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Regional differences of the sleep electroencephalogram in adolescents

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SUMMARY The sleep electroencephalogram (EEG) was recorded from anterior (Fz/Cz) and posterior (Pz/Oz) bipolar derivations in two developmental groups: 20 pre- or early pubertal (Tanner 1/2, mean age 11.4 ± 1.1 years, 11 boys) and 20 late pubertal or mature adolescents (Tanner 4/5, 14.1 ± 1.3 years, 8 boys). A sleep-state independent reduction of EEG power over almost the entire frequency range was present in Tanner 4/5 compared with Tanner 1/2 adolescents. Spectral characteristics of the sleep EEG yielded state- and frequency-dependent regional differences that were similar in both developmental groups. Anterior predominance of power in delta and sigma ranges occurred in non-rapid eye movement sleep. Rapid eye movement sleep EEG power was greater in low delta, alpha, and sigma ranges for the posterior derivation and in theta and beta ranges for the anterior derivation. The decay rate of the sleep homeostatic process – reflected by the exponential decline of the 2-Hz EEG power band across the sleep episode – did not differ for derivations or groups. These results indicate that the nocturnal dynamics of sleep homeostasis are independent of derivation and remain stable across puberty.

KEYWORDS EEG topography, puberty, sleep homeostasis, sleep regulation, sleep spindles, spectral analysis

INTRODUCTION

Recent research indicates that the delay in sleep timing of adolescents is not simply a psychosocial phenomenon. Instead, developmental changes of intrinsic brain processes appear to play an important role in delaying bedtime and rise time in the course of adolescence (for an overview see Carskadon *et al.*, 2004). These processes may include sleep homeostatic mechanisms that are responsible for the rise of sleep propensity during waking (i.e. the increasing pressure to sleep) and its dissipation during sleep (Borbély and Achermann, 2000). The kinetics of sleep propensity have been derived from slow-wave activity (SWA), a spectral measure of electroencephalographic (EEG) slow waves in the frequency range 0.5–4.5 Hz (Borbély, 1982; Daan *et al.*, 1984). We have recently reported that the decay rate of SWA across the sleep episode – essentially reflecting nocturnal recovery processes – remains stable across puberty despite the marked reduction of slow waves in older compared with younger adolescents (Jenni and Carskadon, 2004). A tentative interpretation from our findings was that the reduction of slow waves across adolescence represents maturational changes of neuronal properties rather than changes in sleep regulatory mechanisms (discussed in Jenni and Carskadon, 2004).

Previous sleep EEG studies in adolescents were confined to a single derivation (Coble *et al.*, 1987; Feinberg *et al.*, 1990; Gaudreau *et al.*, 2001; Jenni and Carskadon, 2004; Smith *et al.*, 1977), while regional aspects have been relatively neglected (with the notable exception of Findji *et al.*, 1981). Evidence is accumulating, however, that spectral characteristics of the adult sleep EEG show regional differences (Finelli *et al.*, 2001). Werth *et al.* (1996, 1997) reported that SWA was higher in anterior than in posterior derivations during the initial part of sleep. An anterior predominance was also observed in the frequency range of sleep spindles (12–15 Hz). In view of the role of slow waves and sleep spindles as markers

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of sleep homeostasis (Borbély and Achermann, 2000), these authors suggested that sleep regulatory mechanisms exhibit specific regional features (Werth *et al.*, 1996, 1997).

The objectives of the present study were to: (1) examine regional aspects of the adolescent sleep EEG from two bipolar derivations along the anterior–posterior axis, (2) compare the regional distribution of sleep EEG characteristics in two developmental groups, and (3) address the hypothesis that the decay rate of SWA (i.e. the dissipation of homeostatic sleep drive) across the sleep episode does not differ between derivations and developmental groups. This hypothesis is based on the observation that sleep quantity *per se* is not altered and sleep need does not decrease across puberty (Carskadon *et al.*, 1980).

METHODS

Subjects and procedures

Forty sleep recordings were analyzed from two developmental groups: 20 pre- or early pubertal children [pubertal stages Tanner 1 and 2 (Tanner 1/2); mean age 11.4 years, SD ± 1.1; range 9.1–12.9 years, 11 boys] and 20 late pubertal or mature adolescents [Tanner 4 and 5 (Tanner 4/5); 14.1 ± 1.3 years; 12.7–17.6 years, 8 boys]. The participants were selected from two different studies performed in 2003 and 2004. For the phase shift study (PS, Tanner 1/2: $n = 9$ and Tanner 4/5: $n = 8$), the participants were sleeping at least 10 days on a fixed 10-h sleep schedule without daytime naps. Their in-lab recordings were scheduled accordingly (bedtime 22:00–08:00). For the phase preference study (PP, Tanner 1/2: $n = 11$ and Tanner 4/5: $n = 12$), sleep schedules were close to habitual, but optimized for at least 2 weeks beforehand (constant schedule without weekend variation and no naps). The duration of in-lab recordings of the PP study varied between 9 and 10 h (maximal common sleep duration after sleep onset = 500 min). Wrist activity recordings, diary and daily phone calls (for reporting bedtimes and rise times) allowed verification of the compliance with the requested regularity of the habitual (PP) or scheduled (PS) sleep period. Melatonin onset did not differ between developmental groups (Tanner 1/2 = mean clock time 20.2 ± SE 0.36 min and Tanner 4/5 = 20.3 ± 0.25, n.s.). It is important to note that all participants were well slept during the days before the laboratory visit and no clinical signs of insufficient sleep were apparent.

In 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. No adaptation nights were acquired because the major focus of both studies was on the circadian timing system, not on the sleep–wake system. EEG data of both studies have not been published before.

Tanner staging (Tanner, 1962) was performed by independent research physicians. Pubertal stage Tanner 1 represents absence of secondary sexual characteristics (prepubertal) and Tanner 5 indicates adult sexual maturity. Tanner stage and sex were distributed evenly across studies. The protocols of both studies were approved by the Lifespan Institutional Review Board for the Protection of Human Subjects. Informed consent was obtained from the participants and their parents. Participants received monetary compensation.

Polysomnographic recordings and EEG analysis

Overnight polysomnographic recordings in individual, darkened bedrooms included EEG (electrodes placed along the midline at Fz, Cz, Pz, Oz, and at C3, C4, O2 according to the international 10–20 system), electrooculogram, electromyogram, and electrocardiogram. The bipolar derivations Fz/Cz (anterior) and Pz/Oz (posterior) were used for power spectral analysis and the referential derivation C3/A2 for sleep-stage scoring. The recordings were performed using the Albert Grass Heritage System (Astromed, Grass, West Warwick, RI, USA). The signals were on-line digitized (12-bit AD converter; low pass filter, −6 dB at 35 Hz; time constant 1.0 s; storage resolution of 128 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, USA). Power spectra of consecutive 30-s epochs (Hanning window, averages of six 5-s epochs) were computed, resulting in a frequency resolution of 0.2 Hz. The lowest two-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. Spectral data were analyzed up to 25 Hz. The sleep stages were visually scored from the digital recordings for consecutive 30-s epochs according to the standard criteria of Rechtschaffen and Kales (1968). The 30-s sleep scores were then matched with the 30-s power spectra. Non-rapid eye movement sleep–rapid eye movement sleep (NREMS–REMS) cycles were defined as described in our previous publication (Jenni and Carskadon, 2004). All participants completed at least four NREMS–REMS cycles.

Statistics

The SAS general linear model procedure was used for statistical analyses (Version 8.02; SAS Institute, Inc., Cary, NC, USA). Two-way analyses of variance (ANOVA) included the between-subject factors 'developmental group' (Tanner 1, Tanner 5), and/or the within-subject factors 'derivation' (anterior, posterior), and/or 'episode' (first four NREMS episodes) as appropriate. Probability values presented are based on Greenhouse–Geisser corrected degrees of freedom,

but original *F*-values are reported. The significance level was set at $P < 0.05$. Sleep variables and EEG power spectra were log-transformed prior to statistical testing in order to approximate normal distributions. Comparisons between and within developmental groups were performed by *post-hoc* unpaired or paired two-tailed *t*-tests, respectively.

To assess the homeostatic process, the mean 2-Hz power per NREMS episode in each participant (as a percentage of the overall nocturnal mean) was plotted at episode midpoint times relative to sleep onset for both anterior and posterior derivations. Mean 2-Hz power values of all NREMS episodes were then pooled for all participants, and an exponential function was fitted to the data (Fig. 3). Differences in the parameter estimates of the exponential function (time constant, lower asymptote, and power in the 2-Hz band at sleep onset) between Tanner groups and derivations were considered statistically significant if the 95% confidence intervals of the parameter estimates did not overlap.

RESULTS

Nocturnal sleep and episode variables

Table 1 summarizes sleep measures derived from visual scoring. Sleep variables did not differ significantly between developmental groups, except for NREMS stage 4 and slow-wave sleep.

Table 1 Nocturnal sleep variables (derived from visual scoring of the C3/A2 derivation) in the first 500 min after sleep onset corresponding to the maximal common duration of all sleep episodes

	Tanner 1/2 (n = 20)	*Tanner 4/5 (n = 20)*
SEF (%)	95.7 (1.2)	93.5 (1.3)
Stage 1	47.3 (5.6)	42.9 (4.0)
Stage 2	202.8 (8.6)	234.6 (7.5)*
Stage 3	45.3 (4.6)	34.0 (3.5)*
Stage 4	109.9 (5.8)	75.3 (4.7)†
SWS	155.1 (8.0)	109.4 (5.2)†
REMS	73.5 (5.5)	80.8 (6.0)
MT	7.8 (0.9)	7.2 (0.7)
WASO	19.3 (6.4)	25.1 (6.8)
SL1	9.8 (1.7)	14.6 (2.8)
SL2	17.6 (2.5)	20.7 (2.8)
REML	181.4 (12.8)	145.2 (14.1)*
NREMS episode	84.8 (3.9)	76.0 (2.6)*
REMS episode	15.8 (1.4)	17.0 (1.5)

Values represent mean ± standard error of means (SE) in minutes (for NREMS and REMS episodes = mean duration of the first four episodes). SEF, sleep efficiency (total sleep time as % of the first 500 recording minutes after sleep onset); REML, latency to REMS; SL1, sleep latency to stage 1 sleep; SL2, sleep latency to stage 2 sleep; WASO, waking after sleep onset; stage 1, 2, 3, 4 – NREMS stages; SWS, slow-wave sleep; REMS, rapid eye movement sleep; MT, movement time. 'Skipped' first REMS episodes as defined in our previous publication (Jenni and Carskadon, 2004) occurred in $n = 16$ in the Tanner 1/2 and $n = 12$ in the Tanner 4/5 group.
*$P < 0.1$.
†Significant ($P < 0.05$) differences between groups (unpaired *t*-tests).

All-night EEG power spectra in anterior and posterior derivations

No differences in EEG power spectra were observed between boys and girls. Thus, data of boys and girls were pooled for the final analysis. The typical frequency-related changes in EEG power were observed in both anterior and posterior derivations (Fig. 1). An anterior predominance was present over almost the entire frequency range in NREMS of Tanner 1/2 children, while in Tanner 4/5 adolescents, the anterior predominance was restricted to the delta and sigma ranges. In REMS, the overall regional pattern of the sleep EEG was remarkably similar in both developmental groups (i.e. a posterior predominance in the low delta, alpha, and sigma ranges and an anterior predominance in the theta and beta ranges).

Differences between developmental groups

A two-way ANOVA on log-transformed absolute power values with the between-factor 'group' (Tanner 1/2, Tanner 4/5) and the within-factor 'derivation' (anterior, posterior) yielded significant main effects of 'group' in most frequency bins for both sleep states, indicating differences in overall EEG power between developmental groups (Fig. 1, bottom panels). Power in both sleep states was significantly lower in Tanner 4/5 than in Tanner 1/2 children (compare absolute mean EEG power spectra between both developmental groups in Fig. 1). The ANOVA showed only few frequency bins in the low sigma range (10.4–11.8 Hz) during NREMS with a significant 'group × derivation' interaction. This finding indicated that the effect of group varied across derivations in this frequency range. No significant 'group × derivation' interaction was found for any frequency bin during REMS.

Time-dependent changes of the 2- and 11-Hz bands

The typical modulation of EEG power across NREMS–REMS cycles and the declining trend of power in the 2-Hz band across the sleep episode occurred in anterior and posterior derivations (Figs 2 and 3). Furthermore, NREMS power was higher in anterior derivations for the first four NREMS episodes in both frequency bands and across developmental groups. In REMS, the posterior derivation predominated in the 11-Hz band. A three-way ANOVA on relative power values in the 2-Hz band with the between-subject factor 'group' (Tanner 1/2, Tanner 4/5) and the within-subject factors 'derivation' (anterior, posterior) and 'episode' (first four NREMS episodes) showed a significant main effect 'episode' ($F = 288.6$, $P < 0.0001$), but no other significant main effects or interactions. The non-significant three-way interaction indicated that the nocturnal trend in the 2-Hz band did not vary between developmental group and derivation.

To assess the nocturnal dynamics of the homeostatic process in each derivation, the participants' mean 2-Hz power values

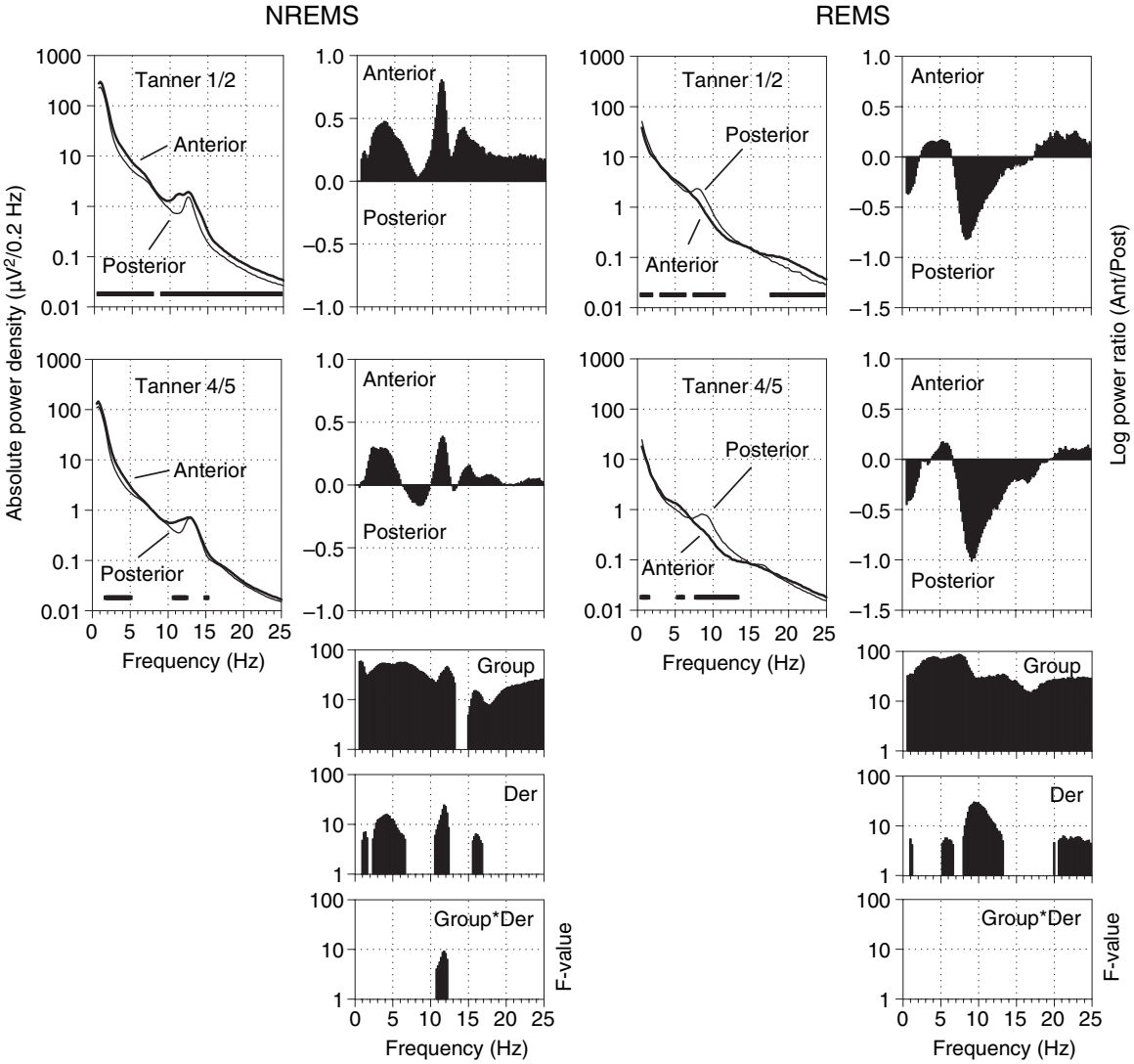

Figure 1. First two columns: *Left*: Mean absolute all-night EEG power spectra in NREMS from an anterior (Fz/Cz, thick lines) and a posterior (Pz/Oz, thin lines) derivation in Tanner 1/2 ($n = 20$) and Tanner 4/5 ($n = 20$). Bars indicate bins for which absolute power was significantly different between derivations ($P < 0.05$, paired t-test). *Right*: Power ratio between anterior and posterior derivations plotted on a log-10 scale. Positive values indicate higher power in anterior, negative values higher power in posterior derivations. In Tanner 1/2, power dominated over almost the entire frequency spectrum in the anterior derivation (except for the 7.8–9 Hz bins). In Tanner 4/5, more power was observed in the delta (1.8–5 Hz) and the sigma range (10.8–12.4) for anterior derivations. *Bottom panels at right*: Statistics for differences of EEG power between derivations and developmental groups. Black areas represent significant F-values of a two-way ANOVA on log-transformed absolute power values with the between-factor 'group' (Tanner 1/2, Tanner 4/5) and the within-factor 'derivation' (anterior, posterior). **Last two columns:** Mean absolute all-night EEG power spectra (*left*) and power ratio (*right*) for REMS. Statistics equal as for NREMS. The overall pattern of differences between derivations was quite similar for both developmental groups; a posterior predominance of EEG power was present in the low frequency range up to 2 Hz and in the alpha/sigma range. In Tanner 1/2, power in the range 3–6 Hz and above 17.6 Hz was higher in anterior derivations. In Tanner 4/5, the anterior predominance in the theta band was restricted to the 5.2–5.8 Hz bins.

per NREMS episode (as a percentage of the overall nocturnal mean) were plotted at episode midpoint times relative to sleep onset (Fig. 3). Parameter estimates (time constants, lower asymptotes, and 2-Hz power values at sleep onset) of exponential functions fitted to the data pooled for all participants did not differ between anterior and posterior derivations or developmental groups, as the 95% confidence intervals overlapped (Table 2).

DISCUSSION

Two main findings emerge from the present study: (1) spectral characteristics of the adolescent sleep EEG show state- and frequency-dependent regional differences which are similar in younger and older adolescents; (2) nocturnal kinetics of the sleep homeostatic process do not differ between derivations and developmental groups, corroborating our earlier findings

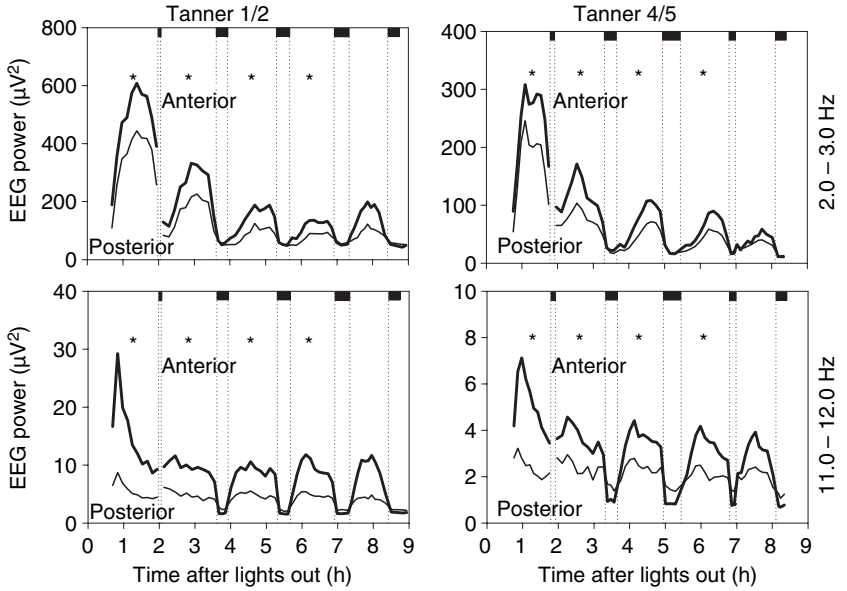

Figure 2. Time course of mean absolute EEG power ($n = 20$ in each developmental group) in the 2-Hz (bins 2.0–3.0 Hz) and 11-Hz (bins 11.0–12.0 Hz) bands from an anterior (Fz/Cz, thick lines) and a posterior derivation (Pz/Oz, thin lines). Individual NREMS episodes for each subject were subdivided into 10 equal parts and individual REMS episodes into three equal parts. Black bars on top and dashed vertical lines delimit REMS episodes. A two-way repeated measures ANOVA on log-transformed absolute power values showed significant main effects for the factors 'derivation' (anterior, posterior), 'episode' (first four NREMS episodes), and significant interactions 'derivation × episode' for each developmental group and each Hz band. Asterisks indicate significant differences between corresponding derivations (*post-hoc* paired *t*-tests). All participants completed four sleep cycles (five cycles: $n = 18$ in Tanner 1/2, $n = 15$ in Tanner 4/5). Note different scaling of *y*-axis for developmental groups, reflecting overall EEG power reduction in Tanner 4/5.

that homeostatic sleep pressure dissipation does not change across pubertal development (Jenni and Carskadon, 2004). This finding is in accordance with the notion that sleep need does not decline in the course of puberty (Carskadon *et al*., 1980).

The anterior predominance of power in the delta and sigma ranges of the adolescent sleep EEG during NREMS is in agreement with findings derived from young and middle-aged subjects (Landolt and Borbély, 2001; Werth *et al*., 1996). Thus, basic conceptual facets of homeostatic sleep regulation as described in adults seem to be valid for older children and adolescents as well. Also in REMS, large segments of the regional spectra of the adolescent sleep EEG concurred with the adult spectra (Landolt and Borbély, 2001; Werth *et al*., 1996): a posterior predominance was observed in the low delta, alpha and sigma range, while anterior power values exceeded posterior values for the beta range. On the contrary, regional distribution in the theta/alpha range during NREMS and in the theta range during REMS differed markedly between adolescents (age 9–18 years) and young adults (20–26 years) (Landolt and Borbély, 2001; Werth *et al*., 1996). Our data did not manifest a topographical gradient in the theta/alpha band during NREMS, although a posterior predominance was reported for the 5–9 Hz frequency range in young adults (Werth *et al*., 1996). In REMS, an opposite regional pattern of theta activity (5–7 Hz) was seen in adolescents (anterior dominance) compared with adults (posterior dominance). One explanation for these differences between age groups may lie in different derivations used in our study (Fz/Cz, Pz/Oz) compared with adult studies (F3/C3, P3/O1) (Landolt and Borbély, 2001; Werth *et al*., 1996). Nevertheless, we speculate on the basis of our findings that *sleep* EEG theta/alpha activity during adolescence may exhibit a more protracted course of maturation and/or a different functional role compared with adults. Recently, it was reported that power in the theta/alpha range of the *waking* EEG in young adults can serve as an indicator for the increasing homeostatic sleep pressure during the day (Cajochen *et al*., 1995; Finelli *et al*., 2000). Whether theta/alpha activity during wakefulness plays a similar role in pubertal children remains to be investigated.

The present study confirms and extends our previous findings that the sleep EEG exhibits a state-independent power reduction across puberty in a wide frequency range (Jenni and Carskadon, 2004). Interestingly, the power reduction appears to be largely independent of EEG electrode site [with the notable exception of the low sigma range (10.4–11.8 Hz) during NREMS, see below], which may reflect relatively synchronous maturational processes of the brain (discussed in Jenni and Carskadon, 2004, p. 779). At first glance, this finding might contrast neuroimaging and histological data reporting regional and asynchronous brain development across adolescence (Giedd *et al*., 1999; Huttenlocher and Dabholkar, 1997). The present analyses, however, were restricted to two bipolar derivations along a single spatial orientation and two developmental groups within a narrow age range (mean age 11.4 and 14.1 years). Further studies are

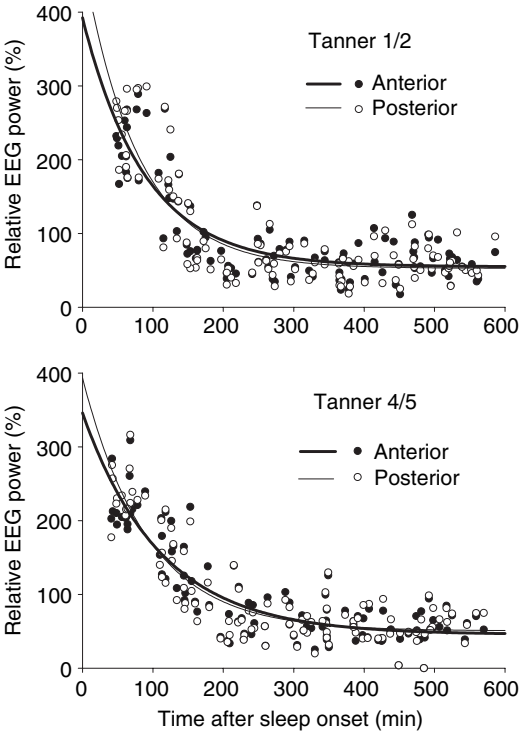

Figure 3. Dynamics of power in the 2-Hz band across the sleep episode (expressed as a percentage of the average nocturnal value during NREMS). Individual means per NREMS episode are plotted at episode midpoint times relative to sleep onset for both derivations (●, anterior; ○, posterior) in both developmental groups. The lines represent exponential functions for anterior (thick lines) and posterior derivations (thin lines) that were fitted to the data. Parameters of the function did not differ between developmental groups (for equation and parameters see Table 2).

needed with incorporation of subjects of a wider age range (as from late childhood to young adulthood), longitudinal designs, and EEG mapping techniques (Finelli *et al.*, 2001). Another shortcoming in the design of this study is omitting the adaptation night that was unavoidable for practical reasons. Thus 'skipped' first REMS episodes (see Table 1) may be related to a first-night laboratory effect in some participants. We note, however, that 'skipped' first REMS episodes are a developmental phenomenon independent of laboratory conditions (Carskadon, 1982; Coble *et al.*, 1987).

Several authors have suggested that 'the hyperfrontality of SWA' may be an indication for increased regional-dependent sleep intensity, reflecting a more profound recovery process in brain regions of most intensive daytime use (i.e. frontal cortical areas) (Borbély and Achermann, 2000; Finelli *et al.*, 2001; Landolt and Borbély, 2001; Werth *et al.*, 1996). The basis for this assumption was the observed shift of EEG power from anterior to posterior derivations in the course of the sleep episode (Werth *et al.*, 1996, 1997), which we did not see across the first four NREMS episodes in adolescents. We also did not find differences in the decay rate of the homeostatic process – reflected by the exponential decline of the 2-Hz band across the sleep episode – between derivations and across developmental groups. We note that the time constants in this study were faster than previously reported (Jenni and Carskadon, 2004), most likely due to different derivations (Fz/Cz, Pz/Oz) used for the analysis of this study compared with the previous report (C3A2) (Jenni and Carskadon, 2004).

An interesting finding was the significant interaction 'group × derivation' in the low sigma range (10.4–11.8 Hz) during NREMS indicating a regional shift of EEG low sigma power across puberty. Landolt *et al.* (1999) found regional shifts of power between 9 and 12 Hz after selective blockade of serotonin-2A (5-HT_{2A}) receptors in young men. We may speculate that the local shift of EEG low sigma power during adolescence may be associated with known developmental changes in cortical 5-HT_{2A} receptor properties (Spear, 2000).

In conclusion, spectral characteristics of the sleep EEG show state- and frequency-dependent regional differences which are similar in prepubertal and mature adolescents despite the marked difference in total EEG power. The nocturnal dynamics of the sleep homeostatic process are independent of derivation and remain stable across puberty. Thus, sleep appears to be a fairly robust process at the transition from childhood to adulthood, although major maturational changes of the brain occur. This interpretation is in accordance with the experience that sleep need is not altered in the course of puberty (Carskadon *et al.*, 1980), rather its timing: adolescents tend to go to bed later and get up later in the course of their pubertal development (Carskadon *et al.*, 2004). We recently reported preliminary findings that sleep homeostatic mechanisms during wakefulness may be altered in mature adolescents compared with prepubertal children, such that the increase of sleep pressure during the day appears to be slower in older versus younger adolescents contributing to their differences in sleep timing (Jenni *et al.*, 2004). These developmental changes are in line with puberty-related alterations of the circadian timing

Table 2 Parameters describing the time course of mean power in the 2-Hz band per NREMS episode in anterior and posterior derivations for both developmental groups (see Fig. 3). Equation of the exponential function: Power (t) = $power_0 \times e^{-t/\tau}$ + $power_\infty$, in which τ = time constant; $power_\infty$ = asymptote; $power_0$ = initial value minus asymptote

	Derivation	τ *(min)*	*Power$_0$ (%)*	*Power$_\infty$ (%)*	r^2
Tanner 1/2	Anterior	88.8 (64.5–113.1)	337.5 (266.7–408.3)	54.8 (44.0–65.6)	0.73
	Posterior	78.4 (58–98.8)	420.3 (327.4–513.2)	52.6 (41.6–63.6)	0.75
Tanner 4/5	Anterior	111.2 (82.4–140)	300.4 (254.5–346.3)	45.5 (32.8–58.2)	0.78
	Posterior	92.6 (70.1–115.1)	343.0 (287.3–398.7)	50.5 (39.5–61.5)	0.80

Values in parentheses represent 95% CI.

system (reviewed in Carskadon *et al*., 2004). Taken together, maturational processes of the sleep homeostat and the circadian system – the principal biological forces for sleep timing – are permissive for later bedtimes of adolescents.

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REFERENCES

Borbély, A. A. A two process model of sleep regulation. *Hum. Neurobiol*., 1982, 1: 195–204.

Borbély, A. and Achermann, P. Sleep homeostasis and models of sleep regulation. In: M. Kryger, T. Roth and W. Dement (Eds) *Principles and Practice of Sleep Medicine*. W.B. Saunders Co., Philadelphia, 2000: 377–390.

Cajochen, C., Brunner, D. P., Kräuchi, K., Graw, P. and Wirz-Justice, A. Power density in theta/alpha frequencies of the waking EEG progressively increases during sustained wakefulness. *Sleep*, 1995, 18: 890–894.

Carskadon, M. A. The second decade. In: C. Guilleminault (Ed.) *Sleep and Waking Disorders: Indications and Techniques*. Addison Wesley, Menlo Park, CA, 1982: 99–125.

Carskadon, M. A., Harvey, K., Duke, P., Anders, T. F., Litt, I. F., Dement, W. C. Pubertal changes in daytime sleepiness. *Sleep*, 1980, 2: 453–460.

Carskadon, M. A., Acebo, C. and Jenni, O. G. Regulation of adolescent sleep: implications for behavior. *Ann. N. Y. Acad. Sci*., 2004, 1021: 276–291.

Coble, P. A., Reynolds, C. F., Kupfer, D. J. and Houck, P. Electroencephalographic sleep of healthy children. Part II: Findings using automated delta and REM sleep measurement methods. *Sleep*, 1987, 10: 551–562.

Daan, S., Beersma, D. G. and Borbély, A. A. Timing of human sleep: recovery process gated by a circadian pacemaker. *Am. J. Physiol*., 1984, 246: R161–R183.

Feinberg, I., March, J. D., Flach, K., Maloney, T., Chern, W. and Travis, F. Maturational changes in amplitude, incidence and cyclic pattern of the 0 to 3 Hz (Delta) electroencephalogram of human sleep. *Brain Dysfunct*., 1990, 3: 183–192.

Findji, F., Catani, P. and Liard, C. Topographical distribution of delta rhythms during sleep: evolution with age. *Electroencephalogr. Clin. Neurophysiol*., 1981, 51: 659–665.

Finelli, L. A., Baumann, H., Borbély, A. A. and Achermann, P. Dual electroencephalogram markers of human sleep homeostasis: correlation between theta activity in waking and slow-wave activity in sleep. *Neuroscience*, 2000, 101: 523–529.

Finelli, L. A., Borbély, A. A. and Achermann, P. Functional topography of the human non-REM sleep electroencephalogram. *Eur. J. Neurosci*., 2001, 13: 2282–2290.

Gaudreau, H., Carrier, J. and Montplaisir, J. Age-related modifications of NREM sleep EEG: from childhood to middle age. *J. Sleep Res*., 2001, 10: 165–172.

Giedd, J. N., Blumenthal, J., Jeffries, N. O., Castellanos, F. X., Liu, H., Zijdenbos, A., Paus, T., Evans, A. C. and Rapoport, J. L. Brain development during childhood and adolescence: a longitudinal MRI study. *Nat. Neurosci*., 1999, 2: 861–863.

Huttenlocher, P. R. and Dabholkar, A. S. Regional differences in synaptogenesis in human cerebral cortex. *J. Comp. Neurol*., 1997, 387: 167–178.

Jenni, O. G. and Carskadon, M. A. Spectral analysis of the sleep electroencephalogram during adolescence. *Sleep*, 2004, 27: 774–783.

Jenni, O. G., Achermann, P., Carskadon, M. A. Evidence for maturational changes in Process S during adolescence based on empirical data and simulations. *Sleep*, 2004, 27: A111.

Landolt, H. P. and Borbély, A. A. Age-dependent changes in sleep EEG topography. *Clin. Neurophysiol*., 2001, 112: 369–377.

Landolt, H. P., Meier, V., Burgess, H. J., Finelli, L. A., Cattelin, F., Achermann, P., Borbely, A. A. Serotonin-2 receptors and human sleep: effect of a selective antagonist on EEG power spectra. *Neuropsychopharmacology*, 1999, 21: 455–466.

Rechtschaffen, A. and Kales, A. (Eds). *A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects*. UCLA Brain Information Service/Brain Research Institute, Los Angeles, CA, 1968.

Smith, J. R., Karacan, I. and Yang, M. Ontogeny of delta activity during human sleep. *Electroencephalogr. Clin. Neurophysiol*., 1977, 43: 229–237.

Spear, L. P. The adolescent brain and age-related behavioral manifestations. *Neurosci. Biobehav. Rev*., 2000, 24: 417–463.

Tanner, J. M. *Growth at Adolescence*. Blackwell, Oxford, 1962.

Werth, E., Achermann, P. and Borbély, A. A. Brain topography of the human sleep EEG: antero-posterior shifts of spectral power. *Neuroreport*, 1996, 8: 123–127.

Werth, E., Achermann, P. and Borbély, A. A. Fronto-occipital EEG power gradients in human sleep. *J. Sleep Res*., 1997, 6: 102–112.