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Clinical Application of Amplitude-Integrated Electroencephalography among Neonatal and Intensive Care Units Patients

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Abstract:Background: Amplitude integrated electroencephalography (aEEG), cerebral function monitoring (CFM) or continuous electroencephalogram (CEEG) is a technique for monitoring brain function in intensive care settings over longer periods of time than the traditional electroencephalogram (EEG), typically hours to days. By placing electrodes on the scalp of the patient, a trace of electrical activity is produced which is then displayed on a semilogarithmic graph of peak-to-peak amplitude over time; amplitude is logarithmic and time is linear. In this way, trends in electrical activity in the cerebral cortex can be interpreted to inform on events such as seizures or suppressed brain activity.[1] aEEG is useful especially in neonatology where it can be used to aid in diagnosis of hypoxic ischemic encephalopathy (HIE), and to monitor and diagnose seizure activity

Keywords:*Amplitude integrated electroencephalography, NICU, PICU*

Introduction

The neurological assessment of paediatric intensive care patients continues to be challenging for nurses and physicians. Evidence that electrocortical activity in this patient group needs to be continuously monitored is growing **(1)**

the gold standard, which is continuous full-channel electroencephalography (EEG), is rarely available and time-consuming to provide. An easy-to-use alternative is amplitude-integrated electroencephalography (aEEG), which is a simplified, time-compressed EEG with a reduced set of electrodes. The interpretation is based on the evaluation of trends, but also allows staff to assess the raw EEG curve(**2**).

aEEG was originally developed as a cerebral function monitor for adult patients after resuscitation, but it has mainly been investigated and applied in newborn infants with seizures and hypoxic ischaemic

encephalopathy. A further, mainly scientific, use is to predict neurological long-term outcomes in preterm infants. **(3)**

In line with its original purpose, aEEG is increasingly used for monitoring brain activity in adults after cardiac arrests. Paediatric intensive care staff also use aEEGs, but clinical guidelines are lacking and its scientific evaluation in such patients is less advanced than for neonatology and adult medicine. **(3)**

Due to their importance in neonatology, aEEG devices are widely used in children's hospitals and are also available to paediatric intensive care staff, which has led to their increasing use in this field. Even though more trend parameters exist for EEG, aEEG is still the default feature of cerebral function monitors, making it particularly relevant for paediatric intensive care physicians. **(3)**

How Electrocortical activity is reflected by the aEEG

aEEG is based upon conventional electroencephalography that is recorded with two or four scalp electrodes, depicting the amplitude of the raw EEG on a time-compressed semi-logarithmic scale. The signal from two or four electrodes placed in the C3, P3, C4, and P4 positions of the international 10-20 system is passed through a bandpass filter, which enhances frequencies between 2 and 15 Hz. Frequencies under 2 Hz and above 15 Hz are attenuated in order to eliminate artefacts, such as sweating, movement, muscle activity, and electrical interference, as much as possible (**4).**

Further processing includes filtering, rectification, smoothing, semi-logarithmic amplitude compression, and time compression. Amplitudes <10 μV are displayed on a linear scale and amplitudes >10 μV on a logarithmic scale. The lowest-detected amplitude is shown as the lower border, and the highest amplitude is shown as the upper border. By this means, even small changes in the lower amplitude remain visible, while an overloading of the display at high amplitudes is avoided (**Figure 1**). Due to time compression, 5 - 6 cm on the time scale represents 1 h, thus making the review of brain activity for hours and even days possible **(5).**

The visible information in the aEEG tracing is limited to changes of the amplitude. Modern devices offer the possibility of viewing the raw EEG, so the frequency and morphology of the raw EEG curve can also be considered for interpretation. This helps to distinguish between artefacts and real seizure activity during suspicious sections of the aEEG band. (**4).**

Some aEEG devices can record a simultaneous video of the patient for even better identification of seizures and artifacts. Electrode impedance is monitored during the entire recording. In two-channel aEEG devices that use four electrodes, the investigator can switch between two intraparietal curves or one transcerebral curve. Depending upon the manufacturer, software offers additional features, like seizure detection, burst rate analysis, electromyography, etc. It is also possible to derive an aEEG from a full-channel EEG device that offers video recording, electromyography, electrooculography, electrocardiography, etc. **(5).**

The qualitative interpretation of aEEG

The qualitative interpretation of aEEG generally includes three categories: classification of the background pattern, sleep-wake cycling, and the presence of seizures. Several authors have made suggestions for classifications and scores that describe brain maturation. The quantitative analysis of aEEG is less common, even though it is possible in modern devices, and few research groups made use of this approach. (**6)**

Hellström-Westas:

The assessment of the tracing is solely qualitative, and the results are not transformed into a score. The classification allows for the description of pathological conditions. Normative values for gestational ages have been published to help interpret whether a pattern is adequate for the age: (1) background patterns: continuous normal voltage (physiological), discontinuous normal voltage (physiological in preterm infants), burst suppression pattern (pathological), continuous low voltage (pathological), and flat trace (pathological); (2) sleep-wake cycling: none, imminent, mature (physiological/pathological, depending on the infant's age); and (3) seizure activity: none, single seizures, repetitive seizures, and status epilepticus. (**4).**

Burdjalov:

The approach of this classification is the qualitative assessment of the tracing and its transformation into a score. The score rises with gestational age, and normative score values for each corresponding gestational age have been published: (1) 0 - 2 points for continuity, (2) 0 - 5 points for sleep-wake cycling, (3) 0 - 2 points for the amplitude of the lower border, (4) 0 - 4 points for the bandwidth, and (5) 0 - 13 points for the total score. **(8).**

Olischar/Klebermass:

Percentiles regarding the percent duration of background patterns (i.e., discontinuous normal voltage, discontinuous low voltage, and continuous normal voltage) and burst rate were developed for gestational ages. Tracings are evaluated for an age-adequate background pattern, the presence of sleep-wake cycling, and the presence of seizure activity (i.e., repetitive seizures or status epilepticus). Then, the tracings are classified into a graded score as follows: (1) normal aEEG (all categories normal), (2) moderately abnormal (1 out of 3 categories classified as abnormal), and (3) severely abnormal (2 or 3 out of 3 categories classified as abnormal). This score has been shown to have a predictive value for neurodevelopmental outcome at 3 years of corrected age. **(8)**

Changes in the aEEG tracing are caused by numerous extracortical factors, such as changes in cerebral blood flow, medication (e.g., opiates, sedatives, and caffeine), acidosis, changes in carbon dioxide tension, clinical conditions (e.g., hypogylcemia, sepsis, meningitis, and patent ductus arteriosus), etc.(**8).**

Methods of conduction of aEEGs :

The presented protocol follows the guidelines of the institution's human research ethics committee.

1. Gather the Needed Supplies

1. Connect the eEEG device to electric power in the place where the monitoring will take place and plug the module box to the aEEG device.
2. Ensure that there are four electrodes for a two-channel aEEG and two electrodes for a single-channel aEEG. Choose either needle electrodes, gold cups, or hydrogel electrodes. Additionally, have one hydrogel electrode ready to serve as a reference electrode. NOTE: Gold cups can be disinfected and reused for up to two years. Needle and hydrogel electrodes are single-use only. Needle electrodes can be used in infants at 23 weeks of gestation without causing skin lesions or infections. Here, the best results were achieved using needle electrodes in older infants as well.
3. Prepare the following supplies: a positioning strip provided by the manufacturer (to help place the electrodes correctly), tape appropriate for use in neonates (e.g., viscose mull), skin disinfectant appropriate for use in neonates (e.g., alcohol-based or octenidinhydrocholoride-based), swabs, skin preparation gel, a module box, and contact gel for gold cups. NOTE: Once disconnected from electrical power, the device will shut down, and the recording will need to be restarted. Some devices have internal batteries, however, and can be moved after being switched on or during the recording.

2. Apply the Electrodes

1. Respecting the principals of minimal handling(**9).** apply the electrodes during routine care or delivery room care. Wear (unsterile) gloves, a gown, a hood, and a mask, according to the institution's guidelines and the patient's infectious status.
2. Prepare the skin for the reference electrode, as follows:
    1. Disinfect the skin. Place skin preparation gel on a cotton swab until it is moist. Apply a few gentle strokes with the cotton swab, using very little pressure. Be very cautious in extremely premature infants between 23 and 25 weeks of gestation to avoid causing lesions on the immature skin.
    2. Place the reference electrode on the back or the chest of the infant.

3. Place the measuring device on the infant's head, and line up the same letters/signs on the infant's tragus and sagittal suture; the two arrows indicate where to place the electrodes (positions C3, P3, C4, and P4 of the 10 - 20 system).

3. Place the electrodes on the infant's head, following the instructions, below, corresponding to the type of electrodes selected.
4. **Needle electrodes.**
    1. Disinfect the area indicated by the measuring device.
    2. Stretch the skin slightly and insert the needle tangentially, just underneath the skin at the markings, with the tip of the needle pointing in the caudal direction. Use tape to keep the electrode in place.
    3. Repeat the procedure for both/all four electrodes. NOTE: Use needle electrodes in very premature infants, as rubbing for skin preparation is not necessary.
5. **Gold cups.**
    1. Disinfect the area indicated by the measuring device.
    2. Prepare the skin in the marked areas, as described in step 2.2.
    3. Fill each cup with contact gel. Place the cup in the proper position, with the cable running towards the head end; tape it into place.
6. **Hydrogel electrodes.**
    1. Disinfect the area indicated by the measuring device.
    2. Prepare the skin in the marked areas, as described in step 2.2.
    3. Place the electrodes with the cable running towards the head end. Fix the electrodes with tape in case they do not stay in place.

3. Connect the Wires to the Monitor

1. Insert the cables into the module box, as indicated by the legend on the box.
2. The default starting screen includes impedance monitoring for all electrodes.
3. Make sure that all electrodes are in place and that there is no mechanical contact between electrodes. If the impedance of one or more electrodes is not satisfactory, remove the corresponding electrode and perform one or two more strokes with the cotton swab, but do not apply more pressure.
4. Start the recording when everything is set. NOTE: Obligatory recording parameters are raw EEG and impedance. According to the device and clinical indication, additional options are burst suppression ratio, sharp transient intensity, and spectral edge frequency, among others. Standard parameters for review include raw EEG, amplitude-integrated EEG curve, and impedance. Depending on the device, there is the opportunity to view more features, like spectral edge frequency, or different forms of the presentation of the lower, mean, and upper border. Additional features are seizure detection and burst rate analysis.

4. Optional: Place a CPAP Hat

1. If required, place a CPAP hat or head band on top of the aEEG electrodes.

5. Aspects to Keep in Mind During the Recording

1. Regularly check for impedance and the dislocation of electrodes to obtain quality recordings. Also, check the infant for skin irritation to avoid lesions or infections.
2. Mark events (e.g., handling, kangaroo care (skin-to-skin care), apnea with bradycardia, intubation, and administration of sedatives or opioids) to facilitate the identification of artifacts using the provided button on the screen of the cerebral function monitor. Leave aEEG electrodes in place during kangaroo care to resume the recording afterwards.
3. Leave aEEG electrodes in place for intubation or other invasive measures to resume the recording later. In case the cables are not long enough to move the infant within the incubator, disconnect them from the module box and reconnect them after the procedure.

6. Review of the aEEG Tracing and Storing

Review the tracing at the end of the recoding on the monitor or transfer it to an external storage device.

Some normal and pathological aEEG Tracing

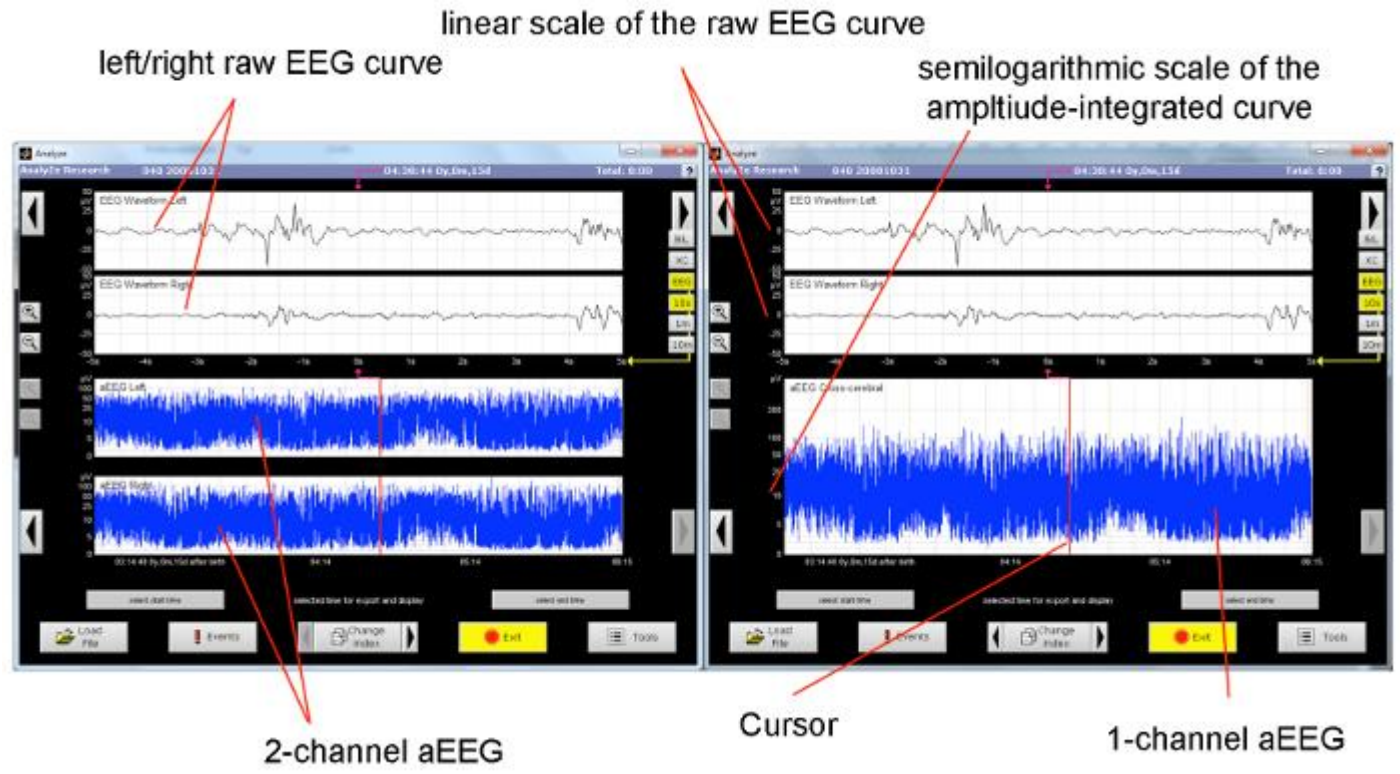

Figure 1. Formation of the aEEG Tracing. The signal from the raw EEG (upper curve) is processed, resulting in the amplitude-integrated EEG band (lower curve). High amplitudes form the upper border, whereas low amplitudes form the lower border. While strong variation in the height of the amplitude leads to a broad aEEG band, the aEEG band is narrow if there is little variation in the height of amplitude. The scale of the y-axis is linear up to 10 µV and logarithmic above 10 µV. **(10).**

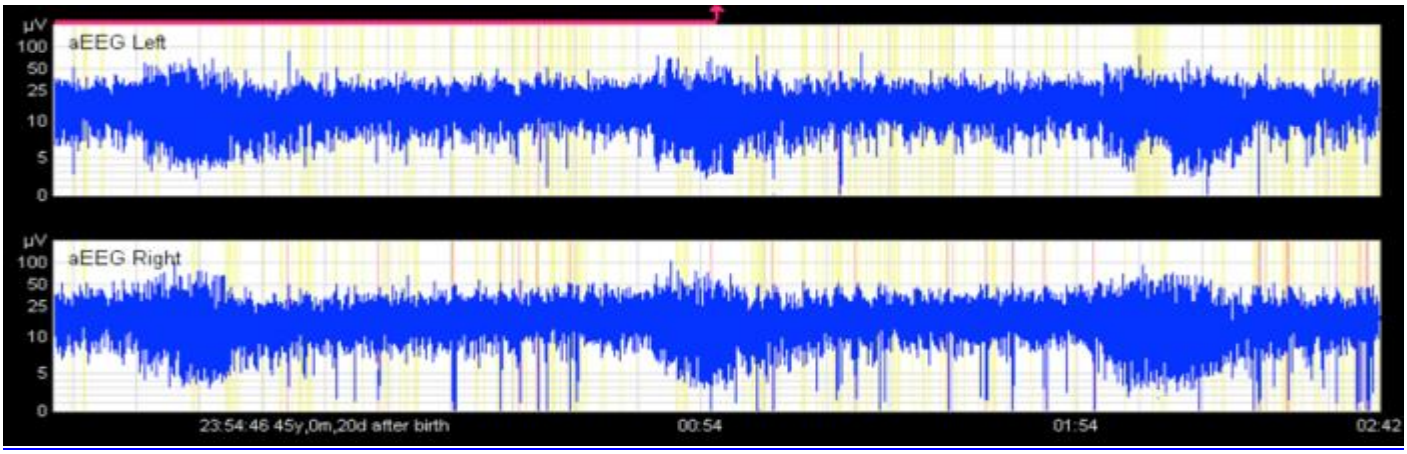

Figure 2. Typical Display of an aEEG Monitor. The upper half of the monitor displays the raw EEG curve (the displayed section equals 10 s). On the left display, the lower half shows the unilateral aEEG tracing (the displayed section equals approximately 3 h). On the right display, the corresponding cross-cerebral tracing is shown. The cursor indicates the section of the amplitude-integrated tracing from the raw EEG. **(10).**

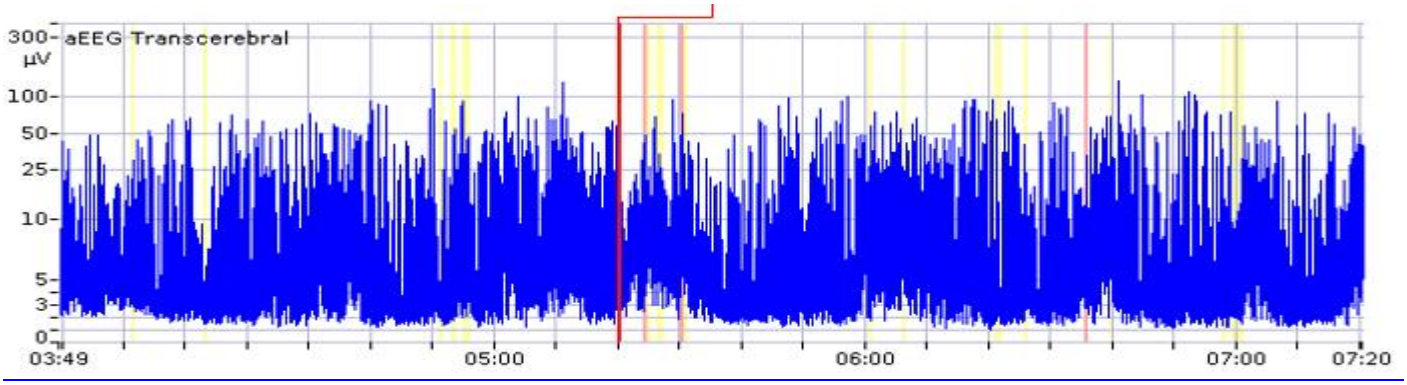

Figure 3. Continuous Normal Voltage Pattern. Continuous background pattern with sleep-wake cycling. The x-axis equals time (one square = 10 min). **(10).**

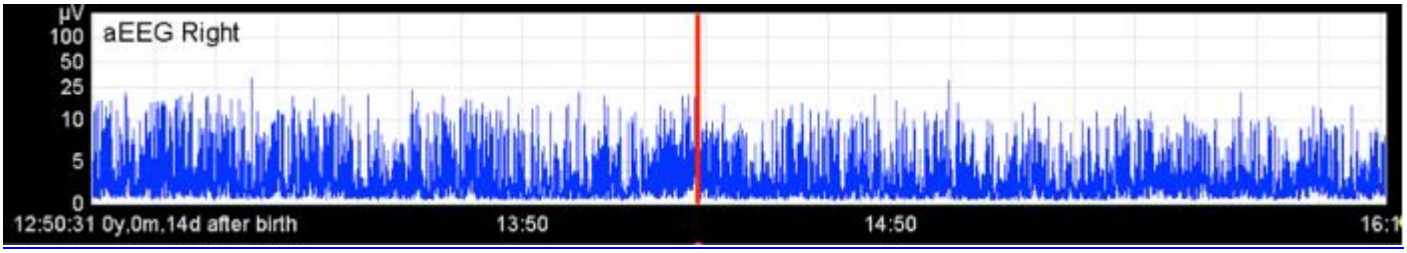

Figure 4. Discontinuous Normal Voltage Pattern. Discontinuous background pattern with imminent sleep-wake cycling. The x-axis equals time (one square = 10 min). **(10).**

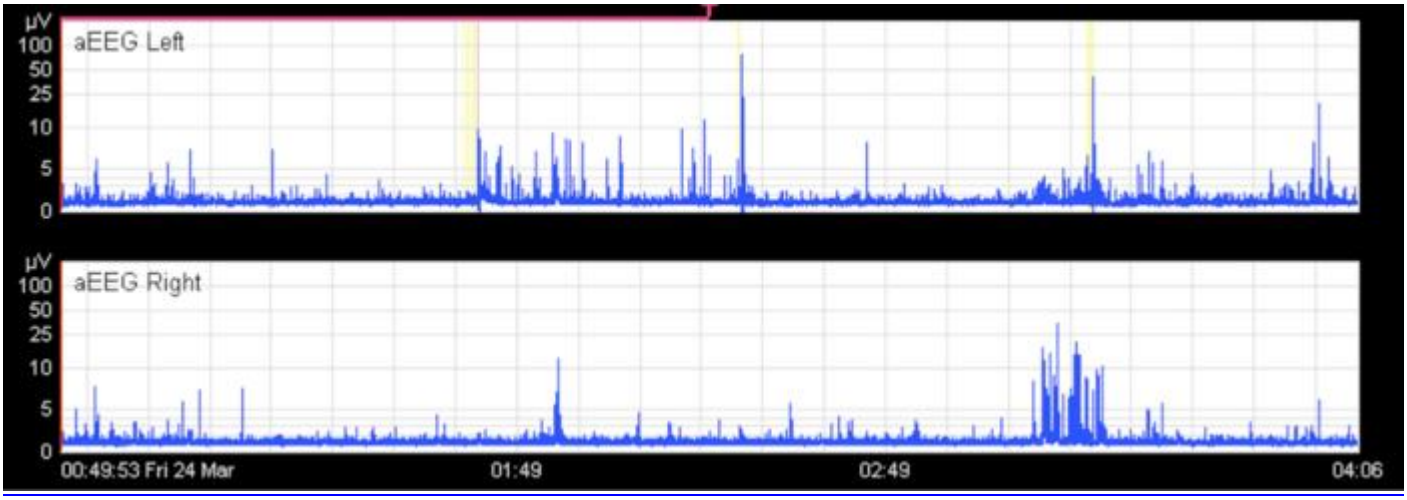

Figure 5. Burst Suppression Pattern. Burst suppression pattern, with the lower amplitude continuously low and without alteration. The x-axis equals time (one square = 10 min). **(10).**

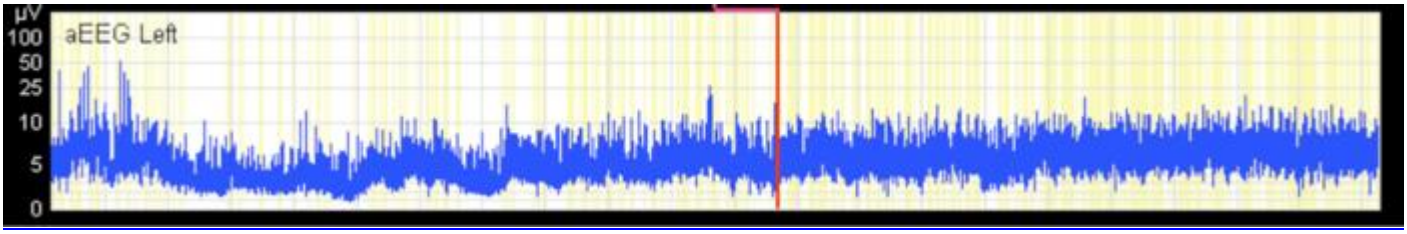

Figure 6. Flat Trace. Flat trace on both sides in a term infant with severe meningoencephalitis. The x-axis equals time (one square = 10 min). **(10).**

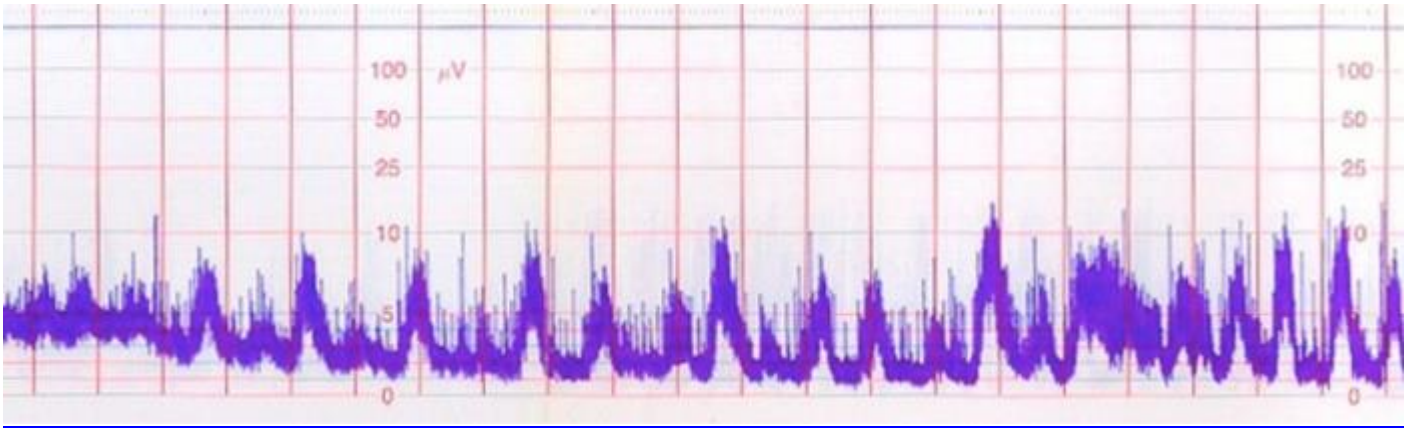

Figure 7. Continuous Low-voltage Pattern. Continuous low-voltage pattern without sleep-wake cycling. The x-axis equals time (one square = 10 min). **(10).**

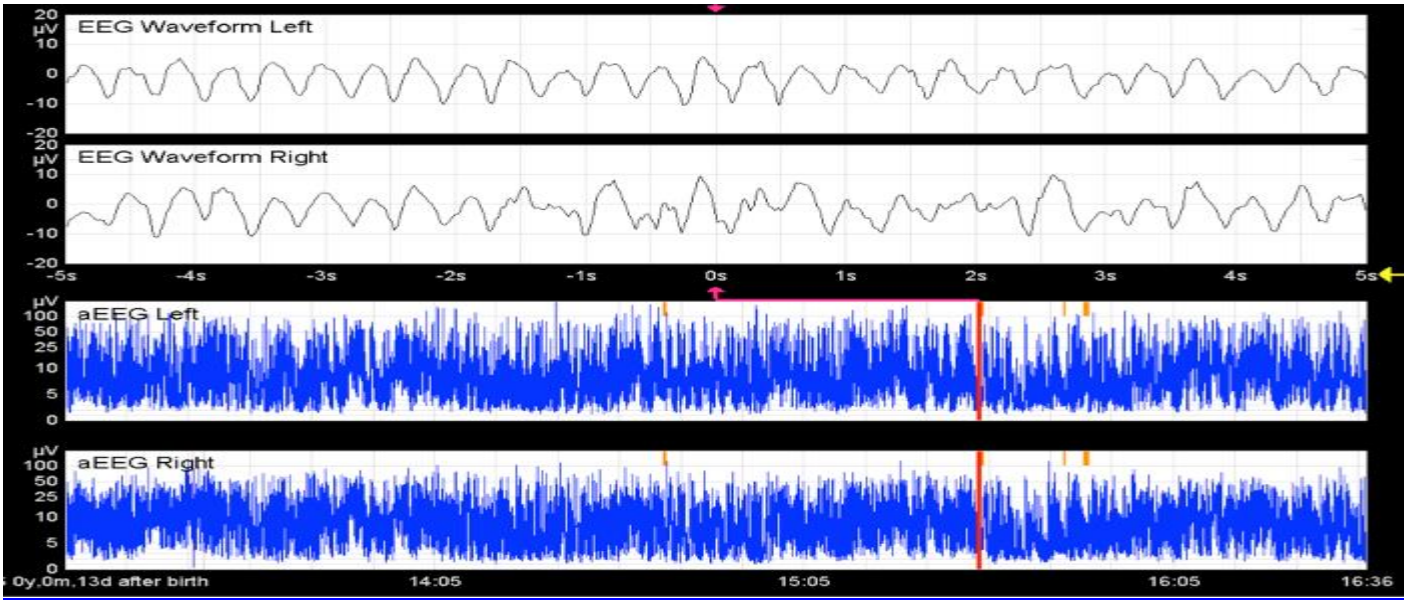

Figure 8. Seizures in Term Infants. Typical depiction of a seizure in the aEEG: a sudden rise of the lower and upper margin is followed by a short period of decreased activity. Repetitive seizures for approximately 3.5 h. The x-axis equals time (one square = 10 min). **(10).**

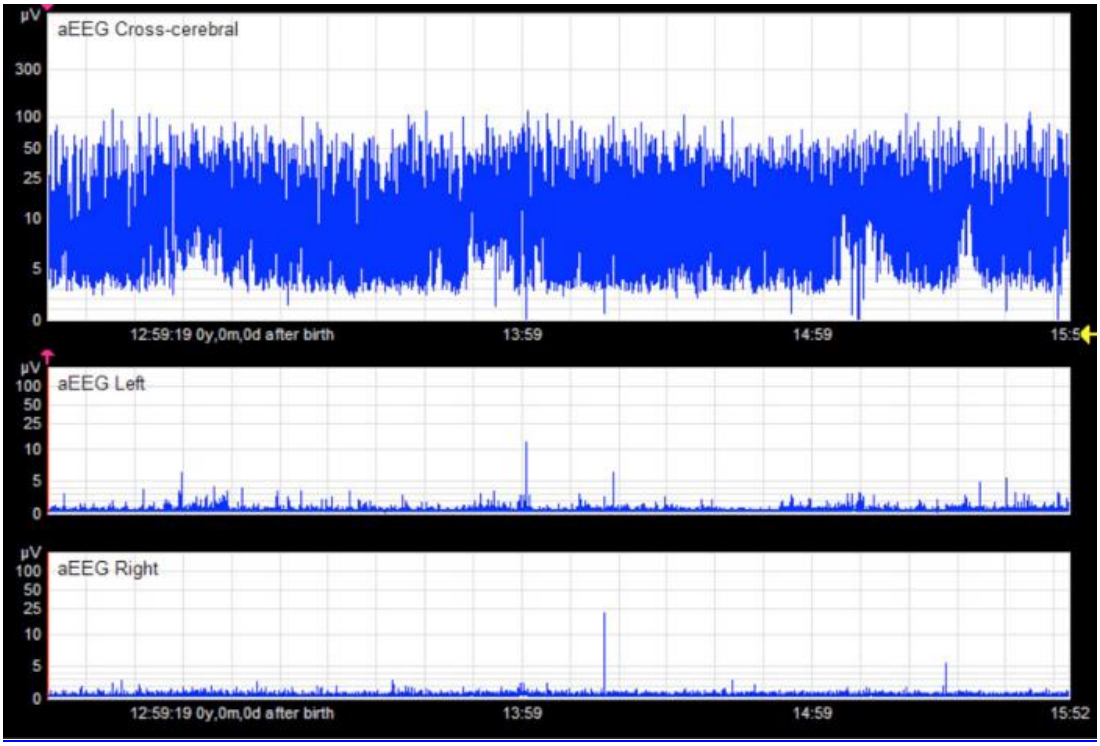

Figure 9. Seizures in Preterm Infants. Without the raw EEG, the hypersynchronous activity in both hemispheres would remain undetected. The x-axis equals time (one square = 10 min). **(10).**

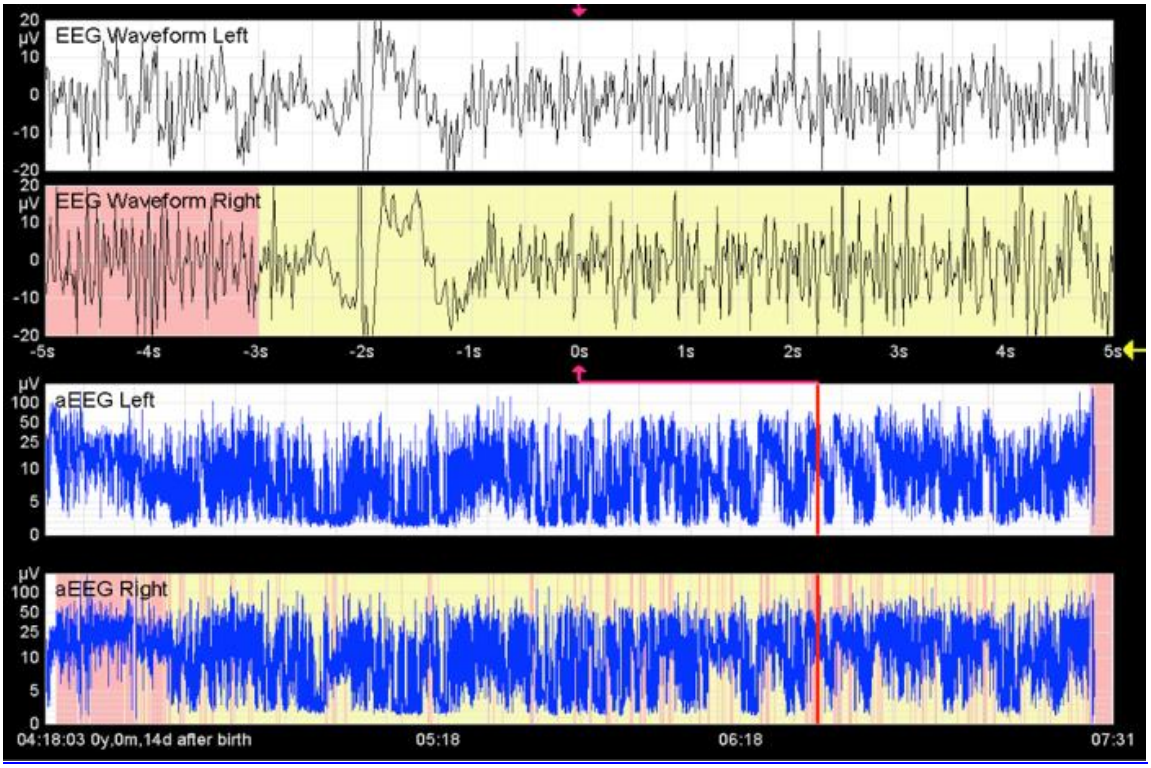

Figure 10. Apparent Flat Trace. In the unilateral tracings, there appears to be a pathological flat trace pattern in an infant without cerebral injury. The cross-cerebral tracing shows a physiological discontinuous background pattern with short sections of continuous activity. In this case, the flat trace is an artifact caused by liquid bridging between electrodes (especially hydrogel electrodes). The x-axis equals time (one square = 10 min) **(10).**

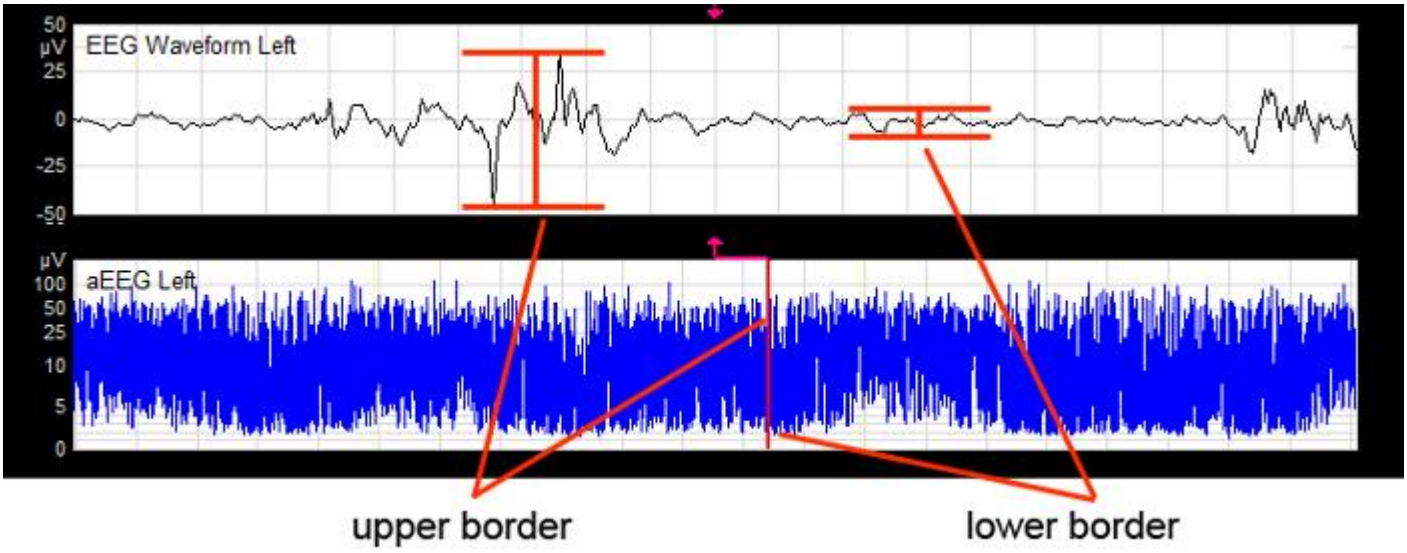

Figure 11. Apparent Seizures. This image shows high-frequency activity over a long period of time. Without seeing the raw EEG curve, status epilepticus is indicated. This artifact is caused by muscle activity. The x-axis equals time (one square = 10 min) **(10).**

Clinical Applications of aEEG:

1- aEEG in Neonates With Hypoxic-Ischemic Encephalopathy

Neonatal HIE remains one of the leading causes of neonatal mortality and long-term disability worldwide. It results from severe hypoxia before, during or after birth, and 42% of asphyxiated infants suffering from HIE . Moderate to severe HIE may result in neurological sequelae, including cognitive and neurodevelopment problems with disabilities or death (**11).**

Recently, several randomized clinical studies have proven that a reduction in brain/body temperature (therapeutic hypothermia) significantly decreased mortality and improved neurodevelopmental outcomes in neonates with HIE. The predictive value of early aEEG recordings on the neurodevelopmental outcome of infants with HIE who were either cooled (received the therapeutic hypothermia) or maintained at normothermia has become a hotspot of research (**11).**

The abnormal aEEG background pattern for longer than 60 h provides a reliable prediction of adverse outcome in hypothermia-treated HIE infants. In (**11).**

2 - Use of aEEG in paediatric intensive care units

Our review showed that the number of scientific studies and case reports on the use of aEEG in children beyond the neonatal period is increasing. In addition to reports on seizures, research suggests that the background pattern may have diagnostic value. **(12)**

It is not knowen how common the use of the aEEG actually is in older infants and children. A telephone survey carried out in East England found that only one of the 17 hospital general paediatric wards used aEEG and another had access to conventional EEG on-call/during weekends. According to an online survey of paediatric intensive care units (PICUs) in Germany, about half of the 43 units who took part had access to conventional EEG during on-call periods and weekends and 93% had access to aEEG devices. **(12)** Of these PICUs, 64% used aEEG on infants and children with altered mental states. The respondents particularly appreciated how aEEG could detect non-convulsive epileptic states, that they could start using it without contacting the EEG service and that it offered the possibility of continuous recording. **(12)**

3 - Interpretation of recordings

aEEGs are interpreted by recognising patterns that reflect long-term trends in amplitude height. Generally, the assessment focuses on the background pattern, seizures and sleep–wake cycling. Clinical information, such as the patient's age, sedation or circulatory instability, must be taken into account when interpreting the tracings. Reference values of the upper and lower margins only exist for neonates and infants up to 3.5 months of age. **(12)**

No common references or classifications exist for older infants and children. For that reason, researchers and clinicians often use the neonatal Hellström–Westas classification for infants, children and even adults.' This includes visually assessing the background patterns, seizures and sleep–wake cycling. It is easy for clinicians to learn how to perform aEEGs, even if they are not EEG experts. One study found that, after a short training period, PICU personnel performed well when it came to detecting severely altered background patterns using the Hellström–Westas classification (kappa 0.71, 95% confidence interval 0.57–0.85), but moderate changes were more difficult to identify. **(13).**

Another study explored whether medical students improved how they interpreted trends in a modified aEEG when it came to identifying wakefulness, sleep and encephalopathic patterns compared to conventional EEG. The study found that their performance improved significantly. **(14).**

Other studies showed that interrater agreement between EEG experts on the aEEG background pattern was good in preterm and term infants. **(10).**

4 - Seizures

Seizures in full-term neonates and older children are typically seen as abrupt rises in the upper and lower margins of the aEEG band for the duration of the incident. Several case reports and case series have

illustrated the usefulness of aEEG in children with seizures. aEEG has helped to detect subclinical seizures, continuously monitor seizure activity and guide anticonvulsant therapy in patients aged between one month and 16 years. Underlying conditions included acute encephalopathy, bacterial meningitis, head injuries and epilepsy. **(15)**

Epileptogenic areas were identified by a conventional EEG in an 11-year-old non-critically ill patient with frontal lobe epilepsy and then monitored with aEEG for days, allowing clinicians to detect frequent seizures and titrate treatment. In a series of patients with genetic epilepsy, the seizure pattern showed a specific triphasic shape that differed from the typical seizure patterns usually observed in an aEEG. **(16).**

Being able to display the long-term trend of cerebral activity makes it possible to identify seizures in aEEG tracings. In a retrospective analysis in our PICU, aEEG helped staff to detect epileptic states more frequently than clinical observation on its own or intermittent conventional EEG. Nevertheless, there are pitfalls in interpreting suspicious sections, because artefacts can cause seizure-like patterns. Prospective studies on the ability of staff to detect seizure activity after short-term training have yielded varying results**(16).**

Nurses who received short-term blended learning only agreed moderately with aEEG specialists when it came to detecting seizures in infants and children with a low incidence of seizures. **(16)**

More encouraging results were obtained by a study on seizure detection by briefly trained neurophysiologists without prior aEEG experience. That study found that using an eight-channel aEEG, without access to raw EEG, yielded a low false-positive rate for seizure identification, of 0.05 false positives per hour, and sensitivity was good (81.5%). **(17).**

Similarly, after short training, critical care providers detected seizures with a sensitivity of 77% and specificity of 65%. While the negative predictive value was good (88%), the false-positive rate was high, with a positive predictive value of 46%. When a study compared a modified aEEG with a colour density spectral array to conventional EEG, medical students performed equally well in both.**(18).**

Another study that compared automated seizure detection by commercially available software packages to experts yielded heterogenous results. While the experts recognised 74% of the seizures in an aEEG and 77% in colour density spectral array, the software ranged between 37% and 92%. These false-positive rates were generally lower for the experts than for the software and differed greatly between different software packages. **(18).**

In a prospective study that evaluated the implementation of aEEG for seizure detection in a PICU, 101 patients underwent quantitative EEG monitoring, including aEEG and colour density spectral array. The diagnoses of the seizures were retrospectively confirmed by a neurophysiologist. The sensitivity and negative predictive value were 100%. However, the high false-positive rate was 52% and this presented similar challenges to previous studies. Treatment was initiated after a median time of 25 min and ranged from five minutes to more than three hours. **(18).**

To conclude, seizure recognition by non-experts was possible and showed high sensitivity. The high false-positive rates displayed in the studies that we reviewed highlight the need for suspected seizures to be confirmed by raw EEG reviews by experts. The rate of seizures missed in children, due to the reduced number of electrodes used, has not been investigated. This is a limitation, especially for the detection of focal seizures. Neonates have a high proportion of focal seizures, and one study showed that only about 68%–85% of those detected by full-channel EEG were also detected by aEEGs. **(18).**

The present data support the use of aEEG for seizure detection and treatment when continuous full-channel EEG is unavailable. However, the method should only be used in conjunction with expert raw EEG reviews and cannot replace intermittent full-channel EEGs. **(18).**

4 Predicting outcomes

One of the most important aspects to guide care after a critical event is estimating the outcome. The evolution of aEEG background patterns predicts outcomes in newborn infants with hypoxic ischaemic encephalopathy and in adults after a cardiac arrest. Normal background patterns and normalisation are associated with better

outcomes than failure to normalise. Preterm infants with normal or normalisation of background patterns within the first 72 h of life achieved better neurodevelopmental outcomes at two years of age than those who displayed a persisting pathological background. **(19).**

The aEEG background improved postoperatively in a study of young infants undergoing cardiac surgery due to congenital heart disease. A lack of sleep–wake cycling was associated with severe infections. The same research group found that preoperative and postoperative aEEGs correlated with neurological development at one year of age. **(19).**

Abnormal preoperative background patterns, and the absence of postoperative sleep–wake cycling, independently predicted poorer motor and cognitive outcomes. **(19).**

In another study on young infants undergoing cardiac surgery with cardiopulmonary bypasses, abnormal postoperative background patterns, and a lack of return to sleep–wake cycling, predicted poorer intelligence quotients at four years of age. However, no such association was found for motor outcomes. **(19).**

One study looked at 30 patients, of up to three years of age, after they had a cardiac arrest and found that the aEEG background correlated with the neurological outcomes when they were discharged from the PICU **(13).**

The aEEG recordings were divided into three-hour sections, evaluated using the Hellström–Westas classification and transformed into a 24-hour summary score according to the background pattern. The scores were significantly associated with neurological outcomes and a cut-off value discriminated between favourable and poor outcomes. **(13).**

In addition, the evolution of the background pattern was examined. This showed that only one patient with a pathological background had a favourable outcome and only one patient with a normal background showed an unfavourable outcome. **(13).**

This was in line with the findings in a mixed patient population, where pathological background patterns and adverse evolutions of background were associated with poor outcomes. In adolescents and young adults with anti-N-methyl-D-aspartate receptor encephalitis, a greater parietal aEEG bandwidth predicted poorer neurological outcomes after 12 months. **(14).**

Although evidence is still sparse, these results show that pathologies of different aetiologies may affect aEEG bandwidth. Long-term outcomes after cardiac surgery have been associated with perioperative aEEG patterns. The post-resuscitation summary score offers the possibility to stratify the severity of brain injuries in cardiac arrest patients. In the long term, this could further promote the use of aEEGs in paediatric intensive care medicine and facilitate clinical studies on neuroprotective strategies and post-cardiac arrest care **(14)**.

5- aEEG during anaesthesia

Sedatives affect aEEG values in neonates and adults by lowering the amplitudes or causing depressed background patterns. Minimum and maximum amplitudes of parietal aEEG became higher after induction in children undergoing anaesthesia with inhaled gases and opioids, and these changes were age-dependent and less pronounced in younger infants. **(20).** However, the electronically measured mean aEEG amplitude in children under two years of age did not correlate with the alveolar sevoflurane concentrations in another study. **(10).**

children's background patterns can be continuous, in spite of continuously administered sedatives. However, it is observed one infant who had a burst suppression pattern that was caused by a severe midazolam overdose. The patient took more than a week to re-establish a continuous background **(10).**

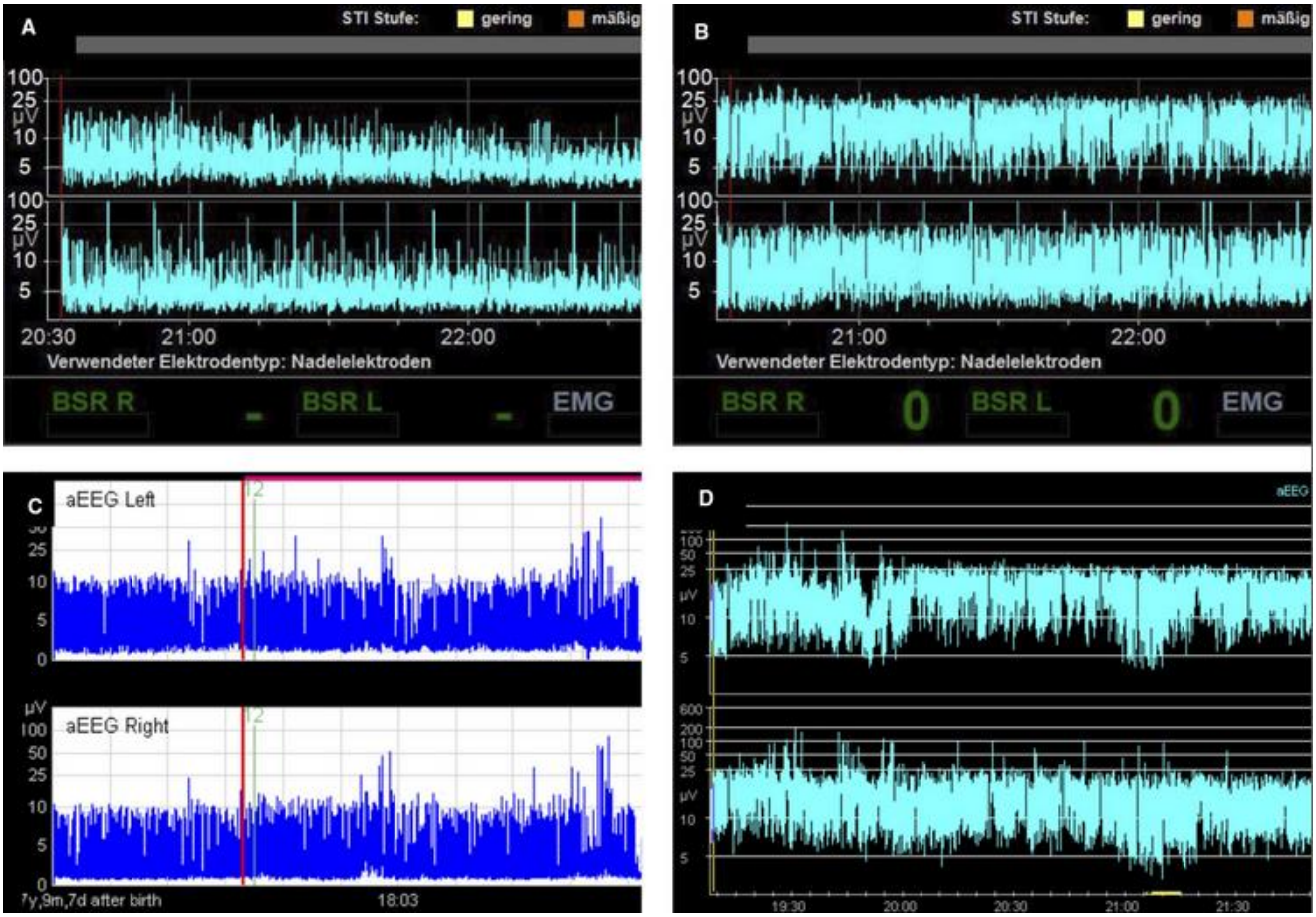

FIGURE 1: Examples of the evolution of aEEG traces over time. A, Preterm infant at an actual age of four months, and corrected age of one month, with septic shock and arterial hypotonia. The background pattern is a very low continuous voltage that can only be distinguished from burst suppression pattern by the variation of the lower amplitude. B, Afterstabilisation and resolution of arterial hypotonia, the background pattern changed to discontinuous normal voltage. C, Two-month-old comatose infant with midazolam intoxication. The initial tracing showed a burst suppression pattern that was not resolved by two doses of flumazenil (vertical green line). D, Over the course of more than one week, the background pattern changed to continuous, as shown here, and the patient became vigilant

Existing studies demonstrate that changes in aEEG occur during anaesthesia and help to discriminate between children who are awake and anaesthetised. However, they do not support the use of aEEG to monitor the depth of anaesthesia. On the other hand, many children admitted to PICUs receive sedative treatment. Analgosedation has been shown to lower the median aEEG amplitude and increase the burst suppression rate in adults who have had cardiac arrests. **(20)**

Given the effects of sedation on neonates and adults, comprehensive knowledge about sedative-induced aEEG changes is relevant for paediatric critical care providers and further research is needed into this. **(20)**

6 - Limitations and outlook

The main limitation of the aEEG is the fact that only a small area of the brain surface is covered by the tracing. Thus, alterations of electrocortical activity in different areas of the brain surface may remain unnoticed. Due to the time compression, short-lasting changes of cerebral activity are difficult to detect without using the

raw EEG curve. Further interpretation of the raw EEG curve requires knowledge about the conventional EEG or close cooperation with neurophysiologists or pediatric neurologists. **(21)**.

aEEG has several limitations due to the underlying technique. A major concern is the reduced set of channels, as this causes loss of information from brain areas not covered by electrodes. While aEEG enables clinicians to carry out long-term trend monitoring, its short-term evolution is difficult to assess due to the compressed time scale. The height of amplitudes may be altered by artefacts, medication, state of consciousness and other clinical conditions. (**22).**

Scientific articles that have evaluated the use of aEEG in older infants and children are still scarce. The number of papers on aEEG in preterm infants and newborn infants was similar 10 and 20 years ago. Today, there are an exhaustive number of papers and aEEG has become standard care for newborn infants after birth asphyxia. With increasing evidence on continuous neuromonitoring, studies on aEEG in children are likely to increase in the coming years. In particular, predicting outcomes is of major interest and will probably be comprehensively investigated. In this context, reference values for infants and children who are older than three months of age are urgently needed to distinguish physiological and pathological patterns. **(22)**.

As scientific and clinical experience grow, aEEG is likely to find a place in bridging the time to full-channel EEG and the rapid assessment of unresponsive children. Coma, seizures, traumatic brain injuries and post-resuscitation management are some of the clinical settings where this technique may be helpful. (**22).**

To address the loss of information, due to the reduced number of channels, intermittent EEG and continuous aEEG monitoring could be combined to identify seizure foci via EEG. aEEG electrodes could be placed above seizure foci to enable long-term monitoring of these areas. Even when continuous full-channel EEG is available, additional trend monitoring may help to identify sections where seizures are suspected and to direct expert reviews of the raw EEG to these sections. (**22).**

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