Age-related modifications of NREM sleep EEG: from childhood to middle age

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Accepted in revised form 26 March 2001; received 16 February 2000

SUMMARY This study investigated the modifications in non-rapid eye movement (NREM) sleep electroencephalogram (EEG) power in 54 subjects, from children to middle-aged adults. Spectral analyses were performed on 5 h of NREM sleep. A marked decrease of absolute slow-wave activity (SWA) was observed with increasing age; children had significantly more SWA than adolescents, young and middle-aged adults. The decline of SWA across the night seems to level off with increasing age, suggesting an age-related attenuation of homeostatic sleep pressure. Absolute theta power was higher for children compared with the other three groups, and adolescents had more theta power than young and middle-aged adults. In comparison to young and middle-aged adults, alpha power was higher for children and adolescents. Children and adolescents had more sigma power than middle-aged adults. Absolute beta power was higher for children than for the other age groups. Therefore, the major alterations of NREM sleep EEG occurring between childhood and middle age are not restricted to SWA, but encompassed the theta, alpha, sigma and beta frequency bands.

KEYWORDS aging, electroencephalogram, maturation, sleep, spectral analysis

INTRODUCTION Polysomnographic sleep undergoes marked modifications from childhood through adolescence. The most obvious sleep change across the maturational process is the decrease in slow-wave sleep (SWS). Children’s sleep pattern is characterized by important amounts of SWS, mostly in the first third of the night (Bee et al. 1991; Coble et al. 1984; Feinberg 1989; Williams et al. 1974). However, when the reduction in SWS first appears it is still a matter of controversy. A quantitative change in SWS occurs somewhere during puberty (Carskadon 1982; Coble et al. 1984; Feinberg 1989; Williams et al. 1972, 1974). Carskadon (1982) observed a reduction in SWS by almost 40% during the second decade of life. Similarly, Coble et al. (1984) reported that, in 6–15-year-old children, NREM sleep was marked by a progressive decrease in the percentage of delta sleep (stage 3 and 4). Kahn et al. (1996) described a gradual decline in SWS across the Tanner puberty stages, with approximately 35% of decline from Tanner stages 1–5. An increased proportion of stage 2 sleep, a reduction of total sleep time and a phase delay of the sleep-wake cycle have also been reported between childhood and adolescence (Carskadon 1982, 1997; Coble et al. 1984; Williams et al. 1972, 1974). Some authors have observed that the transition between childhood and adolescence was characterized by the appearance of sleep complaints and an increase in daytime sleepiness (Carskadon 1982; Williams et al. 1974). It was thus suggested that most changes occurring between childhood and adolescence may be a consequence of pubertal or hormonal changes rather than a strict reflect of age (Carskadon 1982; Karacan et al. 1975; Williams et al. 1972). Carskadon et al. (1997) indicated that sleep-phase delay, which is one of the most consistent modifications in sleep patterns between children and adolescents, may reflect developmental alterations in circadian timing mechanisms. They also proposed that sleep pressure during the day builds up more slowly, enabling individuals to stay awake longer as adolescence progresses. Using preliminary data, they have demonstrated, following sleep deprivation, a reduced amount of slow-wave sleep in more mature
adolescents than in less mature ones, suggesting a possible maturational influence on sleep homeostatic regulation (Carskadon et al. 1998).

During adulthood, SWS begins its sharpest decline across the twenties (Feinberg 1982, 1989; Williams et al. 1974). Young adults’ sleep is also characterized by an increase in REM percent, a shorter latency to the first REM period, and a further decrease in sleep duration compared with adolescents (Williams et al. 1974). As aging proceeds, sleep patterns become more disturbed, with more frequent awakenings across the night, increases in stages 1 and 2 sleep, and a significant and gradual decline in SWS (Bliwise 1993; Carrier et al. 1997; Feinberg 1987; Miles and Dement 1980; Williams et al. 1974).

Spectral analysis makes possible the quantitative description of the time course of sleep EEG across the night. Hence, it is a powerful tool to explore alterations in sleep regulation mechanisms. For instance, spectral analysis of slow-wave activity (SWA) is a quantitative measure of slow-wave sleep dynamics, and represents a physiological marker of homeostatic regulation of sleep (Borbély 1982; Daan et al. 1984). The robustness of the homeostatic marker has been challenged in many protocols using total and partial sleep deprivations, or nap studies (Borbély et al. 1981; Dijk et al. 1987). Sleep deprivation not only increases SWA and theta activity but also reduces sleep spindle activity in the night following deprivation. The reverse effect is produced by a nap in the early evening, producing a decrease in sleep pressure.

Few studies have assessed the effect of age on quantitative measures of the sleep EEG. Most observations describe changes from young adulthood to middle age (Carrier et al. 2000; Dijk et al. 1989; Landolt et al. 1996). These studies have mostly reported a decrease in NREM sleep EEG power density for SWA, theta and sigma activity in middle-aged subjects compared with young adults. Furthermore, the decay rate of EEG power density during NREM sleep is slower in middle-aged subjects than in young adults for SWA and theta bands, so that the between-group difference diminished over the course of sleep. In addition, the difference in sigma activity (frequency range of sleep spindles) increases with time-of-night. These results were interpreted as possibly reflecting an attenuation of the build-up of sleep pressure with increasing age. To our knowledge, no studies investigating alterations of the quantitative sleep EEG, especially SWA, between childhood and young adulthood have yet been undertaken. If EEG SWA power before adulthood is considered, important information may emerge on the appearance of modifications in NREM sleep EEG, reflecting homeostatic sleep regulation mechanisms.

The aim of the present study was to investigate age-related modifications of EEG power spectra in NREM sleep across the night, from childhood to middle age. Furthermore, we explored the alterations in the dynamics of SWA during NREM sleep with increasing age, representing the strength of the homeostatic process.

METHODS

Subjects

Fifty-four subjects between the ages of 6 and 60 years were studied. Four groups, with a female/male ratio of 1:2, were defined as: children (three girls and six boys; mean age 7.11 years; range 6–10 years), adolescents (five girls and 10 boys; mean age 15.33 years; range 14–16 years), young adults (five women and ten men; mean age 23.73 years; range 19–29 years) and middle aged adults (five women and ten men; mean age 45.4 years; range 36–60 years). All subjects reported to be in good health and to be free of sleep complaints. They did not abuse drugs or alcohol, and did not take medications known to influence sleep. Subjects were screened for the presence of sleep apneas (index >10) and periodic limb movements during sleep (index >10). All subjects with an index >10 were excluded. Sleep efficiency was set at a minimum of 85% to obtain comparable sleep parameters for all groups. Bedtime and waketime for the different groups were: 20.30–07.00 h for the children group, 22.30–07.30 h for the adolescents, 23.00–8.30 h for the young adults and 23.00–07.00 h for the middle-aged group.

Sleep recordings

All subjects underwent one night of polysomnographic recording in a sleep laboratory. Children and middle-aged adults were recorded at the Sacré-Cœur Hospital, whereas adolescents and young adults were studied at the Louis-H Lafontaine Research Center. The setting of the two laboratories has been elaborated by the same staff, and according to the same specifications (polygraphs). This minimized the possibility of differences caused by methodology. Experimental conditions such as EEG montages and data acquisition parameters were also strictly the same in the two laboratories. Electrodes were placed according to the international 10–20 system, using a referential montage with at least central and occipital EEG derivations, and left and right electro-oculogram (EOG) and chin electromyogram (EMG). A Grass polygraph (sensitivity 7.0 μV mm⁻¹, bandpass 0.3–100 Hz) was used to amplify signals. The signals were also relayed to a PC computer where they were digitized at a sampling rate of 128 Hz and filtered with a digital filter having an upper cutoff frequency of 64 Hz. Only frequencies up to 31.0 Hz were considered for spectral analyses. Sleep stages were visually scored on screen by 20-s epochs using the C3/A2 lead, according to the standard criteria (Rethschaffen and Kales 1968).

EEG spectral analysis

To quantify the dynamics of NREM sleep EEG over the course of the night, spectral analyses were performed for the first 5 h of NREM sleep (Stage 2, 3 and 4 sleep). In order to obtain data which are equivalent with most studies investigating sleep regulatory mechanisms (Achermann et al. 1993;
Aechbach and Borbély 1993; Dijk et al. 1989) and because it is SD for sleep scoring (Retschaffen et al. 1968), spectral analyses were performed on the C3/A2 derivation.

Power spectral analyses were performed with a commercial software package (Eclipse 3.0, Stellate Systems, Montreal, Canada) which computes fast Fourier transforms (FFT) on 4-s epochs with a cosine window tapering. This yielded a spectral resolution of 0.25 Hz. Artifacts were rejected by visual inspection and analyses were performed on artifact-free epochs. Epochs with artifacts were considered as missing data in order to preserve sleep continuity. After spectral analyses, five 4-s epochs were averaged to keep a correspondence with the 20-s sleep scoring windows. Then, spectral activity was averaged per hour for the first five NREM hour of sleep. Five frequency bands were defined as: SWA (0.75–4.5 Hz), theta (4.0–7.75 Hz), alpha (8.0–12.0 Hz), sigma or spindle frequency activity (SFA: 12.25–15.0 Hz) and beta (15.25–31.0 Hz). Absolute power was used for all frequency bands.

Statistical analyses

To evaluate the differences in sleep architecture, one-way ANOVA with one independent variable (Age group) and one dependent factor (individual sleep parameter) were performed. Significant F-values were adjusted with Bonferroni correction for multiple testings. For a quantitative description of EEG power for each age group during the night, the first statistical analyses were performed on log-transformed power values, to normalize data distributions. Two-way ANOVAs with one independent factor (Age group) and one repeated measure (NREM hour) were performed to illustrate the effects of age and time-of-night on EEG power in the various frequency bands during NREM sleep. P-levels (alpha) were adjusted with Huynh-Feldt correction for sphericity, and considered significant when ≤ 0.05. Contrast analyses and post hoc Tukey HSD (P-level ≤ 0.05) comparisons were used to decompose the interaction effects and identify the nature of significant results, or to locate the differences in main effects.

To assess the dynamic of SWA over the course of the night, further analyses were performed on percent of mean SWA during NREM sleep for the entire night. Two-way ANOVAS with one independent factor (Age group) and one repeated measure (NREM hour) were used to investigate the effects of age on the dynamics of changes in EEG during NREM sleep. Then, trend analyses were performed for each group with a between-group comparison of the rates of change.

RESULTS

Sleep variables

Table 1 presents sleep parameters (mean ± SD) derived from visual scoring. Children and adolescents had longer sleep latency than young adults and middle-aged subjects. REM sleep latency was longer for children than for young adults and middle-aged adults. REM latency was also longer for adolescents than young adults. Sleep efficiency was higher only for the young adults compared with middle-aged subjects. Important differences with regard to percentage of time spent in the various sleep stages were also observed between age groups. The middle-aged group had a higher percentage of wakefulness, stages 1 and 2 sleep, compared with children and adolescent group. Percentage of Stage 2 sleep was higher for adolescents and young adults than for children. In contrast, the percentage of SWS (Stages 3 and 4 sleep) was significantly more important for the children than for the other three groups. The percentage of SWS was also higher for adolescents, than for young adults or middle-aged subjects. There were main effects of gender and age for the percentage of stages 3 and 4, but no interaction. With age, the percentage of SWS decreased, and women had a higher percentage of SWS compared with men. Young adults presented a higher percentage of REM sleep than the other three groups. Total sleep time was reduced for middle-aged subjects compared with the younger groups.

<table>
<thead>
<tr>
<th>Sleep variables</th>
<th>Children</th>
<th>Adolescents</th>
<th>Young adults</th>
<th>Middle-aged adults</th>
<th>F</th>
<th>P</th>
<th>Post-hoc HSD Tukey HSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep lat. (min)</td>
<td>25.04 (12.74)</td>
<td>24.38 (13.91)</td>
<td>9.58 (6.11)</td>
<td>12.71 (6.22)</td>
<td>7.76</td>
<td>0.0002*</td>
<td>CH &gt; YA, MA; AD &gt; YA, MA</td>
</tr>
<tr>
<td>REM lat. (min)</td>
<td>163.52 (54.43)</td>
<td>124.98 (39.94)</td>
<td>86.69 (26.30)</td>
<td>100.89 (20.67)</td>
<td>10.01</td>
<td>&lt; 0.0001*</td>
<td>CH &gt; YA, MA; AD &gt; YA</td>
</tr>
<tr>
<td>Sleep effect (%)</td>
<td>95.39 (4.73)</td>
<td>94.38 (3.43)</td>
<td>96.55 (1.62)</td>
<td>91.12 (5.31)</td>
<td>5.08</td>
<td>0.004*</td>
<td>YA &gt; MA</td>
</tr>
<tr>
<td>Stage 1 (%)</td>
<td>6.84 (3.5)</td>
<td>6.71 (3.05)</td>
<td>8.61 (2.97)</td>
<td>11.21 (4.16)</td>
<td>7.14</td>
<td>0.0004*</td>
<td>MA &gt; CH, AD</td>
</tr>
<tr>
<td>Stage 2 (%)</td>
<td>41.26 (10.46)</td>
<td>53.47 (3.81)</td>
<td>54.78 (4.95)</td>
<td>62.40 (8.01)</td>
<td>17.45</td>
<td>&lt; 0.0001*</td>
<td>MA &gt; AD; CH; YA &gt; CH</td>
</tr>
<tr>
<td>Stages 3 and 4 (%)</td>
<td>34.18 (10.16)</td>
<td>23.63 (6.74)</td>
<td>14.48 (5.82)</td>
<td>7.75 (6.65)</td>
<td>30.73</td>
<td>&lt; 0.0001*</td>
<td>CH &gt; AD; YA; MA; AD &gt; MA</td>
</tr>
<tr>
<td>Stage REM (%)</td>
<td>17.72 (1.26)</td>
<td>18.17 (2.83)</td>
<td>22.13 (3.68)</td>
<td>18.64 (4.07)</td>
<td>5.32</td>
<td>0.003*</td>
<td>YA &gt; CH, AD; YA &gt; MA</td>
</tr>
<tr>
<td>Wakefulness (%)</td>
<td>4.35 (4.81)</td>
<td>4.92 (3.29)</td>
<td>2.86 (1.74)</td>
<td>8.86 (5.30)</td>
<td>6.25</td>
<td>0.001</td>
<td>MA &gt; CH; AD; YA</td>
</tr>
<tr>
<td>TST (min)</td>
<td>528.63 (36.82)</td>
<td>494.24 (23.12)</td>
<td>502.53 (46.32)</td>
<td>439.49 (34.54)</td>
<td>13.44</td>
<td>&lt; 0.0001*</td>
<td>CH &gt; MA; AD &gt; MA; YA &gt; MA</td>
</tr>
</tbody>
</table>

*P-values were considered significant when < 0.05; †mean (Standard deviation); ‡CH: children; AD: adolescents; YA: young adults; MA: middle-aged adults.

Spectral activity

**NREM hours vs. NREM–REM cycles**

NREM hour timebase was chosen for spectral analysis in order to compensate for the differences between the groups in the duration of the first NREM period (REM latencies: Children: 163.52 ± 54.43; Adolescents: 124.98 ± 39.94; Young adults: 86.69 ± 26.30; Middle-aged: 100.89 ± 20.67 min ± SD; \( P < 0.0001 \)). Analyses per NREM hours allows to measure the intensity of EEG spectral power on the same averaging unit (e.g. 60 min), and to compare subjects with different number and duration of NREM–REM cycles. For illustrative purposes, we added a graph of absolute SWA across NREM–REM cycles (Fig. 1). Further analyses were performed on the first 5 NREM hours of sleep.

As illustrated in Fig. 2, a marked decrease of SWA is observed with increasing age. In the four age groups, SWA declined over the first five NREM hours of sleep. A two-way ANOVA (on log transformed values) with Age group as the independent factor and NREM hour as a repeated measure revealed a significant interaction effect \( (F_{12} 200 = 1.93; e = 0.90; P = 0.04) \), showing that the decay rate of SWA was not the same for the different groups; between-group differences in SWA power was larger at the beginning of the night and decreased over the five NREM hours. Contrast analyses were performed to evaluate the effects of age group at each NREM hour, and showed significant between-group differences for each hour \( (P < 0.001) \). Post hoc Tukey HSD mean comparison tests demonstrated that SWA was significantly higher for children compared with adolescents for NREM hours 1 and 4. Children and adolescents had more SWA power than young adults and middle-aged subjects throughout the night. Furthermore, young adults showed a significantly higher level of SWA than the middle-aged for the first 2 h.

Absolute theta power was significantly higher across the night for children compared with the other three groups. Theta power also showed a declining profile over consecutive NREM hours, as illustrated in Fig. 3. A significant interaction between age group and NREM hour was observed \( (F_{12} 200 = 8.16; e = 0.85; P < 0.0001) \). Between-group differences were present at each NREM hour \( (P < 0.0001) \). In comparison to children, theta power was lower for adolescents, young adults and middle-aged subjects throughout the night. Theta power was higher for adolescents compared with young adults for hours 1, 2 and 4. Compared with middle-aged subjects, adolescents had more theta power for all hours. The interaction may be explained by the variations of the effect of age across the night. Children showed, indeed, a steeper decline of theta power especially during the first 2 h of NREM sleep.

**Figure 1.** Absolute SWA power across 4 NREM cycles for children (-----), adolescents (-----), young adults (-----) and middle-aged adults (-----).

**Figure 2.** Absolute SWA power across 5 NREM hours for children (○), adolescents (■), young adults (▲) and middle-aged (●) adults.

**Figure 3.** Absolute theta power across 5 NREM hours for children (○), adolescents (■), young adults (▲) and middle-aged (●) adults.
A significant Age group X NREM hour interaction was found for alpha power ($F_{12,200} = 2.90; \varepsilon = 0.76; P = 0.003$). Significant between-group differences were noted for each hour ($P < 0.0001$). Alpha power was higher for children than for young adults and middle-aged subjects at all hours. Adolescents had also more alpha power compared with middle-aged at hour 1 (Fig. 4).

For sigma power, a significant interaction between Age group and NREM hour was found ($F_{12,200} = 2.17; \varepsilon = 0.99; P = 0.015$). Sigma power was significantly different between the four groups for NREM hours 1, 2, 4 and 5 ($P < 0.05$). Children had more sigma power than middle-aged subjects for hour 1. Sigma power was higher for adolescents compared with middle-aged adults, except for hour 3 (Fig. 5).

The ANOVA revealed significant main effects of both Age group and NREM hour ($F_{350} = 3.44; P = 0.024; F_{4200} = 10.55; \varepsilon = 0.92; P < 0.0001$) for beta power, but no interaction. Beta was significantly higher for children compared with young and middle-aged subjects. A very high tendency for more beta power in the children than in the adolescent group was also observed ($P = 0.052$) (Fig. 6).

Dynamics of SWA and theta power: Integrity of the homeostatic process

To study the individual profile of EEG power spectra within each group, spectral activity was expressed as a percentage of the mean power during NREM sleep for the entire night. Figure 7a and b represent the percentage of SWA and theta band in the course of the night, and show that the effect of age on EEG power varied across the night. A significant Age X NREM hours interaction effect was noted for both frequency bands ($F_{12,200} = 2.55; \varepsilon = 0.78; P = 0.008; F_{12,200} = 13.36; \varepsilon = 0.80; P < 0.0001$). Trend analysis revealed a linear component for the dynamics of SWA and theta decrease for the four groups ($P < 0.002$) a quadratic component ($P < 0.002$, children and adolescents and $P < 0.05$, young adults) for all but the middle-aged subjects. Between-group comparisons on linear trend showed that the rate of decline was different for the four groups. The decrease of SWA and theta during the night displayed a similar profile for children and adolescents. The two younger groups had a higher rate of decline than the two older groups and SWA and theta decrease in young adults was steeper compared with middle-aged. It is interesting to note that for children and adolescents, the build-up of SWA and theta power at the beginning of the night is higher than that of young adults and middle-aged adults. The decline of SWA and theta during the night seemed to approach a plateau value with increasing age.
To our knowledge, this study is the first to describe the major age-related alterations of EEG SWA occurring from childhood to middle age. Absolute SWA undergoes a marked reduction throughout the aging process. The modifications in EEG power across age groups were not restricted to SWA, but included the theta, alpha, sigma and beta frequency bands as well. The dynamics of decline of SWA and theta power across the night seem to approach a plateau with increasing age, suggesting an age-related attenuation of homeostatic sleep pressure dissipation.

We can not rule out the possibility of a first-night effect on sleep architecture. Sleep latency and REM latency during the first night of polysomnographic recordings has been reported to be longer, especially in children. In this study, sleep variables for the younger groups are similar to those reported previously (Benoit 1981; Carskadon et al. 1987; Coble et al. 1987; Palm et al. 1989). Moreover, in our study, sleep efficiency was very high in children and also in adolescent groups, indicating that sleep quality after sleep onset was good.

An important decrease in the percentage of SWS (Stages 3 and 4 sleep) occurs across the process of aging. A major reduction of absolute SWA power was also observed across age-group, starting as early as adolescence. Moreover, the appearance of the age-related decrease of SWA power was paralleled with the decline of SWS. Theta power showed similar variations as SWA across the night and age-groups. The reduction of absolute SWA suggests that it may play a role in the intense physiological transformations occurring during maturation. As such, it has been proposed that the changes of EEG during sleep could reflect the kinetics of the underlying metabolic processes (Church et al. 1975; Feinberg 1982; Feinberg et al. 1990). The early modifications in sleep structure across childhood and adolescence has been related to ontogenetic alterations in cortical synaptic density, which peaks in the first decade of life, and then undergoes a substantial reorganization during the second decade (Feinberg 1982, 1990). The higher EEG power of young subjects was also seen as a possible reflect of a higher level of synchronization of cortical neurons, compared with older individuals (Astrom and Trojaborg 1992).

The age-related alterations of EEG power in this study also affected alpha, sigma and beta frequency bands. Overall, younger subjects exhibited higher power for all these bands than the older groups. The age-related reduction of power in frequencies up to 15 Hz for NREM sleep EEG, has already been reported (Carrier et al. 2000; Dijk et al. 1989; Landolt et al. 1996).

This study also brings new data concerning the dynamics of NREM sleep EEG before adulthood. The decay rate of SWA across the night was similar for children and adolescents. However, both groups showed a higher build-up of SWA early in the night and a steeper decay across the night compared with young and middle-aged subjects. Theta activity displayed a similar dynamics as SWA during NREM sleep. It has already been reported that theta is also sensitive to sleep deprivation (Dijk et al. 1993). The precocious modifications of SWA and theta power highlight the possible maturational influences on sleep regulatory mechanisms. According to previous reports, the present study shows that the time course of SWA decline across the night was slower and shallower for middle-aged, compared with young adults (Carrier et al. 2001; Dijk et al. 1989; Landolt et al. 1996). The decline of SWA and theta during the night seem to approach a plateau value with increasing age. Our results suggest that the dynamics of SWA decline during NREM sleep, reflecting the dissipation of homeostatic sleep process, is already attenuated in early adulthood.

It was proposed that adolescents may present a reduction in the rate of accumulation of the ‘sleep drive’ or sleep/wake homeostatic process compared with children (Carskadon et al. 1997). Preliminary data showed that after sleep deprivation,
more mature adolescents have a lower rebound of SWS than less mature adolescents (Carskadon et al. 1998). It was recently reported that following 25-h of sleep deprivation, middle-aged subjects present a lower rebound of SWA compared with young adults during daytime recuperative sleep, suggesting a reduction in homeostatic recuperative drive (Gaudreau et al. 2001). These studies support the suggestion of an attenuation of build-up of homeostatic sleep pressure with advancing age. However, further studies measuring the age-related differences in the build-up of SWA after different amounts of wakefulness are essential to confirm this hypothesis.

CONCLUSIONS

The dynamics of NREM sleep EEG undergo important agerelated modifications, from childhood to middle-age. The precocious changes in EEG SWA power suggest a peak associated with the maturational process, followed by the already reported decline with advancing age. Aging seems to be linked to an attenuation of homeostatic sleep drive.

ACKNOWLEDGEMENTS

The authors are grateful to Dominique Petit for her helpful comments on the manuscript, Gaétan Poirier for his assistance with the spectral analysis and Jean Paquet for statistical analysis. This study was supported by grants MT-11051 (Montplaisir) and MT-14999 (Carrier) from the Medical Research Council of Canada.

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