American Journal of Epidemiology

Vol. 164, No. 6
DOI: 10.1093/aje/kwj231
Advance Access publication July 7, 2006

Original Contribution

Cigarette Smoking and Nocturnal Sleep Architecture

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Received for publication September 26, 2005; accepted for publication March 6, 2006.

Cigarette smoking has been associated with a high prevalence of sleep-related complaints. However, its effects on sleep architecture have not been fully examined. The primary objective of this investigation was to assess the impact of cigarette smoking on sleep architecture. Polysomnography was used to characterize sleep architecture among 6,400 participants of the Sleep Heart Health Study (United States, 1994–1999). Sleep parameters included total sleep time, latency to sleep onset, sleep efficiency, and percentage of time in each sleep stage. The study sample consisted of 2,916 never smokers, 2,705 former smokers, and 779 current smokers. Compared with never smokers, current smokers had a longer initial sleep latency (5.4 minutes, 95% confidence interval (CI): 2.9, 7.9) and less total sleep time (14.0 minutes, 95% CI: 6.4, 21.7). Furthermore, relative to never smokers, current smokers also had more stage 1 sleep (relative proportion = 1.24, 95% CI: 1.14, 1.33) and less slow wave sleep (relative proportion = 0.86, 95% CI: 0.78, 0.95). Finally, no differences in sleep architecture were noted between former and never smokers. The results of this study show that cigarette smoking is independently associated with disturbances in sleep architecture, including a longer latency to sleep onset and a shift toward lighter stages of sleep. Nicotine in cigarette smoke and acute withdrawal from it may contribute to disturbances in sleep architecture.

nicotine; polysomnography; sleep; sleep stages; smoking; tobacco

Abbreviations: RDI, respiratory disturbance index; REM, rapid eye movement; SHHS, Sleep Heart Health Study.

Cigarette smoking is a major cause of preventable morbidity and mortality in the United States (1). Although the medical hazards of smoking have been studied for decades, its effects on sleep generally and on sleep architecture specifically are not well characterized. Cigarette smoking can alter nocturnal sleep architecture through a number of distinct mechanisms. First, nicotine from cigarette smoke can stimulate the release of several key neurotransmitters that collectively participate in regulating the sleep-wake cycle (2–5). Second, habitual smokers often experience acute withdrawal as the intake of nicotine is curtailed during sleep (6). Third, the medical consequences associated with cigarette smoking, such as chronic obstructive lung disease, can disrupt sleep continuity and have a negative impact on sleep architecture (7, 8). Epidemiologic investigations indicate that, compared with never smokers, current smokers experience greater difficulty in initiating and maintaining sleep and are generally more dissatisfied with their sleep quality (9–14). Although subjective assessments of sleep are easily acquired in the context of large epidemiologic studies, an inherent limitation is the poor correlation of these assessments with physiologic recordings of sleep (15–18). Research studies using polysomnographically defined sleep show that, compared with nonsmokers, current smokers manifest longer latency to sleep onset but otherwise have comparable sleep architecture (19). However, studies using objective sleep data have limited sample sizes and do not fully account for several confounding factors that can

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influence sleep architecture, such as age, alcohol or caffeine consumption, and the presence of medical comorbidity.

The Sleep Heart Health Study (SHHS) is an ongoing, multicenter, longitudinal study examining the effects of sleep-disordered breathing on the risk of cardiovascular disease (20). As part of the baseline examination, a large cohort of community-dwelling individuals underwent home polysomnography to assess sleep quality. The availability of objective data on sleep architecture, with self-reported information on smoking status, provides an opportunity to characterize sleep architecture among current, former, and never smokers in a large community-based sample. Previous analyses of a subset of the cohort have shown that current smokers and former smokers, compared with never smokers, have greater amounts of stage 1 and 2 sleep (21). The present study extends these preliminary analyses by examining the associations between cigarette smoking and sleep architecture while more fully considering potential confounding and using data from the entire SHHS cohort on a larger repertoire of sleep parameters.

MATERIALS AND METHODS

Study sample

The present report is based on data collected in the SHHS, a multicenter study on sleep-disordered breathing, hypertension, and cardiovascular disease. SHHS participants were recruited from ongoing cohort studies on cardiovascular and respiratory disease. The design, rationale, and methods of SHHS have been described previously (20). Briefly, between 1995 and 1997, a sample of 6,441 subjects was recruited from the following studies: Atherosclerosis Risk in Communities Study, Cardiovascular Health Study, Framingham Offspring and Omni Cohort Studies, Health and Environment and Tucson Epidemiologic Study, Strong Heart Study, and New York City Studies of Hypertension. Participants were required to be age 40 years or older at the time of enrollment. Each participant had an in-home polysomnogram and completed several interviewer-administered questionnaires. Approval for the study protocol was acquired from the institutional review board of each participating institution, and informed consent was obtained from all study participants.

Polysomnography

The Compumedics P-series recording system (Compumedics Ltd., Abbotsville, Australia) was used to conduct an unattended overnight polysomnogram in the home. The recording montage included a C3-A2 and C4-A1 electroencephalogram, right and left electrooccullograms, single-lead electrocardiogram, chin electromyogram, measurement of abdominal and thoracic effort by impedance plethysmography, oxyhemoglobin saturation by pulse oximetry, airflow (with an oral-nasal thermistor), body position (by mercury gauge), and ambient light. Nocturnal recordings from each study site were sent to a centralized reading center for scoring. Sleep-stage scoring was performed by trained technicians according to the current guidelines (22). Apneas were identified if airflow was absent or nearly absent for at least 10 seconds. Hypopneas were identified if discernible, discrete reductions in airflow or thoracoabdominal movement (at least 30 percent below baseline values) occurred for at least 10 seconds. The respiratory disturbance index (RDI) was defined as the number of apneas or hypopneas, each associated with a 4 percent decrease in oxygen saturation, per hour of sleep.

Arousals were identified as abrupt shifts of at least 3 seconds' duration in electroencephalogram frequency. In rapid eye movement (REM) sleep, scoring of arousals also required concurrent increases in electromyogram amplitude. An arousal index was defined as the average number of arousals per hour of sleep. Parameters of sleep architecture included total sleep time; sleep efficiency (total sleep time/time in bed); and percentages of stage 1, stage 2, slow wave, and REM sleep. Latencies to sleep onset and REM onset were also determined. Sleep latency was defined as the time from lights ''off'' to sleep onset. REM latency was defined as the time from sleep onset to the first episode of REM sleep. Lights ''on-off'' detection by the portable sleep monitor was considered accurate if a clear transition of lights ''on'' to ''off was visually detected in the sleep recording. Studies showing no change in the light channel or a constant fluctuation between ''on'' and ''off'' were considered to have inaccurate lights ''on/off'' information and thus could not provide data on sleep latency.

Determination of sleep efficiency and its associated parameters (i.e., time in bed) was also affected by whether a recording ended before the final awakening because of limitations in the monitor's battery or memory, or whether the subject slept beyond the preset wake time. Furthermore, data in some sleep studies were scored as sleep or wake when the technical quality of the electroencephalogram did not allow distinction between different sleep stages but allowed a differentiation between sleep and wakefulness. For studies including sleep-wake scoring only, total sleep time was available, but individual sleep-stage data were not. Limitations in the quality of physiologic recordings led to varying sample sizes for the different sleep variables. Analyses restricted to those subjects for whom data on all of the variables were complete showed no significant differences compared with analyses that used any data when available. Therefore, results from the latter are reported herein.

Covariate data

The SHHS baseline visit involved several interviewer-administered questionnaires to collect data on age, gender, race, educational level, marital status, smoking history (current, former, never), caffeine and alcohol consumption, medication use, and medical comorbidities, including cardiovascular and pulmonary disease. Anthropometric measurements included height, weight, and neck circumference. The morning after the sleep recording, information on cigarette smoking, alcohol consumption, and caffeine consumption 4 hours prior to the study was ascertained by using a self-administered questionnaire. Smoking status was based on responses to the following questions: 1) Have you ever smoked cigarettes (yes or no)? and 2) If you

smoked before, do you smoke now (yes or no)? For current smokers, lifetime smoking exposure was quantified in pack-years, where 1 pack-year was considered 20 cigarettes smoked per day for 1 year.

Prevalent cardiovascular disease (self-reported angina, myocardial infarction, coronary artery bypass surgery, coronary angioplasty, stroke, or congestive heart failure), pulmonary disease (self-reported history of emphysema, chronic bronchitis, or asthma), and the use of specific medications (e.g., antidepressants, antihypertensives, β-blockers, nitrates, and estrogen replacement therapy) were ascertained. Psychotropic medication use was confirmed if the participant was taking nontricyclic antidepressants, tri- and tetracyclic antidepressants, monoamine oxidase inhibitors, benzodiazepines, or a drug combination (e.g., tricyclics and antipsychotics). Self-reported information on the use of a sleep aid was assessed with the following question: Do you take sleeping pills at least 1 day per week? Finally, information derived from the Medical Outcomes Short-Form (SF-36), a self-reported, generic, quality-of-life instrument, was used as a measure of mental health (23). Specifically, the mental component summary score of the Medical Outcomes Short-Form was included as a covariate in multivariable models relating smoking status to parameters of sleep architecture.

Statistical analysis

The primary dependent variables included sleep efficiency, initial sleep latency, REM latency, total sleep time, and percentages of stage 1, stage 2, slow wave, and REM sleep. Unadjusted differences in continuous and categorical variables across categories of smoking status were assessed for significance by using t tests or χ^2 tests, as appropriate. The Kaplan-Meier method (24) and the proportional hazards model (25) were used to assess associations of smoking status with the latency to sleep onset and the first episode of REM sleep. The assumption of proportional hazards was assessed by examining the distribution of the scaled Schoenfeld's residuals (26).

For the parameters of sleep architecture, quantile regression models were used to examine differences between never, former, and current smokers given the highly skewed and nonnormal distribution for some of these variables. Quantile regression models describe specific quantiles of a response variable as functions of an observed set of covariates (27). Models were parameterized such that the resulting regression coefficients described the relative proportions of each sleep stage comparing current or former smokers with never smokers (reference group). Multivariable models were developed that included age, gender, race, educational status, marital status, alcohol and caffeine consumption, and use of specific medications (e.g., psychotropics). Marital status was also dichotomized as married versus not married. Other variables were body mass index, neck circumference, prevalent respiratory and cardiovascular disease, and severity of sleep-disordered breathing as assessed by the RDI. Body mass index was categorized as follows: <18.5, 18.5–24.9, 25.0–30.0, and >30.0 kg/m^2. Sleep-disordered severity was assessed with the RDI by using the following cutpoints: <5.0 events/hour (normal), 5.0–14.9 events/hour (mild sleep-disordered breathing), and ≥ 15.0 events/hour (moderate to severe sleep-disordered breathing). Effect modification of smoking status by other covariates, such as alcohol and caffeine consumption, was assessed by including appropriate interaction terms in the multivariable model. Analyses were conducted with the R statistical package for quantile regression (28) and SAS version 9.0 software (SAS Institute, Inc., Cary, North Carolina) for other analyses.

RESULTS

Sample characteristics

Of the 6,441 participants in the SHHS cohort, data on smoking status were available for 6,400 of them. There were 2,916 (45.6 percent) never smokers, 2,705 (42.3 percent) former smokers, and 779 (12.2 percent) current smokers. Table 1 summarizes the sample characteristics of the 6,400 participants by smoking status. Current smokers on average were younger (mean age: 59.6 years) than former smokers (mean age: 64.6 years) or never smokers (mean age: 63.5 years, $p < 0.001$). Current smokers also included the greatest number of African Americans and American Indians compared with former and never smokers. Men constituted the greatest proportion of former smokers (58.1 percent), followed by current smokers (51.9 percent) and never smokers (35.9 percent, $p < 0.001$). Statistically significant differences were not noted in educational level or marital status when former and never smokers were compared (table 1). However, current smokers included a statistically significant lower proportion of married participants (65.9 percent vs. 76.6 percent, $p < 0.001$) and, on average, had less education (13.3 years) than either former smokers (14.3 years) or never smokers (14.2 years, $p < 0.001$).

As expected, daily caffeine and alcohol consumption 4 hours before polysomnography was higher among current smokers than among former or never smokers (table 1). Anthropometric data revealed that, compared with former or never smokers, current smokers had a lower body mass index. The prevalence of self-reported cardiovascular disease was higher among current smokers than never smokers (15.9 percent vs. 13.3 percent, $p < 0.001$), as was the prevalence of respiratory disease (17.0 percent vs. 11.4 percent, $p < 0.001$). Psychotropic medication use did not differ between the three groups. However, former and current smokers reported greater use of sleep aids compared with never smokers (table 1). Among female participants, 27.6 percent of never smokers, 32.2 percent of former smokers, and 29.1 percent of current smokers reported current use of estrogen replacement therapy ($\chi^2 = 7.10$, $p < 0.03$). Finally, among current smokers, the median lifetime exposure to smoking was 27.5 pack-years (interquartile range: 14.4–42.0).

Smoking and sleep architecture: bivariate analyses

Parameters derived from overnight polysomnography are summarized by smoking status in table 2. Information on

TABLE 1. Characteristics of the study sample by smoking status,† Sleep Heart Health Study, United States, 1994–1999

Covariate	Smoking status		
	Never smokers ($n = 2,916$)	Former smokers ($n = 2,705$)	Current smokers ($n = 779$)
Age in years	63.5 (11.5)	64.6 (10.5)*	59.6 (9.5)**
Male gender (%)	35.9	58.1*	51.9**
Race (%)			
White	76.4	81.3*	62.3**
African American	8.3	7.1*	9.9**
American Indian	7.2	8.3*	22.5**
Other	8.1	3.3*	5.2**
Educational level in years	14.2 (3.6)	14.3 (3.4)	13.3 (3.3)**
Married (%)	76.6	77.6	65.9**
Alcohol consumption before the sleep study (%)‡	7.0	13.0*	16.4**
Daily caffeine consumption (%)§	74.2	79.3*	90.6**
Body mass index group (%)			
<18.5 kg/m^2	1.1	0.4*	0.4**
18.5–24.9 kg/m^2	29.5	25.0*	35.2**
25.0–30.0 kg/m^2	40.2	42.6*	37.8**
>30.0 kg/m^2	29.2	31.9*	26.7**
Respiratory disturbance index group (%)			
<5.0 events/hour	55.9	48.2*	64.6**
5.0–14.9 events/hour	27.1	31.9*	21.7**
≥ 15.0 events/hour	17.0	19.8*	13.7**
Cardiovascular disease (%)	13.3	20.2*	15.9**
Respiratory disease (%)	11.4	14.8*	17.0**
Use of a sleep aid (%)	6.2	7.2*	7.7**
Use of psychotropic medication (%)	10.8	10.7	10.7

* $p < 0.02$ comparing never smokers with former smokers; ** $p < 0.001$ comparing never smokers with current smokers.

† Group differences by smoking status for each of the above covariates were determined by the χ^2 test for categorical variables and the *F* test for continuous variables. Continuous variables are expressed as mean (standard deviation).

‡ Alcohol consumption (yes or no) represents intake of any alcohol products 4 hours before the sleep study.

§ Categorical (dichotomous) variable indicating consumption of one or more cups of caffeinated tea, coffee, or soda.

time to sleep onset and sleep efficiency was available for 3,664 participants for whom lights on-off information was sufficiently accurate. Median latency to sleep onset among current smokers was longer than that among never smokers (21.5 minutes vs. 16.5 minutes, $p < 0.0001$). However, former and never smokers had similar latencies to sleep onset (16.0 minutes vs. 16.5 minutes, $p > 0.05$). Latency to the first REM episode was slightly longer among current smokers compared with the other two groups (table 2). In addition, current smokers had less total sleep time, lower sleep efficiency, higher percentages of stage 1 and 2 sleep, and a lower percentage of slow wave (stage 3 or 4) sleep compared with never smokers (table 2).

The median RDI was 3.9 events/hour (interquartile range: 1.2–10.5) among never smokers, 5.3 events/hour (interquartile range: 1.6–12.4) among former smokers, and 2.7 events/hour (interquartile range: 0.8–8.1) among current smokers (F statistic $= 43.8$, $p < 0.0001$). Bivariate analyses revealed that factors including age, body mass index, neck circumference, RDI, history of respiratory disease, estrogen replacement therapy, and use of a sleep aid were associated with the distribution of sleep stages (data not shown). Psychotropic medications, including monoamine oxidase inhibitors, nontricyclic antidepressants, tri- and tetracyclic antidepressants, and benzodiazepines, did not influence the distribution of sleep stages or other parameters derived from overnight polysomnography. No associations were noted between use of other medications (e.g., antihypertensives, β-blockers, nitrates) and distributions of polysomnographic variables.

TABLE 2. Distributions†,‡ of sleep architecture indices by smoking status,§ Sleep Heart Health Study, United States, 1994–1999

Sleep parameter	Smoking status		
	Never smokers	Former smokers	Current smokers
Sleep latency (minutes)	16.5 (9.5–28.8)	16.0 (9.0–27.0)	21.5 (12.0–37.5)**
REM latency (minutes)¶	75.0 (57.0–109.0)	71.0 (54.5–103.5)*	76.0 (58.0–108.5)
Total sleep time (hours)	6.1 (5.4–6.7)	6.0 (5.2–6.6)**	5.9 (5.2–6.6)**
Sleep efficiency (%)	84.1 (76.9–89.3)	83.4 (75.5–88.8)*	83.0 (75.1–88.2)*
Stage 1 sleep (%)#	4.2 (2.6–6.6)	4.8 (2.9–7.5)**	5.5 (3.3–8.7)**
Stage 2 sleep (%)#	56.2 (48.4–64.3)	58.1 (50.1–65.4)**	59.8 (51.3–67.4)**
Slow wave sleep (%)#	18.6 (10.0–26.6)	15.9 (7.9–24.2)**	12.2 (4.2–21.7)**
REM sleep (%)#	20.1 (15.8–23.9)	19.7 (15.6–23.9)	20.6 (16.8–24.4)*

* $p < 0.05$ and ** $p < 0.0001$ compared with never smokers (reference group).
† Values are expressed as median (interquartile range).
‡ Data on sleep latency and sleep efficiency, rapid eye movement (REM) latency, and total sleep time were available for 3,664, 5,798, and 4,398 participants, respectively.
§ Group differences across smoking status were determined by the *t* test.
¶ Denotes latency to the first episode of REM sleep.
# Expressed as percentage of total sleep time.

Smoking and sleep architecture: multivariable analyses

Figure 1 shows the adjusted survival curves from a Cox proportional hazards model for initial sleep latency by smoking status. The previously noted unadjusted differences in initial sleep latency remained after adjustment for age, gender, marital status, neck circumference, RDI, alcohol consumption, and history of respiratory disease. In contrast, differences in REM latency were not observed between the three groups after multivariable adjustments. To assess the independent association of smoking status with the distributions of the sleep-stage parameters, quantile regression models were constructed for the 25th, 50th, and 75th percentiles of each sleep stage as derived from the overnight polysomnogram. Linear regression models were also developed to assess differences between the three groups. Although inferences regarding the associations between smoking status and polysomnographic data from the linear and quantile regression models were consistent, results from the quartile regression analyses are presented here to avoid modeling of skewed parameters (e.g., stage 1, slow wave sleep) and to simplify interpretation of associated regression coefficients.

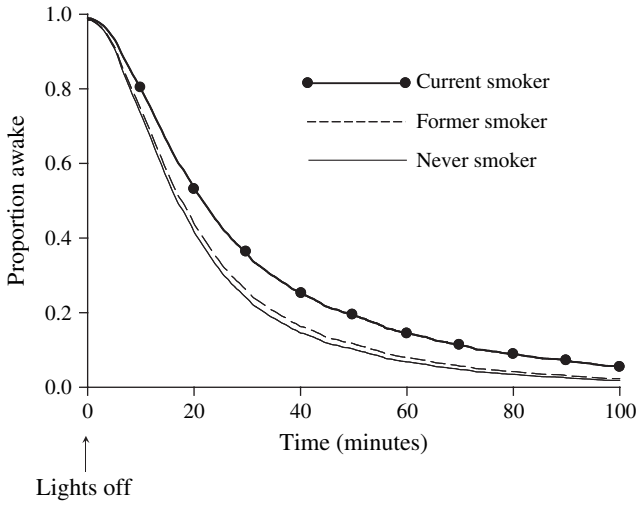

FIGURE 1. Adjusted survival curves for time to sleep onset by smoking status, Sleep Heart Health Study, United States, 1994–1999. Survival curves were based on the Cox proportional hazards model using a reference population with the following characteristics: age, 63.4 years (study sample average); White race; female gender; no self-reported alcohol or caffeine consumption; body mass index, <25 kg/m^2; neck circumference, 38 cm (study sample average); respiratory disturbance index, <5.0 events/hour; and no history of cardiovascular or respiratory disease ($n = 3,167$).

Quantile regression models revealed that, irrespective of the cutpoint modeled (25th, 50th, or 75th percentile), current smokers had less adjusted total sleep time and lower sleep efficiency than never smokers (figure 2). In contrast, differences were not noted between former and never smokers in total sleep time or sleep efficiency (figure 2). Analyses of sleep-stage distribution showed several statistically significant and meaningful differences between current, former, and never smokers in both univariate and multivariable models (table 3). The adjusted relative proportions comparing current and never smokers on the percentages of stage 1 and 2 sleep were 1.24 (95 percent confidence interval: 1.14, 1.33) and 1.01 (95 percent confidence interval: 0.98, 1.04), respectively. Thus, current smokers had 24 percent more stage 1 sleep relative to never smokers. Moreover, current smokers were noted to have 14 percent less slow wave sleep than never smokers (relative proportion = 0.86, 95 percent confidence interval: 0.78, 0.95). In contrast, statistically significant differences in the amount of slow wave sleep were not noted between former and never smokers. However, the amount of REM sleep was similar across the

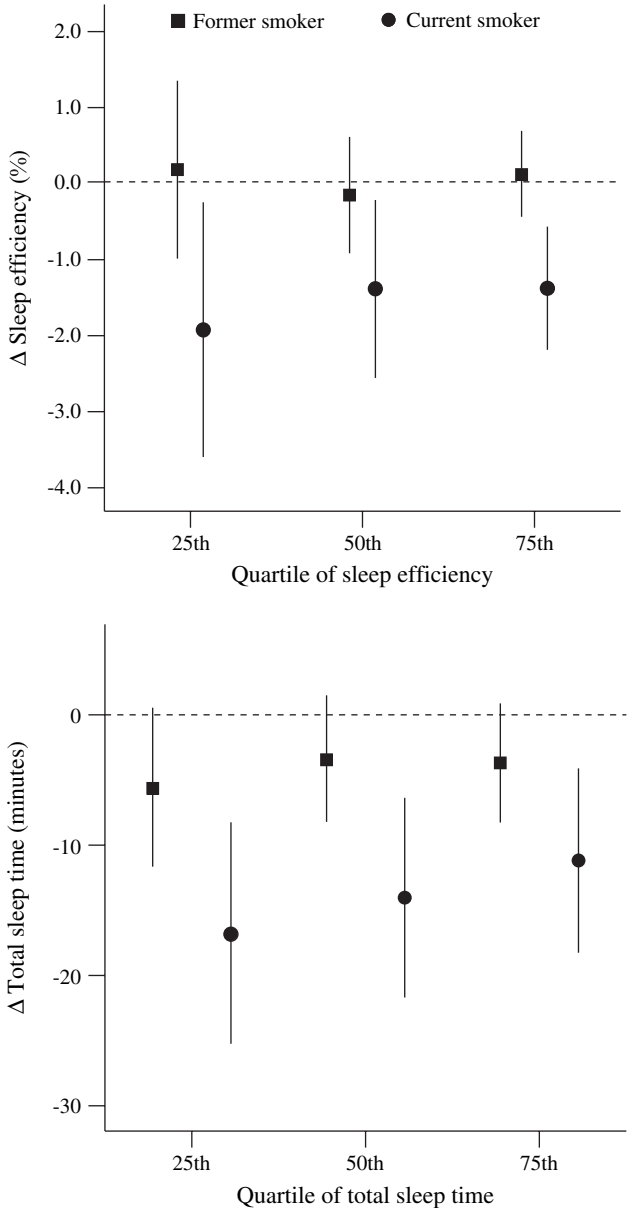

FIGURE 2. Adjusted differences (Δ) and 95% confidence intervals for the quartiles of sleep efficiency and total sleep time between current, former, and never (reference) smokers, Sleep Heart Health Study, United States, 1994–1999. Point estimates were derived from quantile regression models and were adjusted for age, race, gender, marital status, neck circumference, respiratory disturbance index, prevalent respiratory disease, and consumption of caffeinated beverages. Complete data were available for 3,166 and 3,874 subjects regarding sleep efficiency and total sleep time, respectively.

three smoking status groups. Figures 3 and 4 show the adjusted relative proportions comparing current and former smokers with never smokers regarding the percentages of stage 1, stage 2, and slow wave sleep at each quartile (25th, 50th, and 75th percentiles). Finally, among current smokers ($n = 779$), associations were not noted between

TABLE 3. Relative proportions of each sleep stage comparing current smokers and former smokers with never smokers (reference group), Sleep Heart Health Study, United States, 1994–1999*

Sleep stage and model†	Current smokers		Former smokers	
	Relative ratio	95% confidence interval	Relative ratio	95% confidence interval
Stage 1 sleep				
Unadjusted	1.30	1.20, 1.40	1.14	1.09, 1.19
Adjusted	1.24	1.14, 1.33	1.01	0.96, 1.06
Stage 2 sleep				
Unadjusted	1.06	1.05, 1.08	1.03	1.02, 1.05
Adjusted	1.01	0.98, 1.04	0.99	0.98, 1.01
Slow wave sleep				
Unadjusted	0.65	0.59, 0.73	0.85	0.81, 0.89
Adjusted	0.86	0.78, 0.95	1.02	0.92, 1.13
REM‡ sleep				
Unadjusted	1.02	0.99, 1.05	0.98	0.96, 1.00
Adjusted	1.03	1.00, 1.06	1.00	0.98, 1.03

* The regression coefficients represent the relative proportion comparing current smokers or former smokers with never smokers regarding the median percentage of each sleep stage.

† The models are based on median regression analyses and were adjusted for age, race, gender, body mass index, sleep disordered breathing severity (i.e., respiratory disturbance index), prevalent respiratory disease, consumption of caffeinated drinks, estrogen replacement therapy, mental component Medical Outcomes Short-Form summary score, and use of a sleep aid.

‡ REM, rapid eye movement.

life-time exposure (i.e., pack-years) or whether they had smoked 4 hours before the sleep study ($n = 663$) and any of the parameters of sleep architecture.

DISCUSSION

The primary objective of the current study was to characterize differences in sleep architecture between current, former, and never smokers. Using polysomnographic data from the multicenter SHHS cohort, we found that, compared with never smokers, current smokers had less total sleep time, lower sleep efficiency, longer latency to sleep onset, and a shift toward lighter stages of sleep. Specifically, current smokers, compared with never smokers, had more stage 1 sleep with a concomitant decrease in slow wave sleep. In contrast, differences were not noted in the amount of REM sleep between current, former, and never smokers. The associations between smoking status and the distribution of polysomnographic indices were independent of factors such as age, gender, race, body mass index, RDI, and prevalent cardiovascular or respiratory disease. Interestingly, a dose-response relation was not identified between lifetime exposure (i.e., pack-years) and sleep architecture among smokers. Finally, significant differences were not noted in any of the

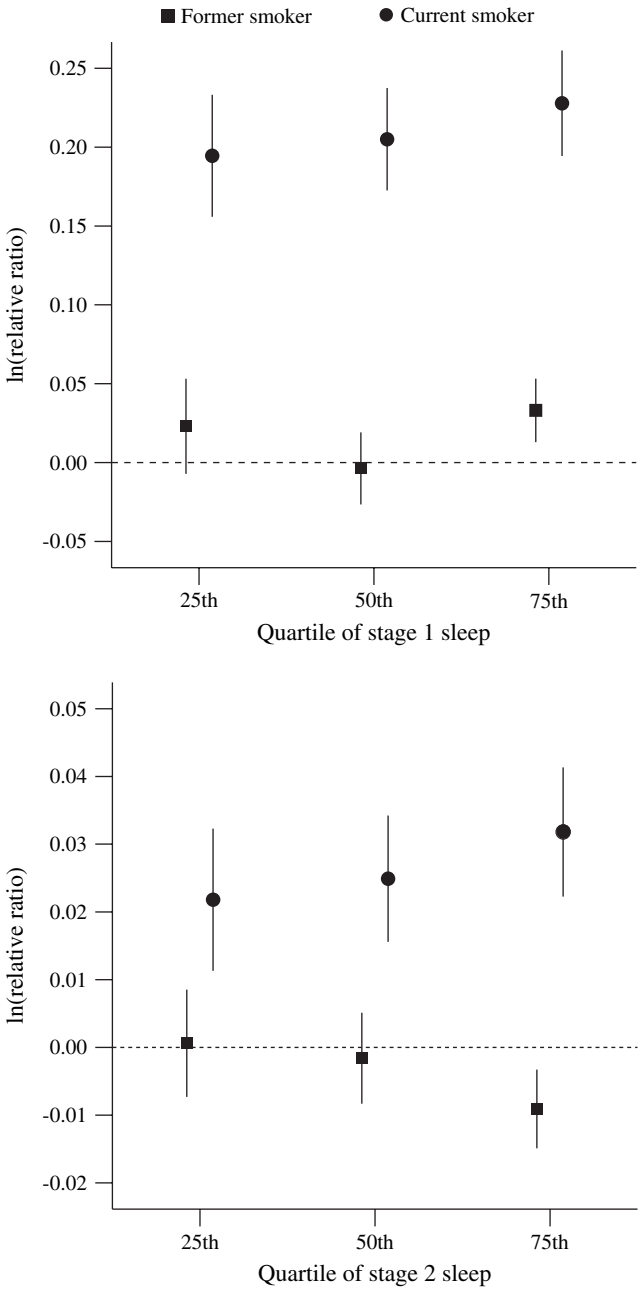

FIGURE 3. Adjusted ln(relative ratios) and 95% confidence intervals for percentages of stage 1 and 2 sleep for current and former smokers compared with never (reference) smokers, Sleep Heart Health Study, United States, 1994–1999. Point estimates were derived from quantile regression models and were adjusted for age, race, gender, marital status, neck circumference, respiratory disturbance index, prevalent respiratory disease, and consumption of caffeinated beverages. Complete data were available for 5,502 subjects.

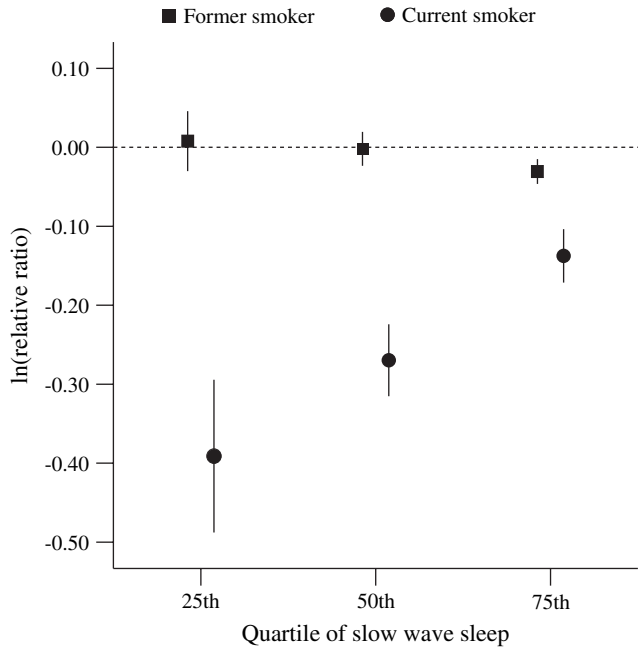

FIGURE 4. Adjusted ln(relative ratios) and 95% confidence intervals for percentages of slow wave sleep for current and former smokers compared with never (reference) smokers, Sleep Heart Health Study, United States, 1994–1999. Point estimates were derived from quantile regression models and were adjusted for age, race, gender, marital status, neck circumference, respiratory disturbance index, prevalent respiratory disease, and consumption of caffeinated beverages. Complete data were available for 5,502 subjects.

sleep parameters between former and never smokers after adjustment for relevant covariates.

The results of this study are consistent with several previous reports demonstrating a higher prevalence of sleep disturbances among current versus former or never smokers. Data from the population-based Wisconsin Sleep Cohort Study have shown that current smokers report greater difficulty than never smokers in initiating and maintaining sleep (11). Symptoms of poor nocturnal sleep quality, including nonrestorative sleep, difficulty with morning awakening, and subsequent excessive daytime sleepiness, were also more common in current smokers than in never smokers. Although the association between cigarette smoking and poor sleep quality has been described in other smaller studies (9, 10, 13, 14), only the Wisconsin Sleep Cohort Study (11) had a potentially informative sample size and considered the potential effects of age and gender in assessing the independent relation between smoking and subjective sleep quality. Nonetheless, to our knowledge, analyses relating smoking status to parameters of sleep architecture from the Wisconsin Sleep Cohort Study have thus far not been published. While subjective reports provide a convenient means for assessing sleep disturbance in field studies, they cannot characterize the range of physiologic disturbances that can be detected with overnight polysomnography.

In one of the few studies with objective measures of sleep, Soldatos et al. (19) found that current smokers had a longer latency to sleep onset than age- and gender-matched nonsmokers did but were otherwise similar regarding the distribution of sleep architecture. However, limitations of that

study include a small sample size with inadequate power to detect differences in sleep architecture and omission of several confounding covariates such as alcohol or caffeine consumption. The current investigation adds to the body of existing literature by showing that the sleep architecture of current smokers and nonsmokers differs. Moreover, our findings extend previous, limited analyses (21) on a subset of the SHHS cohort by including the entire study cohort and considering potential confounding factors, with an in-depth focus on the effects of smoking on a larger repertoire of parameters derived from the overnight sleep study.

The association of cigarette smoking status with altered sleep architecture is not surprising given the effects of nicotine on the central nervous system. Nicotine, the primary pharmacologically active component of cigarette smoke, acts centrally by stimulating nicotine-acetylcholine receptors (29). These receptors are widely distributed in presynaptic neurons located in areas such as the rostral hypothalamus and the brainstem reticular formation (29). Activation of nicotinic receptors leads to the release of several neurotransmitters, including actelycholine, dopamine, serotonin, norepinephrine, and gamma-amino butyric acid. The detrimental effects of nicotine on sleep architecture are likely due to the independent and interactive effects of these neurotransmitters on the central mechanisms that regulate the sleep-wake cycle. One of the major findings in the current study is that smokers and nonsmokers manifest differences in non-REM sleep but not in REM sleep. Regulation of non-REM sleep depends on a decrease in aminergic neuronal activity within the locus coeruleus and dorsal raphe. By stimulating the release of aminergic neurotransmitters (e.g., dopamine and serotonin), nicotine in cigarette smoke may disturb the normal regulation of non-REM sleep and shift the distribution of sleep architecture toward lighter stages of sleep. The comparability in the amount of REM sleep for current smokers and never smokers was likely found because nicotine does not inhibit cholinergic regulation of REM sleep. Alternatively, the use of tabulated sleep-stage statistics (i.e., percentage of REM sleep), which cannot describe temporal changes, may mask nicotine-related alterations in the cycling of REM episodes during the course of the night. With sleep onset, blood nicotine levels gradually decrease and induce a state of nicotine withdrawal that can, in turn, modify sleep continuity. Subtle changes in the temporal distribution of non-REM and REM sleep would not be evident within the overall percentages of non-REM and REM sleep across the night.

In addition to the direct effects of nicotine on the central nervous system, medical conditions and other adverse consequences of cigarette smoking can also affect nocturnal sleep quality. Alcohol and caffeine consumption and the presence of cardiovascular and respiratory disease were associated with alterations in sleep architecture in the current study. Despite adjustment for such factors, results of this investigation support the hypothesis that cigarette smoking is independently associated with physiologic alterations in sleep architecture. Although prevalent medical conditions or other factors do not fully account for the alterations in sleep observed among current smokers, our results also show that, after adjustment for such confounding, sleep architecture is comparable in former and never smokers. Contrary to our expectation, the distribution of sleep architecture among current smokers was not a function of lifetime exposure to cigarette smoking as quantified by pack-years. The lack of an association suggests the hypothesis that sleep disturbance in smokers is not dependent on cumulative exposure and/or that pack-years is a crude measure of the amount smoked.

The current study has several strengths, which include a large sample size, the use of a community-based cohort, the availability of objective sleep measures, and the inclusion of key confounding covariates. Moreover, the use of quantile regression methods illustrates a simple, but appropriate means for modeling skewed distributions of sleep stages that would have otherwise required complex transformations. Nevertheless, the current study has a number of limitations. First, smoking status was based on self-report without corroborating objective documentation. However, we speculate that any misclassification in smoking status is not likely to be associated with the findings of the sleep study and thus could have introduced minimal, if any, bias in the results. Second, restricting the analysis to participants with high-quality polysomnograms may have omitted the most susceptible individuals with disrupted sleep (e.g., smokers whose sleep quality is poor) and diluted the associations of interest. Third, given the cross-sectional nature of our data, causality could not be established definitively. It is certainly plausible that fatigue and sleepiness that result from sleep disruption might lead to smoking given its associated mild stimulant effects. Fourth, data on other tobacco use (e.g., cigars and pipes) or secondhand exposure to smoke were not available for the cohort. Finally, although sensitivity analyses were conducted to determine whether specific medications (i.e., psychotropics) were associated with alternations in sleep architecture, the lack of specific information on psychiatric disorders leaves the possibility of residual confounding by such disorders.

We conclude that the consequences of cigarette smoking extend beyond the long list of well-established causal and detrimental effects on health to sleep. Disturbances in nocturnal sleep architecture can lead to dissatisfaction with sleep quality, decrease daytime alertness, and diminish quality of life. With a better understanding of the adverse effects of cigarette smoking on sleep architecture, methods of smoking cessation might be tailored to curtail the disruption of sleep that is, in part, related to withdrawal from nicotine. In addition, our data suggest that smoking cessation can reverse the disturbances in nocturnal sleep as evident by the finding that former and never smokers showed similar sleep-stage distributions. Finally, the results of this investigation provide empirical evidence for understanding the biologic basis of sleep-onset insomnia and poor sleep quality associated with cigarette smoking.

ACKNOWLEDGMENTS

Supported by the National Heart, Lung, and Blood Institute through the following cooperative agreements: UO1HL53940 (University of Washington), U01HL53941

(Boston University), U01HL63463 (Case Western Reserve University), U01HL53937 (Johns Hopkins University), U01HL53938 (University of Arizona), U01HL53916 (University of California, Davis), U01HL53934 (University of Minnesota), U01HL63429 (Missouri Breaks Research), and U01HL53931 (New York University). Dr. Punjabi has also received support from National Institutes of Health grants HL7578 and AG025553.

The opinions expressed in this paper are those of the authors and do not necessarily reflect the views of the Indian Health Service.

Conflict of interest: none declared.

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