clinical symptoms

- Subtle seizures (50%)
  - Ocular movements
  - Oro-buccal-lingual movements
  - Progression movements (pedaling, bicycling, etc)
  - Autonomic symptoms
  - Complex purposeless movements (arousals, crying, hyperactivity)
- Tonic seizures (5%)
- Clonic seizures (25%) → Multifocal, generalized, symmetric, asymmetric
- Myoclonic seizures (20%)
- Non-paroxysmal repetitive behaviors
- Spasms

Volpe Mizhari

The ILAE Classification of Seizures & the Epilepsies: Modification for Seizures in the Neonate. Proposal from the ILAE Task Force on Neonatal Seizures

Ronit M Pressler[1,2], Maria Roberta Cilio[3], Eli M Mizrahi[4], Solomon L Moshé[5], Magda L Nunes[6], Perrine Plouin[7], Sampsa Vanhatalo[8], Elissa Yozawitz[9], Sameer M Zuberi[10]

Sequential Seizures:

(ILAE Neonatal Task Force and the 2017 ILAE classification manual)

-difficult to identify the dominant feature,

-typically in longer seizures

-sequence of clinical features was seen, often with changing lateralization

Seizure type	Modifiers
Automatisms	Unilateral Bilateral asymmetric Bilateral symmetric
Clonic seizures	Focal Multifocal Bilateral
Epileptic spasms	Unilateral Bilateral asymmetric Bilateral symmetric
Myoclonic seizures	Focal Multifocal Bilateral asymmetric Bilateral symmetric
Sequential seizure type	Depending on components
Tonic seizures	Focal Bilateral asymmetric Bilateral symmetric

Table 2: Modifiers of motor seizures in the neonatal period

Neonatal seizures: location
Premature versus Term babies

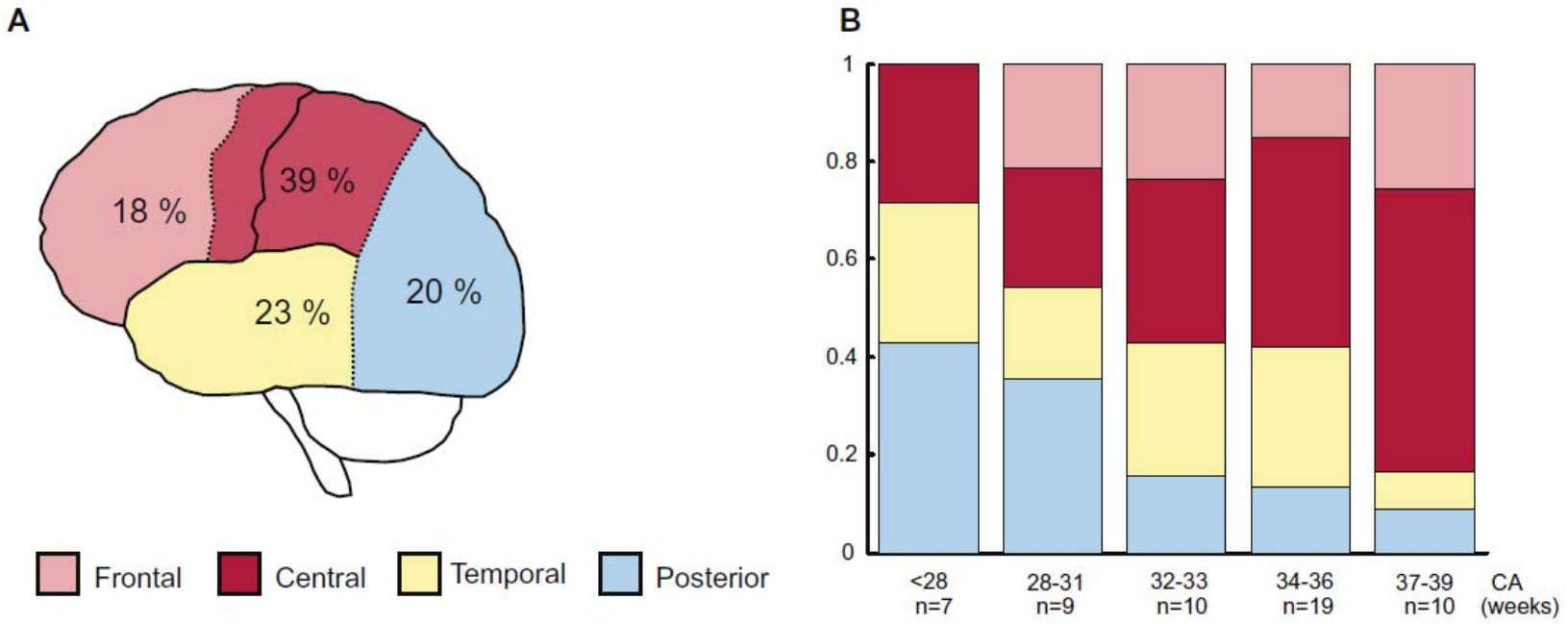


Fig. 2. Localisation of seizure onset. (A) Onset of focal seizures was observed in all cerebral regions and on the whole, the central regions predominated. (B) We observed differences depending on age. In the youngest neonates, the onset over posterior regions predominated, whereas frontal onset was observed only after 28 weeks CA.

S. Janáčková et al. / Clinical Neurophysiology 127 (2016) 2721–2727

Relation between etiology and seizure types in neonates

ETIOLOGY	Hypoxia-Ischemic Encephalopathy	Vascular	Genetic	Metabolic/ Electrolytes	Inborn Error of the Metabolism	Infection	Cortical Malformation
SEIZURE TYPES							
EEG seizures							
Sequential seizures							
Clonic seizures							
Tonic seizures							
Myoclonic seizures							
Autonomic seizures							
Spasms							

Received: 6 October 2018 | Revised: 11 December 2018 | Accepted: 11 December 2018
DOI: 10.1002/epi4.12298

CRITICAL REVIEW AND INVITED COMMENTARY

Epilepsia Open® Open Access

Neonatal seizures: Is there a relationship between ictal electroclinical features and etiology? A critical appraisal based on a systematic literature review

Magda L. Nunes[1] | Elissa G. Yozawitz[2] | Sameer Zuberi[3] | Eli M. Mizrahi[4] | Maria Roberta Cilio[5] | Solomon L. Moshé[6] | Perrine Plouin[7] | Sampsa Vanhatalo[8] | Ronit M. Pressler[9] | Task Force on Neonatal Seizures, ILAE Commission on Classification & Terminology

DEGREE OF ASSOCIATION

= VERY COMMON ASSOCIATION

= VERY RARE ASSOCIATION

Neonatal Status Epilepticus

- Single seizure lasting more than 30 minutes
- Multiple seizures that account for 30 minutes over one hour period
- Recurrent seizures for over 50% of 1-3 hours of recording time (Nash KB et al. Neurology 2011; 76: 556-62)

Table 2
Quantitative seizure characteristics and comparisons between conventional and single channel EEG

	Conventional EEG	$C_3 \rightarrow C_4$	p-Value
Seizures detected	$N = 851$	$N = 664$ (78%)	N/A
Mean seizure duration (s)	132 (10–2314)	100 (10–2313)	$p \leqslant 0.001$[b]
Mean ictal peak-to-peak amplitude (μV)	145 (13–1166)	111 (5–739)	$p \leqslant 0.001$[b]
Mean ratio of ictal to interictal peak-to-peak amplitude (μV)	2.19 (0.5–27.1)	2.27 (0.4–33.8)	$p = 0.47$[b]
Mean seizure burden (percent record with seizure)	24.8%[c] (0.7–86.9)	17.6% (0–18.0)	$p = 0.004$[b]
Mean seizures per hour	7.0[c] (0.5–21)	5.2 (0–18)	$p = 0.003$[b]
Status epilepticus[d]	17/125 (14%)	7/125 (6%)	$p = 0.038$[a]

[a] Chi-squared.
[b] Student's t-test.
[c] There is only a moderate correlation (Spearman coefficient = 0.58) between the number of seizures per hour and the seizure burden.
[d] Status epilepticus was defined as greater than 50% of the tracing with seizures.

Pathophysiology

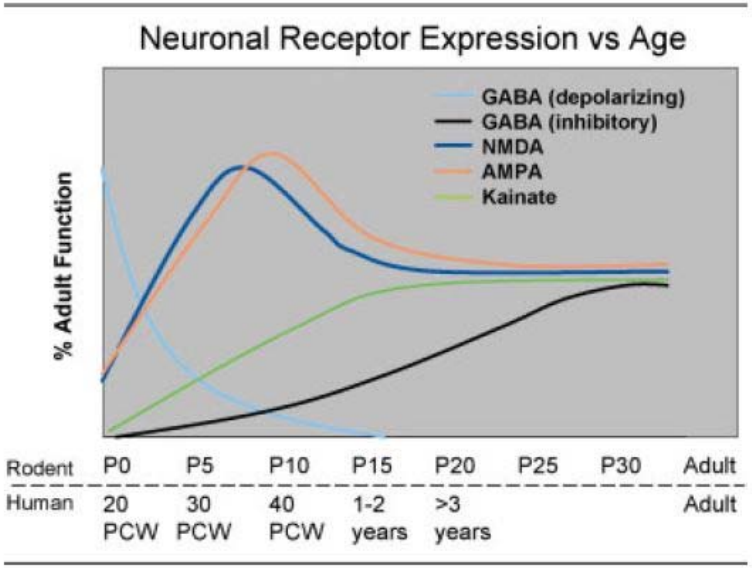
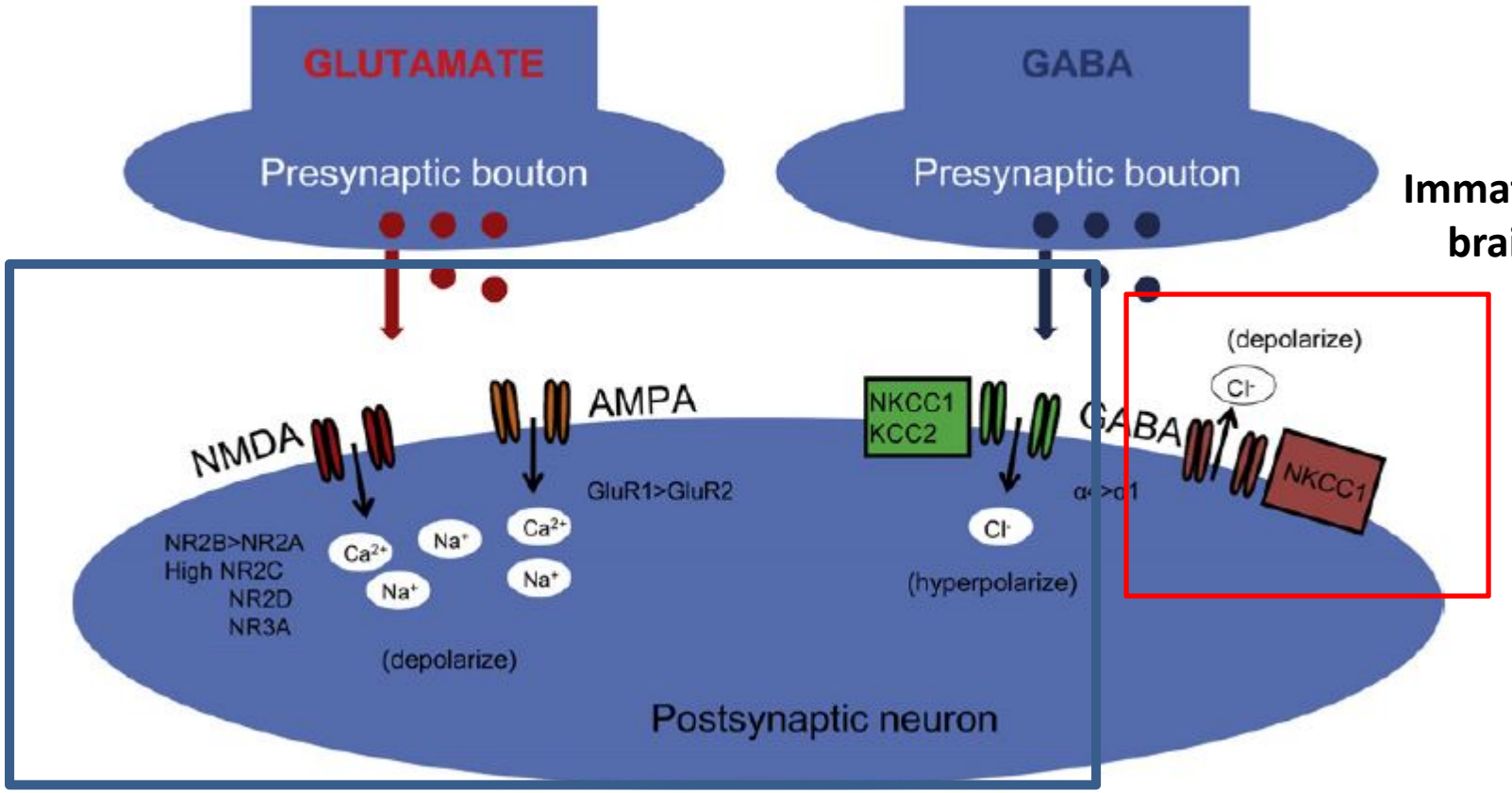


Fig. Schematic depiction of maturational changes in glutamate and GABA receptor expression and function in the developing brain. Developmental pattern for rat (top x*-axis) and human (bottom* x*-axis) are shown, based on recent literature.*[37,39,40,69] *GABA receptors are depolarizing* (light blue line) *early in the first postnatal week in the rat and up to and including the neonatal period in the human, whereas functional inhibition* (black line) *is gradually reached over development.*[69] *Before full maturation of GABA-mediated inhibition, the* N*-methyl-*D*-aspartate (NMDA;* dark blue line*) and* α*-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA;* orange line*) subtypes of glutamate receptors peak between the first and second postnatal weeks in the rat and in the neonatal period in the human. Kainate receptor binding* (green line) *is initially low and gradually increases to adult levels by the fourth postnatal week.*[94]

Ann Neurol 2007; 62:112-120

Clin Perinatol 36 (2009) 881–900



Mature Brain

Clin Perinatol 36 (2009) 881–900

Treatment

- First line
  - phenobarbital (doses ranging from 20–40 mg/kg),
  - phenytoin (20 mg/kg), or fosphenytoin, and/or
- Second-line adjuvant (first line in some centers)
  - benzodiazepines such as lorazepam (0.05–0.1 mg/kg)
  - midazolam
- Other:
  - Lidocaine (77% response versus Midazolam 50% for HIE)
  - Topiramate
  - Levetiracetam
  - Bumetanide 0.3mg/kg -> concern for hearing loss (Pressler RM et al. 2015)

HIE = hypothermia

Ann Neurol 2007;62:112–120; Semin Pediatr Neurol 17:163-168

Table III. Seizure management among 426 neonates with clinically suspected and/or EEG confirmed seizures who were monitored by cEEG

	Overall, n = 426
Initial loading medication and dose	
Phenobarbital (20 mg/kg, IQR 20, 20 mg/kg)	379 (89%)
Levetiracetam (20 mg/kg, IQR 20, 32 mg/kg)	22 (5%)
Fosphenytoin (20 m/kg, IQR 15, 20 mg/kg)	4 (1%)
No loading dose	18 (4%)
Seizure medications administered during the admission	
Phenobarbital	393 (92%)
Levetiracetam	134 (31%)
Fosphenytoin	119 (28%)
Benzodiazepine – intermittent doses	84 (20%)
Benzodiazepine infusion	31 (7%)
Topiramate	17 (4%)
Carbamazepine/oxcarbazepine	9 (2%)
Vitamin(s): (pyridoxine, folic acid, pyridoxal 5 phosphate)	32 (8%)
Number of antiseizure medications administered	
0	10 (2%)
1	194 (46%)
2 Treatment => 2 or more AED 52%	101 (24%)
3	68 (16%)
≥4	53 (12%)

Glass HC et al. 2016

NEONATAL ENCEPHALOPATHY

Neonatal encephalopathy
Clinical manifestations

- Alter mental status
- Seizures
- Hypotonia
- Abnormal primitive reflexes
- Apneas and difficulty breathing
- Feeding problems
- Abnormal cry

Etiology

- Hypoxia Ischemia
- Intracranial infection
- Ischemic perinatal stroke
- Intracranial hemorrhage
- Brain malformations
- Inborn Error of the Metabolism
- Neonatal Onset Epileptic Encephalopathy
  - KCNQ2, KCNQ3, SCN1A, SCN2A, SLC12A5, STXBP1, KCNT2, GDLC, CDKL5, CHD7
- Transient encephalopathy

Neonatal Onset Epileptic Encephalopathy

- Ohtahara syndrome or Early Infantile Epileptic Encephalopathy (EIEE) and Early Myoclonic Epileptic Encephalopathy (EME)

- KCNQ-related epilepsy
  - Benign familial neonatal seizures (BFNS)
  - Benign familial neonatal-infantile seizures (BFNIS)
  - KCNQ severe encephalopathy

Neonatal Onset Epileptic Encephalopathy (Cont.)

- SCN2A- related neonatal epilepsies
- CDKL5 encephalopathy
- STXBP1 encephalopathy
- Other genetic early onset developmental and epileptic encephalopathies

Neonatal encephalopathy with Burst suppression pattern
Clinical features

Ohtahara or EIEE with BS

- Tonic seizures
- Onset in the first week of life
- Grossly abnormal brain MRI

Early Myoclonic Epileptic Encephalopathy (EMEE)

- Myoclonic seizures
- Onset in the first week of life or prenatal
- Normal brain MRI

Etiology

- Brain structural abnormalities
  - hemimegalencephaly, magalencephaly, lissencephaly, polymicrogyria, focal or multifocal cortical dysplasia, poroencephaly, agenesis of the corpus callosum or the mamillary bodies, posterior fossa abnormalities, etc
  - HIE
- Genetic metabolic
  - ARX, CDKL5, SLC25A22 and STXBP1, KCNQ2, SCN2A and ALDH7A1; mitochondrial diseases, inborn error of the metobolism such as non-ketotic hyperglycinemia or glycine encephalopathy, propioic or methylmalonic acidemia, molybdenum cofactor deficency, and other more rare inborn errors of the metabolism

Treatment

Neonatal Epileptic Encephalopathy	treatment
Ohtahara and EMEE	Topiramate, other AED, Steroids, pyridoxine (Evidence Class C, poorly effective, weak recommendation)
KCNQ2 - EE	carbamazepine, oxcarbazepine, phenytoin
SCN2A - EE	carbamazepine, phenytoin
CDKL5 - EE	????
KCNT1 - EE	bromides, levetiracetam, quinidine ???
STXBP1 -EE	???

QUESTIONS