AMPLITUDE INTEGRATED ELECTROENCEPHALOGRAPHY

The term amplitude integrated electroencephalography (aEEG) is used to denote a method for electro-cortical monitoring whereas cerebral function monitor (CFM) is used to refer to specific equipment.

The aEEG allows evaluation of long term changes and trends in electro-cortical background activity by simple pattern recognition.

aEEG is derived from raw EEG signals collected from scalp electrodes situated over the cerebral hemispheres.

Eligibility for cerebral function monitoring

1) **Infants ≥ 35 weeks with one or more of the following:**
    a) Evidence of encephalopathy
    b) Evidence of perinatal distress suggestive of hypoxic-ischemic encephalopathy (HIE)
    c) Seizures, definite or possible
    d) Paralyzed infants where there are concerns over potential HIE or seizures
2) **Other indications:**
    a) Meningitis requiring intensive care
    b) Evidence of extensive structural brain injury or serious congenital brain anomalies (eg cerebral infarction, congenital brain haemorrhage, tumour, hydrocephalus)
3) **preterm infants:**
    a) aEEG is less easy to interpret in preterm infants. Nevertheless monitoring may provide useful information and should be considered in the following situations:
        i. Suspected seizures
        ii. Encephalopathy
        iii. Grade 3 or 4 intraventricular haemorrhage (IVH)

When should monitoring be commenced?

- For suspected HIE commence monitoring as soon as possible and preferably before commencing sedative or anticonvulsant drugs.
- Early application will help facilitate a reliable baseline
- CFAM should preferably be obtained before 6 hours (ideally a precooling trace).

Electrode placement and recording

See guides to CFM set-up in Equipment Guidelines

For term babies use disposable needle electrodes with small drops of colloidon to secure them at the entry point. When inserting the needles aim sub-dermally and towards the back of the head so the leads come anteriorly

from a hat that can be placed to keep the electrodes lying flat against the head. Secure the leads to the hat.

Needle electrodes are usually easy to keep in for long durations but they have some disadvantages including discomfort on insertion and removal, potential risk of infection, needle-stick injury to staff and potential puncture of the cooling mattress.

Gel electrodes are used for preterm babies.

Routine use of two channel recording is recommended. Although there are no major differences between seizure detection with one or two channel aEEG, two channel aEEG provides additional information for unilateral brain lesions. Attention should be paid to correct placement and it is important to keep away from muscles in the scalp area. Needle electrodes in muscle will pick up EMG and cause an aberrant aEEG.

For how long should cerebral function monitoring be continued?

Generally continue monitoring until the patient has clinically stabilized with no risk of further cerebral insult. Aim for the following:

- background recording normalised and stable for 24 hours
- no seizures for 12–24 hours
- for infants with HIE that have been cooled monitor for the first 4 days. A further 4-6 hour recording may be useful on day 7 in conjunction with a documented clinical neurological examination. The CFAM remains on during rewarming.

Interpretation and classification of aEEG

The raw electrical signal (EEG) is collected directly from the electrodes and displayed in real time by the CFM. The EEG is rectified and compressed by the monitor to produce an aEEG trace. The trace reflects variations in minimum and maximum amplitudes of EEG wave forms. EEG processing attenuates activity below 2Hz and above 15Hz.

One hour of EEG is compressed to form 6 cm of aEEG trace. The amplitude display is linear between 0 and 10 microvolts and logarithmic between 10 and 100 microvolts. This semi-logarithmic display enhances identification of changes in low-voltage activity and avoids overloading the display at high amplitudes.

It is important to inspect the raw EEG especially when identifying seizure activity, artefacts and looking for background patterns such as burst suppression. A standard EEG is recommended to support clinical decision making and confirm interpretation of difficult aEEGs or to help exclude artifactual traces.

It is important to accurately interpret, classify and document aEEG findings. Assessing aEEG over time is the key to assigning prognosis.

It is recommended that the EEG and aEEG tracings are reviewed at each ward round. For term babies with HIE a record of neurological and aEEG findings should be recorded during cooling at 6, 24 and 48 hours and again after rewarming.

aEEG may be interpreted and classified according to voltage limits or pattern recognition of background activity. There is a move towards the more descriptive classification as it can be used for all gestations and it is more in keeping with EEG terminology.

1) aEEG classified according to upper and lower voltage limits (Naqueeb et al):

Classification	**Voltage limits**
Normal	Lower limit>5 µV and upper limit>10 µV
Moderately abnormal	Lower limit<5 µV and upper limit>10 µV
Severely abnormal	Lower limit<5 µV and upper limit<10 µV

2) aEEG classified according to pattern recognition of background activity (Toet *et al*.):

- **Continuous normal voltage with sleep-wake cycling**. Continuous background activity with voltage 10–25µV, with the band of aEEG activity altering in width, indicating cycling of sleep stages.
- **Continuous normal voltage**. Continuous background activity, voltage 10–25 µV but without sleep stages.
- **Discontinuous normal voltage**. Discontinuous trace, voltage predominantly >5 µV.
- **Burst suppression**. Discontinuous trace with periods of very low cortical activity (<5µV), intermixed with bursts of higher amplitude.
- **Continuous low voltage**. Continuous background pattern of very low voltage (around or below 5 µV).
- **Flat tracing**. Mainly inactive (isoelectric tracing) of extremely low voltage (<5 µV).

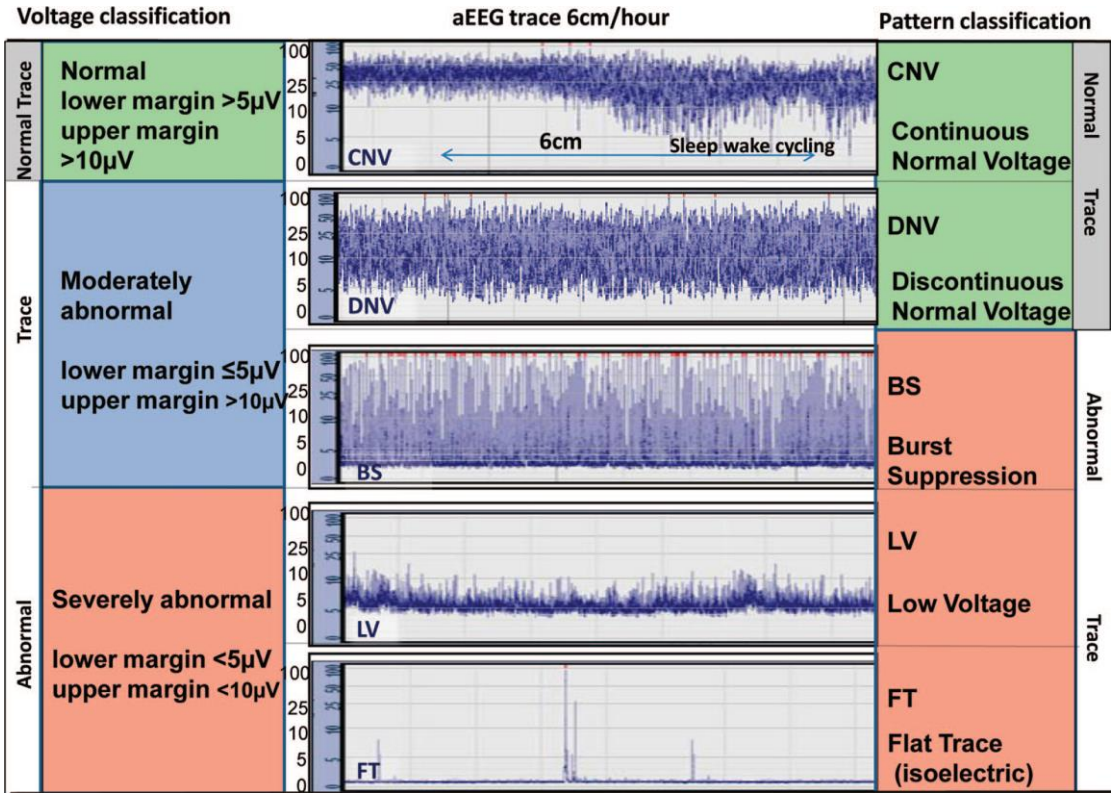

Figure 1: Classification of aEEG using voltage and pattern recognition methods

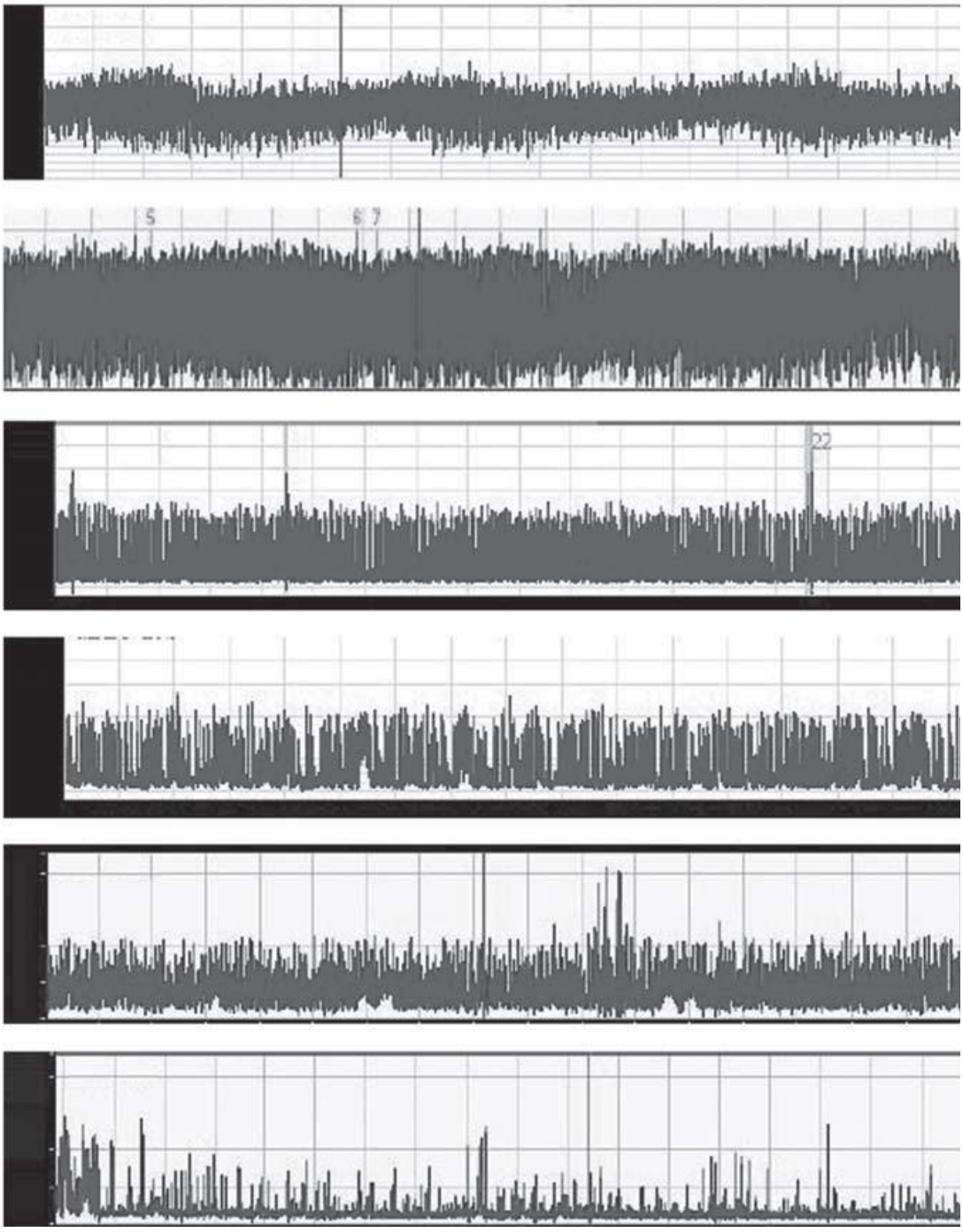

Figure 2: Examples of aEEG background activity patterns:
(a) Continuous background pattern, with prominent SWC: upper-margin voltage is >10 mV and lower margin voltage is >5 mV.
(b) Discontinuous background pattern: upper margin is >10 mV and lower margin is <5 mV.
Burst suppression pattern: upper and lower margin voltages are <10 and <5 mV,
respectively, with >100 bursts per hour (c) and <100 bursts per hour (d).
(e) Continuous low voltage: upper margin is <10 mV and lower margin is <5 mV. Occasional
spikes are seen over 10 mV.

(f) Isoelectric or flat tracing: both margins are <5 mV and prominent spikes are likely due to patient movement. aEEG, amplitude-integrated electroencephalography

Sleep-Wake Cycling

Sleep-wake cycling (**SWC**)**:** A normal finding in the aEEG, characterized by smooth sinusoidal variations, mostly in the minimum amplitude. Broader bandwidth represents discontinuous background activity during quiet sleep, and narrower bandwidth corresponds to the more continuous activity during wakefulness and active sleep. SWC can be seen from the gestational age of 29 weeks.

- **No SWC**: No cyclic variation of the aEEG background
- **Imminent/immature SWC**: Some, but not fully developed, cyclical variation of the lower amplitude; not developed as compared with normative gestational age-representative traces
- **Developed SWC** Clearly identifiable sinusoidal variations between discontinuous and more continuous background activity, with cycle duration >20 min

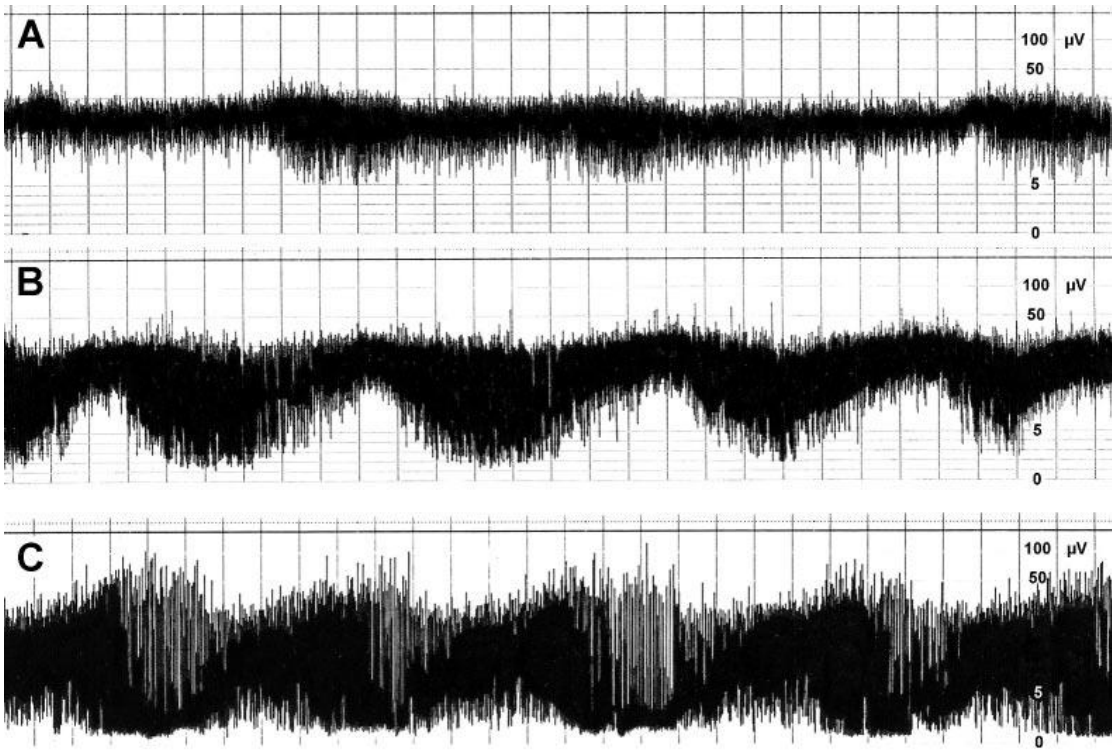

Figure 3: Sleep wake cycling patterns
A, Normal SWC. SWC on a CNV background pattern, with the lower margin of the bandwidth >5µV. Cycle period is unusually prolonged in this sample. B, Normal SWC (suboptimal variant). The lower margin of the bandwidth is <5 µV during quiet sleep. C, Abnormal SWC. SWC on a discontinuous background pattern, with the lower margin of the bandwidth <5µV at all times.

Seizures

Epileptic seizure activity is usually seen in the aEEG as an abrupt rise in the minimum amplitude and a simultaneous rise in the maximum amplitude, often followed by a short period of decreased amplitude. The raw EEG should show simultaneous seizure activity, with a gradual build-up of high amplitude waves and then decline in frequency and amplitude of repetitive spikes or sharp-wave or activity with duration of at least 5 to 10 seconds. Status epilepticus is defined as ongoing seizure activity for >30minutes.

Note on seizures: Only one third of electrographic seizures have overt clinical signs.
Neonatal seizures tend to be over-diagnosed by aEEG and standard EEG confirmation prior to implementing treatment therapy may be considered if readily available.

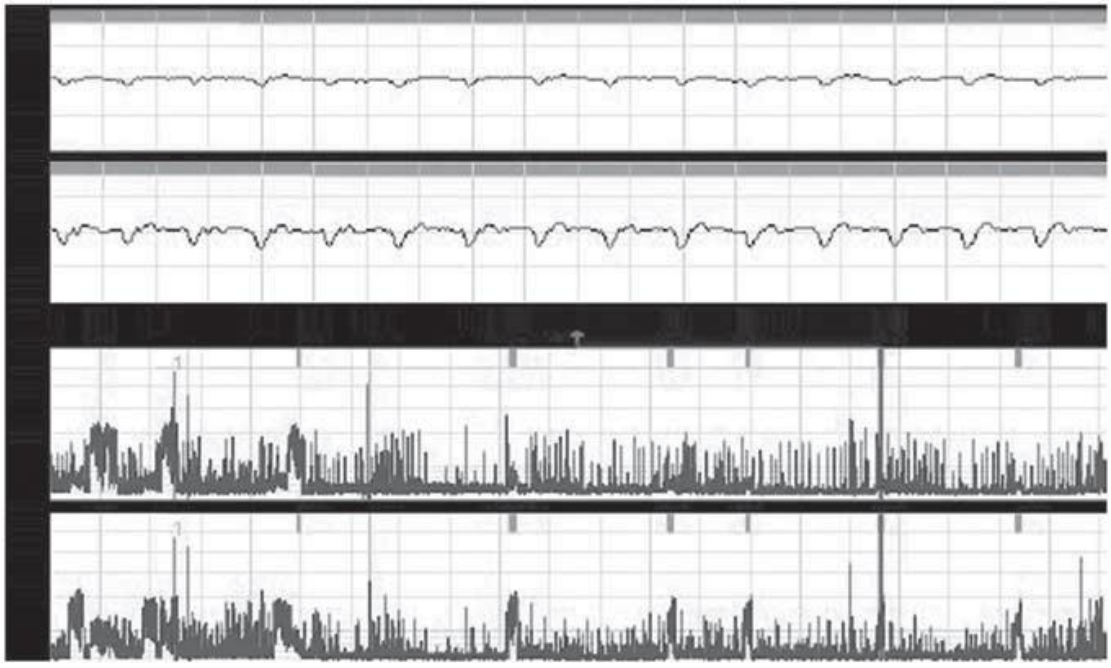

Figure 4: Several discrete seizure episodes on a background of burst suppression; seizures clearly show an abrupt rise in both upper and lower margins.

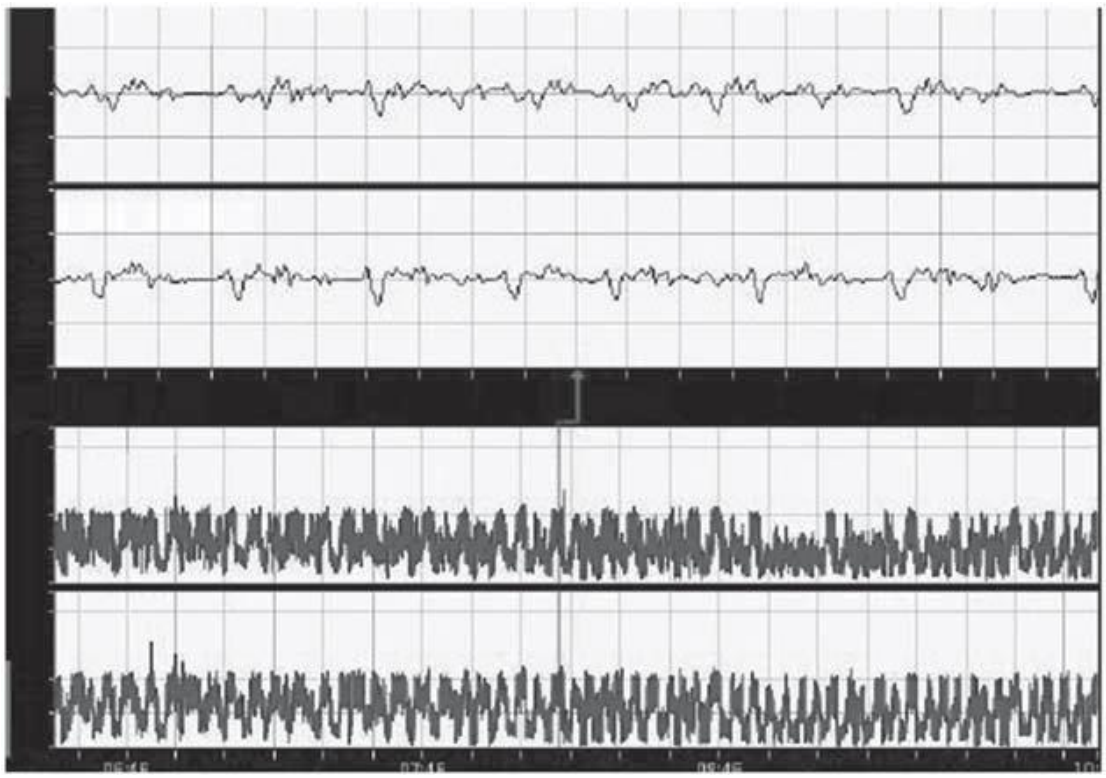

Figure 5: Status epilepticus: multiple marked seizure events dominating nearly the entire tracing.

Artefacts:

Impedance: A measure of how good the contact is between the electrode and the scalp. Loss of contact will cause aEEG artefact. Impedance is measured in Ohms (Ω). <5 Ω is good and 5 to 10 Ω is acceptable.

Inspecting the impedance and raw EEG will help in identifying artefact. General movement or loss of contact will result in a disorganised appearance on the raw EEG with a huge variance in voltage in the aEEG trace which may be suggestive of a seizure. Documentation of cares, change in head position and procedures are of great value in the post hoc evaluation of the aEEG.

Artifact on aEEG traces may mimic seizure activity with an upward shift of baseline voltage. The raw EEG in seizures shows repetitive rhythmical spike and wave discharges. The fine toothed rhythmical activity of HFOV and EMG should be easy to identify. ECG activity on raw EEG can be seen in synchrony with the ECG trace.

Rarely a ventilated infant with continuous gasping will have an aEEG trace consistent with burst suppression. The true background activity if revealed by a muscle-paralysing drug may in fact be a flat trace.
aEEG artefact may also be recognised as baseline drift. Here the baseline tracing becomes falsely elevated in the setting of a previously severely suppressed background activity. The rise in baseline above 5 microvolts may be mistaken as a reassuring sign. Baseline drift may be due to extracranial

activity. Sometimes head turn results in electrodes being pressed into the bed causing an unintentional mechanical contact.

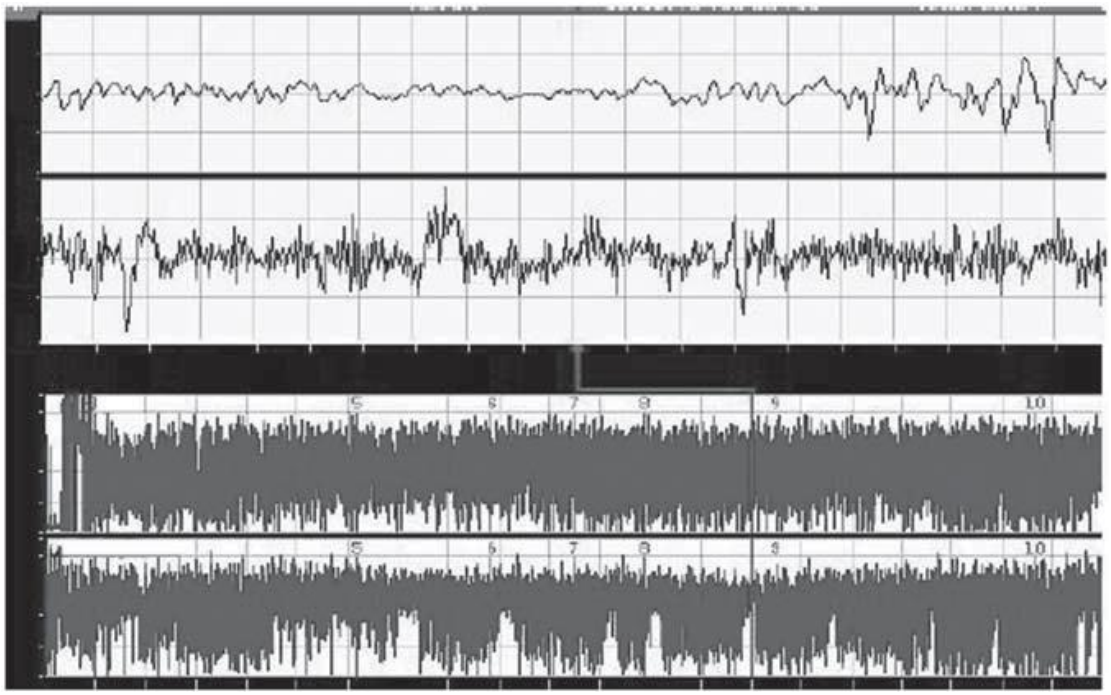

Figure 6: High-frequency oscillatory ventilation (HFOV) may cause significant artefact resembling seizures. Correlation with the raw electroencephalography (EEG) tracing above is essential.

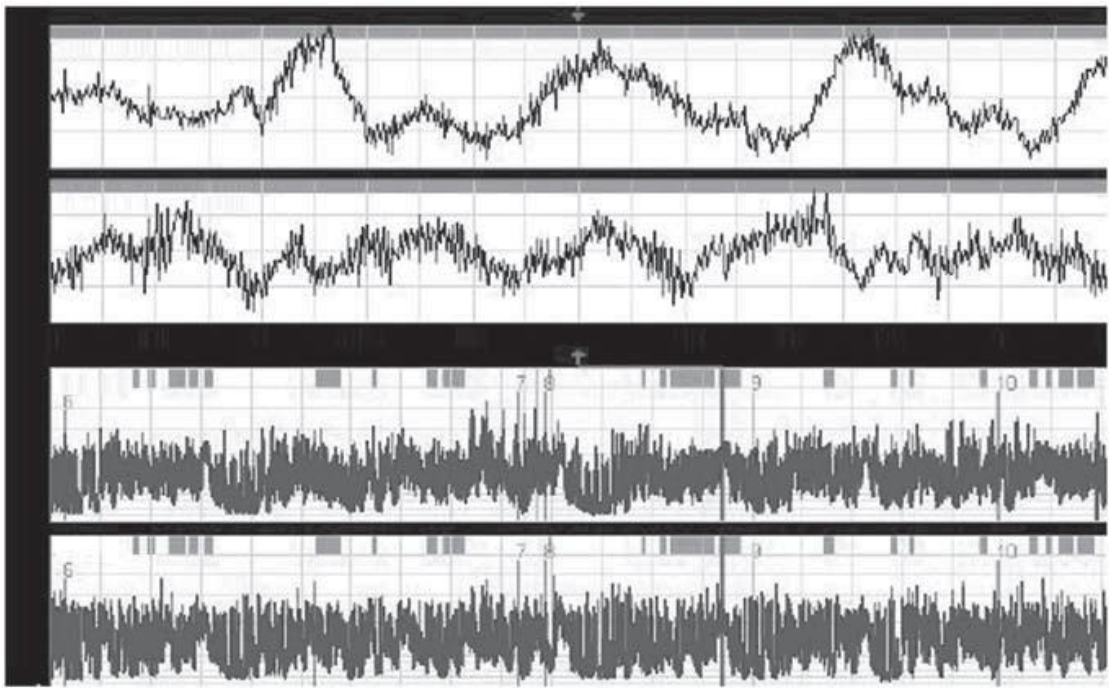

Figure 7: A similar effect is seen from muscle artefact in both hemispheres

<u>Effect of drugs on aEEG:</u>

Administration of morphine, phenobarbitone and midazolam may depress aEEG activity. Prolonged and severe depression is likely to indicate more severely compromised cerebral function. Hypothermia in the therapeutic range has no effect on the aEEG. It may prolong recovery and delay the onset of sleep wake cycling probably due to prolongation of the half-life of anticonvulsant and sedative medications.

Role of aEEG in preterm infants:

Hydrogel electrodes are recommended for use in preterm infants and should be gently removed using Appeel. The use of subdermal needles is strongly discouraged.

aEEG may prove useful in some situations:

1) Infants with IVH: IVH grades 3 and 4 may show decreased continuity, lower voltage patterns and more seizures. The presence of burst suppression has been associated with death and poor outcome at 2 years.
2) Infants with abnormal movements
3) Post-haemorrhagic ventricular dilatation. Infants with PHVD may show burst suppression and decreased continuity even before signs of increased intracranial pressure become apparent. These changes are seen to resolve with CSF drainage.
4) Sequential recordings: Short weekly recordings may provide information on brain development and maturation of function. Continuity of EEG increases with gestational age in the preterm population without brain injury. This maturation can be a sign of healthy brain development. The presence of continuous background activity with sleep wake cycles within the first postnatal week has been associated with a good neurodevelopmental outcome. Dysmaturity (or no maturation) may be a sign of brain injury and altered brain function and may identify vulnerable infants.

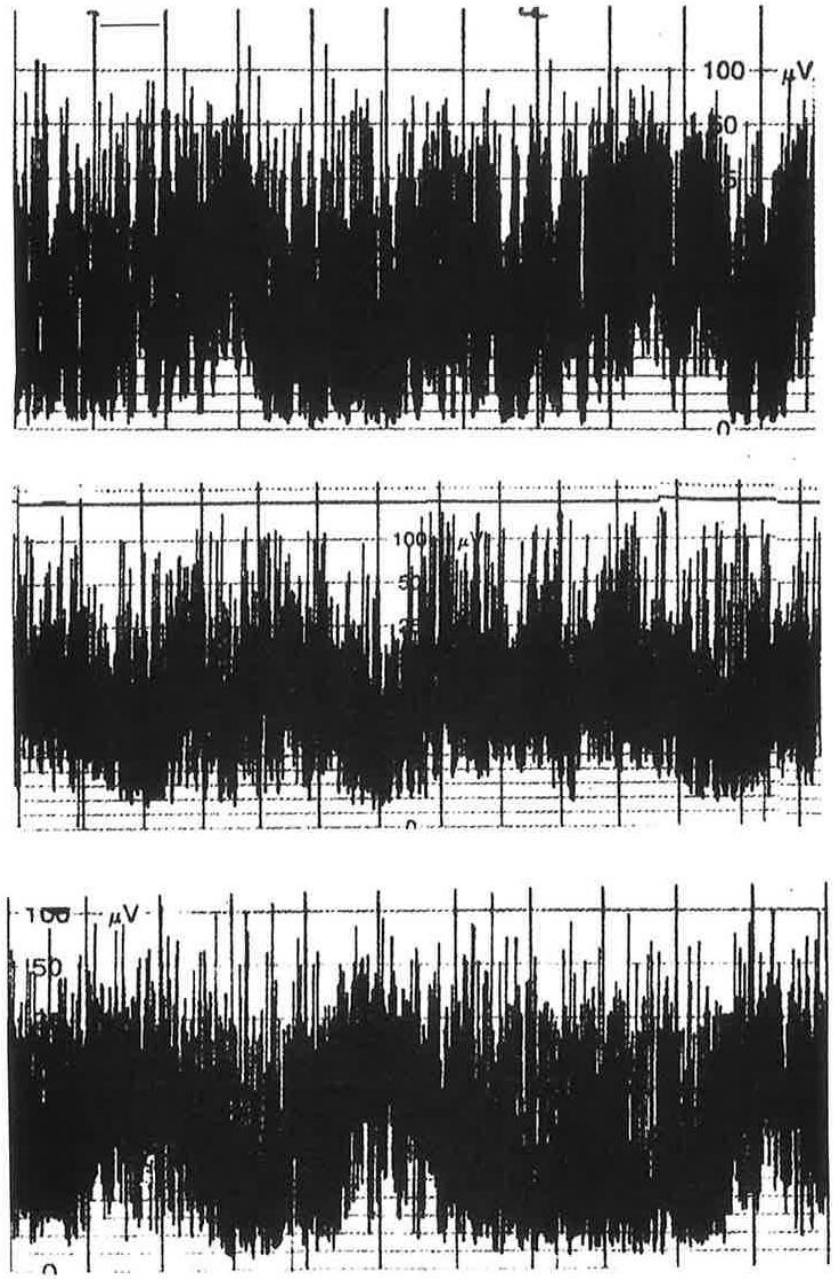

Figure 8: aEEG in extremely preterm infants

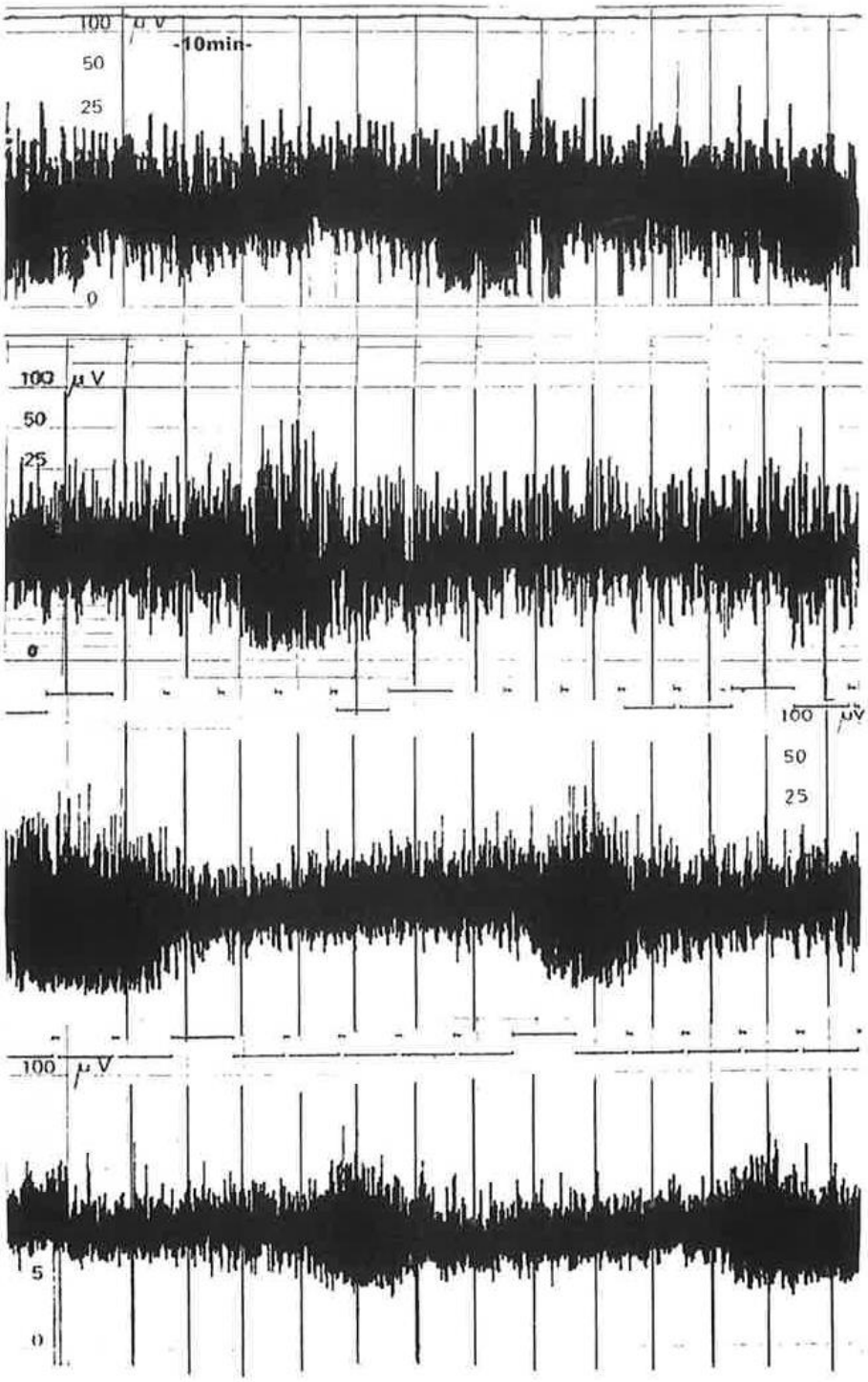

Figure 9: Normal development of aEEG in infants from 31 to 37 weeks' gestation

Prognosis

aEEG patterns in the first days of life have been shown to correlate well with later neurodevelopmental outcome.

Progress of abnormal aEEG background patterns are associated different outcomes in term HIE (adapted from Hellström-Westas et al., 2006)

Age of assessment	Background Pattern	Outcome
6 hours	Continuous with SWC	Good prognosis – consider rewarming
	Discontinuous	High chance of a normal outcome if recovers within the first 6–12 hours
	Burst suppression	Risk of poor outcome. If normal by 12 to 24 hours, 60% mild or no disability
	Low voltage / Flat trace	Severely abnormal outcome
48 hours	Continuous with SWC by 12 to 24 hours	Good outcome possible: 97% if clinically moderate HIE 91% if moderate to severe 75% if severe
	Burst suppression Low voltage / Flat trace	Severely abnormal outcome (death or major handicap). 73% if clinically moderate HIE 89% if moderate to severe 96% if severe

Notes on Prognosis:

1. The combination of the abnormalities in both the neurological examination performed within 12 hours after delivery and the aEEG yield the highest specificity and positive predictive value (94% and 85% respectively) for the short term outcome in HIE.
2. SWC is considered to reflect brain integrity. The presence, time of onset and quality of SWC are influenced by the degree of hypoxic-ischemic insult. A good neurodevelopmental outcome is associated with early onset and normal SWC.
3. Early recovery of an initially abnormal aEEG background pattern is of predictive value.
4. A poor background pattern seen within the first 6 hours after birth predicts a poor outcome with a positive predictive value of 86% and the onset of SWC after 36 hours after birth predicted a poor outcome.
5. When considering a burst suppression trace, the number of bursts per hour during the first 24 to 48 hours after birth seems to be of predictive outcome. Fewer bursts on aEEG and longer inter burst intervals on raw

EEG tend to indicate a worse outcome in HIE and preterm infants with grade 3 or 4 IVH.

6. Burst Suppression, Low Voltage, or Flat Trace in the first 48 hours following an IVH Grade 3 to 4 in a preterm infant is associated with severe handicap or death.

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