

Cerebral function monitoring in term or near term neonates at MDH: preliminary experience and proposal of a guideline

Stephen Attard, Doriette Soler, Paul Soler

Abstract

Introduction: Cerebral function monitoring (CFM) is a simplified EEG device that is used to monitor cerebral function at the cot-side. Various studies have shown its value in detecting neonatal encephalopathy and electrographic seizures, prognostication of neonatal cerebral insults, assessment of response to anticonvulsant therapy and in selecting encephalopathic infants for therapeutic hypothermia. This paper describes our preliminary experience with this monitoring device at Mater Dei Hospital, and a draft of a protocol for its clinical application.

Methods: Fourteen recordings were performed on neurologically normal and abnormal term neonates. The quality of the records and their correlation with other imaging and standard EEG findings was assessed. A dataset including technical and clinical particulars of these cases was then compiled, analyzed and discussed.

Results: Amplitude aEEG traces were recorded from a total of 14 patients, 4 of whom were normal term or near term infants, and 10 were infants with a neurological abnormality.

All records were of satisfactory quality, and all showed very high impedance levels. Five out of 11 neurologically-abnormal patients had signs of seizure activity on CFM. A technical fault caused high impedance level in the first 2 traces. Annotations were generally lacking. Five out of 10 infants with CNS problems had clinical seizures of which 4 had electrographic seizures on CFM, 4 had electrographic seizures on formal EEG, and 3 had abnormal MRI findings.

Conclusion: Our local experience has confirmed the usefulness of CFM monitoring in the setting of a neonatal intensive care unit. Despite some initial problems with high impedance levels and electrode attachment, the tracings obtained were reproducible and of good quality. Almost half of the neurologically-abnormal neonates showed signs of seizure activity on CFM with good correlation with clinical and standard EEG. The timely diagnosis enabled the clinicians to confirm seizure activity, initiate anticonvulsant therapy and monitor the response. Staff training is vital in order to improve utilisation of CFM in neonatal practice.

Background

Neonatal Encephalopathy (NE) is a clinically defined syndrome of disturbed neurological function in the earliest days of life in term infants, manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, subnormal level of consciousness and often seizures. Although hypoxic-ischaemic insults remain a distinct and important cause, NE can be a result of various other causes and continues to be a major problem in neonatal practice.

Clinical assessment using Sarnat staging remains the method of choice for the clinical assessment of degree and prognosis of NE.¹ This can however be difficult to carry out reliably due to certain factors like muscle paralysis and the effects of anticonvulsant drugs.

Standard electroencephalography (EEG), continuous two-channel EEG and cerebral function monitoring (CFM) have all been studied, and are used to assess the functional integrity of the neonatal brain. Khan et al 2008 assessed the predictive value of sequential EEG in neonates with seizures and its relation to neurological outcome. Results showed that as compared to single EEGs, sequential EEG in neonates with seizures had greater predictive value for outcome of NE in terms of neurodevelopmental delay, epilepsy, and postnatal death. In addition, abnormal background activity (defined as

Keywords

Neonatal encephalopathy (NE); amplitude-integrated electroencephalography (aEEG); electroencephalography (EEG); cerebral function monitoring (CFM); neonatal and paediatric intensive care unit (NPICU)

Stephen Attard* MD, MRCPCH
Paediatric Department,
Neonatal and Paediatric Intensive Care Unit
Mater Dei Hospital, Tal-Qroqq, Malta
Email: stephen.attard@gov.mt

Doriette Soler MD, MRCP
Paediatric Department, Mater Dei Hospital, Tal-Qroqq, Malta
Email: doriette.m.soler@gov.mt

Paul Soler MD, MRCP
Neonatal and Paediatric Intensive Care Unit
Paediatric Department, Mater Dei Hospital, Tal-Qroqq, Malta
Email: paul.r.soler@gov.mt

*corresponding author

the prevailing cortical electrical activity) on a single EEG record had a greater prognostic power than other abnormal findings like epileptic activity or abnormalities in the organisation of sleep state. This finding inspired the development of a CFM as a real-time monitoring device using amplitude-integrated EEG (aEEG).²

Aims

This study had two main aims. We were interested in describing our practical experience and the problems we encountered while recording and interpreting our first few aEEG traces. We then used these observations to draft a protocol for the local use of CFM at NPICU.

Methods

A small number of neonates were selected from NICU admissions at Mater Dei Hospital in 2009: (a) term or near-term neonates without any CNS problems, and (b) term neonates with neurological problems mainly HIE, seizures and other neurological problems. These were selected randomly by PS or SA with parental consent and CFM leads were attached by SA who also closely supervised these recordings. Verbal and practical instructions were given to all nurses caring for these infants.

Single-channel CFM recordings were performed using the *NicoletOne* monitor (Viasys Healthcare). Three 1 x 1 cm areas of scalp were first cleaned with alcohol wipes and LemonPrep™ to maximize electrical conduction. Gold-plated re-usable electrodes were placed over the right and left parietal areas (P3 – P4) or frontal areas (F3 – F4) according to the 10 – 20 system. Two other electrodes corresponding to the reference and neutral electrodes were placed over one or other frontal area. Standard conductive gel (Electro-Gel™) was used to minimise electrical impedance and the electrodes were secured using standard skin

tape and head caps as appropriate. No electrodes were placed over any fontanelle (Figure 1). No needle electrodes were used as it was not deemed suitable to use invasive electrodes for the purposes of this study. The leads were connected to a 16 channel NicoletOne pre-amplifier (C16050143-1 issue 07) that was connected to NicoletOne monitor. Readings of impedance were taken prior to starting any recording aiming for impedance <10mΩ. The trace was recorded at an optimal speed of 10cm/20 min, but being a digital system this could be reviewed at different 'paper-speed' and adjusted at all times. Clinical events, seizures and procedures requiring change of head position or disturbance of scalp electrodes were annotated using an event button or via the monitor touch-screen. Electrode placement, impedance, presence of artefacts and significant CFM signs were checked regularly as appropriate.

CNS-normal neonates were monitored for 3 to 24 hours, while neurologically-abnormal neonates were recorded for up to 3 days, depending on the clinical situation. The traces were displayed in the form of standard single-channel CFM traces showing a semi-logarithmic amplitude and impedance bar together with the corresponding raw EEG signal. Records of all infants with CNS problems were reviewed daily and print-outs of representative samples of all CFM traces were inserted in the patients' files. A dataset comprising details of history and diagnosis, CFM traces, standard EEG and neuro-imaging findings (cranial ultrasound and/or brain MRI) was compiled.

Results

Fourteen infants were selected from all the NPICU admissions during the year 2009. They were all term neonates except for one 34 week gestation preterm infant. Four had non-CNS related conditions, while 10 had CNS abnormalities.

Details of the 4 neonates with non-CNS related conditions are shown in Table 1. Two had mild to moderate respiratory

Table 1: Details and CFM results of the four infants without CNS disorders

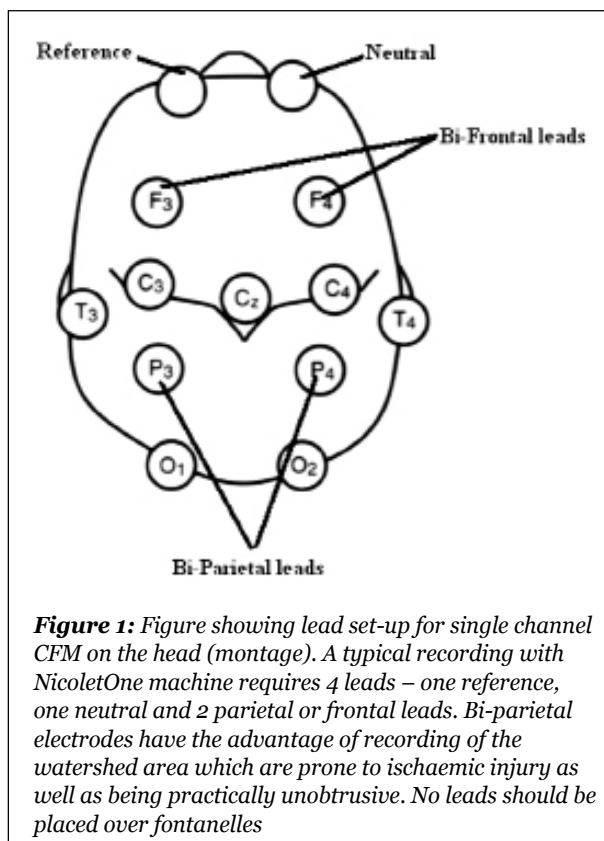
Patient No.	Diagnosis	Findings
1	Term infant with transient tachypnoea of the newborn; Infant of diabetic mother	16 hour recording on day 2 Satisfactory quality; High impedance Normal amplitude aEEG Artefacts detected
2	34 week gestation premature infant. Breastfeeding.	3 hour recording on day 1 Satisfactory quality, high impedance Normal amplitude aEEG Muscle artefacts detected
3	Term neonate with mild respiratory distress syndrome on nasal CPAP. Hungry and active.	12 hour recording on day 2 Satisfactory quality, normal impedance Normal amplitude; sleep / wake cycles seen Artefacts during nursing detected
4	Term neonate with congenital lobar emphysema	4 hour recording on day 3 Satisfactory quality; normal impedance Normal amplitude aEEG Artefacts during nursing detected

Table 2: Data relating to the infants with CNS abnormalities

Patient No.	Diagnostic information	Cerebral ultrasound / MRI results	EEG results	CFM findings
5	Term neonate with HIE grade II secondary to tight cord round neck. Apgars 4, 8, 9. Cord gas not available. Multi-focal seizures at 30 hours without desaturation. Discharged on day 9. On review at 4 months of age, the infant was seizure-free and was making normal developmental progress.	US on day 2 -Normal MRI brain at 6 weeks – thin corpus callosum only	Day 2. Normal background activity. Left fronto-central electrographic discharges.	20 hour recording on day 2. Satisfactory quality. Normal aEEG amplitude. Normal impedance. Appropriate annotations. Seizure activity detected, correlating with clinical clonic seizures of upper and lower limbs and facial twitching.
6	Term neonate with precipitate delivery and foetal bradycardia. HIE grade I. Apgars 3, 7. Bag mask valve ventilation for a few minutes. Cord pH 6.99, BE -16. Opisthotonic in first few hours. Short episodes of opisthotonic posturing and oxygen desaturation to 60%. Discharged on day 3. On review at 6 months of age, there was normal developmental progress.	US brain on day 3 and at 6 weeks - normal	Not done (rapid improvement)	3 hour recording on day 1. Satisfactory quality. Normal aEEG amplitude. Normal impedance. Poorly annotated. No signs of seizure activity.
7	Term infant with congenital hydrocephalus requiring external ventricular shunting. No clinical seizures. The child died from septicaemia.	Obstructive hydrocephalus.	Normal	4 hour recording on day 2. Satisfactory quality. Normal aEEG amplitude. Normal impedance. Appropriate annotations. Normal amplitude. No signs of seizure activity.
8	Term neonate with HIE grade III secondary to cephalo-pelvic disproportion. Needed CPR on delivery. Developed repeated seizures and in the first 2 days of life requiring mechanical ventilation. On review at 6 months of age, the infant was seizure-free, but there were signs of global developmental delay and early signs of a motor disorder.	US brain – normal. MRI brain – Bilateral internal capsule infarcts	Focal electrographic seizures over the right central and temporal area	3 hour recording on day 1. Satisfactory quality. Normal aEEG amplitude. Normal impedance. Lacking annotations. Electrographic seizure activity seen.
9	Term neonate born by emergency section for severe foetal distress. Perinatal asphyxia without clinical signs of encephalopathy. Cord gas – pH 7.03, BE -13. Apgars 6, 7, 9.	Normal US brain day 1.	Normal on day 3	6 hour recording on day 1. Satisfactory quality. Normal aEEG amplitude. Normal impedance. Lacking annotations. No seizures seen.
11	Term neonate with HIE grade II secondary to shoulder dystocia. Cord gas – pH 7.21, BE -8.3. Apgars 3, 3, 7. No seizures. Mild left arm neurapraxia with good recovery.	Normal on day 2	Normal on day 4	22 hour recording on day 1 – 2. Normal aEEG amplitude. Normal impedance. Lacking annotation. No seizure activity. ECG artefacts were seen.

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Patient No.	Diagnostic information	Cerebral ultrasound / MRI results	EEG results	CFM findings
12	Right congenital middle cerebral territory infarct presenting with neonatal seizures	US brain: Abnormal echogenic area right side. MRI brain: extensive old right sided infarct involving right basal ganglia and a recent extensive left sided infarct involving left basal ganglia	Attenuated background activity over the right hemisphere; Electrographic focal discharges over the left fronto-central area	12 hour recording on day 2. Normal aEEG amplitude. Normal impedance. Appropriate annotations. Occasional electrographic seizures seen.
13	Precipitate delivery with HIE grade I. Apgars 7, 9. pH 7.3. BE -4.5. Improved rapidly. No seizures.	Normal on day 1	Normal on day 3	4 hour recording on day 2. Normal aEEG amplitude; Normal impedance. Appropriate annotations. No seizures seen
14	Term neonate with foetal bradycardia and HIE grade I. Cord gas pH 6.98, BE -23. Apgars 4, 8. Rapid recovery.	Normal on day 1	Not done	6 hour recording on day 1. Normal aEEG amplitude; Normal impedance. Lacking annotations. No seizures seen
15	HIE grade III. Cord pH 6.8. Ventilated. Renal impairment and heart failure.	Normal brain ultrasound, Brain MRI not done	Left fronto-central discharges	8 hour recording. Normal aEEG voltage. Normal impedance. Lacking annotations. Frequent electrographic seizures.



distress, one was a normal 34 week gestation infant and 1 had congenital lobar emphysema. They all had satisfactory CFM recordings for 3-16 hours showing normal aEEG amplitude. One showed clear sleep/wake cycles (Figure 2). The first two records showed very high impedance that turned out to be due to a fault in the neutral input of the pre-amplifier. After replacing the pre-amplifier, this problem did not recur.

The group of 10 neonates with CNS problems were the following (Table 2): 8 infants had NE secondary to perinatal asphyxia, 1 had congenital hydrocephalus: 1 presented with perinatal ischaemic stroke. Although annotations were again generally lacking, we could still manage to correlate most of the major clinical and CFM events. Of these 10 infants with CNS problems, 5 had clinical seizures on CFM recording, 4 of these 5 infants had signs of electrographic seizure activity (Figure 3). On formal EEG, 4 infants had focal electrographic seizure activity and 4 had normal EEG findings. EEG was not performed in 2 patients, because of rapid clinical improvement. MRI brain was performed in 4 of these 5 infants, 3 showed abnormal findings in keeping with HIE (2 infants) and Perinatal Ischaemic Stroke (1 infant). The 5th patient had a normal MRI.

Table 3: Data showing how aEEG traces at 48 hours can refine the prognostic prediction of outcome in hypoxic-ischaemic encephalopathy (adapted from Allen WC, 2002).⁴

	Mild (Sarnat 1)	Moderate (Sarnat 2)	Moderate to severe	Severe (Sarnat 3)
Mental Status	Hyperalert	Lethargic	Lethargic	Comatose
Need for Ventilator	No	No	Yes	Yes
Feeding Problems	Mild	Moderate	Moderate	Severe
Tone	Jittery	High	High	Flaccid
Seizures	No	Yes	Yes	Yes (early)
Empirical probability of severe handicap or death based solely on clinical grading *	< 1%	25%	50%	75%
		Odds of 1:3	Odds of 50:50	Odds of 3:1
Probability of severe handicap or death if aEEG IS severely abnormal †		73%	89%	96%
		Odds of 2.7:1	Odds of 8:1	Odds of 24:1

† From Allan WC (2002) compiled from pooled data analyses of infants (n=411) in multiple studies of EEG and showing predicted outcome and odds ratios for EEG or aEEG performed at ~48 hours postnatal. Severely abnormal EEG in these studies referred to low voltage, electrocerebral inactivity, or burst suppression patterns.
* from Levene MI, et al. (1986) using Sarnat & Sarnat classification of HIE.

Discussion

Single-channel aEEG is acquired from two active bi-parietal or bi-frontal electrodes in relation to one reference lead. The signal is amplified and passed through an asymmetrical band pass filter that strongly attenuates activity below 2Hz and above 15Hz in order to minimise artefacts while enhancing clinically relevant low amplitude activities <5µV. Semi-logarithmic amplitude compression, rectification, and time compression are then carried out through additional processing. aEEG amplitude is then plotted on a semi-logarithmic scale on the Y axis against time on the X axis at slow speed (6cm/h) at the cot side. Many commercially available CFM monitors also show raw EEG signal in real-time.

Rationale for the use of CFM in NICU

It has been established that in conjunction with neurological examination, CFM is a powerful tool for the assessment, management and prediction of prognostic category of infants with neonatal encephalopathy. It has been shown that CFM patterns in the first few days of life correlate well with later neurodevelopmental outcome. Very abnormal traces in the first 6 hours after birth define a group of infants at highest risk for death or survival with disability. Conversely, infants who show continuous normal voltage or discontinuous normal voltage patterns (without seizures) in the first 6 hours are likely to survive without sequelae.³

Use of CFM monitoring to refine prediction of prognosis in HIE

CFM is a useful tool when confronted with difficult decisions regarding continuation or withdrawal of intensive care. A normal or normalising aEEG is very reassuring, and in the context of an infant with respiratory failure with a history of episodes of hypoxic ischaemia, would suggest that neurological recovery may still be possible, and therefore continuation of intensive care is worthwhile.⁴

In infants with moderately severe HIE clinically, a severely abnormal EEG suggests a poor prognosis. However, spontaneous recovery of aEEG patterns that were severely abnormal in the first few hours of life is not uncommon⁵, and such an early aEEG may reflect transient dysfunction without permanent brain injury. In one study, 6 out of 65 with a severely abnormal aEEG tracing done at <6 hours of birth, achieved recovery to a continuous normal background pattern within the first 24 hours. Sixty percent of these survived with or without only mild disability.⁶

Table 3 shows how the finding of the presence or absence of a severely abnormal aEEG tracing alone at around 48 hours from birth helps to refine the prediction of prognosis for infants with HIE as compared with relying only on the clinical features of HIE.

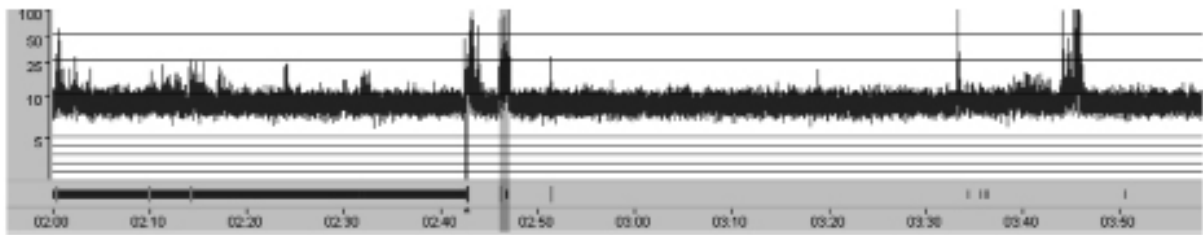


Figure 2a: This figure shows a typical normal CFM trace with an upper border voltage of $>10\mu\text{V}$ and a lower border voltage $>5\mu\text{V}$. There are no sleep-wake cycles in this trace. The black horizontal bar shows high impedance level. A few spiky changes are seen that are due to movements or nursing care, hence the importance of proper annotation

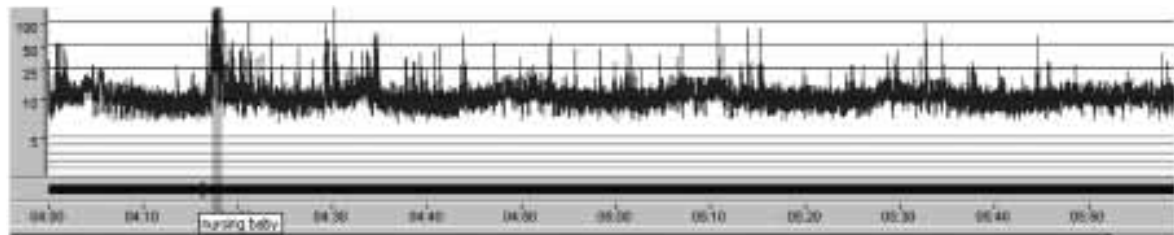


Figure 2b: This figure shows a normal CFM trace. An undulating baseline indicates the presence of sleep-wake cycles (physiological feature). A typical annotation is also shown

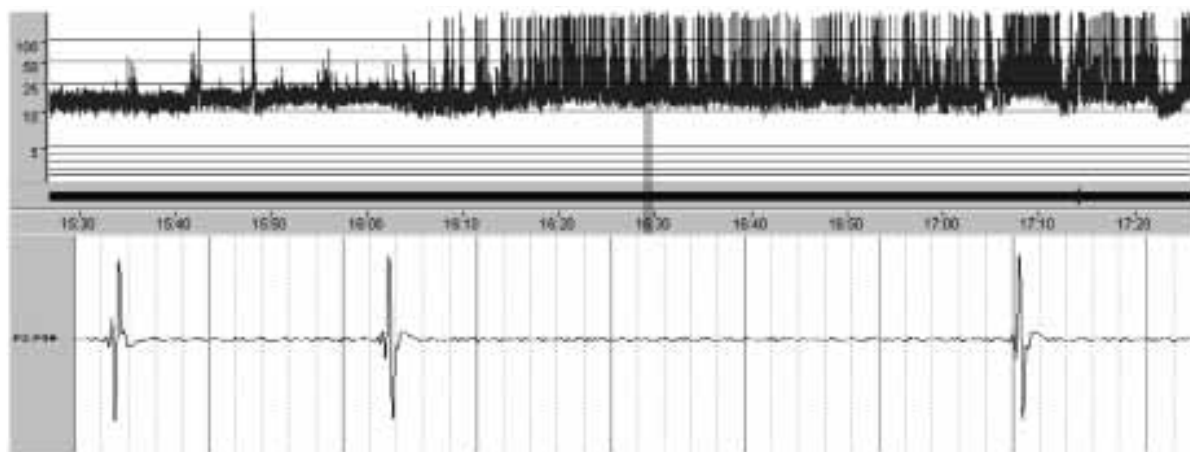


Figure 2c. This figure shows a normal CFM trace associated with intermittent ECG artifact. The lower figure shows the raw EEG pertaining to the portion of aEEG denoted by the vertical bar in the upper figure at 16.30. Reviewing CFM with raw EEG is a useful feature of NicoletOne monitor. This can for example help differentiate between artifacts and genuine abnormalities

Role of aEEG in therapeutic hypothermia

CFM has an established role in the identification of candidates for therapeutic hypothermia.⁷ It is worth noting that although it is known that severe hypothermia can depress aEEG, temperatures above 33.5°C do not interfere with the normal upper and lower margins of aEEG readings.⁸ Hypothermia does however delay the onset of physiological sleep wake cycling as a sign of delay in recovery of aEEG to recover⁹, and this should therefore be interpreted in the context.

aEEG – some advantages over standard EEG findings

Advantages of CFM compared with standard EEG are that CFM monitoring is more easily applicable and available, especially during out of hours, and is especially suitable for continuous monitoring. CFM is a reliable tool for monitoring both background patterns (especially normal and severely abnormal) and ictal activity, and aEEG recordings correlate well with full EEG findings.¹⁰ However, foal, low amplitude and very short periods of seizure discharges (less than 30 seconds) can be missed on CFM. Thus, notwithstanding the utility of CFM on NICU, CFM should never replace a formal EEG where the latter is indicated.

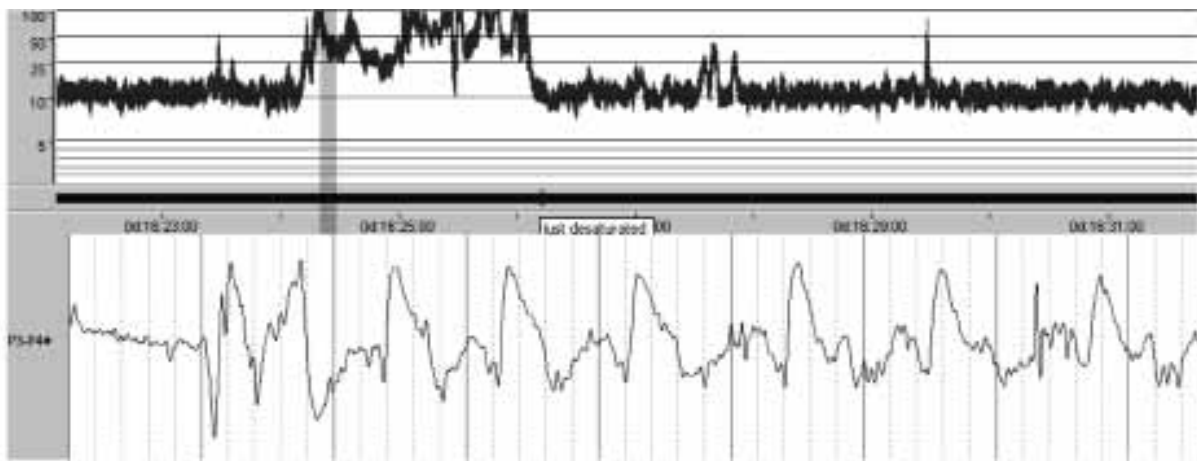


Figure 3a.

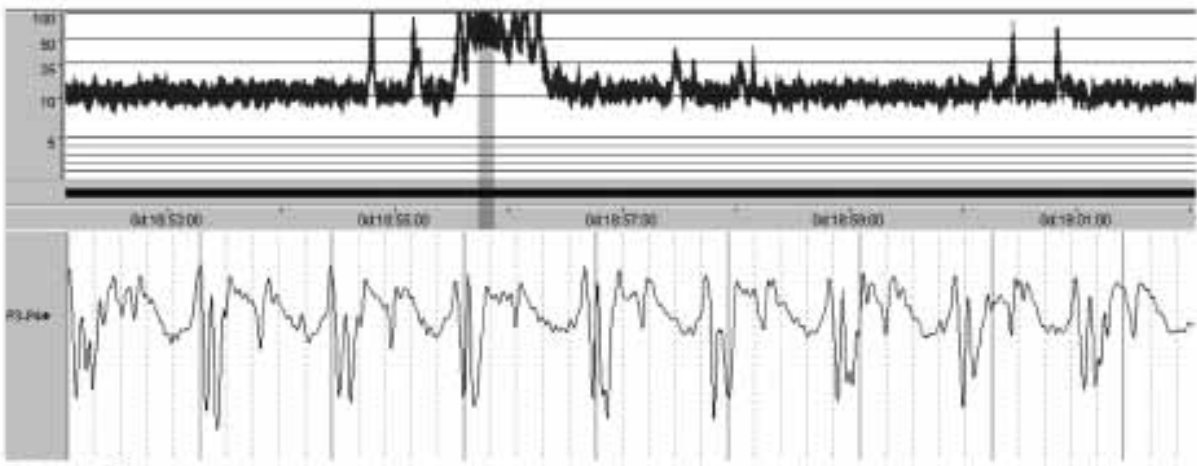


Figure 3b

Figures 3a & 3b: show typical appearances of neonatal seizures that were recorded from patient no 8. The raw EEG traces in the lower parts of both figures shows typical epileptiform discharges corresponding to the parts of the CFM traces indicated by the vertical grey bar. Note how during a seizure CFM amplitude narrows and rises.

Overview of local preliminary experience with CFM

The above described 14 recordings demonstrate a few problems that need to be rectified before CFM can be successfully implemented into local neonatal practice:

1. Staff training

Although an attempt was made to instruct neonatal nurses involved with these infants about CFM recording, the lack of formal training in CFM was a significant drawback. It is now clear that all staff needs to be adequately trained particularly with respect to proper placement of the leads, annotations and interpretation. This can be performed by adopting a 'train the trainer' approach followed by organising local workshops.¹¹

2. CFM machines

NicoletOne, the CFM machine currently available at MDH, is a complex EEG monitoring device, and is therefore not the most suitable clinical monitor for routine neonatal practice. It has complex protocols, and needs four electrodes instead of three for single channel aEEG. The absence of a fast print-out facility on the monitor makes it cumbersome to use in routine practice. These technical problems can be resolved by staff training in the use of NicoletOne and the use of a small portable printer in the first instance.

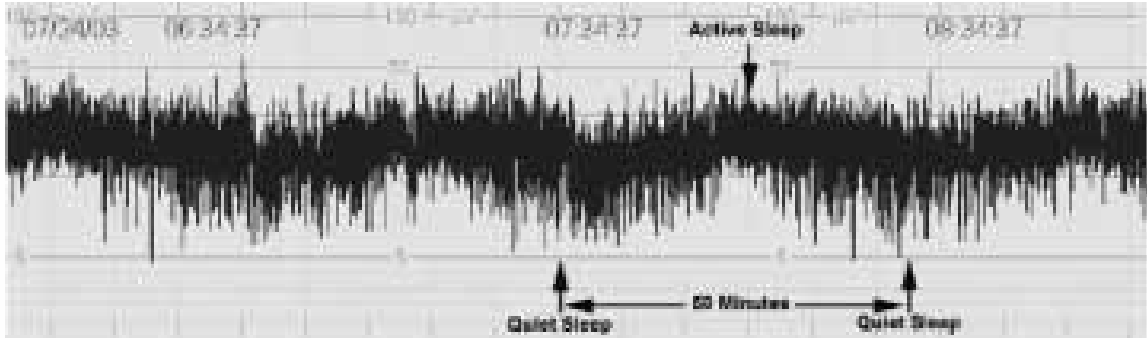
Highlights of a protocol for CFM recording at NICU

Indications for CFM monitoring

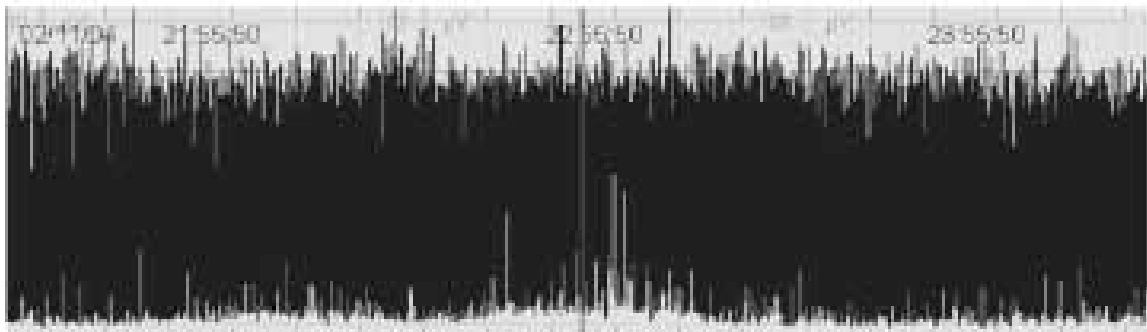
- a) Term or near term infants. CFM should routinely be used for all infants of gestational age >35 weeks who have one or more of the following:
- i) Evidence of encephalopathy.
 - ii) Evidence of perinatal distress suggestive of possible hypoxic-ischaemic encephalopathy (HIE) and

who required admission to NICU. Monitor infants who have any of the following features of perinatal compromise:

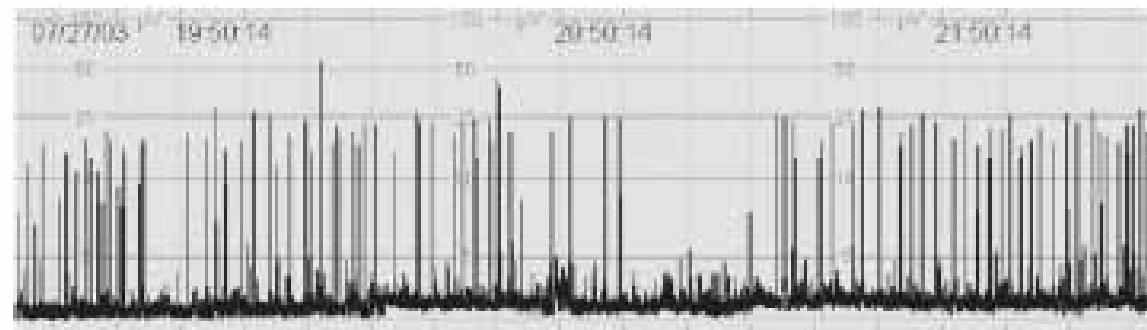
- foetal/neonatal acidaemia with cord pH or arterial pH within 1 hour of birth showing pH<7.0 or base deficit of > 15, and/or
 - APGAR score of <5 at 5 minutes.
- iii) Seizures, definite or possible.
- iv) Muscle relaxed infants where there are concerns over potential HIE or seizures.



Normal trace. Upper margin is > 10µV & lower margin is > 5µV. The widening and narrowing of the trace implies periods of waking and sleep (Sleep Wake Cycling).



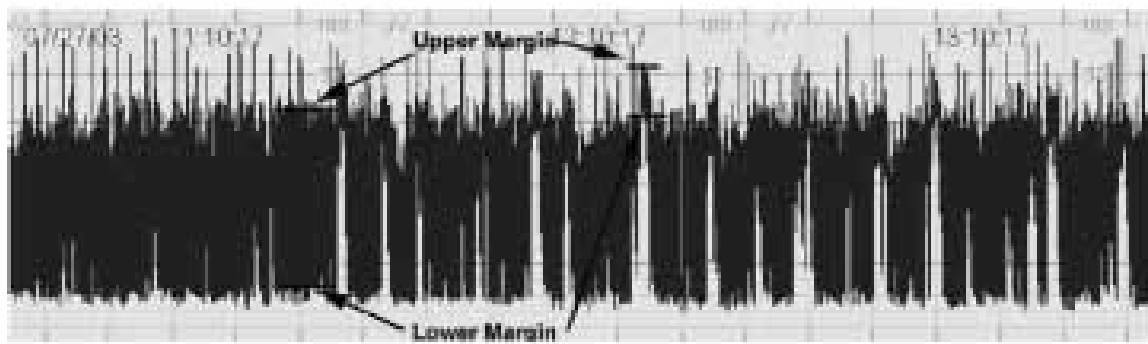
Moderately abnormal trace. Upper margin is > 10µV & lower margin is < 5µV throughout the trace. No sleep wake cycles



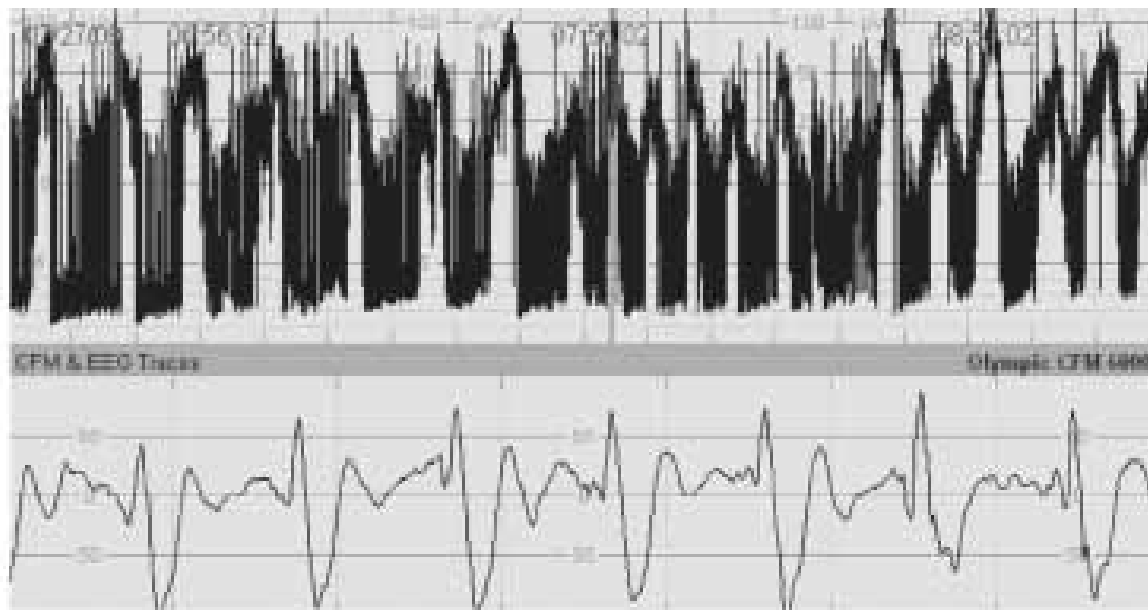
Severely abnormal trace. Upper margin is < 10µV & lower margin is < 5µV throughout the trace. There is evidence of SWS. Periodic bursts of electrical activity

Figure 4: Brief guide to single channel CFM interpretation as described by al Naqeeb et al, 1999

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Seizures. Rising and narrowing pattern in the CFM tracing. In the gaps of the rising and narrowing (lower margin becomes suddenly raised for several minutes), the EEG tracing show a distinct repetitive pattern



Moderately abnormal trace with multiple seizures. Upper margin is $> 10\mu V$ & lower margin is $< 5\mu V$ throughout the trace. No sleep wake cycles. Frequent and prolonged periods of elevation in both the lower and upper margins coinciding with repetitive rhythmic pattern on the EEG. This is characteristic of seizure activity

Figure 4 Continued

b) CFM may also provide useful information in meningitis (requiring intensive care), and cases of extensive structural brain injury or serious congenital brain anomalies (e.g. cerebral infarction, congenital brain haemorrhage/ tumour, hydrocephalus).

c) Preterm infants

The CFM may be less easy to interpret in preterm infants. Nevertheless it can provide very useful information and so may be considered in some infants of < 35 weeks' gestation, in cases of:

- Clinical or suspected seizures
- Encephalopathy
- Grade 3 or 4 intraventricular haemorrhage. CFM monitoring of preterm infants should be at the discretion of the attending consultant.

When should CFM be commenced?

- Apply as soon as possible following admission to the NICU of any infant with suspected hypoxic-ischaemic encephalopathy within the first hour.
- Apply the CFM as soon as possible to at-risk infants in whom there are any neurological concerns.

Who should attach CFM?

- The CFM should be attached only by personnel who have been trained in its application to infants.
- It is important that appropriate annotations regarding events that occur during the period of monitoring are done (suctioning, X-ray, re-intubation, and episodes of overt/ possible seizures). This will facilitate proper retrospective interpretation of the traces and help distinguish artefact.

Attachment of the CFM

Either standard EEG electrodes or gel electrode sets or disposable sub-dermal needle electrodes (in conjunction with needle adapter set) should be used to attach the CFM to the infant. Lead attachment requires time, patience, and careful skin preparation and is a skill that is acquired with practice. Care must be taken when using sub-dermal needle electrodes in order to avoid local scalp infection, needle stick injury for staff and risk of the needle electrode puncturing cooling wraps/mattresses in infants undergoing therapeutic hypothermia. Needle electrodes should be avoided if there is evidence of clotting abnormalities or active bleeding.

Interpretation of the CFM traces

It is recommended to follow the 3 basic categories of aEEG patterns described by al Naqeeb et al¹² (Figure 4).

Documentation of the findings

The clinician attending the infant and reviewing the aEEG tracing should make a written entry into the infant's case notes regarding their impression of the tracing. It is recommended the tracings are reviewed at each ward round. At the end of the recording period the aEEG trace should be formally reported by a clinician experienced in the interpretation of aEEG.

For how long should CFM monitoring be continued?

CFM should generally be continued until the patient has stabilised with no risk of further cerebral insult, and at least until:

- the aEEG pattern has become stable for 24 hours
- there have been no seizures for 12–24 hours.

This will often necessitate continuous monitoring for the first 4 days of clinical encephalopathy. A further 4–6 hour recording on day 7 done in conjunction with a documented clinical neurological examination is recommended.

All infants having cerebral function monitoring should have a formal EEG performed. In the case of the encephalopathic baby undergoing therapeutic hypothermia, this should be done on day 1. Ideally the EEG should be repeated on day 4 (after re-warming) and again on day 7–10 if previously abnormal. In other infants, timing and frequency of EEG examination is left to the discretion of the attending neonatal consultant.

Conclusion

CFM is a useful tool in the assessment of NE, seizures and selection of encephalopathic neonates for therapeutic hypothermia. Out first few recordings show that with appropriate staff training and attention to technical detail, CFM can be used effectively in NPICU at Mater Dei Hospital. A local protocol based on the local resources needs to be drawn up.

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