Acta Medica et Biologica
Vol. 43, No. 1, 17-23, 1995

The Quantification of EEG Continuity by 24-hour Recordings in Intraventricular Hemorrhaging and Periventricular Leukomalacia: Its Prognostic Value in Comparison with Conventional EEG Recordings

Kazuya GOTO, Teruyuki OGAWA and **Hirotomi SONODA**

Department of Pediatrics, Oita Medical University, Oita, Japan

Received August 8 1994; accepted December 26 1994

Summary. **Investigation was made of the prognostic value of quantified 24-hour electroencephalogram (EEG) continuity by 24-hour EEG recordings early in the postnatal period as compared follow-up, conventional EEG recordings up to fullterm was evaluated for low-birth weight infants with intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL).**

Of twelve infants, 24-hour EEG recordings were performed on eight, and a total of 58 follow-up EEG recordings were obtained from the twelve. The 24-hour EEG continuity was quantified by calculating values of five parameters, including percentages of discontinuous type, and duration of interburst interval.

There were no clear differences in the prognostic value between the two methods. However, many follow-up EEG recordings on infants with abnormal neurological outcome showed a mildly abnormal background rhythm which was difficult to differentiate from normal patterns.

Considering the need for EEG recordings in the acute stage of perinatal brain damage, quantification of EEG continuity by 24-hour recording is considered to have merit.

INTRODUCTION

The value of electroencephalogram (EEG) in both full-term and preterm infants is well recognized as an index of cerebral function and as a means for predicting later neuro-developmental outcome.[1-7] In addition, the necessity of an EEG record early in the postnatal period is emphasized to give a more precise prediction of the neuro-developmental outcome in high-risk preterm infants. Tharp et al. showed the need for not only serial EEG recordings but also an initial EEG recording obtained early in the postnatal period to predict more precisely the neuro-developmental outcome in high-risk preterm infants.[2] In addition to conventional EEG recording, Connell et al. showed the usefulness of a continuous 24-hour EEG recordings in evaluating the prognosis of infants with intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL) and seizures.[1,4-6] They stated that the resolution of an initially abnormal EEG by the end of the first week of life does not necessarily indicate a normal neuro-developmental outcome in an infant with IVH.[5]

On the other hand, recent studies concerning EEG in preterm infants have shown that EEG continuity shows remarkable change with maturation and is a sensitive marker of cerebral functioning in such infants.[1,2] Therefore, the analysis of EEG continuity early in the postnatal period is expected to provide important information on neuro-developmental outcome in preterm infants.

The aim of the present study is to determine the prognostic value of quantified 24-hour EEG continuity by 24-hour EEG recordings in the acute stage in low-birth-weight infants with IVH and PVL. Moreover, we compared the prognostic value of this method with follow-up, conventional polygraphic EEG recordings which were performed through full-term postconceptional age (PCA).

Correspondence: Dr. Kazuya Goto, Department of Pediatrics Oita Medical University, 1-1, Idaigaoka, Hazamamachi, Oita 879-55, Japan.

SUBJECTS AND METHODS

Subjects

Twelve low-birth-weight infants with IVH and PVL diagnosed by cranial ultrasound sonography were admitted to our neonatal nursery from January 1989 to June 1991. Subjects included five infants with IVH and seven infants with PVL. All were infants with IVH and PVL in our nursery and were selected from a total of only 92 infants having less than 2,500 g birth weight during the study period. Ultrasound sonography was performed daily during the first week of life and then twice weekly or more if necessary until discharge from the hospital. IVH was graded I to IV in a way similar to that of Papile et al.[8] The ultrasound findings in all seven infants with PVL showed a typical evolution; that is, bilaterally increased echo-genicity seen within 48 h after birth evolved into cyst formation around two weeks after birth.

Method of recording and analysis

Continuous 2-channel EEG recordings

Continuous 2-channel EEG recordings were made for 24 h. A bipolar montage of F3-C3 and F4-C4 using silver/silver chroride cup electrodes attached with electrode cream was applied and skin/electrode impedances were kept below 10 kΩ during recording. EEG records were obtained using a Biophysiological Preamplifier (Nihon Kohden AB 622M). The amplifier time constant was 0.3 sec and high-frequency filter setting was 30 Hz. The EEG signal was digitized at 20 msec interval/channel by an A-D converter (Shoei AD 812) and 24-hour EEG data was stored in a personal computer (Panafacom C280) in the nursery. The 24-hour EEG record was printed on an X-Y plotter using a compressed scale of 12 cm/min and 500 μV/cm.

The method by Connell et al.[1] was used for analysis of the compressed EEG, except for the epoch length, which had to be modified for our computer program, in which sample of 1024 EEG signals was obtained at 20 msec intervals. A period with 16 samples (total time = 327.7 sec, roughly 5.5 min) was obtained and printed per line. The whole 24-hour EEG record was divided into 5.5 min epochs, which were then classified visually into the following 5 categories according to the degree of continuity, as shown in Fig. 1:

(1) Continuous type: complete continuity of activity throughout the epoch.

(2) Predominantly continuous type: continuous activity for at least 80% of the epoch but with at least one interval of activity attenuated to 10-20 μV for at least 5 sec.

(3) Mixed type: both continuous and discontinuous types of activity present with no clear dominance of one over the other.

(4) Predominantly discontinuous type: a mainly discontinuous epoch, which nevertheless contained continuous activity for at least 20% but less than 50% of the time. It included at least one but no more than two bursts longer than 1 min in duration.

(5) Discontinuous type: activity for less than 20% of the epoch, with no burst of activity exceeding 1 min.

If artifacts occupied more than 20% of an epoch, that epoch was excluded from analysis. As an example, representative sequences of epochs over 6 h at at 26, 29 and 33 weeks of PCA are shown in Fig. 2.

General changes in EEG continuity in a given period were characterized by the following measurements:

(1) The number of continuous epochs of each series of the discontinuous types (DTs).

(2) The number of epochs between two series of discontinuous type (IDTIs: inter-discontinuous-type intervals).

(3) The total number of epochs in continuous type and discontinuous type.

The mean number of DT and IDTI durations were expressed in minutes. These measurements for a 24-hour record were analyzed. In addition to these, interburst intervals (IBIs) were also analyzed. In a similar way to that of Connell,[1] the most discontinuous periods of 3 epochs from every 6 h were identified and the mean duration of IBI was calculated from a total of 12 epochs in a 24-hour record.

We have already established mean values of: (1) the percentage of continuous type, (2) the percentage of discontinuous type, (3) DTs duration, (4) IDTIs duration, and (5) IBIs from 26 to 34 weeks PCA based on the data of a total of 122 days of recordings for 28 preterm infants without any neurological impairments.

Twenty-four-hour EEG continuity of infants with IVH and PVL was classified into one of three categories:

(1) Normal: all items (2)-(4) are less than 1 standard deviation (SD) above the mean and items (1) and (5) are above [−1]SD.

(2) Mildly abnormal: one item (2)-(4) is between 1 SD and 2 SD above the mean or item (1) or (5) is between [−1]SD and [−2]SD.

(3) Markedly abnormal: more than two of the items (2)-(4) are between 1 SD and 2 SD above the mean and/or at least one of items (2)-(4) is greater than 2 SD above the mean. Or, items (1) and/or (5) are below [−2]SD.

We analyzed the 24-hour EEG only after abnormal ultrasound findings.

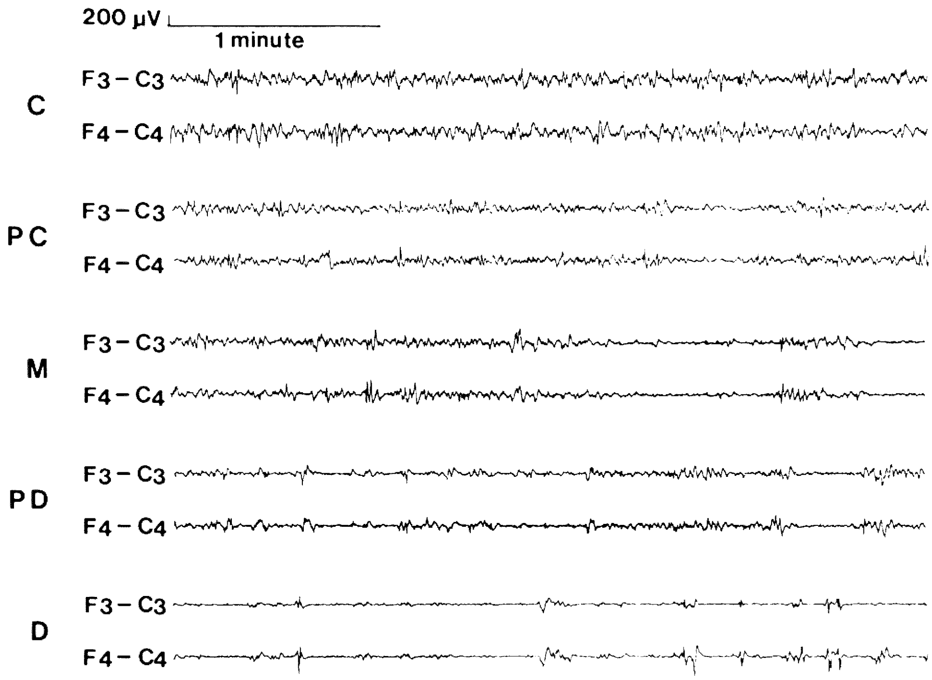

Fig. 1. Five EEG types. (C. continuous type; PC, predominantly continuous type; M, mixed type; PD, predominantly discontinuous type; D, discontinuous type).

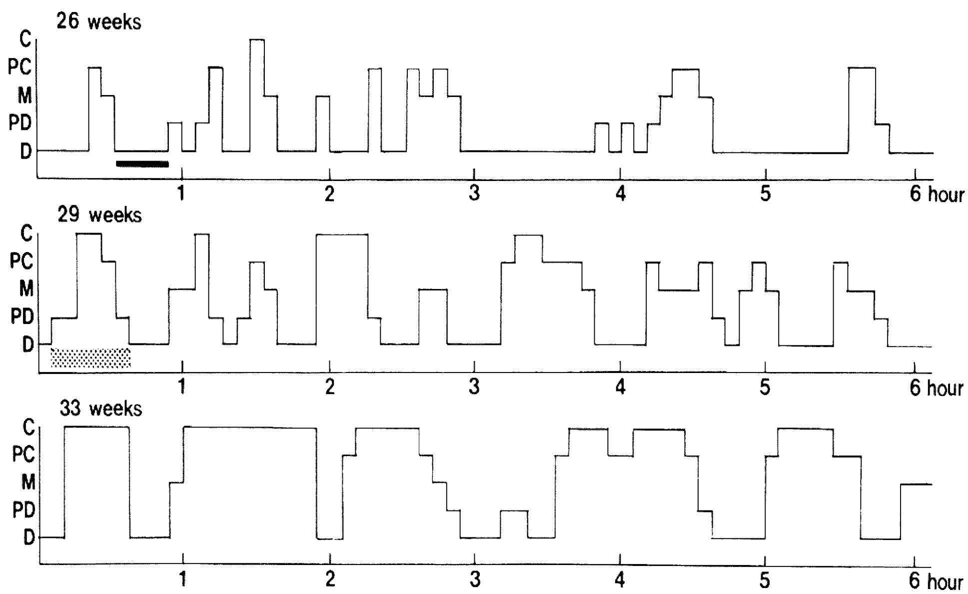

Fig. 2. Representative sequences of EEG types over 6 h at 26, 29 and 33 weeks PCA. (C. continuous type; PC, predominantly continuous type; M, mixed type; PD, predominantly discontinuous type; D, discontinuous type). The solid bar indicates a DT duration. The stippled bar indicates an IDTI duration.

Table 1. 24-hour EEG findings, follow-up EEG finding and neurological outcomes

Case No.	Sonographic findings*	24-hour EEG findings	Follow-up, conventional EEG findings**																		Neurological outcomes
1	IVH(**I**)	normal							[		○	○	○	○	○	○		○[1]			normal
2	IVH(**I**)	normal					[		○	○	○		○			▲			○[2]		normal
3	IVH(**I**)	mildly abnormal							[							▲	▲	○	○[3]		normal
4	IVH(**III**)	mildly abnormal	[																	○[4]	borderline
5	IVH(**III**)	abnormal			[							▲				■				▲[5]	abnormal
6	PVL	—														[			○[6]	○	normal
7	PVL	normal			[				○			○	○						○[7]		normal
8	PVL	—								[									▲[8]	▲	abnormal
9	PVL	—					[								▲		▲[9]				abnormal
10	PVL	abnormal								[			■	▲	▲	▲	▲	▲	○[10]	○	abnormal
11	PVL	—						[	■	■	■	▲	○	▲	▲	▲	▲	▲	○[11]	○	abnormal
12	PVL	abnormal										[		■	■	■	■	■	■[12]	▲	abnormal
			24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	

Postconceptional age (weeks)

Sonographic findings* IVH: intraventricular hemorrhage; PVL: periventricular hemorrhage; **I**: subependymal hemorrhage; **III**: IVH with ventricular dilatation.
Follow-up, conventional EEG findings** [: gestational age; ○: normal background; ▲: mildly abnormal background ■: moderately abnormal background; EEG with postscript number was analyzed as EEG around the fullterm postconceptional age of each infant.

Follow-up conventional EEG recordings

Follow-up EEGs were obtained at the patient's bedside or in the laboratory with a 16-channel Nihon Kohden electroencephalograph. Nine silver/silver chroride cup electrodes were applied to the scalp according to the international 10-20 electrode system modified for neonates. Four polygraphic parameters including electrooculogram, chin electromyogram, electrocardiogram and respiration were also recorded. The EEG background was judged as (1) normal or (2) mildly abnormal, (3) moderately abnormal or (4) markedly abnormal, according to the criteria of Clancy and Tharp.[3]

Neuro-developmental outcome

Assessment of neuro-developmental outcome was made at the Neonatal Follow-up Clinic of our hospital. Sequential neurologic examinations and developmental assessments were performed at 2-month intervals from discharge up to 18 months of corrected age. At 18 months, a Developmental Quotient (DQ) test by Tumori-Inage developmental test[9] was performed. Neurodevelopmental outcome was classified as normal, borderline (i.e. transient abnormality of muscle tone during the first year of life) or abnormal (i.e. DQ less than 80 and/or unequivocal motor dysfunction such as diplegia and quadriplegia).

RESULTS

Patient demography

The gestational ages of 11 infants in this study were less than 34 weeks. One infant with PVL was at 37 weeks of gestation. The mean gestational age was 29.8 weeks (range 24–37 weeks) and mean birth weight was 1178 g (range 566–1736 g). The 24-hour EEG records were obtained from 8 of 12 infants. In seven of these infants, the dates of 24-hour EEG analysis ranged from one to five postnatal days. In one infant with IVH whose gestational age was 24 weeks, the 24-hour EEG recorded on the 14th postnatal day was analyzed because normal values concerning EEG continuities in this study were only established in infants ranging from 26 to 33 weeks of PCA. A total of 58 follow-up, conventional EEGs were obtained from all 12 infants. The number of follow-up EEGs varied from 1 to 12 per infant with a mean of 4.8. Follow-up EEGs were recorded from 2 to 12 postnatal weeks. Table 1 shows sonographic findings, EEG findings and neurological outcomes for each of the 12 infants.

24-hour EEG continuity

The values for each of five parameters concerning EEG continuity obtained by 24-hour recordings in eight infants are shown in Table 2. In four of seven

Table 2. 24-hour EEG findings

Case No.	Sonographic findings*	Postnatal day of EEG recordings	24-hour EEG continuity**				IDTI duration	Neurological outcomes
			% CT	% DT	IBI	DT duration		
1	IVH(**I**)	2	○	▲	○	▲	○	normal
2	IVH(**I**)	1	○	○	○	○	○	normal
3	IVH(**I**)	2	○	○	○	○	○	normal
4	IVH(**III**)	14	○	○	▲	○	○	borderline
5	IVH(**III**)	2	○	▲	○	▲	○	abnormal
7	PVL	4	○	○	○	○	○	normal
10	PVL	5	○	■	○	▲	○	abnormal
12	PVL	3	▲	■	■	▲	▲	abnormal

Sonographic findings* IVH: intraventricular hemorrhage, (**I**): subependymal hemorrhage, (**III**): IVH with ventricular dilatation, PVL: periventricular leukomalacia
** 24 hour EEG continuity, % CT: % of continuous type, IDTI duration: Inter-discontinuous type interval duration, ○: above [−1] SD from the mean, ▲: between [−1] SD and [−2] SD from the mean, ■: below [−2] SD from the mean, % DT: % of discontinuous type, IBI: interburst interval, DT duration: discontinuous type duration, ○: less than [1] SD above the mean, ▲: between [1] SD and [2] SD above the mean, ■: above [2] SD above the mean

infants, the percentage of discontinuous type was increased. In all four of these infants, DT duration was also increased. As for the other three items, a maximum of two infants showed abnormal values for each item. The relation between EEG continuity and neurological outcome is shown in Table 2. Three infants with abnormal outcome exhibited markedly abnormal EEG continuity. Three infants with normal EEG continuity had normal outcomes. Of two infants with mildly abnormal EEG continuity, one had a normal outcome and the other had transient dystonia.

Follow-up EEG

In a total of 58 follow-up EEGs, there were 28 with normal backgrounds, 21 with mildly abnormal backgrounds and 11 with moderately abnormal backgrounds. Markedly abnormal EEG backgrounds were not obtained. The contents of the abnormal EEG backgrounds are shown in Table 3. Mild excessive discontinuity and mild poverty of auticipated background rhythms for PCA typically were represented by increased or decreased delta brushes. Although moderately abnormal backgrounds were obtained in 11 EEGs, one infant (Case 12) with extended PVL, which showed marked laterality, had duplicated abnormal EEG features such as marked focal abnormalities and excessive spikes and sharp waves. The relations between follow-up EEGs recorded up to full-term PCA and neuro-developmental outcomes are shown in Table 1. Although the EEG recordings during the postnatal weeks varied from infant to infant,

Table 3. Conventional EEG findings

EEG findings	No. of EEG/No. of infants
Total	58/12
Normal	28/ 8
Mildly abnormal	21/ 8
Mildly excessive discontinuity	17/ 8
Mild poverty of anticipated background rhythm for PCA	11/ 5
Mild focal abnormalities	5/ 4
Poor concordance between clinical and EEG sleep state	1/ 1
Moderately abnormal	11/ 4
Marked focal abnormalities	6/ 1
Moderately excessive discontinuity	5/ 3
Poverty of anticipated background rhythm for PCA	2/ 1
Excessive spikes and/or sharp waves	2/ 1

PCA: postconceptional age

infants with moderately abnormal EEGs obtained at least once were associated with a poor neuro-developmental outcome. Morever, even for patients with mildy abnormal EEGs, if they were obtained consecutively over two or three weeks, the cases were also associated with a poor outcome. Of 12 EEGs obtained around the fullterm PCA for each patient, eight normal EEGs were associated with five normal, one borderline and two abnormal outcomes. Abnormal EEGs were always associated with abnormal outcomes.

DISCUSSION

Continuous 24-hour EEG recording, in which 2 channels are used in general, has both advantages and disadvantages in comparison with conventional EEG recordings.[1,2] However, because of its minimal interference during the handling of infants and its ease of quantification, we apply it to infants less than 34 weeks PCA, especially in the acute stage. In reports by Connell et al., gradings of EEG abnormalities were based on the quantification of interhemispheric synchrony, symmetry and amplitude of burst activity in addition to EEG cuntinuity.[4-6] Although all these items enable us to judge EEG background in detail, it is a considerably difficult task to quantify all of them through 24-hour EEG recording. In this study, we focused on EEG continuity, which is thought to be the most sensitive EEG marker in preterm infants.

The observed prognostic value of 24-hour EEG continuity in this study was similar to earlier observations,[2-6] in which the grading of EEG abnormalities was based on several parameters. That is to say, normal EEG findings were correlated with normal outcomes. Conversely, markedly abnormal EEG findings were correlated with abnormal outcomes. Therefore, our present study demonstrated that a simple quantification of 24-hour EEG continuity could provide sufficient information on neuro-developmental outcome in preterm infants with IVH and PVL. On the other hand, there were no clear differences in prognostic value between continuous 24-hour EEG recordings and conventional EEG recordings in this study. Infants with abnormal outcomes showed abnormal EEG continuity followed by persistently abnormal EEG backgrounds in follow-up conventional EEG recordings. However, in these follow-up EEG recordings, EEG background abnormalities were resolved around the time of fullterm PCA in some of the infants with abnormal outcomes. Moreover, many follow-up EEG recordings in infants with abnormal outcomes showed a mildly abnormal background such as mildly excessive discontinuity and mild poverty of anticipated background PCA which needed considerable effort to be discriminated from a normal one. Considering the circumstances mentioned above, quantification of 24-hour EEG continuity was useful in predicting neuro-developmental outcome in preterm infants.

Among the five parameters measured, the most common abnormalities regarding continuity appeared in the percentage of discontinuous type and DT duration. A series of DTs which consists of tracé discontinue would most probably correspond to some extent to a period of quiet sleep. On the basis of our previous report,[7] changes in DT duration and IDTI duration appear related to the development of sleep state organization from 26 to 33 weeks of PCA. It is impossible to state that increases in DT duration and IDTI duration observed in this study are directly related to abnormalities of sleep state organization, because other physiological parameters characterizing the sleep state were not analyzed.

However, burst suppression, which is a prolonged discontinuous EEG activity, represents markedly abnormal EEG findings in full-term infants. In order to assess its prognostic significance, we must identify the sleep state in which it appears.[10] It is also a great concern in preterm infants to clarify the relation between changes in EEG continuity and changes in sleep state organization. Recently, computer analysis of both 24-hour EEG continuity and EEG sleep state in neonates has become available.[11,12] The analysis of sleep state organization in addition to EEG continuity through a 24-hour period will provide important information on the cerebral function in premature infants, especially in those with neurological impairments.

Acknowledgements. This study was supported by a Grant for Scientific Research (No. 02670450) from the Ministry of Education of Japan.

REFERENCES

1) Connell JA, Oozeer R, Dubowitz V: Continuous 4-channel EEG monitoring: a guide to interpretation with normal values in preterm infants. *Neuropediatrics* **18:** 138-145, 1987.
2) Tharp BR, Scher MS, Clancy RR: Serial EEGs in normal and abnormal infants with birth weights less than 1200 grams—a prospective study with long term follow-up. *Neuropediatrics* **20:** 64-72, 1989.
3) Clancy RR, Tharp BR, Enzman D: EEG in premature infants with intraventricular hemorrhage. *Neurology* **34:** 583-90, 1984.
4) Connell J, Oozeer R, Regev R, de Vries LS, Dubowitz LMS, Dubowitz V: Continuous four-channel EEG monitoring in the evaluation of echodense ultrasound lesions and cystic leukomalacia. *Arch Dis Child* **62:** 1019-1024, 1987.
5) Connell J, de Vries L, Oozeer R, Regev R, Dubowitz LMS, Dubowitz V: Predictive value of early continuous electroencephalogram monitoring in ventilated preterm infants with intraventricular hemorrhage.

Pediatrics **82:** 337-343, 1988.
6) Connell J, Oozeer R, de Vries L, Dubowitz LMS, Dubowitz V: Continuous EEG monitoring of neonatal seizures: diagnostic and prognostic considerations. *Arch Dis Child* **64:** 452-458, 1989.
7) Goto K, Wakayama K, Sonoda H, Ogawa T: Sequential changes in electroencephalogram continuity in very premature infants. *Electroencephalogra Clin Neurophysiol* **82:** 197-202, 1992.
8) Papile LS, Burnstein J, Burnstein R, Koffler H: Incidence and evolution of the subependymal intraventricular hemorrhage: a study of infants with weights less than 1500 grams. *J Pediatr* **92:** 529-534, 1978.
9) Tsumori M, Inage N: Psychological developmental screening test. Tokyo, *Dainippon Tosho* 1961. (in Japanese)
10) Grigg-Damberger MM, Coker SB, Halsey CL, Anderson CL: Neonatal burst suppression: its developmental significance. *Pediatr Neurol* **5:** 84-92, 1989.
11) Scher MS, Sun M, Hatzilabrou G, Greenberg NL, Cebulka G, Krieger D, Guthrie RD, Sclabassi RJ: Computer analyses of EEG-sleep in the neonate: methodological considerations. *J Clin Neurophysiol* **7:** 417-441, 1990.
12) Wertheim DFP, Murdoch Eaton DG, Oozeer RC, Connell JA, Dubowitz LMS, Dubowitz V, Willetts R, Wootton R: A new system for cotside display and analysis of the preterm neonatal electroencephalogram. *Dev Med Child Neurol* **33:** 1080-1086, 1991.