# Developmental outcome and types of chronic-stage EEG abnormalities in preterm infants

**Akihisa Okumura*** MD, Department of Paediatrics, Nagoya University Graduate School of Medicine, Nagoya;
**Fumio Hayakawa** MD, Department of Paediatrics, Okazaki City Hospital, Okazaki;
**Toru Kato** MD;
**Kuniyoshi Kuno** MD, Department of Paediatrics, Anjo Kosei Hospital, Anjo;
**Kazuyoshi Watanabe** MD, Department of Paediatrics, Nagoya University Graduate School of Medicine, Japan.

**Correspondence to first author at* Department of Paediatrics, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, Aichi 466-8550, Japan. E-mail: okumura@med.nagoya-u.ac.jp

**The aims of this study were to determine the types of chronic-stage EEG abnormalities that exist and to clarify their relation to neurodevelopmental outcome in preterm infants. We evaluated 183 preterm infants with gestational ages of less than 33 weeks (mean age 29.2 weeks) and weighing less than 2000g (mean weight 1275g). The first EEG was performed within 72 hours of life; thereafter, EEG was performed once every 1 to 4 weeks until the infant reached a post-conceptional age of 40 to 42 weeks. Two kinds of EEG abnormalities, acute- and chronic-stage abnormalities, were evaluated and we assessed mainly the latter. Chronic-stage EEG abnormalities were divided into two patterns: disorganized and dysmature. Periventricular leukomalacia (PVL) and intraventricular haemorrhage (IVH) were diagnosed on the basis of ultrasound findings. Psychomotor development was examined every 3 months after discharge until at least 18 months of the infants' corrected age. Disorganized and dysmature patterns were observed in 52 and 28 infants respectively. Among the 52 infants with disorganized patterns, PVL was observed in 31 and IVH in seven infants. Thirty-nine infants had cerebral palsy (CP). Twenty-six achieved normal cognitive development. Of the 28 infants with dysmature patterns, PVL was seen in one and IVH in 11 infants. CP was seen in five infants. Only eight infants achieved normal cognitive development. Gestational age and birthweight were significantly lower in infants with dysmature patterns than in those with disorganized ones. Results indicate that types of chronic-stage EEG abnormalities are related to types of neurological sequelae and are useful for assessing the mode of brain injury in preterm infants.**

Despite recent advances in perinatal care resulting in improved neonatal morbidity and mortality, the incidence of cerebral palsy (CP) and/or mental retardation* (MR) in preterm infants has not decreased. Periventricular leukomalacia (PVL) and intraventricular haemorrhage (IVH) are the principal brain lesions accounting for the majority of neurological sequelae in preterm infants. Extensive studies have demonstrated the usefulness of serial ultrasound in detecting these lesions and for predicting the neurological prognosis (Papile et al. 1978, Shankaran et al. 1982, McMenamin et al. 1984). EEG is also useful for evaluating brain function. It is generally accepted that some EEG abnormalities, such as positive rolandic sharp waves, are highly correlated with brain damage and with an abnormal neurological outcome (Novotny et al. 1987, Watanabe 1992, Baud et al. 1998, Okumura et al. 1999).

EEG can show various changes according to the mode of brain insult. When an acute brain insult has occurred, EEG activity shows various degrees of depression, i.e. acute-stage EEG abnormalities. The severity of acute-stage EEG abnormalities parallels the magnitude of the brain insult. Acute-stage EEG abnormalities gradually improve with time and are replaced by chronic-stage EEG abnormalities. Chronic-stage EEG abnormalities consist mainly of two patterns: dysmature and disorganized (Hayakawa et al. 1997a, b). A disorganized pattern appears after an acute and strong depression and is characterized by a deformity of delta waves and brushes without definite findings of acute-stage EEG abnormalities (Hayakawa et al. 1997a). A disorganized pattern is closely correlated with deep white-matter injury and later with CP (Hayakawa et al. 1997a). A dysmature pattern is appears after mild prolonged depression and is characterized by the appearance of some EEG components which are immature when compared with post-conceptional age (PCA; Hayakawa et al. 1997b). Our previous study suggested a correlation between dysmature patterns and cognitive impairment (Hayakawa et al. 1997b).

The aims of the present study were to assess the types of chronic-stage EEG abnormalities and clarify their relation to ultrasonographic findings and developmental outcome in preterm infants.

## Method

### PATIENTS

We studied 227 preterm infants of 32 weeks' or less gestation (mean age 29.2 weeks, range 25 to 32 weeks) and weighing less than 2000g (mean weight 1276g, range 566 to 1992g) who were admitted to Anjo Kosei Hospital from 1987 to 1992. Gestational age was determined from the mother's last menstrual period and confirmed by the New Ballard Score (Ballard et al. 1991). The latter was used if the mother's last menstrual period was unknown or if the gestational age was discordant with physical examination data. Small-for-date status was defined as having a birthweight of more than 2SD below the mean.

We investigated the serial EEG and ultrasonographic findings and developmental outcomes in these infants. Results from eleven infants who died in the early neonatal period and three with chromosomal abnormalities and/or multiple congenital anomalies were excluded from the study. Results from thirty-three infants who did not attend our hospital

*UK usage: learning disability.

until 18 months of age were also excluded from the study. None of the infants studied had ultrasonographic abnormalities during the neonatal period. Twenty-seven infants attended our hospital until 12 months of age. No delayed development or apparent neurological abnormalities were seen in any infant. One hundred and eighty-three infants were evaluated.

Oral parental consent for EEG recordings was obtained. Ethical consent was not necessary because EEG, ultrasonography, and neurodevelopmental evaluation are performed routinely in our hospital. They were not performed for the purpose of this study.

### EEG

EEG is routinely performed in our hospital in all patients with gestational ages of less than 34 weeks. In this study the first EEG was performed within 72 hours of life: if possible within the first 36 hours. Thereafter, EEG was performed once every 1 to 4 weeks until 40 to 42 weeks of PCA. When the initial EEG revealed abnormal findings or some clinical events occurred (e.g. hypotension, cardiac failure, hyperkalemia, systemic infection, etc.), additional EEG recordings were made. EEG comprised polygraphy, with bipolar derivation and eight surface electrodes (AF3, AF4, C3, C4, O1, O2, T3 and T4) were placed in accordance with the International 10–20 system, combined with electro-oculography, ECG, and respiratory movement measurement, as reported previously (Watanabe 1992). EEG was performed for more than 40 minutes during waking through spontaneous sleep, including all states of sleep. The time constant was 0.3 seconds and the paper speed 3cm/s. All EEGs were independently evaluated by three well-trained neonatal neurologists in the team who were blinded to the infants' ultrasonographic findings and clinical data. If there was any difference in the interpretation of an EEG among them, a consensus was reached after re-evaluation.

Two kinds of EEG abnormalities, acute- and chronic-stage, were evaluated in all EEGs according to the criteria described elsewhere (Watanabe 1992, Hayakawa et al. 1999, Watanabe et al. 1999). Although chronic-stage EEG abnormalities usually appeared after acute-stage EEG abnormalities, they were observed in some infants on the initial EEG immediately after birth. In such infants the brain insult was presumed to have occurred antenatally (Hayakawa et al. 1999, Watanabe et al. 1999). Chronic EEG abnormalities could coexist with acute-stage EEG abnormalities during the phase of recovery from the brain insult. The presence or absence of chronic EEG abnormalities was assessed separately from that of acute-stage EEG abnormalities.

Acute-stage EEG abnormalities were judged to be present when at least one of the following was recognized: decreased continuity, voltage suppression, or attenuated faster activities. Chronic-stage EEG abnormalities were diagnosed as present when disorganized or dysmature patterns were observed. A disorganized pattern refers to an abnormal, deformed morphology of background activities without definite findings of acute-stage EEG abnormalities (Watanabe 1992, Hayakawa et al. 1997a). The waveforms of disorganized EEGs were characterized by a lack of smoothness, the presence of abnormal sharp waves, and the presence of mechanical brushes that were cogwheel-shaped, spiky, and of high amplitude compared with normal brushes (Fig.1). A dysmature pattern was defined as the presence of some EEG patterns that were 2 weeks or more immature, compared with PCA (Hayakawa et al. 1997b). The EEGs of infants with dysmature patterns revealed a lack of physiological maturation of EEG patterns such as an increase in the frequency and a decrease in the amplitude of delta waves, an increase in brushes and a decrease in rhythmic temporal theta waves (Fig. 2). Morphological changes seen in a disorganized pattern sometimes include components analogous to dysmaturity. Therefore, when EEGs revealed both disorganized and dysmature patterns in the same infant in single or sequential recordings such infants were categorized as having disorganized patterns. Morphological changes associated with dysmature patterns are ordinarily subtle, if present. Such infants were classified as having dysmature patterns. The features of chronic EEG abnormalities were not greatly different between early and late recordings, although their severity was reduced in the late recordings.

### NEUROIMAGING

Cranial ultrasound was performed at least twice within the first week of life, once per week during the second to the

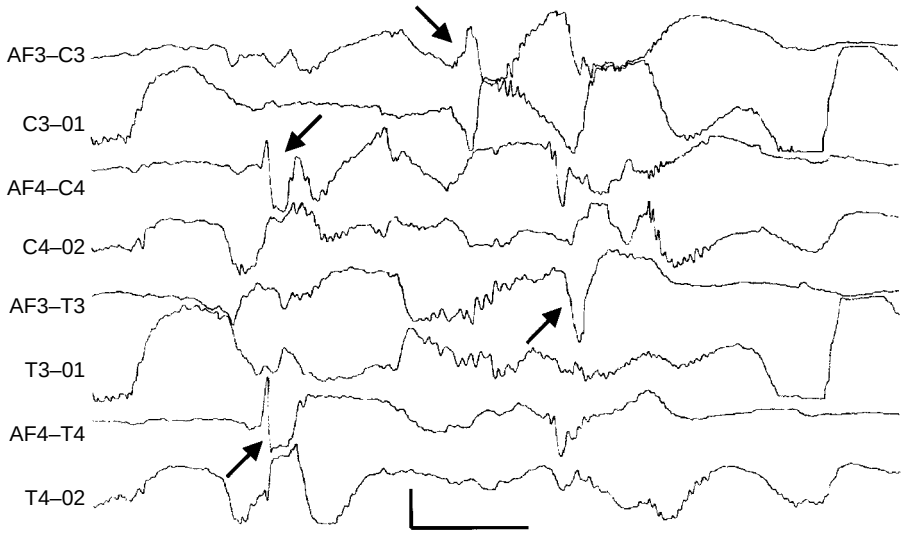


**Figure 1:** *A disorganized pattern. EEG at 32 weeks' postconceptional age. Waveforms of delta waves are distorted and unusual. Some abnormal sharp waves can be seen (arrows). Calibration: 100μV, 1 second.*

fourth weeks of life, and thereafter once every two weeks until discharge, using a 5MHz or 7.5MHz sector SONOS 2000 (Hewlett-Packard, Massachusetts, USA). Coronal and sagittal sections from the anterior fontanel were routinely examined. Cranial MRI was performed during late infancy to early childhood if an infant had an abnormal neurodevelopmental outcome.

PVL was suspected when multiple cystic changes in the deep white matter or periventricular echodensities lasting more than 2 weeks were observed. The diagnosis of PVL was confirmed by MRI during late infancy which revealed ventriculomegaly with irregular margins associated with periventricular high-intensity areas on $T_2$-weighted imaging. MRI was performed in all infants with cystic changes or periventricular echodensities. When infants with periventricular echodensities did not exhibit CP or characteristic MRI findings, PVL was ruled out.

IVH was diagnosed on the basis of ultrasonographic findings. In this study, IVH was divided into two groups: with and without parenchymal haemorrhage. Parenchymal haemorrhage was confirmed to be post-hemorrhagic porencephaly by cranial MRI during late infancy.

### NEURODEVELOPMENTAL OUTCOME

The infants were followed up every 3 months after discharge until at least 18 months corrected age (CA). Their neurodevelopmental outcome was determined on the basis of a complete neurological examination and the Tsumori–Inage developmental quotient (DQ; Tsumori–Inage 1961) between 12 and 18 months CA. When some abnormalities were present, follow-up was continued until at least 3 years CA. The final diagnosis of CP and MR was made at 2 and 3 years CA respectively. The intelligence quotient (IQ) was assessed by means of the Wechsler Preschool and Primary Scale of Intelligence (Wechsler 1974) or the Tanaka–Binet intelligence scale (Tanaka 1970) as appropriate.

Infants with spastic CP were grouped by type and severity of motor impairment as follows: mild diplegia, when an infant could walk with or without support; moderate diplegia, when an infant could sit with support but could not walk; severe diplegia, when an infant could not sit with support; and hemiplegia, when no impairment was observed on the contralateral side.

MR was defined as a DQ or IQ of less than 70. The severity of MR was defined as follows: mild MR when DQ/IQ was between 50 and 70; moderate MR when DQ/IQ was between 30 and 50; and severe MR when DQ/IQ was below 30. Some infants were not suitable for IQ assessment because of severe developmental delay. Such infants were categorized as having severe MR. Infants with a DQ/IQ of between 70 and 85 or with subtle motor impairment without spasticity were classified as borderline.

### STATISTICAL ANALYSIS

Statistical analysis between two groups was performed by means of the unpaired *t*-test for quantitative variables and Fisher's exact test for qualitative variables. Statistical significance was accepted at the level of $p<0.05$.

## Results

Disorganized and dysmature patterns were observed in 52 (28%) and 28 (15%) infants respectively. No chronic-stage EEG abnormalities were present in the other 103 infants (56%).

Follow-up was continued until 18 to 24 months CA in 95 infants who achieved normal development. Eighty-eight infants were followed up until 3 years CA or more because of suspected or confirmed neurological abnormalities. Seventy-nine infants were judged to have some neurological sequelae: 23 infants had both CP and MR, 25 had CP without MR, and 10 infants had MR without CP; 21 infants were judged to have borderline development.

### INFANTS WITH DISORGANIZED PATTERNS

PVL was observed in 31 infants (60%) and IVH in seven infants (13%) (Table I). Ultrasound showed no abnormalities

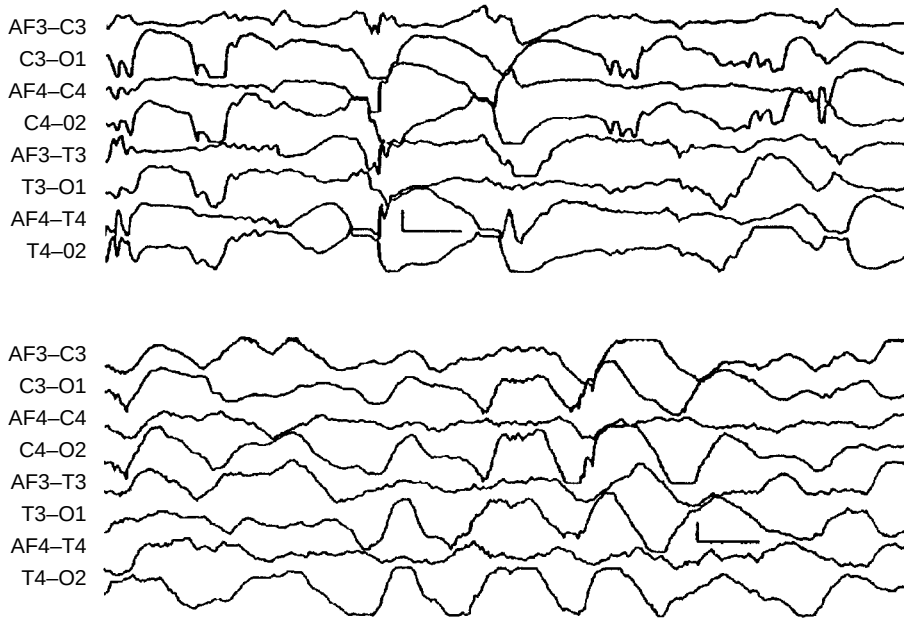


**Figure 2:** *Dysmature pattern. Top: EEG at 28 weeks' post-conceptional age. Infant was born after 26 weeks' gestation. Presence of high-voltage (>300μV) and extremely slow (<1Hz) delta activities can be seen which are characteristic of EEG at this post-conceptional age. In contrast, fast waves were attenuated, which is suggestive of mild acute-stage EEG abnormalities. Bottom: EEG of same infant at 32 weeks' post-conceptional age. High-voltage and extremely slow delta activities were still present. This represents a 2–4-week discrepancy from physiological EEG patterns at 32 weeks' post-conceptional age. Calibration: 100μV, 1 second.*

in fourteen infants (27%). Mild diplegia was observed in 13 (25%) infants, moderate diplegia in 11 (21%), severe diplegia in 13 (25%), and hemiplegia in two (4%). Twenty-six infants (50%) had normal cognitive development and five (10%) had borderline development. Mild MR was recognized in nine infants (17%), moderate MR in one (2%), and severe MR in 11 (21%).

CP was seen in all infants with PVL or IVH with parenchymal haemorrhage. Six of the 14 infants without ultrasonographic abnormalities also had CP. In contrast, no infants with IVH without parenchymal haemorrhage had CP.

Moderate or severe MR was seen exclusively in infants with severe diplegia. When the 13 infants with severe diplegia were excluded, 26 of the remaining 39 infants achieved normal cognitive development even though ultrasonographic abnormalities were present in 17 of the 26 infants.

#### INFANTS WITH DYSMATURE PATTERNS

IVH without parenchymal haemorrhage appeared in 11 of 28 infants and PVL in one (Table II). Sixteen infants had no ultrasonographic abnormalities. Mild diplegia was observed in two infants, moderate diplegia in one, and hemiplegia in two infants. Eight infants had normal cognitive development and 10 had borderline development. Mild MR was was seen in seven and moderate MR in three infants.

CP appeared in five of the 12 infants with ultrasonographic abnormalities, whereas no infants without ultrasonographic abnormalities had CP. Although the percentage of infants with moderate MR was small, only eight of the 28 infants achieved normal cognitive development. Even when limited to those without ultrasonographic abnormalities, only four of the 16 infants had normal cognitive development.

#### INFANTS WITHOUT CHRONIC-STAGE ABNORMALITIES

IVH was revealed in 19 infants (18%) and PVL in one infant (1%; Table III). Eighty-three infants (81%) had no ultrasonographic abnormalities. Mild diplegia was observed in only four infants. Ninety-five infants (92%) had normal cognitive development and six (6%) had borderline development. Mild MR was observed in two infants. No infant had moderate or severe diplegia, nor moderate or severe MR.

#### DISORGANIZED PATTERNS VERSUS DYSMATURE PATTERNS

Gestational age and birthweight were significantly lower in infants with dysmature patterns than in those with disorganized ones (Table IV). In contrast, the proportion of infants who were small-for-date was not different between the two groups. The percentages of those with ultrasonographic

**Table I: Infants with disorganized patterns (*n*=52)**

| *Ultrasound assessment* | *CP* | | *Type of CP* | | *Cognitive development* | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | *Normal* | *Borderline* | *Mild MR* | *Moderate MR* | *Severe MR* |
| PVL (*n*=31) | Yes | 31 | Mild DP | 9 | 8 | | 1 | | |
| | | | Moderate DP | 10 | 7 | | 3 | | |
| | | | Severe DP | 12 | | | 1 | 1 | 10 |
| IVH | | | | | | | | | |
| with PH (*n*=2) | Yes | 2 | Hemiplegia | 2 | 1 | | 1 | | |
| without PH (*n*=5) | No | 5 | | | 1 | 3 | 1 | | |
| Normal (*n*=14) | No | 8 | | | 6 | 2 | | | |
| | Yes | 6 | Mild DP | 4 | 3 | | 1 | | |
| | | | Moderate DP | 1 | | | 1 | | |
| | | | Severe DP | 1 | | | | | 1 |
| Total | | 52 | | 39 | 26 | 5 | | 1 | 11 |

CP, cerebral palsy; MR, mental retardation; PVL, periventricular leukomalacia; DP, diplegia; IVH, intraventricular hemorrhage; PH, parenchymal hemorrhage.

**Table II: Infants with dysmature patterns (*n*=28)**

| *Ultrasound assessment* | *CP* | | *Type of CP* | | *Cognitive development* | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | *Normal* | *Borderline* | *Mild MR* | *Moderate MR* | *Severe MR* |
| PVL (*n*=1) | Yes | 1 | Moderate DP | 1 | | | 1 | | |
| IVH without PH (*n*=11) | No | 7 | | | 2 | 3 | | 2 | |
| | Yes | 4 | Hemiplegia | 2 | 1 | | 1 | | |
| | | | Mild DP | 2 | 1 | | 1 | | |
| Normal (*n*=16) | No | 16 | | | 4 | 7 | 4 | 1 | |
| Total | | 28 | | 5 | 8 | 10 | 7 | 3 | |

CP, cerebral palsy; MR, mental retardation; PVL, periventricular leukomalacia; DP, diplegia; IVH, intraventricular hemorrhage; PH, parenchymal hemorrhage.

abnormalities and those with CP were significantly larger in infants with disorganized patterns than in those with dysmature ones. In contrast, the proportion of infants with normal cognitive development was lower in infants with dysmature patterns, although the difference was not statistically significant.

## Discussion

The present study has demonstrated that ultrasonographic findings and neurodevelopmental outcome in preterm infants are closely related to the type of chronic-stage EEG abnormalities, which reflect the mode of brain injury. Preterm infants are prone to suffer various kinds of brain insult at different times during the neonatal period. The process of development of brain lesions should differ according to the manner in which the brain insult occurs. The results of this study revealed the usefulness of chronic-stage EEG abnormalities for analyzing the evolutional changes in brain function that lead to organic lesions and/or neurological sequelae.

Infants with disorganized patterns were characterized by frequent development of PVL. About 60% of the infants with disorganized patterns developed PVL. This was rare among infants with dysmature patterns or normal EEGs. CP or ultrasonographic abnormalities were more frequent in infants with disorganized patterns than in those with dysmature ones. In contrast, normal cognitive development was more common in infants with disorganized patterns. Two-thirds of these infants achieved normal cognitive development when those with severe diplegia were excluded. These results suggest that disorganized patterns are closely related to destruction of the deep white matter with relative sparing of the cerebral cortex.

Our study revealed that dysmature patterns were correlated with cognitive impairment regardless of the ultrasonographic findings. Ultrasonographic abnormalities were not observed in the majority of infants with dysmature patterns, whereas IVH without parenchymal haemorrhage was relatively common. Despite the lack of severe ultrasonographic changes, MR or borderline development was more common in infants with dysmature patterns than in those with disorganized patterns. This is compatible with some previous studies which revealed that MRI or ultrasonographic abnormalities are not closely related to cognitive impairment (Biagioni et al. 1996, Skranes et al. 1998, Cooke and Abernethy 1999, Pinto-Martin et al. 1999). These results imply that dysmature patterns might be more closely related to cortical injury than to lesions in the white matter. Dysmature patterns could be a more sensitive marker of cognitive impairment in preterm infants than ultrasonographic abnormalities. Some authors have reported that dysmaturity of EEG activities is correlated with cystic PVL (Scher 1997, Biagioni et al. 2000). However, the concept of disorganized patterns was not introduced into such studies. In contrast, in our study disorganized patterns were more closely related to PVL than dysmature patterns. Further detailed studies will be necessary to clarify the relation between neurological outcome and types of EEG abnormalities in preterm infants.

It is noteworthy that gestational age and birthweight were lower in infants with dysmature patterns than in those with disorganized ones. This may be related to the fact that more immature infants are likely to suffer severe complications that can lead to prolonged hypoxic–ischemic stress or malnutrition. Such adverse factors might cause brain maturation delay which will be reflected by dysmature patterns.

**Table III: Infants without chronic-stage abnormalities ($n$=103)**

| *Ultrasound assessment* | *CP* | | *Type of CP* | | *Cognitive development* | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | *Normal* | *Borderline* | *Mild MR* | *Moderate MR* | *Severe MR* |
| PVL ($n$=1) | Yes | 1 | Mild DP | 1 | 1 | | | | |
| IVH | | | | | | | | | |
| with PH ($n$=1) | No | 1 | | | 1 | | | | |
| without PH ($n$=18) | No | 18 | | | 17 | 1 | | | |
| Normal ($n$=14) | No | 80 | | | 73 | 5 | 2 | | |
| | Yes | 3 | Mild DP | 3 | 3 | | | | |
| Total | | 103 | | 4 | 95 | 6 | 2 | | |

CP, cerebral palsy; MR, mental retardation; PVL, periventricular leukomalacia; DP, diplegia; IVH, intraventricular hemorrhage; PH, parenchymal hemorrhage.

**Table IV: Disorganized patterns versus dysmature patterns**

| *Parameter* | *Disorganized patterns (n=52)* | *Dysmature patterns (n=28)* | *Significance* |
|---|---|---|---|
| Gestational age (weeks) | 29 (2) | 28 (2) | $p<0.01$ |
| Birthweight (g) | 1321 (314) | 1086 (268) | $p<0.01$ |
| Small-for-date | 7 | 4 | *ns* |
| Cerebral palsy | 39 | 5 | $p<0.001$ |
| Normal cognitive development | 26 | 8 | *ns* |
| Ultrasonographic abnormalities | 38 | 12 | $p<0.05$ |

Values for gestational age and birthweight are shown as mean (SD). *ns*, not significant.

Ultrasonography demonstrated no abnormalities in 83% of the infants without chronic-stage EEG abnormalities. Ninety-two per cent of the infants without chronic-stage EEG abnormalities had achieved normal development. These results indicate that the absence of chronic-stage EEG abnormalities could be highly predictive of a normal developmental outcome.

One of the shortcomings of this study is that a considerable number of infants were lost to follow-up. Thirty-three infants (15%) failed to attend our hospital until 18 months CA. Ultrasonography and EEG were normal in most infants who were lost to follow-up except for those with congenital and/or chromosomal abnormalities. Twenty-seven of these infants attended our hospital within 12 months and were judged to have normal psychomotor development. For these reasons the percentage of infants with CP among the studied infants was very high. We consider that this fact does not reduce the value of this study because the main focus was on serial EEG findings in infants with neurological sequelae.

In conclusion, our results indicate that the type of chronic-stage EEG abnormalities is not only of significant prognostic value but is also useful for assessing the mode of brain injury in preterm infants.

*Accepted for publication 28th June 2002.*

**References**

Ballard J, Khoury J, Wedig K, Wang L, Eilers-Walsman B, Lipp R. (1991) New Ballard Score, expanded to include extremely premature infants. *Journal of Pediatrics* **119:** 417–23.

Baud O, d'Allest AM, Lacaze-Masmonteil T, Zupan V, Nedelcoux H, Boithias C, Delaveaucoupet J, Deban M. (1998) The early diagnosis of periventricular leukomalacia in premature infants with positive rolandic sharp waves on serial electroencephalography. *Journal of Pediatrics* **132:** 813–7.

Biagioni E, Bartalena L, Biver P, Pieri R, Cioni G. (1996) Electroencephalographic dysmaturity in preterm infants: a prognostic tool in the early postnatal period. *Neuropediatrics* **27:** 311–6.

Biagioni E, Bartalena L, Boldrini A, Pieri R, Cioni G. (2000) Electroencephalography in infants with periventricular leukomalacia: prognostic features at preterm and term age. *Journal of Child Neurology* **15:** 1–6.

Cooke RWI, Abernethy LJ. (1999) Cranial magnetic resonance imaging and school performance in very-low- birthweight infants in adolescence. *Archives of Disease in Childhood, Fetal and Neonatal Edition* **81:** F116–21.

Hayakawa F, Okumura A, Kato T, Kuno K, Watanabe K. (1997a) Disorganized patterns; chronic stage EEG abnormality of the late neonatal period following severely depressed EEG activities in early preterm infants. *Neuropediatrics* **28:** 272–5.

Hayakawa F, Okumura A, Kato T, Kuno K, Watanabe K. (1997b) Dysmature EEG pattern in EEGs of preterm infants with cognitive impairment: maturation arrest caused by prolonged mild CNS depression. *Brain and Development* **19:** 122–5.

Hayakawa F, Okumura A, Kato T, Kuno K, Watanabe K. (1999) Determination of timing of brain injury in preterm infants with periventricular leukomalacia with serial neonatal electroencephalography. *Pediatrics* **104:** 1077–81.

McMenamin JB, Shackelford GD,Volpe JJ. (1984) Outcome of neonatal intraventricular hemorrhage with periventricular echodense lesions. *Annals of Neurology* **15:** 285–90.

Novotny EJ, Tharp BR, Coen RW, Bejar R, Enzmann D, Vaucher YE. (1987) Positive rolandic sharp waves in the EEG of the premature infant. *Neurology* **37:** 1481–6.

Okumura A, Hayakawa F, Kato T, Kuno K, Watanabe K. (1999) Positive rolandic sharp waves in preterm infants with periventricular leukomalacia: their relation to background electroencephalographic abnormalities. *Neuropediatrics* **30:** 278–82.

Papile LN, Burnstein J, Burnstein R, Koffler H. (1978) Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birthweights less than 1500g. *The Journal of Pediatrics* **92:** 529–34.

Pinto-Martin JA, Whitaker AH, Feldman JF, Van Rossem R, Paneth N. (1999) Relation of cranial ultrasound abnormalities in low-birthweight infants to motor or cognitive performance at ages 2, 6, and 9 years. *Developmental Medicine & Child Neurology* **41:** 826–33.

Shankaran S, Slovis TL, Bedard MP, Poland RL. (1982) Sonographic classification of intracranial hemorrhage. A prognostic indicator of mortality, morbidity, and short-term neurologic outcome. *The Journal of Pediatrics* **100:** 469–75.

Skranes J, Vik T, Nilsen G, Smervik O, Andersson HW, Brubakk AM. (1998) Can cerebral MRI at age 1 year predict motor and intellectual outcomes in very-low-birthweight children? *Developmental Medicine & Child Neurology* **40:** 256–62.

Tanaka KK. (1970) *Taken Tanaka Binet Chino Kensabo.* Tokyo: Taken Shuppan. (In Japanese).

Tsumori M, Inage N. (1961) *Nyuyoji Seishin Hattatsu Shindanho. 0–3 Sai Made.* Tokyo: Dainihon Tosho. (In Japanese).

Scher MS. (1997) Neurophysiological assessment of brain function and maturation. II. A measure of brain dysmaturity in healthy preterm neonates. *Pediatric Neurology* **16:** 287–95.

Watanabe K. (1992) The neonatal electroencephalogram and sleep-cycle patterns. In: Eyre JA, editor. *The Neurophysiological Examination of the Newborn Infant. Clinics in Developmental Medicine No. 120.* London: Mac Keith Press. p 11–47.

Watanabe K, Hayakawa F, Okumura A. (1999) Neonatal EEG: a powerful tool in the assessment of brain damage in preterm infants. *Brain and Development* **21:** 361–72.

Wechsler D. (1974) *Preschool and Primary Scale of Intelligence.* New York: The Psychological Corporation.