Amplitude-integrated EEG Classification and Interpretation in Preterm and Term Infants

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Objectives   After completing this article, readers should be able to:

1. Understand the amplitude-integrated electroencephalography (aEEG) method and its utility and limitations.
2. Classify and interpret typical aEEG background patterns.
3. Identify epileptic seizure activity in the aEEG.
4. Describe features in the aEEG recording that are associated with prognosis.

Introduction

Amplitude-integrated electroencephalography (aEEG) is a method for continuous monitoring of brain function that is used increasingly in neonatal intensive care units (NICUs). The method is based on filtered and compressed EEG that enables evaluation of long-term changes and trends in electrocortical background activity by relatively simple pattern recognition. The cerebral function monitor (CFM) was created by Prior and Maynard in the 1960s for use in adult intensive care. Prior and Maynard aimed for a brain monitoring system that had the following features: simplicity, reasonable cost, reliability, direct information about neuronal function, noninvasiveness and wide applicability, quantification and output, automatic operation, and flexibility. (1) The method was applied to newborns in the late 1970s and early 1980s. (2)(3)(4) The original CFM concept has been developed, and several new machines are now available, all including the aEEG trend recording with simultaneous display of the raw EEG. We and others have chosen to call the method aEEG to distinguish it from a special monitor. Published studies on neonatal aEEG include both clinical and experimental investigations. (5) The finding that the aEEG is suitable for very early prediction of outcome after perinatal asphyxia has resulted in more widespread use of the method, not least since abnormal aEEG readings were an inclusion criterion in one of the recently published hypothermia studies. (6)

For new users of aEEG, the potential of this method is usually striking when clinical aEEG monitoring reveals abnormal brain activity that would otherwise pass unrecognized, such as subclinical seizure activity or transient background deterioration during hypoglycemia or pneumothorax. (7) However, it is also extremely important to be aware of limitations and risks of overinterpretation of aEEG readings. (8)(9) The possibility of detailed evaluation is lost at the same time as another important feature is gained: the possibility to follow continuously online long-term trends and changes in cerebroelectrical activity. In this context, the aEEG could be compared with monitoring the electrocardiogram (ECG) in the NICU; the ECG monitor shows trends in cardiac activity but cannot be used for detailed analysis of rhythms and blocks or evaluation of ST-segment and electrical axis. We recommend recording at least one standard EEG, preferably including a period of quiet sleep, in infants monitored with aEEG.

This review summarizes recent knowledge on practical aEEG in the newborn period, discusses classification of aEEG recordings, and provides some tutorial examples of aEEG.

Correlation Between aEEG and EEG

aEEG is derived from a reduced EEG; usually one (from a pair of biparietal electrodes) or two channels (from four electrodes, one channel from each hemisphere) are used. The

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EEG processing includes an asymmetric band pass filter that strongly attenuates activity below 2 Hz and above 15 Hz, semilogarithmic amplitude compression, rectifying, smoothing, and time compression. The bandwidth reflects variations in minimum and maximum EEG amplitude. The amplitude display is linear between 0 and 10 mcV and logarithmic from 10 to 100 mcV. This semilogarithmic display enhances identification of changes in low-voltage activity and avoids overloading of the display at high amplitudes. The aEEG recording previously was printed on paper, but it is digitally stored and displayed on a computer screen in the newer monitors. The electrode impedance is monitored continuously to supervise the technical quality of the recording.

The aEEG has been compared with the EEG in terms of background features and epileptic seizure detection. In general, there is good correlation between primary findings in the aEEG/CFM and EEG. Although all seizures with durations of more than 30 seconds could be identified in the biparietal single-channel CFM, when five channels of tape-recorded EEG are recorded simultaneously, some focal, low-amplitude, and brief seizures may be missed by the aEEG, as well as continuous spiking. (3)(8)(9)(10) The possibility that some seizures will be missed with a reduced number of electrodes is also evident from EEG studies. (11)(12) The recognition of background activity sometimes differs slightly between the aEEG and the EEG; the most common discrepancy is probably that a discontinuous aEEG with low interburst amplitude is classified as a burst-suppression pattern in the EEG. This difference is usually due to either the high sensitivity of the aEEG for recording very low-amplitude electrocortical activity that is difficult to visualize in the EEG or to interference from ECG or electrical equipment that is picked up by the aEEG.

Practical aEEG in the NICU
Normal aEEG
The normal aEEG changes with gestational age. (2)(4)(13)(14)(15)(16) In parallel with the EEG, the aEEG in the very preterm infant is primarily discontinuous and becomes gradually more continuous with increasing gestational age. (17) The normal discontinuous EEG in very preterm infants is called "tracé discontinu" and should be distinguished from the abnormal burst-suppression pattern. (18)

One primary difference between the two background patterns is the inactive (isoelectric) suppression period in burst-suppression compared with the low-voltage period in tracé discontinu that contains low-amplitude activity. This difference frequently is possible to distinguish in the

aEEG, with the burst-suppression pattern having a generally straight lower margin at 0 to 1 (to 2) mcV and the tracé discontinu EEG pattern corresponding to an aEEG that has a lower margin varying between 0 and 5 (to 6 to 7) mcV. Cyclic variations in the aEEG background suggestive of immature sleep-wake cycling (SWC) can be seen in healthy infants from around 26 to 27 weeks' gestation. SWC also develops with increasing maturation, and from 31 to 32 weeks' gestation, quiet sleep periods are clearly discernible in the aEEG as periods that have increased bandwidth. At term, the more discontinuous aEEG pattern during quiet sleep represents the tracé alternant pattern in the EEG.

aEEG in the Term Infant
In term infants, aEEG is an excellent method for evaluating cerebral function and cerebral recovery after hypoxic-ischemic insults such as perinatal asphyxia and apparent life-threatening events (ALTE). (3) Besides contributing to the clinical evaluation, the immediately available information provides early data for the parents. Infants who need intensive care treatment are at higher risk for cerebral complications due to circulatory instability (eg, sepsis), hypoxia (eg, persistent pulmonary hypertension, meconium aspiration, cardiac malformations, or diaphragmatic hernia), hypoglycemia, or seizures. (7)(19) Clinical symptoms of cerebral dysfunction can be difficult to detect due to the illness itself or because sedatives or analgesics have been administered. In such infants, electrocortical background activity usually remains unaffected or only moderately depressed unless high doses of antiepileptic medicines or sedatives have been administered. A continuous aEEG with amplitudes between 10 and 25 mcV, some smooth or cyclic variation, or fully developed SWC is usually a reassuring sign of noncompromised brain function.

The aEEG has proven to be very sensitive for early prediction of outcome in asphyxiated term newborns. (20)(21)(22)(23)(24)(25)(26)(27) A continuous or slightly discontinuous aEEG pattern during the first 6 hours is associated with a high chance of cerebral recovery and normal outcome. Presence of SWC in the aEEG within the first 36 hours in infants who have moderate hypoxic-ischemic encephalopathy (HIE) was associated with a favorable outcome compared with infants in whom the SWC appeared later. (26) Presence of seizures in aEEGs of asphyxiated infants have not been as clearly associated with outcome as has background activity. This may be due to the clinical demeanor of HIE, in which fewer seizures are seen in the most severely asphyxiated infants who have poor outcome (HIE grade 3) than

in more moderately asphyxiated infants (HIE grade 2). However, it is our impression that recurrent seizure activity, or status epilepticus, is associated with a worse outcome, but this has not been studied from a perspective that includes quantification of seizures.

There are no published studies on the use of aEEG during extracorporeal membrane oxygenation in newborns. An abstract, indicating that aEEG is of value in these infants, was presented recently, (28) and this also has been our experience. Brain function may be affected by prior hypoxia-ischemia and seizures, often without clinical signs, which is not uncommon.

aEEG in the Preterm Infant

Although the aEEG has not been evaluated in preterm infants as extensively as in term infants, several studies have shown its utility in this population. Two prospective evaluations of aEEG in very preterm infants during the first postnatal days have been published. Both showed correlation between degree of intraventricular hemorrhage (IVH) and depressed aEEG background activity expressed as amount of activity ("continuous activity") over 3 mcV. Most infants developing IVH had epileptic seizure activity, often subclinical. (29)(30) Burst density was associated with outcome in preterm infants who already had large (grade 3 to 4) IVH during the first 24 to 48 hours after birth. (31) A relatively good outcome could be predicted when the maximum number of bursts per hour exceeded 135. Presence of SWC during the first week after birth was associated with better outcome, but the presence of epileptic seizure activity was not associated with a worse outcome in these infants.

Cyclical aEEG patterns indicating SWC are present in some extremely preterm infants at 25 to 27 weeks' gestation. (30)(32) A recently published study evaluating SWC in relation to standard EEG in stable preterm infants between 25 and 30 weeks' gestation supports the aEEG findings. (33) Although the aEEG background patterns correspond with different sleep states in somewhat more mature preterm infants, this finding has not been shown in extremely preterm infants. (34)

Effect of Medications on aEEG

Administration of morphine, phenobarbital, lidocaine, and midazolam may depress aEEG activity. (35)(36)(37) Other medications, such as morphine and sufentanil, are known to depress EEG activity. (38)(39) Lidocaine infused for treatment of recurrent seizures often results in a discontinuous or burst-suppression pattern that is gradual and more evident when the infusion is stopped and the aEEG background recovers to a more continuous pattern. Our experience is that a loading dose of phenobarbital (10 to 20 mg/kg) may result in moderate depression of background activity, but in term infants, there is usually no major change in background activity. The phenobarbital loading resulting in severe depression is often a sign of more severely compromised cerebral function. This is similar to the findings of van Leuven and associates (37) in their evaluation of midazolam in neonates who had HIE. Diazepam often results in profound depression of aEEG activity in preterm infants, although the effect in term infants frequently is less marked. Other factors that have been described to cause transient depression of aEEG include hypoglycemia and pneumothorax. In preterm infants, surfactant administration may result in a transient aEEG depression for about 10 minutes. (40) The cause of the aEEG depression is not known; it is associated with a rise in cerebral blood volume (as measured with near-infrared spectroscopy), but there is no relation to transient hypotension or changes in blood gases. (41)

Classification of aEEG Recordings

aEEG tracings are described and classified in several different ways, depending on whether normal or abnormal circumstances were evaluated and whether term or preterm infants were studied. At least six publications have described normal aEEGs in term and preterm infants. (2)(4)(13)(14)(15)(16) A summary of normal findings at different gestational ages, based on these studies, is shown in Table 1.

Verma and associates (4) studied 49 term and preterm infants, including six infants born before 30 weeks' gestation. Recordings obtained on the second postnatal day contained both active and deep/quiet sleep. The investigators used a monitor that is not currently available (the Critikon CFM Critikon), which showed cerebral activity as three continuously running lines depicting maximum, mean, and minimum amplitudes. The general forms of the aEEG pattern were described as "wave-form," "flat," or "spiky" and included minimum, maximum, and mean voltage. All infants had wave-form background patterns. The amplitude of the minimum level in deep/quiet sleep showed a significant positive correlation with gestational age. The same investigators also studied 31 asphyxiated preterm and term neonates after emergency support had been started. (44) Eighteen of the 20 infants who had normal background patterns appeared neurologically normal at discharge, three infants who had "immature" aEEG readings showed signs of brain injury, and all eight infants who had flat aEEG recordings died. Viniker and colleagues (2) recorded 107 neonates, born at 29 to

Table 1. **Summary of Normal Single-channel aEEG features in Newborns at Different Gestational/Postconceptional Ages**

Gestational or Postconceptional Age (wk)	Dominating Background Pattern	SWC	Minimum Amplitude (mcV)	Maximum Amplitude (mcV)	Burst/h
24 through 25	DC	(+)	2 to 5	25 to 50 (to 100)	>100
26 through 27	DC	(+)	2 to 5	25 to 50 (to 100)	>100
28 through 29	DC/(C)	(+)/+	2 to 5	25 to 30	>100
30 through 31	C/(DC)	+	2 to 6	20 to 30	>100
32 through 33	C/DC in QS	+	2 to 6	20 to 30	>100
34 through 35	C/DC in QS	+	3 to 7	15 to 25	>100
36 through 37	C/DC in QS	+	4 to 8	17 to 35	>100
38+	C/DC in QS	+	7 to 8	15 to 25	>100

Modified data from references 2, 4, 13–18, 42, 43. Sleep-wake cycling: SWC (+)=imminent/immature; SWC +=developed SWC; QS=quiet/deep sleep; DC=discontinuous background pattern, (C)=continuous

43 weeks' gestation, on 175 occasions. Similar to Verma, these investigators found that the clearest change with increasing maturation was a rise of the lower edge (amplitude) of the quiet sleep tracing. In 1990, Thornberg and Thiringer (13) presented a study on normal aEEG development in preterm and term infants who had uneventful neonatal periods and were neurologically normal at follow-up. Their findings were similar to the previous two studies, and normative data for minimum and maximum amplitude during wakefulness and sleep, including bandwidth, was presented. Thornberg and Ekström-Jodal (20) later published a study of 38 asphyxiated infants. All 17 infants who had normal outcomes had continuous aEEG during the first 1 to 2 days after birth; infants who either died or survived with handicap had burst-suppression or paroxysmal tracings.

Burdjalov and colleagues (14) studied 30 infants with gestational ages of 24 to 39 weeks serially on 146 occasions, twice during the first 3 days after birth and then weekly or biweekly. A scoring system evaluating continuity, cyclic changes, amplitude of lower border, and bandwidth was created. The minimum and maximum summarized scores of the variables were 0 and 13. The total score correlated with gestational and postconceptional ages, with the highest total scores attained at 35 to 36 weeks postconceptional age, although very few recordings were made after 36 weeks' gestation. Abnormal patterns (eg, burst-suppression and seizures) were not included in the scoring system.

Olischar and associates (15) recorded very preterm infants, born at 23 to 29 weeks' gestation, who had no cerebral ultrasonography abnormalities. The recordings were classified as: discontinuous low-voltage pattern

(lower amplitude <3 mcV and higher amplitude 15 to 30 mcV), continuous pattern (lower amplitude >5 mcV and higher amplitude 20 to 40 mcV), and discontinuous high voltage pattern (lower amplitude 3 to 5 mcV and higher amplitude 20 to 40 mcV). Bursts were defined as activity greater than 100 mcV; the median number of bursts per hour showed an inverse correlation to gestational age, decreasing from 20.4/h at 24 to 25 weeks to 14.9/h at 26 to 27 weeks and 4.4/h at 28 to 29 weeks. In a recent publication by Sisman and associates, (16) 31 preterm infants who had no neonatal neurologic abnormalities and were born between 25 and 32 weeks' gestation were recorded biweekly from the first 24 to 48 hours after birth to 35 postmenstrual weeks. Recordings were evaluated for continuity, amplitude, and SWC. Clear SWC was present from 29 gestational weeks. Amplitude measures were very similar to the ones previously published by Viniker and Thornberg and Thiringer.

Several studies include classification and evaluation of abnormal aEEGs (Table 2). Bjerre and associates, (3) in one of the earlier publications on aEEG, described background patterns as continuous or interrupted (discontinuous). The recorded infants included asphyxiated preterm infants, term asphyxiated infants, and infants up to 5 months of age who had suffered ALTE. Recovery was associated with an initial continuous tracing or a change in background pattern from interrupted to continuous within 1 to 2 days of the hypoxic-ischemic incident. Hellström-Westas and associates (21) classified aEEG from asphyxiated term infants as continuous normal voltage (CNV), burst suppression (BS), continuous extremely low-voltage (CLV), and flat (FT). Toet and colleagues (23) created a similar classification with four

Table 2. ## Overview of Abnormal aEEG Background Features and Their Association With Outcome at Different Gestational Ages

Gestational Age (wk)	Background Pattern	Outcome
<33	Reduced continuity first 7 days	Associated with large IVH; long-term outcome not assessed
<33	BS, LV, or FT first 48 h after birth	Severe handicap/death in infants with IVH 3 to 4
≥37	DC	Normal outcome if present only during the first 6 to 12 h after perinatal asphyxia
≥37	LV	Abnormal outcome after perinatal asphyxia
≥37	BS	Abnormal outcome after perinatal asphyxia; some infants healthy if aEEG background becomes continuous within 12 to 24 h
≥37	FT	Severely abnormal outcome (death or major handicap) after perinatal asphyxia

IVH=intraventricular hemorrhage, BS=burst-suppression, LV=low voltage, FT=inactive, flat, DC=discontinuous
Note: Presence of epileptic seizure activity is always abnormal at all gestational ages. Background activity, including sleep-wake cycling, may be depressed by medications.

different background patterns: continuous normal voltage (CNV), discontinuous normal voltage (DNV), burst-suppression (BS), and inactive (flat, FT). Both classifications show very high correlation with outcome. (21)(23)(45)(46) Infants who exhibit CNV or DNV recordings during the first 6 hours after birth are likely to survive without sequelae; infants who have BS, CLV, or FT tracings have a high risk for death or handicap.

Al Naqeeb and colleagues (24) created a classification that includes three categories for normal and abnormal aEEGs in term infants. The classification is based on amplitude, with 14 healthy controls defining the normal pattern. In the healthy infants, the median upper margin of the widest band of aEEG activity was 37.5 mcV (range, 30 to 48 mcV) and the median lower margin was 8 mcV (range, 6.5 to 11 mcV). The aEEG background activity was classified as normal amplitude when the upper margin of the aEEG activity was more than 10 mcV and the lower margin was more than 5 mcV, moderately abnormal when the upper margin of aEEG was more than 10 mcV and the lower margin less than 5 mcV, and suppressed when the upper margin of the aEEG was less than 10 mcV and lower margin less than 5 mcV. Seizure activity was defined, but not SWC. This

classification was used recently in a randomized multicenter study on postasphyctic head cooling. The intervention improved outcome in infants who had moderately abnormal aEEG patterns before 5.5 hours after birth. (6)

Recovery over time is a general feature of electrocortical background abnormalities after an insult. This is relevant for very preterm infants in whom the early abnormal aEEG tracing of infants developing IVH is characterized by increased discontinuity, epileptic seizure activity, and absence of SWC. The aEEG abnormalities correspond well with findings in EEG studies, showing a correlation between depression of electrocortical activity and extent of brain injury. (47)(48) This was evaluated prospectively in two aEEG studies of very preterm infants recorded during the first days after birth. (29)(30) Because the normal aEEG background in very preterm infants is primarily discontinuous, changes in background activity were measured by counting the amount of activity above an empirically chosen level of 3 mcV and by counting the number of bursts per hour. There was a clear correlation between early aEEG continuity and brain injury, with infants who had large IVHs tending to have a lower number of bursts per hour. The number of bursts per hour during the first 24 to 48 hours after birth seems to be predictive of outcome in infants who have IVH grade 3 to 4. (31)

Proposal for a New Classification

It is clear that many of the previous classifications describe aEEG features relevant only for a certain group of NICU patients (eg, asphyxiated term infants or normal preterm infants). We, therefore, propose a classification of aEEG background patterns based on EEG terminology that could be used in all newborns (Table 3 and Fig. 1). (18)(49) In this proposal, we have used and modified some of the classifications described previously. The classification does not include evaluation of background patterns and amplitudes in relation to normative data for different gestational ages because several publications already cover this. (2)(4)(13)(14)(15) It should be

Table 3. Suggested Classification of aEEG Patterns in Preterm and Term Infants

Background Pattern

Describes the dominating type of electrocortical activity in the aEEG trace.
- Continuous (C): Continuous activity with lower (minimum) amplitude around (5 to) 7 to 10 mcV and maximum amplitude of 10 to 25 (to 50) mcV.
- Discontinuous (DC): Discontinuous background with minimum amplitude variable, but below 5 mcV, and maximum amplitude above 10 mcV.
- Burst-suppression (BSA): Discontinuous background with minimum amplitude without variability at 0 to 1 (2) mcV and bursts with amplitude >25 mcV. BS+ denotes burst density ≥100 bursts/h, and BS− means burst density <100 bursts/h.
- Low voltage (LV): Continuous background pattern of very low voltage (around or below 5 mcV).
- Inactive, flat (FT): Primarily inactive (isoelectric tracing) background below 5 mcV.

Sleep-wake Cycling

Sleep-wake cycling (SWC) in the aEEG is characterized by smooth sinusoidal variations, mostly in the minimum amplitude. The broader bandwidth represents discontinuous background activity during quiet sleep (tracé alternant EEG in term infants), and the more narrow bandwidth corresponds to the more continuous activity during wakefulness and active sleep.
- No SWC: No cyclic variation of the aEEG background.
- Imminent/immature SWC: Some, but not fully developed, cyclic variation of the lower amplitude, but not developed as compared with normative gestational age representative data.
- Developed SWC: Clearly identifiable sinusoidal variations between discontinuous and more continuous background activity, with cycle duration ≥20 min.

Seizures

Epileptic seizure activity in the aEEG usually is seen as an abrupt rise in the minimum amplitude and a simultaneous rise in the maximum amplitude, often followed by a short period of decreased amplitude. The raw EEG should show simultaneous seizure activity, with a gradual build-up and then decline in frequency and amplitude of repetitive spikes or sharp-wave or activity with duration of at least 5 to 10 sec.
- Single seizure: A solitary seizure.
- Repetitive seizures: Single seizures appearing more frequently than at 30-minute intervals.
- Status epilepticus: Continuously ongoing seizure activity for >30 minutes.

noted that many EEG terms (eg, focal, multifocal, sharp waves, delta pattern) are not relevant for aEEG because a trend monitor does not provide this type of information. Similar to basic EEG interpretation, we suggest that pattern recognition forms the base of aEEG interpretation.

The amplitude of the electrocortical activity is extremely important, but this measure must be interpreted with caution because voltage may be affected by inter-electrode distance, scalp edema, and extracerebral signals such as ECG and high-frequency oscillation ventilation. Such interference especially may disturb evaluation of very low-amplitude activity. Nevertheless, normative values for minimum and maximum amplitudes of the aEEG at different gestational ages have been published. (2)(4)(13)(16) These figures are very helpful for assisting in evaluation of aEEG recordings in relation to normal traces for a certain gestational age. The minimum amplitude is especially valuable to assess because it rises with increasing gestational age up to term. Furthermore, short-time variability of the minimum amplitude is usually a sign that a discontinuous aEEG corresponds to a discontinuous EEG and not to a burst-suppression EEG.

Discussion

aEEG is a method for continuous long-term monitoring of brain activity that has proved to be very successful in newborns of all gestational ages and that probably will gain more widespread use in NICUs. The simplicity of the method makes it possible to apply and interpret around the clock by the neonatal staff, and the interrater reliability is usually excellent. (8)(24)(45)(46) Due to the low number of electrodes, single-channel aEEG also is suitable for monitoring the most preterm infants.

A common classification of patterns would be beneficial and increase the understanding of the method. A number of studies have shown that the previous classifications are relevant for identifying abnormalities that could lead to early intervention, but they all have been created for specific purposes and, therefore, are limited to evaluation of certain groups of patients (eg, asphyxiated term infants or preterm infants). Because the aEEG method is based on EEG, a classification based on EEG terminology is optimal, although direct interpretation or translation of features is not possible. For example, amplitudes cannot be extrapolated directly from the EEG to the aEEG or vice versa. Interelectrode distance, high impedance, and ex-
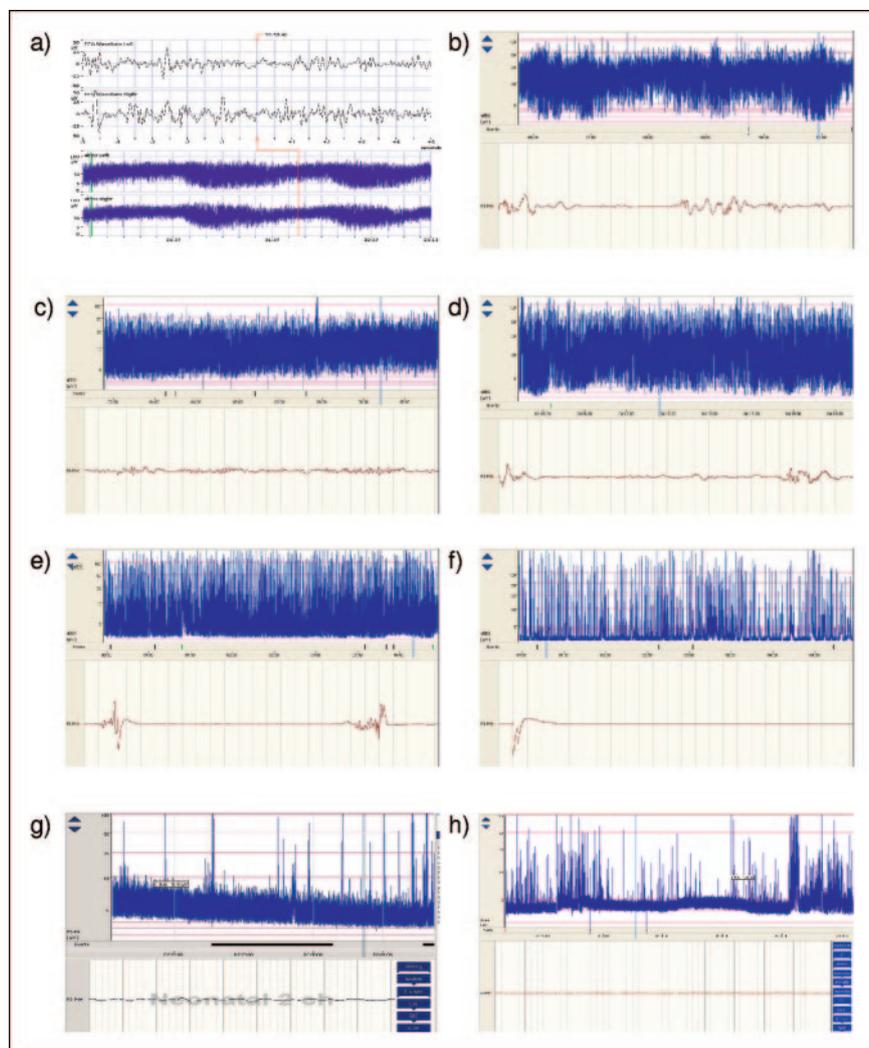
Figure 1. The classification of primary aEEG background patterns, as well as the three degrees of sleep–wake cycling (SWC). a) Continuous background (C) with SWC in healthy term infant (two channels, EEG upper panel, aEEG lower panel). b) C and discontinuous (DC) aEEG background with immature SWC in an infant who has Dandy Walker malformation at 35 weeks' gestation (one channel, aEEG upper panel, EEG lower panel). c) DC background that gradually becomes more continuous, as seen by the rise in the minimum amplitude, in a term infant after cardiac surgery. d) DC background in normal very preterm infant, in whom the maximum amplitude is often higher and the variability in the minimum amplitude is larger than in term infants who have DC patterns. e) Burst-suppression with ≥100 bursts/h (BS+) in a moderately sedated preterm infant. f) Burst-suppression with <100 bursts/h (BS−) in a severely asphyxiated term infant. g) Low voltage (LV) in a severely asphyxiated infant. h) Flat (FT) aEEG and EEG in a term infant who has severe asphyxia. The aEEG baseline between 3 and 5 mcV is due to interference from electrocardiography, which can be seen in the EEG trace. The burstlike pattern is caused by movement artifacts.

tracerebral artifacts (ECG and high-frequency oscillation ventilation) may interfere with the amplitude evaluation. Still, we would like to emphasize the finding from several studies that a primary feature of increasing maturation in healthy infants is an increase in the minimum amplitude during quiet sleep. We have not included the feature "asymmetry" in the current aEEG classification because we believe that this evaluation should be made with standard EEG. However, asymmetries in general amplitude or burst appearance may be visible in two-channel aEEG recordings. (7)

The aEEG identifies subclinical seizure activity that otherwise would pass without detection (Figs. 2 and 3) (Video 1 VIDEO and 2 VIDEO), although we still do not know the best treatment of clinically silent seizure. However, for the neonatologist caring for a sick infant, knowledge about such seizure activity is of great clinical value because it may direct further treatment and investigations. In this context, however, all users of aEEG must be aware that seizure identification with a single- or two-channel monitor is good but that some seizures may pass unrecognized. Especially short single or focal seizures as well as continuous spiking may not be detected by the aEEG. (8)(10) Close collaboration with neurologists and neurophysiologists is, therefore, recommended, and standard EEGs should be recorded frequently in infants with aEEG, especially when the aEEG tracing is abnormal. More advanced systems for neurophysiologic monitoring, such as video-EEG, also are available in the NICU. However, to our knowledge, video-EEG has not been used for standard clinical monitoring in a large population of high-risk new-
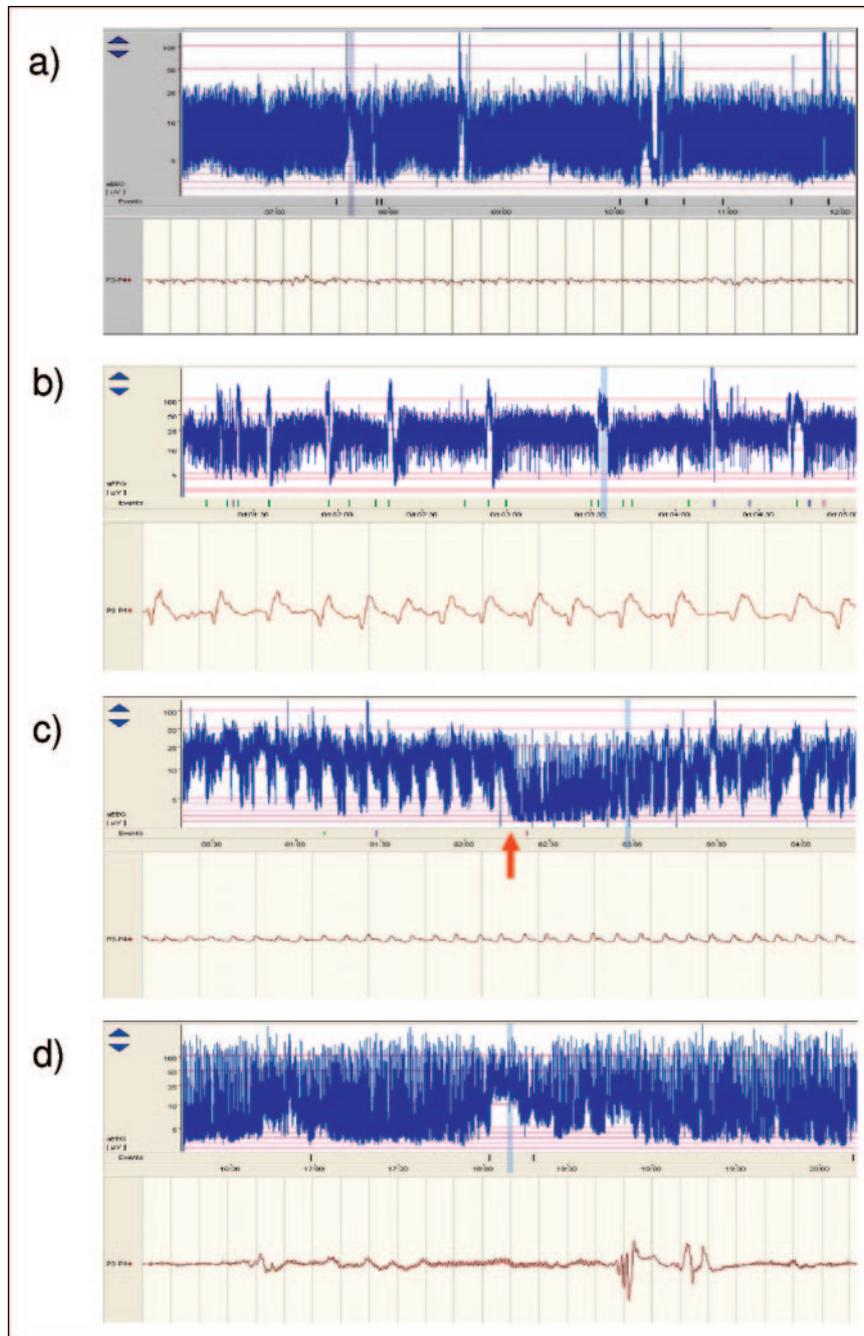
Figure 2. Classification of seizure activity and seizurelike appearance due to interference from high-frequency oscillation ventilation. a) Three single seizures, each lasting for 2 to 4 minutes and appearing at 1- to 1.5-hour intervals on a discontinuous background. Twenty-five seconds of EEG corresponds with the first seizure. The left margin of the blue vertical bar in the aEEG corresponds with the displayed EEG. b) Repetitive seizures with 10- to 35-minute intervals on a continuous background aEEG. The 12-second EEG display is from the seventh seizure (counting from left) with the blue vertical bar. c) Status epilepticus ("saw-tooth pattern") after perinatal asphyxia. Administration of midazolam (red arrow) results in temporary depression of seizures and background activity. The blue vertical bar in the aEEG corresponds with the 12 seconds of EEG. d) This is not a seizure pattern! High-frequency oscillation ventilation resulted in a very variable and raised minimum aEEG amplitude and clearly visible high-frequency interference in the EEG. The 25 seconds of EEG shows the aEEG at the blue vertical bar in this 4-hour aEEG recording. The discontinuous background in this extremely preterm infant is still possible to appreciate, but seizure activity, if present, probably would be missed. The risk of interference from mechanical ventilation on the aEEG is reduced if care is taken that electrodes are not pressed against bedding.
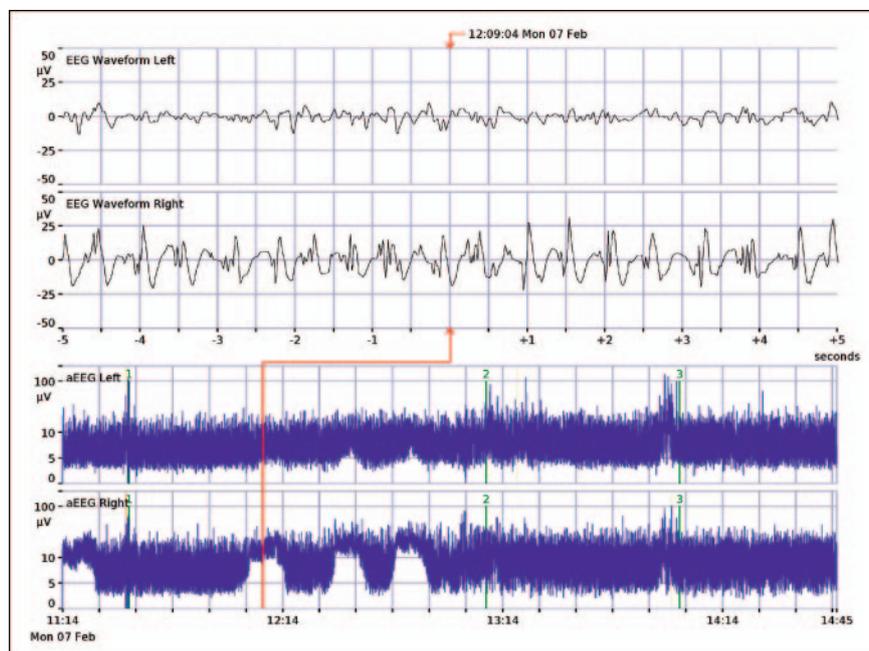
Figure 3. A two-channel record from a term baby who has had a stroke. The EEG waveform from the right hemisphere shows a classic epileptic pattern with monotonous spike waves that repeat at a frequency of about 2/sec. The aEEG from the right hemisphere shows three periods lasting about 10 minutes with markedly increased lower margin. The EEG and aEEG from the left hemisphere show no clear evidence of seizures.

borns in the NICU because the method is more elaborate. A period with video-EEG is probably the best method for continuous monitoring of infants who have severe and recurrent seizures.

Studies in adult intensive care indicate that use of EEG monitoring decreases costs, but no such studies have been conducted in newborns. Furthermore, other than the possibility of early identification of risk for brain injury and the possibility of intervention with hypothermia, no studies have evaluated whether use of aEEG actually improves outcome. For comparison, we are not aware of any studies showing that monitoring of oxygen saturation or blood pressure actually improves outcome in sick newborns.

When interpreting aEEG recordings, attention must be paid to evaluation of possible artifacts, such as ECG and respiratory movements. The study by Burdjalov and associates (14) contains an excellent description of normal aEEG changes with increasing maturation, although the definition of continuity differs from the current proposal. The article is recommended for new users of aEEG because the scoring system clearly shows how to ap-

proach and interpret aEEG tracings. One drawback of the article is that abnormal patterns were not defined.

An important issue is how many channels of EEG should be recorded. For standard monitoring, one or two channels is probably sufficient. When abnormalities are found in the EEG, the number of channels should be individualized. For most infants, one or two channels probably still will be sufficient; only a few infants require more advanced multichannel monitoring. A multichannel system usually is not feasible for standard monitoring because it may disturb other care and the patient, a particularly important consideration in fragile very preterm infants. Although aEEG provides clinically valuable information, the optimal EEG trend measure still is not known. The new aEEG monitors all display the raw EEG continuously, which increases correct identification of seizure activity but also increases the need for adequate training of the staff caring for the patient. For experienced interpreters, some seizures are easier to identify when two channels are used rather than one. Automatic seizure detection is an issue that is being developed for some systems.

Methods for continuous monitoring of brain function will be developed further in the future. In this respect, it is possible that EEG trends will be combined with other methods such as near-infrared spectroscopy for improved evaluation of brain function. Electrodes must be developed further; needle electrodes are easy and fast to apply and usually give good quality recording, but they are invasive. Silver-silver chloride disc electrodes are not invasive and are used for standard EEG, but operators must be trained for them to provide good quality recording. Some adhesive electrodes seem to work after skin preparation, but they should not be placed on the forehead because eye and temporal muscle activity probably will interfere with findings.

In conclusion, aEEG is a standard method for simple brain monitoring. New instruments also simultaneously display the raw EEG signal and provide different meth-

ods of analysis. Further research may show if these options are clinically useful.

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NeoReviews Quiz

4. Amplitude–integrated electroencephalography (aEEG) is based on filtered and compressed electroencephalography (EEG) that enables evaluation of trends in electrocortical activity by simple pattern recognition. Of the following, the aEEG feature contributing *most* to its widespread use in neonates is:

   A. Automatic operation.
   B. Early prediction of neurologic outcome.
   C. Noninvasiveness with wide applicability.
   D. Reasonable cost.
   E. Reliability of recording.

5. aEEG is derived from processing of the raw EEG. Of the following, the *most* important aspect of aEEG is that it:

   A. Filters frequency around 10 Hz and rectifies zero scale.
   B. Compresses several hours of monitoring into one display.
   C. Incorporates activity in all (alpha, beta, delta, and theta) bands.
   D. Integrates signals from several electrodes.
   E. Smoothes signals by filtering technical artifacts.

Continued

6. The aEEG pattern changes with advancing gestational age of the newborn. Of the following, the *most* common aEEG pattern in a healthy infant at 36 weeks of postmenstrual age is:

   A. Burst suppression.
   B. Continuous.
   C. Continuous low voltage.
   D. Continuous with sleep–wake cycling.
   E. Discontinuous.

7. An infant is delivered by cesarean section at 27 weeks of gestational age. The maternal history is significant for worsening pregnancy–induced hypertension necessitating the delivery. The infant's Apgar scores are 7 and 9 at 1 and 5 minutes, respectively. At 24 hours of age, the infant is breathing spontaneously in room air, has normal neurologic examination results, and shows no abnormalities on cranial ultrasonography. The infant has received no sedatives or anticonvulsants. aEEG is obtained. Of the following, the aEEG pattern in this infant is *most* likely to be:

   A. Burst suppression.
   B. Continuous.
   C. Continuous low voltage.
   D. Continuous with sleep–wake cycling.
   E. Discontinuous.