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Authors

Park, Heejung
Tsai, Kim M
Dahl, Ronald E
et al.

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Sleep and Inflammation During Adolescence

Heejung Park, PhD, Kim M. Tsai, PhD, Ronald E. Dahl, MD, Michael R. Irwin, MD, Heather McCreath, PhD, Teresa E. Seeman, PhD, and Andrew J. Fuligni, PhD

ABSTRACT

Objective: To investigate the associations between objective and subjective dimensions of adolescent sleep and C-reactive protein (CRP), a key biomarker of inflammation that predicts chronic health problems in adulthood, and whether the associations vary as a function of adolescents' age.

Methods: A total of 315 adolescents (14.5–18.4 years) wore wrist actigraphs at night to objectively estimate their sleep duration and variability across nights, and completed the Pittsburgh Sleep Quality Index to assess their subjective sleep quality. CRP levels were assayed from dried blood spots obtained from finger pricks. To control for adiposity, age- and sex-specific body mass index percentiles were obtained from height and weight measurements.

Results: Nightly variability in sleep duration was associated with higher levels of CRP ($b = 0.13$, $p = .045$). Shorter average sleep duration was associated with higher CRP, but only among younger adolescents ($b = -0.11$, $p = .041$). Subjective sleep quality was not associated with CRP.

Conclusions: The association of sleep with inflammation during adolescence seems more evident in objective dimensions of sleep duration and variability than in the subjective dimensions of sleep quality. Insufficient sleep may be particularly consequential for younger adolescents.

Key words: sleep, inflammation, C-reactive protein, body mass index, adolescence, actigraphy.

INTRODUCTION

Biological and social changes during adolescence heighten the importance of a good night's sleep (1–3), but many adolescents report getting considerably less than the recommended 8 to 10 hours of nightly sleep (3,4). Shorter sleep duration and diminished sleep quality are associated with poor decision making, risk taking, mood disruptions, and decreased academic performance (1,2,5–7). Although the negative repercussions of sleep problems on psychosocial and behavioral issues are well understood, less is known about the association between sleep and biological markers of physical health during adolescence.

Inflammation has received increased attention as a biomarker of risk for several chronic adult health conditions (e.g., cardiovascular disease [CVD]) that may be sensitive to sleep difficulties. Although CVD is typically a concern among older individuals, the development of CVD risk factors is a lifelong process. Inflammation—as measured by C-reactive protein (CRP)—is predictive of future CVD even among healthy individuals (8–10). Research among adults has suggested that chronic sleep problems contribute to increased inflammation, with laboratory studies bolstering the causal links by demonstrating up-regulated inflammatory responses following sleep loss (8,9,11). Disrupted nocturnal sleep influences the production and activation of cells that are responsible for the regulation of immunity, leading to an alteration of inflammatory markers such as CRP (12,13).

Limited research has explored the linkage between sleep duration and inflammation during adolescence (14), but a few existing studies suggest that sleep problems may be associated with inflammatory markers during this developmental period. One study found that self-reported shorter sleep duration was associated with higher CRP among Spanish 13- to 17-year-olds (15). Using more objective tools such as actigraphy and polysomnography, two studies in the United States also showed an association between shorter sleep duration and higher CRP (10,16). Interestingly, despite the evidence that poor perceived sleep quality is more

BMI = body mass index, **CRP** = C-reactive protein, **CVD** = cardiovascular disease, **PSQI** = Pittsburgh Sleep Quality Index

From the Department of Psychology (Park), Bryn Mawr College, Bryn Mawr, Pennsylvania; Department of Psychology (Tsai), California State University, San Marcos, California; School of Public Health (Dahl), UC Berkeley, Berkeley, California; Department of Psychiatry and Biobehavioral Sciences and Division of Geriatrics (McCreath, Seeman), David Geffen School of Medicine (Irwin, Fuligni), UCLA, Los Angeles, California; Department of Psychology (Fuligni), UCLA, Los Angeles, California; Semel Institute for Neuroscience and Human Behavior (Irwin, Fuligni), UCLA, Los Angeles, California.

Address correspondence and reprint requests to Heejung Park, PhD, Department of Psychology, Bryn Mawr College, 101 N. Merion Ave, Bryn Mawr, PA 19010. E-mail: hpark2@brynmawr.edu

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robustly associated with inflammation than sleep quantity among adults (12), little research has examined the role of perceived sleep quality among adolescents. A more comprehensive understanding of the role of sleep in inflammation during adolescence would be obtained by measuring both objective measures of sleep duration and subjective indices of sleep quality.

The current study expands upon emerging work on the interplay between sleep and inflammation during adolescence in three key ways. First, multiple dimensions of sleep were assessed. Actigraphy was used to estimate the objective sleep dimensions of duration and daily variability in duration. Daily variability was examined in addition to sleep duration given prior work demonstrating the importance of sleep regularity for children and adolescents (5). Self-reports on the Pittsburgh Sleep Quality Inventory (PSQI) (17) were used to assess global and subdimensions of adolescents' subjective sleep quality.

Second, the moderating role of age was examined. Sleep shows age-related changes, with declines in sleep quantity and quality across the life span (2,18). Therefore, shorter duration, greater variability, and poorer quality may be more consequential to physical health if they are present at younger ages. For instance, *shorter* sleep duration has been linked to *higher* levels CRP among adolescents (10,15,16), but sleep duration is inconsistently associated with markers of inflammation in adult populations (12,19). Together, these findings suggest that the negative repercussion of short sleep for inflammation is more evident earlier in the life span. Younger populations may be more sensitive to the restorative role of sleep in their physical health because their immune systems are still developing (12,20).

Small age variations may reveal differential associations of sleep with CRP, especially during adolescence when significant biological and social changes take place. There are relatively dramatic changes in sleep and circadian regulation during pubertal maturation, which is a set of processes that continues into late adolescence with hormone rises and rapid physical growth often extending through the midteens (2,21–24). Therefore, we examined whether the sleep-CRP link differed between younger and older adolescents in this study.

Lastly, our study expanded the ethnic diversity of participants represented in the literature, as well as improved the data analysis approach by considering additional covariates. Ethnicity is associated with inflammatory markers (25), but prior research linking sleep and inflammation during adolescence has had limited ethnic diversity in the adolescent samples. Participants in the study by Martinez-Gomez et al. (15) were adolescents in Spain, and ethnicity was not discussed in the study. Both Larkin et al. (16) and Hall et al. (10) focused on white and black adolescents. The present study included adolescents from Asian, Latino, and European American backgrounds and controlled for ethnicity.

Furthermore, in addition to typical covariates such as sex, socioeconomic status, and ethnicity, our analytic models also controlled for perceived stress and age- and sex-specific body mass index (BMI) percentiles. Stress is associated with both inflammatory markers (25–27) and sleep disturbances (28,29) and could partially account for the relation between sleep and inflammation. As for BMI, an index of adiposity, sleep problems are associated with adiposity during adolescence (30–32). Adiposity is associated with inflammation as adipose tissue releases bioactive mediators that influence body weight homeostasis and alter inflammation (33,34). In previous studies with adolescents, BMI attenuated the association between shorter sleep and higher CRP (15) and accounted for as much as 21% of the variance in CRP levels (10). Therefore, adolescents' sex, ethnicity, parental education, perceived stress, and age- and sex-specific BMI percentiles appropriate for adolescents were all examined as covariates.

In sum, the present study aimed to contribute to the limited literature on sleep and inflammation during adolescence. A main goal was to investigate which dimensions of sleep would be associated with inflammation during adolescence by assessing both objective measures of sleep duration and subjective indices of sleep quality. Another main goal of the study was to examine whether age would moderate the link between sleep and inflammation during adolescence. Our study goals were examined in an ethnically diverse sample of adolescents, and analyses included multiple covariates including perceived stress and age- and sex-specific BMI percentiles appropriate for adolescents.

METHOD

Participants

Participants included 315 adolescents (range = 14.50–18.42 years, mean age [SD] = 16.39 [0.71], 57% female) from diverse ethnic backgrounds (23% Asian, 29% European American, 42% Latino, 6% other ethnicity) who were recruited from four public high schools in the Los Angeles metropolitan area between October 2011 and July 2012. Adolescents' primary caregivers reported both their and their spouse's highest level of education (1 = *some elementary school;* 2 = *completed elementary school*; 3 = *some junior-high school*; 4 = *completed junior-high school*; 5 = *some high school*; 6 = *graduated from high school*; 7 = *trade or vocational school*; 8 = *some college*; 9 = *graduated from college*; 10 = *some medical, law, or graduate school*; *11 = graduated from medical, law, or graduate school*). Averaging the primary caregiver's and spouse's level of education indicated that half of the parents completed at least trade or vocational school, with the entire sample ranging from some elementary school to graduating from medical, law, or graduate school (range = 1.5–11, M [SD] = 7.19 [1.81]).

Procedures

Research staff described the study and distributed flyers to students in classrooms. Flyers also were mailed to the students' homes around the same time

that presentations were made. Research staff called interested families to discuss the study, obtain verbal consent, and schedule a visit with both adolescents and parents. Written consents were obtained during the first visit that took place in the family's home or a local research center.

Adolescents completed measures on subjective sleep quality and stress, and primary caregivers reported demographic information. Research staff measured adolescents' height and weight, and obtained finger-prick blood samples. In addition, adolescents were instructed to wear a wrist actigraph and complete daily sleep reports for eight consecutive days. Adolescents completed diaries for an additional week (data not reported). Research staff returned to the participant's home to collect the materials at the end of the 2-week period. Families received $130 and two movie passes for participating in the study. All procedures were approved by the University of California, Los Angeles Institutional Review Board.

Measures

Sleep Duration and Variability

Adolescents were instructed to place an actigraphy watch that measured body movement (Micro Motionlogger Sleep Watch, Ambulatory Monitoring, Inc) on their nondominant hand before going to bed for eight consecutive nights, and to keep it on until the following morning when they woke up and got out of bed. They were asked to push a button on the actigraph when they a) turned off the lights to go to sleep at night; b) got out of bed in the middle of the night, such as to use the bathroom; or c) got out of bed in the morning. Adolescents wore the wrist actigraph on an average (SD) of 6.58 (1.45) nights (median [Mdn] = 7 nights). The number of nights was nonnormally distributed, with skewness of −1.39 (standard error [SE] = 0.14) and kurtosis of 1.90 (SE = 0.28).

We used the software package Action4 (Ambulatory Monitoring, Inc) to code and score the actigraphy data. The in-bed period began at the time of the first event marker indicating when participant turned off the lights to go to sleep and ended at the time of the last event marker indicating when the participant got out of bed in the morning. If event markers were not present for a particular night, we used adolescents' daily sleep reports to identify the time at which they went to bed and got up in the morning (19). Actigraphy and diary data were correlated for the average sleep duration across nights ($r = 0.63$, $p < .001$).

To calculate sleep duration, we scored 1-minute epochs using the Sadeh actigraph scoring algorithm, which had been validated and used in studies with children and adolescents (35–38). Sleep onset time was the first of at least three consecutive minutes of sleep, and sleep offset time was the time of the last five or more consecutive minutes of sleep (36). The total sleep duration for each night was the total hours scored as sleep during the in-bed period. We averaged adolescents' sleep duration across the eight nights to assess their mean nightly sleep duration (M [SD] = 7.46 [0.99] hours, Mdn = 7.53 hours, skewness = −0.94 [SE = 0.14], kurtosis = 3.24 [SE = 0.28]).

In addition, we calculated nightly variability in sleep duration by taking the mean of the absolute differences between a participant's mean nightly sleep duration and each individual night's sleep duration (M [SD] = 0.96 [0.55] hours, Mdn = 0.86 hours, skewness = 2.38 [SE = 0.14], kurtosis = 11.72 [SE = 0.28]) (5).

Subjective Sleep Quality

Adolescents completed the PSQI, a widely used 18-item self-report questionnaire assessing subjective sleep quality and disturbances during the past month (17). Items were administered based on an open-ended format (e.g., usual bedtime) or a 4-point Likert scale (e.g., overall sleep quality during the past month: very good, fairly good, fairly bad, and very bad). Using the traditional scoring, items were recoded and used to compute seven sleep components (e.g., subjective sleep quality, use of sleep medications), which then were summed to yield one global score (range = 0–12), with higher scores indicating poorer sleep quality (17,39,40).

We also computed three subscales suggested as an alternative scoring model for the PSQI, because the three-factor model (perceived sleep quality, sleep efficiency, and daily disturbances) may be statistically favored over the global score (41). *Perceived sleep quality* included the components of subjective sleep quality (i.e., overall sleep quality), latency (e.g., number of minutes to fall asleep each night), and use of sleep medications (i.e., how often participant took prescribed or over-the-counter medicine to help sleep). *Sleep efficiency* was based on adolescents' subjective report of sleep duration (i.e., hours of actual sleep per night) and habitual sleep efficiency (i.e., proportion of time spent actually sleeping in bed). *Daily disturbances* tapped subjective reports of sleep disturbances (e.g., how often participant woke up in the middle of the night or early morning) and daytime dysfunction (e.g., how often participant had trouble staying awake while driving, eating meals, or engaging in social activity). Across the three subscales, higher scores indicated poorer sleep quality.

C-Reactive Protein

Inflammation was assessed by assaying levels of CRP from dried blood spots (DBS) obtained from finger pricks during the health examination. The use of DBS is a well-validated and relatively noninvasive procedure, with validation studies showing high correlations between matched blood spot and plasma CRP samples (42,43).

After trained research staff cleaned participants' fingers with alcohol, a sterile, disposable microlancet was used to puncture their fingers. After wiping away the first drop, up to seven drops of capillary blood were allowed to fall onto standardized filter paper. Blood spot samples were subsequently allowed to dry overnight, then stored at −80°C. Two spots per participant were shipped to the Laboratory for Human Biology Research at Northwestern University, where they were processed to assess levels of CRP using high-sensitivity enzyme-linked immunosorbent assay. The assay had a lower detection limit of .030 mg/l. Seven samples fell under the lower detection of limit, and intra-assay and interassay coefficients of variation were <6.4% and <9.3%, respectively. All samples were run in duplicate.

According to clinical cutoff points used to assess risk for CVD (44), 83% of the adolescents in our study were in the low-risk category (CRP < 1 mg/l), 12% were in the moderate-risk category (CRP = 1–3 mg/l), and 5% were in the high-risk category (CRP > 3 mg/l). Four participants had values of CRP above 10 mg/l, reflecting temporary acute inflammatory response likely due to infection (44,45), which was confirmed by participants' self-reports. Therefore, the four participants were excluded from analyses including CRP as a variable of interest. Given that CRP values were skewed, we performed a logarithmic data transformation.

We used the log-transformed DBS-assayed values of CRP for all analyses and results. For descriptive purposes, we converted the DBS-assayed values into serum-equivalent values using a conversion formula (serum [mg/l] = 1.84 × DBS [mg/l]) presented by McDade et al. (42). After this conversion, the clinical cutoffs for the sample were as follows: 72% of the adolescents in our study were in the low-risk category (CRP < 1 mg/l), 17% were in the moderate-risk category (CRP = 1–3 mg/l), and 11% were in the high-risk category (CRP > 3 mg/l).

Control Variables

Sex, ethnicity, and perceived stress were obtained based on adolescents' self-report questionnaires. The widely used Perceived Stress Scale (25–27) was administered to assess participants' reports of stress in the past month (e.g., "how often have you felt nervous or stressed?" "how often have you found that you could not cope with all the things you had to do?") on a 5-point scale (0 = *never,* 4 = *very often*). Scores were averaged across the 10 items (range = 0.33–3.56, M [SD] = 1.94 [0.62], $\alpha = .84$). Mean parental education also was used as a control variable.

An index of adiposity, BMI, also was included as a covariate. Height and weight measurements were obtained using portable stadiometers and scales during a health examination in the first visit. BMI raw values and percentiles were obtained using the Centers for Disease Control and

Prevention online calculator for children and teens. BMI raw values were calculated using the standard formula (kg/m^2; range = 14.68–47.58, M [SD] = 23.16 [5.01]), and BMI percentiles expressed participants' BMI relative to adolescents of the same age and sex in the United States (range = 1–99, M [SD] = 60.82 [29.15]). We used BMI percentiles, which is recommended given physical growth and development during adolescence. Fifteen percent of the participants were classified as overweight (85th–95th percentile) and 11% as obese (>95th percentile) (28,29).

Data Analysis

Data were analyzed using SPSS Version 22. We first ran correlations to examine the bivariate associations between our variables of interest. Then a series of stepwise multiple regressions were conducted to examine the main effect of sleep (Step 1) and the interactive effect of sleep and age (Step 2) on CRP, controlling for sex, ethnicity, parental education, perceived stress, and BMI percentile. Tests of simple slopes were conducted in the case of significant interaction of sleep with age. Separate regression models were run for each sleep indicator to avoid problems of multicollinearity among the indicators. All noncategorical variables were centered at the sample mean.

RESULTS

Table 1 presents the range, mean, SD, and correlations of the study variables. Shorter actigraphy sleep duration was correlated with higher BMI ($r = -0.18$, $p = .002$), and greater actigraphy sleep variability was correlated with higher CRP ($r = 0.12$, $p = .039$). Higher scores on the PSQI perceived sleep quality subscale, indicating poorer sleep, were correlated with greater CRP ($r = 0.12$, $p = .037$). None of the other PSQI subscale scores or global PSQI score were related to BMI or CRP. Older age was correlated with shorter sleep duration ($r = -0.13$, $p = .028$) and higher CRP ($r = 0.24$, $p < .001$). Greater BMI was correlated with higher CRP ($r = 0.33$, $p < .001$).

Sleep, Age, and CRP

Table 2 shows the results for the actigraphy sleep indicators. Testing the regression models without the sleep by age interaction terms did not change the results of the main effects for all sleep indicators, as well as all control variables. For simplicity, results from the final models including the interaction terms are reported. Consistent with the bivariate association, greater actigraphy sleep variability was associated with higher CRP ($b = 0.13$, $p = .045$). Although there was no direct association between actigraphy sleep duration and CRP, adolescents' age moderated the association between actigraphy sleep duration and CRP ($b = 0.10$, $p = .046$). To interpret the interaction, we tested the significance of the simple slopes (46) at the sample mean in age (16.40 years), 1 SD below the mean (15.66 years), and 1 SD above the mean (17.14 years). As shown in Figure 1, shorter actigraphy sleep duration was associated with higher CRP only among the younger adolescents ($b = -0.11$, SE = 0.05, $p = .041$). Actigraphy sleep duration was not associated with CRP levels among the mean-aged ($b = -0.04$, SE = 0.04, $p = .31$) or older adolescents ($b = 0.03$, SE = 0.05, $p = .49$).

Table 3 shows the results for the PSQI sleep indicators. Unlike the more objective, actigraphy-based measures of sleep duration and variability, none of the self-reported PSQI indicators measuring subjective sleep quality were associated with CRP, either directly or differentially according to adolescents' age. Older age and lower parental education level were associated with higher CRP, and adolescents from Asian backgrounds had lower CRP than did their European American peers. Higher BMI was associated with higher CRP.

DISCUSSION

This study with healthy adolescents aimed to investigate the associations of objective and subjective sleep dimensions with CRP, a key biomarker of inflammation that predicts chronic health problems in adulthood, and whether the associations varied as a function of adolescents' age. Greater actigraphy sleep variability in duration across the week was directly linked to higher levels of CRP. The association between shorter average sleep duration and greater CRP was evident only among younger adolescents. Subjective sleep quality, as measured by adolescents' responses to the PSQI, was not associated with CRP.

Results in this study contribute to the literature in three distinct ways. First, multiple dimensions of sleep were assessed, expanding emerging research on adolescent sleep and inflammation that has focused on duration (15,16). Results suggest that variability in sleep duration across week is just as important as sleep duration in the upregulation of inflammation, evidenced by higher CRP. In fact, whereas greater variability was associated with higher CRP overall, shorter duration was associated with higher CRP only among younger adolescents. The findings also expand previous work that has demonstrated the association of greater sleep variability with poorer psychological well-being among adolescents (5).

Interestingly, whereas sleep duration and variability in duration derived from actigraphy data were associated with CRP, none of the PSQI sleep variables were associated with the biomarker of inflammation in the regression models. Actigraphy is a more objective tool for assessing sleep (14) and average sleep duration and variability in sleep duration across week are more objective, quantifiable sleep dimensions. In contrast, PSQI assesses participants' self-reported subjective sleep quality. Thus, our findings suggest that objective, but not subjective, sleep dimensions may be related to inflammation during adolescence. There has been limited research on sleep and inflammatory risk during adolescence (14), and to our knowledge, our study was the first to examine the link between adolescent sleep and inflammation by objective and subjective sleep dimensions. Interestingly, our findings diverge from research with clinical or adult populations, where markers of inflammation tend to be more consistently associated

TABLE 1. Descriptive Statistics and Bivariate Correlations

Variables	Range	M (SD)	1	2	3	4	5	6	7	8	9	10	11
1. Actigraphy sleep duration, h	2.20–10.05	7.46 (0.99)											
2. Actigraphy sleep variability	0.00–4.99	0.96 (0.55)	−0.12*										
3. PSQI global	0.00–16	5.15 (2.97)	−0.15*	0.25***									
4. PSQI perceived sleep quality	0.00–3	0.80 (0.53)	−0.05	0.20***	0.83***								
5. PSQI sleep efficiency	0.00–3	0.32 (0.56)	−0.17**	0.15*	0.67***	0.33***							
6. PSQI daily disturbances	0.00–3	1.08 (0.61)	−0.14*	0.20**	0.74***	0.43***	0.29***						
7. CRP	0.001–8.45	0.69 (1.27)	−0.07	0.12*	0.09	0.12*	0.03	0.05					
8. BMI (percentile)	1–99	60.82 (29.15)	−0.18**	0.11	0.05	0.02	0.00	0.11	0.33***				
9. Age, y	14.50–18.42	16.39 (0.71)	−0.13*	0.03	0.03	−0.02	−0.08	0.04	0.24***	−0.01			
10. Sex (female = 1)		57% female	0.16**	0.06	0.10	0.08	0.08	0.09	0.05	0.01	0.05		
11. Parent education (1–11)	1.50–11.00	7.19 (1.81)	0.01	0.02	−0.04	−0.03	−0.04	−0.04	−0.18**	−0.11	−0.13*	−0.12*	
12. Stress (0–4)	0.33–3.56	1.94 (0.62)	0.03	0.06	0.42***	0.35***	0.12*	0.46***	0.06	0.05	−0.04	0.23***	0.05

M = mean; SD = standard deviation; PSQI = Pittsburgh Sleep Quality Index; CRP = C-reactive protein; BMI = body mass index.

Sex was coded such that male = 0 and female = 1. Higher PSQI scores indicated poorer sleep. Range, mean, and SD for CRP were based on untransformed CRP values; correlations were based on log-transformed CRP values.

Parent education was an average of the primary caregiver's and spouse's level of education, where 1 = some elementary school, 2 = completed elementary school; 3 = some junior-high school, 4 = completed junior-high school; 5 = some high school; 6 = graduated from high school; 7 = trade or vocational school; 8 = some college; 9 = graduated from college; 10 = some medical, law, or graduate school; and 11 = graduated from medical, law, or graduate school. Stress was participants' reports of stress in the past month, averaging across 10 items, on a 5-point scale, where 0 = never and 4 = very often.

* $p < .05$, ** $p < .01$, *** $p < .001$.

TABLE 2. Predicting CRP as a Function of Actigraphy Sleep and the Interaction Between Actigraphy Sleep and Age (n = 277)

	Actigraphy Sleep Duration		Actigraphy Sleep Variability	
Variable	*b* (SE)	*β*	*b* (SE)	*β*
Intercept	−0.56 (0.08)		−0.56 (0.08)	
Sex (female = 1)	0.04 (0.07)	0.03	0.03 (0.07)	0.03
Parent education	−0.05 (0.02)	−0.15*	−0.05 (0.02)	−0.15*
Stress	0.06 (0.06)	0.06	0.06 (0.06)	0.06
Asian	−0.17 (0.10)	−0.10	−0.19 (0.10)	−0.13
Latino	0.00 (0.09)	0.00	0.01 (0.09)	0.01
Other ethnicity	0.08 (0.15)	0.03	0.08 (0.15)	0.03
Age	0.17 (0.05)	0.19**	0.18 (0.05)	0.20***
BMI (percentile)	0.01 (0.00)	0.29***	0.01 (0.00)	0.27***
Sleep	−0.01 (0.04)	−0.01	0.13 (0.06)	0.11*
Sleep by age	0.10 (0.05)	0.11*	0.10 (0.10)	0.05

CRP = C-reactive protein; SE = standard error; BMI = body mass index.

Sex was coded such that male = 0 and female = 1. Parent education was an average of the primary caregiver's and spouse's level of education, where 1 = some elementary school, 2 = completed elementary school; 3 = some junior-high school, 4 = completed junior-high school; 5 = some high school; 6 = graduated from high school; 7 = trade or vocational school; 8 = some college; 9 = graduated from college; 10 = some medical, law, or graduate school; and 11 = graduated from medical, law, or graduate school. Stress was participants' reports of stress in the past month, averaging across 10 items, on a 5-point scale, where 0 = never and 4 = very often. European Americans were coded as the reference group for ethnicity. All noncategorical variables were centered at the sample mean. CRP values were log transformed (mg/l).

* $p < .05$, ** $p < .01$, *** $p < .001$.

with subjective sleep assessment (e.g., poor quality, complaints of sleep problems) than sleep duration (12,47). Continued research would need to elucidate the reasons for this divergence.

Second, the moderating role of age during the adolescent years was identified, suggesting that shorter sleep duration is associated with up-regulated inflammation at younger ages. This finding may offer some insight into inconsistency in the literature on the role of sleep duration in inflammation. Research on adult populations has led to the understanding that the association between sleep duration and inflammation is rather inconsistent (12,19,48), questioning the reliability of sleep duration as a precursor to elevated levels of inflammation. In fact, *longer* sleep

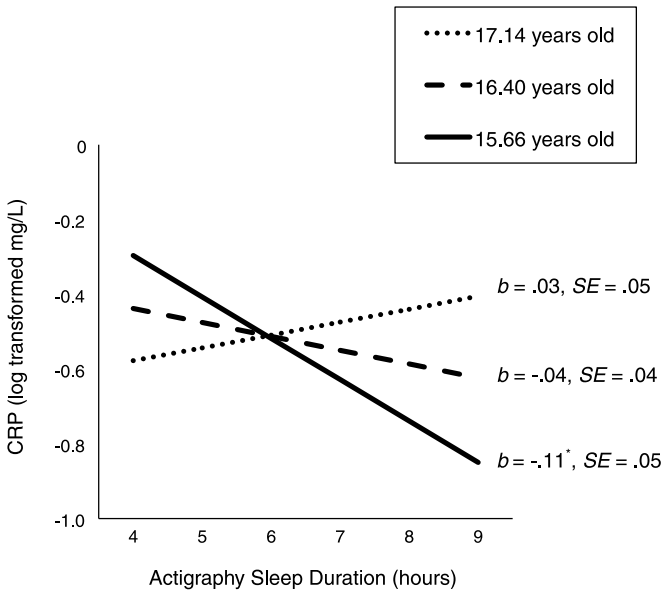

FIGURE 1. Moderating role of age in the association between sleep duration and CRP. Note: 17.14 years = +1 SD of the sample mean age, 16.40 years = sample mean age, 15.66 years = −1 SD of the sample mean age. CRP = C-reactive protein; SD = standard deviation.

TABLE 3. Predicting CRP as a Function of PSQI Sleep and the Interaction between PSQI Sleep and Age (n = 297)

	PSQI Global		PSQI Perceived Sleep Quality		PSQI Sleep Efficiency		PSQI Daily Disturbances	
	b (SE)	*β*	*b* (SE)	*β*	*b* (SE)	*β*	*b* (SE)	*β*
Intercept	−0.59 (0.10)		−0.53 (0.08)		−0.52 (0.08)		−0.46 (0.11)	
Sex (female = 1)	0.02 (0.07)	0.02	0.03 (0.07)	0.02	0.02 (0.07)	0.01	0.02 (0.07)	0.01
Parent education	−0.05 (0.02)	−0.13*	−0.05 (0.02)	−0.13*	−0.05 (0.02)	−0.14*	−0.05 (0.02)	−0.15*
Stress	0.04 (0.06)	0.04	0.02 (0.06)	0.02	0.06 (0.06)	0.06	0.09 (0.06)	0.09
Asian	−0.20 (0.10)	−0.14*	−0.20 (0.10)	−0.13*	−0.20 (0.10)	−0.13*	−0.21 (0.10)	−0.14*
Latino	−0.03 (0.09)	−0.03	−0.02 (0.09)	−0.02	−0.04 (0.09)	−0.03	−0.05 (0.09)	−0.04
Other ethnicity	0.00 (0.16)	0.00	−0.04 (0.16)	−0.02	0.06 (0.16)	0.02	0.02 (0.16)	0.01
Age	0.21 (0.05)	0.23***	0.21 (0.05)	0.23***	0.21 (0.05)	0.23***	0.20 (0.05)	0.23***
BMI (percentile)	0.01 (0.00)	0.28***	0.01 (0.00)	0.28***	0.01 (0.00)	0.28***	0.01 (0.00)	0.29***
Sleep	0.01 (0.07)	0.06	0.13 (0.07)	0.10	0.03 (0.07)	0.07	−0.05 (0.06)	−0.04
Sleep by age	−0.02 (0.02)	−0.07	−0.15 (0.09)	−0.09	−0.11 (0.09)	−0.07	0.01 (0.08)	0.01

CRP = C-reactive protein; PSQI = Pittsburgh Sleep Quality Index; SE = standard error; BMI = body mass index.

Sex was coded such that male = 0 and female = 1. Parent education was an average of the primary caregiver's and spouse's level of education, where 1 = some elementary school, 2 = completed elementary school; 3 = some junior-high school, 4 = completed junior-high school; 5 = some high school; 6 = graduated from high school; 7 = trade or vocational school; 8 = some college; 9 = graduated from college; 10 = some medical, law, or graduate school; and 11 = graduated from medical, law, or graduate school. Stress was participants' reports of stress in the past month, averaging across 10 items, on a 5-point scale, where 0 = never and 4 = very often. European Americans were coded as the reference group for ethnicity. Higher PSQI scores indicated poorer sleep. All noncategorical variables were centered at the sample mean. CRP values were log transformed (mg/l).

* $p < .05$, ** $p < .01$, *** $p < .001$.

is sometimes associated with biomarkers of CVD risk factors such as cholesterol and inflammatory markers for older adults (19). By contrast, emerging work on adolescents, including ours, suggests that *shorter* sleep is associated with higher CRP (10,15,16). By identifying the differential association of sleep duration with CRP between younger and older adolescents within the same study, our study bolsters the possibility that the implications of sleep duration for physical health may vary across the life span. At younger ages when longer sleep is recommended (49), physical health may particularly suffer if insufficient amount of sleep is obtained, whereas in older adults, sleeping longer may be indicative of sedentary lifestyles or medical conditions. In future research, it will be important to use longitudinal designs to examine whether obtaining sufficient amounts of sleep during early periods of the life span may delay the up-regulation of chronic inflammation associated with diseases of aging.

Our results may be explained by younger adolescents' susceptibility to stressors. Acquisition of immune competence is thought to continue in adolescence, and the continuous growth during adolescence plays an important role in susceptibility to toxic exposures (20). Given that nocturnal sleep regulates immune responses (12), short sleep is likely more taxing for younger adolescents whose biological systems are still maturing. It is also possible that some younger adolescents were still going through aspects of pubertal maturation, influencing our results. The role of sleep is heightened during pubertal maturation, although it remains unclear which aspects of pubertal maturation are specifically linked to particular dimensions of sleep and immune changes (21–24). Pubertal status was not assessed in our study, but younger adolescents' sensitivity to the role of sleep duration in our study suggests future research to assess different aspects of pubertal maturation and examine the associations with various dimensions of sleep.

Lastly, our adolescent participants from Asian, Latino, and European American backgrounds expand the ethnic diversity of participants represented in the limited literature on sleep and inflammation during adolescence. Furthermore, in addition to typical covariates such as sex, socioeconomic status, and ethnicity, our analytic models also controlled for perceived stress. Age- and sex-specific BMI percentile was also included as a covariate, revealing an association between higher BMI and higher CRP as with prior work with adolescents (10,15).

Our findings should be interpreted with caution given that causal links between sleep and CRP cannot be established. The limitations of our cross-sectional design should be addressed in future longitudinal studies. For instance, examining change in CRP over the course of adolescent years can shed light onto the age-dependent link between sleep and physical health during adolescence. It will be also important to examine the association of adolescent sleep with additional biomarkers such as cortisol.

In conclusion, irregular sleep duration across the week during adolescence is associated with higher levels of inflammation, which implies increased risk for chronic health

problems in adulthood. For younger adolescents, shorter average sleep duration is also associated with the elevated chronic inflammation. During adolescence, the association of sleep with inflammation seems evident in the objective dimensions of sleep duration and variability in duration, rather than in the subjective dimensions of sleep quality.

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