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ORIGINAL ARTICLE

Daytime Sleepiness Increases With Age in Early Adolescence: A Sleep Restriction Dose–Response Study

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Study Objectives: Daytime sleepiness increases across adolescence. This increase is commonly attributed to insufficient sleep durations resulting from increasingly limited time in bed. We tested the effects of 3 sleep schedules on daytime sleepiness and whether these effects changed with age in early adolescence.

Methods: In 77 children ranging in age from 9.9 to 14 years, objective (multiple sleep latency test [MSLT]) and subjective (Karolinska sleepiness scale [KSS]) sleepiness was measured following 4 consecutive nights of either 7, 8.5, or 10 hours in bed. All participants completed all 3 sleep schedules. The order in which they completed the schedules was not randomized but was accounted for in all statistical analyses.

Results: Time in bed restriction decreased sleep duration and increased objective and subjective daytime sleepiness. Although the sleep durations did not change with age, the likelihood of falling asleep during the MSLT increased with age. Nevertheless, sleep restriction produced a greater increase in MSLT-measured sleepiness in younger participants. Subjective sleepiness measured with the KSS increased with shorter sleep duration, but this effect did not change with age.

Conclusions: Increasing objective daytime sleepiness in early adolescence cannot simply be attributed to reduced sleep due to restricted sleep schedules. We propose that some of the increased daytime sleepiness of adolescents is a consequence of adolescent brain reorganization driven by synaptic pruning which decreases the intensity of waking brain activity.

Keywords: sleep deprivation, MSLT, brain maturation.

Statement of Significance

Objective daytime sleepiness, measured with the MSLT, decreased with increasing time in bed, but this decrease weakened with age between 10 and 14 years. Since daytime sleepiness increases in early adolescence even with 10 h in bed, it is unlikely that such sleepiness can be entirely eliminated by increasing time in bed. Further research is needed to determine the trajectory of sleepiness and its correlates across adolescence and into adulthood.

INTRODUCTION

Sleep duration decreases with age across adolescence. Large-scale, cross-sectional surveys report total sleep time (TST) declines by 12 min/year between ages 10 and 18 years in Australian children.[1] In direct longitudinal measurement of sleep electroencephelogram (EEG) changes across childhood and adolescence, we documented a 10 min/year decline in school-night TST between ages 10 and 18; this decline was entirely produced by decreasing non-rapid eye movement (NREM) sleep duration.[2] The reduction in TST was associated with later school-night bed times. Rise time was essentially constant so that time in bed (TIB; and the opportunity to sleep) was reduced. Progressively later bedtimes across adolescence have long been recognized (cf. refs. [3–5]) and are usually attributed to reduced parental control and increases in scholastic pressures, extracurricular activities, social commitments, television, and computer use (reviewed in ref. [6]). In addition, there is evidence that developmental changes in circadian regulation increasingly delay sleep onset (reviewed in ref. [7]).

Daytime sleepiness is also a matter of increasing public health concern. Such sleepiness is rare in preteen children in the absence of illness or sleep deprivation. It emerges in many youngsters during early adolescence, and its prevalence increases across the second decade. This phenomenon has been documented with the multiple sleep latency test (MSLT).[8] Quite naturally, it has been inferred[9] that the increase in adolescent sleepiness is caused by increasingly reduced TIB caused by the factors mentioned earlier: progressively later school-night bedtimes combine with relatively fixed rise times to reduce time in bed and, necessarily, sleep duration. However, it is also possible that maturational factors contribute to adolescent daytime sleepiness. Thus, it is now recognized that the human brain undergoes a major reorganization during adolescence,[10,11] and we have proposed that these developmental changes reduce the need for NREM sleep.[2]

Early empirical evidence for a maturational contribution to daytime sleepiness emerged in a pioneering study by Carskadon et al.[8] They found that pubertally more mature teenagers had greater MSLT-measured daytime sleepiness than less mature teens even when TIB was held constant at 10 h. More recently, we found in a longitudinal study that subjective daytime sleepiness in adolescence increased with age even when statistically adjusting for sleep schedule.[12]

Many detrimental effects have been attributed to adolescent sleepiness. These include poor school performance,[5,13] engaging in risky behavior,[14] and psychiatric illness (notably depression).[15] Recent efforts to ameliorate this problem have largely focused on increasing sleep duration by increasing TIB with later school start times.[16] We believe that programs to reduce adolescent daytime sleepiness would be strengthened by additional evidence on the relation between sleepiness and prior sleep duration and data on how this relation changes with age.

Here we present data from an ongoing longitudinal study of the interrelations of daytime sleepiness, age, and TIB during adolescence. We report cross-sectional measurements of daytime sleepiness in young adolescents of different ages, each studied after 10, 8.5, and 7 h in bed. Our long-term goal is to determine dose–response relations between daytime sleepiness and prior sleep schedules and how these relationships change across adolescence.

METHODS

Participants

A total of 77 children were enrolled and completed the first year of this longitudinal study. In response to newspaper ads, flyers (distributed at youth sporting events, farmers markets, and doctors' offices), and word of mouth from other enrolled participants, potential participants telephoned the laboratory for information about the study. In this initial contact, we screened out children not between ages 10 and 14 years and those who did not reside within 20 miles of the UC Davis Sleep Lab. We mailed a detailed description of the study and an initial screening questionnaire to 120 interested potential participants and received back 107 screening questionnaires. Of these 107 potential participants, 3 were excluded due to meeting one of the health-related exclusion criteria listed subsequently, 10 were lost to follow-up when we were unable to schedule a consent interview, and 4 were excluded due to targeted enrollment for their age range already being met. Targeted enrollment by age was as follows: 14 children between 10 and 11 years, 26 between 11 and 12 years, 26 between 12 and 13 years, and 14 between 13 and 14 years, with girls and boys equally represented in each age-group. Consent interviews were scheduled for 90 potential participants. Parents provided informed consent, and children older than 12 years provided assent. During the consent meeting, the study was described in detail, and children were given the opportunity to try out the psychomotor vigilance test and Sternberg test. During the consent meeting, potential participants were additionally screened for the following exclusion criteria via an interview with a parent: diagnosed psychiatric or behavioral disorder, epilepsy, head injury resulting in loss of consciousness and symptoms persisting longer than 24 hours, diagnosed sleep disorder, a Sleep Disturbance Scale for Children t-score >70, visual problems that could not be overcome with corrective lenses, manual dexterity problems that would interfere with daytime performance testing, and use of medication affecting the central nervous system. Five children opted not to participate after the consent interview, and 85 enrolled in the study. Two of the 85 participants were diagnosed with psychiatric or behavioral disorders after consenting but prior to the first recording, and 6 participants withdrew from the study prior to or during the first recording, leaving 77 participants who completed the first year of the study. Of the 6 participants who withdrew, two reported the restricted sleep of the 7-h TIB schedule as their reason for withdrawing. Participants were mostly from the university town of Davis, California. The sample is not racially/ethnically representative of the United States. Of the 77 participants 53 are non-Latino white.

Data from one participant were not included in this report because this participant failed to keep the assigned sleep schedules. Of the remaining 76 participants, 36 were female and 40 were male. At the time of the first recording week, participant ages ranged from 9.9 to 14.0 years (mean = 12.2, SD = 1.2).

Study Design

In each year of this longitudinal design, participants adhere to each of 3 different sleep schedules. Each schedule begins with 3 nights of 8.5 h in bed which are followed by 4 nights of 7, 8.5, or 10 h in bed. TIB can be restricted by delaying bedtime or advancing rise time. We chose to delay bedtime in order to simulate the changes in sleep schedule that typically occur as children progress through adolescence. Participants keep their own habitual school day rise time for all 3 schedules. Because the 10-h and 7-h schedules can interfere with participants' scholastic or extracurricular commitments, we had to be flexible in assigning the order in which participants completed the 3 sleep schedules. This flexibility prevented us from randomizing or balancing the order. We attempted to arrange recordings so that each participant completed all 3 schedules within a 3-month period (defined as the time between the first and third lab days of sleepiness and performance testing). Despite conflicts from scholastic and extracurricular activities, 71% of participants completed all 3 schedules within 3 months and 90% completed within 4 months. Participants spent at least 1 week on their habitual sleep schedule between studies. The number of days between the first and third test days ranged from a minimum of 34 days to a maximum of 160 days.

Participants wore actigraphy watches for 2 weeks for each sleep schedule. Actigraphy recordings from the first week documented the participants' habitual sleep schedule. Recordings from the second week established whether the participant successfully adhered to the assigned sleep schedule. If actigraphy or EEG recordings established that the participant's TIB deviated from the assigned schedule by more than 1 h, the participant's data were excluded.

EEG Recording and Analysis

All night EEG was recorded on the second and fourth night of the prescribed sleep schedule (ie, 7, 8.5, or 10 h). Ambulatory recordings at the participants' homes in their habitual sleep environment were made with Grass Aura recorders (400 Hz digitization rate). The Aura amplifiers have single pole low-frequency filters with a −3 dB point at 0.5 Hz and a 6 dB/octave slope and three pole high-frequency filters with a −3 dB point at 100 Hz and an 18 dB/octave slope. EEG was recorded from electrodes applied at F3, F4, C3, C4, P3, P4, O1, and O2 referred to contralateral mastoid (A1 or A2). Right and left eclectro-oculogram (EOG) was referred to a forehead electrode. Chin electromyogram (EMG) was recorded bipolarly. The all night ambulatory recording was not monitored, as laboratory staff left the participants' homes after starting the recording.

All night recordings were imported into Pass Plus software for sleep stage scoring and spectral analysis. Sleep stages were scored according to 2007 American Academy of Sleep Medicine standards with some exceptions. We scored 20- rather than 30-second epochs in order to facilitate comparisons with the data from our previous longitudinal study.[2] We used a 5-channel montage comprised of the 2 central leads, an occipital lead, an EOG, and chin EMG. At the age of the participants included here, slow-wave amplitude is similar in the central and frontal leads. Finally, we did not use a 75-μV criterion for slow waves.

Daytime Sleepiness and Performance Testing

The fourth night of the prescribed sleep schedule was always a Friday or Saturday night. On the following weekend day, participants awoke at their habitual school day rise time and reported to the sleep lab for a full day of performance testing. We could study up to 4 participants simultaneously. Testing took place

in the bedrooms furnished with a desk, chair, extra-long single bed, and a night stand. Participants were alone in the room during testing but monitored via video cameras. They communicated with laboratory staff via microphones and speakers. Participants spent their break time in the kitchen, supervised by undergraduate assistants. Lighting was dim (<100 lux at 6') throughout the laboratory. Temperature in the laboratory was maintained between 72°F and 76°F. To prevent exposure to sunlight, participants were not allowed to leave the building during the test day.

Participants reported to the laboratory at 0830, and we reattached any loose electrodes prior to the first test battery at 0900. The day was comprised of 4 test batteries each about 1 hour long with approximately 1-h break between. Participants were provided with snacks and water during the morning and afternoon breaks and with a pizza lunch during the noon break. During the noon break, participants provided a urine sample that we tested for evidence of drug and caffeine consumption. The second and fourth test batteries were a modified Sternberg task, a Karolinska drowsiness test / alpha attenuation task (KDT/AAT), a psychomotor vigilance test (PVT), and a multiple sleep latency test (MSLT). Prior to the KDT, participants completed a Karolinska Sleepiness Scale (KSS). Prior to the PVT, participants completed a Positive and Negative Affect Schedule for Children (PANAS-C).[17] Prior to the MSLT, participants completed another KSS. The Sternberg task was not included in the first and third test batteries. After completion of the final test battery, we removed all electrodes and sent the participants on their way by 1630. Data from the PVT, Sternberg, KDT/AAT, and PANAS-C and waking EEG will be presented in future reports.

Multiple Sleep Latency Test

Each test battery concluded with a MSLT performed according to procedures specified in Carskadon et al.[18] Each participant lay down in a bed and assumed a comfortable position. They were instructed to try to fall asleep, and the lights were turned off. Their positions were monitored via infrared video camera. Central and occipital EEG, along with EOG and chin EMG, were monitored for each participant. Participants were awakened following 5 consecutive 20-second epochs of stage N1 sleep or a single epoch of stage N2, N3, or REM sleep. The test was terminated upon this awakening or after 20 min if the participant failed to fall asleep.

KSS

The KSS is a 9-point Likert-type scale ranging from "very alert" to "very sleepy (fighting sleep)." Scores have been shown to increase following sleep deprivation and are related to objective sleepiness measures.[19,20] The two KSS scores in each test battery were averaged prior to pooling the data.

Tanner Staging

All participants except one visited a pediatrician for Tanner stage ratings of pubertal maturation.[21] For females, the pediatrician rated pubic hair and breast development on separate 5-point scales. For males, she rated pubic hair and genital development on separate 5-point scales. For statistical analysis, the Tanner stage pubic hair (Tph) and Tanner breast / genital (Tbg) ratings were used to divide the participants roughly into thirds: 26 participants had Tph ratings of 1, 25 participants had ratings of 2 or 3 for Tph and Tbg ratings but not 3 for both Tph and Tbg, and 24 participants had ratings of 3 or above for both Tph and Tbg. Mean ages for the 3 groups were 11.1, 12.4, and 13.0 years. To compare age versus pubertal maturation group effects on sleepiness, participants were also divided into 3 groups by age <11.8 years, 11.8–12.7 years, and >12.7 years. Pubertal maturation is, of course, associated with age, but the age-group and Tanner stage group membership differed. For example, the oldest third of participants and most mature third of participants were each comprised of 24 participants; they shared 13 members and had 11 unique members.

Statistical Analysis

For each analysis, the independent variables of interest were TIB, age, and the interaction between TIB and age. Variability due to time of day was controlled by including a time of day factor. Potential adaptation to the environment for the MSLT was controlled by including an order factor that indicated first, second, or third day of testing. We used various forms of SAS mixed effects analysis for the MSLT and KSS. Mixed effects analysis is appropriate for within participant studies because it accounts for the inherent correlation of multiple observations from the same participant.[22,23] In the KSS analysis, a linear mixed effects model was fit with age and TIB as continuous measures, an age by TIB interaction, and a series of dummy-coded variables to account for time of day and order effects.

The MSLT includes a cutoff of 20 min; therefore, a simple analysis of effects on sleep latency is not appropriate. Instead, we used a nonlinear mixed effects survival analysis that determined the probability of falling asleep in each minute of the test and how these probabilities were affected by TIB, age, time of day, and order as well as the interaction between the TIB and age effects. We tested for sex differences by adding a sex term to this survival analysis. We tested for sleep duration effects by replacing TIB with night 4 TST. We used night 4 rather than night 2 because any cumulative effects of the prescribed sleep schedule would be greatest on the final night of the sleep schedule. These analyses treated time of day, TIB, order, and sex as class (categorical) variables and treated age and TST as continuous measures. For comparison to pubertal maturation, we divided the participants into 3 age-groups and 3 Tanner-stage groups and tested for group differences in the likelihood of falling asleep and interactions with TIB effects. Model fit was compared for a model with both age and Tanner groups along with TIB interactions to models with just age-groups and TIB interaction or just Tanner groups and TIB interaction. The participant without Tanner stage data was also dropped from the age-group analysis.

RESULTS

The prescribed TIB schedules successfully altered participants' sleep duration. On the fourth night of the prescribed schedule, average total sleep durations (±SE) for 7, 8.5, and 10 hours in bed were 405 ± 2 min, 472 ± 2 min, and 534 ± 3 min, respectively. Decreasing TIB reduced both NREM and REM sleep duration.[24] There were no age-related differences in TST, NREM sleep duration, or REM sleep duration for the different

TIB schedules.[24] As stated in a previous report, participants did pretty well at adhering to their assigned schedules, but they lengthened the 7-h TIB schedule by about 6 min and shortened the 10-h TIB schedule by about 10 min. On the 7-h TIB schedule, participants went to bed an average of 1 min prior to their assigned bedtime and arose an average of 5 min after their assigned rise time. On the 10-h TIB schedule, participants went to bed an average of 6 min after their assigned bedtime and arose an average of 4 min prior to their assigned rise time.

Sleep Schedule and Age Effects on the MSLT

Decreasing TIB increased the percentage of participants who fell asleep during the 20-min MSLT and decreased the latency to sleep onset. Pooling all participants and the 4 MSLTs across the day, participants who kept the 10-h TIB schedule fell asleep during 41% of the MSLTs. This percentage increased to 58% for the 8.5-h schedule and to 80% for the 7-h schedule. As mentioned in the Methods, statistical analyses of TIB effects controlled for significant time of day and order effects. Participants were most likely to fall during the 1300 MSLT and least likely to fall asleep during the 0900 MSLT (1300 vs 0900, $t_{75} = 8.54$, $p < .0001$). Participants were most likely to fall asleep on their third visit to the lab and least likely to fall asleep on their first visit (first vs third, $t_{75} = -7.97$, $p < .0001$). With these time of day and order effects accounted for, survival analysis showed a significant TIB effect. Compared to 10 h in bed, reducing time in bed to 8.5 or 7 h significantly ($t_{75} = 6.93$, $p < .0001$; $t_{75} = 14.3$, $p < .0001$, respectively) increased the likelihood of falling asleep. Analyzing the effect of prior sleep duration rather than prior TIB produced the same result. With night 4 TST as a continuous measure, the likelihood of falling asleep during the MSLT decreased significantly ($t_{75} = -12.75$, $P < .0001$) with increasing night 4 sleep duration.

Older participants were more likely to fall asleep during the MSLT than were younger participants (Figure 1). With 10 h TIB, the oldest third of participants fell asleep in 60% of the MSLTs, whereas the youngest third of participants fell asleep in only 23%. The increased percentage of sleep in the older participants was also evident following 8.5 h TIB (67% vs. 55%) and following 7 h TIB (88% vs. 75%). Survival analysis showed that the likelihood of falling asleep increased significantly ($t_{75} = 3.24$, $p = .0018$) with increasing age of study participants. Furthermore, age and TIB effects showed a significant interaction ($t_{75} = -3.40$, $p = .0011$ for age × 8.5 h TIB; $t_{75} = -4.25$, $p < .0001$ for age × 7h TIB), such that the size of the TIB effect decreased with increasing age of study participants. This interaction is evident in Figure 1 which shows that, for younger participants, sleep restriction produced a greater increase in percentage of participants falling asleep and the speed at which they fell asleep. Or stated another way, in younger participants, sleep extension provided a greater reduction in objectively measured daytime sleepiness. This improvement is evident in Figure 2 which shows that increasing TIB from 8.5 to 10 h in younger participants steeply decreased the percentage of participants who fell asleep. Increasing TIB from 8.5 to 10 h did not produce as large a decrease in the older participants.

Sleep onset REM periods during the MSLTs were very rare in this data set with less than 1% of tests containing an epoch of REM sleep.

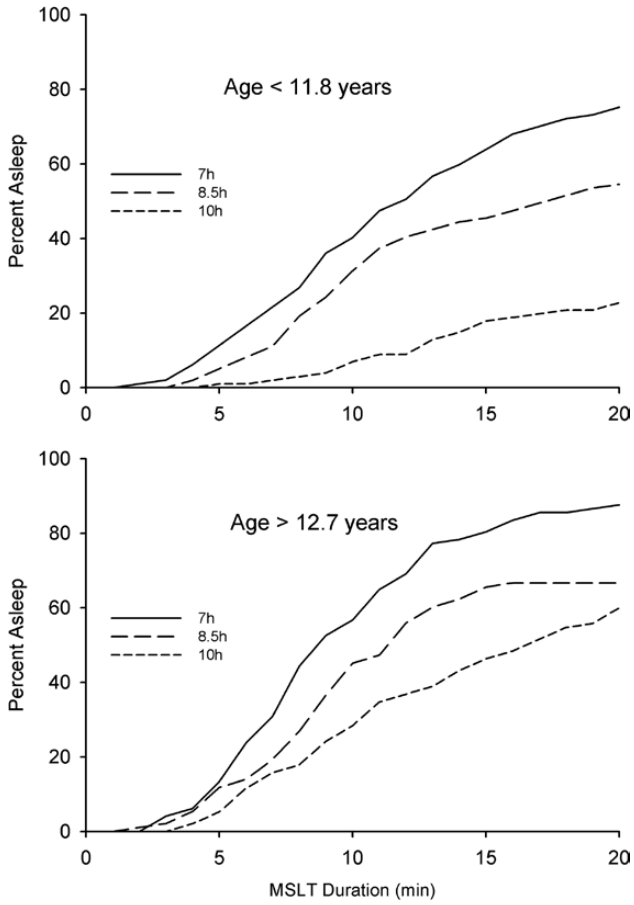

Figure 1—The percentage of participants asleep is plotted against multiple sleep latency test (MSLT) minute for participants younger than 11.8 years (top) and those older than 12.7 years (bottom). Participants were least likely to fall asleep during the MSLT following 4 nights with 10-h (short dashed line) time in bed (TIB). Likelihood of falling asleep increased when TIB was restricted to 8.5 h (long dashed lined) and increased further with TIB restricted to 7 h (solid line). Likelihood of falling asleep increased with age. The benefit of extending TIB decreased with age.

Sex and Tanner Stage Effects on the MSLT

The likelihood of falling asleep during the MSLT did not differ ($t_{75} = 0.097$, $p = .93$) between boys and girls (Figure 3). Analyzing the sexes separately showed a significant TIB effect for both boys and girls ($p < .0001$ for all comparisons) and a significant age × TIB interaction ($p < .05$ for all comparisons).

Dividing the participants into thirds by age and into thirds by Tanner stage revealed very similar effects of age and Tanner stage (Figure 4). The likelihood of falling asleep during the MSLT increased with increasing age (youngest vs. oldest group, $t_{74} = 3.85$, $p = .0002$) and with increasing pubertal maturation (least vs. most mature group, $t_{74} = 3.49$, $p = .0008$). However, the increased likelihood of sleep was more strongly associated with age. Adding age-group effects on objective sleepiness to a model already containing Tanner stage group effects significantly improved the model fit (decreased −2 log likelihood, $\chi^2_6 = 17.7$, $p = .0070$). Adding Tanner group effects to a model

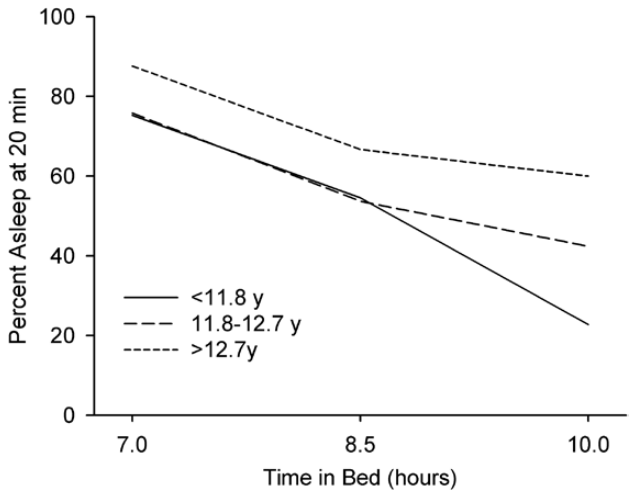

Figure 2—Age effects on the percentage of participants who fell asleep by the 20th minute of the MSLT. Percentage asleep is plotted against time in bed (TIB). Likelihood of falling asleep was greatest for oldest participants (short dashed line) at all TIB durations. The youngest group (solid line) showed the greatest improvement from extending TIB to 10h.

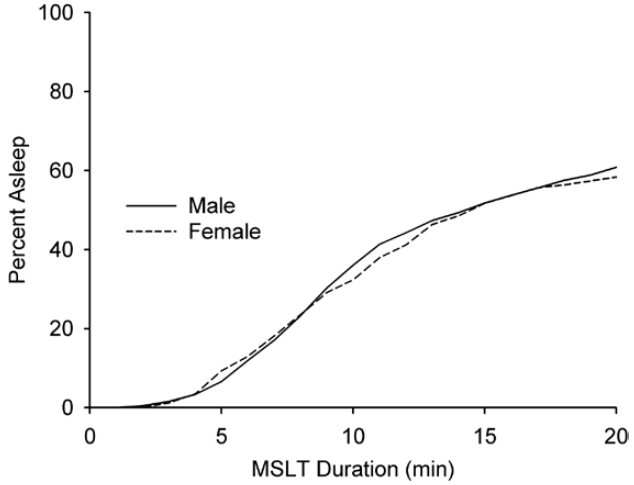

Figure 3—The percentage of participants asleep is plotted against MSLT minute for boys (solid) and girls (dashed). There was clearly no sex difference in objective daytime sleepiness.

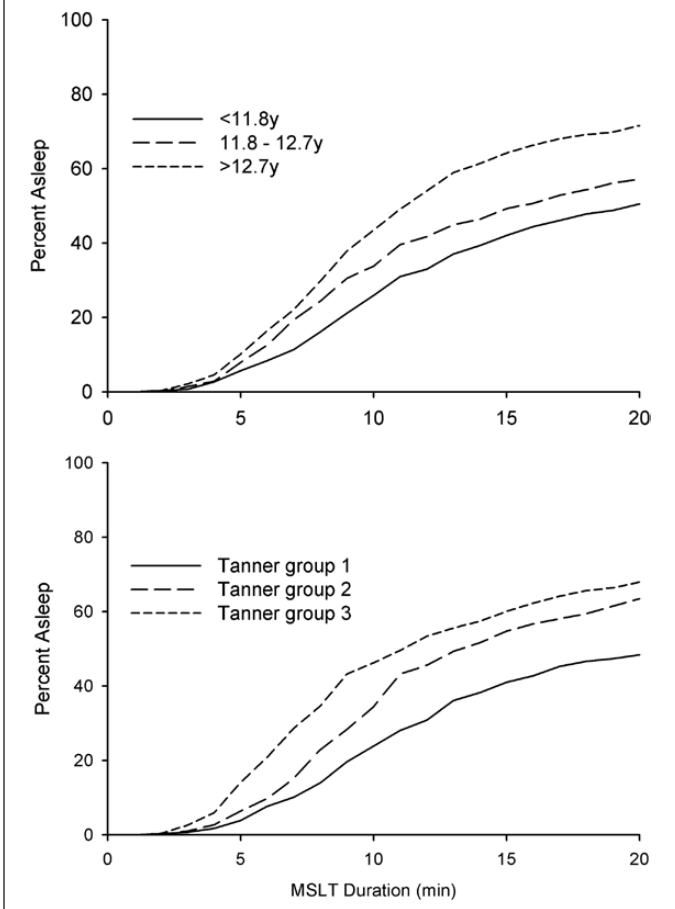

Figure 4—The percentage of participants asleep is plotted against MSLT minute by age-groups (top) and Tanner stage groups (bottom). Statistical analyses showed that age was a more potent determinant of daytime sleepiness.

already containing age-group effects did not improve the fit ($\chi^2_6 = 6.3$, p = .39).

Summer Vacation Effects on the MSLT

We recorded both during the school year and during summer vacation, and we allowed flexibility and participant input on the scheduling of recordings. This flexibility led to an imbalance in the sleep schedules completed during summer vacation with 24 participants completing the 7h condition in the summer, 26 completing the 8.5-h condition, and only 9 completing the 10-h condition. To test the possibility that this imbalance contributed to the TIB effect on MSLT sleep likelihood, we added a summer versus School-year factor to the survival analysis. There was no effect of summer vacation on MSLT sleep likelihood ($t_{75} = 0.71$, p = .48) nor was there an interaction of summer vacation with the TIB effect ($t_{75} = 0.53$, p = .60 for summer × 8.5h TIB; $t_{75} = 0.02$, p < .98 for summer × 7h TIB).

Sleep Schedule and Age Effects on KSS

Subjective sleepiness rating on the KSS (Figure 5) increased with decreasing TIB ($F_{1,810} = 68.6$. p < .0001). Linear mixed effects analysis estimated that for the third lab visit at 15:00, the average KSS rating for 7-h TIB was 6.33 (±0.28 SE) points and decreased by 0.56 (=/− 0.07) points for each additional hour in bed. KSS ratings did not change with age ($F_{1,74} = 0.16$, p = .69) nor did the TIB effect on KSS ratings differ by age ($F_{1,810} = 0.24$, p = .63).

Relation Between KSS Ratings and MSLT

When all other factors were dropped from the survival analysis and replaced with KSS ratings, the likelihood of falling asleep during the MSLT increased significantly ($t_{75} = 8.13$, p < .0001) with increasing KSS rating. With time of day, order, TIB, age, and the age by TIB interaction effects accounted for, the likelihood of falling asleep during the MSLT still increased

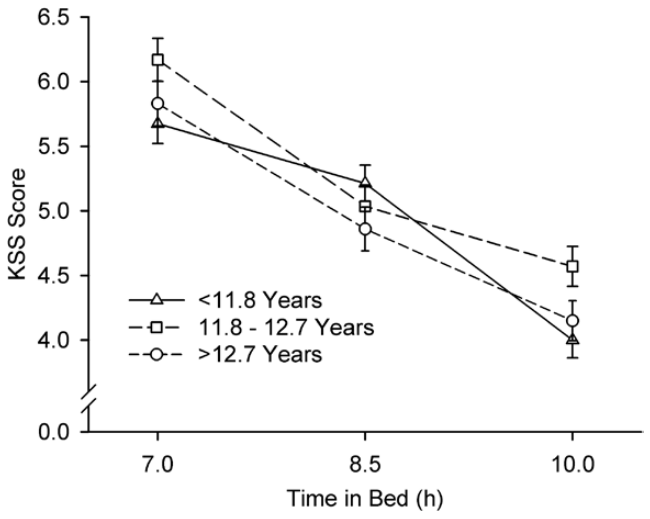

Figure 5—Karolinska Sleepiness Scale (KSS) score decreased with increased TIB. Average (±SE) KSS score is plotted against TIB for participants younger than 11.8 years (solid line, triangles), participants between 11.8 and 12.7 years (long dashed line, squares) and participants older than 12.7 years of age (short dashed line, circles). KSS score did not differ by age.

significantly ($t_{75} = 4.65$, $p < .0001$) with increasing KSS rating, and the model fit improved compared to a model without KSS ($\chi^2_1 = ,22.0$, $P < .0001$).

DISCUSSION

The main findings of this study are (1) that objectively (MSLT) measured daytime sleepiness increases with age and (2) that increasing TIB decreases daytime sleepiness, but this effect declines with age across early adolescence. Actual sleep duration varied systematically with TIB in each experimental condition, but these durations did not differ significantly with age. Nevertheless, objectively measured daytime sleepiness increased with age in all 3 TIB (and sleep duration) conditions. It was the younger participants who benefited more from sleep extension.

Reducing TIB (and TST) in young adolescents increased daytime sleepiness in a dose-dependent manner. The proportion of participants who fell asleep during the MSLT and the speed at which they fell asleep was greatest for 7-h TIB, lowest for 10-h TIB, and intermediate for 8.5-h TIB. These results are similar to those of Voderholzer et al.[25] who found that MSLT sleep onset latency in young adults increased steadily from 7 to 8 to 9 h in bed. In Voderholzer's study, sleep onset latency did not continue to decline when TIB was restricted to 6 or 5 h. Neither our study nor Voderholzer et al.'s was designed to determine an optimum TIB duration at which objective daytime sleepiness is at a minimum or a point at which further increases in TIB do not further reduce sleep propensity. Such data, in relation to age, could be of considerable interest.

For all TIB durations, younger participants were less likely to fall asleep during the MSLT. This finding is consistent with Carskadon et al.'s[8] observations in 19 adolescent subjects studied with TIB at 10 h. They found that more pubertally mature (and older) adolescents were more likely to fall asleep during the MSLT.[8] The finding also agrees with the subjective Epworth sleepiness ratings in our longitudinal study of adolescent sleep.[12] Epworth sleepiness ratings increased with age across adolescence even with sleep schedule statistically controlled.[12] These results argue against the widespread assumption that sleep restriction is the exclusive cause of adolescent sleepiness. They also argue against the assumption that sleepiness can be eliminated by increasing adolescents' TIB, even to an impractical 10 h.

Before discussing the neuroscience implications of the relation of objective sleepiness to age, we briefly take note of the subjective sleepiness and Tanner stage results. Both will require additional data before they can be fully interpreted.

Subjective Sleepiness

Sleep restriction significantly increased subjectively rated sleepiness on the KSS. Thus, sleep reduction elevates sleepiness both as measured objectively with the MSLT and as subjectively rated with the KSS. However, unlike the MSLT measures, subjective sleepiness ratings did not differ by age, nor did the relation between TIB and KSS-rated sleepiness show the age effect found with the MSLT. In our previous longitudinal study,[12] subjective sleepiness rated on the Epworth sleepiness scale (ESS) increased across adolescence even with sleep duration statistically controlled. The lack of an age effect in the KSS data may be due to the limited age range we have studied thus far and/or the cross-sectional nature of the current (year 1) data. Alternatively, the difference between these subjective sleepiness age effects may reflect the different rating scales. The KSS is a single instantaneous measure of how sleepy the subject feels at the time of the rating. In contrast, the ESS is a multiple question scale in which the subject rates, based on recent history, how likely he or she is to fall asleep in a variety of situations.

Apart from the absence of an age relation in the KSS ratings, they showed many similarities to the MSLT results. Both demonstrated similar effects of TIB, time of day, and order. Even with these effects controlled, the MSLT showed a significant relation to KSS ratings. Thus, the relation between objective (MSLT) and the KSS subjective sleepiness ratings is not completely explained by these variables.

Absence of Sleepiness Relations to Sex or Pubertal Status

Boys and Girls in this age range did not differ in their MSLT sleep likelihood. This absence of a sex difference agrees with Carskadon et al.'s[8] original adolescent MSLT study. That study also attributed the adolescent increase in sleepiness to sexual maturation. However, our present cross-sectional data show that objective sleepiness is more strongly related to chronological age than to sexual maturation. A three-group analysis of age and Tanner stage effects on MSLT sleep likelihood showed that adding age groupings improved the fit of a model containing Tanner stage groupings, whereas the converse was not true. We previously found a relation between pubertal maturation and the decline in delta EEG activity that became apparent only after we had collected multiple years of longitudinal data.[26] That study found that the age of most rapid decline in delta power occurred earlier in girls and followed by about 1 year the age of most

rapid pubertal maturation. Sex differences and *timing* of pubertal maturation explained fully 67% of the between participant differences in the *timing* of the brain maturation as reflected in the delta decline.[26] The possible biologic significance of this relation between brain-endocrine maturation is discussed elsewhere.[26] It will be interesting to determine whether a relation between sexual maturation and daytime sleepiness emerges in the longitudinal data now being collected.

Adolescent Brain Maturation and the Emergence of Daytime Sleepiness

Our laboratory was among the first to recognize that the human brain undergoes a fundamental reorganization during adolescence and that this reorganization involves massive changes in the sleep EEG.[10] In our model, adolescent synaptic elimination[11] progressively decreases the intensity of waking brain activity as evidenced by declining brain metabolic rate.[27,28] Decreasing waking brain activity decreases the need for the restorative changes in NREM sleep, whose intensity is proportional to the level of high-amplitude delta EEG.[29,30] These relations would account for the roughly parallel 50% declines in synaptic density, cerebral metabolic rate, and NREM delta EEG activity across the second decade of life.[31] They would also account for the fact that NREM but not REM sleep duration declines across adolescence.[2] We previously hypothesized that the high level of waking neuronal activity in childhood itself increases arousal level and prevents daytime sleepiness.[12] Another possibility is that the profound brain rearrangements of adolescence involve changes in feedback and other integrative circuits that have developmental lags which give rise to daytime sleepiness. Finally, since delta intensity is a putative index of synaptic density,[10,32] it will be interesting to determine whether the emergence of daytime sleepiness is temporally related to the decline in NREM delta power. The longitudinal continuation of years 2 and 3 of our ongoing study should provide a good test of this possibility.

One remaining question raised by our data is why children who show less daytime sleepiness at 10 h in bed have a stronger increase in sleepiness when nighttime sleep is restricted. The intense waking brain activity of younger children is associated with a more rapid accumulation of sleep need[33] as would be expected from the long-recognized high levels of slow-wave EEG activity in children (cf. [30]). The increased accumulation of sleep need produces a higher level of sleep-dependent recuperation. Interfering with this recuperation by restricting TIB exacerbates sleepiness more in younger children. In the present experiment, reducing TIB from 10 to 7 h produced a greater reduction in MSLT sleep latency in younger participants. This occurred even though, as noted above, younger participants on the 10-h sleep schedule were less susceptible to daytime sleepiness, rarely falling asleep during the MSLT.

LIMITATIONS

This study is longitudinal, but only cross-sectional data from the first year are presented here. The main findings of TIB and age effects on MSLT sleep likelihood are robust and are unlikely to differ in the final longitudinal data set. However, some findings, such as the age effect being stronger than the sexual maturation effect may be considered preliminary. The scarcity of sleep-onset REM periods may be related to the young age of the participants and their high need for NREM delta. Delta pressure can suppress REM sleep as seen in recovery sleep following total sleep deprivation in young adults, where delta EEG activity is elevated and the first REM period is more often skipped.[34] Again, the longitudinal data will allow us to better evaluate these relations. There are covariates associated with age that we can account for statistically, but the effects of these covariates may be more prominent as participants progress into later adolescence. For example, sleep duration did not differ with age in the current data set, but in later years of the study, circadian phase delays may impair older participants' ability to adhere to the 10-h TIB schedule. Another limitation is that the current analyses do not control for participants' prior sleep history. It is possible that some participants carried a sleep debt into the week of enforced sleep schedules and that 3 days of 8.5-h in bed did not put all participants at the same level of sleep debt prior to the 4 nights of prescribed TIB schedules. The study design attempts to achieve the scientific goals of the study without overly altering the participants' daily lives. The necessary scheduling flexibility prevented us from randomizing the order in which participants completed the 3 TIB conditions. Instead, we statistically accounted for order effects.

The participants who enrolled and completed the first year of recording are those who were willing to accept the TIB schedules required. Therefore, our sample may be more resistant to the effects of sleep loss than the age population from which they were drawn. It is likely that children who could not tolerate sleep restriction (or those whose parents decided that the children could not tolerate sleep restriction) chose not to participate when they learned the details of the study procedures. Finally, despite our outreach to underrepresented groups, our participant pool, drawn primarily from a university town, does not reflect the ethnic / racial makeup of this country.

CONCLUSION

These data demonstrate that daytime sleepiness increases with age across adolescence. This age trend is most striking in the 10-h TIB condition. While daytime sleepiness increases following sleep restriction, daytime sleepiness cannot be fully explained by reduced TIB. We propose that the brain reorganization of adolescence, driven by synaptic elimination, is itself a major contributor to adolescent daytime sleepiness. Completing our longitudinal data collection on these participants should shed further light on these questions, which bear on important issues in public health and basic neuroscience.

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