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The aEEG Booklet

A quick overview for the practical routine

NIHON KOHDEN

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1. Foreword

If I have learned one thing during the writing of this book, it is that you are never finished. You always keep having new ideas, or keep thinking you could still improve something. With this in mind, I would like to think of this first edition as a beginning - as the beginning of a book which will grow with time and with the aEEG method. Practically every month, there are new studies published on the subject, and new ideas are constantly being born. At this point I would like to call on all readers to send me their comments for improvements, ideas, publications and examples, so that later editions of this book will be kept up-to-date.

I owe particular thanks to Helmut M. Becker and Nihon Kohden Corporation - it is their commitment and enthusiasm for the subject that have made this book possible at all. I also owe a debt of thanks to my colleagues Dr. Richter and Dr. Klebermass-Schrehof for their support and collaboration over the years in the field of cerebral function monitoring and on the many training events we have conducted in the German-speaking region.

Finally, my thanks go to my family. To my parents, who gave me my grounding in life, and who have always helped me to realize every one of my dreams. And thanks to my wife Esther, for her inexhaustible patience with me and for our wonderful life together.

Munich, May 2011 Karl Florian Schettler

2. Basics of the method

2.1. History

The method of amplitude-integrated EEG has already been around for far longer than might be presumed. As early as 1969, Prior and Maynard[1] first described the method in adults. In the 1970s and 1980s, the method was increasingly used with children[2], and the advantages of its use investigated. The aEEG method experienced its first renaissance and significant improvement in the 1990s, when digital technology increased greatly and now the original raw EEG was displayed and recorded together with the aEEG. Particular recognition was ultimately achieved by the aEEG as a method of identifying asphyctic neonates suitable for hypothermia studies, such as the Cool Cap trial.

2.2. Technical background

The technical set-up is, to over-simplify, that of a conventional EEG, with the signal received being filtered, aligned and compressed after appropriate amplification. The filter reduces the frequencies to the range between 2-15 Hz (Fig. 1), which is intended to minimize electrical interference from other equipment used in an intensive care unit environment.

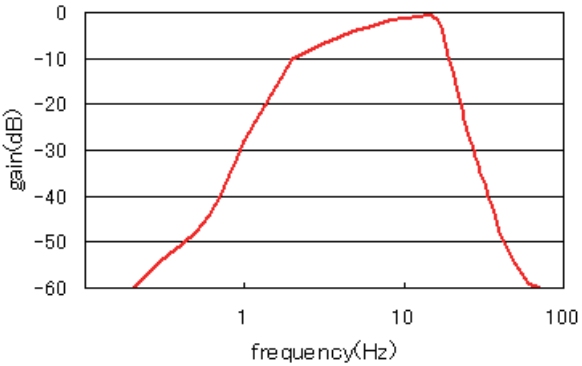


Fig. 1: Filtering the signal to frequencies between 2-15 Hz

Time compression is standardized to one millimeter per minute and thus 6 cm per hour. (Fig. 2)

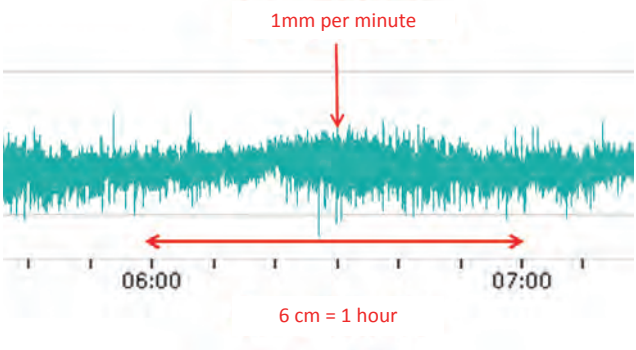


Fig. 2: Time compression in the aEEG

The amplitude of the signal is displayed semi-logarithmically, which means that the scale of amplitudes (measured in µV)

initially runs from 1-10µV in a linear manner and from 10-100µV in a logarithmic manner (Fig. 3). The reason for this is that the amplitudes of interest for the evaluation and differences in neonates are located roughly between 0-20µV. At the same time, however, it is not uncommon for very high amplitudes to occur due to bursts or artifacts, where it is not necessary to differentiate the absolute height with the same degree of fine detail. Thus a semi-logarithmic display provides the best overview.

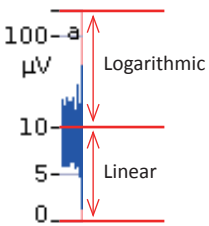


Fig. 3: Semi-logarithmic display of amplitude

The resulting band-shaped pattern of peak-to-peak values of the raw EEG (Fig. 4) can be compared to the principle of cardiotocography (CTG) familiar in obstetrics.

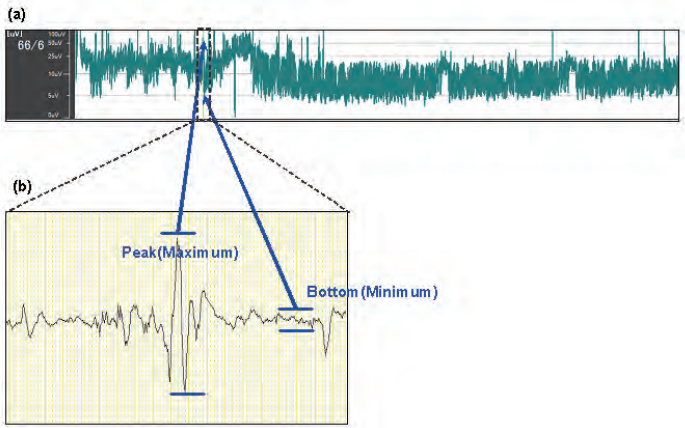


Fig. 4: creating the aEEG from the raw EEG

There are differences in the number of aEEG channels recorded. Originally there was only one "crosscerebral" channel, derived from EEG positions F3 to F4 or P3 to P4 (named by the 10-20 system of Fig. 5). The frontal leads became less relevant, especially for recognizing seizures, because it is possible to miss more pathologies over that region. With the desire to be able to differentiate whether the aEEG signal has a hemispherical difference (e.g. in case of unilateral damage) the 2-channel aEEG was introduced. It is derived from positions C3 to P3 and C4 to P4. In addition to the possibility of being able to identify unilateral pathologies in brain activity, Lavery et. al. additionally demonstrated that in certain cases more pathologies can be missed with a 1-channel aEEG than with the 2-channel method[3]. Some modern devices now permit for any preferred number of aEEG channels, to be derived from a wide range of electrode

positions. It could probably be demonstrated that with more simultaneously recorded aEEG channels there is an associated further increase in the sensitivity of the method, until ultimately as many channels are recorded as for a conventional EEG. The question should be asked whether this is reasonable for the aEEG, which is intended to fulfill the function and practicability of a monitor in the intensive care unit. For that reason, it is suspected that not significantly more than 2 channels will be used for cerebral function monitoring.

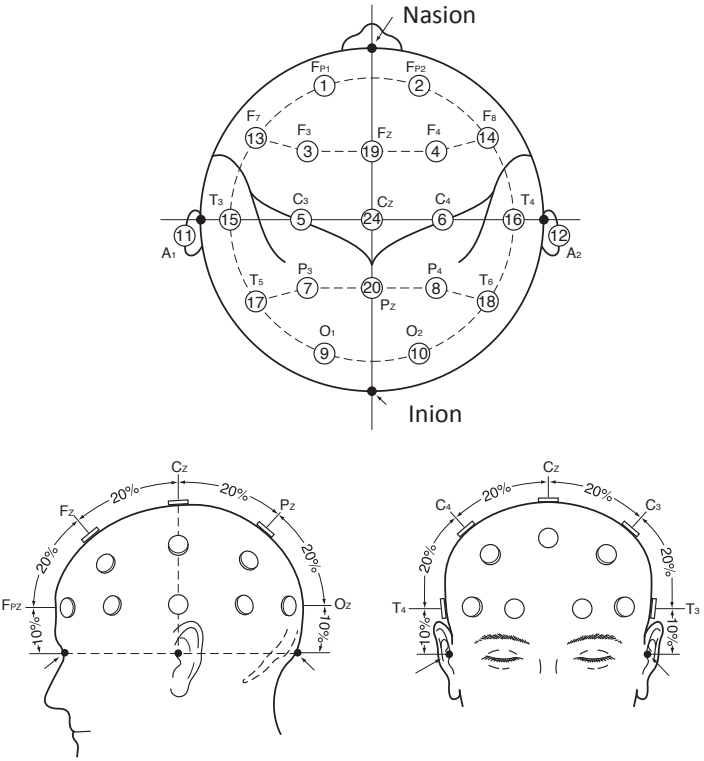


Fig. 5: International 10-20 system of electrode positions, where the spacings between electrodes are given as percentages, in order to remain constant positions for different head sizes

All aEEG monitors show and record the impedance. The impedance corresponds to the quality of the electrode contact and recording. The tolerable range of impedance is indicated differently from device to device, and is generally in the region of 0-20kOhm. If an electrode shows a high impedance outside

the acceptable range, it needs to be reattached. If a sudden change is spotted in the aEEG, then a simultaneously registered significant increase in impendence would indicate an artifact. In the days before simultaneous recording of the raw EEG, this was often the only indication available of an artifact.

2.3. Advantages and intention of aEEG

After these technical details, it is appropriate to ask about the advantages and intention of the method. Amplitude-integrated EEG is intended to be used as a cerebral function monitor in the modern intensive care unit. It is therefore comparable to a traditional ECG monitor in an ICU, which provides us with key points of orientation about the patient's health status, using heart rate and rhythm. The aEEG shows us important information about the neurological activity of our patient, thereby extending our points of orientation and providing critical assistance in identifying cerebral function disturbances at an early stage. In a study of mine on the current use of the aEEG in Germany, over 85% of users interviewed indicated that the aEEG provided valuable information for them which also had an effect on decisions relating to therapy. The method should not be overly relied on, since it is only a "monitor". It is not, as often stated, a major disadvantage of the aEEG that it provides less information than a conventional EEG, which is simply a fact due to its role and practicability as a monitor. But this does not diminish the benefits of the aEEG, or would you fundamentally prohibit the use of your 3-channel ECG in the intensive care unit, since the 12-channel ECG might be able to provide you with more information in certain situations?

Since aEEG is a monitoring solution for the brain it suggests itself to be integrated in a patient monitor which is used anyway at an ICU. This kind of solution has been just introduced into the market and it will be interesting to see if the integration with other patient data will lead to new findings e.g. was the seizure first or the SpO_2 drop?

3. Electrodes

The optimal electrode would have the lowest possible impedance, and thus high lead quality. It should be as easy as possible to fix and should not become immediately loosened again during care measures. To that end, they ought to be as insensitive to artifacts as possible, and at the same time cost-effective.

To derive the electrical signals and thus the raw EEG, there are various types of electrodes, and no single type is always "the best". It is not only the individual situation, but also personal preferences due to experience and possibly the resulting costs that determine the choice.

3.1. Positioning of electrodes

In naming the correct positions, the internationally-valid 10-20 nomenclature of positions is employed when preparing an EEG.

1-channel aEEG usually uses electrode positions P3 and P4. The reference or neutral electrode is generally placed centrally at the front (Fig. 6).

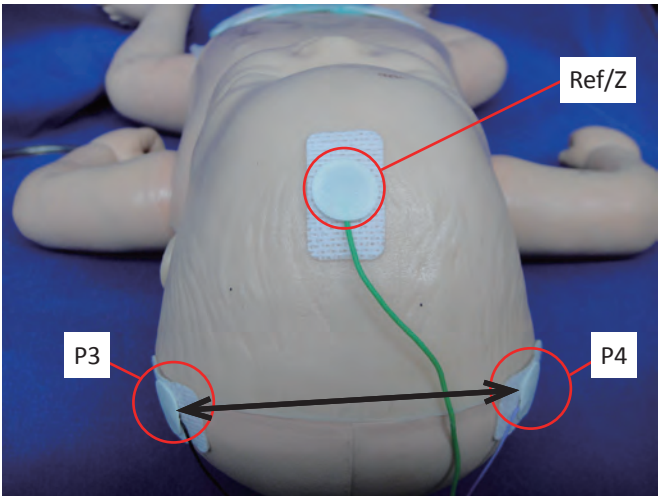


Fig. 6: 1-channel aEEG cross-cerebral from P3 to P4 and a reference or neutral electrode

2-channel aEEG uses the electrode positions C3 and P3, and C4 and P4. Here the reference or neutral electrode is usually positioned in the shoulder area or centrally to the front, depending on company recommendations for the specific monitor type (Fig. 7).

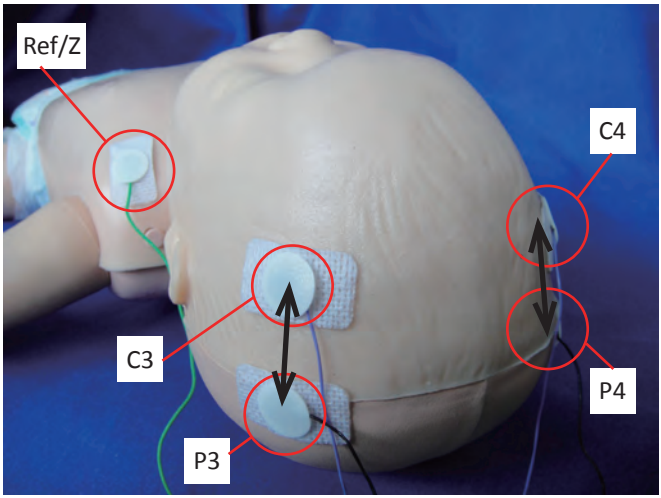


Fig. 7: 2-channel aEEG with unilateral leads from C3 to P3 and C4 to P4 and a reference or neutral electrode

The specified standardized positions are to be respected if possible in all cases. The use of new positions is not sufficiently evaluated in studies and in doing so this often changes the distance between electrodes and thus the measured amplitude height. This effect is already modestly observable in a comparison of 1-channel and 2-channel aEEGs. If there should nevertheless be a need to depart from the standard positions, e.g. for one of the reasons set out below, it must be considered that the new distance between the electrodes might have an influence on the amplitude height. The smaller the distance between the electrodes, the smaller the measured amplitude, and vice versa. The necessary use of substitute positions should therefore also be mentioned in the findings.

More frontally positioned electrodes in the 1-channel-aEEG (Position F3 to F4) should probably no longer be used, since there is a higher risk in missing of seizures. Unfortunately, users generally tend to fix more frontally, since this is sometimes where fewer hairs are disturbing. When positioning the electrodes, it should always be ensured that these are not fixed over the fontanelles, sutures, edemas, hematomas or skin lesions. Unnecessary contact with the patient's bed or positioning aids should be avoided.

3.2. Hydrogel electrodes

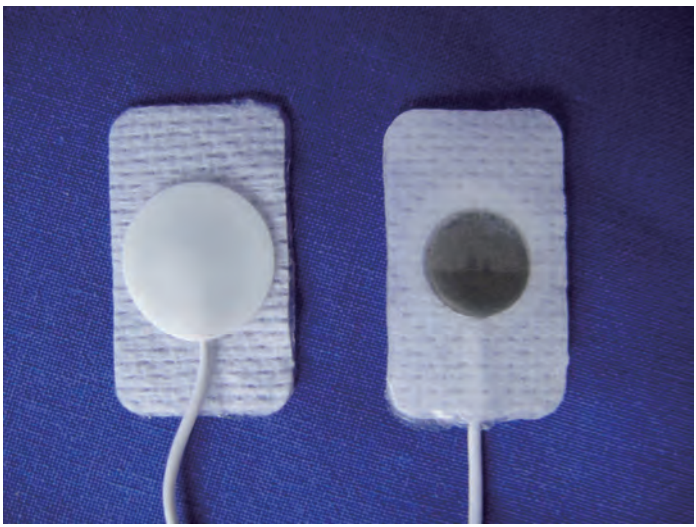


Fig. 8: Example of a hydrogel electrode

Hydrogel electrodes (Fig. 8) are self-adhesive electrodes. Their advantage is primarily that application is considered to be a

relatively simple matter which is not irritating for the neonate. In reality, however, there are some obstacles to be overcome: Firstly, the skin on the head needs to be appropriately prepared and cleaned to achieve reasonable impedance and thus lead quality. The presence of hair makes fixing and preparation more difficult. This is frequently a very frustrating experience, particularly for new users attaching their first electrodes. It is an easier process in very immature preterms with less head hair.

If a good lead quality has been achieved, perhaps only after a few attempts, it is relatively easy to lose the contact again, e.g. because of movement of the infant during care, where often only a tug to the cables worsens the impedance. Even the possible presence of high air humidity in the incubator means there is a more rapid loss of contact. If a 2-channel aEEG is being recorded, then you need to keep a total of 5 electrodes "running", which can certainly be very time-consuming. The skin needs to be re-prepped each time an electrode is re-fixed, which can cause the infant to be woken from sleep under some circumstances and is often not compatible with minimal handling.

As the hydrogel electrodes cannot be reused, these generate higher costs than gold electrodes. On the market, there are a wide range of electrodes from a large variety of companies. The advice is to start by using those supplied with your equipment from the same company, and then simply look around to see what is available and try out others. A check for compatibility of plug contacts is required, although these days practically all devices use standardized contacts or offer appropriate adapters.

Use the experience of the nurses working in your neurological department, whose working day is often entirely taken up with attaching electrodes for EEGs. They are the best to demonstrate how good impedances and lead quality can be achieved.

A step-by-step introduction into how hydrogel electrodes are applied and especially how the skin is prepared for a good contact can be found in Appendix 12.3.

3.3. Gold electrodes

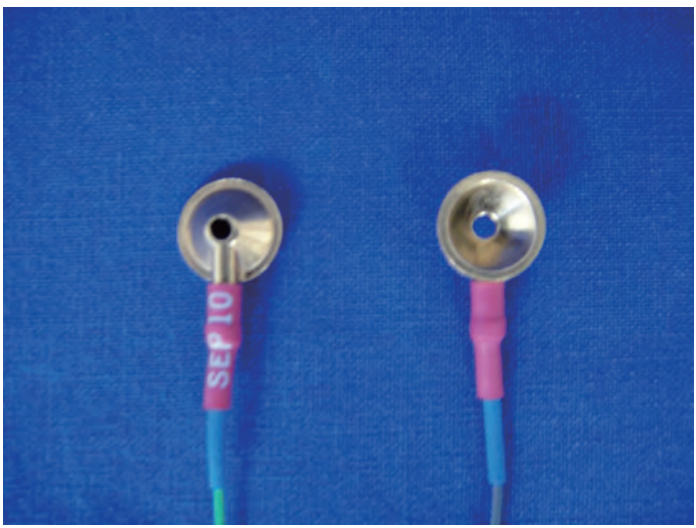


Fig. 9: Example of a gold electrode

Gold electrodes (Fig. 9) are particularly preferred for use in more neuropediatric-oriented departments. If correctly attached, they generally offer better impedances than hydrogel electrodes,

and are more easily fixed to hair-covered areas. Procurement costs are initially higher than for individual hydrogel electrodes, but the gold electrodes can be reused and thus generate significantly lower total costs. In neonatal units where hydrogel and gold electrodes are simultaneously in use, it might be wise to label the gold electrodes clearly, as otherwise inexperienced personnel are often unable to differentiate between the two and the gold electrodes are similarly thrown away. Preparation of the skin of the head is analogous to the preparation when using hydrogel electrodes as described in Appendix 12.3. Gold electrodes are being attached by using a conductive adhesive cream, which fixes the electrode in place when it dries. The cream should not be applied directly onto the hair, but (as with the hydrogel electrodes) in a parting in the hair (see Fig. 10). After use, the cream and electrode can easily be removed using water.

Fig. 10: Correct attachment of a gold electrode on a hair-covered skin

3.4. Needle electrodes

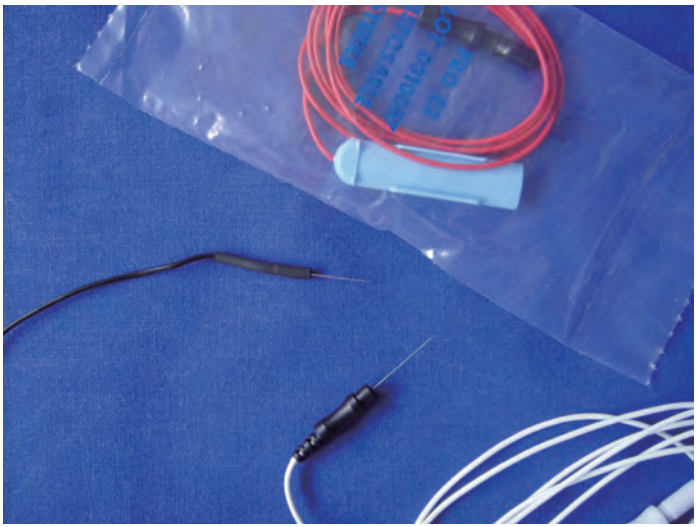


Fig. 11: Examples of needle electrodes

The use of needle electrodes (Fig. 11) is often highly disputed amongst neonatologists. The reason is probably that as soon as the word "needle" is used one automatically assumes a significantly more invasive procedure and there is usually also an increased concern about infections. The advantage of using needle electrodes lies very clearly in the speed with which these can be attached, and also in the perfect impedance thereby achieved over a long period of time. A practical trial is recommended - it will be seen that the laborious application of adhesive electrodes, often with repeated manipulations and rubbing of the infant´s head, stresses the infant significantly more and generates more crying than the quick performed

insertion of needles. Consideration should also be given to the fact that needle electrodes then usually remain in position, with generally good impedances, whereas the hydrogel electrodes often require the contact to be improved after a few hours, with again further manipulation of the infant required. However, one major disadvantage of needle electrodes is the significantly higher cost for material which is single-use only.

The typical patient group where needle electrodes can be used are term infants with asphyxia. Here initially there is generally little spare time for attaching electrodes, and often more extended aEEG recordings over several days are necessary and desirable.

When positioning needle electrodes, the skin should first be adequately cleaned and disinfected, as for any transcutaneous puncture. To minimize pain, the skin should be pretensioned slightly, and the subdermal insertion should be executed rapidly. When introducing the needle electrodes, they should not face towards another, so they do not come into contact with each other. This could cause a "short circuit" and an aEEG artifact that can easily be misinterpreted as a flat trace. The needle must be placed completely as far as the end of the needle shaft. Direct positioning too deeply in the temporal muscle needs to be avoided, as this will cause extreme muscle artifacts. A wide range of methods is used to attach the needle electrodes (Fig. 12). The most advantageous is a method where the insertion point can be sufficiently assessed with regard to early signs of a possible local infection. However, the risk of infection should be considered relatively low. These days only sterile disposable

needle electrodes are being used. Specific studies regarding a possible infection risk because of the use of needle electrodes in neonates still have to be published.

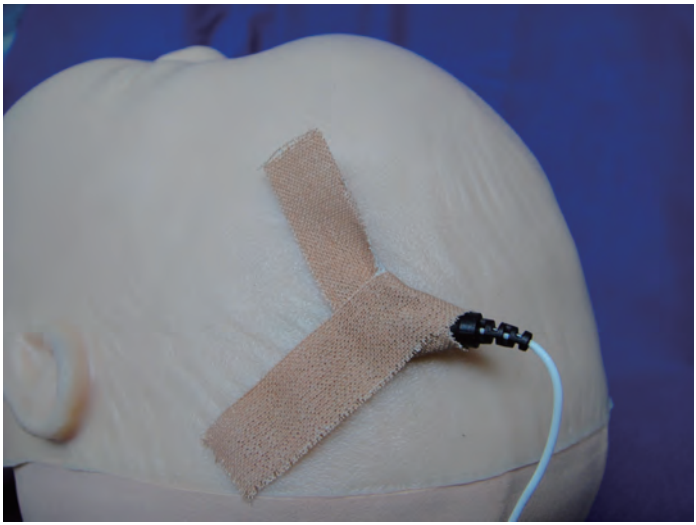


Fig. 12: Possible simple fixation of a needle electrode

4. Background activity and classification

The assessment of cerebral background activity in the aEEG is undertaken primarily through simple pattern recognition. Initially there were similar but different classifications which were used for different patient groups (asphyxia, preterms etc.). Hellström-Westas et al. proposed a classification in their publication in NeoReviews in 2006[4] that is suitable for all patient groups and that is universally recognized and used.

A table with a full overview of all patterns can be found in Appendix 12.1.

4.1. Continuous pattern, continuous normal voltage, C

The continuous normal voltage pattern (Fig. 13) is a relatively narrow band which represents a persistently normal high level of amplitude in the raw EEG. It has a defined minimum amplitude (lower margin) of (5-)7-10µV and a maximum amplitude (upper margin) of at least 10-25 (max. 50) µV. In neonates, a lower margin of 5µV can be assumed. The differing information regarding the limit of the lower margin came about to some extent due to different distances between electrodes for 1-channel and 2-channel aEEG and other technical issues. At the moment increasingly 5µV is generally accepted as the lower limit.

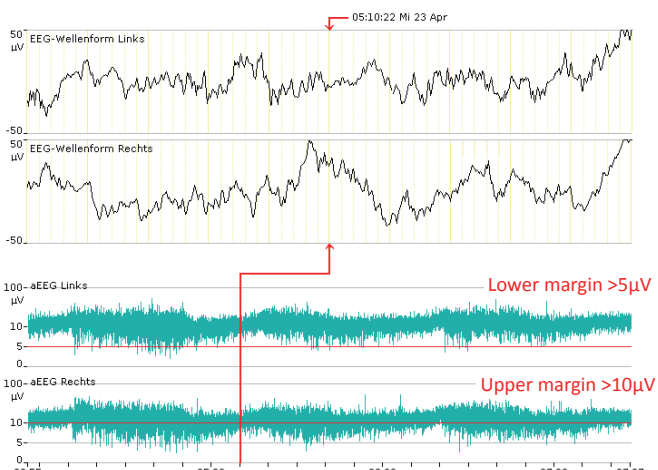


Fig. 13: Continuous pattern

4.2. Discontinuous pattern, discontinuous voltage, DC

The discontinuous pattern (Fig. 14) is characterized by a minimum amplitude (lower margin) of under 5µV, which is however still variable. The maximum amplitude (upper margin) must be at least 10µV. Phases with higher amplitude activity and phases with a lower level of amplitude occur and result in a broader band. In immature preterms this activity is physiological[5], but for a healthy term infant with no influence of any drugs a constant discontinuous pattern is no longer normal.

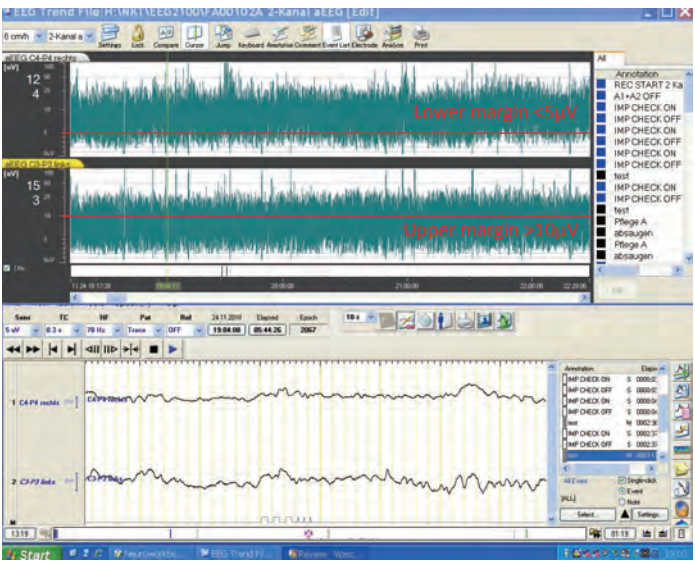


Fig. 14: Discontinuous pattern

4.3. Burst suppression pattern, BS

With the burst suppression pattern (Fig. 15), the minimum amplitude loses its variability. At the same time, however, the aEEG still has individual "peaks" similar to a comb, arising from the high amplitude of individual bursts in the raw EEG. Since suppressed EEG activity follows a burst, the lower margin obtained is correspondingly permanently low. The minimum amplitude (lower margin) in the burst suppression pattern is around 0-1(-2)µV. The observable bursts, by contrast, have a high amplitude of >25µV.

Corresponding to the frequency and density of the occurrence of bursts, the burst suppression pattern can be distinguished between a BS- pattern (under 100 bursts/hour, Fig. 15) and a BS+ pattern (over 100 bursts/hour, Fig. 16). This results according to whether you have a shorter (BS+) or longer (BS-) interburst interval. Many aEEG devices can now also display the interburst interval and the burst suppression ratio in graph format, and it should be included in the assessment of a burst suppression pattern. However, it can also be measured easily using the gap between two bursts in the raw EEG.

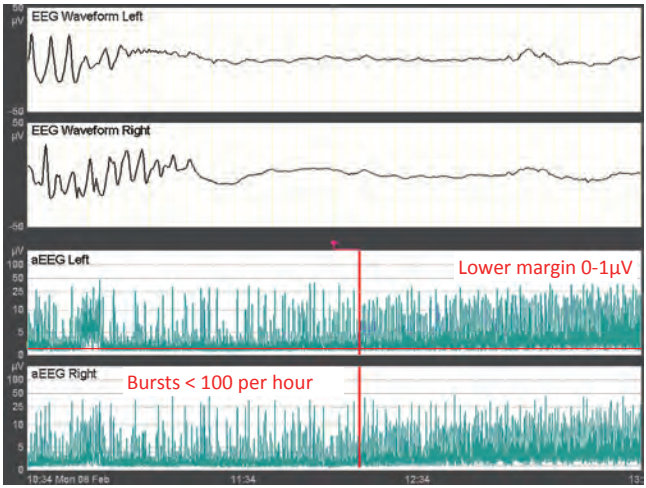


Fig. 15: BS(-) pattern

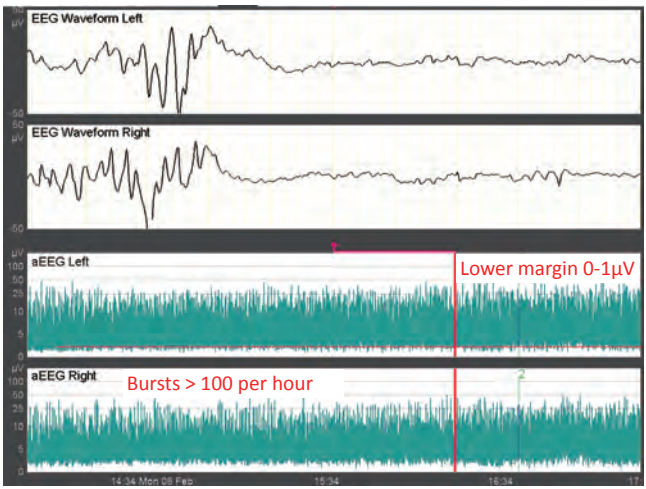


Fig. 16: BS(+) pattern

Beginners in aEEG need to be particularly careful with the BS+ pattern, because at the first superficial glance this can certainly resemble a discontinuous pattern. The critical feature for identification in the aEEG is the lack of lower margin variation in the burst suppression pattern. An additional disturbance can be a "shift of baseline" occurring as artifact (Fig. 17), as a result of which the lower margin of the burst suppression pattern is no longer located around 0-1µV. A short glance at the raw EEG similarly helps in distinguishing this pattern reliably. For easier determination, one manufacturer has introduced a grayscale where bursts in the aEEG pattern can be better visualized.

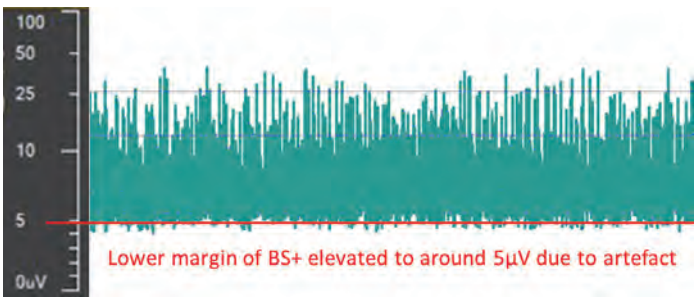


Fig. 17: BS(+) pattern with shift of baseline

4.4. Low voltage, LV

The low voltage pattern (Fig. 18) arises from persistently low amplitude activity. Accordingly, the minimum amplitude (lower margin) is continuously and without much variability at or below 5µV and the maximum amplitude (upper margin) does not exceed 10µV.

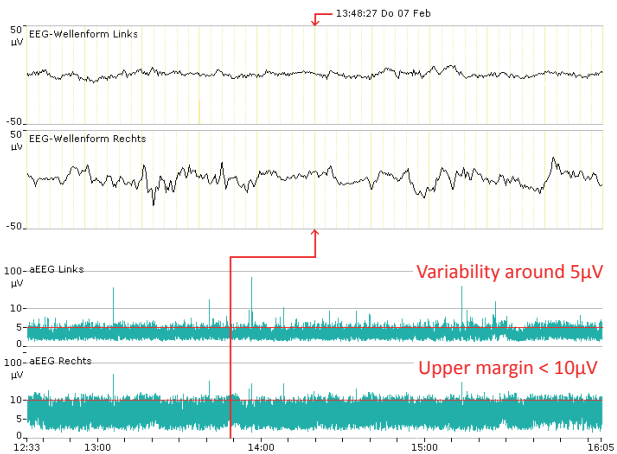


Fig. 18: Low voltage pattern

4.5. Inactive, flat trace, FT

The flat trace pattern (Fig. 19) corresponds, as the name indicates, to a continuous general amplitude depression. There is a very narrow band along the lower margin. The raw EEG is inactive and isoelectrical. The background activity remains continuously below 5µV. Individual peaks in the aEEG are mostly triggered by artifacts and not by bursts. In the case of uncertainty as to whether a long interburst interval exists, a review of the raw EEG assists with identification.

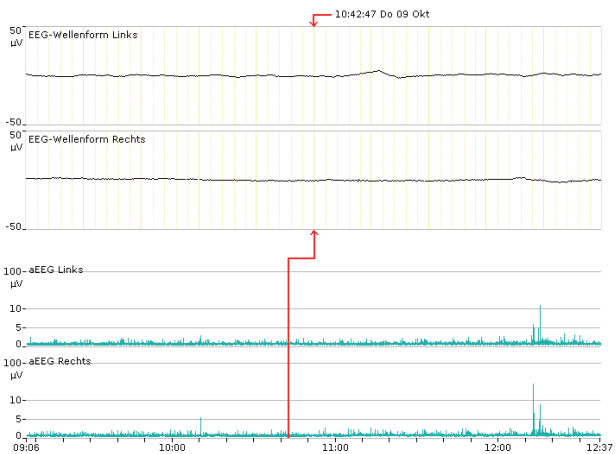


Fig. 19: Flat trace without activity

4.6. Sleep-wake cycles, SWC

Sleep-wake cycles describe the regular occurrence of phases with more continuous activity (being awake, active sleep, AS) alternating with phases of more discontinuous activity (deep sleep, quiet sleep, QS). The phase of continuously cerebrally more active, higher-amplitude active sleep is shown correspondingly in the aEEG as a narrower band, whereas the quiet sleep phase is wider in the aEEG due to greater variability and lower amplitudes (Fig. 20). The quiet sleep phase in the aEEG is comparable with the tracé alternant (alternating trace) in the EEG of a term infant.

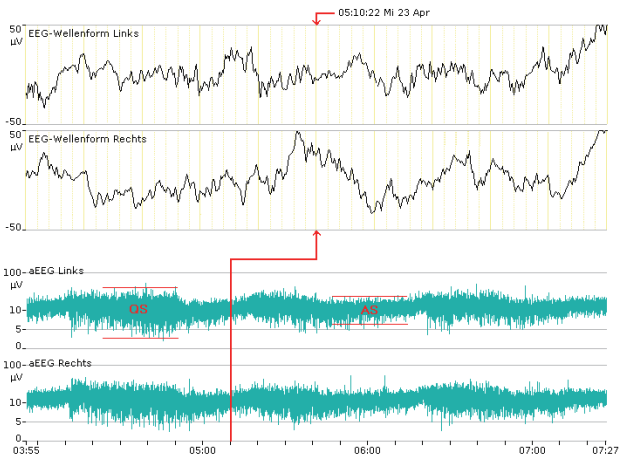


Fig. 20: Continuous pattern with sleep-wake cycles, QS=Quiet sleep, AS=Active sleep

The alternation of active and quiet sleep produces a regular sinusoidal periodic pattern, particularly in the lower margin of the aEEG. The duration of a complete sinusoidal pattern, with active and quiet sleep together, usually lasts over one hour, with the amount of quiet sleep normally being around 20-30minutes.

The presence of sleep-wake cycles can be viewed as indicating the existing integrity and coordinating ability of the brain, and its increasing occurrence in preterms as indication of brain maturation. In preterm infants, the cycles are already apparent from the 25th-26th week of pregnancy[6,7], and generally fully developed from the 29th-30th week of gestation[7]. This sign of maturation and function of the brain can however be impaired and slowed down by asphyxia or cerebral hemorrhaging.

In accordance with the current generally valid classification[4], sleep-wake cycles can be assessed as follows:

No SWC = no cyclic variations in background activity are observed (Fig. 21 A)

Immature or incomplete SWC = by reference to gestational age, the cyclic variations observable in the minimum amplitude are too sparse and not fully developed (Fig. 21 B)

Developed SWC = clearly identifiable, age-appropriate sinusoidal variations between more discontinuous and more continuous background activity, with a cycle period of at least 20 minutes (Fig. 21 C)

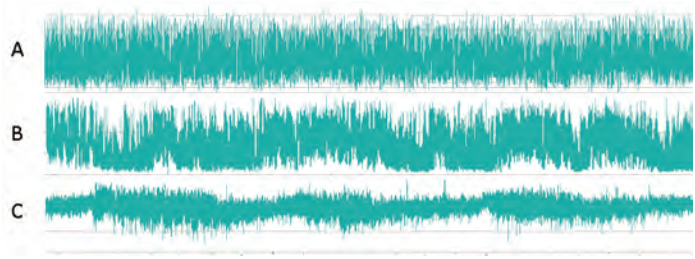


Fig. 21: A. No sleep-wake cycles, B. immature or incomplete SWC, C. developed SWC

4.7. Artifacts

Artifacts are found on average in approx. 12% of the recording period[8]. Of these, around 45% are caused by movement and the remaining 55% by electrical interference[8]. By implementing the raw EEG in the recording, it became significantly easier to identify artifacts reliably.

Shift/Drift of baseline: Permanent artifacts in the raw EEG often lead to what is termed a shift or drift of the baseline. The steadily-repeating artifact amplitudes in the raw EEG mean that, for example, in the burst suppression pattern there are no longer any suppression phases without an amplitude, because during the suppression phase the artifact amplitude is still recorded. As a consequence, the lower margin of the aEEG increases and the actual baseline of 0µV now lies e.g. at 3 µV, since the artifact constantly interferes with an amplitude of 3 µV (Fig. 22).

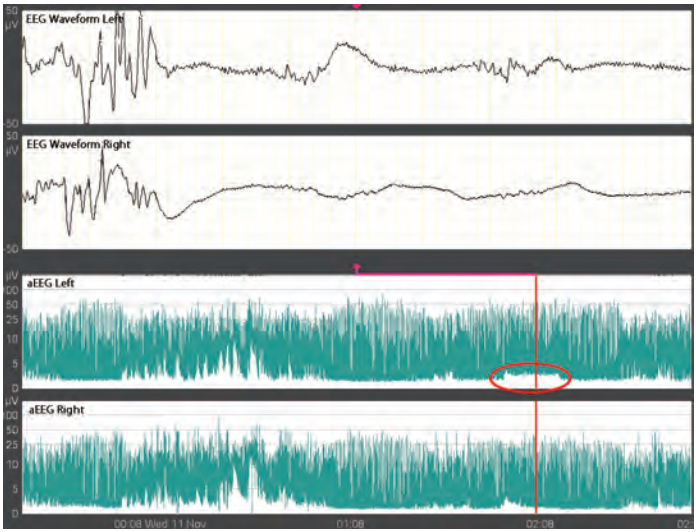


Fig. 22: Small shift of baseline of 1-2µV in the marked area on the left side in a burst suppression pattern

Movement artifact: Artifacts due to movement generally produce a sudden shift in the aEEG and can be misinterpreted as seizures if the raw EEG is not reviewed. Often they look like large-amplitude waves in the raw EEG, but they can also appear with a low-amplitude (Fig. 23). Good documentation of the child's care rounds, and if possible a camera recording, assist in identifying these artifacts more reliably. The regular patting of a baby during feeding can trigger a distinctive movement artifact, known as the patting artifact. Due to the often very regular displacements in amplitude and the frequency, here it is sometimes even more difficult to differentiate from seizures.

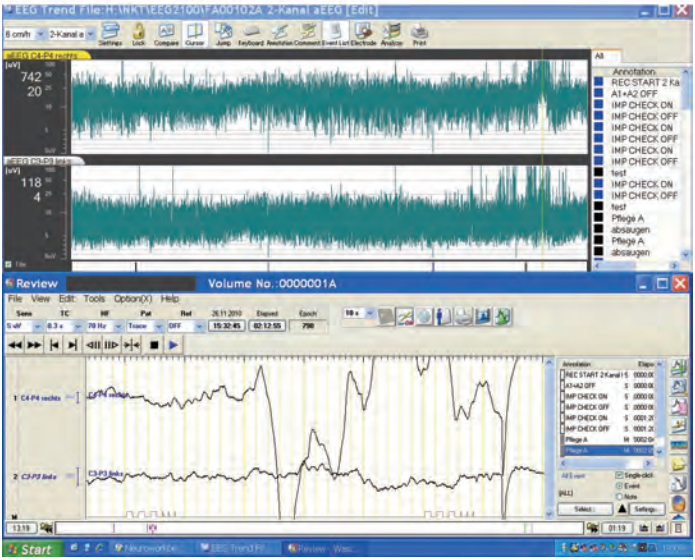


Fig. 23: Unilateral movement artifact, visible on the large-amplitude waves in the raw EEG

Respiratory artifacts: Respiration can similarly be a process which creates a lot of movement. In the raw EEG, this generates a constant interference signal (Fig. 24), which not only lifts the lower margin of the aEEG but can also make the entire recording useless. Here it is helpful to determine the frequency of the artifact with precision and to compare it with the respiratory parameters. The amplitude height can be very variable and is, for example, often low during high-frequency respiration.

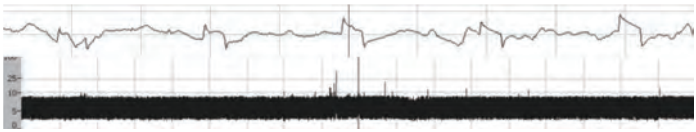


Fig. 24: Respiration artifact, the aEEG shows only the breathing amplitudes and the patient's background activity can no longer be assessed. Used by kind permission of J. W. Richter

Muscle artifact: In proximity to the usual electrode positions of the aEEG there are very strong muscles, notably the Musculus temporalis. In particular, needles placed directly into the muscle result in recording an electromyogram rather than the intended aEEG. Muscle artifacts are characterized by the very high frequency, and are therefore generally easy to identify (Fig. 25). One could practically say the raw EEG looks like "muscle tremor".

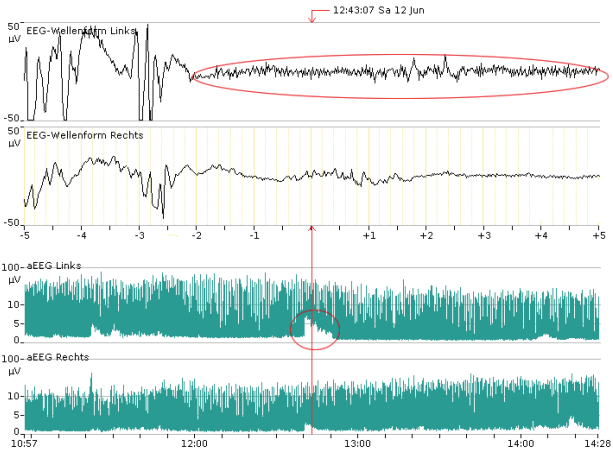


Fig. 25: Muscle artifact in a burst suppression pattern in the upper raw EEG, with associated increase in the lower margin of the aEEG

ECG artifact: Occasionally, the aEEG derives heart activity and thus an ECG. Depending on the strength of the interference signal, the resulting artifact has different-height amplitudes. Classically, this similarly results in baseline drift (Fig. 26). With a very powerful artifact signal, it is even possible to identify elements such as the P and T wave and the QRS complex. Here, again, help can be found by determining the frequency of the artifact and comparing it with the patient's heart rate, in order to identify it reliably as ECG.

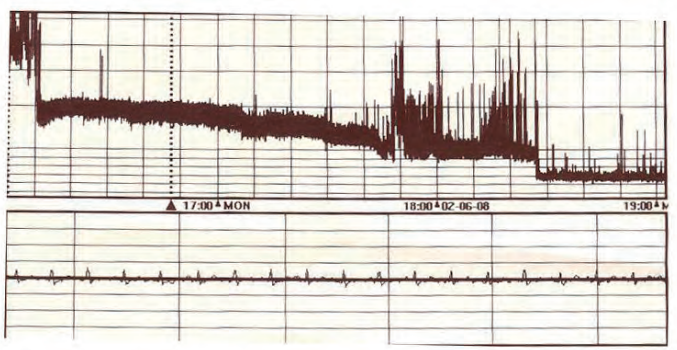


Fig. 26: Example of an ECG artifact, where the frequency of the low amplitudes in the raw EEG corresponds precisely to the patient's heart rate, with this causing a shift of the baseline in the aEEG. Image used by kind permission of K. Klebermass-Schrehof

Sensor contact or "short circuit" artifact: If the lead electrodes come into direct contact or some kind of direct electrical contact, one obtains what is practically a flat trace, which can occasionally also have the appearance of a burst suppression pattern in the aEEG thanks to other artifacts. The confusing

aspect in this is that a very good impedance is measured and therefore the user does not immediately think that anything is wrong with the electrodes. This artifact tends to occur when using needle electrodes if these are inserted facing towards one another or too close to one another. It is also possible for a direct short-circuit contact to be created externally, as in the example given below due to the strong conductivity of a 5.85% saline solution used for contact cleaning (Fig. 27).

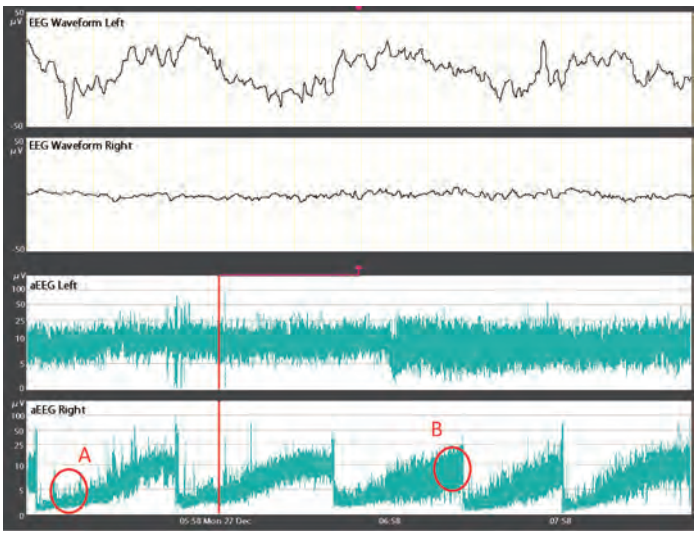


Fig. 27: A shows low amplitude after repositioned electrodes, using 5.85% saline solution with good impedance; B shows correct background activity after some time, but at this moment now has a measured worse impedance. Image used by kind permission of M. Schmid

Edema or hematoma: Fixing an electrode over a hematoma or larger edema similarly results in an artifact. The EEG signal is weakened and generally produces electrical "shunting", whereby it is again possible to give the appearance of absent brain activity (similar to Fig. 27).

4.8. Identifying and evaluating the pattern step-by-step

For correct identification and evaluation of background activity, a step-by-step approach should be adopted and the variables detailed below should be recorded:

1. **Are the impedances** and thus your recording quality adequate?

2. **Background activity:** Record the upper and lower amplitude limit and ignore any short "outliers". Check whether the lower margin is variable or runs "flat". Assign the background activity accordingly to one of the patterns detailed in this chapter. In preterm infants particularly, you should also indicate the percentage of time showing how long particular patterns predominate (see Chapter 7). With a burst suppression pattern, you can indicate the number of bursts per hour (BS+/-) and the interburst interval.

3. **Sleep-wake cycles:** Identify and describe whether SWCs are present or not, and whether normal, incomplete or immature. Particularly in preterm infants, their occurrence needs to be referenced to gestational age. If initially sleep-wake cycles are absent, e.g. following asphyxia, then

describe the point from when these reappear (important for prediction!)

4. **Seizures:** Search your recording for notable areas, particularly sudden changes in background activity such as the lower margin lifting or sudden contraction in the amplitude range (see Chapter 6). View these areas in the raw EEG and check them firstly for artifacts. If you identify seizures in the raw EEG, describe them for duration and number (individual or repeated seizures, status epilepticus). In the 2-channel aEEG, check whether seizures are generalized or just on one side. If you have a device with automatic seizure detection, each marked section needs to be reviewed.

5. **Event markings:** Check the places in your aEEG for which comments have been entered. For example, did a clinically marked seizure correlate to your aEEG or what kind of effect had a given anti-epileptic drug, etc.?

6. **Symmetry:** If you have a 2-channel monitor, compare and check whether the aEEG pattern of the two brain sides is symmetrical or differs from side to side.

7. **Indication-specific view:** Assess the informational findings regarding why the aEEG was initially indicated, and review from this aspect (e.g. search for seizures, effect of anti-epileptic drugs, background activity after asphyxia).

8. **Assessment:** Always make a concluding assessment taking account of influencing factors such as gestational age and drugs. Mention limitations on predictive reliability which have arisen during the recording (e.g. influence of drugs, too

many artifacts, poor impedance, etc.).

4.9. Influence of drugs

Sedating and anti-epileptic drugs have an effect on brain activity and can therefore also cause changes in the aEEG. This sometimes makes it harder to view the actual brain function and thus evaluate real background activity. For an accurate assessment of the aEEG signal, it is essential to know the precise nature, dosing and application time of relevant drugs, and correspondingly important here is good documentation.

Generally, sedatives and anti-epileptic drugs depress background activity and the shaping of sleep-wake cycles[9,10,11]. The aEEG therefore becomes more discontinuous (Fig. 28). Accordingly, a continuous pattern can become a discontinuous pattern and, in the extreme case, a discontinuous pattern can also cross over into a burst suppression pattern. The nature of this influence depends not only on the type of drug, but also on the used dose. Likewise, clinical practice shows that a previously-damaged brain appears to be more sensitive to influence than the brain of a healthy neonate. However, there are no proofs of this in corresponding studies yet.

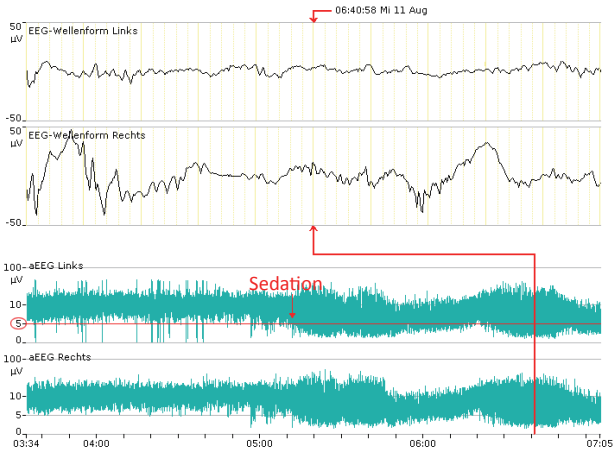


Fig. 28: The image shows how the aEEG becomes more discontinuous through sedation and thus the lower margin crosses below the 5µV limit. Sleep-wake cycles still remain present and visible, but at a lower level

Typical drugs in use are e.g. morphine, fentanyl, benzodiazepines (e.g. midazolam) and phenobarbitone. Marked effects are generally only short-term for these, and observed for not longer than 2 hours following administration. When using a drug as a continuous infusion, one therefore has a permanent influence and thus increased discontinuity in the aEEG.

The administration of surfactant often causes noticeable depressions in brain activity, lasting generally for around 10 minutes[12]. Here, however, there needs to be critical investigation as to whether what is observed is really a direct effect of the drug. Surfactant has marked effects on hemodynamics and CO_2

blood gas, which can also be responsible. This shows how a wide range of systems in our small patients work together, and how a respiratory measure can also have a relevant effect on the brain function.

However, positive use of the influence of sedatives on background activity might be possible. In the intensive care setting the physician is usually only getting informed if a child is too little sedated and too awake. On the other hand, there is little information and clinical observation whether a sedation level is unnecessarily high. In the future perhaps cerebral function monitoring can be used to better control the level of sedation.

The use of the aEEG in connection with asphyxia in neonates was one of the essential reasons why the aEEG has enjoyed such a renaissance in recent years. On account of its predictive value, a pathological aEEG was a required inclusion criteria for some hypothermia studies.

5.1. Background activity and assessment

Serious changes in the perfusion and oxygenation of the brain cause depressed brain activity, which can be shown using the aEEG. The changes thereby observed can not only be used predictively, but also serve simultaneously for monitoring to identify possible seizures due to asphyxia.

To assess the extent of an asphyxia in the aEEG, the pattern recognition is sufficient. Studies oriented to absolute amplitude values were not able to provide more predictive information. Background activity after asphyxia is often classified into 3 types, after Naqueeb[13]: Normal, moderately abnormal and severely abnormal (Fig. 29). This classification was primarily used in the context of intervention studies such as the Cool Cap Trial, and is oriented to the upper and lower margin of the amplitude.

Normal background activity after Naqueeb[13] corresponds to a continuous pattern under the new classification (continuous normal voltage, CNV). The lower amplitude is above 5µV and the upper amplitude above 10µV.

Moderately abnormal background activity after Naqueeb[13] corresponds to a discontinuous pattern in the new classification (discontinuous voltage, DC). The lower amplitude is below 5µV

and the upper amplitude still above 10µV.

Severely abnormal background activity after Naqueeb[13] corresponds to a burst suppression (BS+/-), low voltage (LV) or flat trace (FT) pattern under the new classification. The lower amplitude is below 5µV and the upper amplitude is below 10µV (except for bursts).

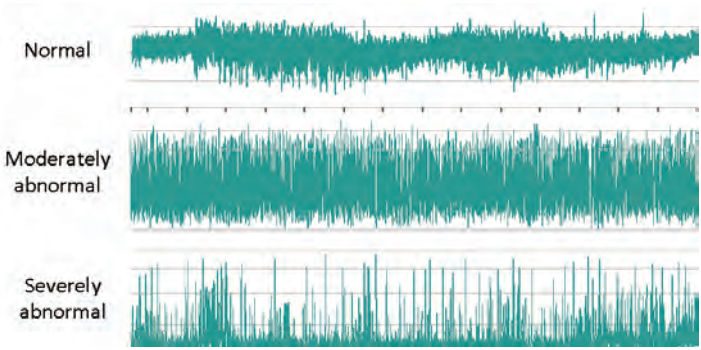


Fig. 29: Classification of aEEG patterns after Naqueeb

When assessing the background activity following an asphyctic event, it is recommended to describe the pattern using both the current classification for background activity and also to assign the pattern to one of the abovementioned three types after Naqueeb.

5.2. Predictive value for asphyxia

In the literature, the ability of the aEEG to predict a bad neurological outcome in the event of asphyxia is indicated with a sensitivity of generally >90% (aEEG discovers cerebral damage)

and specificity of generally >80% (aEEG excludes cerebral damage). Its use as the only indicator, e.g. in identifying patients for hypothermia treatment, is however to be viewed critically, since - particularly with only basal ganglia lesions or smaller one-sided brain damage - a false negative result is possible. For that reason, even an initially unremarkable aEEG following asphyxia requires a later standard EEG. As a functionally-oriented method, the aEEG is superior to some morphological methods such as ultrasound in the first hours following the asphyctic event. The combination of the aEEG with other parameters, such as clinical scores, blood investigations and increasingly also MRI, is important for a reliable and profound prediction of the outcome. Correspondingly, for instance, a study by Shalak et al. showed that the combination of aEEG with a clinical score achieved a better predictive value than using any method on its own.

Background activity classified after Naqueeb in the event of asphyxia (Chapter 5.1) correlates with the extent of the cerebral damage that can be found using MRI[14]. Accordingly, a deeper lower amplitude margin in background activity correlates with a worse neurological outcome.

In addition to the initial background activity following asphyxia, it is also important to review how long it takes for the background activity to normalize again. Van Rooij et al. demonstrated that recovery in the pattern within 24 hours is to be assessed as positive as 61% of these patients have the chance of a better outcome[15]. Thoresen et al. showed that in combination with hypothermia treatment the predictive value

of aEEG background activity becomes lower and the background activity recovery period with hypothermia can be up to 48 hours, in order for the patient still to have a relatively good chance of a better outcome[16]. However, this could also be assessed as a success of the hypothermia treatment, since patients now have a better neurological outcome than might have been expected given the extent of the asphyxia.

The assessment of sleep-wake cycles following asphyxia has proven to be a further important component in assessing the prognosis. The longer it takes following the hypoxic event for sleep-wake cycles to be demonstrated again, the higher the degree of Hyopoxic Ischemic Encephalopathy and thus the worse the outcome[17]. Osredkar and colleagues found a re-emergence after an average of 7, 33 and 62 hours correlating to Sarnat Stage I, II and III of HIE[17]. The predictive value of sleep-wake cycles seems to be increased in patients treated with hypothermia. The time to re-emergence of SWC was a better predictive value of outcome for children treated with hypothermia (88.5%) than for normothermia (63.6%)[16].

The final feature of the aEEG to be assessed is the occurrence of seizures. Seizures in moderate to severe asphyxia or a low voltage EEG has a negative predictive value for the patient's outcome[18].Since in hypothermia studies no difference was shown in relation to the relative risk for the development of seizures between the normothermia and hypothermia groups, it could be that the predictive value of this parameter of the aEEG is not influenced by hypothermia.

	0-12 hours	12-24 hours	24-48 hours
Background activity	++	+	-
Sleep-wake-cycles	+	+	-
Seizures	-	+	-
Reaction to care	-	-	-

Fig. 30: Value of the aEEG parameters for prediction, depending on time following asphyxia, based on Literature 19 and 20

Guidelines for prediction using aEEG following asphyxia
A normal aEEG in a term asphyctic infant in the first hours after the event is predictive for a good outcome.
An abnormal aEEG in a term asphyctic infant with e.g. burst suppression or flat trace is predictive for a bad outcome.
Apporox. 60% of children with a recovery of the background pattern in first 24 hours have a better outcome, in patients treated with hypothermia this time-window is 48 hours.
The time until reoccurrence of sleep-wake cycles needs to be documented and has a predictive value.
The occurrence of seizures following asphyxia with pathological background activity is predictive for a poorer outcome.
To assess the recovery period of an abnormal aEEG and the reoccurence of sleep-wake cycles, longer-term recording is required.
Sedatives, anti-epileptic drugs and hypothermia can have an influence on the aEEG and thus its predictive value.
The aEEG should not be used on its own for prediction, but supplemented at least by a clinical score.
In the asphyctic infant, even a normal aEEG from the beginning must be completed later by a standard EEG.

Fig. 31: Guidelines for prediction of outcome with aEEG in infants with asphyxia

6. Seizures

Seizures at neonatal age are most frequently only the symptom or consequence of another illness. They occur particularly in connection with hypoxia, intracerebral hemorrhage, metabolic disorders, meningitis and encephalitis, drug withdrawal syndromes, hemodynamically significant congenital heart defects, inherited brain defects and serious general illnesses such as multiple organ failure or systemic inflammatory response syndrome. The increasing use of the aEEG demonstrates to us how often epileptiform discharges and seizures were missed by clinicians in the past. While the therapy indication for a status epilepticus is clear, with short and isolated seizures in particular the question still remains which seizures are to be treated in which patients, with which drug and how aggressively. In part, this uncertainty also lies in the fact that the perfect anti-epileptic drug without negative side-effects on the developing preterm brain remains to be discovered.

The use of the aEEG to identify and verify seizures is highly valuable since there is a high dissociation between clinical and electrophysiological observed seizures. Thus in only around 70%[21] of clinically observed seizures an electrophysiological correlate can be found. On the other hand, one can often prove seizures electrophysiologically without discovering them clinically[22]. Even further complicating is that it is possible to demonstrate ongoing electrophysiological seizures even though clinical symptoms cease after anti-epileptic drugs are administered[23]. This high degree of uncertainty amongst clinicians when discussing seizures in neonates shows the importance of longer-term neurophysiological monitoring alongside the standard EEG.

Seizures show in the raw EEG as stereotypical, repeating forms such as spikes or sharp waves. In many studies a duration of at least 10 seconds is generally required in order to speak of a seizure. Shorter epileptiform activities are however likewise not to be categorized as non-dangerous, and there is a need for more research in future regarding the effects of these short events[24].

The repeating, often high-amplitude spikes and wave forms in the raw EEG in connection with a seizure show in the aEEG primarily as a sudden rise in the lower amplitude margin and, to some extent, in the upper margin (Fig. 32).

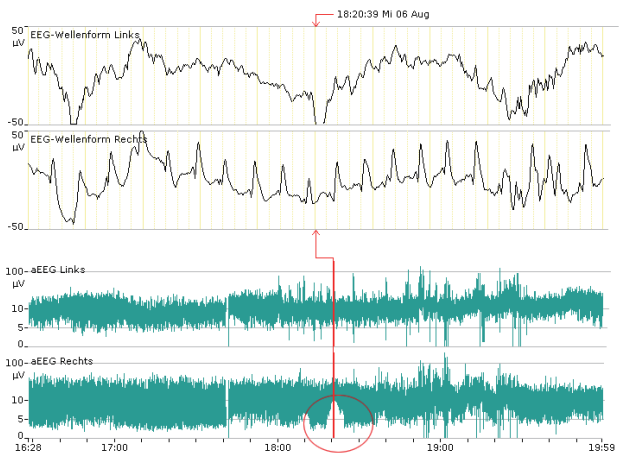


Fig. 32: Right-side seizure, with simultaneous recognizable side difference in background activity

Depending on the interictal background activity, this can give rise to different patterns. Often post-ictally there is a widening of the aEEG to a more discontinuous pattern. In rare cases, this sudden change to a different background activity in the aEEG can be the only recognizable evidence of seizure activity, if the epileptic discharges only lasted for an extremely short period. In these cases it is recommended to review the raw EEG closely shortly before the sudden change in background activity. It is known that extremely short isolated seizures, focal seizures or continuous spiking in the aEEG pattern can more easily be missed[25]. Each seizure seen in the aEEG pattern must be confirmed by viewing the raw EEG, since it is not uncommon that it might also relate to an artifact. The differing appearance of seizures sometimes causes problems particularly for neonatologists lacking EEG knowledge. Fig. 33 shows various seizures as they may appear in the raw EEG.

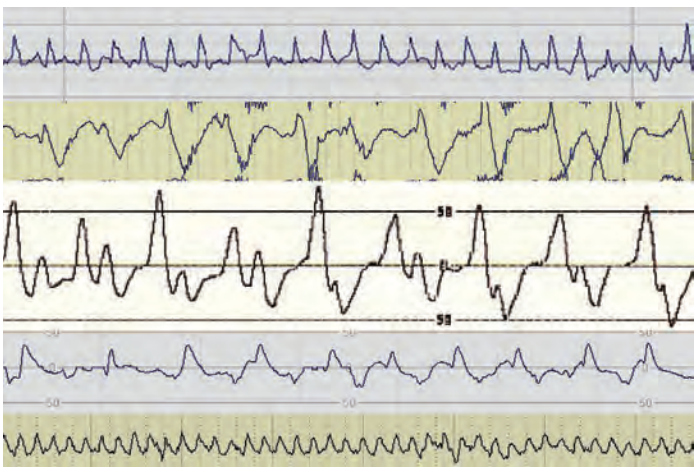


Fig. 33: Various raw EEGs of seizures

If one or more seizures were identified in the aEEG, these should be classified based on the frequency of their occurrence (Fig. 34).

Classification of seizures	
Single seizure	A solitary seizure
Respetitive seizures	Seizures at intervals of less than 30 minutes
Status epilepticus	Seizure activity which lasts for longer than 30 minutes

Fig. 34: Classification of seizures in the aEEG

A status epilepticus can have a different appearance in the aEEG, depending on the underlying background activity (Fig. 35).

Fig. 35: Status epilepticus following asphyxia with a flat trace background activity

Recurring seizures are often referred to as “saw tooth pattern” in the aEEG, if the pattern looks like in Fig. 36.

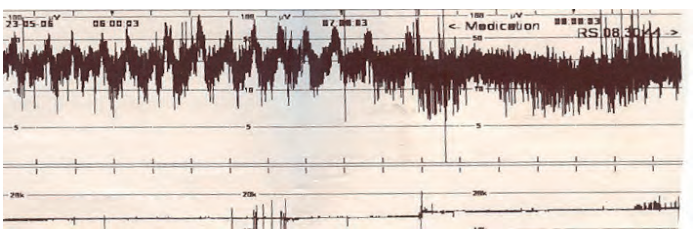


Fig. 36: "saw tooth pattern", after medication transition to continuous pattern.
Image used by kind permission of K. Klebermass-Schrehof

78% of all seizures in neonates can be recognized via electrode position C3/C4[26]. In principle, it can be assumed that by using more channels and more electrode positions this figure could be increased. However, the scope of this improvement has not yet been adequately clarified and thus the question remains open as to whether cross-cerebral 1-channel aEEG discovers relevantly fewer seizures than a side-separated 2-channel aEEG. When considering using increasing numbers of channels, it should always be kept in mind that more channels means more electrodes and more data to evaluate, and that at some point the actual purpose of the aEEG as a monitor becomes lost and it would probably be better to conduct a standard EEG.

With the publication of algorithms to identify seizures, automatic seizure detection has also been implemented in modern aEEG devices. Given their high sensitivity, they are well-suited to identifying very short epilepsy-type discharges which might otherwise be overlooked in the time-compressed aEEG. However, they are also certainly susceptible to artifacts, and each event displayed should be verified in the raw EEG so that no automated false seizures are diagnosed. It should also be noted that, to a significant extent, it is not at all clear whether these now newly-discovered, very short epilepsy-type discharges actually play a relevant role and how aggressively these are to be treated. Similarly, it is particularly young medical personnel with little aEEG experience in the middle of the night who can quickly become unsure about the need to treat what has been displayed, and there is the danger that treatment may be initiated using a potentially harmful antiepileptic drug, although there was no real seizure. For that reason, it is still always very

important to train staff extensively and well in evaluating the aEEG and raw EEG when using automated seizure detection.

7. The aEEG in preterm infants

Not so long ago, in very small preterm infants the focus was primarily on the outcome of "survival". Thanks to modern medicine, the question often is no longer whether they will survive, but how they will survive. It is therefore surprising, when we see how much is monitored on our patients (saturation, CO_2, blood pressure, respiration pressures, laboratory parameters, temperature, humidity, etc) why we do not monitor brain function at all. We generally only concern ourselves with that if there are already bigger problems, such as a brain hemorrhage or a hydrocephalus. In adult medicine nowadays, there are special neurological ICUs set up specifically for cerebral risk patients, to optimize their treatment. Since our little preterm infant in the early weeks is really likewise a patient with continuous neurological risk, functional monitoring should become established in order to make a key contribution to improving the neurological outcome. The aEEG offers us the opportunity to conduct functional monitoring alongside our morphological methods like ultrasound and MRI.

7.1. The physiological aEEG in preterm infants

The brain of a preterm infant, e.g. in the 25th week of pregnancy, undergoes constant maturation through to the estimated birth date. This level of maturity also has direct effects on the background pattern observed in the aEEG. Depending on the time when the aEEG is recorded in the preterm, however, its natural maturity as it would have been prenatally was already influenced. Thus brain activity matures more quickly extrauterinely after the child has been born[27,28]. This means that a child born in the 25th week of pregnancy can, at the age

of 5 weeks, already have a more mature pattern than a child just born in the 30th week of pregnancy. Drugs which stimulate breathing, such as theophyllin and caffeine also seem to accelerate this maturation further, by increasing cerebral cortical activity[29]. Still relatively unclear is the individual effect of further influencing factors such as stress, pain, light, noise and touch, although it can be assumed that these certainly play a part in the accelerated extrauterine maturation. Similarly unknown is whether this accelerated maturation is to be assessed overall as positive or negative for the long-term neurological development of the infant.

The difficulties in assessing background activity in a preterm is therefore in identifying what is normal and age-appropriate and what is not/no longer - with the complication as to what constitutes normal, since there has already been postnatal influence. In very preterm infants, there are many periods of "high voltage activity" (= bursts) with interlying periods of low amplitude height (= interburst interval). The aEEG produces a largely discontinuous pattern with differing proportions of burst suppression patterns and of continuous patterns depending on the level of maturity (Fig. 37). The Interburst Interval (IBI) in preterm infants is physiologically not longer than 30-40 seconds, which would correspond to a burst density of at least 100 per hour in a continuous burst suppression pattern.

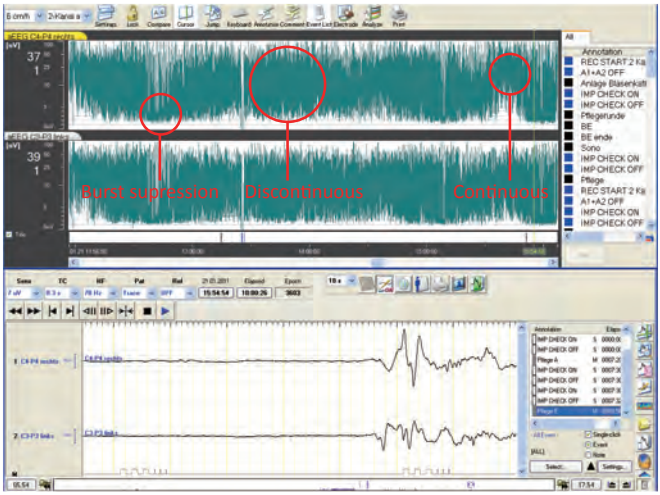


Fig. 37: aEEG of an infant 26th week of gestational age with different parts of background activity; the raw EEG shows a moment with burst suppression activity

The more mature the background activity becomes in the aEEG, the less the burst suppression pattern is evident and the greater the proportion of continuous pattern becomes. The IBI reduces accordingly. The percentage share of the individual activities plays an important role in assessing the degree of maturity, and should therefore be measured and documented when evaluating a preterm infant's aEEG. Olischar and Klebermass defined standard values for preterms in the 24th-29th week of pregnancy[30] (Fig. 38). For a percentage determination of the different patterns, the recording was divided into 10-minute sections and the dominating pattern identified

in each of the 10-minute sections. In this study, different from the now standard nomenclature, a distinction is made between a discontinuous low voltage (minimum amplitude <3µV, corresponding to the burst suppression pattern) and a discontinuous high voltage pattern (minimum amplitude 3-5µV, corresponding to the discontinuous pattern).

Standard values for 24th-25th week of gestational age					
Pattern	**Median**	**5.**	**25.**	**75.**	**95.**
Burst suppression (discontinuous low voltage)	55.6%	0%	46.2%	70%	88.5%
Discontinuous (discontinuous high voltage)	33.3%	11.5%	17.6%	54%	100%
Continuous	0%	0%	0%	8.7%	14.8%

Standard values for 26th-27th week of gestational age					
Pattern	**Median**	**5.**	**25.**	**75.**	**95.**
Burst suppression (discontinuous low voltage)	34%	0%	3.3%	59%	79.8%
Discontinuous (discontinuous high voltage)	56.4%	5.9%	31.4%	65%	95.9%
Continuous	5.9%	0%	0%	21%	58.6%

Standard values for 28th-29th week of gestational age					
Pattern	**Median**	**5.**	**25.**	**75.**	**95.**
Burst suppression (discontinuous low voltage)	7.1%	0%	0%	32%	82.6%
Discontinuous (discontinuous high voltage)	51.8%	2.9%	26.2%	74%	100%
Continuous	16.9%	0%	0%	67%	76.9%

Fig. 38: Percentiles (5., 25., 75., 95.) of normal aEEG values in preterm infants 24-29 weeks of gestational age, indicated as percentage of time in the background pattern, modified from Literature 30

Sleep-wake cycles are observed in all preterm infants, right from the 24th week of gestational age. These are initially immature and are generally fully-formed in the 29th-30th week of gestational age[7].

7.2. The pathological aEEG in preterm infants

Despite the variation in preterm infants of the same gestational age, relevant and significant impairments of brain function continue to be recognizable, since e.g. a constant burst suppression pattern or a flat trace is no longer normal even for a preterm in the 25th week of gestational age (Fig. 39).

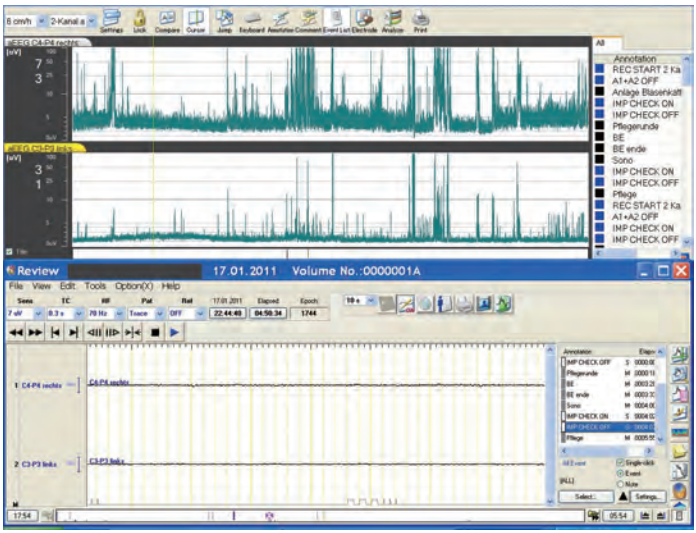


Fig. 39: Severely abnormal aEEG in an extremely small preterm following difficult initial resuscitation

A cerebral hemorrhage (ICH) in the preterm is reflected in the aEEG with more discontinuous and flattening background activity. The degree of severity of this flattening correlates with the degree of severity of the ICH. Thus the observed percentage of continuous activity is significantly lower in preterms with ICH III°-IV° compared with ICH I°-II° [6]. In addition to increased discontinuous and burst suppression patterns, there is a possible loss of sleep-wake cycles and the probability of seizure activity increases[31].

Seizures can be recognized in the aEEG comparably to term infants, as an increase in the lower amplitude margins and sometimes also in the upper margin. However, they are often more difficult to recognize due to the mainly discontinuous background activity with burst suppression elements. In addition to use in identifying clinically-suspected seizures, the aEEG can also be used as a monitor for early detection of subclinical seizures after a brain hemorrhage. It is similarly suitable for monitoring an anti-epileptic drug therapy initiated in preterm infants for effectiveness. Too high dosing of antiepileptic drugs such as phenobarbital can sometimes be identified by too long-sustained burst suppression patterns following administration.

A further area of use in preterm infants is monitoring brain function in a post-hemorrhagic hydrocephalus (see Chapter 9.2).

Fig. 40 shows the aEEG of a 25th week of gestational age shortly after birth, with an average arterial blood pressure around 25mmHg. After increasing blood pressure using catecholamines to above 30mmHg, background activity immediately normalized to an age-appropriate level. In line with this, West et al.

described that early low cardiac output in very small preterm infants is associated with reduced electroencephalographical activity[32]. Despite a direct correlation of the two phenomena being difficult, the aEEG nevertheless also serves its purpose here as a monitor in giving early warning if cerebral function is not appropriate. Using this information, it is then our task to reevaluate the patient in order to find out the cause of this. Without an aEEG, an insufficient perfusion pressure might not be noticed at all, or only very much later.

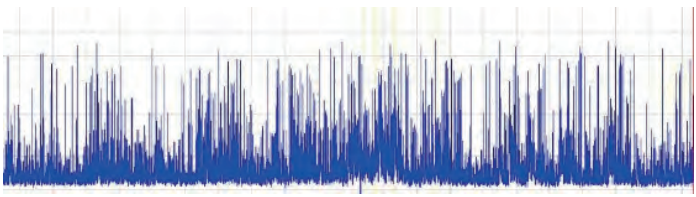


Fig. 40: Preterm infant 25th week of gestational age with average arterial blood pressures around 25mmHg

Smaller differences in background activity in very small preterm infants can be very difficult to detect and some experience may be needed for assessment. However, attention should always be given to the aspects named in Fig. 41:

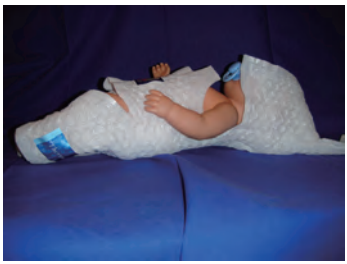
Notice these aEEG changes in preterm infants
Flattening of the amplitude height
Increased discontinuity or burst suppression pattern
Loss of sleep-wake cycles
Seizure activity
Side difference in background activity

Fig. 41: Pathological changes of the aEEG in preterm infants

The aEEG can be an early aid to prognosis with regard to later outcome in extremely small preterm infants. Background activity in the first 2 weeks of life correlates with the later neurological outcome and the MDI (Mental Developmental Index) and PDI (Psychomotor Developmental Index)[33]. There was a specificity of 73% in the first week of life, increasing to 95% for assessment in the second week of life. Sensitivity remained practically unchanged, at 87% and 83%. Cranial ultrasounds carried out in the same study revealed a specificity of 86% in the first and second weeks of life, and sensitivity of 74% and 75%[33].

In the future, it would be desirable to use the aEEG in preterm infants as instinctively as an ECG monitor for observing patterns and trends, for early recognition of changes, for monitoring a therapeutic intervention and predicting the long-term prognosis.

8. Hypothermia and the aEEG



A large part of the rediscovery of the aEEG and its increasing spread of use is thanks to its use as an inclusion criteria in hypothermia studies such as Cool Cap or the TOBY trial[34,35].

The first question which arises is whether the aEEG should be used on its own for indication of hypothermia. While having a very high sensitivity and specificity, however, there are patients with an unremarkable aEEG, but proven damage in an MRI[36]. Many abnormal aEEGs following asphyxia recover quickly. If the time of the asphyxia was significantly prenatal, or the aEEG was applied too late, it can be that abnormal patterns have already recovered. A further cause for a falsely unremarkable aEEG can be a pure basal ganglion or a small isolated one-sided brain lesion. Here the cortex can still be unimpaired to such a degree that the aEEG shows a regular pattern. With sole use of the aEEG as an inclusion criteria, it can therefore certainly be the case that the patient would benefit from cooling despite an unremarkable aEEG. It is useful when evaluating for hypothermia treatment to permit other criteria as well, and to take seriously any noteworthy neurological status even if the aEEG shows a normal pattern.

aEEG monitoring can be used continuously uninterrupted even

during hypothermia. It is useful to monitor these neurological high-risk patients continuously throughout the duration of the hypothermia and the re-warming phase, even if the background pattern has already recovered, since e.g., for example, seizures could still occur.

There are few studies looking at the technical effects of the lower temperature during hypothermia on the aEEG. Horan and colleagues were not able to identify any change in amplitude height and thus any change of the background pattern because of the hypothermia[37].

It is worth reflecting on the fact that, given a hypothermia treatment, the predictive value of the aEEG background activity is reduced. Where in normothermia patients aEEG recovery within 24 hours is considered favorably for the prognosis, this time-frame for hypothermia patients is more like 48 hours[38]. However, this could also be assessed as a success of the hypothermia, since the aim of this treatment is that patients have a better neurological outcome than might have been expected given the extent of the asphyxia.

Conversely, the predictive value of sleep-wake cycles seems to be increased in patients treated with hypothermia. The time to re-emergence of SWC was a more reliable predictive value of outcome for children treated with hypothermia (88.5%) than for the normothermia group (63.6%)[38].

In fetal sheep the amplitude of seizures can be found reduced during hypothermia[39], which means that it might be more difficult to discover seizures during hypothermia in the aEEG pattern.

9. Further possible indications for aEEG

Monitoring cerebral activity in neonates offers countless, and partly previously unimaginable, new possibilities. Accordingly, the range of indications quickly expanded from the original main use in seizures and asphyxia. Further possible indications are presented below.

9.1. Focal hemorrhagic and ischemic lesions

Term infants with seizures without fundamental encephalopathy often have originating one-sided hemorrhagic or ischemic lesions[40]. Accordingly, there is often side asymmetry in brain activity, which can be well displayed particularly using a 2-channel aEEG. This functional disorder is generally recognizable earlier than the morphological change in the ultrasound[41]. The aEEG can thus give earlier indication of such a lesion in a patient with seizures of unknown origin.

Very small preterm infants, despite modern medicine, continue also to have a not inconsiderable number of brain hemorrhages. They can be considered from birth onwards as high-risk neurological patients. It therefore seems reasonable to monitor the cerebral function of this patient group at an early stage. The aEEG provides information about both acute and chronic changes in brain function, in the event of a cerebral hemorrhage or ischemia.

In the acute stage of impairment, there is increased discontinuity, depression in amplitude height, seizures and a loss of sleep-wake cycles[42]. The severity of the changes in background activity correlates with the scope of the impairment and the size of the hemorrhage[43]. Similar to asphyxia, it is

possible to anticipate outcome based on the period until normalization of the background pattern[44].

Chronic changes in the aEEG of preterm babies following the impairment appear primarily as delayed maturation of the background pattern. It appears more disorganized, and sleep-wake cycles can similarly be delayed or influenced in their development. An interburst interval extension in preterm infants of over 30 seconds can be observed, and is associated with a poorer outcome[45]. However, these chronic changes can often be shown better in a standard EEG.

9.2. Posthemorrhagic ventricular dilation in the neonate (PHVD)

Olischar and Klebermass reported for the first time on changes in the aEEG observed in connection with monitoring a posthemorrhagic ventricular dilation[46]. Increasing intracranial pressure (ICP) in the brain causes increased discontinuity and a loss of sleep-wake cycles. A critical intracranial pressure with clear effects on cerebral blood flow in the anterior cerebral artery can trigger a sudden change of the aEEG to a burst suppression pattern[46]. Following drainage of the cerebrospinal fluid (CSF), these changes are again reversible, and sleep-wake cycles particularly improve in 75% of patients[47] (Fig. 42). The aEEG offers the possibility of direct cerebral function oriented monitoring, whereas our previous parameters were mostly more morphologically-oriented (head circumference, ventricle dilation). PHVD has significantly earlier effects on cerebral function compared to changes in blood flow in the anterior cerebral artery[47]. But it is still unclear whether these early

functional changes have already long term relevance. The aEEG can be used for permanent monitoring of a critical PHVD and in some cases might give an earlier indication of critical intracranial pressure, since it would be a continuous monitoring as opposed to time-limited screening using ultrasound. Which method (functional or morphological) is fundamentally more suitable to determine the perfect time for an intervention still needs to be clarified.

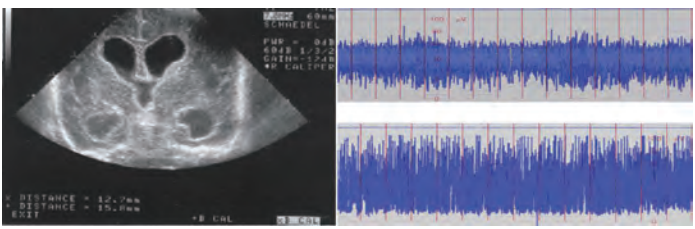


Fig. 42: Example of a posthemorrhagic ventricular dilation with aEEG before and after drainage. Image used by kind permission of K. Klebermass-Schrehof

9.3. Metabolic disorders

Inherited metabolic diseases often cause seizures and encephalopathies during metabolic crisis. These can be monitored and displayed using the aEEG. An initial overview of experience to date was published by Theda[48], involving 25 patients from the "International Registry for Cerebral Function Monitoring in Patients with Genetics Disorders and Brain Malformations". These patients were suffering from hyperammonemia, defects in energy metabolism, disorders in metabolizing amino acids and organic acids, and peroxisomal disorders. In 60% of patients, encephalopathic changes in background activity were discovered,

with the exception of the peroxisomal disorders. Epileptic activities were discovered with a similar frequency. Patients with peroxisomal disorders frequently exhibit epileptic activity with a relatively normal background activity. This is probably because the seizures are the consequence of neuronal migration defects and not of a general encephalopathy. Even if at present there is only limited experience in the use of aEEG with metabolic disorders, it can provide important additional information about brain activity, particularly in connection with metabolic crises. The aEEG should therefore also be used with this group of patients, and we are all called upon to forward further cases to the International Registry (via christiane.theda@thewomens.org.au), so more experiences can be gathered for these relatively rare diseases.

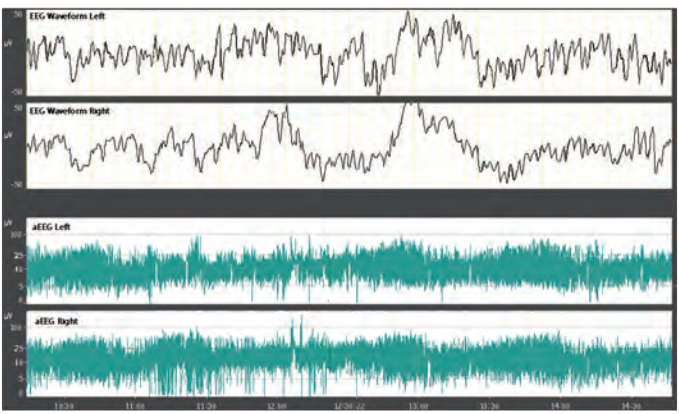


Fig. 43: Term infant with mitochondrial disease. Background activity borderline continuous, as the 5µV limit is partly reached. Sleep-wake cycles are still identifiable. Repeated very short raising of the lower amplitude margin, caused by short epileptic activity. See also case study 11.3

9.4. Muscle relaxed patients

Muscle relaxed patients in an intensive care unit generally have severe illnesses with a metabolically and hemodynamically challenging crisis. Accordingly, in the course of serious illnesses more frequently seizures can occur, e.g. after cardiac surgical interventions. Due to muscle relaxation, it is practically impossible to observe and recognize a seizure clinically. Other clinical symptoms such as an increase in heart rate, temperature or low blood pressures are very non-specific and will often be explained by other causes. Here the aEEG allows for long-term brain function monitoring and thus discovery of seizures. (see case study, Chapter 11).

9.5. Cardiac patients

Relevant neurological damage following cardiopulmonary bypass operations (CPB) in young children seem to be rarer than in adults, averaging 2.3%[49]. However, in more complex cases such as Stage 1 palliation for a hypoplastic left heart syndrome, the incidence for neurological damage can increase to 45%[50]. In the Boston Circulatory Arrest study, the incidence of clinical seizures in the first post-operative week was 6%. Epileptic activity could be proven in 20% of patients in continuous EEG monitoring[51]. At increased risk are children with transposition of the major arteries, hypoplastic left heart syndrome and obstructions of the aortic arch[52]. Further risk factors are the duration of the cardiopulmonary bypass and d-transposition diagnosis of the great arteries (d-TGA) in combination with a ventricular septum defect (VSD) by comparison with d-TGA with intact septum[53]. In conclusion these patients can similarly be considered as

neurological risk patients. Hypoxias can be indicated, as in the asphyctic infant, in a depression of background activity. Accordingly, continuous neurological monitoring can be helpful here in discovering pathologies such as neurological damage and seizures early on. A combination of a cerebral function monitor with near-infrared spectroscopy (NIRS) to monitor additionally cerebral oxygenation in this patient group could contribute to further improvement in neurological outcome in the future.

10. Findings and documentation

If an aEEG is evaluated, additional information should be available in order to be able to give a well-differentiated statement (Fig. 44):

Key information
Gestational age / chronological age
Indication or reason and objective of aEEG recording
Key points in patients history (e.g. umbilical cord pH, base deficit, Apgar)
Relevant other pathologies (metabolism, congenital heart defect, multiple organ failure, etc.)
Drugs, particularly sedatives and anti-eplieptics (dose, application times, drug level in the blood)
Device-based and chemical laboratory test results (e.g. ultrasound, MRI, neuron-specific enolase, etc.)

Fig. 44: information necessary for the evaluation of an aEEG

There is no defined standard how detailed reports from an aEEG need to be and what to do with the recorded data file. If, for example, the set-up was geared to a simple monitor in the ICU as for the ECG, then it would be sufficient to document the aEEG pattern e.g. jointly with the course of the patient chart, and individual pathologies could be printed out for the documentation as proof. The individual ECG monitoring recording is generally not stored permanently, and from this one could conclude that the aEEG recording should likewise not need to be archived.

To date, there has been little experience in the forensic consequences of an aEEG recording. What happens if an aEEG is misinterpreted (e.g. undocumented seizures) and at a later time it is claimed that this should have been discovered and should have had consequences on treatment? Even worse, the complaint might arise that this mistake had led to neurological damage.

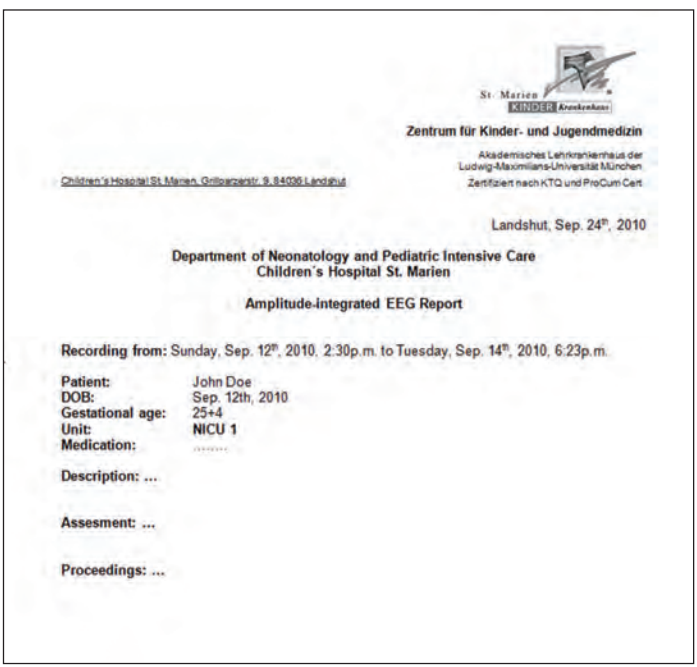
However you handle it in your department, it must at least be ensured that everyone follows the same procedures at all times. Fundamentally, with an aEEG recording, a statement should always be made regarding these 3 points: background activity, sleep-wake cycles, and whether seizures are present. This is the absolute minimum which should be documented.

In my own department, we have this standard: during the recording bedside reports are gathered, which are also mentioned on the patient file along with all other documentation on the course of treatment. This corresponds to the evaluation of what is observed by the doctor on-call when visiting the patient bed. This can be an evaluation by the Resident, Fellow or the senior physician. Once the recording has ended, the senior physician responsible for the aEEG receives the recording for extensive review. This includes a detailed description of all patterns, events, sleep-wake cycles, courses of treatment, seizures etc. A report summarizes everything, assesses it and describes its meaning, e.g. prediction for the patient. Finally, the consequences for the future procedures are set out. Interesting screenshots of the recording are often inserted using copy-and-paste, and the full report is then saved

as a pdf-file and digitally stored. Inserting relevant individual screenshots in the report can have an additional training benefit if Residents and Fellows read the reports.

Each extensive written report requires additional documentation of the patient data: gestational age, indication, time of recording from/to, sedating and anticonvulsive drugs with dosing and application times, place where data is stored (e.g. name of the pdf-file).

An example of what a report may look like is shown in Figure 45.



St. Marien KINDER Krankenhaus

Zentrum für Kinder- und Jugendmedizin

Akademisches Lehrkrankenhaus der Ludwig-Maximilians-Universität München
Zertifiziert nach KTQ und ProCum Cert

Children's Hospital St. Marien, Grillparzerstr. 9, 84036 Landshut

Landshut, Sep. 24th, 2010

Department of Neonatology and Pediatric Intensive Care
Children's Hospital St. Marien

Amplitude-integrated EEG Report

Recording from: Sunday, Sep. 12th, 2010, 2:30p.m. to Tuesday, Sep. 14th, 2010, 6:23p.m.

Patient: John Doe
DOB: Sep. 12th, 2010
Gestational age: 25+4
Unit: NICU 1
Medication: .....

Description: ...

Assesment: ...

Proceedings: ...

Fig. 45: Example of how an aEEG report can look like

11. Case reports

In this chapter you can find case reports where the aEEG provided valuable and interesting results.

11.1. A patient with muscle relaxation

The reported patient is a term infant born with a large abdominal wall defect. A severe SIRS (Systemic Inflammatory Response Syndrome) developed post-op, and the patient required muscle relaxation and high-frequency ventilation. To monitor brain function during this critical condition, an aEEG was applied.

After the first post-operative night the patient developed, starting at around 4:00 am, an increase in heart rate from 180 to 200/min, a rise in body temperature from 37.0°C to 38.0°C and low blood pressure with increasing need of vasopressors (Fig. 46). Reflecting the most likely cause following an abdominal surgical intervention, the initial response of the physician on-call was giving additional volume. It was possible to stabilize the blood pressure, but heart rate and temperature remained increased.

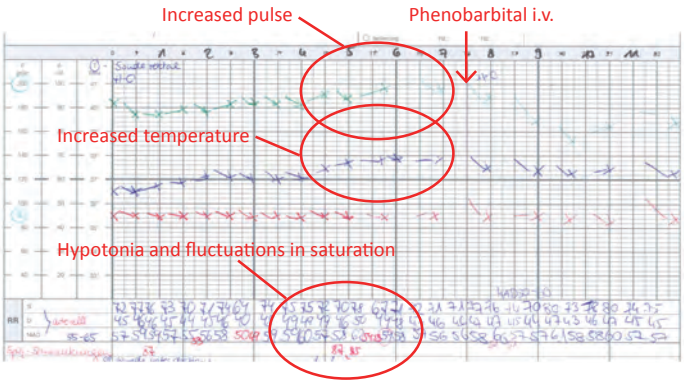


Fig. 46: patient documentation

The patient had meanwhile already received an additional 40ml/kg volume when the aEEG recording in the background was noticed (Fig. 47).

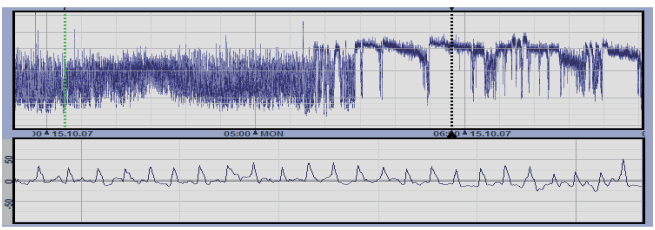


Fig. 47: aEEG of the muscle relaxated patient with seizure

In the aEEG, it was possible to identify a status epilepticus, which was not recognizable because of the muscle relaxation of the patient. The effects of the status epilepticus were clinically misinterpreted as a simple volume deficiency. After identifying the problem, the patient received one single dose of phenobarbital 10mg/kg with immediate effect and return to previous background activity. The heart rate dropped to 160-180/minute, and temperature fell to 37.2°C, with the need for vasopressors likewise reversing. The patient had no further seizures in the course of treatment. This is one example of how the aEEG can improve our often misguided clinical view, and how it enables us to a more cause orientated approach in therapy.

11.2. B-streptococcal meningitis

This patient was presented via the emergency department at age of 14 days, due to an increasingly deteriorating condition in the last few hours. Patient history showed that the mother had been tested positive for B-streptococcus at the time of birth, with no antibiotic treatment being given. At the time of admission to our intensive care unit, the patient already had a massive B-streptococcal sepsis with disseminated intravascular coagulopathy (DIC) and a severe B-streptococcal-meningitis with thrombosis of the sinus vein. The patient survived the infection, but suffered severe brain damage and required feeding by a gastric tube. The patient was readmitted 2 months after being discharged with signs of new individual short cries, unrelated to time or to an event. Since this happened only once or twice a day and it was therefore difficult to record an EEG precisely

during the event of crying, there was initial monitoring using aEEG to clarify whether these cries coincided with increased brain activity or seizure activity. Fig. 48 shows the patient's extreme cortical damage identifiable using ultrasound, which also showed in the aEEG.

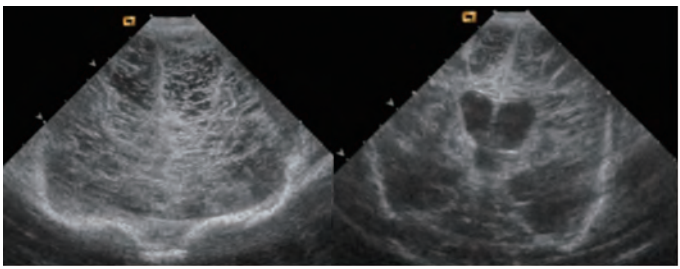


Fig. 48: Ultrasound images showing the extensive cortical damage

The recorded aEEG shows a low voltage aEEG. The left brain side presented even worse. On both sides there is a slight shift of baseline due to artifacts. The patient's cries were marked on the aEEG by the nursing staff. At these times, no change in background activity or a sign of seizures was identifiable in the aEEG. The remaining rises in the lower margin in the picture were artifacts (Fig. 49).

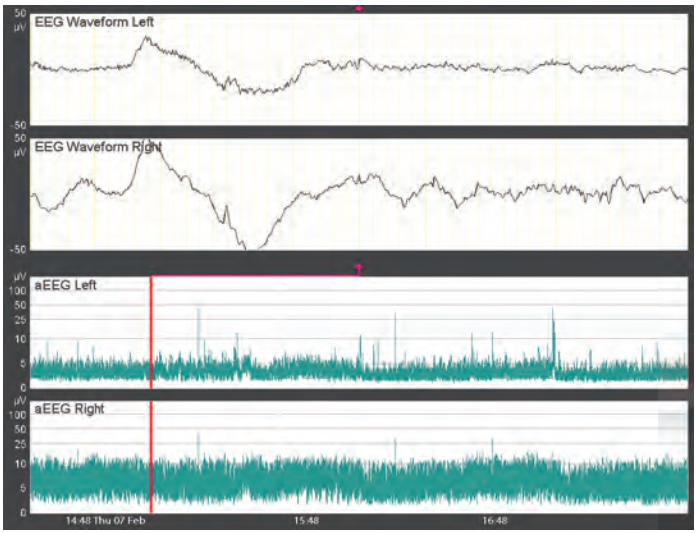


Fig. 49: aEEG of a patient aged 2.5 months after B-streptococcal-menigitis and sepsis as a newborn. There was no influence from sedating or antiepileptic drugs during recording

11.3. Seizures following birth

This case reports on a term male infant from a mother with a dilated cardiomyopathy of uncertain cause. Shortly after birth, the child showed noticeable unusual muscle movements, which was interpreted clinically as seizures. An aEEG recording was started right after admission to our NICU (Fig. 50).

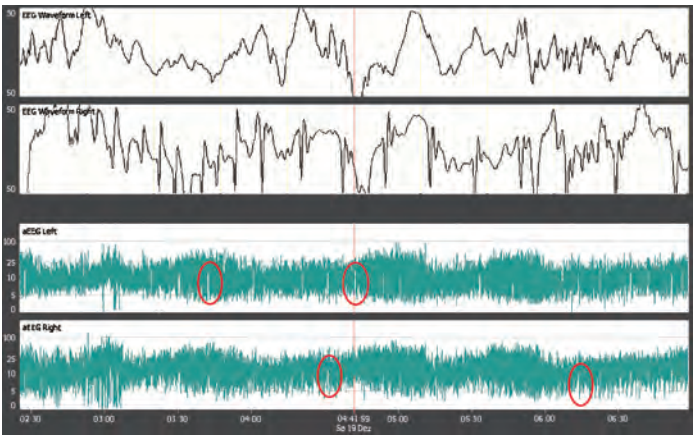


Fig. 50: aEEG with very short epileptic activity (here currently well seen in the right raw EEG), causing repeated short raising of lower margin of aEEG throughout recording (examples circled in red)

The aEEG shows repeated short increases in the lower margin, which are noticeable only as a small white line. In these phases the raw EEG showed epileptic activity of different appearances (see also Fig. 51). The background activity is only borderline continuous, as the 5µV limit is reached. Sleep-wake cycles can still be identified.

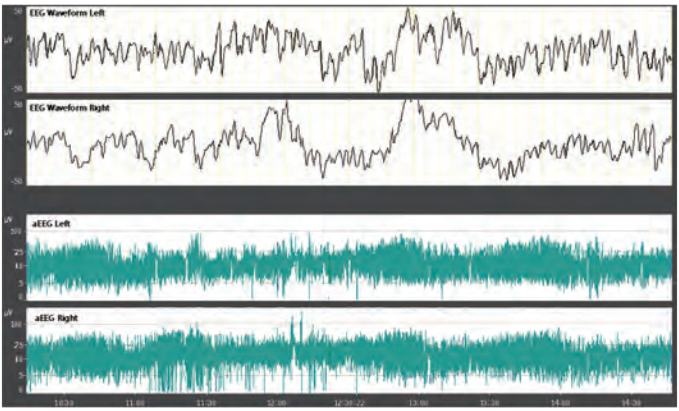


Fig. 51: aEEG with more spindle-shaped phase in the raw EEG, which causes a very short rise of the lower margin in the aEEG

The EEG showed a mixed-amplitude pattern changing between good and low modulation. There were steep spindle-like patterns throughout (Fig. 52). In the video monitoring, isolated myoclonia, matching the spindle-form steep patterns could be recognized.

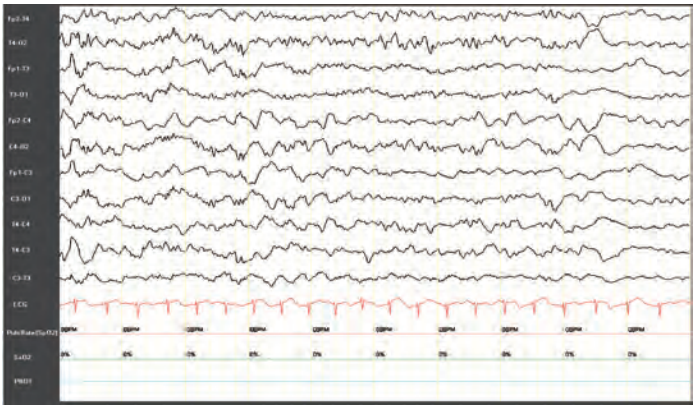
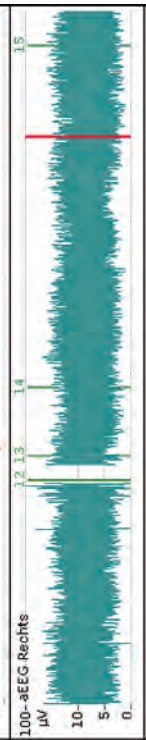
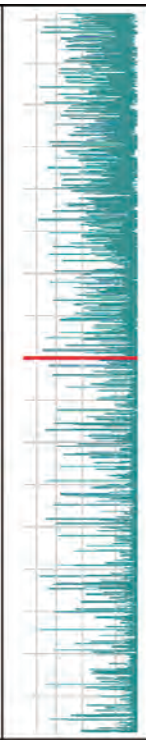
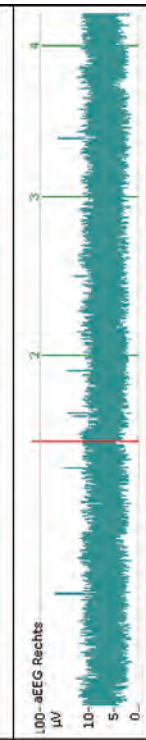
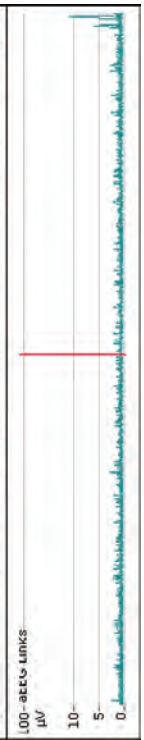


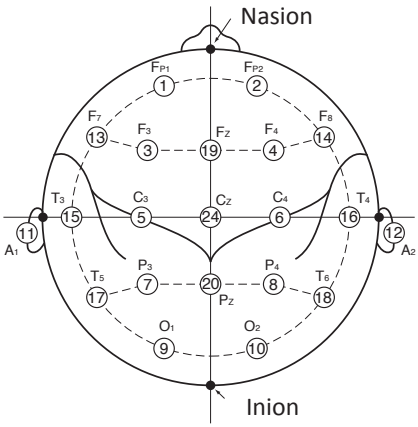
Fig. 52: EEG of the patient

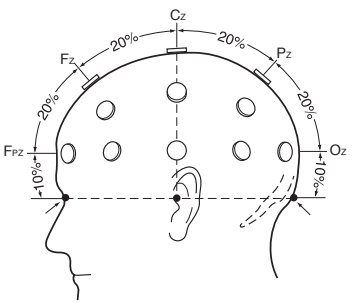
The seizures were difficult to treat with anti-epileptic drugs. Extensive investigations ultimately revealed, under electron microscopy of a muscle biopsy, giant mitochondria with structural impairment of the cristae with an irregular arrangement, and biochemically it was possible to prove a defect in the breathing chain complex I (NADH-CoQ-oxidoreductase) with clearly reduced activity. The mitochondrial disease is now also showing as beginning impairment of cardiac ventricular contraction.

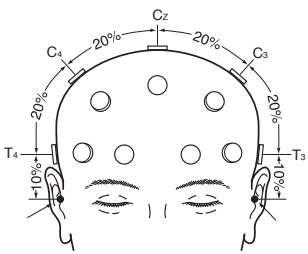
12.1. Overview of background patterns

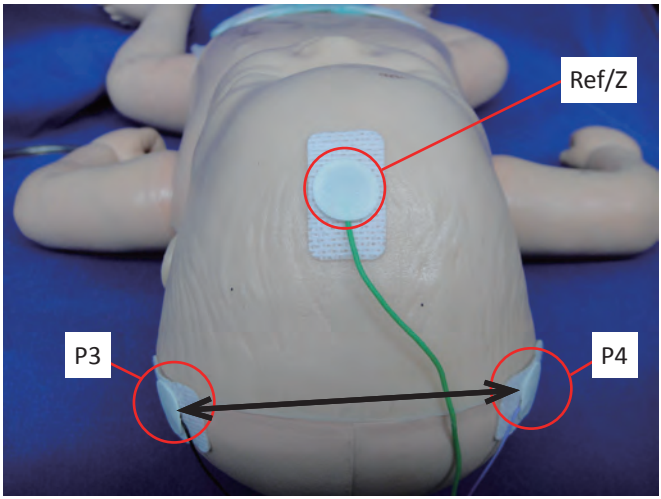
continuous normal voltage pattern, C Upper margin >10-25µV Lower margin >(5-)7-10µV	
discontinuous pattern, DC Upper margin >10-25µV Lower margin <5µV	
Burst suppression pattern, BS Lower margin 0-1(-2)µV Bursts >25µV BS- <100 bursts/hour BS+ >100 bursts/hour	
Low voltage, LV Lower margin at or <5µV Upper margin <10µV	
Inactive, flat trace, FT Upper and lower margin continuously <5µV	

12.2. Electrode positions

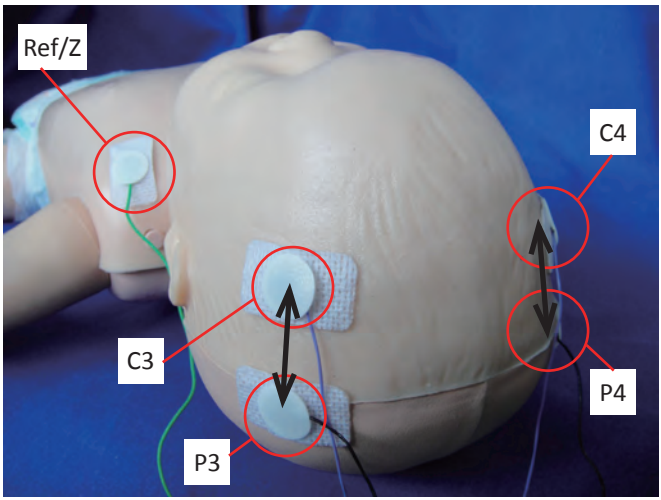








1-channel monitor



2-channel monitor

12.3. Step-by-step placing of hydrogel electrodes

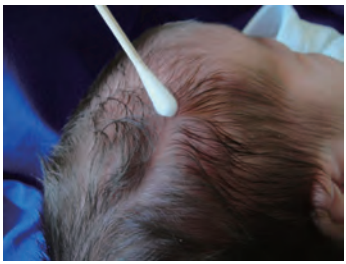
1. Positioning:

Locate the correct position for your electrodes as shown in Chapter 3.1 or Appendix 12.2, and mark if necessary. Alternatively use templates provided by some manufacturers to locate the correct position. If possible, make a plan of the order in which the electrodes are best applied, so that the child requires the minimum amount of head movement and you do not lose the previously-attached front electrode when applying the rear electrode.

2. Cleaning

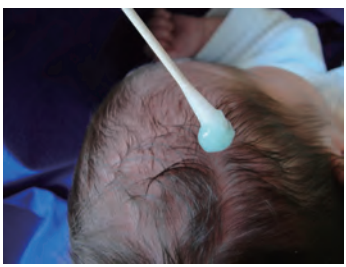
Clean the skin of the head to remove obvious dirt such as blood, vernix or meconium.

3. The hair problem:



Part the child's hair so you can prepare a good area of skin. This can be done e.g. using a toothbrush, a fine comb or wet cotton stick. If you cannot clear a sufficiently large patch, it is possible to remove hairs locally, e.g. using a nasal hair trimmer. Avoid larger shaving of head hair, as this is unnecessary. With very small hair-free areas, gold electrodes generally attach better.

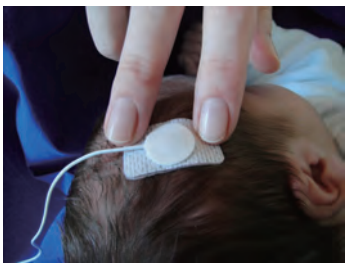
4. Skin preparation:



The most frequent cause of bad impedances with adhesive electrodes is inadequate preparation of the skin. First remove still remaining obvious contaminants such as blood, meconium or vernix. Use a cotton stick to avoid rubbing hair back into your prepared skin area. Now apply your skin peeling cream (e.g. SkinPure®). Stroke it continuously and strongly in the skin area. Generally this procedure is being performed too gently,

since this is certainly the most unpleasant part for the baby when fixing electrodes. With small preterm infants (23-28 week of gestational age), skin peeling should not be used initially as adequate impedances can often already be achieved with simple cleaning using the cotton stick.

5. Fixing the electrodes:



When fixing the electrodes, ensure that the cables always run upwards. Hydrogel electrodes should be sufficiently warm in order to function well. Do not attach them cold, and if possible warm them after applying for a further minute, e.g. using the surface of your hand. When used in an incubator they generally automatically become warmer, but may also become moister, which means they adhere less well and for a shorter time.

5. DO NOT DESPAIR!:

Unfortunately, it is normal that the skin needs to be prepared repeatedly for some electrodes before a good impedance and lead quality is achieved. It is also normal that good impedance is not maintained for ever. At the beginning, also make use of the experience of the nurses from your EEG lab, or visit the lab to pick up tips and to practice applying electrodes.

12.4. Neurological scores

Sarnat stages of HIE Arch Neurol 33:696, 1976
Mild HIE - Sarnat Stage I Hyperalent, eyes wide open, jittery irritable, no seizures, lasts < 24 hours, < 1% poor outcome
Moderate HIE - Sarnat Stage II lethargic, obtunded, hypotonic with flexion, reduced brain stem reflexes (pupils/sucking/choking), clinically apparent seizures possible (variable to multifocal on EEG), lasts > 24 hours, 20 - 40% poor outcome
Severe HIE - Sarnat Stage III comatose, no reaction to stimuli (spinal reflex to pain still possible), weak or absent breathing, floppy infant (tone of torso and extremities severely reduced), reduced or absent brain stem reflexes (pupils/sucking/choking), absent tendon reflexes, EEG severely abnormal (suppressed or flat with/without seizures), lasts > 5 days : 100% poor outcome

Classification of hypoxic-ischemic encephalopathy after Sarnat and Sarnat[54]

Thompson Score Acta Paediatr 1997; 86:757-61				
Indicator	**0**	**1**	**2**	**3**
Tone	Normal	Hypertone	Hypotone	Floppy
Consciousness	Normal	Hyperalert	Rigid, lethargic	Comatose
Seizures	None	1-2/day	3+/day	
Posture	Normal	Chewing fist	Distal flexion	Decerebrate
Moro	Normal	Partial	Absent	
Gripping	Normal	Poor	Absent	
Sucking	Normal	Poor	absent ± biting	
Breathing	Normal	Hyper-ventilation	Short apneas	Persistent apnea
Fontanelles	Normal	Above level	Tense	

Thompson Score	Sarnat HIE stage
0-10	Mild
11-14	Moderate
15-22	Severe

Assessment of neurology using Thompson Score and comparison with Sarnat Stages[55]

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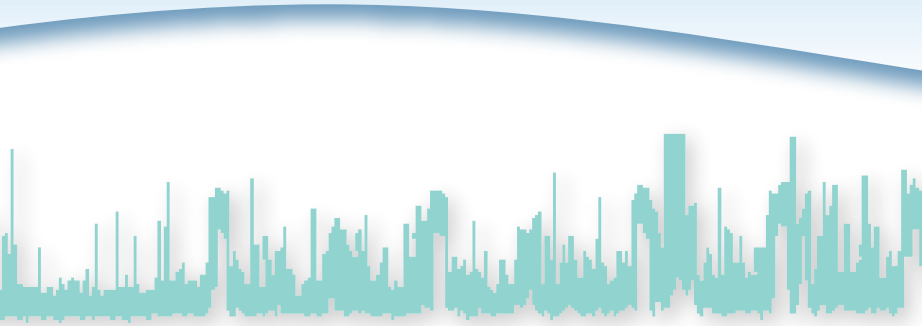

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