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An introduction to neonatal EEG

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ABSTRACT

Electroencephalography (EEG) is used in neonatal care to assess encephalopathy, seizure recognition and classification, to make epilepsy syndrome diagnoses, and to assess the maturity of neonatal brain activity. It forms part of the neurological assessment, alongside clinical history, examination, and neuroimaging, and should not be taken out of this context. The neonatal EEG is complex and accurate interpretation requires detailed clinical information to be provided on request forms. However, the EEG reports returned to the neonatal unit can also be loaded with technical details, making it difficult for neonatal staff to understand them. This article reviews the basics of EEG, the changes seen with increasing gestational age, and changes seen in common pathologies. We also provide a structured approach to the interpretation of the neonatal EEG report, and discuss its role in prognostication. Amplitude integrated EEG is reviewed in our companion paper.

INTRODUCTION

Neonatal electroencephalography (EEG) is an invaluable part of the neurological evaluation of a neonate, alongside clinical history, examination, and neuroimaging. Its complexity can be unravelled by an understanding the basics of EEG, common terminology, and how the EEG changes as the brain develops.

This article provides information on:

- 1) the basics of EEG
- 2) when to order an EEG in a neonate
- 3) what information to provide on the request form
- 4) a glossary of common terminology used in reports
- 5) the features of a normal neonatal EEG at term age
- 6) what happens as preterm EEG matures towards term age
- 7) what to look out for when interpreting the neonatal EEG report
- 8) the role of neonatal EEG in prognostication

WHAT IS EEG?

EEG records the spontaneous extracellular electrical activity of the brain, generated by the action potentials of neurons. The waveforms represent an average of many actions potentials, some of which will be excitatory, some inhibitory. Much of this is driven by subcortical structures, such as the thalamus and brainstem, particularly in pre-term neonates.

The positions of the EEG electrodes are based on the International 10 / 20 system (Figure 1a). This system can be modified in neonates to take account of the smaller head size (dotted circles, figure 1a). Once recorded, the signal is amplified, filtered to reduce artefact, and electronically displayed. The order in which the signals are displayed generates the montage. There are two types of montage: bipolar and

unipolar (also called a referential montage). Bipolar montages measure the potential difference between two adjacent electrodes. Unipolar montages compare each electrode to the same common electrode, or, in the case of the referential montage, to the averaged activity from all electrodes. The EEGs displayed in this paper are bipolar montages, with the order of the electrodes displayed in chains on the left of the figures for reference, as if looking down on the head from above.

Other parameters that can be measured during the EEG recording include: the electrocardiogram (ECG), respiratory patterns, eye movements, submental muscle activity, and simultaneous video recording. These provide important information, but are not all available on every neonatal unit.

WHEN DO YOU REQUEST AN EEG IN A NEONATE AND WHAT INFORMATION IS NEEDED ON THE REQUEST FORM?

The major indications for requesting an EEG are:

- To ascertain if abnormal movements or CFM tracings are seizures or not
- To clarify if seizures have stopped
- This is important as subclinical seizures are frequently seen following treatment with anti-epileptic drugs.
- To monitor the progress of an encephalopathic state and aid prognostication
- To identify rare neonatal epilepsy syndromes

The request form should contain all relevant details for correct EEG interpretation, including:

- Gestation and corrected age of the neonate
- Birth history e.g. CTG abnormalities, method of delivery, Apgar score
- History of possible seizures, including onset, duration, type
- Medication history, including any recent anti-epileptic medications and benzodiazepines
- Current clinical state e.g. ventilated, cooled

- Comorbid medical conditions and neuroimaging results
- Family history of neurological illness
- Specific question for the reviewing neurophysiologist, e.g. the nature of certain movements, effectiveness of anti-epileptic medications, or assessment of background rhythms

COMMON EEG TERMINOLOGY

We have included a glossary of some common terms encountered in neonatal EEG reports (table one). Frequencies, background activity and epileptiform activity deserve further explanation.

Frequencies are how fast the waveforms are oscillating each second, measured in Hertz (Hz). Examples include: alpha (8-13 Hz), beta (14-40 Hz), theta (5-7 Hz) and delta (<4Hz) waveforms. The predominant waveforms in neonatal EEG are “slow waves” in the delta or theta ranges. The regularity (or rhythmicity) and irregularity of the waveforms may also be described.

Background activity – this is the electrical activity that is seen most commonly throughout the recording. It changes with gestational age and is also different in the awake and sleep states. When looking at the EEG, the neurophysiologist will assess the:

- symmetry of activity over the two hemispheres
- synchrony of activity that occurs in bursts (i.e. do the bursts occur at the same time)
- overall continuity (i.e. does activity occur all the time or does it seem to “stop and start”)
- amplitude of the activity (i.e. how big it is)
- presence of sleep wake cycling (SWC)
- reactivity of the EEG (its ability to change) to external stimuli.

Seizures are notoriously difficult to recognise clinically in neonates, with over and under-diagnosis occurring simultaneously. Therefore, EEG or amplitude integrated EEG recordings may be needed to confirm whether seizures are present or not. On EEG, seizures are paroxysmal events that disturb the normal background rhythms. In older children and adults, seizures can comprise runs of either (or combinations of) sharp waves, spikes, spikes-slow-wave, and slow wave discharges. Sharp waves have durations of 80-200ms (figure 1d) and spikes with durations of 20-80ms (figure 1d). Both have a “pointy” appearance, with the ascent of the wave being steeper than the descent. If they are seen briefly in the background without clinical changes, they are interictal discharges.

Neonatal seizures, however, may not show the same EEG changes as children and adults. To make things more complex, some of the interictal abnormalities seen in later life may actually be normal in neonates. For example, “frontal sharp transients” are sharp waves in the frontal region of the brain that are normal in neonates (figure 2). Electrically, neonatal seizures may be defined as sudden, evolving episodes of abnormal activity with an amplitude $\geq 2 \mu\text{V}$ and a duration ≥ 10 seconds. On the EEG, seizures evolve and change with time. The pattern of EEG activity at the start of the seizure can be very different from the middle and end of the seizure (figure 4). For example, seizures often start off low in amplitude and fast in frequency. The amplitude increases and the frequency slows as the seizure progresses. Abnormalities that do not evolve and are rhythmical, fixed, or unchanging are suspicious of artefact.

Neonatal seizures are almost always focal in nature, and a third of neonates have more than one foci for the onset of the seizures, with some occurring simultaneously but independently at different sites (figure 3c). Seizure activity may also move from one hemisphere to another, (figure 4) or may not be associated with any clinical features at all – called electroclinical dissociation. This phenomenon is more common after drug treatment, but up to two thirds of electrographic seizures have no clinical correlate at all.

THE NORMAL NEONATAL EEG

Term neonates

The background of a normal, term neonatal EEG mainly contains irregular activity in the delta, theta and higher frequencies. This activity is constant over both hemispheres and is termed “continuous” (figure 2).

Sleep wake cycling can be seen in term neonates (figure 2). During the awake state and active sleep (AS), which is associated with rapid eye movement, the EEG has continuous, low voltage activity. However, the EEG changes during quiet sleep (QS), with high voltage bursts separated by lower voltage slow waves. This is called tracé alternans (figure 2b). Because the bursts of activity are separated by periods of relative quiescence, the activity is called “discontinuous”. As the term baby gets older, the EEG in quiet sleep becomes more continuous, until mature features like sleep spindles appear around 46 weeks gestational age.

In a term neonate, sleep alternates with wakefulness over a three to four hour period. Background abnormalities are more common in QS, whilst seizures are most frequently seen in AS. In order to capture both sleep states and assess the neurodevelopmental stage of the EEG, a recording should be at least an hour long.

The normal preterm neonatal EEG and its maturation towards term age

The background – the majority of the preterm neonate’s background is discontinuous during awake and sleep states (figure 2). This is called trace discontinue. As a neonate matures, the duration of the flatter, quieter periods shortens and the bursts lengthen. Hence, the “inter-burst interval” reduces, until it becomes continuous by term age in the awake and active sleep states.

Before 30 weeks gestational age, bursts of activity are seen over both hemispheres in a fairly synchronous fashion, i.e. at largely the same time. By definition this means

they are separated by less than 1.5 seconds. This synchrony is reduced temporarily around 30 weeks, as the cortical neuronal networks develop further, and recovers around 34 weeks gestational age as the corpus callosum matures.

A normal preterm EEG can show occasional sharp waves from different regions of the brain. The neurophysiologist interpreting the EEG will take the gestational age, location and frequency of sharp waves into account to decide if they are normal or not. In addition, characteristic, brief waveforms also appear normally in the background at certain gestational ages. These are shown in figure 2, and may be commented on in the report. These waveforms can help the neurophysiologist determine whether or not the recording is appropriate for the gestational age of the baby.

Sleep wake cycling can be seen just before 30 weeks gestational age. From 30 weeks the different phases of the sleep cycle become increasingly distinct (figure 2). The duration of the sleep wake cycle also increases with maturity:

- At 30 weeks, 20 minutes of AS and 10 minutes of QS are typically seen
- At term: 45 minutes AS and 20 minutes of QS are typical.

In general terms, the EEG of preterm neonates acquires the same characteristics expected of those born at later gestational ages, assuming no neurological insults have occurred.

ABNORMAL NEONATAL EEG FINDINGS AND THEIR SIGNIFICANCE

To help decipher the mysteries and terminology used in EEG report, we recommend the clinician looks for information from four areas:

1. Is the EEG background normal or abnormal?
2. Are abnormal focal or generalised abnormalities appearing in the background?

3. Are there seizures?
4. Is there a neonatal epilepsy syndrome?

Clearly, any EEG that contains seizures is abnormal. But determining if the background is abnormal or not from a report can be tricky.

Background abnormalities in a term infant – the normal term EEG is continuous, symmetrical and synchronous in the awake and active sleep states, with occasional sharp waves from a variety of regions of the brain and sleep wake cycling seen. There is no universally accepted grading system to classify abnormal neonatal EEG background patterns. Different authors use slightly different criteria to group certain features and then assign a grade, such as minor, moderate or severe abnormalities. These grades are mainly used in the research setting, and in clinical practice neonatal staff are more likely to be faced with a descriptive account of the EEG instead. Some abnormalities in the background to look out for include:

Discontinuity in the awake or active sleep states should be considered abnormal in the term neonate. It can be associated with a poor outcome, although we advise caution if the EEG is performed early in hypoxic ischaemic encephalopathy (HIE).

Burst suppression (figure 3a) is a characteristic pattern in which there are spells of prolonged electrical inactivity (“suppression”) followed by brief bursts of high voltage activity. In contrast to discontinuity, the suppressed periods are devoid of cerebral activity, and the bursts contain mainly abnormal waveforms. The durations of the “bursts” and the “suppressed” periods vary. Burst suppression is seen in HIE, meningitis, inborn errors of metabolism, drugs, anaesthesia, and two of the neonatal encephalopathies: Ohtahara syndrome and early myoclonic epileptic encephalopathy (EMEE).

Developmental outcome following the appearance of burst suppression is dependent on the cause. Neonates with HIE can have good outcome if the EEG normalises quickly, and pyridoxine dependent seizures can have good outcome if treated. Burst suppression that does not improve, or is associated with a neonatal epilepsy syndrome / a structural brain abnormality not amenable to epilepsy surgery predicts a poor outlook.

“Electrocerebral inactivity” is the absence of EEG activity over 2 μ V. The EEG is flat with markedly reduced electrical activity and the neonate will be encephalopathic. This tracing can be associated with multiple pathologies and is typically associated with a poor outcome, although better outcomes have been reported in HIE if it resolves over the first few days of life.

Dysmaturity is an immature EEG background. Specifically this means there is EEG activity that would be more suitable to a neonate 2 or more weeks younger than their real gestational age. Transient dysmaturity is of uncertain significance, but its persistence is associated with an increased likelihood of neurological disability.

Sharp waves – whilst occasional sharp waves from different regions of the brain can be normal, if there are “too many” present, or if they occur persistently from one or more regions of the brain, this suggests an abnormality.

Focal periodic discharges are brief abnormalities that occur at regular intervals from a specific region of the brain. The most well-known are called “periodic lateralised epileptiform discharges”, abbreviated to PLEDS (figure 3b). They are rare and most commonly seen following perinatal stroke.

The preterm infant

As with term neonates, no universally accepted classification for abnormalities in preterm infants exists, possibly because the EEG changes so significantly between 24 weeks and term. A clinician should look to see if the report comments on whether the report is appropriate for the gestational age of the baby, or if it is dysmature. If there is doubt about this, contact the neurophysiologist, as they may not have been provided with the gestational age of the baby on the request form.

Burst suppression can be seen in preterm infants, but can look similar to the normal tracé discontinu pattern. The important point to note is that the bursts of activity contain normal features in both tracé discontinu and the excessive discontinuity seen in extremely unwell infants. In contrast, burst suppression does not contain normal features in the bursts.

Focal periodic discharges – occasional sharp waves from different regions of the brain can be normal in the preterm EEG; however, positive Rolandic sharp waves (PRSWs) are sharp waves persistently seen over the central or Rolandic region (i.e. around the central sulcus; figure 3d), and may be unilateral. PRSWs are a marker for periventricular leukomalacia, and are claimed to be a sensitive (98%) and specific (84%) markers of motor disability at one year.

CAN EEG OFFER PROGNOSTIC INFORMATION?

EEG does confer useful prognostic information, but should only be part of a comprehensive assessment alongside the history, examination, amplitude integrated EEG and neurological examination.

Preterm neonates

EEG studies performed at 3 points within the first month of life in under 34 week premature babies showed the presence of background abnormalities were associated with developmental delay or cerebral palsy. More severe patterns correlated more strongly with future developmental problems. However, EEG is not a

routine part of preterm clinical care and will not supplant history, examination and neuroimaging.

Hypoxic ischaemic encephalopathy

A normal EEG in the first 8 hours of life is associated with an excellent outcome. Abnormal recordings that improve within 7 days, even those that were relatively inactive, also indicate a good prognosis. For example, neonates in cooling studies whose “severe” EEG abnormalities improved had a normal examination at one year. In contrast, a static or worsening EEG is associated with poor outcome.

Seizures

Some studies suggest that 20% of neonates with seizures develop post-neonatal epilepsy. However, this ignores the most important factor: the aetiology of the seizures.

Cerebral infection

EEG abnormalities can be observed in acute neurological infections, like meningitis or herpes encephalitis. These abnormalities include non-specific background changes and seizures.

Normal background rhythms are associated with a good outcome. Abnormal patterns are associated with neurodevelopmental difficulties. Some authors have suggested a correlation between the degree of EEG abnormality and outcome: normal or isolated mild background abnormalities are associated with normal outcome; more than one asymmetrical, asynchronous background abnormality, a burst suppression pattern, or an isoelectric EEG are associated with poor outcome. As with HIE, the timing of the EEG is important. Abnormalities disappearing after a few days can be associated with normal developmental outcome.

CONCLUSION

Increasingly, neonatal units are using neurophysiology techniques to monitor infants. EEG can provide useful information, including background activity, focal abnormalities, seizure confirmation, and epilepsy syndrome classification. A basic understanding of neonatal EEG helps a clinician decipher the language of the reports, and may provide prognostic information in conjunction with history, examination and neuroimaging.

Table one. Common terms found in EEG reports.

Term	Definition
Alpha frequency	Frequency band of 8-13 Hz
Amplitude	Voltage of EEG waves expressed in microvolts (μV). Measured peak-to-peak
Asymmetry	Unequal amplitude of EEG activities over homologous areas on opposite sides of the head.
Asynchrony	The non-simultaneous occurrence of EEG activities over regions on the same or opposite sides of the head.
Background activity	The EEG activity recorded during the resting state which provides baseline activity on which normal age dependent patterns and abnormal phenomena occur.
Beta frequency	Frequency band from 14 to 40 Hz.
Burst	Group of waves which appear and disappear abruptly and are distinguished from background activity by differences in frequency, form and/or amplitude.
Delta	Rhythm under 4 Hz
Delta brush	Slow waves overlaid with faster frequency waveforms. First seen around 28 weeks, peak at 32 weeks, gone by term. Initially seen at various locations, should be exclusively occipital by 36 weeks.
Discharge	Interpretive term commonly used to designate epileptiform and seizure patterns
Enoche frontale	Sharp appearing waves in the frontal regions appearing at around GA 35 weeks
Fast activity	Activity of frequency higher than alpha, i.e. beta and gamma activity.
Generalized	Occurring over all regions of the head
Multifocal	More than two or more spatially separated foci
Paroxysmal fast	Fast frequencies in the beta range occurring intermittently
Periodic	Applies to: (1) EEG waves or complexes occurring in a sequence at an approximately regular rate throughout the whole recording; (2) EEG waves or complexes occurring intermittently at approximately regular intervals.

Premature temporal theta	Short runs of theta activity in the temporal regions (can take a saw-tooth appearance). Appear at 24 weeks, disappear around 34 weeks
Sharp wave	Transient, clearly distinguished from background activity, with pointed peak and duration of 70-200 ms. The term is restricted to epileptiform discharges
Sharp-and-slow-wave complex	A sequence of a sharp wave and a slow wave.
Slow activity or wave	Activity of frequency lower than alpha, i.e. theta and delta activities.
Spike	A transient, clearly distinguished from background activity, with pointed peak and a duration from 20 to under 70 ms. The term is restricted to epileptiform discharges
Spike-and-slow-wave complex	A pattern consisting of a spike followed by a slow wave.
Symmetry	Approximately equal amplitude, frequency and form of EEG activities over homologous areas on opposite sides of the head.
Synchrony	The simultaneous occurrence of EEG waves over regions on the same or opposite sides of the head.
Theta frequency	Frequency band from 4 to under 8 Hz.
Tracé alternant	A discontinuous pattern of non-REM (quiet) sleep seen in preterm infants of 34 weeks conceptional age or older which can persist up to 3±4 weeks after birth in full term infants. The pattern is characterized by bursts of predominantly slow waves (1±3 Hz, 50±100 µV) appearing approximately every 4±5 s, and intervening periods of low voltage activity of (<50 µV) 4-7 Hz.
Tracé continu	Continuous activity, replacing a previously markedly intermittent record during evolution of EEG in preterm infants.
Tracé discontinue	Pattern of preterm infants below 34 weeks of conceptional age (CA) characterized by mixed frequency high voltage bursts separated by periods of a very low voltage background.
Transient	Any isolated wave or complex, distinguished from background activity.
Wave	Any change of the potential difference between pairs of electrodes in EEG recording. May arise in the brain (EEG wave) or outside it (extra-cerebral potential).

FIGURE LEGENDS:

Figure 1. Electrode placement and output

a, The International 10/20 system of electrode placement (filled circles) results in the electrodes being placed over specific points on the head following detailed measurements drawn from anatomical landmarks. The dotted circles represent the reduced 10/20 system often used in neonates.

b, In bipolar recording the electrical field captured by one potential is compared to another nearby, for example C4 is compared to P4. If the electrodes see the same field, there is no difference between them and so output is flat. The greater the potential difference between the electrodes, the higher the amplitude of the output.

c, Localisation of an abnormality to the C4 electrode. If the discharge occurs under the C4 electrode then it becomes negative with respect to its neighbouring electrodes. In a bipolar montage this leads to a positive (downward) deflection in the F4-C4 channel and a negative (upward) deflection in the C4-P4. When the two channels are displayed next to each other, the waveforms “phase reverse”.

di. Example of a spike wave followed by a slow wave. This is from an older child.

dii. Examples of a sharp wave with phase reversal. The downward point of one sharp wave appears to touch the up going point of the other. This localises the epileptic activity to the area underneath the electrode that is common to both tracings.

Figure 2. Development of the neonatal EEG

a, During development the neonatal EEG undergoes pronounced changes that reflect increased connectivity, neuronal number and sleep-wake cycling. Tracé alternans disappears by 46 weeks and is replaced by high voltage slow wave sleep. At term both active sleep and awake are characterised by mixed frequency activity (also called *activité moyenne*); irregular respirations and intermittent REM distinguish the two states by means of measurement, clinically the baby will have eyes open in awake. The symbols “†” and “*” indicate that there is little to choose between the two EEG patterns, to tell apart the two states one must rely on clinical state and other measures such as respiration and eye movement channels.

b, Examples of developmental transients (bordered in grey) and background patterns (bordered in blue, red, green or gold to match the chart above). Note the increasingly continuous activity seen as gestational age increases. The green border symbolises the awake state (see “a”), the gold border active sleep and the red border quiet sleep.

Figure 3. Examples of abnormal EEG patterns of cerebral activity.

a). Burst suppression. Generalised bursts of irregular spikes and sharp waves discharge synchronously over both hemispheres. In between the trace is flat with no activity above $5\mu\text{V}$. The inter-burst interval is variable but around 15-30s.

b). Periodic lateralised epileptiform discharges (PLEDS); sharp waves can be seen over the left centro-temporal region, discharging at regular intervals.

c). Comparing the right hemisphere (upper 4 traces) and left hemisphere (second set of 4 traces) two distinct seizure patterns can be seen (circles). The seizure discharges have different shaped waveforms, amplitudes and rhythmicity; for example, the rhythmical activity is slower on the right when compared to the left.

d). Positive Rolandic sharp waves. The sharp waves are seen over the C4-Cz and Cz-C3 channels (circled). The waveforms face away as here Cz is made positive by a relative focus of negative charge deep in the brain parenchyma, usually in the periventricular white matter. If Cz is also positive in relation to nearby electrodes then in the C4-Cz channel an upward deflection is seen as C4 is negative relative to Cz; the opposite occurs in Cz-C3. This localises the abnormality to the Cz electrode in the Rolandic region.

Figure 4. Changes in seizure activity on the EEG

ai-iii). Spatial migration of a seizure. Initially irregular discharges of can be seen over the posterior region of the left hemisphere (circles in i). The activity then involves the both hemispheres (central panel ii, circles). Rhythmical sharp waves appear over the right fronto-parietal regions (circle, iii). This neonate had a diagnosis of migrating partial seizures of infancy.

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MAIN POINTS

- Correct interpretation of an EEG requires adequate clinical details, including gestational age at birth and the clinical question being asked
- The EEG changes from preterm to a term pattern as the brain matures. Understanding of these changes is vital to interpret EEG and the reports
- Significant differences exist between the EEG during the awake and sleep states, and recording both will give more information
- When interpreting an EEG report, the features to seek out are: background including sleep waking cycling, focal or generalised abnormalities, and seizures. These may help diagnose a rare neonatal epilepsy syndrome
- EEG can give useful prognostic information, but only alongside other aspects of clinical evaluation, like examination and neuroimaging