



ELSEVIER

Early Human Development 55 (1999) 113–123

**Early Human  
Development**

## Prediction of neurological outcome after birth asphyxia from early continuous two-channel electroencephalography

Denis Azzopardi<sup>b,\*</sup>, Iolanda Guarino<sup>a</sup>, Cindy Brayshaw<sup>b,1</sup>,  
Frances Cowan<sup>b</sup>, Deborah Price-Williams<sup>a</sup>, A. David Edwards<sup>b</sup>,  
Dominique Acolet<sup>a</sup>

<sup>a</sup>Department of Paediatrics, Hillingdon Hospital, Uxbridge, UK

<sup>b</sup>Department of Paediatrics and Neonatal Medicine, Imperial College School of Medicine,  
Hammersmith Hospital, Du Cane Road, London W12 0HS, UK

Received 21 October 1998; received in revised form 1 February 1999; accepted 2 February 1999

---

### Abstract

*Objective:* To determine whether two-channel continuous electroencephalography (EEG) applied within 12 h of birth can predict the severity of neurological complications and neurodevelopmental outcome following birth asphyxia. *Methods:* A continuous two-channel EEG was performed within 12 h of birth in 22 infants suspected of having suffered birth asphyxia and 11 healthy control infants (22 infants at a general and 11 at a specialist paediatric unit). Criteria to categorise normal and abnormal EEG records were defined and compared with the severity of hypoxic/ischaemic encephalopathy (HIE) and with neurodevelopmental outcome, assessed at or after 12 months of age. *Results:* EEG recordings were commenced at a median (range) of 2 h 50 min (1 h 45 min to 12 h) after birth. Technically satisfactory recordings were obtained in all but one infant. All control infants remained asymptomatic and had a normal EEG with discernible sleep/awake periods. 12 h after birth the EEG was normal in all 12 infants suspected of asphyxia who remained well or developed grade I HIE and was abnormal in six of nine infants with grade II or III HIE. Fifteen of 16 infants suspected of asphyxia with a normal neurodevelopmental outcome had a normal EEG at 12 h; transient abnormalities lasting not more than 8 h had been detected in three of these infants. All five infants who died or developed neurodevelopmental abnormalities had an abnormal EEG. At 12

---

\*Corresponding author. Tel.: +44-181-383-1793; fax: +44-181-740-8281.

E-mail address: dazzopar@rps.ac.uk (D. Azzopardi)

<sup>1</sup>Ms C. Brayshaw died since completion of this study.

h of age the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratio for predicting severe (grade II or III) HIE were: 67, 100, 100, 80% and infinity and for subsequent death or neurodevelopmental impairments: 100, 94, 83, 100 and 16%, respectively. Assessment of the EEG before 12 h of age altered prognostic accuracy: 4 h after birth the sensitivity, specificity, positive and negative predictive values and the likelihood ratio for poor neurodevelopmental outcome were 100, 71, 33%, 100 and 3.7%, respectively (16 infants). *Conclusion:* Continuous two-channel EEG is an accurate tool for assessing the severity of neurological insult soon after birth asphyxia. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

*Keywords:* Birth asphyxia; Continuous EEG; Neurological outcome

---

## 1. Introduction

The management of infants suspected of having suffered birth asphyxia is complicated by the difficulty in predicting soon after birth which infants are likely to develop neurological complications and their eventual outcome [1]. A method for predicting, within a few hours of birth, the maximal severity of hypoxic–ischaemic encephalopathy (HIE) and the subsequent neurodevelopmental outcome would facilitate clinical management and counselling of parents, and may aid the selection of infants who might benefit from neuroprotective therapies [2]. Clinical assessment immediately after birth is not sufficiently accurate [1], neither are cranial ultrasound imaging and Doppler measurement of cerebral blood flow velocity during the first 24 h of life [3]; other techniques such as magnetic resonance imaging or proton spectroscopy are not readily available [4,5].

Previous studies indicate that electroencephalography (EEG) during the first week after asphyxia accurately predicts the neurological outcome [6–9], but few studies have been carried out during the first few hours following asphyxia and all have been performed in specialist units and thus may not be generally applicable [3,10]. Our aim was to determine whether two-channel continuous EEG could be applied within 12 h of birth asphyxia to predict the severity of the neurological insult and subsequent outcome. A secondary aim was to examine whether assessment at 4 h of age (for possible selection of infants for neuroprotective therapy) would alter the prognostic accuracy of the EEG.

## 2. Methods

This study was carried out with the approval of the Research Ethics Committees of Hammersmith Hospitals Trust and Hillingdon Hospital and with the verbal informed consent of the parents.

### 2.1. Subjects studied

We studied 22 full-term infants suspected of suffering birth asphyxia: 11 born at Hillingdon Hospital (a District General Hospital) and 11 at Hammersmith Hospital or Queen Charlotte and Chelsea Hospitals—both are referral centres for neonatal intensive care. Eleven healthy full-term infants (all born at Hillingdon Hospital) were also studied for comparison. The principal clinical details of the infants are shown in Table 1.

Infants were suspected of suffering birth asphyxia if there were: evidence of fetal distress (defined as any meconium staining of the amniotic fluid and/or fetal bradycardia) *and* an Apgar score of less than 5 at 5 min or a base deficit of greater than  $-15$  in the cord blood or first arterial blood sample taken within an hour of birth.

Infants with congenital infection, congenital brain abnormalities or proven metabolic disorders were excluded.

### 2.2. Electroencephalography

The EEG was recorded using a small battery powered four-channel tape recorder measuring  $112 \times 86 \times 36$  mm (Oxford Medilog 4–24 monitor). Two channels of EEG were recorded from  $F_4P_4$  and  $F_3P_3$  (International 10/20 system). Six silver/silver chloride electrodes were applied with collodion on the scalp. The tape speed allowed up to 24 h of record to be stored on a conventional 120-min cassette tape. The electrodes were attached and recording initiated by junior medical staff or nursing staff at each hospital.

The tapes were replayed in a visual display unit providing the possibility of rapid visual scanning of 24 h of data in 24 min and analysed visually by CB, who was unaware of the infants' clinical details. An assessment was made of EEG amplitude, continuity, symmetry, synchrony and the presence of seizures. For assessment of prediction of outcome we classified the EEG into two groups: (1) *abnormal*, EEG

Table 1  
Clinical details of study infants<sup>a</sup>

	Control infants ( $n = 11$ ) median (range)	Asphyxiated infants ( $n = 22$ ) median (range)
Gestation (weeks)	39 (37–41)	40 (37–42)
Birth weight (g)	3500 (3180–4055)	3440 (2264–4750)
Delivery	SVD	EmCS (10); Forceps (4); SVD (8)
Apgar score at 5 min	9 (9–10)	4 (0–10)
Age at start of EEG (h, min)	2, 40 (1, 45–7)	3, 15 (1, 40–12)
Duration of EEG record (h, min)	1, 25–8	4– > 8

<sup>a</sup> SVD, spontaneous vaginal delivery; EmCS, emergency caesarean section. Median and range values are shown.

records that were intermittent (defined as a repetitive pattern of attenuation of EEG activity to less than 20  $\mu\text{V}$  for more than 6 s) or of low voltage (less than 20  $\mu\text{V}$ ) or contained bursts of spikes and waves consistent with seizure; (2) *normal*, all other EEG records, including those that showed some asymmetry but were not intermittent. Illustrations of normal and abnormal EEG patterns are shown in Figs. 1 and 2. EEG abnormalities that were present only on part of the recording were called transient abnormalities; such records were also classified normal or abnormal according to the EEG findings at 4 and at 12 h of age. The technical quality of the EEG record was graded by CB as poor, adequate and good for each infant.

### 2.3. HIE and neurodevelopmental outcome

HIE was scored daily for the first 3 days after birth [11]. Neurological outcome was assessed in all the infants suspected of suffering asphyxia at 12 months of age or later by a standardised neurological assessment [12,13] and when possible also by Griffiths developmental assessment [14]. Paediatricians not involved in the EEG analysis carried out neurological assessment.

### 2.4. Data analysis

We determined sensitivity, specificity, positive and negative predictive values and likelihood ratios for the prediction, at 4 and 12 h after birth, of (a) HIE grade II–III, and (b) death or neurodevelopmental impairments.

## 3. Results

One infant (suspected of having suffered birth asphyxia) had a technically unsatisfactory EEG and was excluded from the study. The technical quality of all the other records ranged from adequate to good (the median quality was good). EEG recording commenced from 1 h 45 min to 12 h after birth (median 2 h 50 min) and for 26 of the 32 infants EEG recording commenced within 4 h of birth.

The results are summarised in Table 2.

### 3.1. EEG at 12 h of age and neurological symptoms after birth

All 11 control infants remained well and symptom free in the neonatal period. The EEG was normal and a characteristic pattern of changes in EEG activity due to sleep/wake periods could be observed in each infant.

Twelve of the 21 possibly asphyxiated infants either remained asymptomatic or developed grade I HIE. The EEG was always normal in 11 of these infants and was intermittent but returned to normal within 6 h after birth in the other infant. Two of the five infants with maximal grade II HIE had an intermittent EEG which returned to normal within 12 h of birth; a further two infants had a persistently intermittent EEG, whereas one infant with maximal grade II HIE had a normal EEG throughout. All

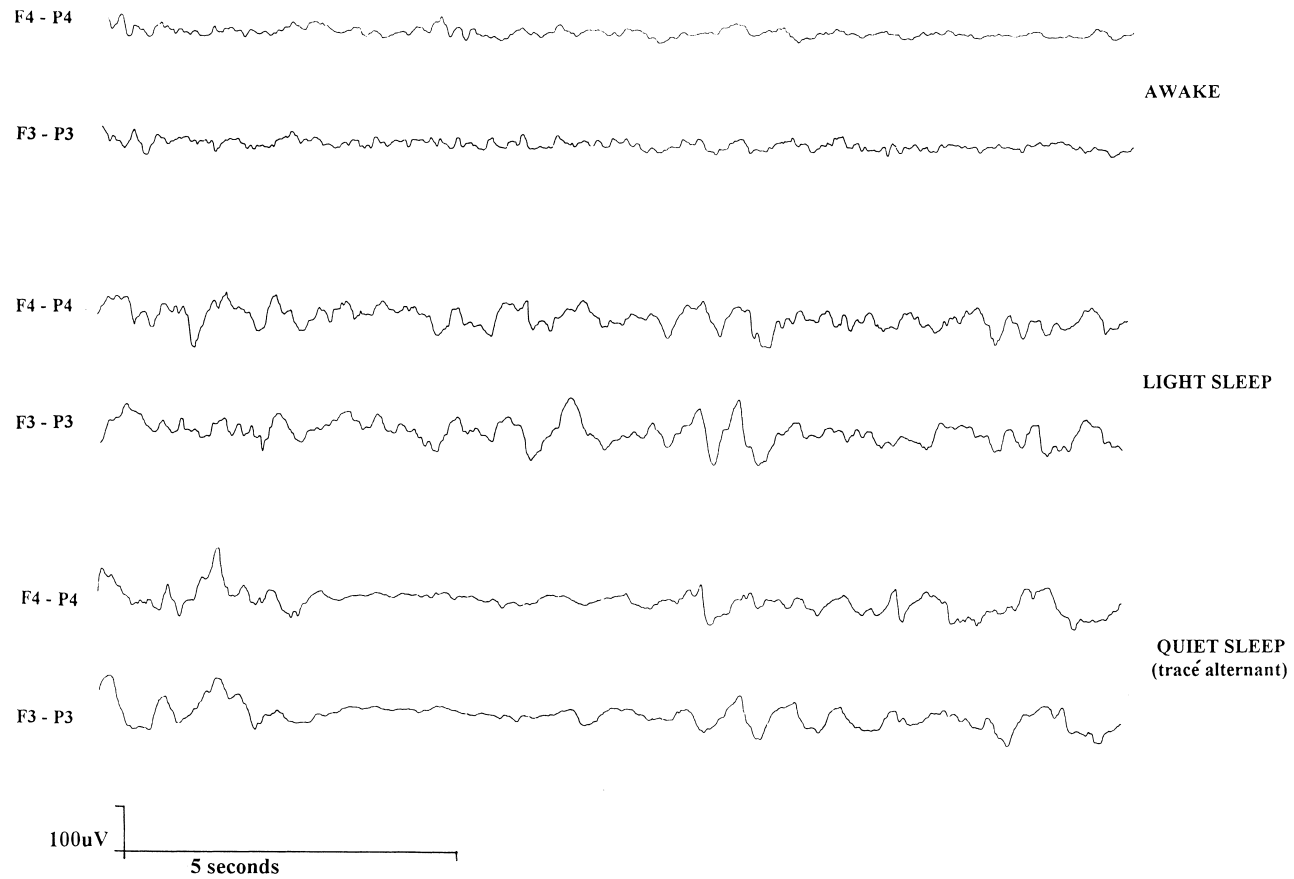


Fig. 1. EEG recording from a normal infant showing EEG in different sleep states.

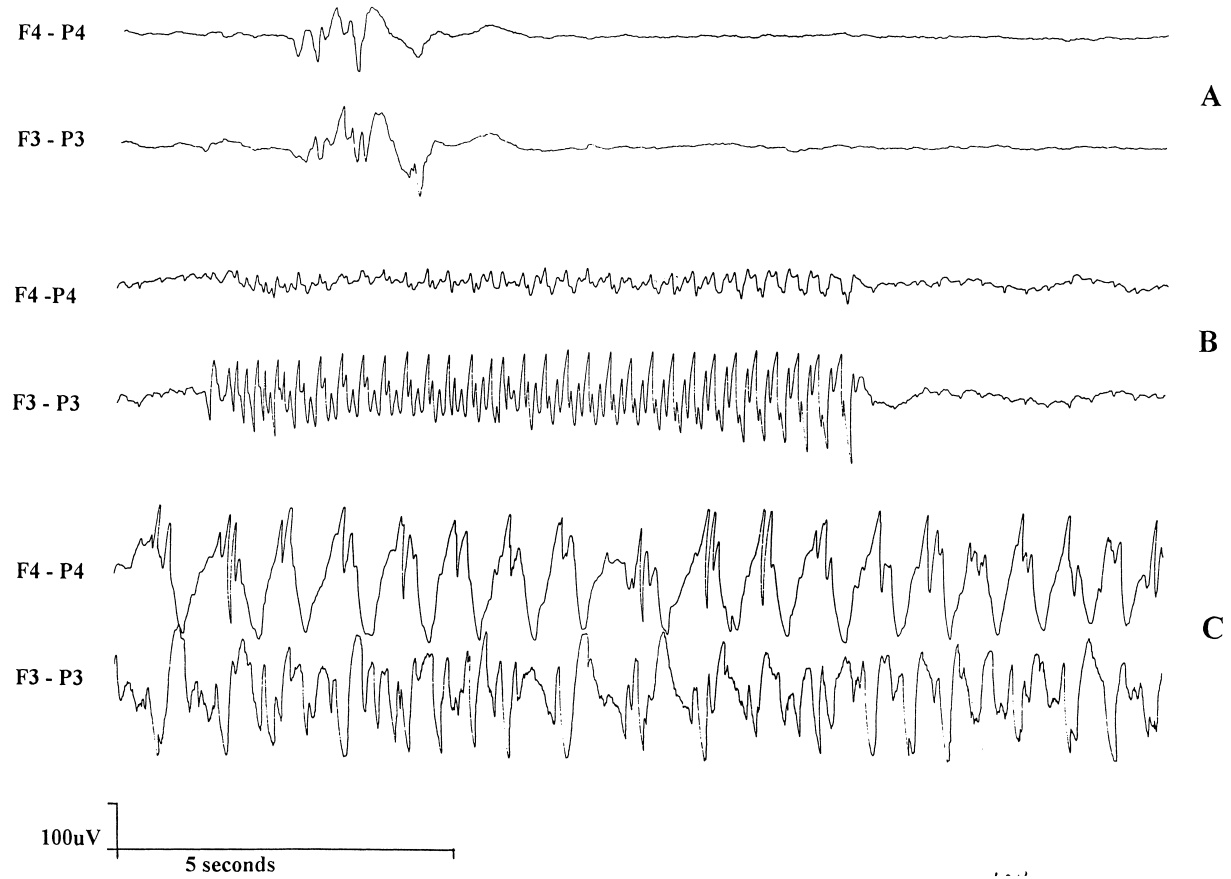


Fig. 2. EEG recording showing intermittent activity (A) and different types of seizure activity (B, C).

Table 2  
EEG findings and neurological outcome in asphyxiated infants<sup>a</sup>

Patient no.	Age at start of EEG (h, min)	EEG	HIE grade	Outcome	GQ	Age at last follow-up (months)
1	5	Very low amplitude	3	Died	NA	NA
2	1, 40	Intermittent; normal at 6 h of age	1	Normal	115	12
3	2, 50	Normal	1	Normal <sup>b</sup>	ND	14
4	3, 25	Normal	1	Normal	ND	24
5	2	Normal	1	Normal <sup>b</sup>	ND	22
6	12	Very low amplitude; frequent seizures	3	Died	NA	NA
7	9	Low amplitude; seizures	3	Died	NA	NA
8	3, 15	Normal	1	Normal	105	24
9	2, 30	Intermittent; normal at 6 h of age	2	Normal	109	12
10	4	Intermittent; seizures	2	Motor, hearing and visual impairments	54	13
11	4	Normal	1	Normal	105	13
12	2, 10	Sharp waves; intermittent	2	Normal	108	15
13	5, 25	Normal	1	Normal	105	13
14	3, 25	Normal	1	Normal	121	12
15	2, 35	Normal	1	Normal	123	12
16	3, 15	Intermittent; frequent seizures	3	Microcephaly severe visual and motor impairments	NA	12
17	2, 35	Intermittent; normal at 10 h of age	2	Normal	104	18
18	3, 15	Normal	2	Normal	94	24
19	2, 05	Normal	1	Normal	109	13
20	4	Normal	1	Normal	96	13
21	8	Normal	1	Normal	107	24

<sup>a</sup> HIE grade I includes infants who remained asymptomatic. GQ refers to Griffiths General Quotient. NA, not applicable; ND, not done.

<sup>b</sup> These infants were examined by the general practitioner.

four infants who developed grade III HIE had an abnormal EEG, characterised by frequent seizures in three and very low voltage in the other infant.

### 3.2. Relation between EEG at 12 h of age and neurodevelopmental outcome

Sixteen of the 21 possibly asphyxiated infants had a normal neurological examination at 12–24 months of age. The EEG was normal at 12 h in 15 of these 16 infants; in three infants there had been transient abnormalities lasting less than 12 h. The EEG of one infant showed intermittent activity and sharp waves persisting beyond 12 h.

Two infants developed major neurodevelopmental problems on follow-up. Both infants had an abnormal EEG at 12 h of age: background activity was intermittent and

Table 3

Prediction by continuous EEG of maximal HIE grade II or III and poor neurological outcome in asphyxiated infants at 4 h after birth

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR
HIE (Grade II, III)	83 (5/6)	90 (9/10)	83 (5/6)	90 (9/10)	8.3 (83/10)
Neurological impairments or death	100 (2/2)	71 (10/14)	33 (2/6)	100 (10/10)	3.4 (100/10)

seizures were noted. Three infants died due to severe hypoxic–ischaemic brain injury and all three had an abnormal EEG that was intermittent in two infants and isoelectric in the other.

### 3.3. EEG findings 4 h following birth asphyxia

The EEG was available for assessment at 4 h of age in 16 infants. Nine of the ten infants who remained asymptomatic or developed maximal grade I HIE had a normal EEG at 4 h, whilst four of five infants with maximal grade II HIE and the single infant with maximal grade III HIE had an abnormal EEG 4 h after birth.

Ten of 14 infants who had a normal neurodevelopmental outcome had a normal EEG at 4 h of age. Both infants who developed neurodevelopmental abnormalities on follow-up had an abnormal EEG at 4 h of age.

### 3.4. Comparison of EEG findings at 4 and 12 h after birth

Ten of the 16 infants in whom the EEG was available for assessment at 4 and 12 h of age had a normal EEG at 4 h of age that remained normal at the later assessment. All ten infants had normal follow-up neurological examination.

The other six infants had an abnormal EEG at 4 h, but the EEG became normal at 12 h in three of these infants. Two of the three infants with a persistently abnormal EEG had an abnormal outcome.

The accuracy of the EEG for predicting neurological symptoms and outcome at four and 12 h following birth asphyxia is shown in Tables 3 and 4.

Table 4

Prediction by continuous EEG of maximal HIE grade II or III and poor neurological outcome in asphyxiated infants at 12 h of age

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR
HIE (Grade II,III)	67 (6/9)	100 (12/12)	100 (6/6)	80 (12/15)	Infinity
Neurological impairments or death	100 (5/5)	94 (15/16)	83 (5/6)	100 (15/15)	16 (100/6)

#### 4. Discussion

Continuous two-channel EEG was recorded successfully very soon after suspected birth asphyxia by clinical staff in a general and in specialist hospitals in 21 of 22 infants and used to predict the severity of neurological complications and subsequent outcome. A control group of healthy infants were shown to have normal EEG and identifiable sleep/wake cycles within a few hours of birth.

Other investigators have reported that the standard EEG and continuous EEG, when performed within 1 week of asphyxia, is predictive of neurological outcome [8,9,15]. However, facilities for performing a standard EEG are not widely available on neonatal units and are unlikely to be available very soon after birth. In our study, an early continuous EEG accurately predicted the severity of neurological symptoms and subsequent neurodevelopmental outcome following birth asphyxia. However, it is not certain whether an early EEG would have identified infants who develop moderate disabilities following asphyxia since all survivors either made a complete recovery or developed severe abnormalities. Although the survivors underwent neurological assessment at 12–24 months of age it is very unlikely that major abnormalities were undetected or would have developed later.

Since the EEG might be of value for selecting infants who might benefit from neuroprotective therapy, we assessed the EEG at 4 h of age and also at 12 h after birth. The EEG was less accurate at the earlier assessment because three infants with a transiently abnormal EEG made a complete recovery. Transient abnormalities lasting less than 12 h have previously been reported to be associated with a good neurodevelopmental outcome [3]. The EEG abnormalities in these three infants were less severe than those observed in infants with a poor neurodevelopmental outcome and the EEG had returned to normal by 12 h after birth. These findings suggest that the prognostic accuracy of continuous EEG would be greater if the EEG is recorded for at least 12 h after birth asphyxia; however, earlier assessment may be required for the selection of infants for neuroprotective therapies.

The prognostic significance of seizures is uncertain. In this study four infants who developed seizures very soon after birth also had abnormal EEG background activity and they all had a poor outcome. However, in other studies seizures did not always indicate a poor prognosis if EEG background activity between seizures remained normal [16].

We found it was possible to teach medical and nursing staff in both specialist and non-specialist units to obtain good quality two-channel EEG recordings very soon after birth. However, although we defined criteria to classify the EEG that might be used by clinicians with little training, in our study an experienced scientist assessed the EEG record. Therefore it is not certain that this technique is applicable in non-specialist units. To simplify assessment we did not attempt to quantify the degree of EEG discontinuity, although a previous study suggested that this would improve the prognostic accuracy of the technique [8].

The Oxford Medilog system does not provide a continuous display of the EEG and visual assessment of the EEG on the playback monitor is time consuming. Computerised automatic analysis of the EEG [17] would simplify assessment further but systems suitable for use in neonates are not widely available.

Amplitude integrated EEG (aEEG) recorded using a cerebral function monitor (CFM) may offer an alternative to continuous EEG recording. The CFM is less expensive, simple to use since only three electrodes are required and a continuous visual record of the signal can be displayed on a chart recorder. Eken et al. [3] found that the aEEG was the best predictor of neurological outcome within 6 h of birth in asphyxiated infants, compared with cerebral ultrasound examination and measurement of evoked potentials. However, there are disadvantages with the aEEG: because the display is time compressed, typically at 6 cm/h, seizures and events lasting up to several seconds may be missed [9] and focal abnormalities will not be observed unless two monitors are used, which would reduce the convenience of the technique. However, these deficiencies do not appear to impair the prognostic accuracy of aEEG [3,10]. Some aEEG recording equipment may also display EEG spectral power and frequency but these have not been found useful in neonates [18].

Knowledge of the likelihood and severity of neurological complications and subsequent outcome very soon after birth asphyxia can be important clinically: appropriate monitoring and treatment can be instituted, the parents counselled about the likely prognosis, and a decision as to the appropriateness of continuing intensive care in the severely asphyxiated infant will be better informed. This information will allow selection of infants who require referral to specialist units for more sophisticated and more expensive investigations. Continuous EEG appears a highly sensitive and specific method for assessing the severity of neurological insult in non-specialist units soon after birth.

## 5. Notation

EEG, Electroencephalography  
aEEG, amplitude integrated EEG  
HIE, hypoxic/ischaemic encephalopathy  
PPV, positive predictive value  
NPV, negative predictive value

## References

- [1] Volpe JJ. Hypoxic-ischemic encephalopathy: clinical aspects. In: Volpe JJ, editor, *Neurology of the newborn*, W.B. Saunders, Philadelphia, 1994, pp. 314–69.
- [2] Edwards AD. Protection against hypoxic-ischaemic cerebral injury in the developing brain. *Perfusion* 1993;8:97–100.
- [3] Eken P, Toet MC, Groenendaal F, de Vries LS. Predictive value of early neuroimaging, pulsed Doppler and neurophysiology in full term infants with hypoxic-ischaemic encephalopathy. *Arch Dis Child Fetal Neonatal Ed* 1995;73:F75–80.
- [4] Hanrahan JD, Sargentoni J, Azzopardi D et al. Cerebral metabolism within 18 h of birth asphyxia: a proton magnetic resonance study. *Pediatr Res* 1996;39(4 pt 1):584–90.
- [5] Cowan FM, Pennock JM, Hanrahan JD, Manji KP, Edwards AD. Early detection of cerebral infarction and hypoxic ischemic encephalopathy in neonates using diffusion-weighted magnetic resonance imaging. *Neuropediatrics* 1994;Aug 75(4):172–5.

- [6] Holmes GL, Lombroso CT. Prognostic value of background patterns in the neonatal EEG. *J Clin Neurophysiol* 1993;10:323–52.
- [7] Obrecht R, Pollock MA, Evans S, Scott DF. Prediction of outcome in neonates using EEG. *Clin Electroencephalogr* 1982;13:46–9.
- [8] Wertheim D, Mercuri E, Faundez JC, Rutherford M, Acolet D, Dubowitz L. Prognostic value of continuous electroencephalographic recording in full term infants with hypoxic ischaemic encephalopathy. *Arch Dis Child* 1994;71:F97–102.
- [9] Selton D, Andre M. Prognosis of hypoxic-ischaemic encephalopathy in full-term newborns—value of neonatal electroencephalography. *Neuropediatrics* 1997;Oct 28(5):276–80.
- [10] Hellstrom Westas L, Rosen I, Svenningsen NW. Predictive value of early continuous amplitude integrated EEG recordings on outcome after severe birth asphyxia in full term infants. *Arch Dis Child Fetal Neonatal Ed* 1995;72:F34–8.
- [11] Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. *Arch Neurol* 1976;33:696–705.
- [12] Amiel Tison C, Albert Grenier A. In: *Neurological examination during the first year of life*, Oxford University Press, 1992.
- [13] Dubowitz L, Dubowitz V. In: *The neurological assessment of the preterm and full term newborn infant*. Clin Dev Med No 79 London SIMP, Heinemann Medical, Philadelphia, 1981.
- [14] Griffiths R. In: *The abilities of babies—a study in mental measurement*, University of London Press, London, 1954.
- [15] Holmes G, Rowe J, Hafford J, Schmidt R, Testa M, Zimmerman A. Prognostic value of the electroencephalogram in neonatal asphyxia. *Electroencephalogr Clin Neurophysiol* 1982;53:60–72.
- [16] Scher MS, Painter MJ. Controversies concerning neonatal seizures. *Pediatr Clin North Am* 1989;36:281–310.
- [17] Wertheim DF, Murdoch Eaton DG, Oozeer RC et al. A new system for cotside display and analysis of the preterm neonatal electroencephalogram. *Dev Med Child Neurol* 1991;33:1080–6.
- [18] Eaton DM, Toet M, Livingston J, Smith I, Levene M. Evaluation of the Cerebro Trac 2500 for monitoring of cerebral function in the neonatal intensive care. *Neuropediatrics* 1994;25:122–8.