Brain monitoring in neonates

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ABSTRACT

Continuous EEG monitoring with amplitude-integrated electroencephalography (aEEG) has become a part of the routine neurological care in the neonatal unit, especially in full-term infants with hypoxia–ischemia and in infants suspected of seizures. Its prognostic value after birth asphyxia is well established and seizure detection has improved with the new digital aEEG devices with access to the "real" EEG, and even with seizure detection in some devices. Recent experience shows that aEEG monitoring also appears to be very helpful in premature infants. One has to be aware of possible artefacts, like ECG or movement artefacts, which can lead to misinterpretation of the background pattern.

Cerebral oximetry records regional saturation of the brain using Near Infrared Spectroscopy (NIRS) and provides a non-invasive method to continuously monitor brain oxygen imbalance. Cerebral oximetry is increasingly being used as a trend monitor in critically ill neonates. Its usefulness has been assessed in cardiac surgery, patent ductus arteriosus, hypoxia–ischemia and ventilation with high mean airway pressures.

A combination of both monitoring modalities will probably become the future for neonatal neuromonitoring.

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Whereas monitoring of physiological parameters such as ECG, heart rate, blood pressure, oxygen saturation and temperature have long since be integrated into neonatal intensive care, continuous EEG monitoring to evaluate brain function is less common. Interest in the neonatal brain has increased considerably during the last decade. This is in part due to better diagnostic methods in the acute and subacute stage. Imaging of the brain, using ultrasound and magnetic resonance imaging (MRI), provides important information about the presence and extent of structural lesions. Information about cerebral metabolism can also be obtained during the same examination using MR spectroscopy. Although MRI is now often performed within a few days after birth, information is preferably obtained within hours after delivery for selection of infants for early intervention, such as cooling after perinatal asphyxia.

EEG or amplitude integrated EEG (aEEG) provides information about brain function. It may detect epileptic discharges and signs of

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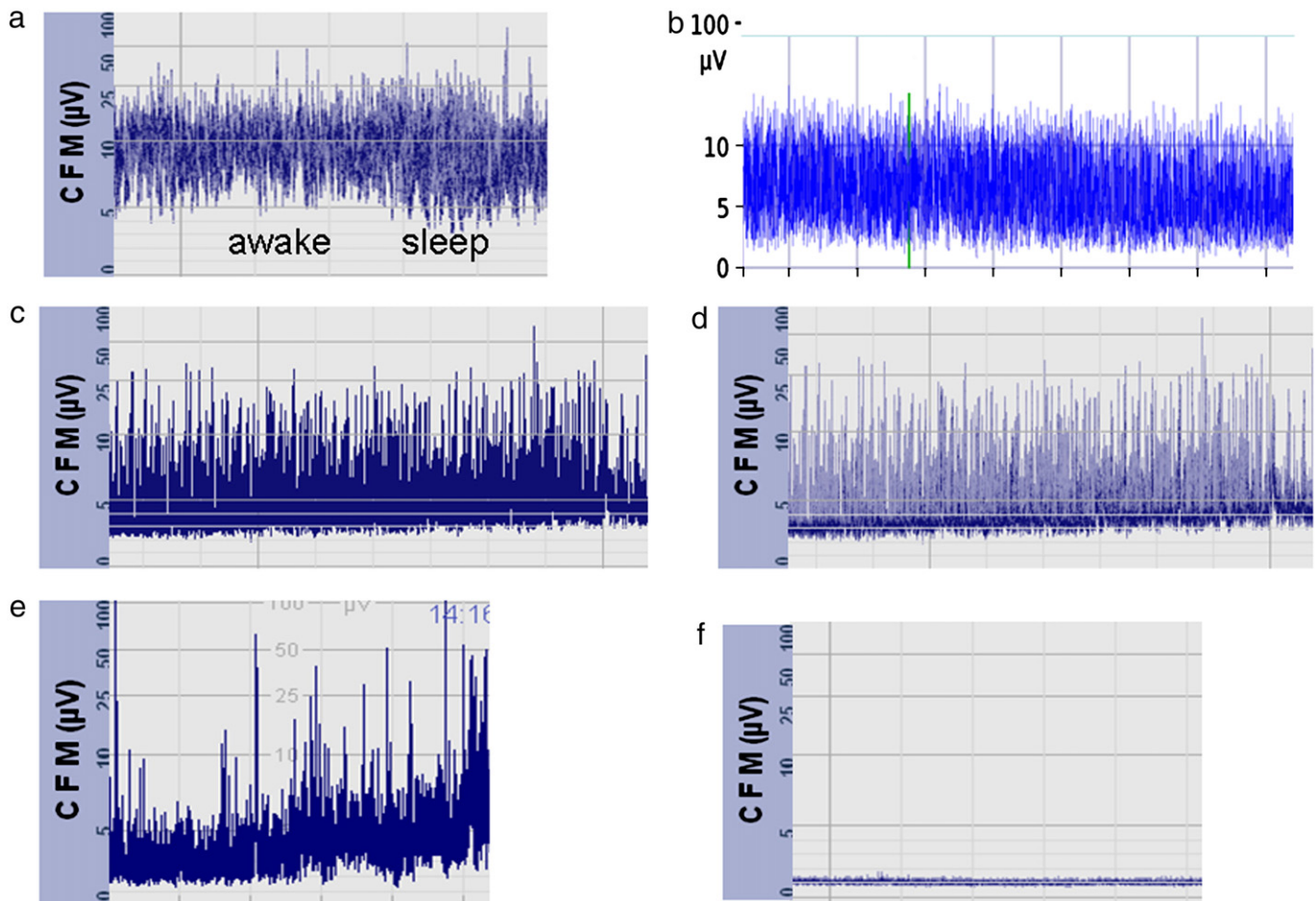
Fig. 1. Different aEEG background patterns: (a) continuous normal voltage, CNV, (b) discontinuous normal voltage, DNV, (c) burst suppression, BS, (d) burst suppression with greyscale (e) continuous low voltage, CLV, (f) flat trace, FT.

hypoxia–ischaemia. Near Infrared Spectroscopy (NIRS) allows non-invasive monitoring of tissue oxygenation and cerebral haemody-namics. aEEG is nowadays used routinely in an increasing number of neonatal intensive care centres. Up till now NIRS is not routinely used in neonatal intensive care, although this is changing rapidly.

1. Amplitude integrated aEEG (aEEG)

Dr. Douglas Maynard constructed the cerebral function monitor (CFM) in the late 1960s for continuous EEG monitoring. His colleague Dr. Pamela Prior later developed the clinical application, mainly for adult patients during anaesthesia and intensive care, after cardiac arrest, during status epilepticus and after heart surgery. The term amplitude integrated EEG (aEEG) is currently preferred to denote a method for encephalographic monitoring while CFM is used to refer to a specific device. The EEG signal for the single channel aEEG is usually recorded from one pair of parietally placed electrodes (corresponding to P_3 and P_4 according to the interna-tional EEG 10–20 classification, ground F_z). The signal is amplified and passed through an asymmetrical band-pass filter that strongly prefers higher frequencies over lower ones and suppresses activity below 2 Hz and above 15 Hz in order to minimise artefacts from such sources as sweating, movement, muscle activity and electrical interference. Additional processing includes semilogarithmic ampli-tude presentation, rectification, smoothing and considerable time compression. The signal is displayed on a semilogarithmic scale at slow speed (6 cm/h) at the cot side. A second tracing continuously displays the original EEG from either one or two channels. The

electrode impedance is continuously recorded but not necessarily displayed, but there will be an alarm when there is high impedance, often due to a loose electrode. The band width in the output reflects variations in minimum and maximum EEG amplitude, both of which depend on the maturity and severity of illness of the newborn infant. Due to the semilogarithmic scale used to plot the output, changes in background activity of very low amplitude (<5 μV) are enhanced. The information in the aEEG trace can be enhanced by modifying the grey scale so that a particular spot is determined by the length of time spent at that spot. This feature is useful when defining the lower border of the trace (Fig. 1d) and analysing changes caused by ictal periods [1,2].

2. Assessment of aEEG background pattern [1]

The aEEG traces are assessed visually based on pattern recognition and classified into the five following categories in full-term infants (Fig. 1):

a) the continuous normal voltage pattern (CNV) is a continuous trace with a voltage 10–25 (−50) μV (Fig. 1a)
b) discontinuous normal voltage pattern (DNV) is a discontinuous trace, where the low voltage is predominantly above 5 μV (no burst suppression) (Fig. 1b)
c) discontinuous background pattern (burst suppression): periods of low voltage (inactivity) intermixed with bursts of higher amplitude (BS) (Fig. 1c and d)
d) continuous background pattern of very low voltage (around or below 5 μV (CLV) (Fig. 1e)

Table 1
Predictive values of abnormal background patterns (BS, CLV, FT) during the first 3 and 6 h (12) of life, to predict adverse outcomes (death or handicap)

Studies	Time hours	N	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Hellström-Westas et al. [3]	6	47	95	89	86	96
Eken et al. [4]	6	34	94	79	84	92
Al Naqeeb et al. [5]	6	56	93	70	77	90
Toet et al. [6]	6	68	91	86	86	96
Shalak et al. [7]	12	15	79	89	73	91
Van Rooij et al. [8]	6	161	83	85	88	91
Shany et al. [9]	6	39	100	87	69	100

e) very low voltage, mainly inactive tracing with activity below 5 μV (flat trace, FT) (Fig. 1f)

3. aEEG in neonatal encephalopathy

The value of the background pattern in the prediction of neurodevelopmental outcome has already been established with the use of the standard EEG. A poor background pattern, persisting beyond the first 12–24 h after birth (burst suppression (BS), low voltage and flat trace), is well known to carry a poor prognosis. There have been several studies where aEEG and standard EEG were performed simultaneously to compare the two techniques. Overall there appeared to be a good correlation between the aEEG and EEG background pattern in the full-term infant with moderate–severe neonatal encephalopathy.

The first studies assessed the aEEG during the first 12–24 h, but with recent interest in early intervention strategies, the aEEG has also been assessed as early as 3–6 h after birth, to establish whether the aEEG could play a role in the selection of infants at risk of developing neonatal encephalopathy. The predictive value of the presence of a poor background pattern (BS, CLV, FT) for subsequent poor neurodevelopmental outcome at 18–24 months was assessed in these studies. The predictive values obtained by different groups were very similar (Table 1 [3–9]). Both positive and negative predictive values were slightly lower when the aEEG was assessed at 3 instead of 6 h after birth, but they were still considered sufficiently high to warrant use of this technique for early selection in hypothermia or other intervention studies. Combining a neurological examination with aEEG performed <12 h after birth further increased predictive accuracy from 75% to 85%. In the meta-analysis of 8 studies described by Spitzmiller et al. [10] a sensitivity of 91% (CI 87–95) and a negative likelihood ratio of 0.09 for aEEG tracings was found to accurately predict poor outcome. The relationship between aEEG amplitude measures, Sarnat grades and MRI abnormality scores has also been reported. The relationship was strongest for the minimum amplitude measures in both hemispheres. A minimum amplitude <4 μV was useful in predicting severe MRI abnormalities.

Recovery of the background pattern within 24 h after perinatal asphyxia with a poor background activity (BS, FT, CLV) has been reported in 20% of the cases. Of these infants 60% survived with mild disability or were normal at follow-up. The patients who did not recover either died in the neonatal period or survived with a severe disability. Another way of looking at recovery of the background pattern is to assess the presence, quality and time of onset of "sleep–wake cycling" (Fig. 1a). The presence, time of onset, and quality of sleep–wake cycling (SWC) reflects the severity of the hypoxic–ischemic insult to which newborns have been exposed. The time of onset of SWC was shown to predict neurodevelopmental outcome

based on whether SWC returns before 36 h (good outcome) or after 36 h (bad outcome). Therefore we recommend continuous monitoring for at least 48 h or until a normal SWC-pattern has been established.

Data about a possible effect of hypothermia on aEEG voltage are scarce. In one study there was no effect of mild hypothermia on aEEG voltage in neonates receiving ECMO. There are no data about a possible effect of mild hypothermia on the rate of recovery of a depressed background pattern [1].

4. Detection of epileptic seizure activity

Seizure burden is known to be very high in encephalopathic neonates. A recent video-conventional EEG study by Murray et al. [11] shows that only one third of neonatal EEG seizures display clinical signs on simultaneous video recordings. Two-thirds of these clinical manifestations are unrecognised or misinterpreted by experienced neonatal staff. Clinical diagnosis is therefore not sufficient for the recognition and management of neonatal seizures.

A rapid rise of both the lower and the upper margins of the aEEG tracing is suggestive of an ictal discharge (Fig. 2a). Seizures can be recognised as single seizures, repetitive seizures and as a status epilepticus (Fig. 2b–c). The latter usually looks like a "saw-tooth" pattern. Correct interpretation is greatly improved by simultaneous "real" EEG recording available on the digital devices (Fig. 2a1–2) and the greyscale software available on some of the newer machines also helps to make the correct diagnosis.

Since the increased use of continuous monitoring, it has become apparent that subclinical seizures are common and occur especially following administration of the first antiepileptic drug. This so-called 'uncoupling' or 'electroclinical dissociation' has recently been reported by several groups and was found in 50–60% of the children studied. The aEEG can play an important role in the detection of these subclinical seizures [1].

Even a status epilepticus is not uncommon and occurred in 18% of 56 full-term infants admitted with neonatal seizures recorded with aEEG. The duration of a status epilepticus may influence prognosis as well. In a group of 48 infants with HIE and an aEEG detected status epilepticus, there was a significant difference in background patterns and in duration of the status epilepticus between infants with a poor outcome, compared with those with a good outcome. The background pattern at the onset of status epilepticus appeared to be the main predictor of outcome in all neonates with status epilepticus.

Being aware of this high incidence of subclinical seizures has made one aware of the poor therapeutic effect of most of the commonly used anti-epileptic drugs. Drugs that were considered to have a good therapeutic effect mainly appeared to suppress the clinical symptoms. Continuous EEG or aEEG recording, preferably with simultaneous video recording, is therefore required to assess the therapeutic effect of the different anti-epileptic drugs.

Due to the nature of the technique it is not surprising that very brief seizure activity as well as focal seizure activity may be missed. This was recently shown by Shellhaas et al. [12] in a large data set of 125 conventional EEGs with 851 neonatal seizures. 94% of the conventional EEGs detected one or more seizures on the C3–C4 channel. Detection of individual seizures appeared to be difficult (12–38%) without access to the "real" EEG, especially when the seizures were infrequent, brief, or of low amplitude. There were no false positives among control records. However, infants with focal seizures tend to develop more widespread ictal discharges during the continuous registration, which will be identified. In addition, 81% of the neonatal seizures originated from central–temporal or midline vertex electrodes, which can potentially be picked up by the aEEG electrodes. Shah et al. [13] showed that the combination of a 2-channel aEEG with the "real" EEG signal detected the majority (76%) of electrical seizures in at risk newborn infants. aEEG in combination
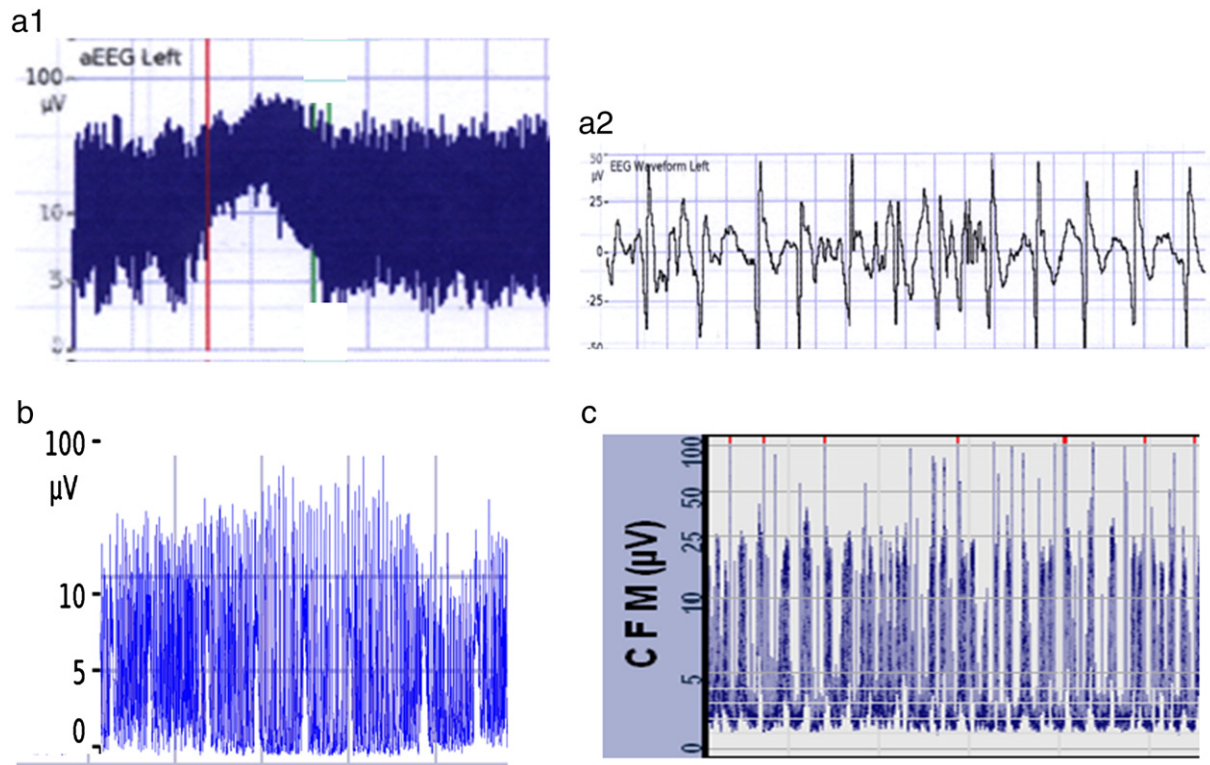
Fig. 2. Different seizure patterns: (a) single seizure: (a1) aEEG; (a2) corresponding "real" EEG during seizure, (b) repetitive seizures, (c) status epilepticus with "sawtooth" pattern.

with the "real" EEG signal was clearly better in seizure detection than aEEG alone.

Whether the use of two channels (or more) is indicated in all infants is still under debate. It seems to be appropriate to use 2 channels instead of one channel (cross-cerebral) in children with unilateral brain lesions. Studies addressing this issue are on their way. Although some ictal discharges arose from the affected hemisphere, the discharge could usually be recognised on the cross-cerebral recording. In general, there seemed to be a good agreement with regard to classification of the background pattern in the one channel recording compared to the two channel recording.

5. Pitfalls and artefacts

One can either use a classification system based on pattern recognition (see above) or look at actual values of lower and upper margins of activity (al Naqeeb criteria [5]), i.e. normal amplitude (maximum amplitude >10 μV, minimum amplitude >5 μV); moderately abnormal (maximum amplitude >10 μV, minimum amplitude ≤5 μV) and severely abnormal (maximum amplitude < 10 μV, minimum amplitude <5 μV). Although one would be inclined to prefer values, rather than patterns, values may be misleading, as the voltage may be affected by scalp oedema and inter-electrode distance. In the studies of Shany [9] and Shah et al. [13] with 2-channel recordings, cut-off values of 4 and 9 μV were used instead of cut-off values of 5 and 10 μV from the al Naqeeb criteria in the 1-channel recording, because of a smaller distance between the central and parietal electrodes (C3–P3 and C4–P4 with an electrode distance of 2.5 cm) in the 2-channel recording compared to the 1-channel electrode distance. Furthermore, the lower margin may be elevated due to extracranial activity, e.g. ECG interference or interference from the high frequency ventilator. This so-called 'drift of the baseline' is especially seen in infants with a severely depressed background pattern, which can be misinterpreted as "normal" background pattern in children who would be eligible for cooling after severe perinatal asphyxia. The simultaneous recording of the real EEG, present on the newer digital devices, may help in the identification of an ECG artefact (Fig. 3).

Artefacts are quite common during long-term recordings. It has been shown that up till 12% of recorded time could be affected by artefacts. This was due to electrical interference in 55%, which could be either ECG artefact (39%) or fast activity (>50 Hz, 61%) and due to movement artefact in the remaining 45%. Therefore the dual facility (aEEG with simultaneous "real" EEG) is crucial for the correct interpretation of the aEEG [14]. Inappropriate electrode position can lead to aEEG recordings with artefact or drift of the baseline. Medication can also affect the background pattern, as was mentioned before. Anti-epileptic drugs can give a temporary decrease in amplitude on the aEEG recording, although this does not influence prognosis. Other drugs, like an overdose of morphine, can also have this effect.

We therefore recommend the use of pattern recognition, taking the values of upper and lower margins into account as well.

6. Seizure like artefacts

Any movement or handling of the baby, with a sudden increase of the baseline of the aEEG recording, can also mimic seizure activity on the aEEG. The simultaneous recorded single channel "real" EEG signal can help to interpret aEEG traces more accurately. In addition marking events on the aEEG recording by nursing staff is very important.

7. aEEG in preterm infants

aEEG is also feasible for monitoring cerebral activity in preterm infants during intensive care. In parallel with multichannel EEG, aEEG background activity is more discontinuous in preterm infants. Normative values for aEEG background activity at different gestational ages have been published [15]. A scoring system for evaluation of brain maturation in neonates has also been developed [16]. Sleep–wake
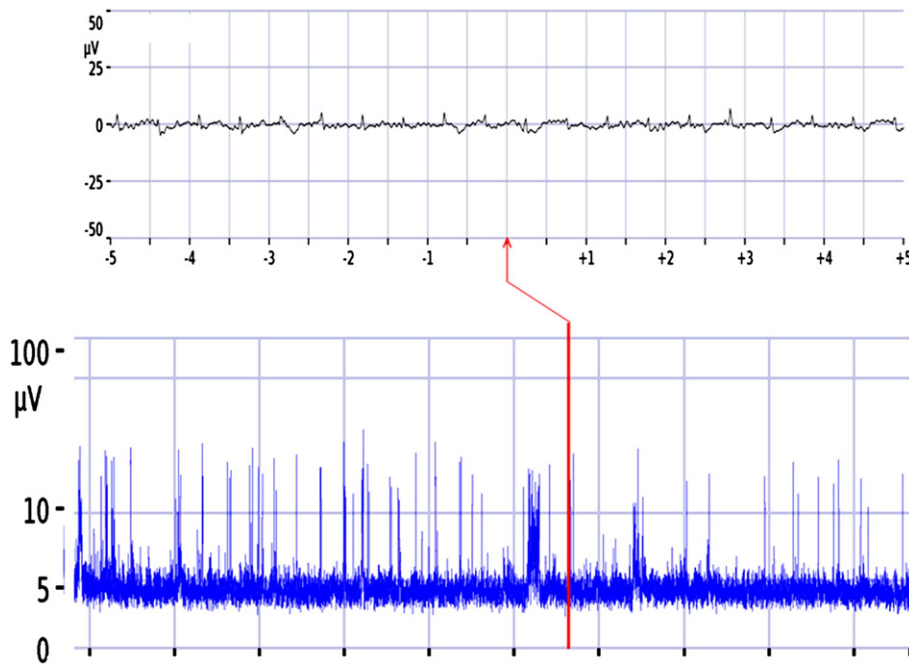
Fig. 3. Flat trace with "drift of the baseline" due to an ECG artefact.

cycling can be clearly identified in the aEEG from around 30 weeks gestation, but also at 25–26 weeks gestational age a cyclical pattern resembling sleep wake cycling can be seen in stable infants. Effects from some common medications, e.g. surfactant, morphine and diazepam can be readily seen in the aEEG of preterm infants.

Early prediction of outcome from aEEG is a more complicated issue in preterm infants than in full-term infants. In the most immature infants, factors other than initial brain function may influence long-term neurodevelopmental outcome, e.g. bronchopulmonary dysplasia and late-onset sepsis, which makes prediction of outcome from early EEG less certain. Nevertheless, several EEG and aEEG studies have shown early background depression to correlate with the severity of a periventricular–intraventricular haemorrhage [17]. A mainly discontinuous background pattern can be considered as normal in most infants below 30 weeks gestation. Consequently, a classification based on the type of background pattern is not feasible for preterm infants.

Epileptic seizure activity in preterm infants can be identified in a similar way as in full-term infants. Epileptic seizure activity, often without clinical symptoms, is very common in the aEEG during development of intracerebral hemorrhages. Identifying seizure activity on a discontinuous background pattern can be very difficult. With access to the real EEG on the digital devices this problem can be handled more easily, especially with the new seizure detection algorithm on some devices (Fig. 4).

As the diagnostic value of aEEG has now been appreciated and experience with this technique is increasing, many neonatal intensive care units would find it hard to imagine treating a full-term infant with HIE without having access to this equipment. New digital aEEG devices have been developed the last few years, even with seizure detection. Some machines offer two channels which may allow better detection of focal seizures, for instance in children with neonatal stroke. Even though it is possible that some focal or very brief seizures will not be detected, the long duration of the aEEG registration outweighs the limitations of obtaining more detailed information during a much shorter 30 minute standard EEG registration.

Amplitude integrated EEG is also useful in the high-risk preterm infant even though this has not yet been evaluated as extensively as in the full-term infant. With the availability of new digital equipment, continuous display of inter burst duration, which differs with gestational age, may become a prognostic factor in preterm infants in the near future [18].

The usefulness of aEEG in older children might be a subject for further study as well. Very few centres use aEEG in their paediatric intensive care unit, for instance after neurosurgery, near drowning or cardiac surgery. Additional information to analyse different frequencies might be one of the possibilities to assess brain function in more detail.

It is most likely that aEEG will soon be part of the routine care not only in the neonatal unit, but in some of the larger district general hospitals as well. This might be particularly important in consideration of early intervention after perinatal asphyxia.

8. Near Infrared Spectroscopy (NIRS)

The use of in vivo NIRS in humans was already introduced in the late seventies for non-invasive monitoring of tissue oxygenation. It has been used mainly as a research tool in premature infants and term infants with perinatal asphyxia and in open heart surgery.

In these studies changes in oxygenated haemoglobin (O_2Hb) and deoxygenated haemoglobin (HHb) as measures of cerebral oxygenation, as well as changes in total haemoglobin (THb) and/or the difference between O_2Hb and HHb (Hb-D) were used. This approach allows the investigation of acute changes in cerebral haemodynamics and oxygenation. However, because of movement artefacts, NIRS is less appropriate for *long-term* monitoring of cerebral oxygenation and saturation, which may be important in the daily surveillance of cerebral oxygen metabolism and perfusion in unstable (preterm) neonates. For this purpose NIRS determined regional cerebral oxygen saturation as a reliable estimator for changes in regional cerebral oxygenation, is used [19]. Because absolute values are provided here, it is less dependent of movement artefacts and important comparisons over time are possible. For reliable NIRS-monitored oxygenation there are 2 promising candidates who are highly comparable: the cerebral tissue oxygenation index (TOI, NIRO-200, Hamamatsu Photonics, Hamamatsu City, Japan) and the regional cerebral oxygen saturation ($rScO_2$, INVOS, Somanetics Corp., Troy, Michigan, USA).
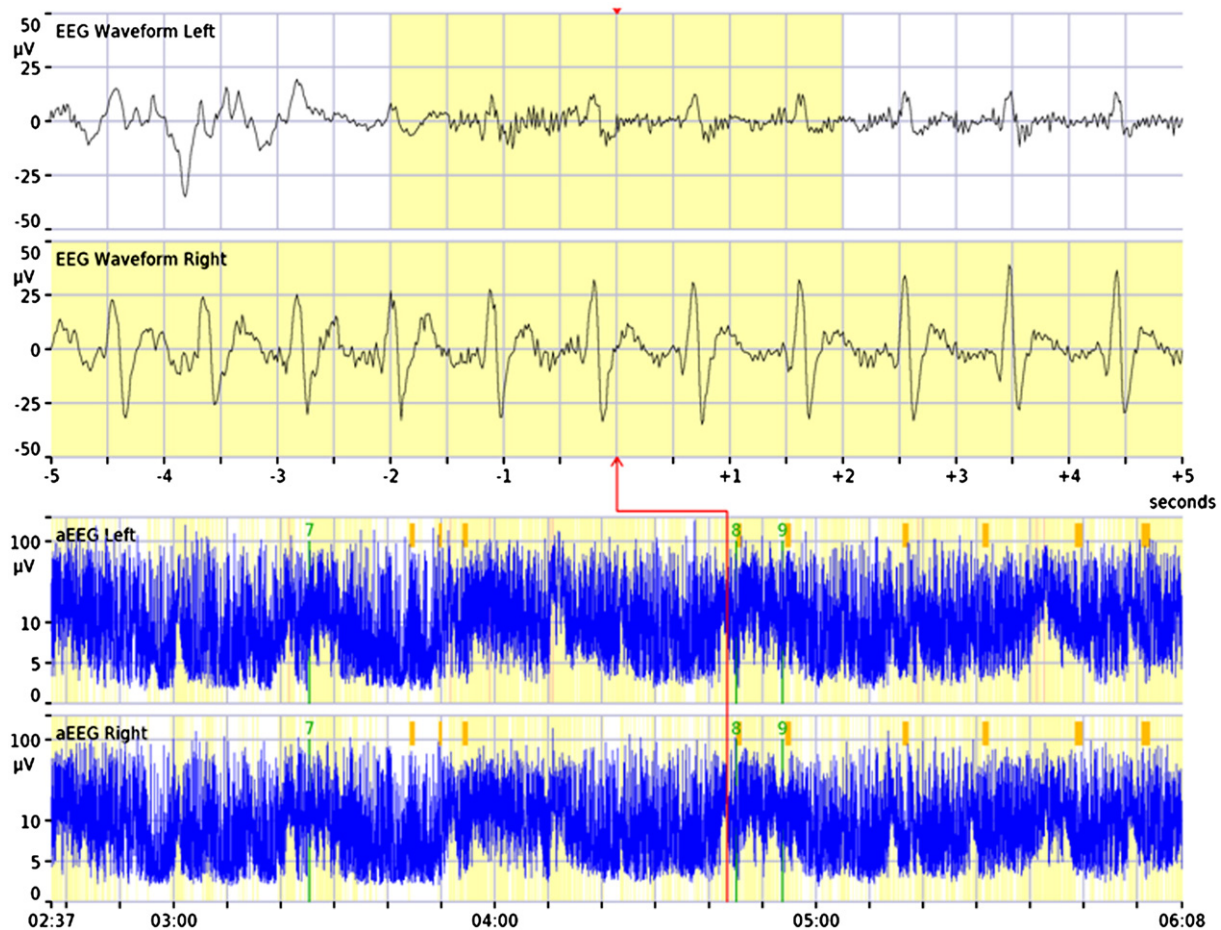
Fig. 4. 2-channel recording of a premature infant (29 weeks) with an intraventricular haemorrhage on both sides. Seizure detection marker presents as blocks on top of each recording. Ictal discharge in the "real" EEG.

In fact both variables are based on the following formula:

$$O_2Hb \cdot k / THb \cdot k \cdot 100 (\%)$$
(k, the constant reflecting the scattering, can be omitted)

However the methods used are different. TOI is calculated by using the diffusion equation, while $rScO_2$ is using a different formula where scattering is measured at the first optode (at 2 cm) and deducted from the measurements at 4 cm.

With the INVOS near infrared spectrometer a transducer containing a light emitting diode and two distant sensors are attached to the fronto-parietal side of the neonatal skull. $rScO_2$ is calculated from the differential signals obtained from these two sensors, expressed as the venous-weighted percent oxygenated haemoglobin (oxygenated haemoglobin/total haemoglobin [oxygenated haemoglobin+deoxygenated haemoglobin]). To investigate the balance between oxygen delivery and oxygen consumption, a relative fractional tissue oxygen extraction (FTOE) measurement can be formulated as a ratio:

$$FTOE = [SaO_2 - rScO_2] / SaO_2.$$
(SaO_2 is the arterial saturation measured by pulse oximetry)

So an increase in FTOE might indicate a reduced delivery with a constant oxygen consumption of the brain or a higher consumption than oxygen delivery. The opposite is true in case of a decrease in FTOE, reflecting a decrease of oxygen extraction due to less utilisation of oxygen or constant oxygen consumption with an increased oxygen delivery.

Both TOI and $rScO_2$ reflect the saturation of oxygen in veins (70-to-80%), capillaries (5%) and arteries (20-to-25%). It has been compared and used as a surrogate measure of the oxygen saturation in jugular venous blood (SvO_2). However, jugular SvO_2 measures pure venous blood, whereas TOI and $rScO_2$ measure a mixed venous saturation. Therefore reference values for (preterm) newborns of these NIRS-derived variables should be extracted from well-designed studies with appropriate numbers of infants. These normative values can then be compared with values obtained during neonatal complications which might affect cerebral oxygenation. Despite the differences in measurement technique and algorithm of both devices to monitor cerebral oxygenation, they appear to be useful as trend monitors in clinical practice.

9. Clinical applications of NIRS

The most important issue regarding clinical application of NIRS-monitored cerebral oxygenation and saturation is the ability to perform reliable and non-invasive long-term monitoring of cerebral oxygenation in the most immature and unstable neonates without the necessity to frequently disturb the infant. The most critical part here is appropriate fixation to the skull of the transducer, which contains the light emitting diode and the distant sensors (reflection method), to allow reliable registration of the $rScO_2$ or TOI for extended periods of time (days). Also, repeated cranial ultrasound investigations, placement of electrodes for amplitude-integrated EEG (aEEG) monitoring or fixation of the CPAP-devices are possible.

Three common clinical conditions in preterm infants can be linked with unusually low $rScO_2$-values:

1) hemodynamically important patent ductus arteriosus (PDA)
2) blood pressure passive oxygenation (TOI-$rScO_2$) of the brain
3) artificial ventilation with high mean airway pressures
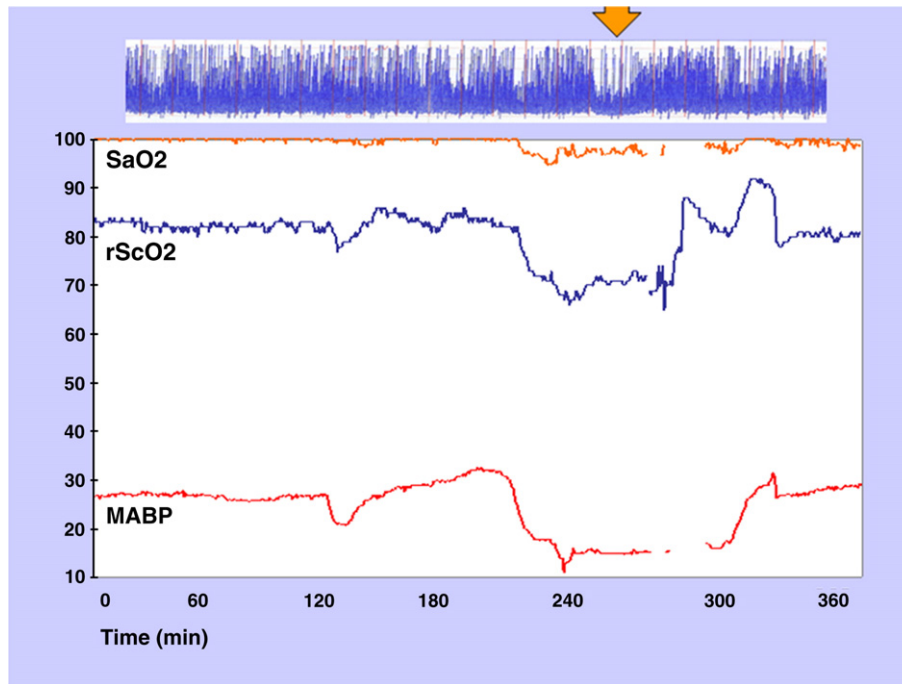
Fig. 5. Simultaneous monitoring of blood pressure (MAP (mean arterial blood pressure)/bottom), aEEG (top), arterial saturation (SaO$_2$) and regional saturation of the brain (rSO$_2$) of a premature infant (28 weeks GA; 800 g) with severe RDS: during a period of hypotension (arrow), a drop in SaO$_2$ and rSO$_2$ with a "fattening" of the aEEG-pattern.

Combining arterial blood pressure monitoring with NIRS-monitored rScO$_2$, TOI and FTOE may be a way to monitor cerebral autoregulation in unstable (premature) infants [19]. A growing number of papers regarding these issues have been published. In case of PDA, mean arterial blood pressure and rSO$_2$ measured by NIRS were significantly lower and the FTOE significantly higher compared to control infants. rSO$_2$ and FTOE were lower and higher respectively, up to 24 h after start of indomethacin treatment, but subsequently normalized to control values. Indomethacin had no additional negative effect on the cerebral oxygenation [20]. Another study showed no negative effect on the cerebral oxygenation (rSO$_2$) in infants with respiratory distress syndrome needing artificial ventilation, except for those with high mean airway pressures [19] (Fig. 5).

Continuous rSO$_2$ monitoring has been used in term infants with HIE after perinatal asphyxia and in infants undergoing cardiac surgery, both together with aEEG [21,22]. rSO$_2$ seems to reflect secondary energy failure, with an increase 24 h after perinatal asphyxia in the infants with poor outcome. In infants with transposition of the great arteries, rSO$_2$ was decreased until 24 h after surgery, despite normal values of arterial blood pressure and arterial saturation.

At present, cerebral oximetry (by recording regional saturation of the brain) provides the only non-invasive means of continuous monitoring of the brain oxygen imbalance. It can guide interventions aimed at correction of this imbalance. NIRS as a monitoring device is less well integrated in neonatal intensive care, compared with aEEG, but this is changing. Recording rSO$_2$ and FTOE, as parameters for oxygenation, is easy to accomplish and very suitable for monitoring of longer duration. It could be used in relation to blood pressure, arterial oxygen saturation and to evaluate cerebral auto-regulation in very ill infants, without interfering with care. In open heart surgery cerebral monitoring should be, together with aEEG, part of routine care, not only during cardiopulmonary bypass, but also before and in the hours to days after surgery. Use of this continuous monitoring device also raises a number of questions. What are normative data for regional oxygen saturation of the brain in premature infants? When does a low blood pressure cause imbalance of brain oxygenation in a particular patient and when should hypotension be treated? Already some research projects, regarding these issues, have started.

Guidelines for aEEG- and NIRS-monitoring overlap and aEEG and NIRS should preferably be used simultaneously.

10. Guidelines for aEEG-monitoring

- Perinatal asphyxia
- Cooling
- Neonatal seizures and/or apneas
- Metabolic disorders
- Meningoencephalitis
- Post-surgery, especially cardiac surgery
- Muscle paralysis

11. Research directions for aEEG-monitoring

Fullterm infant:

- Seizure detection
- Effect of intervention (cooling) on recovery of background patterns and seizure onset

Preterm infant:

- Seizure detection
- Other modalities of background pattern evaluation; i.e. inter burst duration

Older infants (analysis of more than one channel/frequency):

- Cardiac surgery
- Neurosurgery
- Near drowning

12. Guidelines for NIRS-monitoring

(rSO$_2$, FTOE or TOI simultaneous with blood pressure and arterial saturation)

- Critically ill patients
- Hypotension

- PDA
- Prenatal asphyxia
- Cardiac surgery

13. Research directions for NIRS

(Absolute) normative values for rSO$_2$, FTOE and TOI

- at different gestational ages and time after birth
- during cooling or other neuroprotective interventions
- during seizures

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