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The Distribution of Slow-Wave Sleep Across the Night: A Comparison for Infants, Children, and Adults

*†‡F. Bes, †H. Schulz, ‡Y. Navelet, and ‡P. Salzarulo

**University of Amsterdam, Amsterdam, The Netherlands;*
†Max-Planck-Institut für Psychiatrie, Munich, FRG; and
‡INSERM U3, Hôpital de la Salpetrière, Paris, France

Summary: This study describes the temporal distribution of slow-wave sleep (SWS) (defined as the visually scored stages 3 + 4) across the night for 16 infants aged between 20 weeks and 1 year, 17 children between 1 and 6 years, and 17 adults between 20 and 36 years. In all three groups the amounts of SWS peaked during the first nonrapid eye movement (NREM) episode. SWS decreased across the night for adults and children, but not for infants. In infants the amounts of SWS remained at a fairly constant level from the second cycle onward, although many cycles were observed with zero SWS. The latter was evident from the very low tendency for SWS to appear in consecutive NREM/REM cycles. Rather, SWS was observed in alternate cycles. In children this phenomenon was less prominent but still well visible, and the tendency for SWS to appear in consecutive cycles had increased. In adults SWS occurred predominantly in consecutive cycles. The results suggest that whereas REM recurrence time increases twofold from infancy to adulthood, SWS recurrence time remains of similar length in infants, children, and adults. **Key Words:** Slow-wave sleep—Ontogeny—Sleep cycles.

A well-known feature of adult human sleep is the abundance of slow-wave sleep (SWS) just after sleep onset with recurrent bouts of decreasing amount during the remainder of the night. The fundamental nature of this feature has been used in the two-process model of sleep (1) to represent the homeostatic process S (in addition to the circadian process C, the variation in sleep propensity). Commonly, SWS is designated as sleep stages 3 + 4 according to Rechtschaffen and Kales (2).

Studies of SWS in the first year of life have been scant until now. There is no general agreement on the age at which SWS can be identified. Among those authors who distinguish stages 1, 2, 3, and 4 during quiet sleep from the third to fifth month onward (3–6), only a few mention anything specific about the distribution of SWS across the night. Coons and Guilleminault (6) reported that SWS is not uniformly distributed during sleep, peaking in the early portion of the night at 3 months and less sharply at 4.5 and 6 months of age. We reported for infants from 5 to 12 months that SWS displays a maximum in the first nonrapid eye movement (NREM) episode after sleep onset (7) and that SWS recurs predominantly in alternate NREM/REM cycles across the night (that is with one cycle in between, which contains few or no SWS at all) and not in consecutive cycles as observed in adults (7,8).

For children it was reported that at the age between about 1 to 6 years most SWS occurs in the first part of the night (9,10). Often, after sleep onset, SWS appears to make up a very long first NREM/REM cycle with one or several so-called "missed REM episodes" (11–14).

In our previous work (7,8) we reported preliminary results concerning infants and adults. The purpose of the present study is to extend the analysis of these two groups by adding a sample of young children to the samples already used. By comparing infants, children, and adults we may thus gain a better understanding of how the distribution of SWS across the night develops with age.

METHODS

Subjects

As gender was not a selection criterion, subjects of either gender were present in the age groups.

Infants. One night's sleep of 16 infants was poly-

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Address correspondence and reprint request to F. Bes, Freie Universität Berlin, Universitätsklinikum Rudolf Virchow, Standort Charlottenburg, Labor für Klinische Psychophysiologie, Eschenallee 3, D-1000 Berlin 19, FRG.

graphically recorded according to methods described in detail elsewhere (15). The infants were healthy, born full-term, and were generally sleeping throughout the night at the time of the study. They ranged in age from 20 to 54 weeks (mean 35.9, standard deviation 10.4 weeks). These 16 infants were the oldest from an original sample of 54 subjects in the first year of life (cf. 16,17). They were selected according to the criterion that their night sleep manifested sleep stages 3 and 4 according to the manual of Rechtschaffen and Kales (2). Infants of 20 weeks and older met this criterion.

Children. The night sleep of 17 healthy children was analyzed. The children were recorded in the laboratory of O. Benoit (cf. 18,19). Their age ranged from 1 to 6 years (mean 3.5 ± 1.5 years).

Adults. The night sleep of 17 young healthy adults ranging in age from 20 to 36 years (25.3 ± 4.6 years) was analyzed. For each subject, data from 14 consecutive laboratory nights were available, but only the first night was used for the analysis (except for three subjects; see Procedures) in order to be comparable with the single nights of the infants and the children.

Procedures

General. Recordings were made on paper (and also on tape for infants and adults only, permitting automatic analysis; but, given the design with three age groups, the present study will use that analysis only for illustrative purposes). They included electrooculogram (EOG), electromyogram (EMG), and at least a central derivation of the electroencephalogram (EEG) with time constant of 0.3 s. All records were visually scored for sleep stages by experienced raters according to Rechtschaffen and Kales (2). The minimum length of one sleep stage was 2 min, shorter changes being included in the preceding stage [this was the usual method for the evaluation of the infant sleep stages (15), not for those of the adults and children; for comparative reasons we also applied this method in the present study for the adult and children sleep stages]. The number of SWS epochs was counted for each record and later expressed in minutes. To be scored as SWS, at least 20% of an epoch had to consist of waves of 2 Hz or slower, with amplitude greater than 75 μV.

Sleep was then subdivided into cycles, defined from the onset of one NREM episode to the next onset, including one REM episode. Interruptions of up to 15 min between REM segments were accepted within a single REM episode. For further analysis only those sleep records were considered that displayed at least three consecutive NREM/REM cycles without intervening wakefulness of longer than 15 min. The first-night records of three of the adult subjects failed to meet this requirement. In these cases, second-night records were used. For the NREM part of every NREM/REM cycle the duration of SWS was determined. Group differences in total amount of SWS and NREM/REM cycle length were tested with ANOVA.

SWS distribution. In order to establish the SWS distribution across the night, the percentage of SWS per NREM episode was calculated for every NREM/REM cycle. For each age group the percentages were plotted as a function of cycle rank. If the NREM/REM cycle was interrupted by more than 15 min of wakefulness it was skipped.

In order to test general association between SWS percentage and NREM episode rank in each age group, the frequencies of values above versus, respectively, below the group median were tabulated for successive NREM episodes and a chi-square test was performed on these scores. We renounced using a Friedman ANOVA to test differences between the various NREM episodes because the presence of many NREM episodes without SWS would have generated a large number of ties.

SWS recurrence. In order to describe the recurring appearance of SWS in the night, the absolute durations of SWS (in minutes) were compared cycle by cycle for each sleep record. Here, fractions of the registrations of at least three consecutive NREM/REM cycles were used, which were not interrupted by more than 15 min of wakefulness. SWS recurrence time was defined as the time between the first occurrence of SWS within a given NREM/REM cycle and the first occurrence of SWS in the subsequent NREM/REM cycle. REM recurrence time was similarly defined. Group differences in SWS recurrence time as well as in REM recurrence time were tested with ANOVA. The frequency of consecutive NREM/REM cycles with SWS was tabulated across the age groups and tested for association with the chi-square procedure.

Thereafter, whether SWS recurred with decreased or increased durations was investigated. Therefore, with every NREM/REM cycle whether the amount of SWS compared with the preceding cycle was on the one hand equal or larger (both denoted by SWS+), or, on the other hand, smaller or absent (both denoted by SWS−) was determined. To account for SWS in alternate NREM/REM cycles, succession of SWS−/SWS+ after each cycle containing SWS were tabulated and expressed as a proportion of the possible maximum number of such successions.

RESULTS

SWS distribution across NREM episodes

In Figure 1 the relative amounts of SWS within consecutive NREM episodes are plotted as a function of cycle rank for each of the three groups.

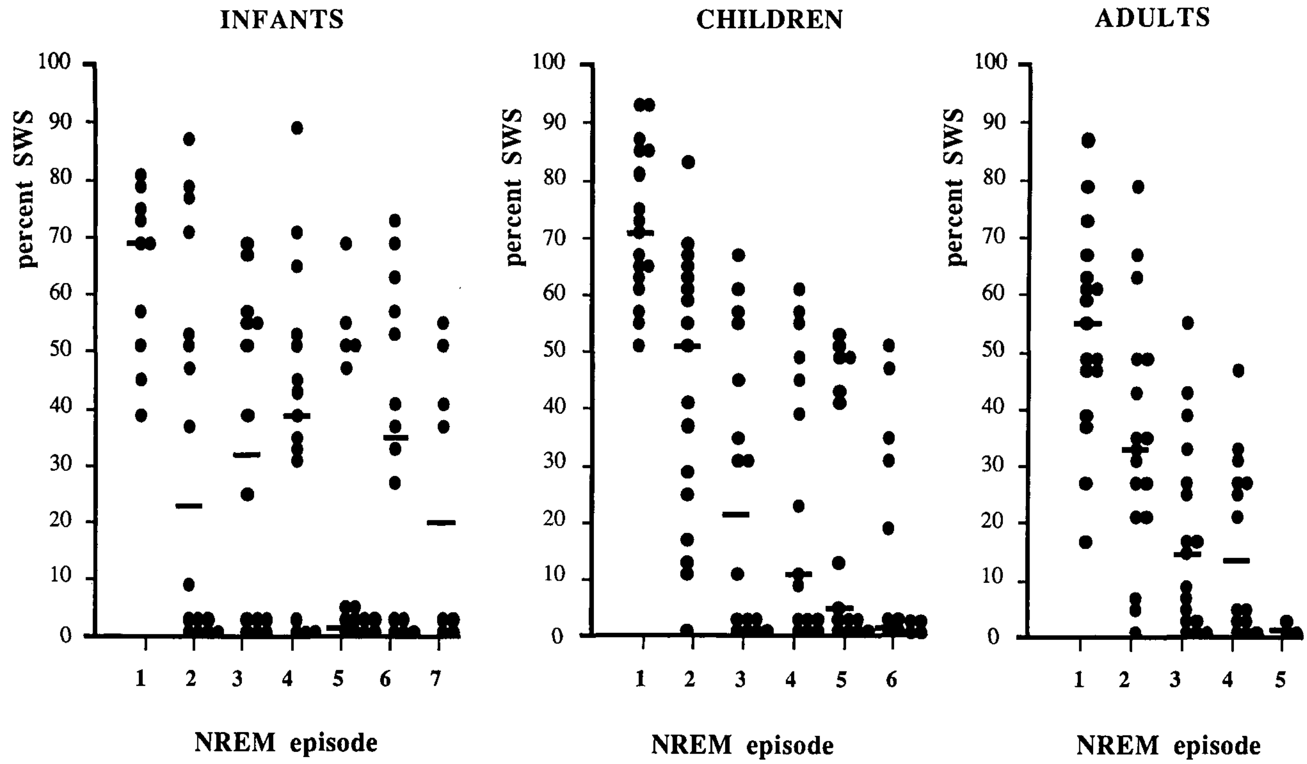

FIG. 1. Distribution of relative SWS amounts, plotted as a function of cycle rank and expressed as percentage of NREM episode, across the first seven NREM episodes for 16 infants, the first six NREM episodes for 17 children, and the first five NREM episodes for 17 adults. The SWS percentages are represented by dots; the median SWS percentage at a given NREM episode rank by a single horizontal dash. Cycles that were interrupted by more than 15 min of wakefulness were considered to be missing values and omitted from the plot. Therefore the data points of each NREM episode do not always add up to the number of subjects in the group.

Infants. With the infants, a maximum percentage of SWS was found in the first NREM episode (median for the first episode, 68.8%; range, 39.5–81.1%). From the second episode onward many zero values were present and the non-zero values maintained a fairly constant level (the medians for episode 2–7 were 23.2, 32.8, 37.3, 0.00, 35.7, and 19.1%). The distribution of the SWS values was clearly bimodal within these episodes, the majority being either greater than 30% or zero.

The median SWS percentage for the whole group was 38.8. After determining the frequency above and below this median for each NREM episode, all percentages in the first NREM episode were found to lie above the median. A barely significant association between percentage SWS and NREM episode rank could thus be shown ($\chi^2 = 12.8$, $p = 0.047$), indicating a decrease of SWS across NREM episodes. However, when this procedure was repeated without considering the first NREM episode (the group median in that case was 34.2), the χ^2 value was no longer significant ($\chi^2 = 2.6$, $p = 0.769$).

Children. The children also had a maximum percentage of SWS in the first NREM episode (the median was 70.8%, with a range of 51.3–95.4%). The SWS percentages decreased across successive NREM episodes, with medians for episodes 1–6 of 70.8, 50.7, 20.9, 9.9, 2.7, and 0.0%. The median value for the whole group was 37.2%. All percentages in the first NREM episode lay above this median. A highly significant association existed between NREM episode rank and SWS percentage ($\chi^2 = 28.1$, $p = 0.0005$). If the first episode was not considered, this yielded a χ^2 of 7.3, which was no longer significant ($p = 0.118$).

NREM episodes without any SWS were observed rather early in the night, the majority from the third NREM episode onward. The SWS values were not clearly bimodally distributed within the NREM episodes, as was seen with the infants.

Adults. In a similar manner the adult group also manifested the greatest relative amounts of SWS in the first NREM episode after sleep onset (median for episode 1 was 54.4%, range 15.9–88.9; medians for episodes 2–5 were 34.0, 15.2, 12.9, and 0.0%). The association between NREM episode rank and SWS percentages was significant ($\chi^2 = 18.9$, $p = 0.001$) and remained significant when the first episode was not taken into consideration ($\chi^2 = 8.5$, $p = 0.037$).

Recurrence of SWS in the night

The data concerning the recurrence of SWS are summarized in Table 1.

TABLE 1. *Data concerning the recurrence of SWS*

	Infants	Children	Adults
Number of sleep records	16	17	17
Number of sleep records with SWS+	16	14	12
Number of NREM/REM cycles (comprising series of at least three cycles)	90	99	68
Average SWS recurrence time (and SD)	104.4 ± 42.5	125.9 ± 50.1	126.7 ± 48.4
Total number of consecutive cycles with SWS (and percentage from number of NREM/REM cycles)	20 (=22.2)	49 (=49.5)	49 (=72.1)
Number of cycles with SWS+	30	26	16
Maximum possible	72	81	51
Percentage from maximum	41.7	32.1	31.4
Number of series SWS/SWS−/SWS+	21	18	8
Maximum possible	31	36	21
Percentage from maximum	67.7	50.0	38.1

Infants. With the infant group, the average SWS recurrence time was 104.4 ± 42.5 min. SWS recurred only occasionally in consecutive NREM/REM cycles: the 16 sleep records comprised 90 NREM/REM cycles, from which 20 cycles (or 22.2%) consecutively contained SWS. Occurrences of SWS+ were found in every record. They comprised 30 out of 72 occasions in which SWS could possibly recur (n = 72, i.e., all NREM/REM cycles occurring in uninterrupted series of at least three, except for the first cycle in every series, where SWS cannot recur by definition; 18 series were counted, amounting to 90 cycles, hence n = 90 − 18, or 72). Successions of SWS−/SWS+ after an SWS-containing NREM/REM cycle were observed on 21 of 31 possible occurrences, equalling 67.7%. In other words, SWS in infants does not recur predominantly in consecutive cycles, but in alternate cycles, with the intermediate cycle containing no SWS.

This tendency is clearly visible in Figure 2, which depicts four typical examples of infant sleep profiles. Below each sleep profile an automatically analyzed EEG parameter is displayed, which shows the degree of synchronization in the background EEG across the night based on 30-s epochs (16,20). The differentiation that is evident in the time course of the EEG parameter corroborates the visually scored sleep profile (21).

Children. The average SWS recurrence time with the children was 125.9 ± 50.1 min. The 17 records comprised 99 NREM/REM cycles, of which 49 (or 49.5%) consecutively contained SWS. From the recurring amounts of SWS, 26 were of the type SWS+, which amounted to 32.1% of the possible occurrences (n = 81). They were found in 14 of the 17 sleep records. Successions of SWS−/SWS+ after SWS containing NREM/REM cycles were observed on 18 out of 36 possible occurrences (50%).

Adults. With the adults, the average SWS recurrence time was 126.7 ± 48.4 min. SWS appeared mainly in consecutive NREM/REM cycles: the 17 sleep records comprised 68 NREM/REM cycles, from which 49 (or 72.1%) consecutively contained SWS. SWS+ was found in 12 sleep records and occurred in 16 of 51 possible cases (31.4%). A succession of SWS−/SWS+ after an SWS-containing NREM/REM cycle was observed on eight occasions. This was 38.1% of the maximum possible number of such occurrences, which equalled 21.

Comparison between the age groups

The groups differed significantly in total duration of SWS (F = 4.84, df = 2, p = 0.012). The mean total amount and standard deviation of SWS per night was 103.3 ± 42.3 min for the infants, 136.3 ± 33.9 min for the children, and 95.8 ± 44.1 min for the adults. Post-hoc comparison between the means (t test) showed that children had significantly more SWS than adults ($p < 0.01$) and infants ($p < 0.05$), but that infants and adults did not differ in this respect.

NREM/REM cycle duration appeared to change significantly with age (F = 77.26, df = 2, p = 0.0001). The infants had a mean cycle duration of 55.7 ± 12.8 min, the children of 81.4 ± 30.9, and the adults of 100.1 ± 24.9 min. Post-hoc comparison between the groups showed that all means differed significantly ($p < 0.01$).

SWS recurrence time did not appear to change significantly with age (F = 2.78, df = 2, p = 0.066). REM recurrence time, on the other hand, did change significantly with age (F = 51.67, df = 2, p = 0.0001). The frequency distributions of SWS and REM recurrence times are depicted in Figure 3. For all groups the range of SWS recurrence times was broad and exceeded the range of REM recurrence times. With the adults a peak in SWS recurrence could be distinguished between 100 and 120 min. With the infants no predominant peak could be found, but the frequency of SWS recurrence seemed somewhat elevated at times corresponding to multiples of their mean REM recurrence time. The frequency distribution of REM recurrence times showed one clear peak for all three groups, and the peak shifted from 40 to 60 min with the infants, to 80–100 min with the adults.

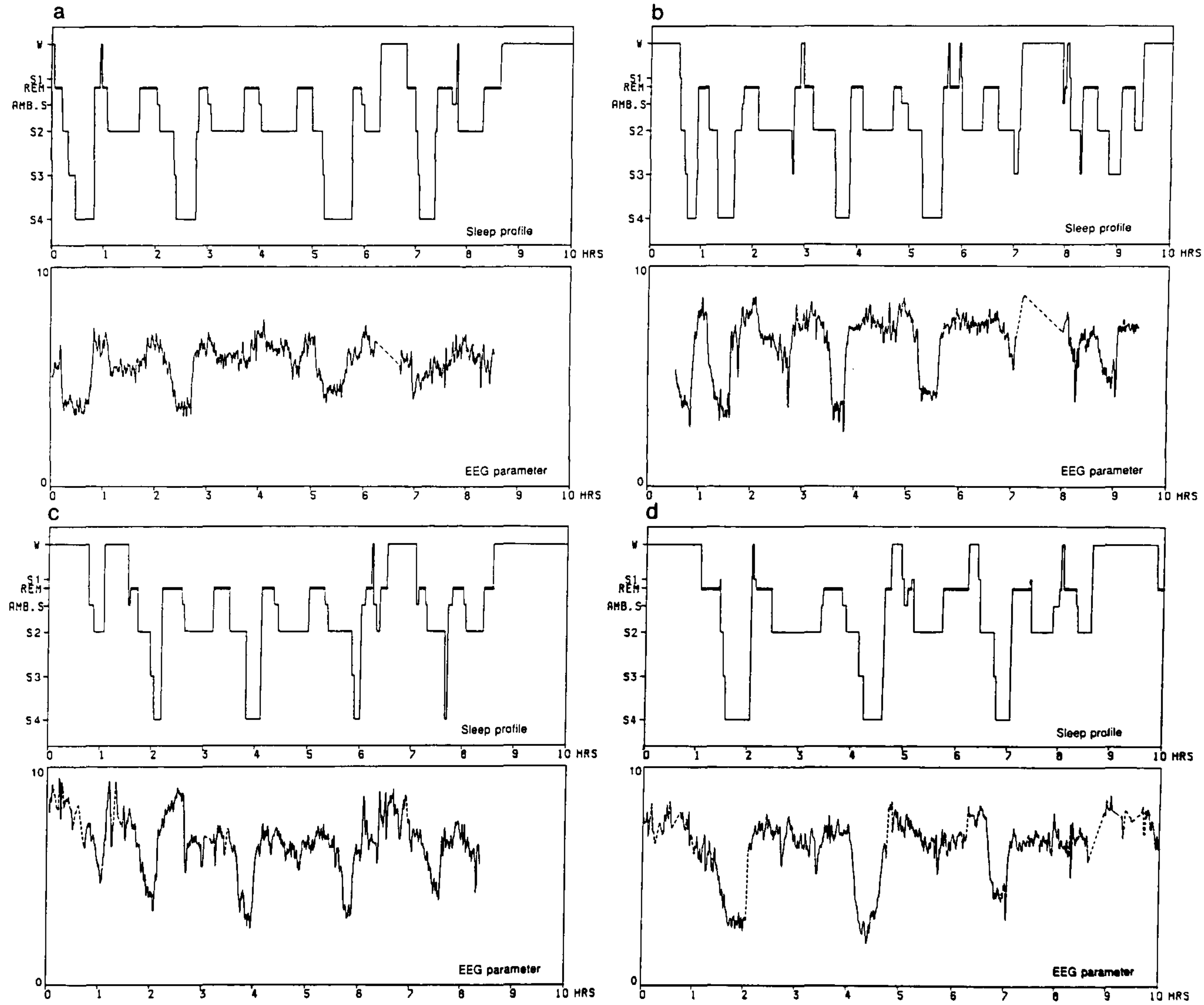

FIG. 2. Visual analysis (sleep profile) and automatic analysis (EEG parameter) of four infants, ages 33 weeks (panel a), 36 weeks (panel b), 44 weeks (panel c), and 47 weeks (panel d). Upper insert within each panel = sleep profile, W = awake, REM = REM sleep, Amb.S. = ambiguous sleep, S1–4 = sleep stages 1–4. The lower insert within each panel denotes the EEG parameter; the dashed sections correspond to artifacts of the EEG; the ordinate represents the degree of EEG synchronization in units running from 0 (synchronization) to 10 (desynchronization).

A significant association between age and the occurrence of SWS in consecutive cycles was demonstrated ($\chi^2 = 39.6$, $p < 0.0005$). Adults had a prevalence for SWS in consecutive NREM/REM cycles (72.1% of all cycles), infants clearly not, with only 22.2% of all cycles consecutively containing SWS. The children were intermediate between infants and adults in this respect (49.5%).

DISCUSSION

The present study demonstrates that for all three groups the amount of SWS reached a maximum in the first cycle after sleep onset. However, it also demonstrates two substantial differences between adults, children, and infants in the distribution of SWS across the night.

First, although in adults the relative proportion of SWS decreases steadily across the night, this is not the case in infants. The SWS percentages in infants display a striking bimodal distribution, with the majority of cycles containing either more than 30% or no SWS at all.

When all NREM episodes are considered, a relationship exists between NREM episode rank and SWS percentage in each group, which is barely significant in the infants and highly significant in children and adults. This indicates a decrease of SWS across successive NREM episodes. However, when the first NREM episode is left out of consideration, this rela-

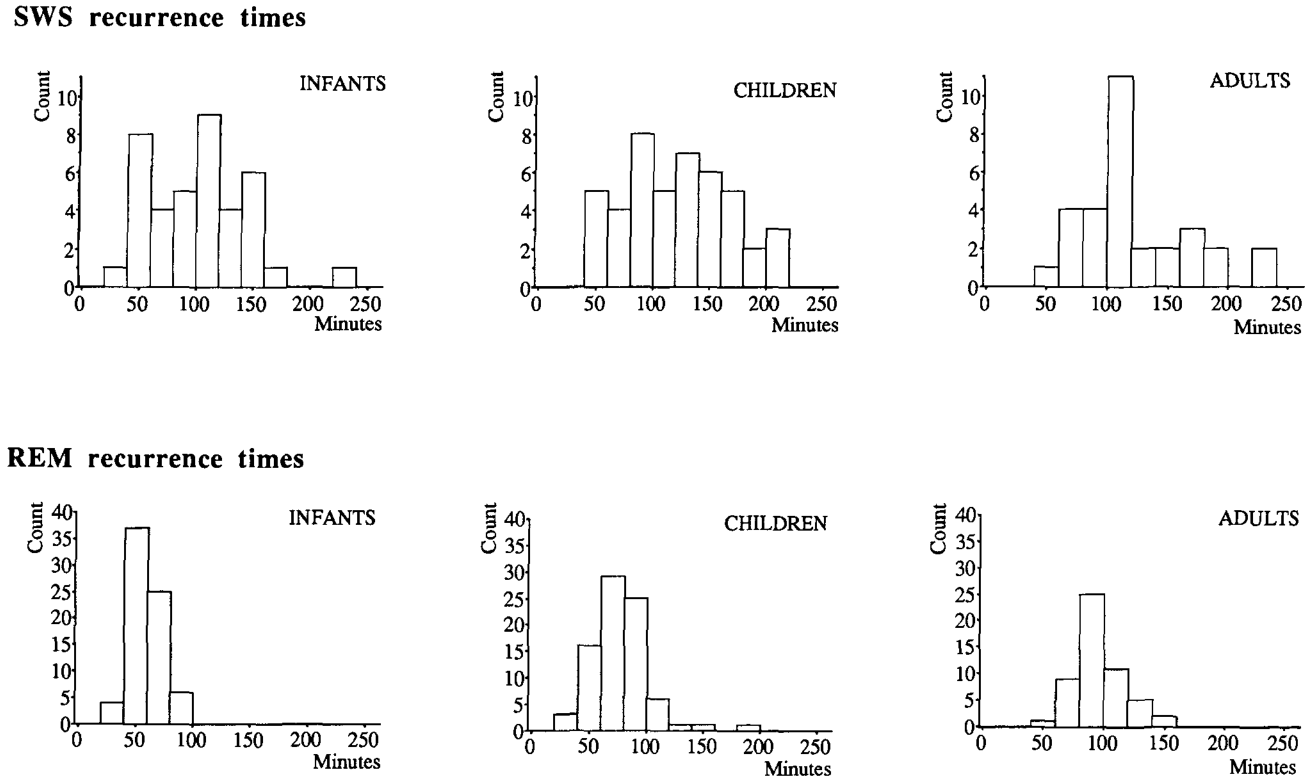

FIG. 3. Frequency distributions of SWS recurrence times (upper panels) and REM recurrence times (lower panels) for infants, children, and adults. The bin width of the histograms is 20 min.

tionship, and hence the decrease, is no longer evident in either infants or children. This suggests that with infants and children the relationship between SWS percentage and NREM episode rank resulted mainly from the high percentage present in the first NREM episode. The results give the strong impression that SWS in infants does not decrease toward a stable minimal level. The large amount of SWS in many NREM/REM cycles later in sleep of infants clearly contrasts with the SWS distribution in adults. The examples of infant sleep profiles in Figure 2 demonstrate that intervening wakefulness, which could stimulate a renewal of SWS, hardly can have played an essential role. There are many cycles with large amounts of SWS, although the preceding sleep phase was not interrupted by wakefulness.

The children manifest an intermediate position between infants and adults. On the one hand, the results of the chi-square test suggest that the relationship between NREM episode rank and SWS percentage in children was mainly due to the high percentages in the first NREM episode, in analogy to the infant group. On the other hand, Figure 1 shows that the median percentage displays a clear decrease across NREM episodes, which is comparable to adults.

The sleep–wake history of the subjects in the present study is unknown, as the amounts and timing of wakefulness prior to night sleep have not been tabulated for either group. Daytime sleep has been shown to exert a strong inhibitory effect on the expression of SWS in the subsequent night (22,23). Presumably, the nights of the infants and to some extent also the nights of the children were preceded by more daytime sleep than the nights of the adults. Nevertheless, the infants have proportions of SWS of up to 80% in the first NREM episode and children of up to even 95%, and although the mean total amount of SWS in the infants was found to be less than that in the children, it does not differ from that of the adults. It remains unclear to what extent the presumed daytime sleep of the infants and children might have influenced SWS expression in their night sleep.

The second difference in the distribution of SWS across the night concerns its recurrence. In the night sleep of adults SWS tends to recur in consecutive NREM/REM cycles. This is in sharp contrast to the night sleep of infants, in which SWS tends to recur in alternate NREM/REM cycles. In the night sleep of children the tendency for SWS to appear in consecutive cycles is increased in comparison with infants, although the tendency to produce SWS in alternate NREM/REM cycles is still visible. In this respect the night sleep of children constitutes a transition between that of infants and adults.

The mean NREM/REM cycle duration for infants is reported to be approximately 40–60 min (17,24,25), the actual duration in our sample being 55.7 ± 12.8 min. As SWS in infants tends to recur every second NREM/REM cycle, this means that on the average it tends to recur about every 100–120 min; this is confirmed by our results. Sterman, in 1979, probably referred to this alternating SWS phenomenon when he described the sleep of infants by means of integrated EEG across the night (26). He remarked that "... when the infant has reached 19 weeks of age ... a new organization has emerged ... periodicity in the 1–3 Hz band has lengthened ... to manifest a coupled cycle of about two hours" (p 220). Moreover, he noted that "... by 10 weeks ... the low frequency component appears to be somewhat attenuated during alternate cycles ..." (with low frequency is meant the 1–3-Hz band). This observation is very interesting, as it suggests that the alternating SWS phenomenon starts as a modulation of the low frequencies in the EEG between 10 and 20 weeks of age.

The frequency distributions of the SWS and REM recurrence times for all groups show a broad range for SWS recurrence as compared to REM recurrence. This indicates that SWS recurrence is a more irregular process than REM recurrence.

The present results suggest that although REM recurrence time is known to lengthen with age (9,10), practically doubling from infancy to adulthood, SWS recurrence time does not change. Indeed, the SWS recurrence time of infants is already comparable to the one of children and adults. Thus, although infants display a 1:2 coupling between SWS and REM sleep, REM and SWS recurrence times in adults tend to manifest a 1:1 coupling. This is based on the conception that not only REM but also SWS constitute rhythmic ultradian phenomena. This is not at odds with the hypothesis that SWS is controlled by homeostatic regulatory mechanisms, for which ample evidence exists in the adult. It is conceivable that SWS is strongly dependent on homeostatic mechanisms, reflected by process S, but nevertheless has a superimposed "sloppy" ultradian component of about 2 h. In adults this component is masked while it runs in counterphase with REM recurrence and moreover while it is damped across the night, reflecting process S. The recurrence of delta activity in the EEG of adults has been described as a semi-independent damped ultradian rhythm by Lubin et al. (27). They concluded that "even though a REM episode always coincides with a delta trough, there is a good deal of independence between the REM cycle and the delta cycle." Independence between REM and delta cycle is emphasized by the different ontogeny of REM and SWS recurrence times.

In brief, we conclude that whereas REM has a relatively regular recurrence time throughout the night, lengthening with age, SWS has a less regular recurrence, which on the average does not change with age, and that infants apparently have two different forms of NREM, one with and one without SWS, which alternate across the night.

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