Spectral Analysis of the Sleep Electroencephalogram During Adolescence

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Objectives: To describe developmental changes of the human sleep electroencephalogram (EEG) during adolescence using EEG spectral analysis and specifically to compare the nocturnal dynamics of slow-wave activity (EEG spectral power 0.6-4.6 Hz, a marker for sleep homeostatic pressure) in prepubertal and mature adolescents.
Design: After 10 nights on a fixed 10-hour sleep schedule without daytime naps, participants were studied during a 10-hour baseline night.
Setting: Data were collected in a 4-bed sleep research laboratory.
Participants: Eight prepubertal children (pubertal stage Tanner 1; mean age 11.3 years, SD ± 1.2, 4 boys) and 8 mature adolescents (Tanner 5; mean age 14.1 years, ± 1.3, 3 boys).
Interventions: Not applicable.
Measurements: All-night polysomnography was performed. Sleep stages were scored according to conventional criteria. EEG power spectra (of derivation C3/A2) were calculated using a fast Fourier transform routine.
Results: A reduction of non-rapid eye movement (NREM) sleep stage 4 (by 40.1%) and greater amounts of stage 2 sleep (19.7%) were found in mature compared to prepubertal adolescents. NREM sleep EEG power was lower in the frequency ranges < 7 Hz, 11.8 to 12.6 Hz, and 16.2 to 16.8 Hz in mature adolescents. A reduction of rapid eye movement sleep spectral power was present in the frequency ranges < 8.6 Hz and 9.6 to 15 Hz for mature compared to prepubertal adolescents. Slow-wave activity showed identical dynamics within individual NREM sleep episodes and across the night in both developmental groups.
Conclusions: The homeostatic recuperative drive during sleep remains unchanged across puberty. The decline of slow-wave sleep during adolescence may reflect developmental changes of the brain rather than changes of sleep regulatory processes.
Key Words: sleep homeostasis, puberty, and adolescent humans
Citation: Jenni OG; Carskadon MA. Spectral analysis of the sleep electroencephalogram during adolescence. *SLEEP* 2004;27(4):774-83.

INTRODUCTION

ONE OF THE MOST CONSISTENT FINDINGS ABOUT ADOLESCENT SLEEP BEHAVIOR IS THE DELAY IN THE TIMING OF SLEEP.[1-6] Adolescents increasingly tend to stay up late at night and sleep late in the morning compared to preadolescents. This adolescent sleep delay has attracted interest of parents, clinicians, and educators concerned about chronic sleep loss in young people who are unable to fall asleep early at night but must wake up for early school days. This concern adds to the urgency of understanding whether developmental changes in sleep regulatory processes are involved.

The shift of the sleep phase has been attributed to altered psychosocial environment and, more recently, to modifications of the circadian clock during puberty.[2,7] The timing of sleep, however, is codetermined by the interaction of the circadian system with a sleep-dependent homeostatic process.[8,9] Therefore, the adolescent delay in sleep timing could well be related to developmental changes of the latter process, but literature on sleep homeostatic mechanisms during adolescence remains scarce. Furthermore, quantitative electroencephalogram (EEG) analysis, a powerful method to investigate underlying regulatory features of sleep, has only been occasionally used in children and adolescents.[10-13]

Disclosure Statement
No significant financial interest/other relationship to disclose.

Submitted for publication October 2003
Accepted for publication January 2004
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The homeostatic process is viewed to reflect sleep pressure or sleep need, which builds up during wakefulness and dissipates during sleep.[8,9] Parameters of the adult homeostatic process (eg, the build-up rate during the day and the nocturnal decay rate) have been derived from the time course of slow-wave activity (SWA, EEG spectral power in the frequency range of 0.75-4.5 Hz, a quantitative measure of EEG slow waves) during daytime naps, baseline nights, and recovery sleep after sleep deprivation.[8,9,14-16] Typically, SWA is high initially in the sleep episode and exhibits an exponential decline across successive non-rapid eye movement (NREM) sleep episodes, reflecting the overnight dissipation of sleep propensity. The time constant of the exponential decay of SWA has been assessed and confirmed in several experiments with young adults.[9,15,16]

Slow wave sleep (SWS, NREM sleep stages 3 and 4) and SWA have been reported to decrease across puberty.[10-13,17-20] By the end of the second decade, time spent in SWS is only 60% of the amount at the beginning of the decade.[20] Thus, a fundamental question is whether the adolescent SWS decrease simply represents developmental changes of SWS-generating brain structures or whether it indicates changes in sleep homeostatic processes as well.

A number of authors have described an age-related reduction of SWA and changes in its nocturnal time course with advancing age.[21-24] Studies estimating the exponential decline of SWA in middle-aged subjects have yielded a longer time constant (ie, shallower decay rate of SWA) compared to young adults,[22] leading to the conclusion that homeostatic recuperative drive attenuates with aging.

Does the nocturnal decay of SWA also change at the transition from childhood to adulthood? One recent study has reported that the nightly decline of SWA was similar between children and adolescents, but a statistical analysis was not provided.[13] Detailed

information about changes in the nocturnal dynamics of SWA across puberty would provide important insights into the development of sleep homeostatic mechanisms.

The principal aim of this study was to use EEG spectral analysis to describe developmental changes of the adolescent sleep EEG. We were in particular interested in whether the dynamics of SWA across the night and within individual NREM sleep episodes changes in the course of adolescent development.

METHODS

Participants

Sixteen sleep recordings from 8 prepubertal children (pubertal stage Tanner 1; mean age 11.3 years, SD ± 1.2; range 9.6-12.9 years, 4 boys) and 8 mature adolescents (Tanner 5; mean age 14.1 years, ± 1.3; range 11.8-15.9 years, 3 boys) were analyzed. Four prepubertal and 1 mature participant had taken part in an investigation of the sensitivity of the circadian timing system to light during the summer months in 2002,[25] and 11 participants were selected from a forced desynchrony study conducted between 1999 and 2002.[26,27] One female participant was studied longitudinally at both developmental stages (Figure 3). Polysomnographic sleep data from these studies have not been reported previously.

Pubertal status was determined at a brief physical examination using the standardized assessment scales developed by Tanner.[28] Tanner staging relies on rating genital development and pubic hair growth in boys and breast development and pubic hair growth in girls. In general, pubic hair growth ratings are more reliable than genital or breast development ratings.[28] Tanner staging was performed by 2 or 3 independent research physicians, and consensus ratings of pubic hair growth were used to classify pubertal stage. Pubertal stage Tanner 1 represents absence of secondary sexual characteristics (prepubertal), and Tanner 5 indicates adult sexual maturity.

For both studies, telephone and questionnaire screenings were performed to exclude children with personal or family history of psychopathologies, sleep disorders, chronic or current illnesses, or evidence of learning disabilities. Participants with sleep schedules that indicated chronic insufficient sleep accompanied by signs of excessive sleepiness were also excluded. On the day of study, the participants were in good physical and mental health, were on no medications, and had no current sleep complaints. The protocols of both studies were approved by the Lifespan Institutional Review Board for the Protection of Human Subjects, and the studies were performed according to the Declaration of Helsinki. A description of the study procedures was given to and informed consent was obtained from the participants and their parents. Participants received monetary compensation.

Procedures

The 2 protocols had identical conditions for the prestudy period and for the first night recording (baseline night = lights off at 10:00 PM, lights on at 8:00 AM, 10-hour bedtime). The protocols started with at least 10 nights on the same fixed 10-hour sleep schedule without daytime naps. Consistent schedules were monitored by daily phone calls, sleep diaries, and continuous wrist actigraphy. Although no adaptation night preceded the baseline night, all participants had slept previously in our lab while taking part in other studies. All were recorded in individual darkened bedrooms using standard polysomnography.

EEG Recordings and Analysis

Overnight monitoring included continuous recordings of EEG (referential derivations, international 10-20 system, C3/A2 or C4/A1, and O2/A1 or O1/A2), electrooculogram (right and left outer canthus), electromyogram (mentalis, submentalis), and electrocardiogram. Derivation C3/A2 was used for sleep-stage scoring and for power spectral analysis. The recordings were performed using the Albert Grass Heritage System (Astromed, Grass, West Warwick, RI). The signals were recorded on polygraph paper (10 mm per second paper speed; high-pass analog EEG filter, -6 dB at 0.3 Hz; low-pass filter, -6 dB at 35 Hz; notch filter at 60 Hz) and were on-line digitized (12 bit AD converter; low-pass filter, -6 dB at 35 Hz; time constant 1.0 second; storage resolution of 100 Hz for the EEG). A trained staff member monitored the quality of the recordings throughout the night. Electrode impedance was checked at the start of each recording. The EEG was subjected to spectral analysis off-line using a fast Fourier transform routine (Matlab, The MathWorks, Inc. Natick, MA). Power spectra of consecutive 30-second epochs (Hanning window, averages of six 5-second epochs) were computed, resulting in a frequency resolution of 0.2 Hz. The lowest 2 frequency bins (0.2 and 0.4 Hz) were not used for further analysis due to their sensitivity to low-frequency EEG artifacts. Artifacts were excluded by visual inspection (artifact-free 30-second epochs of sleep as a percentage of all epochs of sleep; prepubertal: 91.8% ± 1.5% [mean ± SEM]; mature: 87.6% ± 1.3%, unpaired *t* test, NS). Spectral data were analyzed up to 25 Hz. The sleep stages were visually scored from the digital recordings for consecutive 30-second epochs according to the standard criteria of Rechtschaffen and Kales.[29] The 30-second sleep scores were then matched with the 30-second power spectra.

Definition of the Sleep Cycle and the First NREM Sleep Episode

NREM-rapid eye movement (REM) sleep cycles were defined according to the criteria of Feinberg and Floyd.[30] NREM sleep episodes started with stage 2, ended with the beginning of REM sleep, and were required to last for a minimum of 15 minutes. The minimal duration of consecutive REM sleep episodes for completing a NREM-REM sleep cycle was 5 minutes (for the first REM sleep episode, no minimum criterion was applied).

The first trough in the SWA trend usually began at the time when REM sleep actually occurred (Figure 3, upper panel, black arrow). Because 'skipped' first REM sleep episodes critically influence the calculation of the dynamics of SWA across the night, we divided the first NREM sleep episode into 2 separate episodes only when SWS was interrupted by stages 1 or 2, wakefulness, or movement time for more than 12 minutes (for rationale see Appendix).

Statistics

The SAS General Linear Model procedure was used for statistical analyses (Version 8.02, SAS Institute, Inc., NC). One-, 2- or 3-way analyses of variance (ANOVA) included the between-subjects factor 'developmental group' (Tanner 1, Tanner 5), and/or the within-subject factors 'episode' (first 4 NREM sleep

episodes), and/or 'interval' (1-10 parts across the first 4 NREM sleep episodes) as appropriate. Probability values presented are based on Greenhouse-Geisser corrected degrees of freedom. The significance level was set at $P < .05$. Sleep variables and EEG power spectra were log transformed prior to statistical testing in order to approximate normal distributions. Comparisons between and within the developmental groups were performed by unpaired or paired 2-tailed *t* tests, respectively.

To assess the homeostatic process, each participant's mean SWA per NREM sleep episode (as a percentage of the overall nocturnal SWA mean) was plotted at episode midpoint times relative to sleep onset. Mean SWA values of all NREM sleep episodes were then pooled for all participants, and an exponential function was fitted to the data (Figure 4). Differences in the parameter estimates of the exponential function (time constant, lower asymptote, and SWA at sleep onset) between Tanner groups were considered statistically significant if the 95% confidence intervals of the parameter estimates did not overlap.

The mean time course of power in selected frequency ranges (0.6-4.6 Hz, 11.6-12.4 Hz, 12.6-13.4 Hz) was calculated by subdividing each NREM sleep episode into 10 equal intervals and each REM sleep episode into 3 equal intervals. For each interval, mean power was calculated for each participant and then averaged across the group. Two frequency ranges in the sigma band (11.6-12.4 Hz, 12.6-13.4 Hz) were selected on the basis of the sigma peak frequency in the developmental groups.

RESULTS

Nocturnal Sleep Variables Derived from Visual Scoring

Sleep-Stage Variables

Table 1 summarizes the macrostructure of nocturnal sleep in prepubertal (Tanner 1) and mature (Tanner 5) adolescents. An expected finding was the reduction of NREM sleep stage 4 (by 40.1%) and the greater amounts of stage 2 (19.7%) in mature compared to prepubertal adolescents. The reduction of SWS was primarily accounted for by a reduction of stage 4, because stage 3 did not differ between developmental groups. The latencies to stage 1, 2, and REM sleep did not differ significantly between groups. No differences were observed in total sleep time, sleep efficiency, waking after sleep onset, movement time, NREM sleep stage 1, and REM sleep.

Sleep-Episode Variables

A 2-way ANOVA (factors 'developmental group' and 'episode') revealed no differences in the duration of the first 4 NREM and REM sleep episodes between prepubertal and mature children (factor 'developmental group', NS), while the duration of episodes varied across the night for both developmental groups (factor 'episode': for NREM sleep, $F_{3,63} = 27.1$, $P < .05$; and for REM sleep, $F_{3,63} = 8.0$, $P < .05$). No significant interaction 'developmental group' × 'episode' was found. The duration of the first NREM sleep episode (NREM-1) was longer compared to the following episode (in prepubertal children: 130.8 ± 12.2 minutes [mean ± SEM] for NREM-1, 71.1 ± 4.9 minute for NREM-2; in mature children: 131.4 ± 16.7 minute for NREM-1, 70.2 ± 5.2 minute for NREM-2; $P < .05$; 2-tailed paired *t* tests on log transformed values). Because differences in the length of NREM-1 and the following NREM sleep episodes affect the dynamics of SWA across the night,[31] we separated the long NREM-1 into 2 episodes on the basis of the 12-minute rule in 3 prepubertal children and 5 mature children (see Appendix for rationale). Following this procedure, no statistical differences were found for the duration of NREM sleep episodes between developmental groups, nor for the duration of NREM sleep episodes across the night.

EEG Power Spectra

Figure 1 illustrates all-night EEG power spectra for NREM sleep (stages 2, 3, and 4; upper panels) and REM sleep (lower panels). Absolute EEG power densities during NREM sleep were significantly lower in the delta and theta (0.6-7 Hz), in the sigma (11.8-12.6 Hz), and in the lower beta frequency ranges (16.2-16.8 Hz) in mature adolescents compared to prepubertal children. A similar picture emerged for REM sleep: the reduction of EEG power density in mature adolescents compared to prepubertal children was present up to 15 Hz, except for the alpha range (8.6-9.4 Hz), where no difference between developmental groups was found. To visualize more clearly the differences between the age groups, power density of the mature participants was plotted as a percentage of the corresponding frequency bin value of prepubertal children (Figure 1, right panels). In mature adolescents, power in the delta range (0.6-4.6 Hz) during NREM sleep was 41% (42% during REM sleep) of the value in prepubertal children.

An interesting feature was the developmental change in the sigma frequency range (11-15 Hz) during NREM sleep (Figure 1,

Table 1—Nocturnal sleep variables derived from visual scoring (n = 8).

	Tanner 1	Tanner 5
TST	561.3 (5.5)	540.2 (12.4)
SEF (%)	94.4 (0.9)	90.8 (2.1)
Latency to S1	9.2 (2.7)	10.9 (5.7)
Latency to S2	15.2 (2.5)	17.5 (5.7)
REMS latency	123.2 (15.1)	154.6 (20.7)
WASO	14.3 (4.4)	31.1 (11.1)
Stage 1	56.2 (9.1)	62.1 (8.3)
Stage 2	204.9 (12.8) *	255.0 (8.1) *
Stage 3	62.6 (9.0)	49.3 (6.1)
Stage 4	122.6 (10.7) *	73.5 (10.4) *
SWS	185.1 (18.8) *	122.8 (13.2) *
REMS	115.0 (7.3)	100.4 (5.3)
MT	9.9 (1.7)	12.7 (2.0)
Stage 1 (%)	10.1 (1.7)	11.6 (1.6)
Stage 2 (%)	36.6 (2.3) *	47.2 (1.1) *
Stage 3 (%)	11.1 (1.6)	9.1 (1.0)
Stage 4 (%)	21.9 (1.9) *	13.5 (1.8) *
SWS (%)	33.0 (3.3) *	22.6 (2.1) *
REMS (%)	20.5 (1.2)	18.7 (1.0)

The first 595 min of total recording time (TRT) were analyzed. Values represent means ± SEM in minutes or as % of total sleep time (TST). SEF refers to sleep efficiency (TST as % of TRT); REMS = rapid eye movement sleep latency, latency from stage 2; WASO = waking after sleep onset from stage 2 to final awakening; Stage 1, 2, 3, 4 = non-rapid eye movement sleep stages; SWS = slow wave sleep; MT = movement time. Asterisks indicate significant ($P < .05$) differences between groups (unpaired *t* tests).

top panels). A shift of the sigma peak in the mean absolute spectra was evident from prepubertal to mature children, giving rise to a trough and a peak in the relative spectra (see Figure 1, top right panel). Individual mean all-night power spectra of NREM sleep stage 2 were chosen to examine these changes in more detail. Only a single peak was present in the spectra of 6 prepubertal children, while 1 child manifested 2 peaks and no peak was observed in another. Two sigma peaks occurred in the spectra of 6 mature adolescents, while only 1 peak was seen in 2 adolescents. If 2 peaks occurred, peak power was always greater in the high-frequency peak (predominant peak). The center frequency of the predominant sigma peak was visually marked using a manual cursor program. The frequency shift of the sigma peak in the mean spectra was based on significant differences in individual predominant sigma peak frequencies (12.3±0.2 Hz [mean ± SEM] for n = 7 in prepubertal children and 12.9 ± 0.2 Hz for n = 8 in mature adolescents, unpaired *t* test, $P < .05$).

The upper 2 panels of Figure 2 show EEG power values in each frequency bin during the second, third and fourth NREM sleep episodes expressed as a percentage of the corresponding value in the first NREM sleep episode. Significant differences in the second, third, and fourth episode compared to the first episode were found in the range of 0.6 to 12 Hz in both developmental groups, and additionally in the 13.8 to 15 Hz range in prepubertal children. The lower panel of Figure 2 depicts the power density for the first 4 NREM sleep episodes in mature adolescents expressed as a percentage of the corresponding values in prepubertal children (100%). Two-way ANOVAs on log-transformed 0.2-Hz power density values with the between-subjects factor 'developmental group' and the within-subject factor 'episode' showed significant effects for the factor 'developmental group' for all frequency bins below 15.0 Hz ($F_{1,63} > 6.2$, $P < .05$), but no effects for 'episode' and no significant interaction. Power density was lower in mature adolescents compared to prepubertal children across the first 4 NREM sleep episodes in the delta (0.6-4.6 Hz, with exception of the 0.6-3.2 Hz band in the third NREM sleep episode) and the theta band (4.8-7.6 Hz).

Time Course of Nocturnal Sleep Stages and SWA in an Individual Subject

Figure 3 shows the nocturnal time course of sleep stages and SWA (0.6-4.6 Hz range) for a single participant at both pubertal stages, illustrating many of the developmental changes. A decrease of NREM sleep stage 4 as well as an increase in stage 2 is evident in the sleep histogram of the lower panel (Tanner 5) compared to the upper panel (Tanner 1). A substantial shortening of REM sleep latency was present in the participant when she was Tanner 5 compared to Tanner 1. A decrease of overall power in the SWA range from the prepubertal to the mature stage occurred, while the typical declining trend of SWA across the night appeared similar in both recordings.

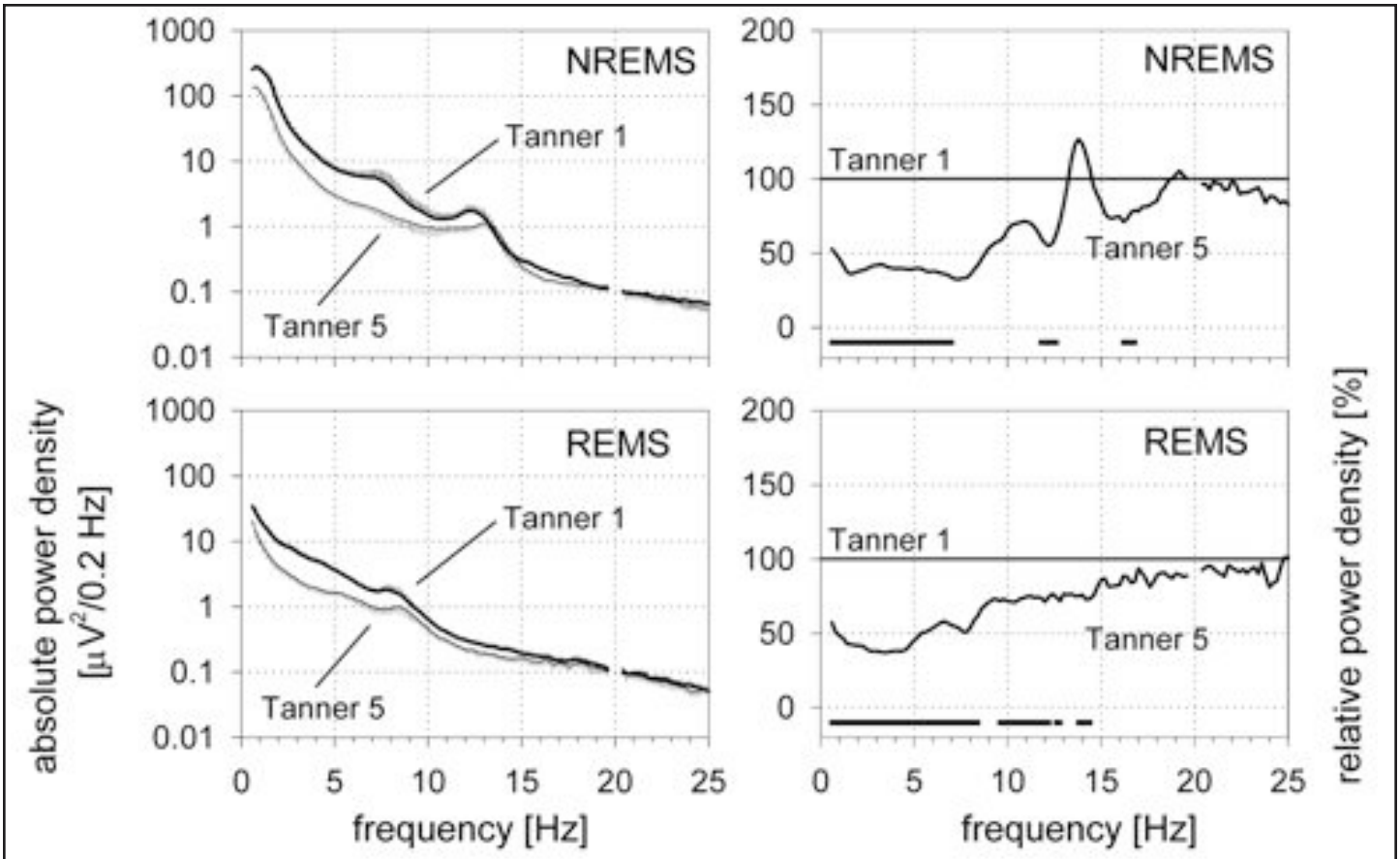


Figure 1—Mean all-night electroencephalogram (EEG) power spectra for non-rapid eye movement (NREM) sleep (stages 2-4, upper panels) and rapid eye movement (REM) sleep (lower panels). Power density values are plotted in the middle of the frequency bins. *Left:* absolute spectra of Tanner 1 (thick line) and Tanner 5 (thin line). Vertical lines represent ±1 SEM (n = 8); *right:* relative spectra (each frequency bin of Tanner 5 expressed as a percentage of the corresponding bin for Tanner 1). Black bars at the bottom of right panels indicate frequency bins in which absolute power density of Tanner 1 and 5 differed significantly ($P < .05$; 2-tailed unpaired *t* tests on log transformed values). The frequency bins 19.8, 20.0 and 20.2 Hz were excluded from the analysis and illustration because of a 20-Hz artifact in some recordings.

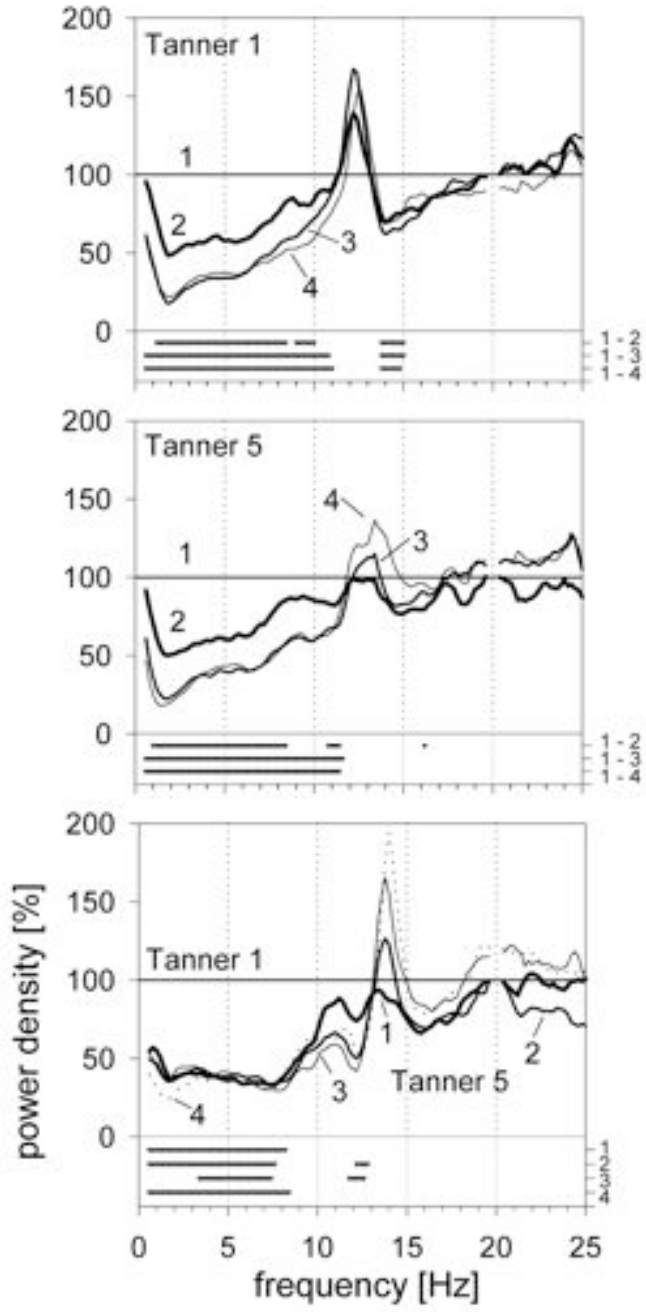


Figure 2—Electroencephalogram (EEG) power density spectra of the first 4 non-rapid eye movement (NREM) sleep episodes in prepubertal (Tanner 1, top panel) and mature (Tanner 5, middle panel) children. Each curve connects average power density values expressed as a percentage of the corresponding value in the first episode (second episode thick line, third episode medium line, fourth episode thin line). Curves were smoothed with a moving median over three, 0.2-Hz bins. Marks below the abscissae indicate 0.2-Hz bins that differed significantly from the first episode ($P < .05$, 2-tailed paired t tests, performed when the 1-way analysis of variance revealed a significant effect of factor 'episode'). In the bottom panel, EEG power density of 4 consecutive NREM sleep episodes (1-4) in Tanner 5 children is expressed as a percentage of Tanner 1 (100%) children (first episode thick line, second episode medium line, third episode thin line, fourth episode dotted line). Marks below the bottom panel indicate frequency bins for which power differed between the 2 developmental groups ($P < .05$, 2-tailed unpaired t test). The frequency bins 19.8, 20.0, and 20.2 Hz were excluded from the analysis and illustration because of a 20-Hz artifact in some recordings.

Dynamics of SWA and Sigma Activity

In both developmental groups, SWA declined across consecutive NREM sleep episodes. Figure 4 displays individual mean SWA values per NREM sleep episodes in each group plotted against corresponding episode midpoint times. Time constants obtained by fitting exponential functions to the data did not differ between prepubertal and mature adolescents, since the 95% confidence intervals overlapped (time constant of Tanner 1 = 143.2 minutes (87.0-199.5); Tanner 5 = 128.2 minutes (80.4-176.9), detailed results of the fitting procedure are reported in the legend of Figure 4).

The cycle-by-cycle dynamics of SWA (0.6-4.6 Hz) and of 2 sigma frequency ranges (11.6-12.4 and 12.6-13.4 Hz) are illustrated in Figure 5. The 2 selected sigma frequency ranges were based on the peak sigma frequency in each developmental group. For both groups, SWA was high during NREM sleep and low during REM sleep and exhibited a monotonic decline across the night. Highest levels of SWA coincided with the intra-episodic trough of activity in both sigma ranges that exhibited a U-shaped pattern in most NREM sleep episodes.

Age-related changes in the dynamics of the selected frequency bands over the course of the night and within episodes were examined using values normalized to individual nocturnal mean values during NREM sleep. A 3-way ANOVA was computed with within-subjects factors 'episode' (first 4 NREM sleep episodes) and 'interval' (1-10 parts across the first 4 NREM sleep episodes) and between-subjects factor 'developmental group' (Tanner 1, Tanner 5). No significant effect of the factor 'developmental group' was observed for any frequency band. The intra-episodic as well as the inter-episodic time course revealed no significant age-related variation ('developmental group' × 'interval' and 'developmental group' × 'episode,' NS for all bands).

DISCUSSION

This paper presents detailed information about state- and frequency-dependent changes of the sleep EEG across puberty and includes 2 major findings. First, EEG spectral power in the low frequency range was lower for mature versus prepubertal adolescents in both NREM and REM sleep. Second, SWA showed identical dynamics within individual NREM sleep episodes and across the night in prepubertal children and mature adolescents.

Visually scored sleep variables reflecting the macrostructure of sleep in both developmental groups are in good agreement with previous reports, confirming a reduction of SWS and greater amounts of NREM stage 2 sleep in mature adolescents compared to prepubertal children.[17,18,32,33] The reduction of SWS was mainly accounted for by less NREM sleep stage 4 and was paralleled by a marked age-related decline of SWA, the computer-derived quantitative measure of SWS. Several authors have previously described the age-related decline of SWA from childhood through adolescence.[10,11,13] In our study, the difference in EEG power between groups was restricted not only to those frequencies that define NREM sleep stage 3 and 4 (ie, the delta frequencies), but also encompassed the theta range up to 7 Hz, the sigma range (11.8 and 12.6 Hz), and the beta range (16.2-16.8 Hz, Figure 1). These findings corroborate the results of an earlier study of age-related changes in the EEG during NREM sleep by Gaudreau and colleagues,[13] who reported that EEG power in the

entire frequency range up to 31 Hz was reduced at age 15 years compared to age 7 years.

A new finding of our study is the decline of low frequency power that we also saw in REM sleep, perhaps indicating sleep state-independent aspects of EEG development. If the EEG power decrease reflects fundamental brain maturational processes, then a decline of EEG waking power would be expected as well. We were, however, unable to record sufficient amount of artifact-free waking EEG data. Another study using frequency analysis of the waking EEG demonstrated a decrease of activity up to 9.5 Hz across the first 2 decades, but this cross-sectional study was not specifically focused on adolescence.[34] One interpretation of the state-independent decline of low frequency power may be that basic EEG-generating mechanisms change across development, and in particular during puberty. The EEG largely results from postsynaptic potentials of large and distributed neuronal populations.[35] The degree of synchronization of these postsynaptic potentials is reflected in the amplitude of the scalp-recorded EEG signal.[35] Thus, the marked decline of EEG power across puberty may reflect the decrease in synaptic connectivity of neuronal assemblies,[36] changes in neurotransmitter or neuroreceptor properties,[37] or reduction of the size of the neurons [38] that occurs at the transition from childhood to adulthood. Such an interpretation is in line with Feinberg's notion[39] that the decrease of delta amplitude across puberty may reflect a decline in synaptic density. The important question remains, however, whether the described changes in sleep and the sleep EEG across adolescence are indeed specifically linked to age-dependent neurologic maturation that is independent of puberty. The relatively small sample size and the cross-sectional nature of our study make this issue difficult to address. Longitudinal investigations with adequate sample sizes are needed to disentangle the effects of puberty from ongoing effects of brain maturation on sleep EEG changes.

A similar decline of low EEG spectral power has been previously reported in studies comparing young adults with middle-aged subjects.[22-24] For example, Landolt and colleagues[23] showed an age-related reduction of EEG power for frequencies below 15 Hz in NREM sleep and below 7 Hz in REM sleep. Although the reduction of EEG low frequency power across several decades

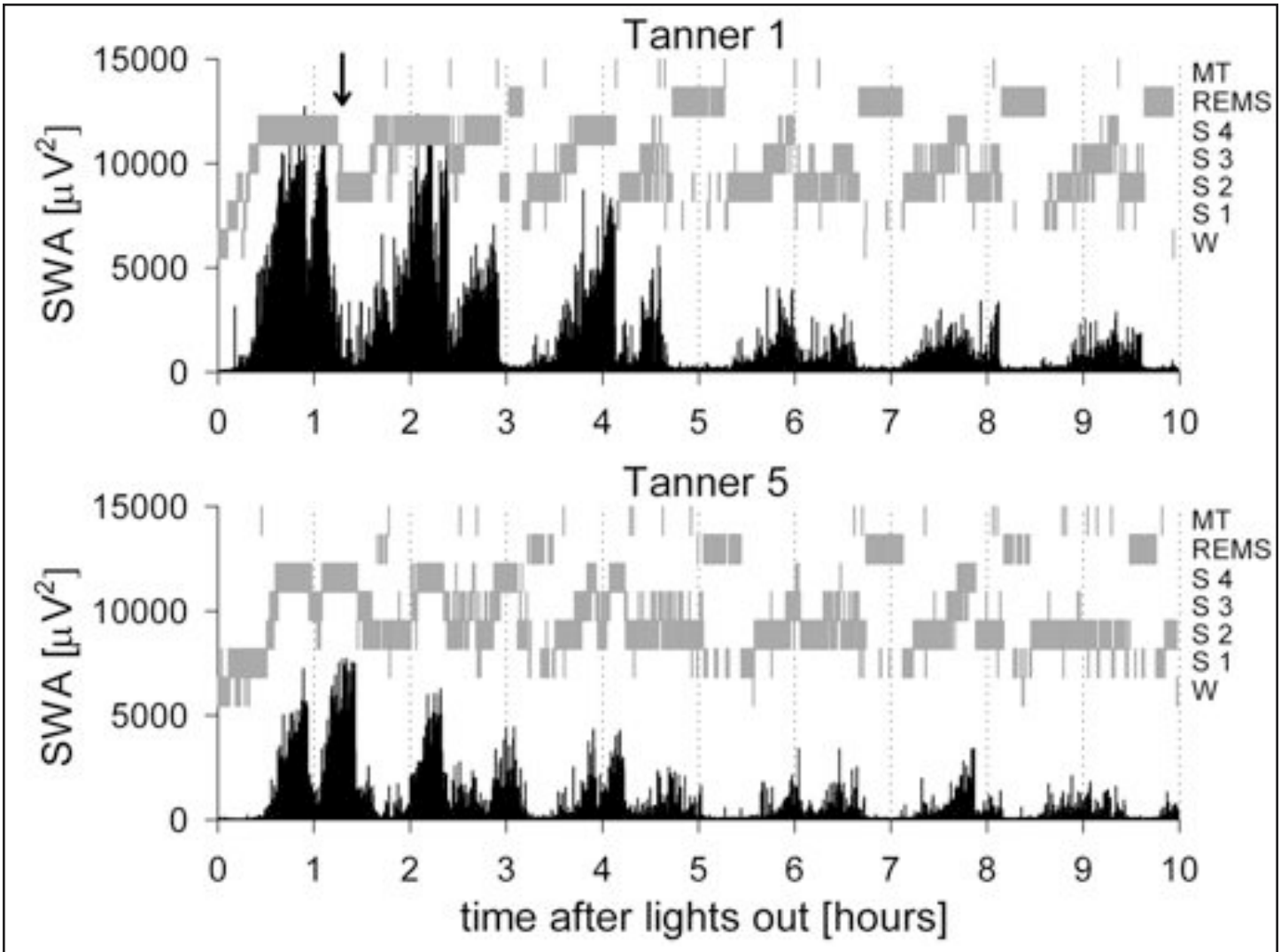


Figure 3—Visually scored sleep stages and time course of electroencephalogram (EEG) slow-wave activity (power in the 0.6 - 4.6 Hz range, derivation C3/A2) during two 10-hour sleep episodes in the same girl at pubertal stage Tanner 1 (upper panel, prepubertal, age 12.3 years) and Tanner 5 (lower panel, mature, age 14.5 years). Slow-wave activity and sleep stages were plotted for 30-second epochs. MT refers to movement time; REMS, rapid eye movement sleep; S1-S4, non-rapid eye movement (NREM) sleep stages; W, wakefulness. The black arrow in the upper panel indicates the epoch where the first NREM sleep episode was divided into 2 episodes. The first NREM sleep episode was treated as 2 episodes when at least 15 minutes of slow wave sleep (S3, S4) were interrupted by more than 12 minutes of S1, S2, W or MT (for details see Appendix).

strikingly resembles the changes across the relatively short span of puberty (mean interval = 2.8 years), the phenomena may represent different underlying processes. Thus, the SWS decline across adolescence may be viewed as a "maturational" process of the developing brain, while "degenerative" changes may be responsible for the SWA decrease during aging. This perspective is consistent with the notion of a different relationship between SWS and growth-hormone secretion across puberty and during aging.[40] Van Cauter and colleagues[41,42] suggested that a simultaneous decrease in SWS generation and growth-hormone secretion during aging may reflect common underlying mechanisms. Such an association is unlikely to be the case during adolescence, since growth hormone reaches maximum levels during puberty at a time when SWS declines.

Additional support for different underlying mechanisms for the SWS decrease across puberty and during aging comes from the view that the decline of SWS may play a major role in the age-related changes of sleep consolidation.[43] Several groups have compared sleep variables between young and older adults reporting more frequent wake after sleep onset, lower sleep efficiency, and increased sleep complaints with advancing age (for a review see[44]). In the present study, by contrast, sleep efficiency and wake after sleep onset were not different between developmental groups (Table 1), indicating that pubertal sleep consolidation remains intact. This finding is consistent with previous data demonstrating that the number of awakenings and arousals during the night do not change in the course of adolescence.[32] In fact, complaints about the timing of sleep (delay of the sleep phase) and daytime sleepiness are more frequent than complaints about disrupted nocturnal sleep in adolescents.

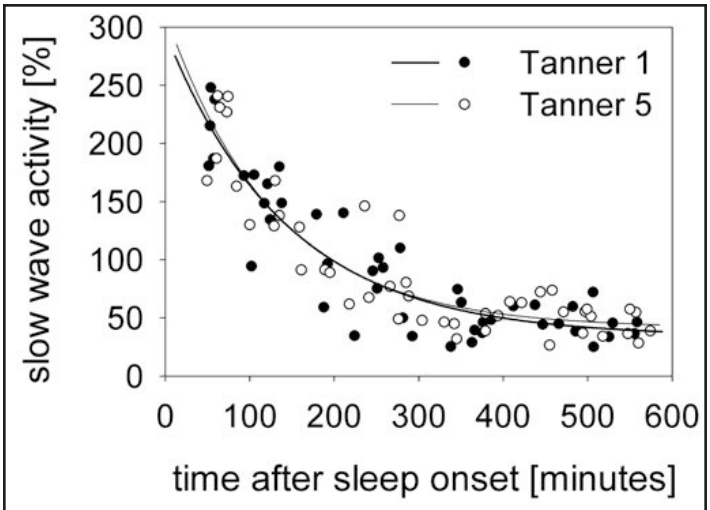


Figure 4—Dynamics of slow-wave activity (SWA) (0.6-4.6 Hz) across the sleep episode. SWA is expressed as a percentage of the average nocturnal value during non-rapid eye movement (NREM) sleep. Individual means per NREM sleep episode are plotted at episode midpoint times relative to sleep onset. The lines represent exponential functions for Tanner 1 participants (●, thick line, $r^2 = 0.83$) and Tanner 5 participants (○, thin line, $r^2 = 0.83$), which were fitted to the data using the following equation: $SWA\ (t) = SWA_0 * e^{-t/\tau} + SWA_\infty$, in which τ = time constant; SWA_∞ = asymptote; SWA_0 = initial value minus asymptote. τ, SWA_∞, and SWA_0 did not differ between developmental groups [τ of Tanner 1 = 143.2 minutes (87.0-199.5, asymptotic 95% confidence interval); Tanner 5 = 128.2 minutes (80.4-176.9); SWA_∞ of Tanner 1=33.8% (12.4-55.4%); Tanner 5=41.2% (24.3-58.1%); SWA_0 of Tanner 1=262.0 % (216.9-307.1); Tanner 5=271.2 % (217.3-325.1)].

Thus, the question arises whether the homeostatic regulatory process during the night manifests a different pattern of developmental change from late childhood to early adulthood than from young adulthood to middle age. In the latter case, an attenuation of sleep recuperative drive has been postulated.[22-24] In agreement with earlier studies in adults[15,16,45] and with the 2-process model of sleep regulation,[8,9] we found that the nocturnal time course of SWA in both developmental groups was closely approximated by an exponential function. The time constant and lower asymptote of the decaying functions did not differ significantly between the groups (see Figure 4 legend for parameters of the exponential functions) and were similar to those reported in young adults [τ, 144.6 minutes; SWA_∞, 41.1%[15]). This finding indicates that the decay rate of SWA is a fairly robust measure of the sleep process from childhood up to young adulthood. The attenuation of the sleep-dependent decay of SWA in older adults may reflect diminishing NREM sleep need.[46] Because the overall decrease of low frequency power from prepubertal to postpubertal children is not reflected in changes of the nocturnal dynamics of SWA, however, the pubertal age-related differences of EEG power do not appear to reflect a reduced need for deep NREM sleep nor a reduced intensity of sleep in older adolescents. This pattern of findings contrasts with those from comparative studies during aging, where a reduced need for NREM sleep[22-24] and a diminished intensity of sleep[47] have been postulated. Developmental variations in auditory arousal thresholds during sleep, reflecting the intensity of sleep, have been reported previously in a study with children and adults,[48] although not specifically focused on the adolescent age range. Whether arousal thresholds during sleep change from Tanner 1 to Tanner 5 remains to be investigated.

A further interesting finding in the current study is that changes were seen in the frequency range of sleep spindles (sigma range, 11-15 Hz), which are a salient feature of the human EEG during NREM sleep. Direct measures of sleep spindles (eg, density, amplitude, frequency) were not obtained in the present analysis. EEG power density in the sigma range, however, is closely related to sleep spindles.[49] The pattern of changes in the sigma range of the absolute and relative curve (Figure 1) is consistent with the interpretation that a shift of the predominant sigma frequency peak in the absolute spectra across puberty underlies a trough and a peak in the relative spectra (see Figure 1, top right panel). A tentative interpretation of this finding is that intrinsic properties of spindle generators in the thalamocortical system change during development.[50] Because of the small sample size and the cross-sectional nature of the study, however, a thorough analysis of the changes in the sigma range was not possible. Our findings need to be confirmed in a longitudinal sample recording from sufficient EEG electrodes to identify spindle generators.

While the amount of SWS decreases dramatically across puberty, our findings indicate that the homeostatic recuperative drive during sleep remains unchanged from late childhood into adulthood. This conclusion still leaves open the possibility that sleep homeostatic mechanisms change in the course of adolescence, namely during the day. We have previously postulated that sleep homeostatic pressure accumulates at a slower daily rate in mature adolescents enabling them to stay awake longer.[27,51] Assessment of this component of the homeostatic process would provide important additional information for understanding adolescent sleep behavior. Such an assumption needs to be investi-

gated using sleep-deprivation protocols or nap studies with different durations of waking episodes. In addition, quantitative EEG analysis with incorporation of current models of sleep regulatory processes needs to be performed in such designs.

ACKNOWLEDGEMENTS

We thank Drs. Christine Acebo, Peter Achermann, and Ronald Seifer for technical and statistical assistance and for comments on the manuscript. Eliza van Reen contributed to the analysis of the data presented in the Appendix, and her contribution is gratefully acknowledged. Tanner staging was done by Judith A. Owens, MD, Henry Sachs, MD, and Susan Labyak, RN, PhD, and we thank them for this important contribution. We also thank our research staff and laboratory technicians. The careful and helpful reviews by 2 referees led to substantial improvements of the final version. Parts of this report were presented at the 17th Annual Meeting of the Associated Professional Sleep Societies and the World Federation of Sleep Research Societies on June 5, 2003, Chicago, Illinois.

This research was supported by the National Institute of Mental Health, grant MH52415 (to MAC) and by the Swiss National Science Foundation, grant 81ZH-068474 (to OGJ).

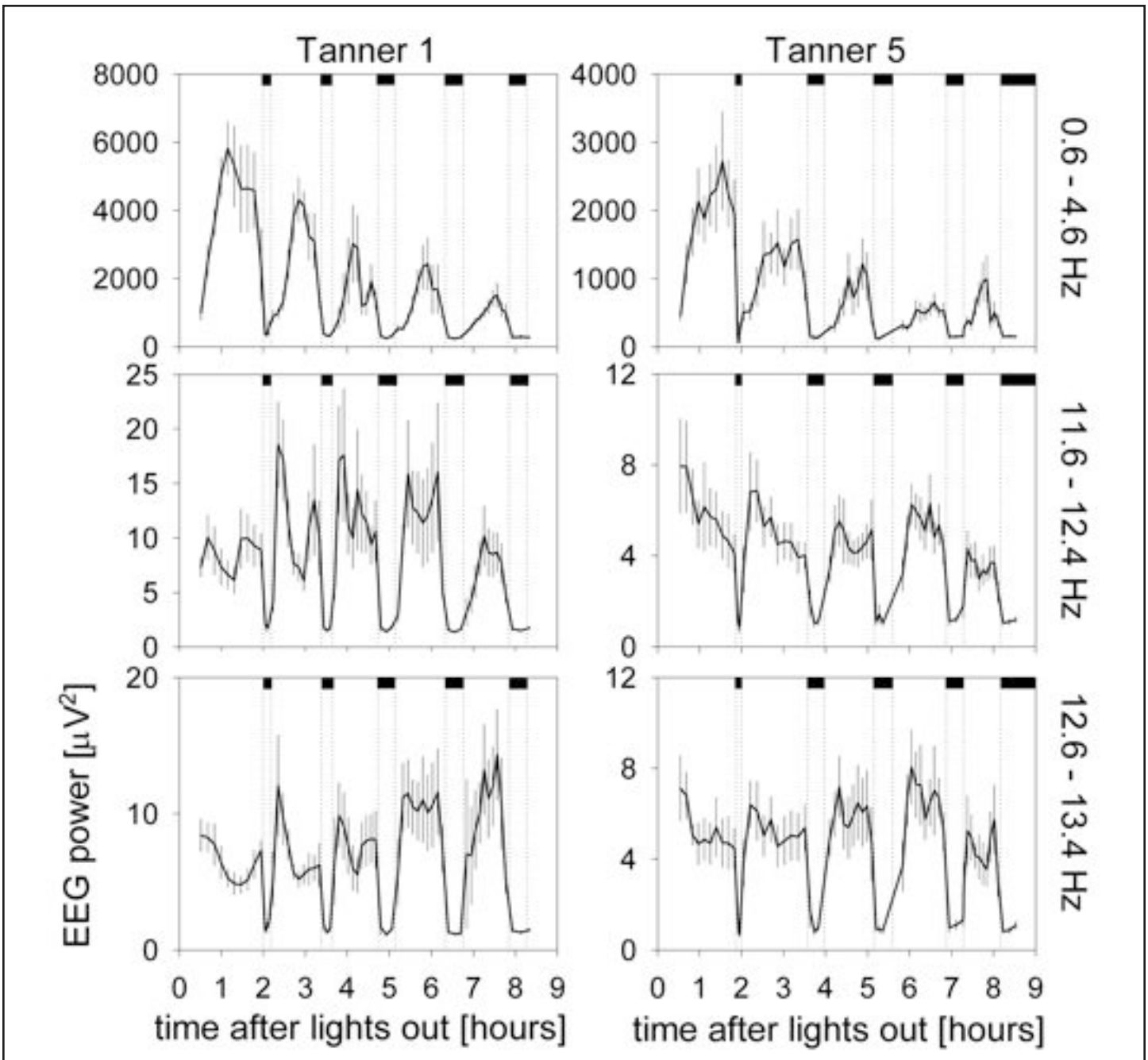
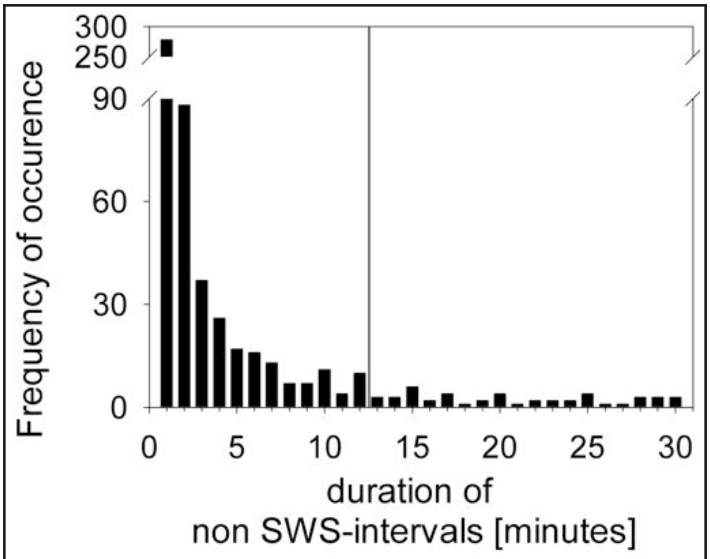


Figure 5—Average time course of slow-wave activity (*upper panels*, power in the 0.6-4.6 Hz range) and for 2 different 1-Hz bands in the sigma range (11.6-12.4 Hz, 12.6-13.4 Hz) for Tanner 1 (prepubertal, left column) and Tanner 5 (mature, right column) children. Non-rapid eye movement (NREM) sleep episodes were subdivided into 10 and rapid eye movement (REM) sleep episodes into 3 equal time intervals and averaged across participants. Vertical lines represent ±1 SEM. Black bars and dotted vertical lines delimit REM sleep episodes. The interval between lights out and sleep onset was not considered. For both developmental groups n = 8, except for cycle 5 where n = 7.

APPENDIX

The 12-minute rule described in the methods section was based on the analysis of 131 polysomnographic all-night recordings (45 participants Tanner 1, 86 Tanner 5) from a previous study performed in the early 1980s.[32] In this data set, the frequency distribution of interval durations with stage 1, 2, wakefulness, or movement time separating the first non-rapid eye movement sleep episode showed a drop below 5 after 12 minutes (Figure Appendix). Of the 561 total intervals, 91.6% were ≤ 12 minutes and 8.4% were > 12 minutes.



Appendix Figure—Frequency histogram displaying the distribution of interval durations with stage 1, 2, wakefulness, or movement time separating the first non-rapid eye movement (NREM) sleep episode. Intervals of > 30 minutes are not displayed (50 intervals).

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