Amplitude-Integrated EEG (aEEG) – What it is and how it is being used

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Amplitude-Integrated EEG (aEEG)

- Down to a single channel portable EEG obtained from bi-parietal or bi-temporal electrodes
- Amplifies and filters (2-15 Hz)
- Gives a compressed, banded, slow (6cm/hr) relatively easy to interpret readout
Cerebral Function Monitor (CFM) - Amplitude-Integrated EEG (aEEG)

• CFM first aEEG developed in the 1960’s in the United Kingdom by Dr. Maynard
• Initially used for monitoring adults undergoing surgery, suffering head trauma, or in a coma
• In the early to mid 1980’s groups in Europe began investigating its use in neonates suffering from birth asphyxia
Cerebral Function Monitor
First aEEG to be available in the US used to screen infants for entry into the “Head Cooling Study for Perinatal Asphyxia”

- Improves accuracy of newborn neurological examinations
- Records and aids in detecting seizures
- Continuously monitors and records brain activity
- Monitors effects of drugs and other therapies on the brain
- Aids in identifying HIE and predicting long-term outcome
- Determines need for further neurological examination or transport
NicoletOne Monitor — previously called “Nervus”

- 16-32 channel high quality EEG recording
- Touch screen operation
- Small footprint - only a panel PC, keyboard & mouse
- Can be mounted on a trolley, wall or stand
- Virtually unlimited recording time
- On-line and remote data access
- Continuous impedance check
‘Brainz’ - Amplitude-Integrated EEG (aEEG) - Bi-Parietal and Cross-Cerebral Methods.
Why is Neurophysiological Monitoring in the NICU Important?

• Mortality Rates in NICU Patients Especially Premature Infants have Dramatically Decreased, while Long Term Neurological Morbidity has not.

• Clinical Advancement in the Use of Neuroprotective Factors in the Past has been Significantly Limited by the Lack of a Continuous Neurophysiological Monitor
Why is the aEEG Important?

- Other means of monitoring neurological status: physical exam, neuroimaging (MRI, CT, U/S -doppler studies)
  - very difficult to impossible to be done continuously
  - when abnormalities detected – often too late to intervene with neuroprotective treatment
Ideal Neurophysiological Monitor

• Non-Invasive
• Simple to Apply, Operate and Interpret at the Bedside in ‘Real’ time
• Able to Run in a Continuous Manner with a Continuous Read Out.
• Able to Detect Subtle and Subclinical Seizures and Neurological Changes at a ‘Reversible’ Stage
• Able to Predict Outcome
Continuous Neurophysiological Monitoring with a Standard EEG

• **Advantages**
  - Composite reflection of cerebral metabolism.
  - Detects Neuronal Dysfunction at Reversible Stage
  - Best method of detecting seizure activity.
  - Very Predictive of Outcome Following Perinatal Asphyxia

• **Disadvantages**
  - Difficult to Obtain Emergently and Run Continuously
  - Difficult to Interpret at the Bedside
  - Difficult to Condense Long Periods of Recordings to Efficiently Read
Standard EEG Equipment
Standard EEG Tracing
aEEG

- Easier to obtain emergently and run continuously
- Easier to condense long periods of recordings
- Easier to interpret at the bedside
Continuous Neurophysiological Monitoring with a aEEG

**Other Advantages**
- Composite reflection of cerebral metabolism. Detects Neuronal Dysfunction at Reversible Stage
- Very Predictive of Outcome Following Perinatal Asphyxia
- Good at Detecting Seizures Activity

**Disadvantages**
- Cannot localize seizure activity well
- May miss very focal seizures if not in the vicinity of the electrodes
Comparison of Standard EEG and CFM

- 14/17 with Normal CFM = Normal EEG
- 26/27 with Abnormal CFM = Abnormal EEG
  - Naqueeib et al. - Pediatrics June 1999
- 15/15 = Agreement between background activity and seizure activity except very short (5-30s) seizures.
Comparison of Standard EEG and CFM

- 100% of severely abnormal CFM’s (BS, continuous extremely low voltage, flat tracing) correlated with a severely abnormal EEG (excessive discontinuity, BS, low voltage undifferentiated, no activity) 100% PPV/Specificity, 80% NPV, 76% Sensitivity

- Agreement of background activity better with CFM than EEG 0.92 vs 0.74

- CFM reliable tool for monitoring normal and abnormal background patterns and ictal activity, but can miss certain focal, low amplitude and very short seizures — *Toet et al. Pediatrics 2002*
Fig 1. Examples of aEEG background activity. A, normal amplitude; B, moderately abnormal amplitude; C, suppressed amplitude.

Fig 2. Examples of seizures. A, seizure with normal amplitude aEEG; B, seizures with moderately abnormal aEEG; C, seizures with suppressed amplitude aEEG.
Normal Trace

- The upper margin of the main band of activity is above 10 µVolts.
- The lower margin is above 5 µVolts.
Moderately Abnormal or Discontinuous Trace with Seizure

- Upper margin is slightly depressed but is still above 10 µVolts.
- The lower margin has dropped below 5 µVolts.
Severely Abnormal or Burst Suppression

- Upper margin is below 10 uV and lower margin is below 5uV
- Note the very narrow, suppressed band of activity with occasional spikes indicating burst suppression.
Severely Abnormal (Continuous Extremely Low Voltage) almost ‘Flat’ or ‘Isoelectric’ Trace
CFM Predictability Early After Perinatal Asphyxia

- 47 Asphyxiated Infants had aEEG Recordings within the First 6 hrs. 
  *Hellstrom-Westas Arch Dis Child 1995*

  - 25/26 with continuous **normal voltage** background were **normal** thru 4 yrs.
  - 2/2 with continuous **very low voltage** background survived with **severe handicap**
  - 4/5 with **isoelectric tracings** died the 5th survived with **severe handicap**
CFM Predictability Early After Perinatal Asphyxia

- 5/14 with burst suppression died. 6 survived with severe handicap and 3 were nl.
- 50% of infants with single seizures had a good outcome.
- 3 hr. EEG prognostic efficiency (True Pos. + True Neg. Div. By # Obs. X 100) was only 74% at 3 hrs. compared to 91.5% at 6 hrs. and 90.5% with standard EEG at 1-4 days.
CFM Predictability Early After Perinatal Asphyxia

• 56 Infants With Neonatal Encephalopathy Along With Controls Were Studied within 12 Hours - Naqueeb Pediatrics 1999
  – 19/21 with normal a EEG were normal at 18-24 months
  – 27/35 with moderately abnormal aEEG died or had handicaps
  – Sensitivity = 0.93, Specificity = 0.7
  – Positive Predictive Value = 0.77
  – Negative Predictive Value = 0.90
  – Interobserver Variability = 0.85 (assessment of amplitude) = 0.76 (identification of seizures)
CFM Predictability Early After Perinatal Asphyxia

• 73 cases of neonatal encephalopathy studied at 3-6 hours after birth - Toet M. Arch Dis Child Fet Neo Ed, 1999.

• 9/9 with ‘Flat Tracing’ died or had major handicap – (7 died, 2 major handicap)

• 6/6 with ‘Continuous Low Voltage’ died or had major handicap – (5 died, 1 major handicap)

- 14/19 with ‘Burst Suppression’ died or had major handicap or global delay – (10 died, 4 major handicap, 1 global delay, 5 normal)
- 2/2 with ‘Discontinuous Normal Voltage’ were normal
- 26/28 with ‘Continuous Normal Voltage’ were normal (1 died, 2 global delay)
- 3h PPV=78%, NPV=84%; 6h PPV=86%, NPV=91%
Overall Predictability of CFM after Perinatal Asphyxia

• In first 6 hours after birth in ≥36 weeks gestation.
  – > 90% negative predictive value (infant will have no long term neurological sequelae from birth event)
  – ~ 80% positive predictive value infant will have long term neurological sequelae from birth event (this may be lessened by alternative treatment ie. Cooling)
  – 100% of Low Voltage or Flat Tracings died or lived with severe disability
  – Predictability better at 6 hours than at 3 hours
Term Perinatal Asphyxia – Prognosis?
Interim Summary

- CFM/aEEG originally came to the US in the late 90’s to be used as a tool for screening newborns at risk of neurological injury following perinatal asphyxia for enrollment into a “Head Cooling” study.
- It is now being used more in NICU’s for other reasons such as: monitoring term and preterm infants for seizures and evidence of neurological damage following “events”, monitoring for ‘sleepwake cycling’ (SWC), as well as studying preterm development.
Neonatal Seizures

- Seizures are more common in the neonatal period than any other time in life (as high as 57.5/1000 in < 1500g and 2.8/1000 in 2500-3999) Volpe JJ. Neonatal Seizures. In: Neurology of the Newborn, 4th edition. 2000.

- Most common type of seizures are subtle or subclinical
Neonatal Seizures

- Recognizing neonatal seizures important for proper evaluation of etiology (i.e., hypoxic injury, sepsis, meningitis, metabolic disorder, or CNS hemorrhage or infarct)
- Neonatal seizures may adversely effect the developing brain
- Certain anti-epileptic drugs may also adversely effect the developing brain
Neonatal Seizures

- Diagnosing neonatal seizures is difficult without an EEG
- Standard EEG usually done for 60 min and often not done during suspected seizure activity
- Continuous aEEG can significantly enhance seizure detection
Case # 1

- 3300g female born to 35 year old G1P1
- 42 weeks
- GBS positive, prenatals otherwise normal
- 3+ meconium, cleared with amnioinfusion
- Mild decels
- Forceps assisted vaginal delivery
- Intubated-no mec below cords
- Brief PPV-Apgars 6\textsuperscript{195}
Case # 1

• Exam is essentially normal.
• To Level I.
• At 12 hours is observed to be dusky and pale, which resolves with BBO$_2$ in SCN.
• Followed by several more episodes of apnea, pallor, and duskiness.
• Requires intubation for apnea with desaturation.
Case # 4 - Initial Labs

- WBC 23.7  80S  0B
- HCT 43.7
- PLT 223
- CRP 1.5
- Na 141, K 5.1, Cl 108, CO₂ 19, Glu 60
- ABG 7.4 / 36 / 95 / 22.1 / -1.7
Case # 1 - CFM Characteristic of Seizures
Right Occipital Hemorrhagic Infarction
Sleep Wake Cycling

- Cyclical pattern occurring ~ every 60-90 minutes
- Broadened band width (discontinuous activity) represents quiet sleep and narrow band width (continuous activity) represents wakefulness or active sleep
- Usually present from ≥ 30 weeks, can be present in an immature form < 30 weeks
- Good prognostic indicator if present shortly (ie < 36 hours) after neurological insult
aEEG in the Premature Infant

• The aEEG background voltage, amount of continuous activity, and sleep wake cycling increases normally as the infant’s gestation increases.

• Premature infants tend to have significantly more background voltage depression with sedative medications (phenobarbital, benzodiazepams) than term infants.
Standard EEG Change with Gestation
% of Continuous Activity Increases and Interburst Interval Time Decreases with Gestation
CFM Use in Premature Infants

- Normal Patterns have been described for Premature Infants.

- Presence of Continuous Activity (Min Voltage > 3uV)(PPV=91%) and Sleep Wake Cycle (SWC)(PPV=69%) are Indicators of favorable outcome.
  - Hellstrom-Westas Neuropediatrics 1991
CFM Use in Premature Infants

• Electrocerebral Inactivity (Max Voltage < 5uv > 2 h) Predicted an Unfavorable Outcome (PPV=100%).

• Epileptiform Activity (EPA) Was only found in infants with Intracranial Hemorrhage (ICH) and 75% of Infants with ICH had EPA (85% with Periods of Subclinical Seizures)

– Hellstrom-Westas Neuropediatrics 1991
27 Week Septic Shock Grade 3 IVH
Required Shunt

29 Week Seizures Grade 3 IVH
Required Shunt
27 Week - Perinatal Asphyxia

Grade 2 IVH

3 days later with SWC
Case #2

- 28 week gestation 2 day old infant with initial generalized tonic and clonic activity lasting for 5-10 minutes stopped only with Versed prior to placement of CFM.
- Suspected recurrent seizures with significant increase in BP treated with Phenobarbital. Head ultrasound showed Grade 1 IVH.
Case #2 CFM
Other Recent aEEG Research

• Continuity and amplitude may increase in the first 3 days of life in premature infants with no brain lesions — Menache C. Neuropediatrics 2006

• aEEG showed increased discontinuity and decreased SWC in 2 premature infants with progressive posthemorrhagic hydrocephalus — Olishchar M. Childs Nerv. Syst. 2004
Tips for Applying CFM Electrodes

• Hydrogel electrodes can be used on scalp or forehead.
  – Require aggressive prep with abrasive scrub to exfoliate top layer of skin prior.
  – Look at impedance on CFM – should be < 20 KOhms and ideally < 5 KOhms

• Important to measure distance between electrodes.
  – Too close could falsely decrease background voltage as less brain tissue and less electrical activity would be between electrodes.
Tips for Applying CFM Electrodes

• Biparietal (scalp) application preferred:
  – ‘Watershed’ area between posterior and middle cerebral arteries.
  – Least likely to be affected by scalp muscle activity and eye-movement artifacts.
  – Needle electrodes are easiest to use with the scalp application.
  – Technique would be same as starting scalp IV with initial prep with alcohol and securing with tape. Can be left in place for days if needed.
Importance for Continuous Ongoing Monitoring with CFM

- Predictive value has been documented to be better at 6 hrs. than 3 hrs. and almost certainly better at 24 hours than 3-6 hrs.
- A baby who progresses to or has a persistent continuous low voltage CFM past 24 hrs. has a very poor prognosis and deserves further discussion/evaluation for possible withdrawing of support.
- Alternatively, a baby who has presence of Sleep Wake Cycling especially with normal background voltage has a very good prognosis.
- Detecting and aggressively treating seizures may impact outcome
Pitfalls of CFM

• Background Voltage can be Artificially elevated by:
  – Handling
  – Muscle Activity
  – High Frequency Ventilation
  – Status Epilepticus
  – Gasp Artifact
  – EKG Artifact
Pitfalls of CFM

• Background Voltage can be Artificially Depressed by:
  – Severe Scalp Edema (ie. Subgaleal Hemorrhage)
  – Leads significantly too close together
  – Significant Sedation
Other Case Presentations
Case #3

- Term infant born by C/S delivery after failed vacuum with mec stained fluid
- Depressed at birth requiring bag mask ventilation and then mask CPAP for ‘several minutes’ after birth
- Apgars = 5\textsuperscript{1}, 6\textsuperscript{5}, 7\textsuperscript{10}; no cord pH done
- Transferred from rural Colorado to The Children’s Hospital at ~ 6-7 hours of age for persistent oxygen requirement and suspected meconium aspiration
Case #3

- Baby was noted to have large ‘caput’ and was very irritable and not consolable during transport
- After admission noted to have mod. Subgaleal, irritable, diffusely hypertonic and jittery/intermittent myoclonus
Case #3 CFM
Case #3 - CT Scan
Case #3

- Physical exam over first 24 hours progressed to moderate encephalopathy with intermittent seizures noted on CFM despite prn ativan requiring 2 (10 mg/kg) Phenobarbital total but not maintenance doses.
- Physical exam slowly improved with residual mild hypotonicity especially around shoulder girdle.
- MRI scan with diffusion weighted images done on DOL# 6 read as normal.
Case #3 Clinical History

• EEG on DOL #5 – moderately abnormal, discontinuous with occasional sharp spikes.
• MRI on DOL #6 – read as normal
• EEG on DOL #7 – still abnormal with discontinuity, occasional spikes but improved.
• Metabolic Work-up = normal
Case #3 Clinical History

- Began feeding at 3 days of age.
- Nippling all feeds by 11 days of age and discharged home at 13 days of age.
- Readmitted at 3 ½ months of age with severe failure to thrive, developmental delay, irritability, abnormal tone
- MRI scan with global myelination delay
- Clinical Presentation, MRI consistent with Cerebral Palsy
Case #4

- 37 week gestation, 2920 gram male
- SVD, Apgars 8₁, 9₅
- Found unresponsive, apneic, limp at ~1h45min.
- Resuscitation included intubation, chest compression – did not require epinephrine
- Post-resuscitation pH=6.74, -28
- Clinical onset of seizures with < 1 hour
- Initial CT Scan = normal, EEG severe burst suppression
Case #4

- Baby transferred ~ 2 hours after insult for further eval and treatment.
- Exam at admission consistent with Sarnat stage 3 encephalopathy – Diffusely hypotonic, with intermittent myoclonus of extremities, absent gag, pupils unreactive, absent corneal reflex
Case #4  CFM
Case # 5

- 3338 gram 38 2/7 wk gestation female born by crash C/S shortly after mother’s arrival secondary to active vaginal bleeding from vasa previa and abruption and fetal bradycardia.
- Baby flaccid and pale at delivery. Resuscitation = immediate intubation, chest compressions x 5 minutes, 2 doses of epinephrine per ETT, volume resuscitation via low UVC with 25 ml/kg normal saline and 10 ml/kg PRBC’s (trauma blood) in delivery room.
- Apgars = 01, 05, 310, 415
- Cord gas: pH = 6.82, base deficit = 18.4
Case #5
Initial CFM trace from ~1 hour to 2 1/2 hours of age:
Case # 5

- Initial arterial blood gas at 1 hour of age: pH=6.95, pCO2 = 12, PO2= 21, bicarbonate = 2.6, base deficit = 29.5
- Other initial labs at 1 hour of age: Ionized calcium = normal, PT = 28.5, PTT = 120, Fibrinogen = 125, Fibrin Split Products > 160, platelet count = 196,000, hematocrit = 36, AST = 148, ALT = 77, Accucheck = 14, Blood pressure initial = 35/19 (24)
- Further management: UAC/UVC placement; 2ml/kg D10W bolus; 20 ml/kg PRBC’s for total of 30 ml/kg from delivery (with follow up hematocrit after = 38), 20 ml/kg FFP
Case #5

- Initial Exam at 30-60 minutes of age = pale, flaccid with only gasping respirations, no spontaneous movements. By 2 hours of age = pink, diffusely hypotonic, occasional spontaneous movements and intermittent eye opening. Intact pupil and gag reflex.
- Transferred to The Children’s Hospital for enrollment in to the “Head Cooling -Continuation Protocol Study”.
- Suspected seizures prior to transfer treated with Phenobarbital 20 mg/kg x 1 (given after initial CFM tracing completed).
Case # 5 - F/U CFM
Case # 5

- Follow up CFM tracing done at ~ 36 hours of age:
- No clinical seizures noted however so baby not treated with further anticonvulsants other than the initial 20 mg/kg Phenobarbital and 1 dose of Ativan.
- Head ultrasound normal at 1 day of life. Brain MRI normal at 5 days of life. Extubated at 5 days of life and initiated on feeds. Discharged home at 9 days of life with normal neurological exam, Breast feeding ad lib, on a small amount of supplemental oxygen and no meds.