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Changes in Sleep and Sleep Electroencephalogram During Pregnancy

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Summary: The impairment of sleep quality is a common complaint during pregnancy. To investigate the changes in sleep in the course of pregnancy, the sleep electroencephalogram (EEG) was recorded and analyzed in nine healthy women on 2 consecutive nights during each trimester of pregnancy. Waking after sleep onset increased from the second (TR2) to the third (TR3) trimester, whereas rapid eye movement (REM) sleep decreased from the first trimester (TR1) to TR2. Spectral analysis of the EEG in nonrapid eye movement (NREM) sleep revealed a progressive reduction of power density in the course of pregnancy. In comparison to TR1, the values in TR2 were significantly lower in the 10.25–11.0-Hz and 14.25–17.0-Hz bands. In TR3, the significant reduction extended over the ranges of 1.25–12.0 Hz and 13.25–16.0 Hz. The largest decrease (30%) occurred in the 14.25–15.0-Hz band. In REM sleep, the spindle frequency range was not affected, and a minor reduction of power density in some frequency bins below 12 Hz was present only in TR3. The study documents major alterations of the sleep EEG that are not evident from the sleep scores and that may be associated with the characteristic hormonal changes occurring during pregnancy. **Key Words:** EEG spectra—Power density—Pregnancy—NREM sleep—REM sleep.

During pregnancy, sleep duration, sleep quality and daytime vigilance may undergo considerable changes. Although excessive sleepiness is a common complaint in early pregnancy, impaired sleep quality is typical for the weeks prior to parturition (1–3). These changes have not yet been investigated systematically, and polysomnographic studies have yielded contradictory results. Thus, whereas earlier studies reported reduced amounts of stage 4 sleep during late pregnancy (4–7) or no change of slow-wave sleep (SWS) (3), a recent investigation revealed an increase of SWS from the first to the third trimester (8). Also, the changes reported for rapid eye movement (REM) sleep are inconsistent (3,4,8–10).

Recent advances in quantitative electroencephalographic (EEG) analysis revealed a relationship of specific electrophysiological parameters (i.e. EEG slow-wave activity, spindle activity) to functional aspects of sleep regulation (11–14). The observation that steroid hormones also affect the sleep EEG (15) prompted us to apply these quantitative techniques to the investigation of sleep during pregnancy. In particular, we wished to explore whether specific aspects of sleep EEG regulation would undergo distinctive changes.

METHODS

Subjects and experimental protocol

Between February and August 1990, nine women (mean age 30.6 ± 2.9 years; range 27–35 years) were recruited in the early stage of pregnancy during visits to the Department of Obstetrics, University Clinic of Zürich. Five women were primiparous and the other four were in their second pregnancy. They reported neither sleep disturbances nor medical or psychiatric problems at the time of admission and gave their informed consent to participate as paid subjects in the study. All remained in good health throughout the study and successfully completed their pregnancies. Polysomnography (PSG) was performed on 6 nights in the sleep laboratory. Recordings were obtained for 2 consecutive nights in the first (TR1; weeks 9–14), second (TR2; weeks 18–23) and third (TR3; weeks 32–35) trimester of pregnancy. Bedtimes in the laboratory corresponded closely to habitual bedtimes at home, which

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were influenced by professional obligations and family life. The mean time of lights off on the experimental nights was 2311 hours (SD 21 minutes) in TR1, 2304 hours (SD 37 minutes) in TR2, and 2305 hours (SD 20 minutes) in TR3. The women were requested to refrain from alcohol, drug intake, excessive caffeine consumption and daytime napping on the days preceding the PSG. A wrist-worn activity-monitoring device worn throughout the study made it possible to recognize daytime napping. Not all subjects were able to avoid napping. Of the 54 recorded sleep episodes, three were preceded by naps in TR1, five in TR2 and six in TR3. Most subjects were prescribed multivitamin tablets as well as magnesium and iron preparations. Moreover, one subject received a subcutaneous injection of heparin (5,000 IU) on the days prior to the TR3 sleep recordings, and the beta-adrenoceptor agonist fenoterol (5 mg per os) for uterus relaxation prior to one of these nights.

Recordings and data analysis

Two EEG signals (C3-A2 and C4-A1), two electrooculogram signals and the submental electromyogram were continuously recorded on paper (10 mm/second). The records were scored for 20-second epochs according to conventional criteria (16). For the EEG signals the high-pass filter setting of the polygraph amplifiers (Grass, 7P511J) was 0.1 Hz, which corresponds to a time constant of 0.9 second. The EEG was low-pass filtered (25 Hz, 24 dB/octave), digitized with a sampling rate of 128 Hz and subjected to spectral analysis by a fast Fourier transform routine. Power spectra were computed on-line for consecutive 4-second epochs and 0.25-Hz bands in the range of 0.25–25.0 Hz by applying a rectangular window. The values of adjacent 0.25-Hz bands were collapsed into 0.5-Hz bins between 0.25 and 5.0 Hz, and into 1.0-Hz bins between 5.25 and 25.0 Hz. A timemark generated in connection with the on-line signal processing was written on the polygraph paper at 20-second intervals to enable synchronization of the sleep stage scoring with the spectral data. The 20-second EEG spectra were calculated off-line by averaging the values of five consecutive 4-second EEG spectra. Four-second epochs containing artifacts were eliminated before averaging. The criteria for artifact elimination have been described in more detail elsewhere (17). Nonrapid eye movement (NREM)–REM sleep cycles were defined according to the criteria of Feinberg and Floyd (18). NREM sleep episodes started with stage 2, ended with the beginning of REM sleep, and were required to contain at least 15 minutes of the sleep stages 2, 3 or 4. The last cycle of a night was considered to be completed when REM sleep was present after the last NREM sleep episode.

Statistics and data presentation

Within subjects the same EEG derivation was used on all nights. Power spectra in NREM sleep were calculated by averaging the power density values of 20-second epochs scored as stage 2, 3 or 4. The longest common sleep time of the 54 nights was 265 minutes. The analysis of sleep stages was performed for the total sleep episode as well as for the longest common sleep time. To test whether sleep stage parameters varied significantly between the three trimesters, the data of 2 consecutive nights were averaged and the mean values analyzed by the Friedman nonparametric ANOVA for repeated measures. Although a potential adaptation effect may have been more prominent on the first night of TR1 than on the first nights of the other trimesters, we included these nights in the computations to base the estimate of the sleep parameters on 2 nights per trimester. Differences between trimesters and between consecutive nights were tested with the Wilcoxon matched-pairs signed-rank test. Spectral data were calculated for the entire sleep episode as well as for NREM–REM sleep cycles. The spectral data from 2 consecutive nights were averaged to obtain a single value per trimester and frequency bin. To test whether power density varied significantly over the three trimesters (Fig. 2) or over the first four cycles (Fig. 4, top panel), a one-way ANOVA for repeated measures was performed on the absolute values in each frequency bin. The Huynh-Feldt corrected probability of 0.05 was used as the significance level. Because the absolute levels of spectral power density varied considerably among subjects, relative values were calculated by expressing the data as a percentage of the corresponding values of the first trimester. Paired t tests on the log-transformed relative values were used to test for differences between corresponding spectral data. The two-sided significance level ($p < 0.05$) was applied in all pairwise comparisons. Because changes in single frequency bins were interpreted only when they occurred in conjunction with a nonrandom pattern of spectral changes persisting for more than 1 night or more than one sleep cycle, no correction for multiple testing was made. For plotting average power spectra (Figs. 2 and 4), the geometric mean ($n = 9$) of the relative values was used.

RESULTS

Sleep parameters

Table 1 contains the data of the 6 individual nights (left side) and the average values of 2 consecutive nights of each trimester (right side). The ANOVA over the three trimesters using the average values showed a significant variation for waking after sleep onset and for

TABLE 1. *Sleep parameters of the entire sleep episode determined for the two individual nights (N1 and N2) of each trimester (TR1–TR3) (left) and for the average of the two nights (right). Mean values are indicated in minutes with SEM in parentheses (n = 9)*

	Individual night data									
	TR1		TR2		TR3		Averaged data (N1 + N2)			p(F)[a]
	N1	N2	N1	N2	N1	N2	TR1	TR2	TR3	(df = 2)
Total sleep time	38.24	394.8	389.5	412.1	384.2	380.0	388.6	400.8	382.1	0.2636
	(14.0)	(8.0)	(21.8)	(10.2)	(17.4)	(16.9)	(10.0)	(14.6)	(14.4)	
Sleep efficiency	84.0	88.2	86.6	89.6	80.4	79.5	86.5	88.0	79.9[d]	0.0970
(%)	(3.3)	(1.3)	(3.8)	(1.4)	(2.5)	(2.0)	(2.3)	(2.5)	(1.6)	
Sleep latency	23.3	16.9[b]	24.1	19.4	21.8	28.3	20.0	21.7	25.0	0.2927
(to stage 2)	(5.3)	(3.5)	(9.5)	(7.3)	(6.6)	(6.2)	(4.2)	(8.4)	(4.0)	
REM sleep latency	94.5	63.0[b]	72.9	67.2	68.6	60.7	78.7	70.1	64.6	0.1211
(from stage 2)	(11.4)	(5.9)	(4.2)	(4.6)	(5.4)	(3.6)	(8.1)	(2.6)	(3.2)	
Wakefulness after	38.0	26.9	25.9	19.6	60.0	56.7	32.5	22.8	58.3[d]	0.0446
sleep onset	(13.9)	(6.0)	(9.9)	(1.6)	(7.3)	(7.8)	(9.6)	(5.0)	(6.1)	
Stage 1	34.5	32.9	31.5	30.6	39.9	32.3[b]	33.7	31.1	36.1	0.4594
	(4.5)	(4.4)	(3.8)	(4.8)	(6.3)	(4.6)	(4.2)	(4.0)	(5.2)	
Stage 2	213.9	215.9	237.2	231.4	218.6	223.3	214.9	234.3[c]	220.9	0.0622
	(16.6)	(11.9)	(18.7)	(16.6)	(15.7)	(15.0)	(13.8)	(17.4)	(14.1)	
Stage 3	37.0	43.0	38.9	39.5	36.0	36.6	40.0	39.2	36.3	0.4594
	(4.3)	(3.2)	(3.4)	(4.0)	(3.6)	(3.7)	(3.5)	(2.8)	(3.3)	
Stage 4	22.9	17.8	20.8	26.8	17.1	19.3	20.4	23.8	18.2	0.0622
	(5.3)	(3.9)	(4.1)	(7.1)	(6.1)	(6.2)	(4.4)	(5.3)	(6.0)	
REM sleep	74.1	85.3	61.2	83.8[b]	72.6	68.4	79.7	72.5[c]	70.5	0.0131
	(4.7)	(2.8)	(6.1)	(6.0)	(6.4)	(7.3)	(2.4)	(2.7)	(5.9)	
Slow-wave sleep	59.9	60.7	59.7	66.3	53.1	56.0	60.3	63.0	54.6	0.2359
	(9.1)	(5.8)	(6.4)	(8.9)	(9.1)	(9.0)	(7.2)	(6.9)	(8.8)	
Movement time	9.8	10.2	11.3	10.2	11.0	11.6	10.0	10.8	11.3	0.5488
	(1.2)	(1.3)	(0.9)	(1.5)	(1.8)	(1.4)	(1.1)	(1.1)	(1.4)	

[a] p(F): Significance level of Friedman two-way ANOVA for repeated measures (df = 2) performed on the values averaged over 2 consecutive nights (N1 + N2).
[b] $p < 0.05$; differences from first night (N1) of the same trimester.
[c] $p < 0.05$; difference from corresponding value of TR1.
[d] $p < 0.05$; difference from corresponding value of TR2.
All differences were tested with the Wilcoxon matched pairs, signed ranks test, two sided.

REM sleep. The pairwise comparison revealed an increase of waking from TR2 to TR3 and a reduction of REM sleep from TR1 to TR2. Caution should be applied to interpreting the latter finding, however, because the 2 consecutive nights of TR2 differed significantly. When only the first 265 minutes of sleep (i.e. the longest common sleep duration) were considered, only waking after sleep onset showed a significant variation over trimesters.

EEG spectra

Figure 1 illustrates the time course of EEG power density in the 0.75–4.5-Hz range [slow-wave activity (SWA)] for a single subject on the 6 experimental nights. The typical declining trend of SWA is evident in all records. There is a striking similarity in the patterns of the 2 consecutive nights in each trimester, whereas the patterns differ between trimesters. The low level of SWA in TR3 is noticeable.

The changes in EEG power density in NREM sleep and REM sleep during pregnancy are shown in Fig. 2. For each frequency bin the values are expressed relative to the mean value of the two TR1 recordings (100%). Because the two pairs of curves for TR2 and TR3 were similar, mean values of the two consecutive sleep episodes were used to evaluate the differences between trimesters. Based on the ANOVA (black bars below the abscissa), EEG power density in NREM sleep showed a significant variation in four frequency bands between 3.25 Hz and 16.0 Hz. The power density exhibited a progressive decline from TR1 to TR2 and from TR2 to TR3. A pairwise comparison revealed that power density was significantly lower in the 10.25–11.0-Hz and 14.25–17.0-Hz bands in TR2 than in TR1. In TR3, the values in the entire 1.25–12.0-Hz range as well as in the 13.25–16.0-Hz band were significantly reduced. However, the latter results must be interpreted with caution because the ANOVA was not significant for the entire range. To exclude the possibility that the attenuation of power density resulted from the presence of daytime napping, the computations of Fig. 2 were repeated by using only those nights that were not preceded by naps. The results from seven subjects who had at least 1 unaffected night in each trimester were very similar to those of Fig. 2. A significant ($p < 0.05$) reduction of EEG activity in TR3 relative to TR1 was present in the 1.75–4.5-Hz and 6.25–12-Hz bands.

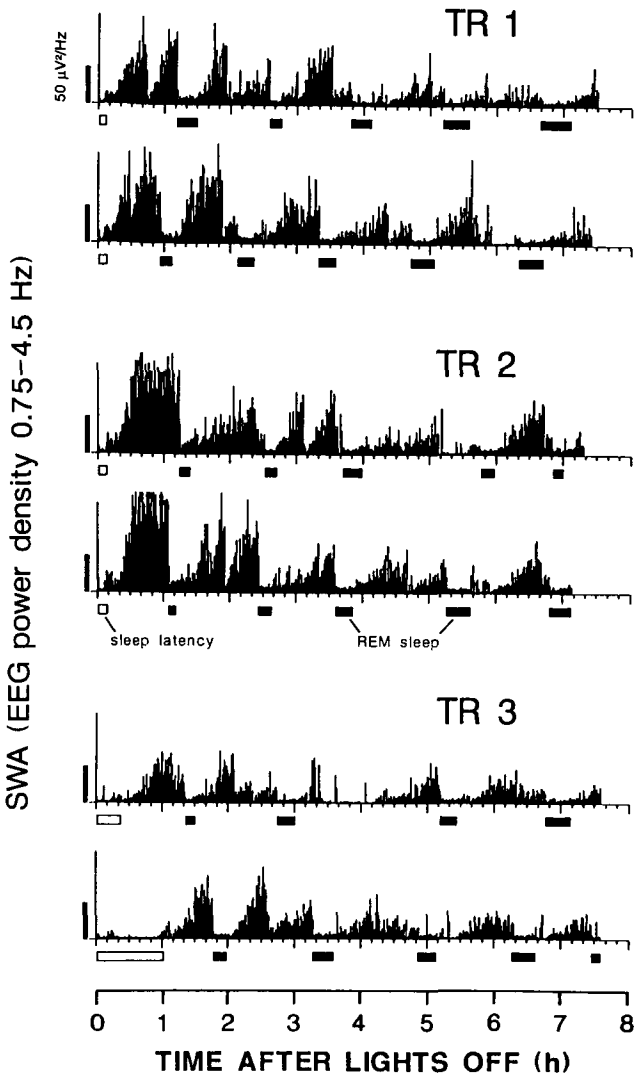

FIG. 1. Time course of EEG slow-wave activity (power density in the 0.75–4.5-Hz band) recorded for one woman on the 2 consecutive laboratory nights of the first (TR1), second (TR2) and third (TR3) trimester. The data are plotted from lights off until the termination of sleep. The REM sleep episodes (solid bars) and the sleep latency to stage 2 (open bars) are indicated below the abscissae, and a calibration mark (50 μV^2/Hz) is shown on the left of the ordinates.

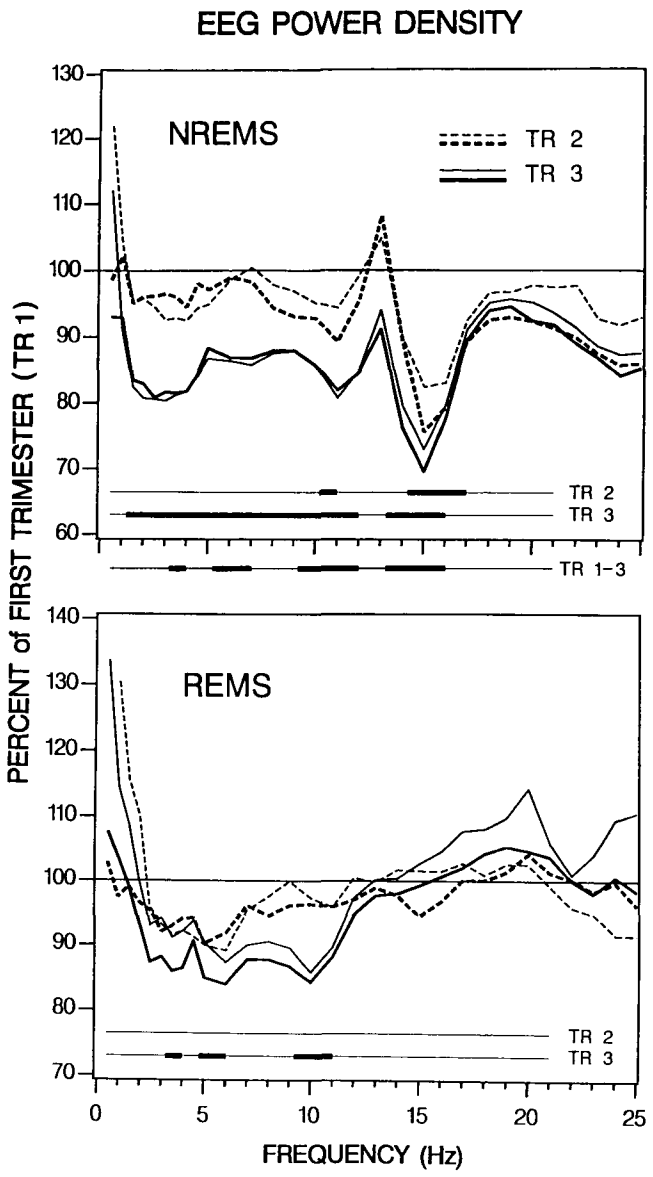

FIG. 2. Relative EEG power density in NREM sleep (top) and REM sleep (bottom) across the three trimesters of pregnancy. For each subject the values obtained in the 2 nights of the first trimester were averaged and used as the reference (100%). For each bin the data of the 2 consecutive nights in the second and third trimesters are expressed relative to the corresponding reference values and plotted as the geometric mean of the nine subjects. Statistics were performed on mean values of 2 consecutive nights. The frequency range in which the values of TR2 and TR3 differed significantly ($p < 0.05$; paired t test) from TR1 are indicated by black bars above the abscissae. The ranges with significant variation ($p < 0.05$; ANOVA) between trimesters are indicated below the abscissa.

The changes in REM sleep (Fig. 2, lower panel) were less prominent than in NREM sleep, and the ANOVA revealed no significant variation over the conditions. In the pairwise comparison, the level of significance was reached only in TR3 in some frequency bands between 3.25 and 11.0 Hz.

In Fig. 3 the relative EEG spectra of NREM sleep (mean values of two consecutive sleep episodes) are shown for three individuals. The most prominent changes were present in the frequency range of sleep spindles. However, these changes occurred at different frequencies. Whereas in subject 5 the largest decrease was present in the 16-Hz bin, in subject 7 it was the 15-Hz bin and in subject 9 the 14-Hz bin which were most affected. The peak in the adjacent lower frequency band also showed corresponding interindividual variations. Differences between subjects were also seen for the values in the delta and theta bands of TR2, which exhibited a rise (subject 5 and subject in Fig. 1), no change (subject 7) or a decrease (subject 9). In contrast,

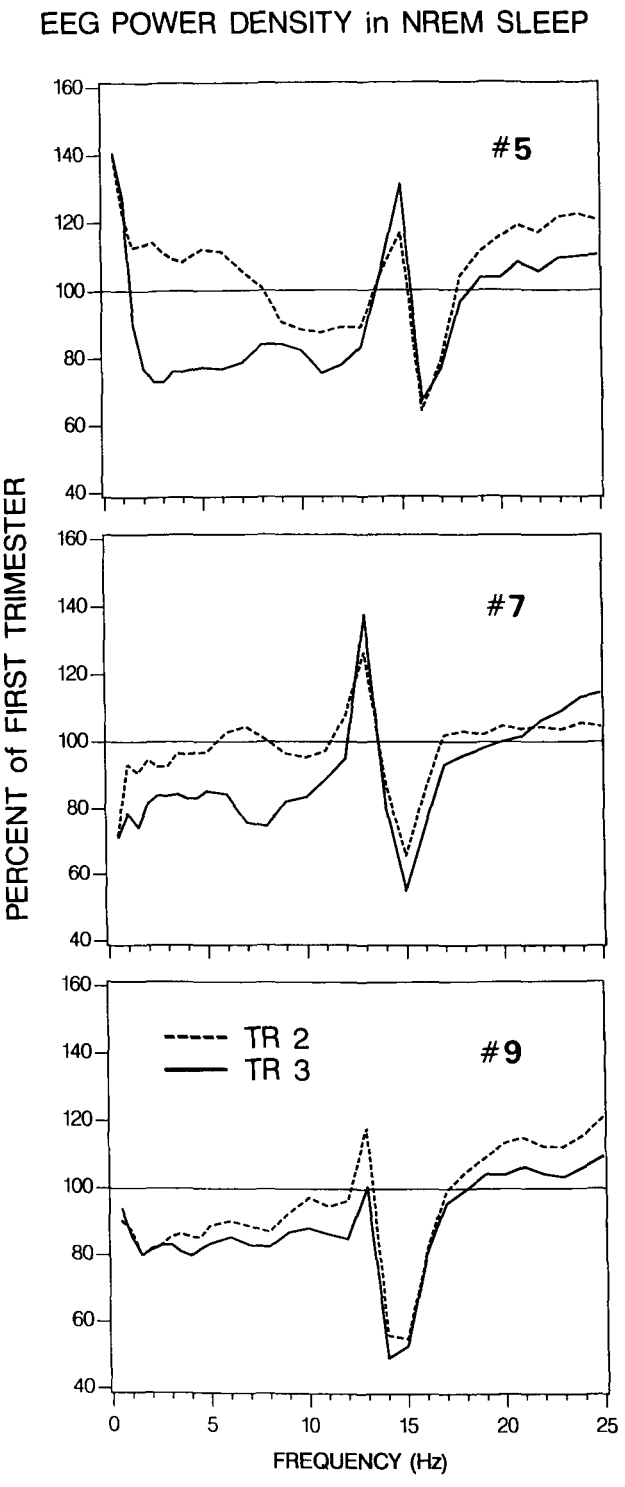

FIG. 3. EEG power density in NREM sleep in three subjects. For each trimester the values (mean of 2 consecutive nights) are expressed relative to the corresponding value in TR1. Large spectral changes in the frequencies of sleep spindles occurred from TR1 to TR2 and persisted in TR3.

power density in the delta and theta bands was invariably decreased in TR3.

Electroencephalogram power spectra calculated for NREM–REM sleep cycles are presented in Fig. 4. The top panel demonstrates for TR1 the changes in the first four sleep cycles relative to the first sleep cycle (100%). The ANOVA revealed a significant variation in the range of 0.25–10.0 Hz and in two higher frequency bands (12.25–14.0 Hz; 16.25–19.0 Hz). The lower two panels of Fig. 4 depict for the first four cycles the power density in TR2 and TR3 expressed relative to the corresponding values in TR1. The similar shape of the curves in TR2 demonstrates that the changes were similar in all cycles. In contrast to TR2, the spectral changes in TR3 differed between the cycles (Fig. 4, bottom panel). The reduction of power density in the low frequencies was most prominent in cycle 1 and smallest in cycle 4. A two-way ANOVA for the factors sleep cycle (four levels) and trimester (three levels) revealed a significant interaction ($p < 0.05$) in three frequency bins (6.25–7.0 Hz, 8.25–9.0 Hz and 14.25–15.0 Hz).

DISCUSSION

On the basis of standard polysomnography, the main finding was the considerable increase in waking after sleep onset in the last trimester. This result confirms previous findings (3) and is probably a consequence of various factors such as nicturia, the difficulty of assuming the habitual sleep posture due to the enlargement of the abdomen, the disturbance of sleep by fetal movements and low back pain in late pregnancy (1,3,10). However, in confirmation of a previous report (8), there was no evidence for sleep fragmentation (i.e. no increase in stage 1 and movement time). Another significant finding was the reduction of REM sleep from the first to the second trimester, an effect that on the basis of the mean values seemed to progress to the third trimester (Table 1). Although this interpretation must be qualified in view of the large night-to-night variability, it agrees with the results of two recent studies (3,8). The amount of SWS did not undergo consistent changes across trimesters.

The new finding of this study is the progressive reduction of EEG power density in NREM sleep. The decrease did not uniformly affect the entire frequency range but showed a specific pattern. Whereas the lowest frequency bin showed no significant change, the other parts of the delta band, as well as the theta and alpha bands, were reduced. A minor peak was evident at the alpha–sigma transition, whereas the most prominent decrease in power density occurred within the sigma band. No significant changes were present in the highest frequencies. The pattern of these changes were already apparent in TR2, although individual variability was high. The major changes were present in TR3 when power density in the 15-Hz band was reduced by as much as 30% relative to TR1. The high night-to-night consistency of the mean spectra provides strong evi-

dence that the progressive modifications of the EEG in NREM sleep were indeed associated with the stage of pregnancy. Because two thirds of the subjects entered the study between June and August, seasonal influences must be considered. In view of the lack of consistent seasonal changes in the sleep EEG spectrum in healthy women and in patients suffering from seasonal affective disorders (Brunner et al., in preparation), a prominent contribution of seasonal factors to the changes observed in the present study is unlikely.

Changes in the REM sleep spectra were less pronounced than in NREM sleep and showed a higher night-to-night variability. Modifications in the sigma frequencies were absent in REM sleep, indicating that the prominent changes in the 13.25–16.0-Hz band of the NREM sleep spectra were due to an effect on sleep spindles. Although direct measures of sleep spindles (e.g. number of occurrence, amplitude and frequency) were not obtained in this study, spectral power density in the spindle frequency range has been shown to be closely related to the spindle parameters (14). The pattern of the relative changes in the mean and individual curves (Figs. 2 and 3) is consistent with the interpretation that a decrease of the predominant spindle frequency in the course of pregnancy gave rise to a peak and a trough in the relative spectra. However, because the trough was much more prominent than the peak, an overall suppression of spindle activity may have occurred. This interpretation is tentative and will have to be confirmed by a direct analysis of sleep spindles.

The pattern of spectral changes observed in the course of pregnancy differed from those induced by sleep deprivation or by pharmacological agents. A sleep deficit is known to increase power density in the delta and theta ranges while reducing activity in the spindle frequency band (11,12). These effects contrast with the changes induced by benzodiazepine receptor agonists, which suppress delta and theta activity while enhancing power density in the spindle frequencies (see reference 19 for an overview). However, these drugs do not appear to shift the frequency of sleep spindles (20). It is reasonable to assume that the modifications of the sleep EEG observed in the present study were a consequence of the marked hormonal changes that are known to occur during pregnancy (21). Activity in the

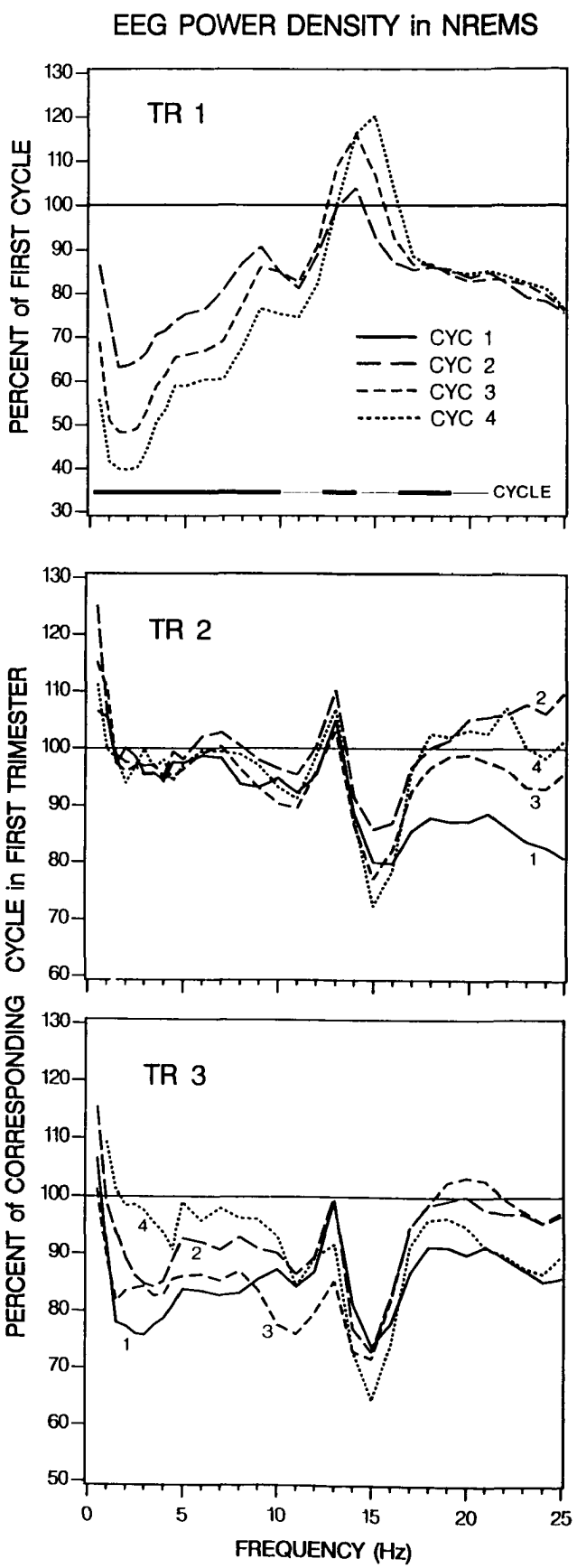

FIG. 4. Changes of EEG power density over the NREM–REM sleep cycles. The curves represent mean values of two consecutive sleep episodes. Power density in each frequency bin is expressed relative to cycle 1 (100%) for TR1, and relative to the corresponding cycle of TR1 for TR2 and TR3; i.e. the top panel shows changes across the sleep cycles for TR1, whereas the middle and bottom panels show deviations from corresponding cycles of TR1 for TR2 and TR3. The heavy lines above the abscissa of the upper panel indicate the ranges in which a significant variation over the first four sleep cycles was observed ($p < 0.05$, ANOVA).

spindle frequencies may be particularly susceptible to endocrine influences, because power density in this frequency range was altered already in TR2. Pregnenolone, one of the hormones whose level increases during pregnancy, was recently shown to attenuate power density in NREM sleep, an effect that was most prominent in the spindle frequency range (15). Further evidence for hormonal influences on spindle activity was obtained in a study in which the spindle frequency was observed to undergo shifts in the course of the menstrual cycle (22). In contrast to power density in the spindle frequencies, activity in the low- and medium-frequency range (1.25–12.0 Hz) was consistently reduced only in late pregnancy when several hormones (e.g. estrogen, progesterone and prolactin) reach their peak level (23). It is unlikely that daytime napping contributed substantially to the reduction of slow-wave activity because similar changes were also observed for nights that were not preceded by naps. In summary, in view of the multiple hormonal changes known to occur during pregnancy (21), it is difficult to attribute the effects on the sleep EEG to specific substances. However, as more information on the action of single hormones becomes available, the results obtained in this study may soon be interpreted in more detail.

It must be pointed out that only the changes occurring within pregnancy were analyzed in the present study, because no "baseline" record before or after pregnancy was available. Thus it is possible that the reference values of TR1 had already been affected by hormonal changes in early pregnancy. In view of the characteristic and consistent effects observed in TR2 and TR3, it will be important to analyze the entire time course in future studies.

In conclusion, the present study demonstrated that in the course of pregnancy the sleep EEG undergoes a characteristic modification that is not apparent from an analysis based on the conventional scoring of sleep stages. The results represent, therefore, further evidence of the necessity to complement sleep recordings by a quantitative analysis of the EEG. As the neurophysiological mechanisms underlying the sleep EEG are being elucidated (24), it is not improbable that the putative hormonal actions leading to the electrophysiological changes in the course of pregnancy will soon be specified.

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