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All Night Spectral Analysis of EEG Sleep in Young Adult and Middle-Aged Male Subjects

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DIJK, D. J., D. G. M. BEERSMA AND R. H. VAN DEN HOOFDAKKER. All night spectral analysis of EEG sleep in young adult and middle-aged male subjects. NEUROBIOLOGI AGING 10(6) 677~82, 1989.—The sleep EEGs of 9 young adult males (age 20–28 years) and 8 middle-aged males (42–56 years) were analyzed by visual scoring and spectral analysis. In the middle-aged subjects power density in the delta, theta and sigma frequencies were attenuated as compared to the young subjects. In both age groups power density in the delta and theta frequencies declined from NREM period 1 to 3. In the sigma frequencies, however, no systematic changes in power density were observed over the sleep episode. In both age groups the decay of EEG power (0.75–7.0 Hz) over successive NREM-REM cycles and the time course of EEG power during NREM sleep was analyzed. The decay rate of both EEG power density over successive NREM-REM cycles and EEG power density during NREM sleep was smaller in the middle-aged subjects than in the young subjects. It is concluded that the age-related differences in human sleep EEG power spectra are not identical to the changes in EEG power spectra observed in the course of the sleep episode. Therefore age-related differences in EEG power spectra cannot be completely explained by assuming a reduced need for sleep in older subjects. The smaller decay rate of EEG power during NREM sleep in the middle-aged subjects is interpreted as a reduced sleep efficiency. The results are discussed in the frame work of the two-process model of sleep regulation.

Aging Sleep EEG Spectral analysis Two-process model

AGE-RELATED changes in human sleep have been studied extensively and profound differences between age groups have been reported [for a review see (13)]. Most studies used conventional sleep scoring techniques and a consistent finding across these studies was a decrease in stage 4 of NREM sleep with increasing age. Changes in stage 3 are less consistently reported. Compared to young adults, both normal and reduced levels of stage 3 have been described with increasing age. These changes in slow wave sleep are accompanied by an attenuation of the amplitude of delta waves (8, 10, 18). One interpretation of this age-related change is that the reduction in SWS reflects a reduced need for deep NREM sleep (1,13). This interpretation is supported by similarities between the age-related differences on the one hand and the changes over a sleep episode and those induced by sleep deprivation on the other. In the young adult the most striking change over a sleep episode is the sleep decrease in the duration of the stages 3 + 4 from the beginning of sleep to the end (22). Also in older subjects SWS is predominantly present in the beginning of sleep (9). In both age groups this sleep-dependent decrease in SWS is thought to reflect diminishing NREM sleep need. Enhancement of sleep pressure by increasing the duration of prior wakeness results in an increase in the amount of SWS both in young adults (3) and older subjects (5,17,20).

In a recently developed model for the timing of sleep and wakeness (4,6) these changes are thought to reflect a sleep regulatory process. In this model the timing of sleep and wakeness results from an interaction between a homeostatic process S and a circadian process C. Process S reflects sleep debt which increases during waking in a saturating exponential way and decreases exponentially during sleep. The circadian process modulates the upper and lower limits of S. If S reaches the lower threshold, sleep is initiated to continue until the lower threshold is reached. Both thresholds covary with the body temperature rhythm. In young adults the time course of process S was quantified on the basis of the changes in EEG power density over a sleep episode and the changes induced by sleep deprivation (3). The shape of the thresholds was derived from an experiment in which the spontaneous termination of sleep was assessed after varying the duration of prior wakeness (2). The parameters obtained allowed computer simulations of the timing of sleep and wakeness in a variety of experimental conditions, including temporal isolation. Whether or not the parameter values in this model are age dependent has not been investigated.

A fundamental question is whether or not the changes in the

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Sleep EEG with increasing age can be explained completely by an attenuation of sleep need (i.e., a reduced level of S at the beginning of sleep). To answer this question we need a detailed analysis of the age-related changes of the sleep EEG. Visual scoring of the sleep EEG is not sensitive enough for such a comparison. This can be concluded from an experiment in which visual scoring was combined with spectral analysis (3). Sleep deprivation not only increased the amount of SWS but power density in the delta and theta frequencies within SWS were also enhanced. Also, within stage 2 and REM sleep, spectral analysis detected changes in specific frequency bands which went unnoticed by the visual analysis. Furthermore, spectral analysis allows a quantitative description of the time course of EEG power density during sleep. The aims of the present paper are 1) to determine if age-related changes in the sleep EEG can be completely explained by reduced need for NREM sleep and 2) to determine if parameter values of the two-process model of sleep regulation vary across age.

To address these questions we compared power density during NREM sleep and REM sleep of young adult and middle-aged male subjects and analyzed the time course of power density in these two groups. The results are interpreted in the framework of the two-process model of sleep regulation.

METHOD

Nine young adult males (mean age 22.8 years; range 20-28) and eight middle-aged males (mean age 49.8 years; range 42-56) were paid to participate in the study. They were all in good health and were free of sleep complaints as assessed by a general sleep complaints scale. For the duration of the experiment the use of alcohol or other drugs was not allowed. The subjects were instructed not to take naps and to avoid irregular activities. The data presented here were collected after one adaptation night in the laboratory. All subjects went to bed in the laboratory at their habitual bedtimes. EEG, EMG and EOG were recorded. The EEG was derived from C4-A1 and C3-A2. All signals were on line analog to digital converted with a sampling rate of 64 Hz. Before the conversion the EEG signals were low pass filtered at 25 Hz (24 dB/octave). Digitized data were stored on magnetic tape. On both analog to digital converted signals power density spectra were calculated for NREM sleep (stages 2, 3, and 4) and REM sleep (stages 1 + 2 + 3 + 4 = REM). All epochs of stages 0, and MT (movement time) were excluded from the analysis. Short lasting disruptions of the EEG signal due to arousals were removed on the basis of the rectified EMG.

Differences between age groups were tested with the Student's t-test, or Mann-Whitney U-test.

RESULTS

Table 1 contains the time spent in the various sleep stages during the first 360 min after sleep onset for the two age groups. Sleep onset was defined as the first occurrence of stage 2 provided that less than 2 minutes of stage 0 or MT was present in the next ten minutes. The middle-aged males had significantly less stage 4 than the young adult males (p<0.05, Mann-Whitney U-test). In 4 of the 8 middle-aged subjects only 1 min or less stage 4 was scored. In the duration of stage 3 no significant differences were observed between the two groups. On average, middle-aged subjects had more stage 0, 1 and 2 than young subjects, but for none of these stages was the difference statistically significant.

Time spent in stage REM during the first 360 minutes of sleep was virtually identical for the two groups. Analysis of the sleep stages during the entire recording period led to similar results as the analysis of the first 360 minutes of sleep.

Power densities during the first 360 minutes of sleep were calculated for NREM sleep (stages 2, 3, and 4) and REM sleep. Statistical significant differences were found between the two age groups. For a visualization of these differences the absolute power densities are not suitable since from 1 to 15 Hz the absolute values encompassed several log units. Therefore, the middle-aged subjects' power density in each frequency bin was expressed as a fraction of the average power density in the young subjects in that bin, for both REM sleep and NREM sleep (Fig. 1). During NREM sleep power densities in the delta and theta band in the middle-aged subjects were on average lower than those of the young subjects. These differences were statistically significant between 2 and 6 Hz (for the statistical evaluation the absolute values were log trans...
formed and then subjected to Student's t-test). The largest attenuation was observed in the 1.25-2.0 Hz bin. In this frequency band power densities in the middle-aged subjects were on average as low as 32 percent of the value in the young subjects. In the sigma frequencies (13 and 14 Hz) power density in the middle-aged subjects were also significantly lower than in the young subjects. During REM sleep power densities over the entire frequency range, with the exception of the lowest frequency bin, were somewhat lower in the middle-aged subjects, although for none of the frequency bins were the values significantly different (p > 0.05, Student's t-test on log transformed absolute values). Power densities during NREM sleep were calculated for the first three NREM-REM cycles, in both age groups. In Fig. 2 the power densities during the second and third NREM period are expressed relative to the values of the first NREM period for both the middle-aged and young subjects. To assess in which frequency bins power density varied significantly over the first 3 cycles, power density in each frequency bin was subjected to Friedman's nonparametric ANOVA for repeated measures. In the young subjects a progressive reduction in power densities between 1 and 11 Hz from cycle 1 to 3 could be observed. The largest change from cycle 1 to 3 was present in the 1.25-2.0 Hz band. In the third cycle power densities in this band had dropped to 32.6 ± 5.0% (S.E.M.) of the value in the first cycle. In the highest frequencies analyzed no significant changes were observed. In the middle-aged subjects the reductions from cycle 1 to 3 were on average smaller than those in the young subjects. In the middle-aged subjects the significant changes from cycle 1 to 3 were limited to 1 to 7 Hz. Also in the middle-aged subjects the largest change from cycle 1 to 3 was located in the 1.25-2.0 Hz band. In this age group power density in the 2 Hz band during the third NREM period amounted to 52.2 ± 3.9% (S.E.M.) of the value in the first cycle. In the frequencies above 7 Hz no significant changes were observed. The somewhat smaller reduction from cycle 1 to 3 in the middle-aged subjects suggests that the changes over the entire sleep period are smaller in the middle-aged subjects than in the young subjects. This further implies that the observed differences in the absolute power densities (Fig. 1) between the age groups change over the sleep period. The changes over the sleep period in the absolute power densities were analyzed by calculating the integral power density (0.75–7.0 Hz) in stage 1, NREM and REM sleep for all NREM-REM cycles in both age groups. The average values per NREM-REM cycle were plotted against the corresponding cycle midpoint (Fig. 3). The difference between the age groups was largest at the beginning of the night, i.e., during the first NREM-REM cycle, and then gradually became smaller.

To quantify the changes over the sleep period integral power densities (0.75–7.0 Hz) per NREM-REM cycle were in each subject expressed as a fraction of the average power densities during the first 360 minutes of sleep of that subject. The "log

FIG. 3. EEG power density (0.75–7.0 Hz) during stages 1, 2, 3, 4 and REM averaged per NREM-REM cycle. Values are plotted at cycle midpoints. Filled symbols: young subjects; open symbols: middle-aged subjects. Number of subjects contributing to each average is indicated. Bars indicate 1 S.E.M. Plotted lines are the exponential decay functions which resulted from linear regression analysis on the "log values of the absolute power densities per NREM-REM cycle. In this regression analysis all individual NREM-REM cycles were included; n = 38 and 32 for the young and middle-aged subjects respectively. (The deviation between this line and the average power density in the first cycle in the young subjects is a consequence of this transformation.)
changes over the sleep episode were different for the two age groups. It could 0.163 elog units/per hour for the young and middle-aged subjects respectively. Thus also after exclusion of REM sleep the changes of 214% was obtained. The accumulation rates were 0.430 and NREM sleep energy, whereas in the middle-aged subjects a value 30 minutes (Fig. 4). In the young subjects EEG transformed values were correlated with the cycle midpoints. In both age groups a highly significant correlation was obtained, r(36) = -.878, p<0.001; r(30) = -.918, p<0.001, for the young and middle-aged subjects respectively. The decay rates were calculated from the slopes which resulted from the linear regression analysis. These decay rates were 0.225 ± 0.021 and 0.155 ± 0.012 °log units (± SE) per hour for the young and middle-aged subjects respectively. The 95% confidence intervals of the two decay rates did not overlap. Adding a quadratic term to the analysis revealed a small but significant positive quadratic term in the young subjects, F(1,35) = 5.826, p<0.05. In the middle-aged subjects the quadratic term was not significant, F(1,31) = 1.528, p>0.1. Since power density during REM sleep is very low, differences between the two groups in the temporal distribution of REM sleep might have caused the different decay rates. If this were the case the different decay rates would not reflect a difference in the time course of the NREM sleep process. To investigate the influence of REM sleep we accumulated EEG power density (0.75–7.0 Hz) during NREM sleep over the first 4 hours of NREM sleep, resulting in NREM EEG energy. The values were expressed relative to the total energy after 4 hours of NREM sleep and plotted at 30-minute intervals (Fig. 4). In the young subjects EEG energy accumulated in a saturating exponential way. Although in the middle-aged subjects the saturation is less clear, also in these subjects a leveling off of EEG energy accumulation towards the end of the period considered, can be observed. For a quantitative evaluation the saturating exponential function $E_t = A(1 - e^{-rt})$ was fitted to the data using the least squares criterion. The normalization points were not included in the analysis. $A$ represents the asymptote, $r$ the accumulation rate (the inverse of the time constant) and $t_0$ allows a correction for the low power densities in the first minutes of sleep. In the young subjects, 95% and in the middle-aged subjects 96% of the total variance could be explained by fitting the 3 free parameters. The resulting parameters were, however, not identical for the two age groups. The asymptote $A$ for the young subjects was 120% of total 4 hour NREM sleep energy, whereas in the middle-aged subjects a value of 214% was obtained. The accumulation rates were 0.430 and 0.163 °log units/hour for the young and middle-aged subjects respectively. Thus also after exclusion of REM sleep the changes over a sleep episode were different for the two age groups. It could be argued though that the assumption of an exponential decline of power density over a sleep episode, which implicates that at $t = 0$ power density = 0 is not valid. The limit might well be different from zero. If this limit is identical in the two age groups the higher absolute power densities in the young subjects could render this limit negligible. In contrast, in the middle-aged subjects its contribution might still be considerable. Excluding this limit from the fitting procedure could then result in a lower decay rate in the middle-aged subjects which, however, does not reflect the rate of change over the sleep episode. Assuming that this limit is positive would mean that the accumulation of EEG energy should be fitted with a saturating exponential function with a additional linear trend $E_t = A(1 - e^{-rt})+c+t$. In both age groups this procedure resulted in a positive linear trend. The difference in the (horizontal) asymptote was highly reduced (65.1% and 98.7% for the young and middle-aged subjects respectively). The difference in the inverse of the time constant of the exponential process however, was preserved (0.713 and 0.265 °log units/hour for the young and middle-aged subjects respectively).

**DISCUSSION**

The analysis of the sleep stages revealed that in the middle-aged males the amount of stage 4 but not stage 3, was reduced as compared to the young adults. These findings are in agreement with those studies in which the 75 μV criterion for the scoring of delta sleep was maintained, as we did in this study [see (13) for references].

Spectral analysis revealed that during NREM sleep power densities between 1 and 6 Hz were significantly lower in the middle-aged subjects. Also in the sigma band (13 and 14 Hz) power densities were attenuated. This latter finding is in accordance with the reduced spindle amplitude reported by Principe et al. (14). Thus the age dependent changes in the NREM sleep EEG are not limited to those frequencies which are typical for stages 3 + 4, i.e., the delta frequencies, as is often suggested in the literature. Another conclusion from Fig. 1 is that not all frequencies are affected equally. The largest reduction is observed in the 2 Hz band. Feinberg et al. (11) analyzed the amplitude/frequency relation during NREM sleep, in young (22.2 years) and older subjects (71.8 years). From their analysis it was also concluded that the amplitude of delta waves decline more with age than amplitude in the higher frequencies. The present analysis, however, shows that these age-related changes in the sleep EEG are already occurring in a relatively young group of subjects (42–56 years). In the present data there is some evidence that these age-related changes are not limited to NREM sleep, but may extend into REM sleep. However, this conclusion must be considered tentative until this finding is replicated in a larger number of subjects.

Despite the large differences in the absolute power densities the changes over the sleep episode were remarkably similar in the two age groups. In both age groups the power densities in delta and theta frequencies decreased. In the young subjects the sleep-related changes extended up to 11 Hz. The present findings are in good agreement with the analysis of Borbély et al. (3), of changes in power density over the sleep period in young adults. Similar spectral changes have been observed in a series of experiments. After sleep deprivation power densities in the delta and theta frequencies were enhanced, and power density in the 15 Hz band was attenuated. In a nap study in young adult female subjects it was shown that the power densities in the delta and theta frequencies during sleep were a monotonic rising function of the duration of prior wakefulness (7). In that study power density in the 15 Hz band decreased with increasing duration of prior wakefulness. In all these studies power density in the 2 Hz band was most strongly affected. Unfortunately, recovery sleep after

**FIG. 4.** Accumulation of EEG energy (0.75–7.0 Hz) during the first 4 hours of NREM sleep plotted against elapsed NREM time. Values are plotted at 30-minute intervals and expressed relative to EEG energy accumulated after 240 minutes of NREM sleep. Filled symbols: young subjects; open symbols: middle-aged subjects. Bars represent 1 S.E.M.
sleep deprivation in aged subjects has not been subjected to spectral analysis, although an increase in SWS after sleep deprivation has been reported also in older subjects (5, 17, 20).

The picture emerging from these experiments is that when sleep debt at the beginning of sleep is high, power densities in the delta and theta frequencies of the sleep EEG are high, whereas power densities of the spindle frequencies are inversely affected. In the course of the sleep episode, when sleep debt is diminishing, power densities in the delta and theta frequencies decay, whereas power densities in the spindle frequencies tend to increase. One interpretation of the observed lower power densities in the delta and theta frequencies in the middle-aged subjects is that in these subjects sleep debt at the beginning of the nocturnal sleep episode is much smaller than in the young subjects. This interpretation is further supported by the finding that the largest difference between the two age groups was present in the 2 Hz bin. This frequency is particularly sensitive to changes in sleep debt. The reduced power density in the spindle frequencies, however, can not be attributed to a reduced sleep debt, since over the sleep period no change or even an increase in power density is observed. So, the age-related changes of the sleep EEG cannot be fully explained by changes in the hypothetical process S which is thought to measure sleep debt. Since this ‘age effect’ or ‘nonprocess S effect’ may also affect power densities in the delta and theta frequencies the reduced sleep debt interpretation is premature. The observed attenuation of power density in the delta and theta frequencies could equally well be explained by assuming that not the level of S is reduced but that the relation between the sleep EEG and process S has changed with increasing age.

In our present sample the decay of power density integrated over 0.75–7.0 Hz and averaged over successive NREM-REM cycles was essentially exponential in both age groups, although in the young subjects a small deviation from an exponential decline could be observed. When disregarding the quadratic term, the time constants of the exponential decay, however, were different for the two age groups. The decay rate in the young subjects (0.225 ±log units/hr) was virtually identical to the decay rate obtained by Borbély (0.238 ±log units/hr) in an independent study in subjects of about the same age (3). The decay rate in the middle-aged subjects, however, was significantly smaller (0.155 ±log unit/hr). In the quantitative formulation of the two-process model (6) the time constant of the decay of process S during sleep was derived from the decay of EEG power density averaged over NREM-REM cycles. This implies that the decay rate of process S will change if the temporal distribution of REM sleep changes. The possible contribution of a different REM sleep distribution, which has been reported in older subjects (16) and was also present in our sample (data not shown) could not explain this different decay rate since the time constant of the accumulation of NREM EEG energy was also different for the two age groups. This difference was preserved when a linear trend was added to the fitting procedure. Keane et al. (12) also reported a flatter distribution of delta waves across the night in older subjects, although they did not analyze NREM sleep separately. So, it can be concluded that with increasing age not only the temporal distribution of REM sleep is changed but the time course of NREM sleep is also affected. One interpretation of this finding is that in the middle-aged subjects sleep is less efficient; i.e., the decay of NREM sleep during sleep is slowed down. This interpretation is in accordance with complaints of older subjects about less restorative sleep (13).

What are theoretically the consequences of this reduced sleep efficiency for the timing of sleep in older subjects? The only parameter of the two-process model which has been measured directly in the present analysis is the decay rate of S during sleep. The time constant for the young subjects, based on the analysis per NREM-REM cycle, is very close to the value originally derived from the data of Borbély (3), which implies that the decay rate is a rather robust characteristic of sleep in young adults. However, this decay rate seems to vary across age. We tried to simulate the timing of sleep and wakefulness in middle-aged subjects by substituting the original time constant of the decay of S by the time constant derived from our middle-aged subjects, while leaving the remaining parameters unchanged. These simulations resulted in a prolonged sleep duration [562 ± 22 (sd) min vs. 497 ± 24 min for the middle-aged and young subjects respectively]. This longer sleep duration is not accompanied with a much earlier sleep onset, but the moment of waking up is delayed for on average 70 minutes. The results of these simulations are at variance with existing data on the timing of sleep in older subjects. No change or a reduction in sleep duration with increasing age is generally reported (13, 19). Furthermore, in contrast to the results of the simulations, sleep end is generally advanced in middle-aged subjects as compared to young subjects (19, 22). Obviously, only changing the decay rate, and leaving the remaining model parameters unchanged does not produce any of the characteristics of sleep timing in aged subjects. For a complete understanding of the age related changes in sleep regulation, in the frame work of the two-process model, experiments designed to measure the remaining parameters are needed.

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