Sleep, 20(5):323–333

Sleep in Children

Sleep Ontogenesis Revisited: A Longitudinal 24-Hour Home Polygraphic Study on 15 Normal Infants During the First Two Years of Life

*Jacqueline Louis, *Christine Cannard, †Hélène Bastuji and *Marie-Josèphe Challamel

**INSERM U.52, Service d'Explorations Fonctionnelles Neurologiques, Centre Hospitalier Lyon-Sud, Pierre Bénite, France; and †Service de Neurologie Fonctionnelle et d' Epileptologie, Hôpital Neurologique, Lyon, France*

Summary: The sleep organization of 15 normal infants (seven boys, eight girls) was studied at their homes during six 24-hour periods, i.e. at 3, 6, 9, 12, 18, and 24 months of age, using the Oxford Medical System. Sleep states and stages were scored visually at 30-second intervals, according to Rechtschaffen and Kales' criteria, adapted for children by Guilleminault. All sleep parameters were analyzed for the entire 24-hour period, i.e. during both the nocturnal and the diurnal part of the nycthemere. The results showed a continuous decrease in total sleep time, rapid eye movement (REM) sleep, and indeterminate sleep, and also an increase in waking time, quiet sleep, and stages 1 and 2 sleep. Except for slow-wave sleep, which remained very stable for the different ages, analysis of variance applied to the data showed clear age and day–night effects on sleep ontogenesis. Modifications with age were more precocious and more pronounced for the diurnal part of the nycthemere, especially as regards REM sleep. For the nocturnal part, there was a significant increase in sleep efficiency and in the length of the REM period after 12 months of age, while total sleep duration and number of awakenings decreased. In addition to normative data for clinical use, this study provides three new interesting results related to the maturation of sleep mechanisms and functions: 1) the high stability of the percentage of slow-wave sleep along these 2 years, 2) the presence (from 12 months of age) of a stage 2/REM sleep ratio equal to one, and a sleep change occuring earlier, during the diurnal rather than the nocturnal part of the nycthemere. The first two points could be regarded as indexes of sleep maturation reflecting developmental and neurophysiological changes in central nervous system structures. The third point underlines the importance of the circadian rhythm and the concept of "experience" in the maturation of sleep. **Key Words:** Sleep development—Maturation—Ontogenesis—Infants—EEG.

Studies on sleep in infants have tended to investigate age-related changes in the organization of the two basic rhythmic sleep processes, i.e. rapid eye movement (REM) and nonrapid eye movement (NREM), which are customarily described in terms of active sleep (AS) and quiet sleep (QS), respectively. In most previous studies, polygraphic data were obtained during the night (1–5) or day (6–15), were of either short (1,6–14) or long duration (2–5), and, essentially, were performed in hospital environments during the first few months of life. Only two such studies were based on 24-hour polygraphic recordings (16,17). Other findings confirm these previous studies using cross-sectional, or a combination of cross-sectional and longitudinal, recordings based on visual and/or actigraphic observations (18,19). The main results on maturational changes in sleep–wake organization may be summarized as follows: 1) an increase in waking time, associated with a decrease in REM sleep and an increase in QS (3–5,8,12–17), and 2) a development of circadian sleep rhythm synchronized with the 24-hour light–dark cycle (18–24).

However, in agreement with Crowell et al. (1982), little is known about the precise evolution of the specific electroencephalograph (EEG) patterns, designated as stages 1, 2, and 3/4 sleep, that occur sequentially during NREM sleep, and less still is known about the reciprocal evolution and/or interaction of the different sleep stages (15). These two points are very important

Accepted for publication January 1996.

Address correspondence and reprint requests to Jacqueline Louis, INSERM U.52, Service d'Explorations Fonctionnelles Neurologiques, Centre Hospitalier Lyon-Sud, 69 495 Pierre Bénite Cedex, France.

in determining the following: 1) the point when infant EEG sleep patterns reach those of adulthood, and 2) the mutual organization of these patterns to give the temporal and sequential sleep structure of adults. Given that infant sleep patterns are not evaluated by the same rules as for adults, only the first point is treated in most studies (2,3,5,15,16). A few authors (25,26) have focused their research on the second point, which essentially concerns the maturation of sleep mechanisms and functions. However, these studies are affected by methodological problems, namely the fact that the data were obtained in hospital environments from different infants at different ages and thus did not allow the interactive evolution of the different sleep stages to be fully examined.

The goal of the present study is to describe the successive steps in sleep ontogenesis, using a more precise methodology involving the following: 1) longitudinal recordings of normal infants for 24-hour periods spaced out over the first 2 years of life in order to limit interindividual variations; 2) observations carried out in the home, given that a laboratory environment affects infant sleep patterns (10,27), 3) scoring of sleep stages using a modified form of the usual criteria for adults (28), and 4) comparative data analysis for the nocturnal and diurnal parts of the nycthemere, in order to evaluate the influence of circadian and ultradian rhythms on sleep maturation. The development of infant sleep toward adult sleep structure will be discussed, as well as the different steps of this process, with reference to the maturation of the central nervous system (CNS). It is hoped that this study will contribute to the understanding of the maturation of sleep mechanisms and will give normative data for clinical use.

MATERIALS AND METHODS

Subjects

Subjects were 15 healthy infants (seven boys, eight girls) selected according to the following criteria: no family history of neurological disease, normal pregnancy and birth, normal postnatal physical and neurological examination, and nonmedicated status. All infants were full-term, with a mean gestational age of 39 ± 1 week, a birth weight of 3.6 ± 0.5 kg, and a height of 51 ± 2 cm; the mean Apgar score at 5 minutes was 9.5 ± 0.8. All the infants were Caucasian and from middle- or upper-class families, as determined by parental education and occupation. They were living with both biological parents in the city of Lyon, France. In six families (for four boys and two girls), the mothers were full-time housewives. Birth order was first (four), second (five), and third (four). Informed consent for recording was obtained from each family.

Sleep records

All the infants were recorded for six 24-hour periods, i.e. at 3, 6, 9, 12, 18, and 24 months of age. They were prepared at home in the late afternoon, between 1800 hours and 2000 hours by one of us, always the same person. Electroencephalograph electrodes were placed on one hemiscalp according to the international 10–20 system (29), with bipolar montages as follows: F3–C3, C3–T3, T3–O1, plus one electrooculogram (EOG), one submental electromyogram (EMG), one electrocardiogram (EKG), and one thoracic respirogram channel. The hemiscalp, always the same one for each particular child throughout, was chosen according to sleeping position preference. Oxford Medilog 9000 eight-channel tape recorders (Oxford Medical System, U.K.) were used to make the recordings, with TDK or Oxford 120 minute cassettes. In order to be sure that the sleep–wake patterns recorded over the 24-hour periods were representative, the parents were asked to complete a sleep log for some days before and after each recording.

Sleep analysis

The results were scored visually by two persons, directly from the screen of the Oxford Medilog 9000 display unit, at 20× the recording speed, which corresponded to a 15-mm paper speed. The reliability of the coding system was assessed by having two training observers code 45% of recordings simultaneously but independently. Percentage agreement was 87%. We scored the different sleep stages at 30-second intervals, according to Rechtschaffen and Kales' criteria (28), adapted for children by Guilleminault (30). These criteria distinguish six sleep states and stages: wakefulness (W), REM sleep, indeterminate sleep (IS), stage 1 (S1), stage 2 (S2), and stages 3/4, which are treated together as slow-wave sleep (SWS). Stage 1 is defined by a 4–5-Hz occipital or diffuse EEG rhythm, closed eyes, possible slow eye movements, and no major movement artifacts. Indeterminate sleep corresponds to periods during which the criteria for W, or for other sleep stages, are not fulfilled. Figure 1 gives an example of a polygraphic sleep recording at 3 months of age for different sleep stages.

Data analysis

Data were analyzed during both the nocturnal and diurnal periods of the nycthemere, delimited by the

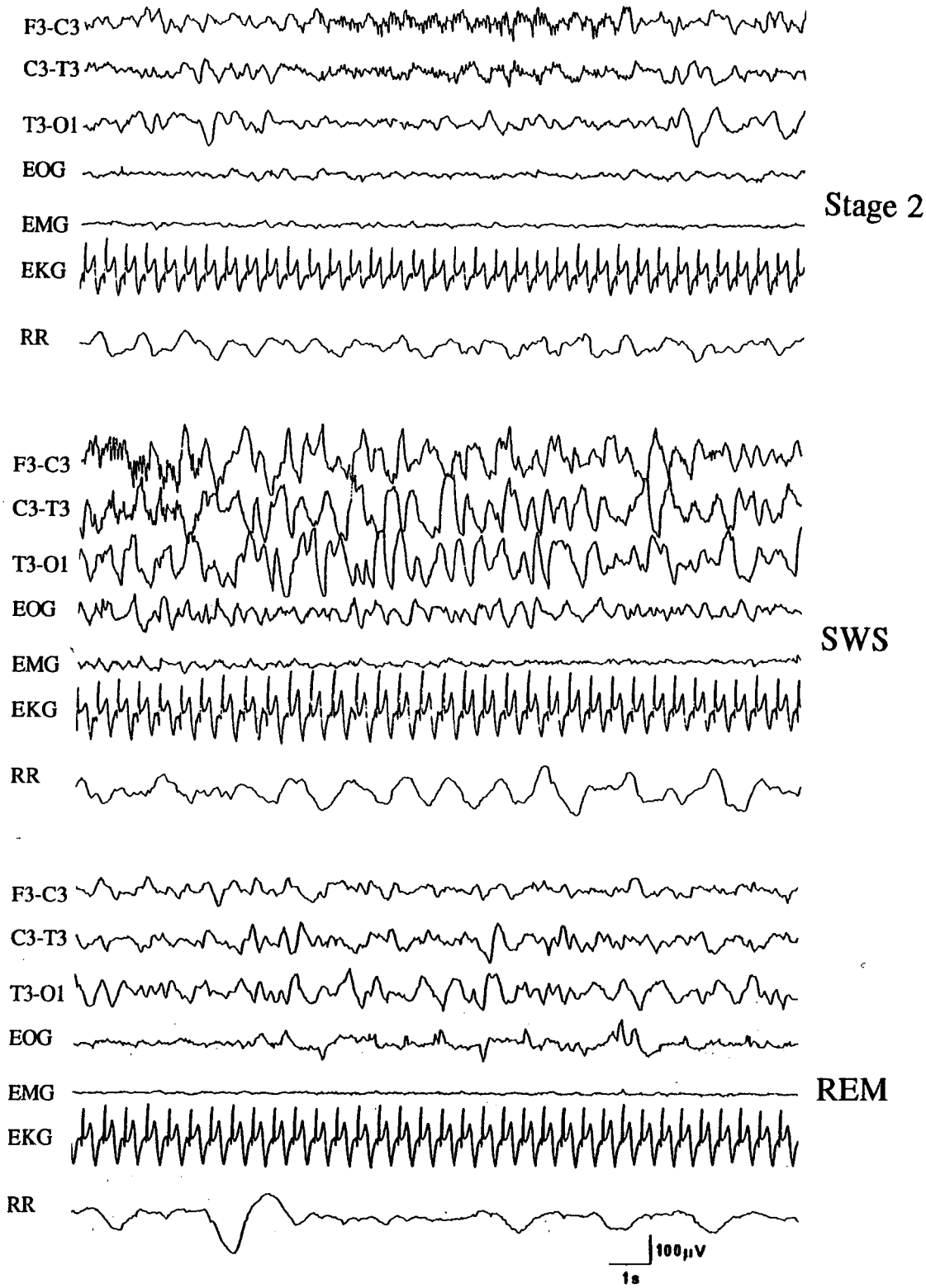


FIG. 1 Electroencephalograph (EEG) recordings representative of stage 2 sleep, slow-wave sleep (SWS), and rapid eye movement (REM) sleep in an infant at 3 months of age.

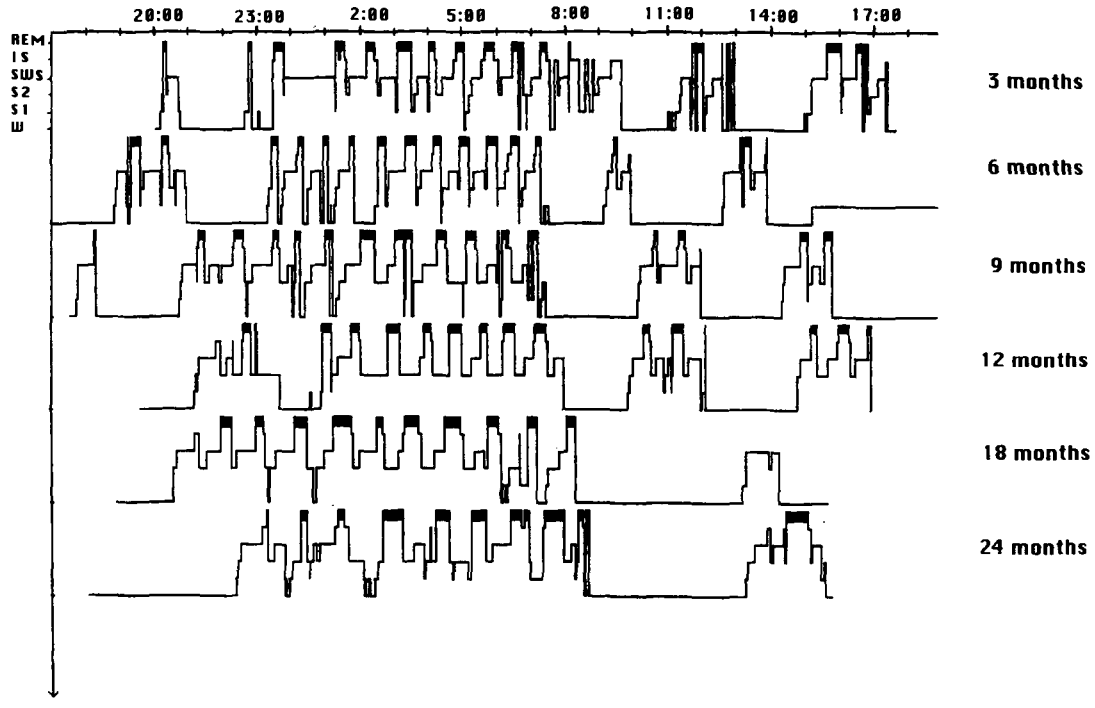


FIG 2. Twenty-four-hour hypnograms for a particular child between 3 months and 2 years of age.

lights-off and lights-on given by the parents. Parameters were defined as follows:

1) Total recording time (TRT) = for night (nighttime duration), the time between lights-off and lights-on, and for day (daytime duration), the remaining periods.

2) Sleep efficiency index (SEI) = total sleep time (TST) as a fraction of TRT.

3) Number of awakenings >1 minute.

4) Duration (minutes) and percentage of TST for W, S1, S2, SWS, IS, and REM sleep (REMS).

5) Number of stage transitions (phase shifts).

For easier comparison with published results, only S1 and IS were defined as transitional sleep (TS) but were treated separately. For the same reason, TS, S2, and SWS were combined as NREM sleep. Finally, in line with Sterman et al.'s definition (2), S2 and SWS were defined as QS. However, all these sleep stages were treated separately to analyze the evolution with age of each of them. For the night, the following parameters were also calculated:

1) Sleep latency = time from lights-off to the first continuous period of sleep.

2) REMS latency = time from sleep onset to the first appearance of a REM episode.

3) REMS stability = ratio of uninterrupted REM sleep to total REM sleep.

4) Duration of REM sleep episodes.

5) Number of sleep onsets in REM mode.

6) Percentage of body movements during REM sleep.

7) REM sleep cycle, defined as the mean interval between the middle of successive REM sleep episodes.

The evolution of sleep parameters with age and/or the two parts of the nycthemere was tested by one- or two-way analysis of variance for repeated measures (ANOVA). The multiple range test (*F* of Scheffé) was then carried out for age comparison and regression analysis for the time evolution of QS and REM sleep.

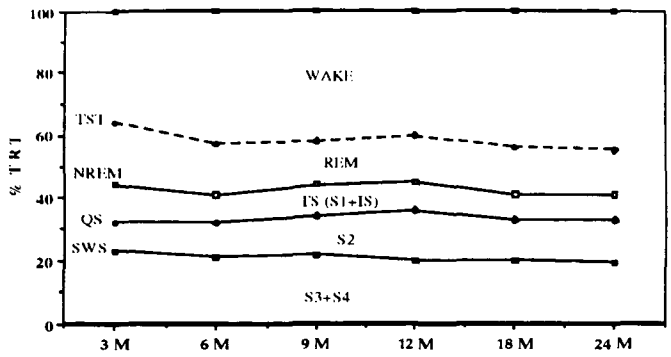
RESULTS

Ninety 24-hour recordings were performed, i.e. six recordings for each of the 15 infants. Five recordings were nonutilizable due to either technical problems, skin allergies, or changes of residence. Finally, a total of 85 recordings were analyzed.

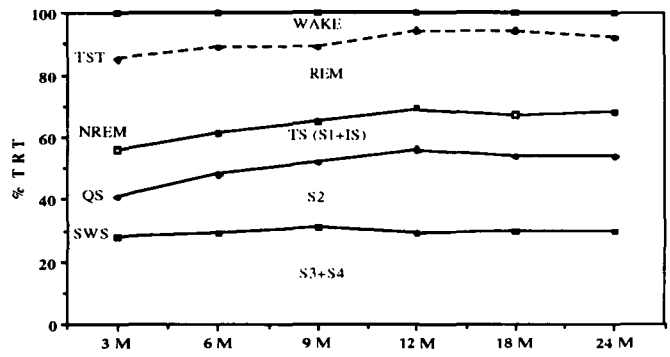
24-hour sleep evolution

Figure 2 shows the different hypnograms obtained for a particular child in the study. The mean duration of TST decreased from 14.5 ± 1.03 hours at 3 months to 11 ± 1.54 hours at 2 years. This was mainly due to a decrease in diurnal naps (from 3 ± 1 hours at 6 months to 2 ± 0.5 hours at 1 year and 1 ± 0 hours at 2 years).

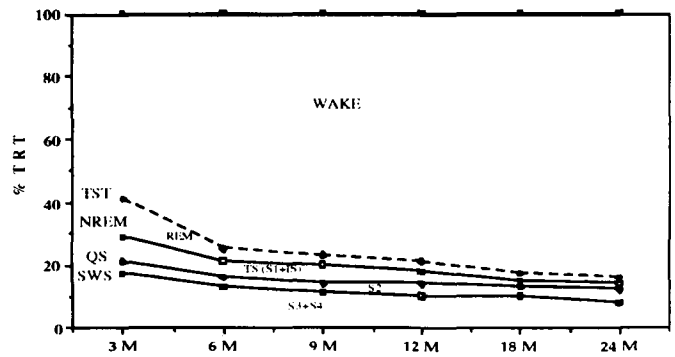
In the evolution of the different sleep states as per-



a: 24 H



b: NIGHT



c: DAY

FIG 3. Proportion of sleep states during the 24-hour period and during the two parts of the nycthemere (night, day). Wake, total sleep time (TST), sleep states, and stages as percentages of total recording time (TRT) are presented for each age.

centages of TRT (Fig. 3a), the decrease of REM sleep was especially strong between 3 and 6 months, when NREM sleep represented a relatively constant proportion of the 24-hour period. Within this period, S2 increased and TS decreased, whereas SWS remained stable. While TST decreased, QS as a percentage of TST increased significantly throughout the first 2 years of life (Fig. 4) ($y = 1.984x + 51.22$; $r^2 = 0.297$; $p \leq 0.001$), while the percentage of REM decreased significantly (Fig. 4) ($y = -1.447x + 31.745$; $r^2 = 0.26$; $p \leq 0.001$). Except for SWS (Fig. 5), ANOVA showed a clear effect of age on sleep evolution ($F = 6.19$, 9.83, 35.40, and 10.64 for S1, S2, IS, and REM sleep, respectively; $p \leq 0.001$) (Fig. 5). These age-related modifications were particularly marked after either 6 months (S1, IS, REM), or 9 months (S2) ($p \leq 0.01$, multiple range test). Sleep stage 2 and IS developed in opposite ways between 3 and 24 months (+12%, −12%, respectively) (Fig. 5).

Nocturnal organization

As we can see in Table 1 total TRT during the night was stable regardless of age. Lights-off ranged from

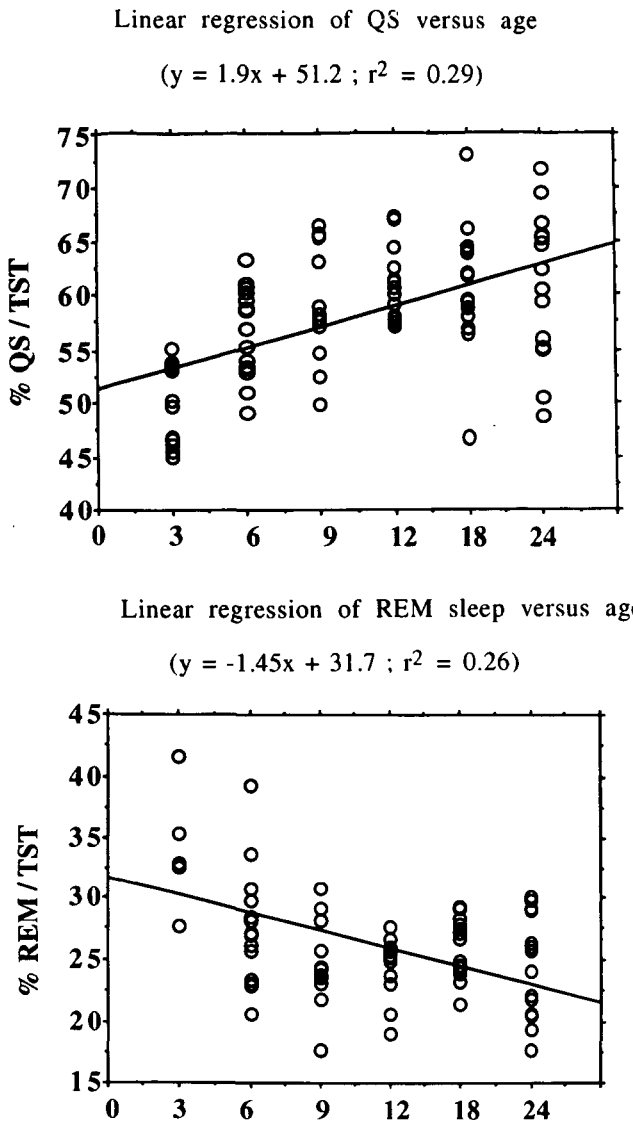


FIG 4. Linear regression analysis versus age for quiet sleep (QS) and rapid eye movement (REM) sleep as percentages of total sleep time (TST) over the 24-hour period.

2030 hours ± 1.5 hours at 3 months of age to 2100 hours ± 1 hour at 24 months of age, with a mean value equal to 2030 hours ± 1 hour. In the same way, lights-on ranged from 0800 hours ± 1 hour to 0730 hours ± 1 hour with a mean value equal to 0730 hours ± 1 hour.

During the night, waking state decreased and TST increased (Fig. 3b). Increases in NREM and QS were essentially due to an increase in S2, given that the percentage of SWS did not change during this part of the nycthemere.

Analysis of variance (Table 1) showed a clear influence of age on all sleep parameters other than SWS ($p \leq 0.001$ for most of the parameters). The duration and number of awakenings decreased significantly with age. The rise between 3 and 24 months of age in the percentage of S1 and S2 was, respectively, 11% and 10%, while the decline in IS was 13% and in REM sleep was only 8%.

This decline in REM sleep can be explained by a significant decrease in the number of REM sleep episodes (ANOVA; $p \leq 0.001$) without any notable change in their mean duration until 24 months of age. There was no modification of sleep latency with age. Rapid eye movement sleep latency increased significantly from 12 months of age, while the number of REM sleep onsets decreased rapidly between 3 and 6 months of age. The duration of the sleep cycle increased slowly, with a significant difference from 9 months of age but without reaching adult values by 2 years of age.

Several of the REM sleep parameters studied were significantly modified from 6 months of age (number of episodes, number of REM sleep onsets, and percentage of body movements), but the percentage of REM sleep changed significantly only at 9 months of age. The multiple range test showed that significant modifications with age of the other states and stages occurred essentially at 9 or 12 months of age. At these ages, it was important to notice that percentages of S2 and REM sleep reached similar values. Finally, it was only at 12 months of age that sleep efficiency and periodicity increased significantly, with a decrease in the duration and number of awakenings.

Diurnal organization

It was during the diurnal period that sleep states and stages underwent the largest modifications (Fig. 3c). There was an overall increase in the percentage of waking periods, which became longer but fewer. The percentages of TST, NREM sleep, QS, and SWS decreased significantly with age (ANOVA; $p \leq 0.001$ for all states and stages) (Table 2). The multiple range test (F of Scheffé), showed that the decline in the percentage of IS and REM sleep occurred from 6 months of age. The rise in the percentages of W and S1 occurred, respectively, at 6 and 9 months of age and only at 24 months for S2.

Comparison between nocturnal and diurnal organization

The duration of diurnal sleep in minutes, or expressed as a percentage of TST, is different from the nocturnal duration (Fig. 6). Two-way variance analysis showed a clear effect of the day–night factor on the development of the different sleep stages other than IS (F = 29.29, 78.13, 59.08, and 370.56 for S1, S2, SWS, and REM sleep, respectively; $p \leq 0.001$). Two-factor interaction analysis showed that both age and day–

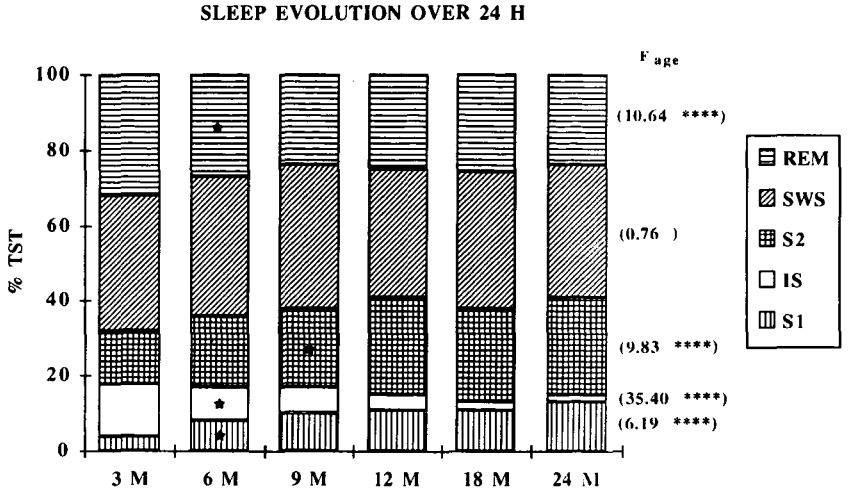


FIG 5. Evolution with age of the different sleep states and stages as percentages of total sleep time (TST) over the 24-h period. The values of the *F* of Snedecor (ANOVA repeated measures) are noted for each sleep stage. ****p ≤ 0.001; * p ≤ 0.01 (multiple range test).

TABLE 1. *Nocturnal sleep variables as a function of age*

	3 months	6 months	9 months	12 months	18 months	24 months	F_{age} (df = 5)	p values
Night time duration	697 ± 74	640 ± 73	683 ± 65	645 ± 55	647 ± 47	618 ± 81		
TST (minutes)	588 ± 81	571 ± 67	611 ± 52	605 ± 50	608 ± 56	571 ± 79		
% TRT (SEI)	84 ± 8	89 ± 6	90 ± 7	94 ± 6[a]	94 ± 6[a]	93 ± 6[a]	5.11	<0.001
Sleep states and stages								
W (minutes)	109 ± 53	69 ± 41	72 ± 54	41 ± 46	39 ± 38	43 ± 41		
% TRT	16 ± 7	11 ± 6	9 ± 6	6 ± 6[a]	6 ± 5[a]	7 ± 6[a]	5.18	<0.001
Number >1 minute	8 ± 4	6 ± 4	7 ± 4	5 ± 3	3 ± 2[a]	5 ± 3	4.57	0.0012
QS (minute)	287 ± 42	312 ± 26	358 ± 29	366 ± 31	353 ± 32	335 ± 52		
% TST	49 ± 4	55 ± 3[a]	59 ± 5[a]	61 ± 4[a]	59 ± 7[a]	59 ± 7[a]	9.88	<0.001
S1 (minute)	14 ± 14	35 ± 31	46 ± 23	55 ± 26	67 ± 43	74 ± 49		
% TST	2 ± 2	6 ± 5	8 ± 3	9 ± 4	11 ± 6[a]	13 ± 8[a]	7.17	<0.001
S2 (minute)	91 ± 36	123 ± 57	144 ± 37	176 ± 49	159 ± 45	149 ± 45		
%TST	16 ± 5	20 ± 9	23 ± 6	29 ± 8[a]	26 ± 7[a]	26 ± 8[a]	7.06	<0.001
SWS (minute)	196 ± 38	189 ± 52	214 ± 31	190 ± 40	194 ± 40	186 ± 49		
%TST	33 ± 5	33 ± 8	35 ± 4	31 ± 6	32 ± 7	33 ± 7	0.41	0.830
IS (minute)	88 ± 28	49 ± 30	46 ± 25	26 ± 23	15 ± 20	12 ± 18		
% TST	15 ± 4	9 ± 5[a]	7 ± 4[a]	4 ± 4[a]	3 ± 3[abc]	2 ± 3[abc]	31.46	<0.001
REMS (minute)	199 ± 46	176 ± 36	164 ± 39	160 ± 22	173 ± 28	150 ± 36		
% TST	34 ± 6	31 ± 5	27 ± 4[a]	26 ± 3[a]	28 ± 2[a]	26 ± 5[a]	7.91	<0.001
Sleep latency (minute)	15 ± 18	18 ± 10	13 ± 11	10 ± 7	10 ± 8	15 ± 13	0.83	0.535
Phase shifts (number)	76 ± 15	64 ± 14	69 ± 14	60 ± 11	52 ± 11[ac]	55 ± 13[a]	7.85	<0.001
REM-sleep parameters								
REMS episodes (number)	12 ± 2	11 ± 1[a]	11 ± 2[a]	9 ± 1[a]	9 ± 1[ab]	8 ± 1[abc]	22.15	<0.001
REMS duration (minute)	18 ± 4	17 ± 4	16 ± 3	18 ± 2	19 ± 3	20 ± 4[c]	3.61	0.006
REMS latency (minute)	15 ± 20	38 ± 23	36 ± 8	55 ± 26[a]	53 ± 22[a]	70 ± 29[abc]	9.63	<0.001
REMS onset (number)	3 ± 2	1 ± 1[a]	1 ± 1[a]	0.5 ± 1[a]	0.4 ± 1.3[a]	1 ± 1[a]	8.21	<0.001
REMS cycle (minute)	55 ± 6	56 ± 4	65 ± 12[a]	66 ± 5[ab]	69 ± 4[ab]	75 ± 9[abc]	18.30	<0.001
Stability index (%)	90 ± 6	94 ± 3	93 ± 5	93 ± 3	96 ± 4[a]	94 ± 6	2.67	0.028
Body movement (%)	7 ± 2	3 ± 2[a]	3 ± 1[a]	3 ± 2[a]	3 ± 2[a]	3 ± 1[a]	15.39	<0.001
Number	14	15	13	15	14	14		

TRT, total recording time; QS, quiet sleep; TST, total sleep time; S1, stage 1 sleep; S2, stage 2 sleep; SWS, slow-wave sleep; IS, indeterminate sleep; REMS, rapid eye movement sleep.

Analysis of variance for repeated measures, *F* of Snedecor (df = 5), and p values. *F* of Scheffé was used to establish at which age the modification was significant.

[a] Significant difference between 3 months and the other ages.
[b] Significant difference between 6 months and the other ages.
[c] Significant difference between 9 months and the other ages.

TABLE 2. *Diurnal sleep variables as a function of age*

	3 months	6 months	9 months	12 months	18 months	24 months	F_{age} (df = 5)	p values
Daytime duration	650 ± 89	668 ± 170	640 ± 217	632 ± 106	635 ± 105	672 ± 90		
TST (minute)	269 ± 70	176 ± 67	147 ± 68	139 ± 64	110 ± 46	110 ± 29		
% TRT	41 ± 6	26 ± 6[a]	24 ± 10[a]	21 ± 8[a]	17 ± 5[ab]	17 ± 5[ab]	26.71	<0.001
W (minute)	381 ± 45	492 ± 129	493 ± 178	493 ± 91	525 ± 75	550 ± 92		
% TRT	59 ± 6	74 ± 6[a]	74 ± 10[a]	78 ± 8[a]	83 ± 5[a]	83 ± 5[abc]	25.91	<0.001
Number >1 minute	4 ± 1	4 ± 1	4 ± 1	3 ± 0	2 ± 0[abc]	2 ± 1[abc]	12.56	<0.001
QS (minute)	141 ± 42	110 ± 47	92 ± 47	89 ± 36	82 ± 28	78 ± 20		
% TST	53 ± 7	62 ± 8	62 ± 8	67 ± 9[a]	78 ± 12[abc]	72 ± 9[a]	13.56	<0.001
S1 (minute)	16 ± 14	26 ± 17	28 ± 18	25 ± 18	14 ± 11	16 ± 9		
% TST	6 ± 4	15 ± 11	19 ± 10[a]	18 ± 9[a]	12 ± 7	15 ± 8	6.28	<0.001
S2 (minute)	29 ± 13	20 ± 23	19 ± 13	27 ± 19	19 ± 16	26 ± 18		
% TST	11 ± 5	11 ± 8	13 ± 8	19 ± 7	17 ± 10	24 ± 15[ab]	5.51	<0.001
SWS (minute)	112 ± 45	90 ± 33	73 ± 39	62 ± 23	63 ± 20	52 ± 19		
% TST	42 ± 10	51 ± 8	49 ± 9	45 ± 13	57 ± 18[ac]	47 ± 13	6.20	<0.001
IS (minute)	36 ± 26	11 ± 8	10 ± 8	3 ± 5	1 ± 1.5	1 ± 4		
% TST	14 ± 8	6 ± 5[a]	7 ± 4[a]	2 ± 3[a]	1 ± 1[ab]	1 ± 3[a]	16.10	<0.001
REM (minute)	75 ± 17	29 ± 15	20 ± 18	22 ± 18	14 ± 14	15 ± 10		
% TST	28 ± 5	16 ± 5[a]	13 ± 7[a]	16 ± 8[a]	13 ± 9[a]	13 ± 7[a]	11.33	<0.001
Phase shifts (number)	44 ± 14	26 ± 9[a]	23 ± 10[a]	19 ± 10[a]	14 ± 6[ab]	14 ± 7[ab]	19.60	<0.001
Number	14	15	13	14	14	12		

W, wakefulness; for definitions of other acronyms, see Table 1.

Analysis of variance for repeated measures, F of Snedecor (df = 5), and p values. F of Scheffé was used to establish at which age the modification was significant.

[a] Significant difference between 3 months and the other ages.

[b] Significant difference between 6 months and the other ages.

[c] Significant difference between 9 months and the other ages.

night factors contributed to variations in the sleep stages. The percentage of SWS was higher during the day than during the night, while the percentage of REM sleep was lower. Moreover, the decrease in the amount of REM sleep between 3 and 24 months was more pronounced during the diurnal part of the nycthemere (−15%) than during the nocturnal part (−8%) (Tables 1 and 2). Diurnal modifications occurred earlier than nocturnal ones, i.e. from 6 months onward and especially during REM sleep. Nevertheless, at 2 years, diurnal sleep was still essentially composed of SWS.

DISCUSSION

Besides differences in experimental conditions (type and duration of recordings, environment, and longitudinal or transverse studies), sleep data presented here corroborate other authors' results with respect to quantitative data on the development of sleep states, i.e. waking, REM sleep, and NREM sleep modifications (3–5,8,12–17). However, the early use of modified adult EEG criteria, providing more precise analysis on the emergence of the different sleep stages (stages 1, 2, and 3/4), creates some difficulties for comparisons with results concerning only the two basic forms of

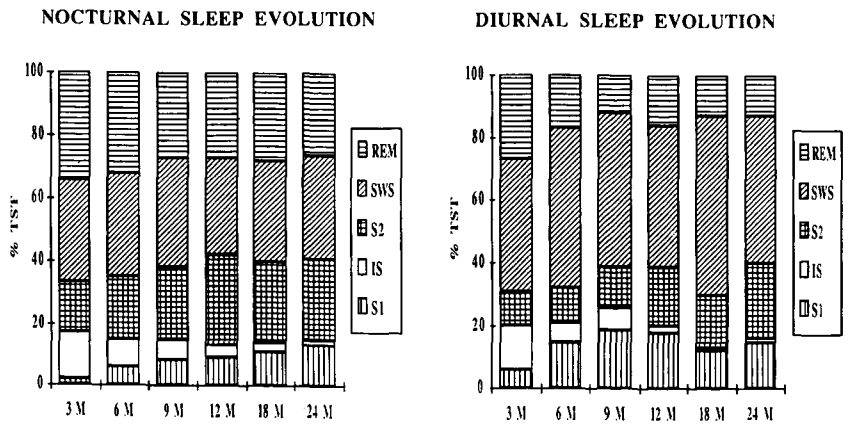


FIG 6. Nocturnal and diurnal evolution, with age, of the different sleep states and stages as percentages of total sleep time (TST).

rhythmic sleep, i.e. AS and QS (1–14). As suggested by Roffwarg et al. (31), the primary function of infant sleep and, particularly, REM sleep, could be to support the development of the CNS. Likewise, the emergence of adult sleep EEG patterns and structures reflects a number of steps in this CNS maturation process and probably also the development of physiological periodicities expressed in different structures of the brain (32). Thus, the early use of adult EEG criteria seems crucial in determining the point in time when adult sleep patterns emerge. This approach was indicated by the results of several studies on the rapid maturation of electrical activity in the brain during the first 3 months of life, i.e. disappearance of the "trace alternant", emergence of sleep spindle activity (12,33,34), and "adult-like" delta-wave activity (35). Moreover, power-spectral EEG analysis has demonstrated that, starting from 16 weeks of age, there is a significant developmental increment in the 4–7-Hz frequency band during NREM sleep (2,36), which confirmed the emergence of S1 at this point and justified our decision [Challamel et al. (37)], to score S1 according to Rechtschaffen and Kales' criteria (28).

The main results of the present study concerned the following three points. First, The percentage of SWS, which can be regarded as a feature of intrinsic sleep production mechanisms, reflecting homeostatic processes is stable. The data revealed a great stability, over the 2 years, in the percentage of SWS. Although we confirmed the increase with age in QS observed by others (3–5,8,12–17), this evolution was essentially due, in our results, to an increase in S2 and not to a reciprocal increase in S2 and decrease in SWS, as reported by some authors (16,17). At 6 months of age, we found more SWS and less S2 than did Coons et al. (16) or Fagioli and Salzarulo (17), where S2 was the dominant component of NREM sleep. Their high proportion of S2 would seem to be due to a lower proportion of SWS, since in our conditions, the proportion of SWS remains stable. In accord with some authors (5,16), we suggest that the discrepancy between our results and theirs was probably due to different recording conditions (home vs. laboratory) rather than to sleep state scoring methods. Stress has been reported to produce an increase in NREM sleep (38), but as Bernstein et al. pointed out, the increase with age in S2 should not be confused with the great proportion of S2 in NREM sleep linked with experimental conditions (10). The stability of the percentage of SWS over the 2 years emphasizes the importance of S2 in maturational changes in the infant sleep development process. However, this quantitative stability does not exclude the nycthemeral SWS organization, with a high proportion of SWS during the first part of the night (25,39,40). This point will be analyzed in a subsequent publication. For the moment, we would suggest that this high degree of SWS stability may reflect certain homeostatic processes involved in sleep production mechanisms (41).

Second, A S2-REM sleep ratio equal to one, which represents an index of sleep maturation linked to developmental neurophysiological changes in some CNS structures is present from 9 months of age onward. Given the stability of SWS within QS, the ratio of REM sleep to S2 would seem to be more representative of this process than the ratio of REM sleep to QS, provided by some authors as an indicator of sleep maturation (5,19). In fact, this ratio is made up of the two main sleep stages, each of which plays a role in the maturational process. The individualization of S2 is linked to the emergence of sleep spindle activity, this activity being considered as an electrophysiological measure of brain maturation (25,34), reflecting developmental changes in thalamocortical structures (34,42), myelination, and growth of dendrites (43,44). Nine months of age appears to be a turning point in the sleep maturation process with, during the night period, a significant decrease in REM sleep and an increase in S2. This is also an important age for frontal area myelination; it comes at the end of the caudorostral myelination phase (44) and promotes the interaction between the brain stem and the thalamocortical system, which are involved respectively in the organization of REM and S2 sleep (32). This result emphasizes the link between sleep maturation and developmental neurophysiological changes in some CNS structures.

Third, An early sleep change during the diurnal part of the nycthemere underlines the importance of the circadian rhythm process and of "life experience" in the maturation of sleep. In the present study, the total amount of sleep, over the 24-hour period did not significantly change, but starting from 3 months of age, day–night differences were observed for most of the sleep parameters except for IS. In this study, transitional sleep was precisely analyzed through S1 and IS and permits us to differentiate transitions between REM and NREM sleep (IS) and those between sleep and waking (S1). Variance analysis showed a clear effect of the day–night factor on the evolution of S1, while IS was not found to vary with the nocturnal or diurnal part of the nycthemere. In fact, our results suggest, in agreement with Ellingson and Peters (14), that IS may provide a quantitative measure of immature sleep and thus should not be identified with the emergence of S1 in NREM sleep. With regard to the other sleep parameters (TST, W, REM sleep, and SWS), the most important modifications begin during the diurnal part of the nycthemere at 3 months of age, which suggests that circadian sleep periodicity occurs as early as 10 weeks of age (18,45–48). Moreover, an interesting

result supports the view that sleep ontogenesis may be related to neurophysiological plasticity, which itself may be influenced by "experience"; sleep spindles develop earlier in premature than in full-term infants, which is probably due to their longer period of extrauterine experience (49) . But how much of this experience is endogenous and how much exogenous? Environmental conditions and interference were not taken into account in our study. Nevertheless, it is known that both components are significant; in a constant light environment, circadian rhythms do not develop (50), and many biological rhythms seem to be coordinated with the sleep–wake cycle (51,52). As far as the ultradian rhythm is concerned, the REM sleep cycle is already present at birth and, in the present study, was found to lengthen only after 12 months. This is in agreement with Meier-Koll et al. (53) who found that modifications of the ultradian rhythm occurred only after the consolidation of the circadian sleep–wake rhythm.

These three points will be more fully developed in subsequent publications. However, this sleep-ontogenesis study provides much information on sleep development and demonstrates that adult sleep characteristics occur early in infancy. The circadian rhythm appears at 3 months, followed by the adult sleep structure between 6 and 9 months, and the lengthening of the ultradian rhythm at 12 months.

Acknowledgements: We would like to thank the families of the babies for their assistance in this study and the babies themselves: Adelin, Anaëlle, Auriane, Antoine, Caroline, Cédric, Cyrielle, Florian, Gonzague, Karine, Magaly, Martin, Mélanie, Michel, and Salomé. Thanks also to John Doherty for checking the English manuscript. This study was supported by grants from INSERM U.52, CNRS URA 1195, DRET 91–1, Claude Bernard University.

REFERENCES

1. Dittrichova J. The development of sleep in infancy. *J Appl Physiol* 1966;21:1243–6.
2. Sterman MP, Harper RM, Havens B, Hoppenbrouwers T, McGinty DJ, Hodgman JE. Quantitative analysis of infant EEG development during quiet sleep. *Electroencephalogr Clin Neurophysiol* 1977;43:371–85.
3. Harper RM, Leake B, Miyahara L, et al. Temporal sequencing in sleep and waking states during the first 6 months of life. *Exp Neurol* 1981;72:294–307.
4. Navelet Y, Benoit O, Bouard G. Nocturnal sleep organization during the first months of life. *Electroencephalogr Clin Neurophysiol* 1982;54:71–8.
5. Hoppenbrouwers T, Hodgman J, Arakawa K, Geidel SA, Sterman MB. Sleep and waking states in infancy: normative studies. *Sleep* 1988;11(4):387–401.
6. Parmelee AH, Winner WH, Schulz HR. Infant sleep patterns from birth to 16 weeks of age. *J Pediatrics* 1964;65:576–82.
7. Monod N, Pajot N. Le sommeil du nouveau-né et du prématuré. *Biol Néonat* 1969;8:281–307.
8. Lenard HC. Sleep studies in infancy: facts, concepts and significances. *Acta Paediatr Scand* 1970;59:572–81.
9. Hagne I. Development of the sleep EEG in normal infants during the first year of life. *Acta Paediat Scand* 1972;219:25–53.
10. Bernstein P, Emde R, Campos J. REM sleep in four-month infants under home and laboratory conditions. *Psychosom Med* 1973;35(4):322–9.
11. Dreyfus-Brisac C, Curzi-Dascalova L. The EEG during the first year of life. In: Rémond A, ed. *Handbook electroencephalogr clin neurophysiology,* vol. 6B. Amsterdam: Elsevier, 1975:24–30.
12. Curzi-Dascalova L. EEG de veille et de sommeil du nourisson normal avant 6 mois d'âge. *Rev EEG Neurophysiol* 1977;7:316–26.
13. Emde RN, Walker S. Longitudinal study of infant sleep: results of 14 subjects studied at monthly intervals. *Psychophysiology* 1976;13(5):456–61.
14. Ellingson RJ, Peters JF. Development of EEG and daytime sleep patterns in normal full-term infants during the first 3 months of life: longitudinal observations. *Electroencephalogr Clin Neurophysiol* 1980;49:112–24.
15. Crowell DH, Kapuniai LE, Boychuk RB, Light MJ, Hodgman JE. Daytime sleep stage organization in three-month-old infants. *Electroencephalogr Clin Neurophysiol* 1982;53:36–47.
16. Coons S, Guilleminault C. Development of sleep–wake patterns and non-rapid eye movement sleep stages during the first six months of life in normal infants. *Pediatrics* 1982;69(6):793–8.
17. Fagioli I, Salzarulo P. Sleep states development in the first year of life assessed through 24h recordings. *Early Hum Dev* 1982;6:215–28.
18. Anders T, Hoffman E. The sleep polygram: a potentially useful tool for clinical assessment in human infants. *Am J Ment Defic* 1973;77:506–14.
19. Thoman EB, Whitney MP. Sleep states of infants monitored in the home: individual differences, developmental trends, and origins of diurnal cyclicity. *Inf Behav Dev* 1989;12:59–75.
20. Kleitman N, Engelmann TG. Sleep characteristics of infants. *J Appl Physiol* 1953;6:269–82.
21. Stern E, Parmelee AH, Akiyama Y, Schultz MA, Wenner WH. Sleep characteristics in infants. *Pediatrics* 1969;43:65–70.
22. Curzi-Dascalova L, Peirano P, Morel-Kahn F. Development of sleep states in normal premature and full-term newborns. *Dev Psychobiol* 1988;21:431–44.
23. Schmid U, Lang R, Hallek M, et al. Maturation of circadian behavior rhythms in the first year of human life. In: Labrecque C, ed. *Annual review of chronopharmacology.* New York: Pergamon Press, 1988:273–6.
24. Pollak CP. Regulation of sleep rate and circadian consolidation of sleep and wakefulness in an infant. *Sleep* 1994;17(7):567–75.
25. Schulz H, Bes E, Salzarulo P. Rhythmicity of slow wave sleep developmental aspects. In: Wauquier A, Dugovic C, Radulovacki M, eds, *Slow wave sleep: physiological, pathophysiological and functional aspects.* New York: Raven Press, 1989:49–60.
26. Salzarulo P, Fagioli I. Post-natal development of sleep organization in man: speculations on the emergence of the 'S process'. *Neurophysiol Clin* 1992;22:107–15.
27. Sostek AM, Anders TF. Effects of varying laboratory conditions on behavioral-state organization in two- and eight-week-old infants. *Child Develop* 1975;46:871–8.
28. Rechtschaffen A, Kales A. *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects.* Washington, DC: U.S. Government Printing Office, National Institute of Health Publication, 1968.
29. Jasper HH. The ten–twenty electrode system of the international federation. *Electroencephalogr Clin Neurophysiol* 1958;10:371–5.
30. Guilleminault C, Souquet M. Sleep states and related pathology. In: Korobkin R, Guilleminault C, eds. *Advances in perinatal neurology.* New York: SP Medical and Scientific Books, 1979:225–47.
31. Roffwarg HP, Muzio JN, Dement WC. Ontogenetic develop-

ment of the human sleep–dream cycle. *Science* 1966;152:604–19.
32. Steriade M. Development of thalamocortical oscillatory patterns and their maturing structural bases. In: Steriade M, Jones EG, Llinas RR, eds. *Thalamic oscillations and signaling.* New York: A Neurosciences Institute Publication, 1990:217–37.
33. Ellingson RJ. The EEGs of prematures and full-term newborns. In: Klass DW, Daly DD, eds. *Current practice of clinical electroencephalography.* New York: Raven Press, 1979:149–77.
34. Louis J, Zhang JX, Revol M, Debilly G, Challamel MJ. Ontogenesis of nocturnal organization of sleep spindles: a longitudinal study during the first 6 months of life. *Electroencephalogr Clin Neurophysiol* 1992;83:289–96.
35. Schechtman VL, Harper RK, Harper RM. Distribution of slow-wave EEG activity across the night in developing infants. *Sleep* 1994;17(4):316–22.
36. Samson-Dollfus D, Nogues B, Menard JF, Bertoli-Lefever I, Geffroy D. Delta, theta, alpha and beta power spectrum of sleep electroencephalogram in infants aged two to eleven months. *Sleep* 1983;6(4):376–83.
37. Challamel MJ, Debilly G, Leszczynski MC, Revol M. Sleep state development in near-miss sudden death infants. In: Harper RM, Hoffman HJ, eds. *Sudden infant death syndrome: risk factors and basic mechanisms.* New York: PMA Publishing, 1988: 423–34.
38. Emde RN, Harmon RJ, Metcalf D, Koenig KL, Wagonfeld S. Stress and neonatal sleep. *Psychosom Med* 1971;33(6):491–7.
39. Bes F, Schulz H, Navelet Y, Salzarulo P. The distribution of slow-wave sleep across the night: a comparison for infants, children and adults. *Sleep* 1991;14(1):5–12.
40. Peirano P, Fagioli I, Bes F, Salzarulo P. The role of slow-wave sleep on the duration of quiet sleep in infants. *J Sleep Res* 1993;2:130–3.
41. Borbély AA. A two-process model of sleep regulation. *Human Neurobiol* 1982;1:195–204.
42. Steriade M, Deschênes M, Domich L, Mulle C. Abolition of spindle oscillation in thalamic neurons disconnected from nucleus reticularis thalami. *J Neurophysiol* 1985;54:1473–97.
43. Schadé JP, Meeter K. Neuronal and dendritic patterns in the uncinate area of the human hippocampus. *Prog Brain Res* 1963;3:89–110.
44. Van der Knaap MS, Valk J. MR imaging of the various stages of normal myelination during the first year of life. *Neuroradiology* 1990;31:459–70.
45. Hellbrügge T. The development of circadian and ultradian rhythms of premature and full-term infants. In: Scheving L, ed. *Chronobiology.* Tokyo: Igaku Shoin, 1974:339–41.
46. De Roquefeuil G, Djakovic M, Montagner H. New data on the ontogeny of the child's sleep–wake rhythm. *Chronobiology Int* 1993;10(1):43–53.
47. Samson-Dollfus D, Vanhulle C, Michaélis L. Rest–activity cycle in normal newborns. *J Sleep Res* 1994;3(Suppl 1):228.
48. Coons S. Development of sleep and wakefulness during the first 6 months of life. In: Guilleminault C, ed. *Sleep and its disorders in children.* New York: Raven Press, 1987:17–27.
49. Metcalf DR. The effect of extrauterine experience on the ontogenesis of EEG sleep spindle. *Psychosom Med* 1969;31:393–9.
50. Martin du Pan R. Some clinical applications of our knowledge of the evolution of the circadian rhythm in infants. In: Schewing LF, Halberg DF, Pauly JE, eds. *Chronobiology.* Stuttgart: 1974: 342–7.
51. Mirmiran M, Kok JH. Circadian rhythms in early human development. *Early Hum Dev* 1991;26:121–8.
52. Glotzbach SF, Edgar DM, Boeddiker M, Ariagno RL. Biological rhythmicity in normal infants during the first 3 months of life. *Pediatrics* 1994;94(4):482–8.
53. Meier-Koll A, Hall U, Hellwig U, Kott G, Meier-Koll V. A biological oscillator system and the development of sleep–waking behavior during early infancy. *Chronobiologia* 1978;4(5): 425–39.