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Prognostic value of sleep analysis in newborns with perinatal hypoxic brain injury

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The correlation between the findings of polygraphic sleep analysis and the late prognosis was studied in 37 full-term newborns after perinatal hypoxic-ischaemic brain injury, and in 9 healthy neonates. The relationship with a poor prognosis was significant if there was (i) a sleep cycle disturbance (decreased level of active sleep; persistence of quiet sleep-trace alternant pattern in the total cycle); (ii) immaturity in bioelectric brain maturation ≥ 4 weeks; (iii) depression of background activity. The correlation with favourable outcome was significant if (i) the EEG was normal; (ii) sleep spindles occurred.

The following findings were unrelated to prognosis: asymmetry, paroxysmal abnormalities, and reactivity of EEG to light or sound stimulation.

Assessment of the degree of perinatal hypoxic-ischaemic brain damage may have major therapeutic and prognostic implications. The neonatal EEG can be used to identify infants liable to future neurologic dysfunction [4, 10, 11].

The purpose of the present study was to investigate the correlation between the findings of polygraphic sleep analysis and the prognosis of full-term newborns with perinatal hypoxic-ischaemic brain injury.

Subjects and Methods

The subjects of the present study were full-term neonates with gestational ages ranging from 38 to 42 weeks and birthweights from 2.6 to 4.2 kg (mean 3.34 kg). Thirty-seven newborns suffered from perinatal hypoxia and 9 newborns were healthy. The newborns with perinatal hypoxic brain damage were selected according to the following criteria.

1. They had neurological signs and symptoms suggestive of encephalopathy during the neonatal period.

2. In their perinatal history signs of fetal distress were documented.

Infants with intracranial haemorrhage, bacterial meningitis and CNS malformation were excluded from the study.

Newborn infants with perinatal hypoxic brain damage were subdivided into groups of moderate and serious injury. The injury was considered serious if the newborn had deep coma (lack of corneal reflex, no response to pain) for more than 48 hours. 19 newborns were in the moderate group and 18 in the serious injury group.

52 daytime sleep-polygrams were recorded in 46 infants. The first record was prepared at mean age of 8.7 ± 5.1 days. The examination was repeated at two months of age in six newborns. An ORION 8 channel electroencephalograph was em-

ployed, using a paper speed of 30 mm/sec, with conventional gain and filter settings [1 11]. During the polygraphic studies, 4 EEG channels were used to monitor activity from the frontocentral and parieto-occipital regions (F_3–C_3, P_3–O_1, F_4–C_4, P_4–O_2). The electrodes were placed using the 10–20 system.

In addition, the following physiological data were recorded:

1. Horizontal ocular movements;
2. muscle activity by a surface electromyograph;
3. heart rate by ECG;
4. respiratory rate by means of a thermistor.
5. The behaviour of the newborn was documented on the polygraph paper.

Polygraphic recordings were performed during the interval between two feedings in the afternoon. Each recording period lasted 90 to 120 minutes. All records were analysed visually page by page (each page epoch = 20 sec). Each epoch was classified as active sleep (AS); quiet sleep (QS); indeterminate sleep (IS) or wakefulness (W) according to the conventional criteria [1].

The maturity of AS and QS patterns was determined on the basis of the data of Parmelee et al [5], Schulte et al [9] and Werner et al [11]. The morphology of quiet sleep and the occurrence of sleep spindles were observed.

The duration of AS and QS in a total sleep cycle was measured and compared in the three groups of newborns. Abnormalities of the recordings were also identified: abnormalities in background activity, asymmetry or sharp transients.

The next step was to determine the reactivity of EEG after light (stroboscope) and sound (slow and quick hand claps) stimulation.

Finally, the duration of apnoea in the different sleep states was observed.

The results of the three groups were compared.

All infants were subjected to a routine paediatric and special developmental neurological and psychological examination every three months. At the time of writing this paper the subjects range in age from 7 to 30 months. The neonatal EEG findings and the outcome of the newborns were compared.

The chi-square test was used to assess differences between the EEG findings and the outcome in the three groups.

Results

The outcome of the three groups of newborns is presented in Table I. The relationship between outcome and the degree of acute clinical signs and symptoms is obvious.

Bioelectric brain maturity in the AS and QS states of the investigated newborns was compared with their postmenstrual age at the time of the recordings (Table II). The EEG was considered immature if the difference between postmenstrual age at the recording and bioelectric brain maturation was four weeks or more. In the most serious cases the discrepancy was 12 weeks. In many cases a heterochronism was observed: the patterns were characteristic of two maturational levels occurring in AS and QS states within the same record. If heterochronism was found, the more immature was always the AS.

In healthy newborns the duration of active sleep was longer than that of quiet sleep in the total sleep cycle, while the proportion of AS state decreased in infants with perinatal hypoxic insult (Table III). In the three most severe cases only QS (tracé alternant pattern) was found during the sleep cycle.

TABLE I

Prognosis of the investigated control (C) and of the newborns with moderate (M) and serious (S) hypoxic brain injury

Outcome	Subjects (n)		
	C n=9	M n = 19	S n = 18
Normal without therapy	9	6	—
Normal after habilitation	—	12	11
Moderate cerebral palsy with or without slight mental retardation	—	1	4
Severe cerebral palsy with mental retardation and epilepsy	—	—	3

Statistical significance (chi-square test) among the three groups, $p < 0.001$.

TABLE II

Bioelectric brain maturation and postmenstrual age of the control (C) newborns, and of the newborns with moderate (M) and serious (S) hypoxic brain injury

Bioelectric brain maturation and postmenstrual age at recording	Subjects		
	C n = 9	M n = 19	S n = 18
Equal (in QS and AS states)	9	10	4
Retardation of bioelectric brain maturation ≥ 4 weeks	—	5	7
Heterochronism AS/QS	—	4/0	7/3

Heterochronism = patterns characteristic of two maturational levels occurring in AS and QS states, discrepancy ≥ 4 weeks
AS/QS = number of infants with immature EEG in AS/QS states
Statistical significance (chi-square test) among the three groups, $p < 0.01$.

TABLE III

Proportion of AS/QS states in the total sleep cycle in the control newborns (C), and in the newborns with moderate (M) and serious (S) hypoxic brain injury

Duration of state	Subjects		
	C n = 9	M n = 19	S n = 18
AS > QS	9	12	9
AS < QS	—	7	6
Only QS was found	—	—	3

Statistical significance (chi-square test) among the three groups, $p < 0.05$.

Table IV

Background activity and sharp transients in the EEG of control newborns (C) and of the newborns with moderate (M) and serious (S) hypoxic brain injury

EEG findings	Subjects		
	C n = 9	M n = 19	S n = 18
Normal background activity	8	15	10
Depressed EEG			
burst suppression	—	—	3
low voltage	—	—	2
Asymmetry	1	4	3
Sharp transients	4	10	8

Statistical significance (chi-square test) among the three groups of background activity: $p < 0.05$, of sharp transients: NS.

A significant difference in background activity could be observed between the three investigated groups. Burst suppression pattern or low voltage EEG was found only in the seriously asphyxiated newborns. Asymmetry and sharp transients were detected in all the three groups (Table IV).

No response to low frequency photic stimulation was obtained in the majority of newborns with and without perinatal hypoxic brain damage. A frequency of 15–25 cycles/sec elicited a reaction in half of the newborns, regardless of the fact whether or not they had a brain injury.

Auditory stimulation by slow and quick hand claps elicited a response in every subject except three infants with nonreactive low voltage EEG. In many cases a pattern similar to K-complexes appeared after the stimulation, and signs of habituation and dishabituation were also observed.

The duration of the breathing interval in the healthy newborns was always less than 3 sec, also during active sleep. In the group of moderate asphyxia, 9 out of 19 infants, and in the group with serious asphyxia, 15 of 19 newborns had apnoeas longer than 3 sec during AS states.

The examinations were repeated in three infants from the moderate, and in three from the serious group. In the newborns with moderate hypoxic brain injury the seizure pattern persisted even at two months of age. At present these children are 7, 18, and 30 months old, respectively, and they have no symptoms of epilepsy. Of the three infants from the serious group who exhibited only a tracé alternant pattern in the total sleep cycle during the neonatal period, in two cases the abnormality was unchanged at the age of two and a half months. The third infant had

TABLE V

Correlation between EEG and prognosis

Findings associated with favourable prognosis:	
normal EEG	$0.05 > p < 0.1$
occurrence of sleep spindles	$p < 0.05$
Findings associated with unfavourable prognosis:	
depressed background activity	$p < 0.05$
QS > AS in the sleep cycle	$p < 0.05$
immaturity ≥ 4 weeks in EEG	$p < 0.01$
apnoea longer than 3 sec	$p < 0.05$
TA predominance during the total sleep cycles	$p < 0.001$
Findings failing to predict prognosis:	
asymmetry	
sharp transients	
non-reactivity to light or sound stimulation (except total lack of reactivity and lability of EEG)	

developed AS by this time but in quiet sleep the tracé alternant could still be observed. One of the infants with disorganization of the sleep cycle at four months of age fell asleep during the examination. During sleep high voltage slow patterns predominated but bursts reminiscent of tracé alternant (TA) were periodically visible in the record. The EEG findings and their correlation with the prognosis can be summarized as in Table V.

Discussion

The present study has shown that neonatal sleep analysis is a good prognostic indicator after perinatal hypoxic insults. Our prospective examinations corroborated the data in the literature in that the depression of background EEG had a high prognostic value, whereas an asymmetry and paroxysmal EEG abnormalities did not predict the outcome [**4**, **7**, **10**, **11**].

We found that the disturbances of the sleep cycle also correlated with the prognosis. When the background activity was depressed, the sleep cycles were always disturbed.

In contrast with the experience of Watanabe et al (10), we found that the duration of quiet sleep increased after perinatal hypoxic brain injury. This finding corresponds to the observations in adult patients with traumatic brain injury [6] and to some experimental findings [8].

The persistence of the QS state (tracé alternant pattern) during the total sleep cycle seems to be an unfavourable prognostic sign. The retardation in biolectric brain maturation after neonatal hypoxic brain damage agree well with the findings of Karch et al. [3]. They interpreted the immature bioelectric brain activity occurring in patients with perinatal hypoxia as an unspecific response to functional and structural changes in the CNS. As to respiration, Haidmayer and Kurz [2] found considerably prolonged apnoea periods in high risk infants. Our experience was the same. The long apnoea of newborns with hypoxic brain injury appeared always during active sleep.

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