

Background electroencephalographic (EEG) activities of very preterm infants born at less than 27 weeks gestation: a study on the degree of continuity

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Abstract

Aims—To clarify the features of the background electroencephalographic (EEG) activities in clinically well preterm infants born at less than 27 weeks gestation and to outline their chronological changes with increasing postconceptional age (PCA).

Methods—EEGs of clinically well premature infants born at less than 27 weeks gestation were recorded during the early postnatal period. The infants were separated into three groups according to their PCA at the time of EEG recording (21–22 weeks PCA, 23–24 weeks PCA, and 25–26 weeks PCA). The mean and maximum duration of interburst intervals (IBIs), the mean duration of bursts, and the percentage of continuous and discontinuous patterns in each PCA group were evaluated.

Results—There were three infants at 21–22 weeks PCA, seven at 23–24 weeks PCA, and five at 25–26 weeks PCA. Eighteen EEG recordings were obtained. The mean and maximum IBI duration decreased with increasing PCA. The percentage of continuous patterns increased with increasing PCA. Conversely, the percentage of discontinuous patterns decreased with increasing PCA.

Conclusions—In premature infants born at less than 27 weeks gestation, the characteristics of the background EEG activities were similar to those of older premature infants. These changes reflect the development of the central nervous system in this period.

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Keywords: electroencephalogram; central nervous system; development; prematurity; extremely low birth-weight infants; neonatal intensive care unit

During the last few decades, advances in neonatal intensive care have resulted in a decrease in neonatal mortality and a dramatic increase in the survival rate of extremely low birthweight infants.^{1–4} However, severe neurological sequelae are common because of the vulnerability of the immature central nervous system.^{1–3 5} Although various techniques such as cranial ultrasonography are used for neurological evaluation, electroencephalography (EEG) is one of the most useful tools for predicting neurological outcome in preterm and term infants.^{6–10}

Several authors have studied EEGs in premature infants.^{11–18} We can recognise two distinct patterns, continuous and discontinuous. The continuity of EEG activities changes considerably with maturation of the brain. In immature infants, discontinuous patterns occur in a large part of the tracing.^{19–23}

Although several studies on EEG findings of premature infants have been published, most were concerned only with those born at more than 27 weeks gestation.^{11–16} The aim of this study was to clarify the features of background EEG activities in clinically well preterm infants born at less than 27 weeks gestation in terms of continuity and to outline their developmental changes with increasing postconceptional age (PCA).

Patients and methods

The subjects were preterm infants born at less than 27 weeks gestation, who were admitted to the neonatal intensive care unit of Ogaki Municipal Hospital from June 1997 to October 1998. Infants were selected who met all of the following criteria: normal neurological examination and cranial ultrasound at least until 24 hours after the last EEG recordings; no evidence of asphyxia (pH > 7.25 in initial blood gas analysis); no congenital anomalies; stable respiratory and circulatory state. Gestational age was determined from the date of the mother's last menstrual period and confirmed by the New Ballard Score.²⁴ The latter was used if the mother's last menstrual period was unknown or if the gestational age estimated from the last menstrual period was discordant with physical examination data.

EEG recordings were performed at the infants' bed side using a Nihon-Koden instrument. Eight bipolar conduction electrodes were placed according to the modified 10–20 international system adjusted to the smaller head size of preterm infants (AF3–C3, C3–O1, AF4–C4, C4–O2, AF3–T3, T3–O1, AF4–T4, T4–O2). Paper speed was 30 mm/second, with a time constant of 0.3 second. Amplitudes were 10 μ V/mm. A high frequency filter was set at 60 Hz. EEGs were recorded for more than 30 minutes in order to include both continuous and discontinuous patterns.

EEG findings were divided into three categories according to the following criteria (fig 1). (1) Continuous patterns: EEG activity mainly consisting of delta waves > 100 μ V that were continuously recognised for more than 20

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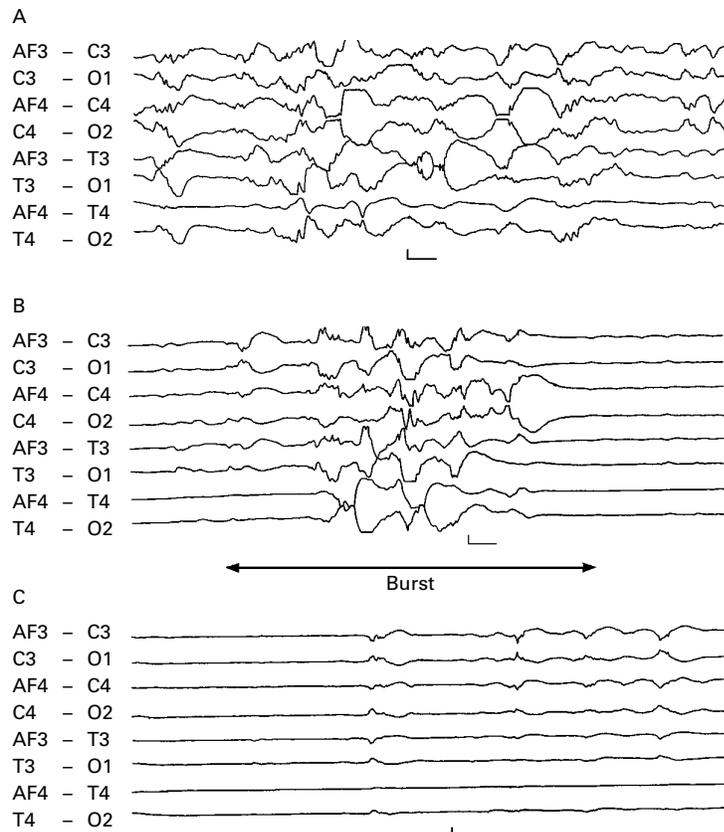


Figure 1 Electroencephalographic (EEG) findings for a very preterm infant (gestational age 23 weeks 6 days; postconceptional age 24 weeks 0 days; birth weight 564 g). (A) Continuous pattern; (B) discontinuous pattern; (C) undifferentiated pattern. Calibrations are 100 μ V and 1 second.

seconds. (2) Discontinuous patterns: bursts of EEG activity separated by low voltage activity < 30 μ V for more than five seconds. Bursts were defined as EEG activity with amplitudes more than 100 μ V lasting for 2–20 seconds in any of the channels. (3) Undifferentiated pattern: EEG activity that did not correspond to either continuous or discontinuous patterns. An interburst interval (IBI) was defined as a period between bursts during which activities were lower than 30 μ V in all leads. The mean and maximum IBI duration and the mean burst duration during discontinuous patterns were determined in each EEG. The percentage of continuous patterns and discontinuous patterns in each EEG was also evaluated. These values were used for the following analysis.

The patients were separated into three groups (21–22 weeks PCA, 23–24 weeks PCA, and 25–26 weeks PCA) according to PCA at the time of recording. We evaluated the mean IBI, the maximum IBI, and the mean burst duration in each PCA group. The percentage

of continuous and discontinuous patterns was also compared among the three groups. Blood pressure, arterial or venous blood gas values, and SpO₂ at the time of EEG recording were analysed in order to evaluate the physiological conditions of the infants.

All numerical data are expressed as mean (range). Statistical analysis between groups was by the Kruskal-Wallis test and analysis of variance, when appropriate. Tukey's HSD was used as a post hoc multiple comparison test. Statistical significance was accepted at the level of $p < 0.05$.

Results

Fifteen infants participated in this study. Their mean gestational age was 24.1 (21.1–26.3) weeks and mean birth weight 638.7 (415–940) g. Eighteen EEG recordings were obtained. Table 1 shows the clinical characteristics at the time of EEG recording. The mean postnatal age at the time of the EEG recording was 1.9 (0–9) days. Mean systolic and diastolic blood pressures were 47.1 (24–62) and 28.6 (15–44) mm Hg respectively. Mean pH was 7.39 (7.34–7.46) and mean base excess was –2.9 (–10.2 to 0.7) mmol/l. Mean SpO₂ was 96.6 (90–100)%. None of patients received sedative or narcotic agents.

Mean IBI duration decreased as PCA increased (fig 2A). The mean IBI duration was 25.8 (14.1–46.3) seconds at 21–22 weeks PCA, 18.4 (11.1–25.2) seconds at 23–24 weeks PCA, and 12.7 (10.3–16.3) seconds at 25–26 weeks PCA. There was a significant difference only between 21–22 weeks PCA and 25–26 weeks PCA ($p < 0.05$).

The maximum IBI duration also showed a decreasing trend from 21 to 26 weeks PCA (fig 2B). The maximum IBI duration was 126.0 (67–218) seconds at 21–22 weeks PCA and 86.6 (43–136) seconds at 23–24 weeks PCA. At 25–26 weeks PCA, the maximum IBI duration was 44.2 (19–76) seconds. A significant difference was seen only between 21–22 weeks PCA and 25–26 weeks PCA ($p < 0.05$).

The mean burst duration during discontinuous patterns increased as PCA increased (fig 3). Burst durations were 4.3 (3.4–5.1) seconds at 21–22 weeks PCA, 5.0 (3.9–7.4) seconds at 23–24 weeks PCA and 5.8 (4.9–7.2) seconds at 25–26 weeks PCA. There was a significant difference only between 21–22 weeks PCA and 25–26 weeks PCA ($p < 0.05$).

The percentage of continuous patterns at each PCA increased as PCA increased (fig 4A). The percentage of continuous patterns at 21–22 weeks PCA, 23–24 weeks PCA, and 25–26 weeks PCA were 5.5 (0.0–17.3), 23.8 (1.3–46.4), and 48.5 (27.3–73.2) respectively.

Table 1 Characteristics of the three groups of preterm infants at time of EEG recordings

PCA (weeks)	No of EEGs	Recording age (day)	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	pH	BE (mmol/l)	SpO ₂ (%)
21–22	5	1.0 (0–3)	37.2 (24–52)	22.2 (15–39)	7.41 (7.35–7.46)	–4.5 (–10.2––1.1)	96.2 (95–97)
23–24	7	2.4 (0–9)	49.0 (45–57)	29.3 (23–36)	7.38 (7.34–7.45)	–2.0 (–3.0–0.7)	96.0 (90–100)
25–26	6	2.0 (0–8)	53.2 (41–62)	33.0 (24–44)	7.38 (7.35–7.41)	–2.5 (–6.4–0.7)	97.7 (97–100)
Total	18	1.9 (0–9)	47.1 (24–62)	28.6 (15–44)	7.39 (7.34–7.46)	–2.9 (–10.2–0.7)	96.6 (90–100)

Values are means (range).

PCA, Postconceptional age; BP, blood pressure; BE, base excess.

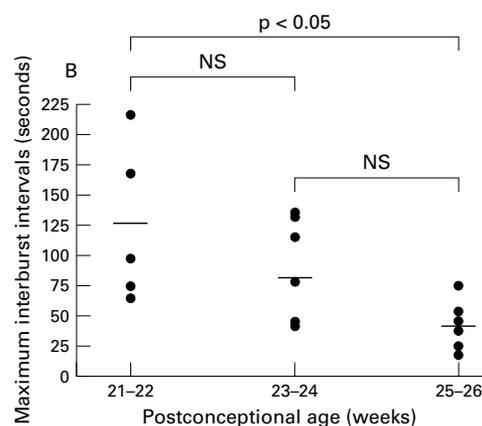
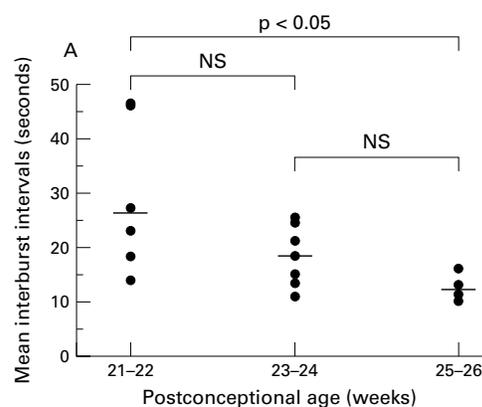


Figure 2 Comparison of the interburst intervals for the three groups of preterm infants. (A) Mean interburst intervals; (B) maximum interburst intervals. The solid line in each case represents the mean value.

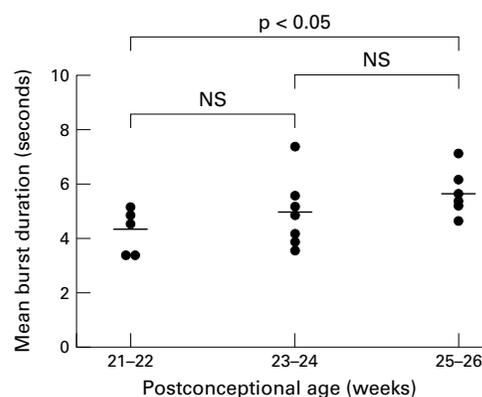


Figure 3 Comparison of the mean burst durations for the three groups of preterm infants. The solid line in each case represents the mean value.

The results were significantly different between 21–22 weeks PCA and 25–26 weeks PCA ($p < 0.01$). In contrast with the continuous patterns, the percentage of discontinuous patterns decreased as PCA increased (fig 4B). The percentage of discontinuous patterns at 21–22 weeks PCA, 23–24 weeks PCA, 25–26 weeks PCA were 69.0 (30.4–96.1), 53.8 (32.8–76.8), and 48.4 (18.9–49.0) respectively. The results were significantly different between 21–22 weeks PCA and 25–26 weeks PCA ($p < 0.05$).

Six of these 15 infants died after the recordings. The causes of death were pneumothorax

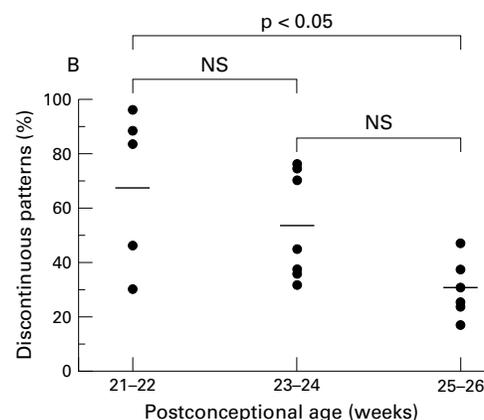
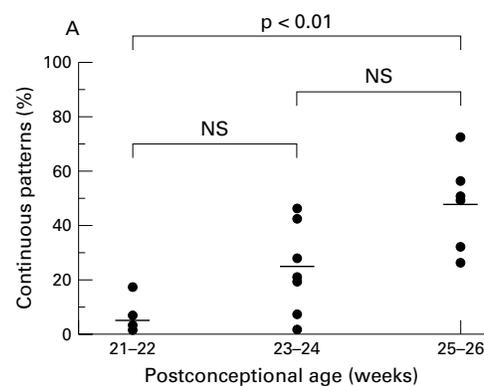


Figure 4 Comparison of the continuities for the three groups of preterm infants. (A) Continuous patterns; (B) discontinuous patterns. The solid line in each case represents the mean value.

in two, necrotising enterocolitis in two, intestinal perforation in one, and pyothorax in one. One infant was blind due to retinopathy of prematurity and another had subglottis stenosis. Although neurodevelopmental outcome was not sufficiently evaluated because three infants were younger than one year of corrected age at their last follow up, six infants had no neurological sequelae.

Discussion

This study illustrates the characteristics and developmental changes in background EEG activities in very premature infants in terms of continuity. The mean and maximum IBI duration decreased as PCA increased, whereas the burst duration and continuity increased with increasing PCA. These findings are consistent with the maturational changes in background EEGs in infants born after 27 weeks gestational age.^{11–16}

The presence of discontinuous patterns is a prominent feature of EEGs of preterm infants. IBI is an easily distinguishable component of EEG activity. Several reports have focused on IBI duration and its maturational change.^{16 17 23} Mean IBI duration has been reported to decrease as PCA increases. Connell *et al*,¹⁷ using continuous four channel EEG monitoring, reported that mean IBI duration fell from 14 to 8 seconds between 26 and 37 weeks. Anderson *et al*¹⁶ showed that mean IBI decreased from 12 to 7 seconds between 27 and 32 weeks. A similar trend is observed in the

results of our study, although mean IBI duration is much longer than that of older preterm infants. The mean IBI duration was 12.7 seconds at 25–26 weeks PCA, 18.4 seconds at 23–24 weeks PCA, and 25.8 seconds at 21–22 weeks PCA.

The maximum IBI is also known to decrease as PCA increases. Connell *et al*¹⁷ reported that maximum IBI fell from 75 to 15 seconds between 26 and 37 weeks. Biagioni *et al*²³ found that maximum IBIs in normal premature infants were 30.7 seconds at 27–28 weeks, 29.5 seconds at 29–30 weeks, 19.7 seconds at 30–31 weeks, and 14.8 seconds at 33–34 weeks. Anderson *et al*¹⁶ reported that the mean of the longest IBI decreased from 48 to 20 seconds between 27 and 32 weeks. In the present study, the maximum IBI was 126.0 seconds at 21–22 weeks PCA, 86 seconds at 23–24 weeks PCA, and 44.2 seconds at 25–26 weeks PCA. Therefore the maximum IBI decreased as PCA increased in agreement with previous studies, but it was longer than that of older preterm infants.

Burst duration increased with increasing PCA in our study, whereas previous studies showed that it was independent of PCA.^{16, 17} Eyre *et al*¹⁸ reported that the duration of bursts was between two and five seconds. Anderson *et al*¹⁶ reported that the duration of bursts during discontinuous patterns was four to five seconds on average at any PCA. However, sufficient statistical analysis was not performed in these studies. In contrast with previous studies, our study showed that the mean burst duration was 4.3 seconds at 21–22 weeks PCA, 5.0 seconds at 23–24 weeks PCA, and 5.8 seconds at 25–26 weeks PCA. Burst duration was significantly longer in infants at 21–22 weeks PCA than in infants at 25–26 weeks PCA.

Several authors have reported that continuous patterns increased and discontinuous patterns decreased with increasing PCA. Anderson *et al*¹⁶ showed that the percentage of discontinuous patterns was 62 at 27–28 weeks PCA, 53 at 29–30 weeks PCA, and 45 at 31–32 weeks PCA. Goto *et al*²² reported that continuous patterns increased from 1.2 to 7.1% and discontinuous patterns decreased from 66.6 to 36.7% from 26 to 30 weeks PCA. In our study, maturational alteration of the percentage of continuous and discontinuous patterns in very preterm infants was consistent with previous reports on more mature preterm infants. However, the percentage of continuous patterns in this study was larger and that of discontinuous patterns was smaller than that of more mature preterm infants in these studies. These differences may be attributable to the difference in the definition of continuous and discontinuous patterns. Goto *et al*²² reported sequential changes in continuity of EEG activities using low amplification and a compressed time scale. Some low voltage EEG activities, which are detectable in our study, may have been missed. Furthermore, they used only two cerebral channels located in the bilateral frontal and central regions. EEG activities from other regions were not detected by their monitoring system. This resulted in longer discontinuous

Key messages

At less than 27 weeks gestational age, the characteristics of background EEG activities were found to be as follows:

- the mean and maximum IBI duration decreased with increasing PCA
- the percentage of continuous patterns increased with increasing PCA
- the percentage of discontinuous patterns increased with increasing PCA
- the mean burst duration during discontinuous patterns increased as PCA increased

patterns in their study. We were able to identify continuous and discontinuous patterns more precisely because we used a higher amplification rate and faster paper speed.

There are two limitations to our study. Firstly, the definition of a normal very preterm infant is difficult because prematurity itself is not physiological. A preterm infant cannot be confirmed as truly healthy during the early neonatal period until normal growth and psychomotor development are achieved. The prognosis of very preterm infants is poor despite recent advances in neonatal intensive care.²⁵ This is especially true for those born at less than 24 weeks gestation. Therefore we cannot decide whether the infants who participated in this study were truly well. We consider that they were healthy and their brain function satisfactory because we carefully selected very preterm infants whose respiratory and cardio-circulatory conditions were stable and cranial ultrasonographic findings were normal. Therefore we believe that EEGs of healthy preterm infants were evaluated in this study. Another limitation is the small number of patients. Severe complications such as intracranial haemorrhage and respiratory or cardiac failure are common among very preterm infants. It is difficult to record EEGs of very preterm infants while they are clinically well. Further multicentre studies will be necessary to determine precisely the physiological EEG findings of very preterm infants.

The central nervous system of very preterm infants is vulnerable because of its prematurity. The main causes of neurological sequelae are intraventricular haemorrhage and periventricular leucomalacia. Previous studies have shown that EEG is useful in predicting neurological outcome of preterm infants.^{19–23} Decreased continuity of EEG activities is known to be related to neurological outcome in preterm infants. This indicates that the continuity of EEG activities is sensitively influenced by acute insults to the brain, although chronic brain injuries cannot be assessed with this variable.²⁶ An assessment of EEG continuity will provide valuable information on brain function. This study shows some important features of background EEG of clinically well very preterm infants born at less than 27 weeks gestational age. Further studies that include impaired infants are needed to establish the

diagnostic and prognostic value of EEG in very preterm infants.

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