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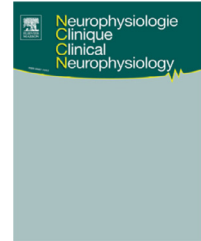
ORIGINAL ARTICLE

CARFS[7]: A guide and proforma for reading a preterm neonate's EEG

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Abstract

Objectives: The important role of the EEG in preterm and term babies in investigating brain function and seizures, predicting outcomes, evaluating therapeutic interventions and decision-making is being increasingly acknowledged. Development of the brain in the last trimester of pregnancy results in rapid changes in the EEG patterns in this period. Acquiring and interpreting the EEG of a preterm baby can be challenging. The aim of this study was to develop a proforma titled CARFS[7] (Continuity, Amplitude, Reactivity, Frequency, Synchrony, Symmetry, Sleep, Sharps, Shapes, Size and Seizures) to enable neurologists to read EEGs of premature babies with greater confidence, ease and accuracy and produce a report more easily repeatable and homogenous among operators.

Methods: The CARFS[7] proforma was developed based on a literature review and the personal experience of the authors. The parameters of the EEG evaluated and scored in the proforma are Continuity, Amplitude, Reactivity/Variability, Frequency, Synchrony, Symmetry, Sleep, Sharps, Shapes/Patterns, Size and Seizures. We also assessed the interrater reliability of the proposed scoring system incorporated in the proforma.

List of abbreviations: AS, active sleep; AS1, active sleep 1, usually seen before an epoch of quiet sleep; AS2, active sleep 2, usually seen after an epoch of quiet sleep; B, bursts (B); BERDs, brief EEG rhythmic discharges of 5—10 s; BIRDS, brief intermittent ictal/interictal discharges; CA, chronological age is the time elapsed after birth; CARFS[7], continuity, amplitude, reactivity, frequency, synchrony, symmetry, sleep, sharps, shapes, size and seizures; ECG, electrocardiogram; ECI, electrocerebral inactivity; ECSz, electroclinical seizures; EEG, electroencephalogram; EMG, electromyogram; EOG, electrooculogram; ESZ, electrographic only seizures; GA, gestational age is the time elapsed between the first day of the last menstrual period and delivery; IBI, interbursts (inter-burst-intervals); LPDs, lateralised periodic discharges; PLEDs, periodic lateralised epileptiform discharges; PMA, postmenstrual age is the gestational age plus the chronological age; PRS, positive rolandic sharps; PTS, positive temporal sharps; PTT, premature temporal theta; QS, quiet sleep; SAD, slow anterior dysrhythmia; STOP, sinusoidal theta in occipital region of prematures; V-EEG, video-EEG; VS, vertex sharps.

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Results: CARFS[7] proforma incorporates a number of parameters that help evaluate the preterm EEG. The interrater reliability of the proposed scoring system in the CARFS[7]proforma was high.

Conclusions: CARFS[7] is a user friendly proforma for reading EEGs in the preterm infant. Interrater reliability using Cohen's k shows high agreement between two child neurologists who independently rated the EEGs of 25 premature babies using this proforma. CARFS[7] has the potential to provide, accurate, reproducible and valuable information on brain function in the preterm infant in clinical practice.

Introduction

Survival of premature babies has improved tremendously over the years. However, morbidity in the form of cognitive disability, motor disability, epilepsy, visual and hearing impairment, sleep disturbances and behavioural difficulties occurs in preterm infants more frequently than in term babies. Poor neurodevelopmental outcomes are still seen [61,92,69−72,67]. The ability to predict outcomes early will enable initiation and targeting of early therapeutic and interventional strategies, as well as make timely decisions regarding options of care.

The conventional EEG has been shown to be a good predictor of outcome in term babies. The important role of the EEG in preterm and term babies in understanding the dynamic structural and functional changes in the brain, predicting outcomes, evaluating therapeutic interventions and decision-making is being increasingly acknowledged [42,95,38,51,30,29,93].

There are many challenges in acquiring and interpreting an EEG in a preterm baby. We know the development of the brain in the last trimester of pregnancy results in rapid evolutionary changes in the EEG patterns in this period [94,88,77,3,17,60,39,75,85,32,28,24,21,8]. One of the problems in this period is deciding what is normal − as preterm birth itself is not a normal event.

There are excellent papers describing in detail the occurrence, maturation and evolution of different patterns (normal and abnormal) from the foetal to preterm to term babies [41,18,86,1,63−65,69,33,83,52,49,48,22−24,16,57,93,6,3,4,82]. Many of these studies illustrate the usefulness of EEG in predicting neurodevelopmental outcome in the term and preterm baby [14,64,23,33,48−51,18−22,16]. A standardised assessment scheme for preterm EEG assessment [63] has been developed to be used by experienced readers of neonatal EEG: the practical utilisation of this scheme may be dependant on the time available and the expertise of the reader. Excellent recent reviews [93,6] outline the maturational aspects of the EEG from preterm to term newborns and discuss the basic substrates and mechanisms involved in the generation of the EEG. However, even today, the task of reporting and interpreting the EEG of a premature baby remains quite daunting for most neurologists in clinical practice. The different definitions, descriptions and values for some of the patterns are not consistent across the many groups who have contributed significantly to our understanding of the EEG of premature babies [1,90,91,6].

The aim of this study was to develop a proforma titled CARFS[7] in order to enable neurologists to read the EEG of premature babies with greater confidence, ease and accuracy and produce a report more easily repeatable and homogenous among operators. Our CARFS[7] proforma has been built through a composite scoring system based on a literature review and personal experience of the authors; some parameters (continuity, amplitude, seizures) have a higher weighting than others. In this paper we also report on the interrater reliability of this scoring system based on the EEGs of 25 premature babies, interpreted and scored independently by two experienced readers of neonatal EEG.

Methods

Parameter selection and scoring was based on literature review and our own experience. We read and considered the manuscripts and book chapters written by important and well recognised scientists in the field. Two of the 3 authors (LN and FP) independently undertook PubMed, Web of Science and Scopus searches for EEGs of premature babies and for each of the parameters outlined in the proforma. Not all the literature we reviewed has been referenced − only those articles that were considered most relevant by the authors, and those that gave details regarding the different patterns described in our manuscript. Furthermore, some articles were manually added from references of pertinent studies not identified through electronic search. Two authors (LN and SG) developed the scoring system and two (LN and FP) did the scoring independently for inter-rater reliability.

CARFS[7]: continuity, amplitude, reactivity/ variability, frequency, synchrony, symmetry, sleep, sharps, shape, size and seizures

Each of these parameters is described and definitions and normal values recommended. We have defined preterm age as follows: gestational age (GA) is the time elapsed between the first day of the last menstrual period and delivery, chronological age is the time elapsed after birth, postmenstrual age (PMA) is the gestational age plus the chronological age [13]. Table 1 outlines the parameters and the weighted scores allocated to each parameter. Some parameters (continuity and amplitude) have more precise definitions than others (frequency and some shapes). Often when abnormality is seen in one parameter, abnormality is also seen in others. An EEG with a score of zero indicates normality, a higher score implies a more abnormal EEG. The CARFS[7] proforma can be used on a standard one hour neonatal Video-EEG (V-EEG) recording, or at specified times during continuous monitoring, or when a sleep-wake cycle is recorded.

Table 1 CARFS[7] scoring sheet.

Parameter	Actual score	Maximum scores (normal 0)
Continuity		3
Amplitude		4
Reactivity/Variability		2
Frequency		1
Synchrony		1
Symmetry		2
Sleep		1
Shapes/Patterns		1
Size		1
Sharps		1
Seizures		3
Total		20

Table 2 Abnormal continuity measures.

Gestational age (weeks)	Longest IBI	Longest B
26−27	>60 s	<60 s
28−29	>30 s	<120 s
30−32	>20 s	<600 s
Scores	Abnormal IBI	Abnormal B
1	<25%	<25%
2	25−75%	25−75%
3	>75%	>75%

Abbreviations: B: burst, IBI: interburst.

Good clinical practice dictates considering relevant clinical situations (e.g. hypothermia, metabolic disturbances, medications etc.) in the final interpretation.

Continuity (scored 0, 1, 2, 3)

Discontinuity of the background is a characteristic feature of the EEG of a premature baby [1,90,91,3,18,86,64,57,25,95]. The percentage of the EEG recording that shows a discontinuous pattern is important and varies with different degrees of prematurity. The percentage of discontinuity decreases with increasing gestational and chronological age. In extreme prematurity (PMA 24−25 weeks), the background is very discontinuous. Most babies will show variable periods of discontinuity in a standard recording. Discontinuity is higher in quiet sleep compared to active sleep and wake state.

The EEG of a premature baby shows bursts of activity (at times called active periods): mostly high amplitude delta, at times with superadded faster frequencies, alternating with interbursts (at times called quiescent periods): mostly periods of low amplitude (15−25 uV). In the literature the accepted amplitude for a burst has varied from >15 to >50 uV. We recommend an amplitude of > 25 uV for a burst and < 25 uV for an interburst (IB). An epoch (usually 15 s) is considered discontinuous if the burst portion is less than 50%.

Table 2a gives the duration of the bursts (B) and interbursts (IBI) that should be considered abnormal at the different GAs. Normal values are available until 32 weeks GA. Beyond that most IBI are < 10 s. In our experience, the majority of IBIs in premature babies, are less than 35 s. If >75% of bursts and IBI are abnormal then a score of 3 is recommended; between 25 and 75% scores a 2 and <25% scores a 1 (Table 2b). Fig. 1 shows different interburst durations (normal and abnormal), Figs. 2−5 illustrate the maturation patterns with greater continuity in more mature babies.

Based on the assessment of continuity a score is allocated, with 3 reflecting severe abnormality and 0 being normal for age. The EEG in Fig. 1D would score 2/3 for excess discontinuity, in Fig. 4D would score 0/3, and n Fig. 6C would score 3/3.

Amplitude (scored 0, 1, 2, 3, 4)

The amplitude of the different frequencies in the recording is important. High amplitude slow delta is common in normal preterm infants. Reduced amplitude suggests background depression and may reflect early or acute changes of brain injury [19−22,44,51,90,91,86,69,6]. Figs. 1−5 demonstrate high amplitude of the delta activity seen at different PMAs. A flat EEG tracing (see Fig. 6) indicates electrocerebral inactivity (ECI) or silence; often what is seen is near ECI because of the difficulty in eliminating all artefact in the neonatal EEG in a sick baby. It is extremely important to ensure that rigorous technical standards are followed before declaring ECI or near ECI. If ECI is seen no other parameters can be scored. Table 3 recommends parameters for assessing low amplitude.

The amplitude is scored out of 4 with 0 being normal and 4 severely abnormal. The EEG in Fig. 1D would be scored 2/4 for amplitude and in Fig. 6C would score 4/4.

Reactivity, variability, lability (scored 0, 1, 2)

Clinical and EEG reactivity is usually evident by PMA 28 weeks and can be seen earlier (see Fig. 6) in some babies [1,90,91,6]. Reactivity to sensory stimulation often results in a change in background with attenuation in the awake and active sleep (AS) states. In quiet sleep (QS) stimulation may result in more continuous activity. At 24−25 weeks stimulation may result in limb withdrawal, though no specific EEG change is evident. The EEG, even in preterm infants, has variability and lability, with bursts and interburst intervals.

A monotonous non changing EEG is abnormal and scored as 2. Other abnormalities, such as lack of reactivity on EEG after 28 weeks, are scored as 1. The EEG in Fig. 6A would score 0/2 for reactivity.

Frequency (scored 0,1)

Most EEGs in premature babies show various combinations of activity in the delta, theta, alpha and beta frequencies, with higher amplitudes in the lower frequencies [90,91,62,26,32,37]. Short bursts of alpha or theta rhythms are well recognised in the rolandic regions of term babies as a normal phenomenon. Frontal alpha bursts may be seen in at PMA 25−26 weeks and is thought to be more common on the left side. Excessive rhythmic alpha or theta frequency activity may be abnormal. Figs. 1−5 show admixture of frequencies at different ages.
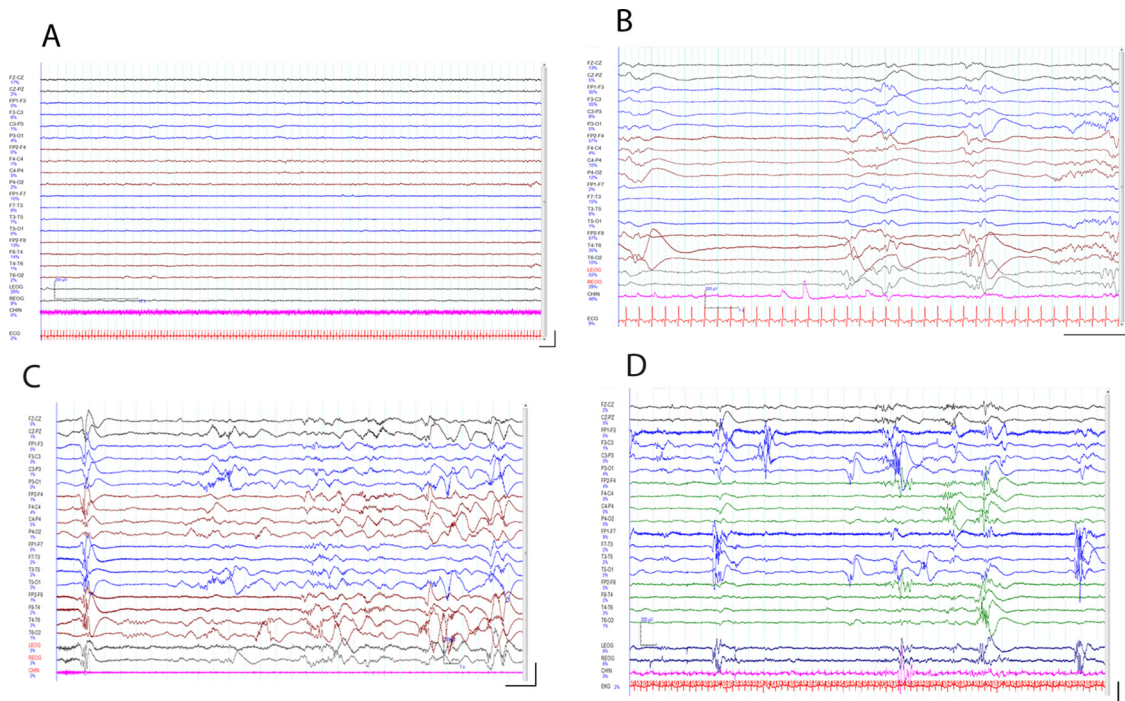
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Fig. 1 EEGs showing variations in continuity and amplitude at different premenstrual ages (PMA); other features are described in individual subfigure legends. Montage is double banana, with left sided derivations in blue, right in red and midline in black. Calibration bars at bottom right of each subfigure: vertical 200uV, horizontal 2 s. Montage and calibration descriptions apply to all figures. Abbreviations: IBI: InterBurst Interval, PTS: Positive Temporal Sharps, PTT: Premature Temporal Theta. A. PMA 25 weeks, IBI>60 s. B. PMA 27 weeks, normal discontinuity, PTS, and mild asymmetry of PTT. C. PMA 31 weeks, normal discontinuity. A, B and C would be scored as 0/3 for continuity. D. PMA 33 weeks, excess discontinuity, low amplitude in IBI, occipital sharps, abnormal delta brushes, excess asynchrony. D would be scored as 2/3 for continuity, 2/4 for amplitude, 1/1 for synchrony, 1/1 for sharps, 1/1 for shape, 1/1 for size.

A score of 0 is given for normal and 1 for abnormal EEG with regard to frequency. The EEGs in Figs. 2C−4D would score 0/1 for frequency.

Synchrony (scored 0,1)

Synchrony of the high amplitude delta bursts is seen in extremely premature babies until about PMA 28 weeks. Asynchrony implies a temporal delay of $> 1.5 − 2$ s between hemispheric bursts, [1,3,6,41,25,57,62,82]. The level of asynchrony is estimated by the number of bursts that show $>1.5−2$ s of difference between the two hemispheres. Physiological transient interhemispheric asynchrony is observed during changes in alertness or vigilance, most prominently between PMA 32 and 36 weeks. Interhemispheric synchrony is almost 80% at most PMAs. Figs. 1−5 show the synchronous and at times asynchronous bursts in babies of PMA 25−33 weeks.

A score 0 for normal and 1 is given for abnormal asynchrony. The EEG in Fig. 1D would score 1/1 for synchrony and EEG in Fig. 2C would score 0/1.

Symmetry (scored 0, 1, 2)

Interhemispheric asymmetry refers to asymmetry of amplitude of $>50\%$, frequency or morphology between the same areas of the two hemispheres [64,86,90,91,1,41,82,62]. Persistent asymmetry is abnormal, transient asymmetries may

be normal. Abnormal amplitude asymmetry is almost always associated with asymmetry in frequency, morphology, shapes and patterns. Figs. 1−8 demonstrate normal and abnormal asymmetry in preterm babies.

Symmetry is scored out of 2 with 0 being normal, a score of 2 with persistent asymmetry ($>75\%$ of the time). A score of 1 would be given for asymmetry present more than 25% of the time. EEGs in Figs. 1C and 3D would score 0/2 for symmetry, and the EEG in Fig. 9B would score 2/2.

Sleep (scored 0, 1)

A standard neonatal V-EEG recording should ideally be at least one hour in duration. Sleep scoring in neonatal EEG is usually visually assessed on the EEG [32,81,80,29,12,1,42,62,37,16,3,73,87,7]. Additional information can be gleaned from the video but is not critical. In neonates less than PMA 26 weeks, one can only distinguish a resting state and an agitated state. Typical sleep states on EEG can be distinguished from 30 weeks onwards; however, some differences between wake and sleep may be discerned earlier. Discontinuity of the EEG reduces as the chronological age increases. Discontinuity of the EEG also varies in the different sleep stages: discontinuity in quiet sleep is more than in active sleep and least in the wake state. The typical trace alternans pattern of quiet sleep is recognised and reported from 37 weeks of age. From about 37 weeks one can distinguish Active sleep 1 (AS1), usually seen before an epoch of

Fig. 2 EEGs at PMA 25 weeks showing variations in continuity, amplitude and synchrony, and admixture of frequencies. Abbreviations: IBI: InterBurst Interval, PRS: PeriRolandic Sharps, PTT: Premature Temporal Theta, STOP: Sinusoidal Theta in Occipital region of Prematures, VS: Vertex Sharps. A: PTT with delta (eye), left sided run of PRS. This would score as 0/1 for shapes and 0/1 for sharps. B. Variable IBI, PTT with delta, PRS, VS, asynchronous and synchronous bursts. This would score 0/3 for continuity and 0/1 for shapes. C. Single PRS, synchronous bursts of activity, mixed frequency activity. This would score as 0/1 for frequency and 0/1 for synchrony. D. PRS on both sides, STOP, right occipital sharp, admixture of frequencies. This would score as 0/1 for frequency and 0/1 for shapes.

quiet sleep and Active sleep 2 (AS2) seen after an epoch of QS. At 40 weeks one should see wakefulness, active sleep and quiet sleep in a 1-h recording. Neonates enter active sleep first, when states can be distinguished. Abnormalities of the background are often more obvious in quiet sleep. Sleep is scored as 0 when normal for age.

Fig. 3 EEGs at PMA 27 weeks with varying bursts and interburst intervals, some asymmetry, and admixture of frequencies. Abbreviations: PRS: PeriRolandic Sharps, STOP: Sinusoidal Theta in Occipital region of Prematures. A. Note frontal sharps. If frequently seen it should be scored as 1/1 for sharps. B. Some asymmetry, delta brushes. The asymmetry is scored as 1/2 if present for more than 25% of the recording and 2/2 if more than 75%. C. Repetitive PRS, sharp/spikey PRS on the right. This PRS is abnormal and would be scored as 1/1 for sharps. D. Bilateral STOP. This would be scored as 0/1 for shapes.
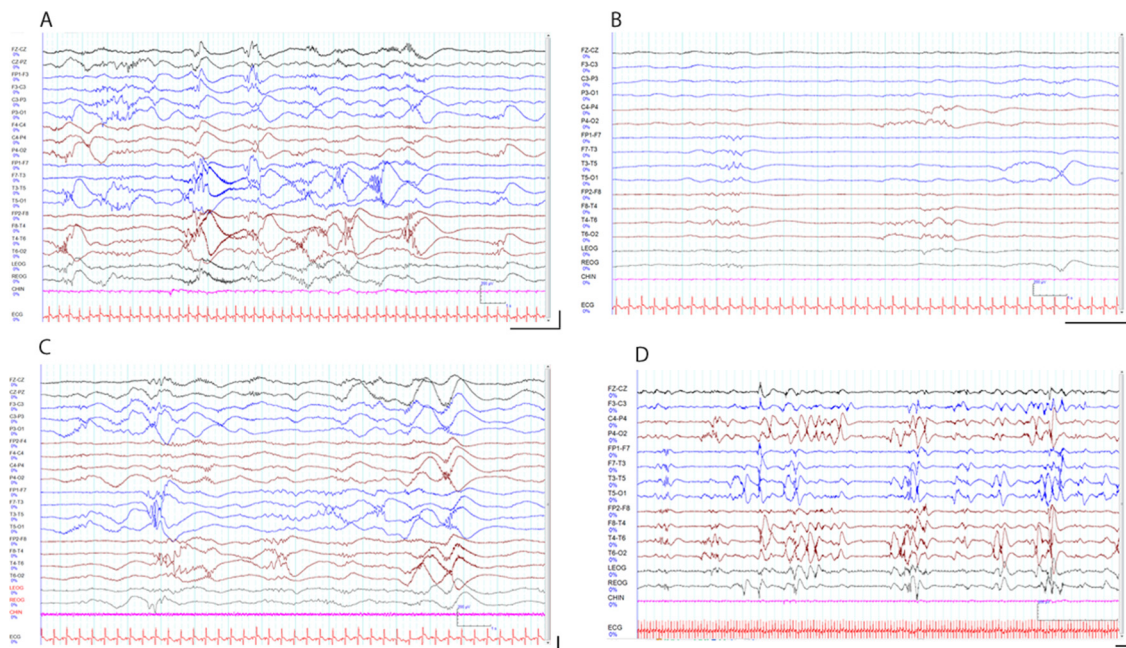
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Fig. 4 EEGs at PMA 29 weeks showing varying bursts and interburst intervals, admixture of frequencies, some asynchrony, and some asymmetry. Abbreviations: IBI: InterBurst Interval, PTS: Positive Temporal Sharps, PTT: Premature Temporal Theta. A. Bursts of PTT followed by delta (eye), occipital sharps, frontal sharps. This would score 1/1 for sharps. B. Note PTS. This is normal and would be scored 0/1 for sharps. C. Delta brushes, PTT with delta, some spikey right temporal theta, left sinusoidal temporal theta. Spiky temporal theta is abnormal. D. A 60 s epoch demonstrating bursts and IBIs. This would score 0/3 for continuity and 0/1 for frequency.
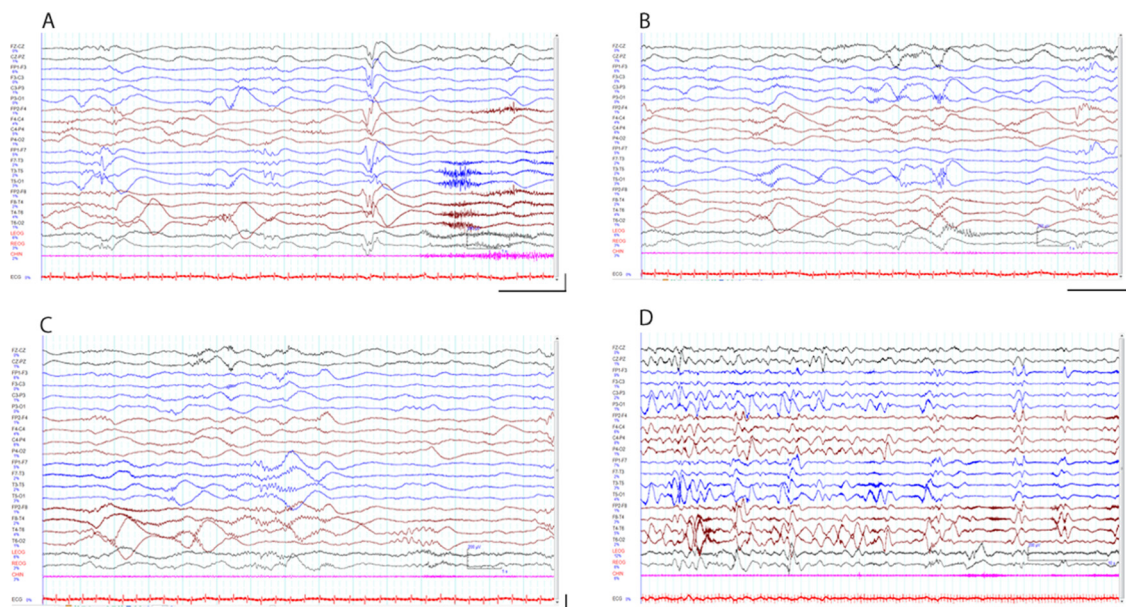

Fig. 5 EEGs at PMA 31 weeks showing increasing continuity, admixture of frequencies, and different shapes and patterns. Abbreviations: PRS: PeriRolandic Sharps, PTT: Premature Temporal Theta, STOP: Sinusoidal Theta in Occipital region of Prematures. A. PRS, left PTS of different amplitudes, PTT followed by delta, frontal sharps, muscle artefact, variability. B. Delta brushes, PTT followed by delta left > right. C. Note continuity, delta brushes, delta activity, admixture of frequencies, asymmetrical STOP right>left. D. A 60 s epoch demonstrating mostly continuous background. Epochs shown in this figure are mostly normal for age. However, if the frontal sharps seen in A occurred frequently, they may be abnormal.
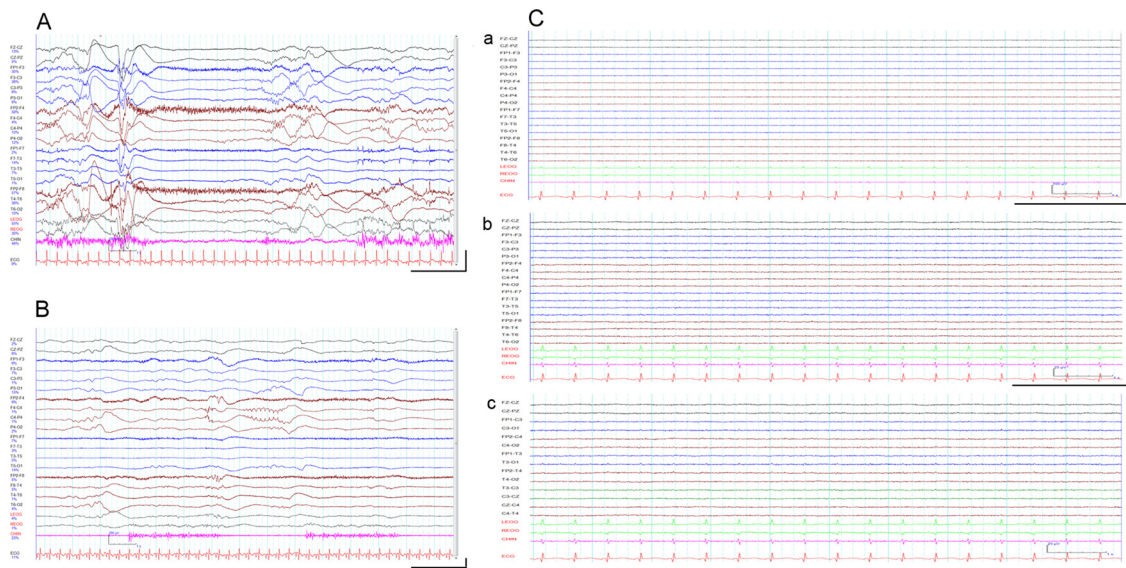
Fig. 6 EEGs showing alerting responses and reactivity. Abbreviations: ECI: Electrocerebral Inactivity, STOP: Sinusoidal Theta in Occipital region of Prematures. A. PMA 27 weeks, alerting response on being touched, varied frequencies and patterns. This epoch is normal for reactivity. B. PMA 27 weeks, repetitive positive rolandic slow sharps on the right, mild asymmetry and asynchrony, STOP. These shapes, sharps, and frequencies are normal for this age group. C. ECI. EEGs with standard view (Ca), increased sensitivity (Cb and Cc), and large inter-electrode distances/ double spacing (Cc). This EEG would be scored 4/4 for amplitude and would not be scored for other parameters.

Table 3 Abnormal amplitude.

Severity	Score	Amplitude
Mild	1	delta <200 uV at 30 wks GA, <150 uV at 32−33 wks GA
Moderate	2	mostly 20−50 uV, some activity 50−100 uV
Severe	3	all activity <20 uV
Profound	4	Electrocerebral inactivity

Abbreviation: GA: gestational age.

Shapes, patterns (scored 0, 1)

Characteristic shapes and patterns occur as the EEG evolves in premature babies, with interactions between neurons in the subcortical and cortical plate, inputs from the thalamus and development of endogenous generators [1,96, 64,4,36,34,93,55,78,59,58,56,43,33,27,20−22,19,2,11,10, 15]. These shapes and patterns are important to assess the maturity of the background.

This parameter is scored as 0 when normal and 1 when abnormal. EEGs in Figs. 1D, 4A, 7B and 7C would be scored as 1/1 for shapes/patterns.

Premature Temporal Theta (PTT): This is sometimes called sawtooth theta. It has a particular shape with a brief run of theta often followed by a delta wave (like an eye), (see Figs. 1, 2, 4, 5 and 7). Theta is often 4.5−6/s, though PTT may encroach low alpha range activity. It starts at GA 24 weeks, peaks at 29−31 weeks and may be present until 34 weeks. Theta in the temporal region usually disappears by 32 weeks in active sleep and by 33−34 weeks in quiet sleep. With increasing PMA the amplitude decreases, although duration and frequency may increase until 31 weeks. It is frequently bilateral, though often asynchronous and is thought to be more frequent on the left side. At times the patterns are distorted (see Figs. 1,2,4,5, and 7), the delta following PTT (the eye) is usually smooth, however in disorganised EEGs it may be abnormal (Fig. 8). Distorted delta, especially if frequent (>1/min in the occipital region) is abnormal.

Occipital theta bursts: It is sometimes called STOP (Sinusoidal Theta in Occipital region of Prematures) or occipital saw tooth. It starts appearing at 24 weeks GA, is most prominent at ∼ 26 weeks and disappears by 28−30 weeks. As occipital infolding occurs earlier than temporal, PTT is of higher incidence than STOP in babies more than 28 weeks PMA. It is mostly asynchronous and ∼ 100−400 uV in amplitude (see Figs. 2, 3 and 7).

Frontal bursts: Waveforms of 100−400 uV in the theta range may be seen in extremely premature babies (< GA 28 weeks). Sharp frontal delta waves may also occur in the premature infant of < 28 weeks, at times of fairly high amplitude (up to 600 uV). They are abnormal if they occur frequently or are persistently asymmetrical.

Anterior Slow Dysrhythmia: Anterior slow dysrhythmia is mono or polymorphic delta of 50−100 μV, located in the frontal area, seen in short bursts in active sleep, and usually at 36−37 weeks PMA. These waveforms are sometimes called slow anterior dysrhythmia (SAD).

Delta Brushes: These are a well-known and characteristic feature of the preterm EEG (Figs. 3−5,7,8). This is a pattern where repetitive delta waves (frequency 0.3−1.5/s, amplitude 50−300 uV) are seen with superimposed faster activity (frequency 8−30 hz, amplitude 10−40 uV) (Whitehead et al. [96]). The delta is usually smooth and fast activity is on the ascending slope of the delta wave. If the delta waves are distorted it is abnormal. Delta brushes are seen at 28 weeks GA,
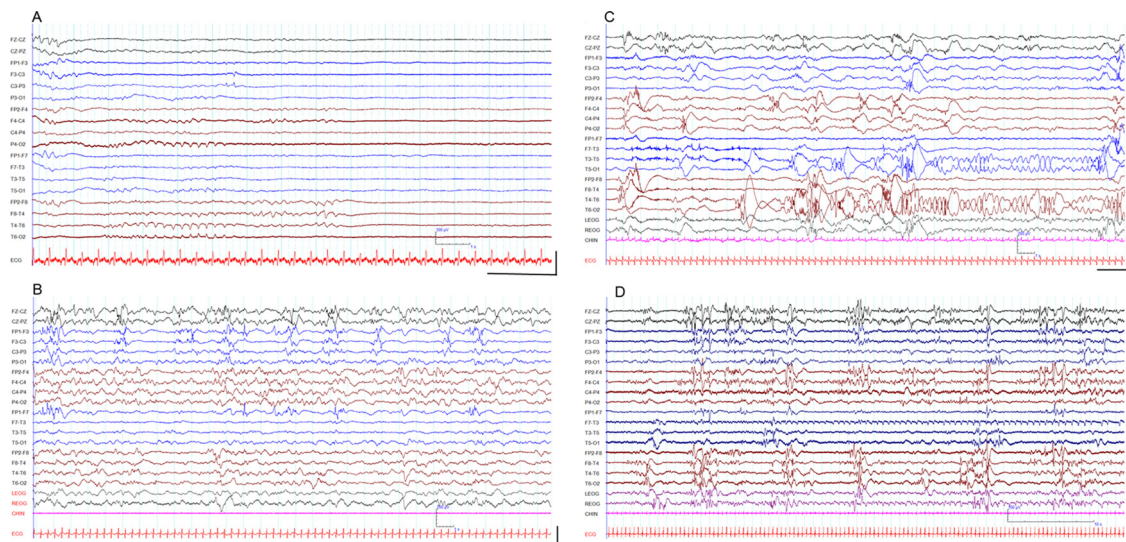
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Fig. 7 EEGs showing normal and abnormal shapes and sizes. Abbreviations: PRS: PeriRolandic Sharps, PTT: Premature Temporal Theta, STOP: Sinusoidal Theta in Occipital region of Prematures. A. PMA 25 weeks, STOP, repetitive PRS, abnormal distorted delta following PTT on the right. STOP is normal for this age, the distorted delta on the right is abnormal. B. PMA 25 weeks, PTT, abnormal spiky right sided PRS. This would score 1/1 for sharps. C. PMA 27 weeks, occipital sharps, left PRS, STOP. This is probably normal, unless the occipital sharps are repetitive. D. PMA 27 weeks with frontal spikes, asymmetrical delta brushes. Repetitive frontal spikes and persistent asymmetry would be abnormal.

may be present from 24 weeks, increase up to 32−34 weeks and then decrease. They have almost disappeared at term. The amplitude of the delta is initially high and then decreases as the PMA increases, whereas the frequency of the delta increases with increasing PMA. Initially they are more diffuse, then temporo-occipital, and by 36 weeks they are occipital

only. During early prematurity they are more frequent during active than quiet sleep. From 29−34 weeks the delta brushes are more frequent and higher in amplitude in QS.

Other Delta Patterns: Delta patterns with superimposed spiky and high amplitude fast activity (Fig. 8D) may indicate hydrocephalus [50].

Fig. 8 EEGs showing abnormal Delta brushes. They would score as abnormal for shapes and sizes. A. PMA 30 weeks mechanistic/cogwheel/mechanical delta brushes. B. Same epoch as in 8A, with changed filters (LFF 10 Hz): note amplitude of beta in right sided delta brush >40 uV. C. PMA 32 weeks, abnormal "crown" delta brush, asymmetric delta brushes. D. PMA 32 weeks, high amplitude delta with high amplitude alpha/beta range spikes suggestive of left ventricular dilatation.

Fig. 9 EEGs showing BERDs, LPDs and ESzs. A. PMA 33 weeks, BERDs. This would score 1/3 for seizures. B. PMA 36 weeks, LPDs over the left hemisphere. This would score 1/1 for sharps. C. PMA 31 weeks, sinusoidal seizure discharge over the temporal derivations. This would score 2/3 for seizures. D. PMA 36 weeks, spiky seizure discharge starting over the left temporal region. This would score 2/3 for seizures.

Size of shapes, patterns (scored 0, 1)

The size of the different waveforms and patterns should be assessed.

The delta activity following PTT (Figs. 1−5,7) is not usually more than 300 uV in premature babies [82,56,55,1]. Higher amplitude of the delta is abnormal, though data regarding this is not robust in the extreme premature babies [6]. It may be difficult to establish whether delta brushes are normal in the extremely premature baby.

The amplitude of the fast activity in the delta brush may be abnormal. Delta brushes with fast activity of > 40 uV, with a cogwheel type pattern are called mechanistic, cogwheel or mechanical delta brushes. They are thought to be abnormal and an indication of dysmaturity if seen repeatedly (Fig. 8). Mechanical delta brushes are best illustrated with a low frequency filter of 10 and high frequency filter of 70 in standard EEGs. Abnormal delta brushes on refiltered EEG are reported to be strongly associated with white matter injury [36,34,33], (Fig. 8).

Size is scored as 0 for normal and 1 for abnormal. EEGs in Figs. 1D, and 8A, B, and D would be scored as 1/1 for size of shapes and patterns.

Sharps (scored 0,1)

Sharp wave transients may be seen in normal preterm and term babies; studies have estimated frequencies varying from 10 ± 7 /h for preterms and 12 ± 12 for term babies. Unless repetitive, periodic, distorted, spiky or confined to one area, they may be normal. In general, positive sharps are more common than negative [78,15,82,56,55]. With increasing GA (>30 weeks), negative sharps occur more often.

Positive Rolandic Sharps (PRS): They are also called central positive slow waves or vertex sharps (VS) [5,43,56,15].

These are surface positive, broad-based waves, less than 500 msec in duration, and localised to C3, C4 or Cz. They are usually 20−200 uV in amplitude, though > 100 uV is thought to be abnormal by some groups. Their morphology may vary. They may or may not be sharply differentiated from background. They may be simple or notched, with superimposed fast activity. They may be isolated or occur in runs (Figs. 2,3,5−7). Although they may be seen in normal backgrounds, they are reported to occur with increased frequency in intraventricular haemorrhage and periventricular leukomalacia. Okumara et al. [59,58] suggest that PRS > 0.1/min and of > 100 uV is abnormal. We suggest that a density of PRS of any kind > 1−2/min is abnormal and may be associated with white matter injury.

Positive Temporal Sharps (PTS): PTS may occur [11,10,91,90,89] in normal preterm infants of 27−36 weeks GA, with peak incidence at 31−32 weeks (Figs. 1,4,5). PTS that remains frequent until term, increases in postnatal life, is long in duration or high in amplitude is abnormal. Abnormal PTS is often associated with other EEG abnormalities and neuroimaging abnormalities.

Transient Frontal sharps: They are sometimes called enoches frontales, may be seen in AS starting at 35−36 weeks GA (sometimes earlier), and may persist till 44 weeks. They are usually <200 uV.

Lateralised Periodic discharges (LPDs): previously called Periodic Lateralised epileptiform Discharges (PLEDs). LPDs are rare in premature babies. They may have variable morphology, and may be biphasic, triphasic or polyphasic. LPDs usually last 200−400 msec and occur repetitively (every 1−10 s), without evolving into an electrographic seizure [45]. Fig. 9B shows LPDs in a preterm neonate with a left middle cerebral artery infarct.

Sharps are scored as 0 when normal and 1 when excessive or abnormal for age. EEGs in Figs. 1D, 3C, and 7C would be scored as 1/1 for sharps.

Seizures (scored 0, 1, 2, 3)

Seizures occur frequently in neonates [52−54,92,79,31, 74−76,72,60,49,29,9,68−70]. Electrographic seizures may occur in neonates with or without clinical correlates [79,48,92,53]. Electrographic seizures, by convention, are at least 10 s in duration. Ictal discharges in preterm neonates may be sinusoidal, sharp or spiky. The discharge may remain focal, may propagate regionally, may migrate to the other side, may flip-flop and remain unilateral, or become bihemispheric. Ictal patterns in preterm neonates may be of lower amplitude and frequency than in term infants. Fig. 9 illustrates a sinusoidal seizure discharge in a 31week PMA infant and a spiky electrographic seizure discharge in a 36week infant.

Brief EEG rhythmic discharges of 5−10 s (BERDS) [52,84], similar to BIRDS (brief intermittent ictal/interictal discharges), are scored as 1. Both electrographic only seizures (ESZ) and electroclinical seizures (ECSz) [53,48,69,31,93] are scored as 2. Status Epilepticus (>50% of EEG with electrographic seizures) [65,79] is scored as 3. The EEG in Fig. 9A would score 1/ 3 for seizure, in Fig. 9C would score 2/3, and in Fig. 9D (infant in electrographic status) would score 3/3.

CARFS[7] score

The scores for different parameters should be based on the complete record. The figures show a variety of normal and abnormal features seen in premature infant EEGs chosen from our personal collection. They include EEGs not used for the interrater reliability study. We have given scores for brief epochs of EEG shown in the figures.

The total CARFS[7] score can vary from 0, when all the EEG parameters considered for this study are normal, up to 20 when the EEG is profoundly abnormal. If the EEG shows ECI or near ECI, then it is assessed as profoundly abnormal and interpreted in the clinical context. In this case the amplitude would be scored as 4/4 and the report should indicate that other parameters cannot be scored. If electrographic seizure activity is present through most or all of the recording, the other parameters cannot be scored. A repeat EEG once the seizures are better controlled would be useful. When only a limited number of parameters can be scored the report should reflect this. The proforma has been developed to help neurologists report preterm EEGs in a standardized, reproducible fashion.

Interrater reliability of CARFS[7]

25 preterm EEGs (in babies born at 31 weeks of gestational age or less) were evaluated blindly by two neurologists experienced in reading neonatal EEGs, using the CARFS[7] protocol. They were blinded to all clinical data except for gestational and chronological age of the baby. The EEGs used to assess interrater reliability of this proforma had been recorded as part of a brain maturation study in premature babies (Institutional Ethics Approval: HREC Reference Number: 2013108EP).

V-EEG recording

The EEGs were recorded after informed consent using the Compumedics system and PSG software. EEGs were recorded mostly between days 5−12 after birth, using cup electrodes, in accordance with the 10−20 system. Additional EMG leads over the chin, EOG leads, and Heart Rate monitoring were simultaneously recorded. The recording was undertaken by an experienced neurophysiology technologist.

Neurodevelopmental outcomes

Neurodevelopmental outcomes were based on medical record reviews. All children, except those lost to follow-up, had a clinical examination done by a Paediatric specialist at varying ages (see Table 5). Some also had standardized neurodevelopmental testing (e.g., Bayley, Griffiths).

Results

The CARFS[7] scores given by the 2 assessors are shown in Table 4. Percentage agreement between raters for subscores and total scores varied from 88 to 100%. Cohen's κ [46] was run to determine agreement between the two raters. There was high agreement for subscores and total scores, κ varied from 0.694 to 1. Cohen's κ could not be calculated for continuity, sleep or seizures as the scores showed no variability.

Table 5 provides the neurodevelopmental outcomes in the 25 babies whose EEGs were scored for interrater reliability. The EEGs were the first 25 recorded in our new hospital, as part of a premature brain maturation study. The majority of these infants had a normal neurodevelopmental profile at last follow-up. The scores in these 25 babies were mostly mildly abnormal or normal (highest score: 5/20). All babies who had any neurodevelopmental impairment on follow-up scored 3−5/20 on EEGs. Eight babies had neuroimaging abnormalities; 7 of these scored 4−5/20 on EEGs. CARFS[7] proforma should help the neurologist report a preterm neonatal EEG. These preliminary results, need to be interpreted with caution: they suggest a predictive value for the proforma. The prognostic value of CARFS[7] scoring system will be/ needs to be assessed on larger cohorts of preterm babies.

Discussion

The EEG in the preterm infant provides a window to evaluate the health of the brain. A systematic review of prognostic accuracy of EEGs in preterm infants concluded that EEG recorded within the first 7 days of life may have potential as a predictor for later neurodevelopmental outcome [16]. Multichannel, serial EEGs have been shown to be a strong predictor of neurodevelopmental outcome in preterm infants, with the 35-week EEG performing the best [40].

The EEGs for interrater reliability were recorded between 5 and 12 days of age, as that was the approved protocol for the brain maturation study. We would recommend an EEG in the first week of life for a preterm infant, with serial EEGs, if possible, every two weeks till 37 weeks. This would enable assessment of the effect of prenatal and postnatal complications and be valuable to prognosticate. More frequent EEGs can be undertaken if clinically indicated: for example, to assess response to a therapeutic intervention. Prolonged V-EEG monitoring may be required for preterm babies with seizures or at high risk for seizures [54].

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Table 4   CARFS[7] scores given by assessors for premature babies' EEGs (Disparate scores have been underlined).

Subject no	Continuity 1	2	Amplitude 1	2	Reactivity 1	2	Frequency 1	2	Synchrony 1	2	Symmetry 1	2	Sleep 1	2	Shapes 1	2	Size 1	2	Sharps 1	2	Seizures 1	2	Total 1	2
1	0	0	1	1	0	0	0	0	0	0	1	1	0	0	1	1	1	1	1	1	0	0	5	5
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	0	0	3	3
3	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1	1	1	1	1	0	0	4	4
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	2	2
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	2	2
6	0	0	0	0	0	0	0	0	0	0	2	2	0	0	1	1	1	1	1	1	0	0	5	5
7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	0	0	3	3
8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1
10	0	0	0	0	0	0	0	0	0	1	1	1	0	0	1	0	1	0	0	1	0	0	3	3
11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	1	1	1	1	1	1	0	0	0	0	0	0	1	1	1	1	0	0	0	0	5	5
13	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	1	1	1	0	0	4	4
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	0	0	3	3
15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	0	0	3	3
16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	0	0	3	3
17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	0	0	3	3
18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	1	1
19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	1
20	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	1	0	0	1	0	0	3	2
21	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	1	1	1	0	0	4	4
22	0	0	1	1	0	0	0	0	1	1	1	1	0	0	1	1	0	0	1	1	0	0	5	5
23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	1
24	0	0	1	1	0	0	0	0	0	0	1	1	0	0	1	1	1	1	1	1	0	0	5	5
25	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	1	1	1	0	0	4	4
Kappa			1	1	1		0.779		0.916	1		0.783	0.818	0.694	1		0.95							
Percentage Agreement	100		100	100	100	96	96	100		92	92	88	100		96									

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Table 5 CARFS[7] Score, neurodevelopmental outcome and neuroimaging.

Number	GA	Scorer 1	Scorer 2	Development	Neurological examination	Follow up age (months)	Imaging - Ultrasound/ MRI
1	27^{+6}	5	5	WNL	WNL	25	R thalamic parenchymal abnormality
2	28^{+6}	3	3	WNL	WNL	6	WNL
3	30^{+3}	4	4	Mild delay	Moderate CP	24	PVL
4	28^{+6}	2	2	WNL	WNL	2	WNL
5	23^{+4}	2	2	WNL	WNL	28	GMH with haemosiderin staining of lateral ventricles and post fossa. right cerebellar parenchymal gliosis
6	23^{+4}	5	5	Mild delay	Mild hemiparesis	28	IVH, IPH, atrophy of R cerebral peduncle. L cerebellar parenchymal gliosis
7	30^{+3}	3	3	WNL	WNL	7	WNL
8	28^{+1}	0	0	WNL	WNL	27	WNL
9	29^{+3}	1	1	WNL	WNL	7	WNL
10	28^{+1}	3	3	WNL	Mild hypotonia	26	WNL
11	28^{+1}	0	0	WNL	WNL	27	WNL
12	29^{+5}	4	5	WNL	WNL	21	WNL
13	29^{+5}	4	4	WNL	WNL	33	Bilateral IVH ($L>R$) and cerebral oedema
14	29^{+4}	3	3	WNL	WNL	8	WNL
15	29^{+3}	3	3	WNL	WNL	33	WNL
16	30^{+3}	3	3	WNL	WNL	30	WNL
17	29^{+1}	3	3	WNL	WNL	24	WNL
18	29^{+4}	1	1	WNL	WNL	12	WNL
19	30^{+2}	1	1	WNL	WNL	34	WNL
20	29^{+6}	4	4	WNL	WNL	31	WNL
21	29^{+2}	4	4	WNL	Moderate hemiparesis	28	IVH, hydrocephalus needing ventriculostomy
22	30^{+1}	5	5	Mild delay	Nystagmus	32	L frontal PVH with porencephalic cyst
23	30^{+2}	1	1	WNL	WNL	12	WNL
24	29	5	5	Lost to FU			WNL
25	29^{+5}	4	4	WNL	WNL	30	R cerebellar haemorrhage

Abbreviations: GMH: Germinal Matrix Haemorrhage; GA: Gestational Age, IPH: Intraparenchymal Haemorrhage; IVH: Intraventricular Haemorrhage; L: Left; PVH: Periventricular Haemorrhage; R: Right; WNL: Within Normal Limits.

A good quality V-EEG recording undertaken by an experienced neurophysiology technologist is an essential requirement to enable proficient interpretation [60]. We apply the full array of electrodes in accordance with the international 10—20 system in most neonates, with some exceptions such as less than 25 weeks of age and those with microcephaly. This provides better coverage of the infant's brain/cranium. In addition, we monitor EMG, EOG and ECG. The CARFS[7] proforma can also be used to interpret EEGs recorded with the modified 8—10 electrode array undertaken by many centres [83]. It would be difficult to evaluate some parameters (such as sharps, shapes, sizes) on the commonly used 4-electrodes for aEEG. Consistency and familiarity with the recording system is useful for visual interpretation.

Standardised reporting may enhance the reliability, reproducibility and ease of interpreting the preterm infant EEG in management and prognostication. CARFS[7] proforma may be used for evaluation of all preterm EEGs. The proforma might enable neurologists to read EEGs of premature babies with greater confidence, ease, and accuracy, as well as produce a report that is repeatable and homogenous among operators.

The EEG abnormalities, in preterm neonates, may help distinguish between acute and chronic changes, though overlap is not uncommon [27,20—22,19,33—36,38,3,96, 59,44,10]. Reduction in amplitude is often the most obvious change with acute impairment of brain function. In chronic

brain injury the EEG may show dysmature patterns (disparity of greater than two weeks between post menstrual age and estimated EEG maturity on visual analysis) or may be disorganised (abnormalities of Shape, Size, Patterns, Sharps) [66,33—37,1]. Interpretation of changing EEG patterns (normal and abnormal) at different PMAs can be challenging. This study and the CARFS[7] proforma may provide a simple, reliable and user-friendly guideline to both the novice and the experienced neurologist.

Serial EEGs [19—22,43,44,97] may help to distinguish between acute transient changes and/ or persistent changes indicating chronic brain impairment. A standardised report, using the CARFS[7] proforma, will facilitate comparison of serial EEGs at different PMAs and interpret differences and changes in a proficient manner.

Abnormality in specific parameters of CARFS[7] proforma may help guide interpretation. A report on the EEG of a premature baby, with brief descriptions of the different parameters along with the individual and total scores, may help in making conclusions regarding aetiopathogenesis and appropriate interventions.

Our preliminary data suggests that CARFS7 may be useful as a prognostic indicator of neurodevelopmental outcome. However, the sample size, the limited variability and spectrum of abnormality (mild abnormality in some parameters, and no abnormality in others), and uniformly good neurodevelopmental outcomes are significant limitations. Any indication of the predictive value of the proforma must be interpreted with caution. The role of the CARFS[7] proforma in prognostication must be evaluated in larger cohorts of preterm babies.

Automated analysis of preterm multichannel EEG [47] has the potential to be available in future in clinical practice. Our proforma, with a scoring system for the important EEG components, may provide supportive data to engineers and neuroscientists in their quest for development of efficient, practical automated programs for interpretation and prognostication based on preterm EEGs.

Conclusion

CARFS[7] is a user friendly proforma for reading EEGs in the preterm infant. Interrater reliability using Cohen's k shows high agreement between two child neurologists who independently rated the EEG of twenty-five premature babies EEGs using this proforma. CARFS[7] has the potential to provide accurate, reproducible and valuable information on brain function in the preterm infant in clinical practice.

Declaration of Competing Interest

None.

Acknowledgments

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