Effects of a 25-h sleep deprivation on daytime sleep in the middle-aged
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Abstract

Our understanding of the mechanisms by which sleep deteriorates with age almost exclusively stems from comparisons of young and elderly subjects. The present study investigated the different effects of a 25-h sleep deprivation on the recovery sleep initiated in the morning (when circadian sleep propensity decreases) of young (20–39 y) and middle-aged subjects (40–60 y). Middle-aged subjects showed a steeper increase in the duration of wakefulness during daytime recovery sleep than the young subjects. Slow-wave sleep (SWS) and EEG slow-wave activity (SWA: spectral power between 0.5–4.5 Hz) were potentiated in both groups following sleep deprivation. However, the rebound of SWS and SWA was significantly less pronounced in the middle-aged than in the young. This reduction in homeostatic recuperative drive in middle-aged subjects might account for the decrease in their ability to maintain sleep when they have to recuperate at an abnormal circadian phase. These results helps to understand the increase in complaints related to shift work and jet lag in the middle years of life. © 2001 Elsevier Science Inc. All rights reserved.

Keywords: Sleep; Sleep deprivation; Aging; Middle-age; Homeostatic; Circadian rhythms

1. Introduction

The modification of sleep organization is a hallmark of the normal aging process. Until now, our understanding of the mechanisms by which sleep deteriorates with age has almost exclusively come from comparisons between young and elderly subjects. However subjective sleep complaints begin to increase significantly in the middle years of life [19] and almost all sleep parameters show significant effects of age between age 20 and age 60 [16,20]. The results of one study of 110 subjects between the ages of 20 and 60 years indicated that, at home, older subjects woke up earlier, went to bed earlier, spent less time in bed, and were more alert at waketime [11]. In the laboratory, increasing age was associated with less time asleep, increased number of awakenings, increased amount of wakefulness during sleep, less slow-wave sleep (SWS) and Rapid-Eye Movement sleep (REM), higher percentages of stage 1 and stage 2 sleep, and shorter REM latency [11].

Results on quantitative sleep EEG also point out significant changes between 20 and 60 years of age [9,16,20]. The most consistent of these modifications is a decrease in SWA (slow-wave activity: spectral power between 0.75 to 4.5 Hz) during NREM sleep with advancing age. These studies also report that the difference in SWA between young (20–39 y) and middle-aged (40–60 y) subjects diminished across the sleep period, leading to a shallower decay rate of SWA throughout the night in the middle-aged subjects.

The interaction of homeostatic and circadian processes regulates the sleep-wake cycle [1,5]. The homeostatic process represents the sleep debt accumulated during wakefulness. As a result, the homeostatic process increases during waking hours and decreases exponentially during sleep. The intensity and dynamic of SWS and SWA provide an estimate of the homeostatic process. Numerous studies have investigated the homeostatic process of sleep regulation in humans by measuring the effects of prior wakefulness and sleep on the sleep EEG. It has been shown that SWS and SWA are enhanced after an extension of prior wakefulness [1]. The increase of SWA following sleep deprivation is more prominent at the beginning of the night. This leads to a steeper decline of SWA through the night following sleep deprivation [1].

The decrease in the amount of SWA and its more shal-
low decay rate across the night in older subjects may reflect an attenuation of sleep homeostatic pressure with increasing age [9,16,20]. More information about the effects of differential amounts of wakefulness on sleep is necessary to support this suggestion. Very few studies to date have evaluated the effects of manipulations of the homeostatic process in aging. Studies in young and old rats have shown that aged rats exhibit reduced responses on SWS and on EEG delta power following sleep deprivation [26,27]. In studies of humans, elderly subjects have been subjected to one or two nights of sleep deprivation or to sleep fragmentation. Although elderly adults respond to sleep deprivation with an increase in SWS, they tend to show a lower rebound of SWS after this challenge than younger subjects [3,4,6]. Therefore it appears that even though the homeostatic process of elderly subjects has the ability to respond to major sleep deprivation challenges, its overall capacity to respond diminishes.

The circadian process of sleep regulation is controlled by an endogenous pacemaker, located in the suprachiasmatic nucleus of the hypothalamus. This circadian pacemaker is responsible for the rhythmic variations of sleep propensity throughout the 24-h day. Sleep propensity increases on the falling limb of the circadian temperature curve and it maximizes near the trough of the curve. Sleep propensity decreases on the rising limb of the circadian curve and it minimizes near the peak of the curve [13,17,21,30]. When required to sleep at a circadian phase of low circadian sleep propensity both young and older subjects will show higher levels of wakefulness compared to baseline sleep [10,17,22,23]. However, it has been suggested that the sleep of aging subjects might be particularly vulnerable to a circadian phase misalignment [8,22]. A forced desynchrony protocol in which sleep episodes were initiated at all circadian phases and preceded by 18.33 h of wakefulness indicated that elderly subjects show more wakefulness than young subjects at each phase. However, this difference between young and elderly subjects was more prominent when sleep occurred on the ascending limb of the circadian temperature rhythm, a point at which circadian sleep propensity is decreasing [15]. These data supported the hypothesis of an increased susceptibility to a phase angle misalignment in elderly subjects.

The aim of the present study was to evaluate the different effects of a phase angle misalignment in young and middle-aged subjects in a situation of enhanced sleep homeostatic pressure induced by an acute sleep deprivation. The study investigated the differences across young and middle-aged subjects in the effects of a 25-h sleep deprivation on recovery sleep initiated in the morning, a time during which circadian sleep propensity decreases. We hypothesize that compared to the young, the strength of middle-aged subjects’ homeostatic response will be less pronounced following sleep deprivation. The dynamics of SWS and SWA throughout the night will serve as measures of the homeostatic process recuperative drive. We predict a lower rebound of these sleep parameters following the sleep deprivation in the middle-aged subjects. We hypothesize further that the sleep of middle-aged subjects will be more vulnerable to an abnormal phase angle between the sleep-wake cycle and the circadian signal as measured by a steeper increase in wakefulness during daytime recovery sleep.

2. Methods

2.1. Subjects

Thirty-three subjects between the ages of 20 and 60 completed the study. They were separated into two groups according to their age: young subjects (8 women and 8 men; 20–39 y; mean age 30.0 y, sem = 1.2) and middle-aged subjects (8 women and 9 men; 40–60 y; mean age 50.2 y, sem 1.4). Subjects were screened to be in good health according to history, normal blood test and urinalysis (complete blood count, chemistry screen, thyroid function tests, prolactin, testosterone in men, and estrogens, FSH, LH in women). Subjects were on no medications and they had no sleep complaints. They reported no history of psychiatric or neurological illnesses. Subjects who experienced night work or transmeridian travel in the three months prior to the study were excluded from the sample. Obese individuals were also excluded (BMI > 27). All subjects had a score lower than 4 on the short version of the Beck Depression Scale [2]. The Screening also included one-night sleep polysomnographic (PSG) evaluation. During the PSG screening, electroencephalogram (EEG), electromyogram (EMG) and electrooculogram (EOG) were recorded. A nasal/oral thermometer and EMG leg electrodes were also used to screen for sleep apnea and for periodic leg movements respectively. Subjects with an apnea-hypopnea index > 10 or a periodic limb movements index > 10 were excluded from the study. Subjects were instructed to abstain from alcohol, caffeine, and medication during the laboratory experience. All subjects were required to be non-smokers because the study took place over an extended period of time in a confined environment. Subjects had also to fill-up a 14-day activity diary. Young and middle-aged subjects did not differ in the mean number of caffeine beverages per day (Young: 1.5, sem 0.3; Middle-aged: 1.7, sem = 0.2), or in the mean number of alcoholic beverages per day (Young: 0.8, sem 0.2; Middle-aged: 0.6, sem = 0.2).

Pre-menopausal and post-menopausal women were included in the study. Peri-menopausal women and women using hormonal contraceptives or receiving hormonal replacement therapy were excluded. Pre-menopausal women were required to have had a regular menstrual cycle (25–32 days) during the year preceding the study, no vasomotor complaints (hot flashes, night sweats), and low FSH levels (<20 iU/liter). They were studied in the laboratory during the follicular phase of their menstrual cycle. Post-menopausal women had to have had no menstrual cycles during...
the past year and FSH levels above 20 iU/liter. In the middle-aged group, four women were pre-menopausal and four women were post-menopausal. Subjects were asked to read and to sign a consent form that provided detailed information about the nature, the purpose, and the risks of the study; they were paid for their participation. The ethical committee of the Hospital approved this project.

2.2. Procedure

Before the laboratory sleep study, subjects completed a French version of the “Pittsburgh Sleep Diary” [24] every day for 14 days, from which means for habitual waketimes, habitual bedtimes, and habitual time spent in bed were calculated. Subjects came to the chronobiology laboratory for 4 consecutive nights and for 2 days (see Fig. 1 for details). The first two sleep episodes (S1 and S2) were used as adaptation nights. For these two nights, subjects arrived at the chronobiology laboratory a few hours prior to their habitual bedtime and they left in the morning; they performed their habitual activities during the day. When subjects were admitted on the third night, they remained in the laboratory for the next 48 h. Night 3 (S3) was used as the baseline sleep episode. The timing of bedtime and waketime for the laboratory sleep study was based on habitual bedtimes and waketimes averaged from the two-week sleep diaries. Participants were subjected to a mini-constant routine for the 25 h that immediately followed their habitual wake-up time on S3. During the mini-constant routine, subjects remained awake in bed in a semi-recumbent position with ambient lighting kept below 15 lux and they were given small snacks on a regular basis. A research assistant was present at all times to administer vigilance and performance evaluations, to collect saliva samples, and to make sure that subjects were not falling asleep. Rectal temperature was measured continuously by a disposable rectal sensor (Yellowspring Inst.) that was inserted 10 cm into the rectum from bedtime of night 3 to the end of the experiment (Mini-Logger, Mini-Mitter). The mini-constant routine ended in the morning, one hour after habitual wake-up time. At the end of the mini-constant routine, lights were turned off and a daytime recovery sleep episode was recorded (S4). Subjects had to stay in bed for the habitual sleep length indicated in their sleep diaries.

![Figure 1](https://example.com/figure1.png)

Fig. 1. Schematic representation of the research protocol for a subject with habitual bedtime at midnight and habitual waketime at 08:00. Hours are from midnight to midnight on the horizontal axis. Each line represents one day of the research protocol. Dashed areas represent sleep episodes. S3 is the baseline sleep episode and S4 is the daytime recovery sleep episode. Vertical lines indicate admission (continuous) and departure (dotted) from the chronobiology laboratory.
Table 1

All-night sleep parameters: mean and SEM. P values were considered significant when <0.05. S3 is baseline sleep episode and S4 is daytime sleep episode.

<table>
<thead>
<tr>
<th>Sleep variables</th>
<th>Young</th>
<th>Middle-aged</th>
<th>Main group effects</th>
<th>Main sleep episode effects</th>
<th>Group X sleep episode interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S3</td>
<td>S4</td>
<td>S3</td>
<td>S4</td>
<td>F</td>
</tr>
<tr>
<td>Sleep latency (min)</td>
<td>11.2 (1.6)</td>
<td>4.4 (1.1)</td>
<td>10.9 (1.7)</td>
<td>5.5 (0.9)</td>
<td>0.5</td>
</tr>
<tr>
<td>REM latency (min)</td>
<td>81.1 (8.7)</td>
<td>67.7 (6.8)</td>
<td>79.2 (5.4)</td>
<td>54.4 (5.1)</td>
<td>1.3</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>90.7 (1.9)</td>
<td>83.3 (3.7)</td>
<td>88.4 (2.0)</td>
<td>70.5 (2.7)</td>
<td>6.8</td>
</tr>
<tr>
<td>Stage 1 (min)</td>
<td>38.8 (3.8)</td>
<td>26.3 (3.5)</td>
<td>33.6 (3.8)</td>
<td>31.5 (3.5)</td>
<td>0</td>
</tr>
<tr>
<td>Stage 2 (min)</td>
<td>267.8 (13.1)</td>
<td>222.9 (13.1)</td>
<td>269.9 (11.2)</td>
<td>212.1 (10.2)</td>
<td>0.1</td>
</tr>
<tr>
<td>SWS (min)</td>
<td>32.0 (6.3)</td>
<td>54.1 (7.5)</td>
<td>12.8 (3.0)</td>
<td>23.4 (5.0)</td>
<td>10.5</td>
</tr>
<tr>
<td>REM (min)</td>
<td>97.0 (6.6)</td>
<td>68.7 (9.2)</td>
<td>93.9 (4.8)</td>
<td>54.3 (5.7)</td>
<td>1.02</td>
</tr>
</tbody>
</table>

1 Log transformation Ln (var + 1) performed before analyses. Mean values presented in original units.
2 Square root transformation performed before analyses. Mean values presented in original units.
3 Log transformation Ln (100 – var + 1) performed before analyses. Mean values presented in original units.

2.2.1. Polysomnographic recordings

EEG electrodes were placed according to the international 10–20 system, using a referential montage with linked ears, a left and right electrooculogram (EOG) and a chin electromyogram (EMG). A Grass Model 15A54 amplifier system (gain 10000, bandpass 0.3–100 Hz) was used and signals were digitalized at a sampling rate of 256 Hz using a commercial software product (Harmonie, Stellate system). Sleep stages were scored visually on screen (LUNA, Stellate System) according to the standard criteria by 20-s epochs [25].

2.2.2. Quantitative EEG

Power spectral analyses were performed on the C3 derivation during NREM sleep with a commercial software package (Electrophysiological Recordings Analyser 2.0) that computes fast Fourier transforms (FFT) on 4-s epochs with a Hanning window tapering. This yielded a spectral resolution of 0.25 Hz. Automatic detection rejected artifacts and analyses were performed on artifact-free epochs [7]. Epochs containing artifacts were regarded as missing data in order to preserve sleep continuity. After spectral analyses, five 4-s epochs were averaged in order to maintain correspondence with the 20-s sleep scoring windows. Then, spectral activity was averaged per 60 min of NREM sleep for the first 180 NREM minutes. SWA was defined as absolute power (μV²) for frequencies between 0.5 and 4.5 Hz. Values were expressed as a percentage of mean SWA during the first 180 min of N-REM sleep for the baseline sleep episode. Analyses on N-REM minutes received preference over N-REM periods because daytime recovery sleep disturbed the dynamic of sleep cycles.

2.2.3. Statistical analyses

Two-way ANOVAs with one independent factor (Group) and one repeated measure (Sleep episode) were performed in order to evaluate group (Young vs Middle-aged) differences in sleep architecture between baseline and daytime recovery sleep. Sleep parameters that did not distribute normally (Shapiro-Wilk test) were transformed prior to statistical analyses (see Table 1). A three-way ANOVA with one independent factor (Group) and two repeated measures (Sleep Episode and Half-hour) was performed to analyze group differences in the number of minutes of wakefulness for each half-hour during baseline and recovery sleep. Wakefulness values were log transformed prior to statistical analysis so that the variation could approximate a normal distribution. A three-way ANOVA with one independent factor (Group) and two repeated measures (Sleep episode and NREM minutes) was used to compare differential effects of age on the SWA dynamic before and after sleep deprivation. P-levels (alpha) were adjusted with Huynh-Feldt correction for sphericity for repeated measures with more than two levels and they were considered significant when α ≤ 0.05. Contrast analyses and post hoc Tukey HSD (p-level ≤ 0.05) comparisons were used either to decompose the interaction effects and to identify the nature of significant results or to locate the differences in main effects. Since no interaction was found between Group and Gender or between Group, Sleep Episode, and Gender on any sleep or SWA parameters, data from men and women were pooled together.

3. Results

Compared to the young subjects, the middle-aged subjects showed earlier habitual bedtime (Young: 23:49, sem = 0:16; Middle-Aged: 22:58, sem = 0:16; P < 0.04) and earlier habitual waketime (Young: 08:26, sem = 0:15; Middle-Aged: 07:19, sem = 0:15; P < 0.01), but similar habitual sleep period length (Young: 07:59, sem = 0:13; Middle-aged: 07:49, sem = 0:13; n.s.). As shown in Table 1, a comparison of baseline sleep and daytime recovery sleep
revealed that both groups of subjects showed reduced sleep latency and REM sleep latency along with a decrease in the number of minutes in stage 2 and of REM sleep (Sleep episode effect: \( P \leq 0.02 \), all cases). There was no interaction between Group and Sleep episode for these variables. There was a significant Group X Sleep episode interaction for the number of minutes of stage 1. Contrast analyses indicated a significant reduction of the length of stage 1 during daytime recovery sleep in the Young subjects (\( P < 0.0009 \)) but not in the Middle-aged subjects (ns).

There was also a significant Group X Sleep episode interaction for sleep efficiency. Contrast analyses revealed a significant decrease of sleep efficiency during daytime recovery sleep in both groups of subjects but that the Middle-aged subjects had a more abrupt decline than did the Young subjects (see Fig. 2; Middle-aged: \( P < 0.000001 \); Young: \( P = 0.002 \)).

The number of minutes of wakefulness per half-hour was averaged for the first six hours of the sleep episode for the purpose of evaluating the dynamic of wakefulness across the sleep episode (Fig. 3). A three-way ANOVA with one independent factor (Group) and two repeated measures (Sleep episode and Half-hour) revealed significant main effects of Group (\( F_{1,31} = 7.9; P = 0.008 \)), Sleep episode (\( F_{1,31} = 53.7; P < 0.001 \)), and Half-hour (\( F_{7,207} = 12.0; P < 0.001 \)). There were also significant interactions between Group and Sleep episode (\( F_{1,31} = 5.3; P < 0.03 \)) and between Sleep episode and Half-hour (\( F_{7,248} = 4.3; P < 0.001 \)). Contrast analyses for the Sleep episode X Half-hour interaction indicated that the number of minutes of wakefulness was higher during daytime recovery sleep than during baseline sleep mostly after the first 120 min of the sleep episode (150 min, 180 min, 240 min, 360 min: \( P < 0.03 \); 270 min, 300 min, 330 min: \( P < 0.0001 \)). Contrast analyses for the Group X Sleep episode interaction showed that both groups of subjects had a significant increase in wakefulness during daytime recovery sleep but that it was larger for the Middle-aged than for the Young subjects (Middle-aged: \( P < 0.000001 \), Young \( P = 0.001 \)).

As shown in Fig. 4, SWS (stages 3+4 in min) duration was significantly enhanced for both groups during recovery daytime sleep but contrast analyses of the interaction revealed that SWS rebound was less pronounced in the Middle-aged group (\( P = 0.0003 \)) than in the Young group (\( P > 0.000001 \)).

Fig. 5 illustrates mean SWA (expressed as percent of the mean of baseline) for the first 180 min of N-REM sleep. Three-way ANOVAs showed significant main effects of Group (\( F_{1,31} = 4.4, P < 0.05 \)), Sleep episode (\( F_{1,31}: 41.4; P < 0.001 \)), and NREM Hour (\( F_{1,7,52.9} = 30.8; P < 0.001 \)) as well as a significant Group X Sleep episode interaction (\( F_{1,31} = 4.3, P < 0.05 \)). SWA was potentiated for both groups of subjects during daytime recovery sleep. However, contrast analyses of the Group X Sleep episode interaction indicated that SWA rebound was lower for the Middle-aged subjects (\( P < 0.004 \)) compared to the Young ones (\( P < 0.000002 \)). Post hoc analyses on the main N-REM hour effect exposed a declining profile of SWA across the sleep episode (\( P < 0.003 \) for all N-REM hour comparisons).
4. Discussion

To our knowledge, this is the first report of differential effects of sleep deprivation on sleep and on sleep EEG spectral power in young and middle-aged adults. Following 25 h of sleep deprivation, there was more disruption in sleep consolidation in middle-aged than in young adults when recovery sleep was initiated in the morning, a time of decreased circadian sleep propensity. A rebound of SWS and SWA was observed during recovery sleep for both groups of subjects but the increase was significantly less in the middle-aged than in the young subjects. These results suggest that the middle years of life are associated with important modifications in sleep regulatory processes.

It has been reported that the circadian phase strongly modulates sleep propensity and REM sleep propensity [12–14]. In this study, the daytime recovery sleep episode was initiated one hour following habitual waketime, a circadian time that is usually associated with high sleep propensity and high REM sleep propensity. The increase in homeostatic sleep pressure following sleep deprivation in conjunction with the still high circadian sleep propensity at the beginning of the daytime sleep episode may account for the reduction in sleep latency observed in both groups of subjects. High circadian REM pressure may explain the significant reduction of REM sleep latency.

The forced desynchrony protocol is one of the techniques often proposed to separate the homeostatic influence from the drive of the circadian timing system. A nonlinear interaction of the circadian and the sleep-dependent components of sleep propensity has been reported in forced desynchrony studies [17]. For instance, the amplitude of the circadian modulation for the amount of wakefulness during sleep has been shown to increase with the number of hours asleep. In the present study, a daytime recovery sleep episode occurred at a circadian time of decreasing sleep propensity. Not surprisingly, sleep efficiency was lower during daytime recovery sleep than during baseline sleep, at the expense of stages 1, 2 and REM sleep. The duration of wakefulness during daytime recovery sleep was more prominent for both groups at the end of the sleep episode, when homeostatic sleep drive decreased. This probably reflects the combined influence of decreasing circadian sleep propensity drive and the evacuation of homeostatic sleep pressure.

It has been suggested that the sleep-wake cycle of older subjects might be particularly vulnerable to an abnormal phase angle between the sleep episode and the circadian timing system [8,22]. In our study, the more important reduction of sleep efficiency in the middle-aged group during daytime recovery sleep shows that the increased vulnerability to an abnormal phase angle is already apparent in the middle years of life. This higher vulnerability is observed despite an increased homeostatic sleep pressure at sleep onset induced by 25 h of sleep deprivation.

SWS was significantly enhanced for both age groups during daytime recovery sleep but SWS rebound was less pronounced in the middle-aged group than in the young group. This corroborates the observation that older subjects preserve the ability to respond to sleep deprivation with a
SWS rebound [22,28]. The only study to date that examined the effects of sleep deprivation on daytime sleep architecture in young and in middle-aged men reported a longer latency to stage 4 during recovery sleep in the middle-aged compared to the young subjects. However, no difference in the amounts of stages 3 and 4 was found [28]. This previous study did not evaluate quantitative EEG parameters and used a more acute sleep deprivation (two days). In the present study, the rebound of SWS and SWA during recovery sleep was significantly lower for the middle-aged than for the younger group. During the extended waking period, the build-up of sleep pressure appears to be weaker in middle-aged individuals than in young adults. The observed reduction of SWA following sleep deprivation in middle-aged subjects suggests that the homeostatic recuperative drive is already attenuated in the middle years of life. However, future research will need to address the effects of homeostatic challenges when sleep is initiated at a normal phase relationship with the circadian signal. This would verify that the smaller rebound of SWA in the middle-aged adults is not directly caused by the steeper increase of wakefulness during daytime recovery sleep.

Knowing the non-additive interaction between the homeostatic and the circadian processes, it is quite possible that the observed reduction in homeostatic recuperative drive following sleep deprivation in the middle-aged subjects may account for their reduced ability to maintain sleep when they have to recuperate at an abnormal circadian phase. In the middle-aged subjects, the shallower homeostatic sleep response following the sleep deprivation may not have been able to “override” the high circadian propensity for wakefulness at this time of day.

5. Conclusion

Results of this study suggest that people in their forties and fifties already show a heightened vulnerability to an abnormal phase angle between sleep and the circadian signal in addition to an attenuation of the homeostatic recuperative drive. These results help to understand why middle-aged individuals demonstrate more difficulties than younger individuals adapting to challenges to the sleep-wake cycle such as shift work and jet lag [18,22,29].

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