Relation of Sleepiness to Respiratory Disturbance Index

The Sleep Heart Health Study

DANIEL J. GOTTLIEB, CORALYN W. WHITNEY, WILLIAM H. BONEKAT, CONRAD IBER, GARY D. JAMES, MICHAEL LEBOWITZ, F. JAVIER NIETO, and CARL E. ROSENBERG, for the Sleep Heart Health Study Research Group

Department of Medicine, Boston University School of Medicine, Boston, Massachusetts; Department of Biostatistics, University of Washington, Seattle, Washington; Department of Medicine, University of California, Davis, California; Department of Medicine, University of Minnesota, Minneapolis, Minnesota; Cardiovascular Center, Cornell Medical Center, New York, New York; Pulmonary Section, Department of Medicine, University of Arizona College of Medicine, Tucson, Arizona; Department of Epidemiology, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland; and Department of Neurology, Case Western Reserve University, Cleveland, Ohio

Obstructive sleep apnea syndrome is a well recognized cause of excessive sleepiness; however, the relation of sleepiness to mild sleep-disordered breathing (SDB), which affects as much as half the adult population, is uncertain. In order to explore this relation, we conducted a cross-sectional cohort study of community-dwelling adults participating in the Sleep Heart Health Study, a longitudinal study of the cardiovascular consequences of SDB. The study sample comprises 886 men and 938 women, with a mean age of 65 (SD 11) yr. Sleepiness was quantified using the Epworth Sleepiness Scale (ESS). Sleep-disordered breathing was quantified by the respiratory disturbance index (RDI), defined as the number of apneas plus hypopneas per hour of sleep, measured during in-home polysomnography. When RDI was categorized into four groups ($<$ 5, 5 to $<$ 15, 15 to $<$ 30, $\geqslant$ 30), a significantly progressive increase in mean ESS score was seen across all four levels of SDB, from 7.2 (4.3) in subjects with RDI $<$ 5 to 9.3 (4.9) in subjects with RDI $\geqslant$ 30 ($p < 0.001$). There was no significant modification of this effect by age, sex, body mass index, or evidence of chronic restriction of sleep time or periodic limb movement disorder. The percentage of subjects with excessive sleepiness, defined as an ESS score $\geqslant$ 11, increased from 21% in subjects with RDI $<$ 5 to 35% in those with RDI $\geqslant$ 30 ($p < 0.001$). We conclude that SDB is associated with excess sleepiness in community-dwelling, middle-aged and older adults, not limited to those with clinically apparent sleep apnea. Gottlieb DJ, Whitney CW, Bonekat WH, Iber C, James GD, Lebowitz M, Nieto FJ, Rosenberg CE, for the Sleep Heart Health Study Research Group. Relation of sleepiness to respiratory disturbance index: the Sleep Heart Health Study. AM J RESPIR CRIT CARE MED 1999;159:502–507.

Excessive sleepiness has been increasingly recognized as an important public health problem, estimated to affect as much as 12% of the general adult population (1) and contributing to both motor-vehicle and work-related accidents, impaired social functioning, and reduced quality of life (2–5). Among the many causes of excessive sleepiness is the obstructive sleep apnea syndrome (OSAS), characterized by repetitive episodes of apnea or hypopnea during sleep (6). Patients with OSAS are sleepier than control subjects when assessed by polysomnographic measurement of mean sleep latency or by sleep symptom questionnaires, and sleepiness in these patients appears to be correlated with OSAS severity, as determined by the respiratory disturbance index (RDI) (7, 8). Although the prevalence of OSAS is estimated at 1 to 4% of the adult population in the United States and other industrialized countries, sleep-disordered breathing (SDB) that is not of sufficient severity to be diagnosed as OSAS is now recognized to be quite common, affecting as much as 25 to 50% of middle-aged and older adults (9–14). Although the RDI is correlated with sleepiness in patients with OSAS, a relation between SDB and sleepiness has not been clearly demonstrated in the general population (15–17). In the present study, we take advantage of polysomnography (PSG) and questionnaire data collected by the Sleep Heart Health Study (SHHS) to investigate the relation of SDB to sleepiness in a community-dwelling cohort of middle-aged and older adults selected independent of the diagnosis of sleep apnea.

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Correspondence and requests for reprints should be addressed to Daniel J. Gottlieb, M.D., M.P.H., The Pulmonary Center, Boston University School of Medicine, 715 Albany Street, R-304, Boston, MA 02118-2394.

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METHODS

Study Sample

All subjects are participants in the SHHS, a multicenter study of the cardiovascular consequences of SDB involving subjects recruited from ongoing epidemiologic studies. The design of the SHHS has been described previously (18). Subjects were recruited independent of reported sleepiness or obstructive sleep apnea; however, subjects who reported habitual snoring were oversampled at some participating centers, and subjects were excluded if receiving supplemental oxygen therapy or current treatment for OSAS. The study protocol was approved by the institutional review board of each participating institution. Recruitment of subjects into the SHHS began in November 1995 and ended in January 1998. Subjects chosen for this analysis included all SHHS participants who had PSG of acceptable quality scored prior to March 7, 1997, and who completed the Epworth Sleepiness Scale (ESS) questionnaire. During this period of recruitment, 27 potential subjects were excluded from participation because they were receiving current therapy for OSAS.

Polysomnography

A single night of unattended polysomnography was performed in the subject's home, using a Compumedics PS-2 system (Compumedics Pty. Ltd., Abbotsford, Australia) with the following montage: central electroencephalogram × 2, electrooculogram × 2, chin electromyogram, electrocardiogram, oximetry, chest and abdominal excursion, airflow (using an oronasal thermocouple), and body position. Recordings were transferred to the SHHS Reading Center (Cleveland) for scoring of sleep stages, arousals, and respiratory events. Approximately 3% of studies were rejected prior to scoring because of poor quality apparent on preliminary review; this varied somewhat among the 11 field centers, from 1.0 to 7.9%. Acceptable studies were those with at least 4 h of recorded data of sufficient quality to allow sleep staging and respiratory event detection. For this analysis, RDI was defined as the number of apneas plus hypopneas per hour of sleep time, where apnea is defined as a reduction in the thermocouple signal to $\leqslant$ 25% of baseline for $\geqslant$ 10 s, and hypopnea is defined as a decrease in the thermocouple signal or thoracoabdominal excursion to $\leqslant$ 70% of baseline for $\geqslant$ 10 s, accompanied by a 4% decrease in oxygen saturation. In order to exclude postarousal respiratory events, apneas or hypopneas were not scored if they immediately followed an isolated large breath or movement.

Sleepiness

Sleepiness was defined as the score on the ESS, a well-validated eight-item self-completion questionnaire that asks the subject to rate his or her likelihood of falling asleep in a variety of commonly encountered situations (19, 20). Possible scores range from 0 (the least sleepy) to 24 (the most sleepy). The ESS score has been shown to correlate positively with RDI and inversely with sleep latency in patients with OSAS (21). A score of 11 or higher is considered to represent an abnormal degree of daytime sleepiness (19).

Analysis

All analyses were performed using SPSS data analysis software. Analysis of variance and analysis of covariance were used to assess differences in mean ESS score between four categories of RDI severity, and to assess potential effect modification by age, sex, body mass index (BMI), duration of usual sleep period, difference between usual sleep time on weekdays (or usual work days) versus weekends (or usual nonwork days), presence of symptoms of periodic limb movement disorder, and center from which the subject was recruited. Contingency table analysis was used to compare the prevalence of excessive sleepiness, defined as a score $\geqslant$ 11 on the ESS, among categories of SDB severity.

RESULTS

Subjects

Between November 1995 and March 1997, 1,907 subjects had PSG performed and scored as part of the SHHS. Of these, 10 were excluded because of unacceptable PSG quality and 73 were excluded for failure to complete the ESS. The remaining 1,824 subjects (938 women and 886 men) form the basis of this report. Subject characteristics are shown in Table 1. The racial/ethnic composition of the study sample reflects the status of recruitment at the time of this analysis, and differs from the anticipated final composition of the SHHS cohort. In particular, the high proportion of Native Americans reflects the high rate of enrollment of subjects from the Strong Heart Study early in the SHHS. Thirty-four subjects (2%) reported a physician diagnosis of OSAS, and they are included in the analysis; four of these had received treatment in the past, two with surgery and two with continuous positive airway pressure.

Respiratory Disturbance Index

The mean RDI was 10.9 events/h (SD, 15.0; median, 5.1; interquartile range [IQR], 1.5 to 13.3). Fifty-one percent of subjects had RDI $\geqslant$ 5, 22% had RDI $\geqslant$ 15, and 10% had RDI $\geqslant$ 30. The mean RDI was greater in men (14.2 events/h) than in women (7.8 events/h), and increased with body mass index from 6.5 events/h in subjects in the lowest quartile (BMI $<$ 25 kg/m^2) to 15.2 events/h in those in the highest quartile (BMI $\geqslant$ 32 kg/m^2). Adjusting for sex and BMI by analysis of covariance, the mean RDI increased with age from 8.5 events/h in subjects $<$ 55 yr of age to 12.1 events/h in those 75 yr of age and older.

Sleepiness

The mean score on the ESS was 7.7 (SD, 4.5; median, 7; IQR, 4 to 11). In univariate analyses, men had higher mean scores on the ESS than did women (8.1 versus 7.4, $p = 0.001$), and subjects $\leqslant$ 65 yr of age had higher mean scores than did those $>$ 65 yr of age (8.0 versus 7.5, $p = 0.012$). The ESS score was inversely correlated with questionnaire-reported usual total sleep time on weekdays ($r_s = -0.09$, $p < 0.001$), and with the difference of usual total sleep time on weekdays minus usual total sleep time on weekends ($r_s = -0.08$, $p = 0.001$). The ESS score was lower in subjects reporting that they were awakened by leg cramps or leg jerks “never,” “rarely,” or “sometimes” than in those reporting these symptoms “often” or “almost always” (7.5 versus 9.2, $p < 0.001$).

The relation of RDI to sleepiness was assessed by dividing the subjects into four categories of RDI severity, using thresholds commonly employed in clinical practice: RDI $<$ 5 (n = 898), 5 $\leqslant$ RDI $<$ 15 (n = 524), 15 $\leqslant$ RDI $<$ 30 (n = 211), and RDI $\geqslant$ 30 (n = 191). A statistically significant linear increase in ESS score was present across all four categories of RDI, with an increased ESS score observed even in those subjects

TABLE 1

SUBJECT CHARACTERISTICS

Subjects, n	1,824
Age, yr*	65 (11)
Sex, female, %	51
Race/ethnicity	
White, non-Hispanic, %	72
Black, non-Hispanic, %	8
Hispanic, %	3
Native American, %	16
Asian/Pacific Islander, %	1
BMI, kg/m^2*	28.8 (5.4)
Usual sleep period, h*	7.4 (1.3)
RDI, events/h*	10.9 (15.0)
Epworth score*	7.7 (4.5)

* Values are mean with SD shown in parentheses.

TABLE 2

RELATION OF SLEEPINESS TO RESPIRATORY DISTURBANCE INDEX

	RDI < 5	5 ≤ RDI < 15	15 ≤ RDI < 30	RDI ≥ 30
Subjects, n	898	524	211	191
ESS score, mean (SD)*	7.2 (4.3)	7.8 (4.4)	8.3 (4.6)	9.3 (4.9)
ESS score, median*	6	7	8	9
ESS score ≥ 11, %*	21	28	28	35

Definition of abbreviations: ESS = Epworth Sleepiness Scale; RDI = respiratory disturbance index, defined as the number of apneas plus hypopneas per hour of sleep.
* $p < 0.001$ for difference between groups.

with the mildest elevation of RDI (Table 2 and Figure 1, *top panel*). The mean ESS score was 7.2 (SD 4.3) for subjects with RDI < 5, 7.8 (4.4) for subjects with RDI 5 to < 15, 8.3 (4.6) for subjects with RDI 15 to < 30, and 9.3 (4.9) for subjects with RDI ≥ 30 ($p < 0.001$ for difference between groups, $p < 0.001$ for test of linear trend). Analysis of variance and analysis of covariance techniques revealed no significant modification of the relation between RDI and ESS score by adjustment for age, sex, BMI, study center, usual total sleep time on weekdays, difference between weekday and weekend usual sleep time, or the presence of nocturnal leg cramps or leg jerks. After adjustment for all of these covariates (including either of the sleep-time variables but not both), the adjusted mean ESS scores for the four RDI categories were 7.3, 7.7, 8.2, and 9.1 ($p < 0.001$), little different from the unadjusted values. When excessive sleepiness was defined as an ESS score ≥ 11, the percentage of subjects with excessive sleepiness increased from 21% in those with RDI < 5, to 28% in those with RDI 5 to < 30, to 35% in those with RDI ≥ 30 ($p < 0.001$).

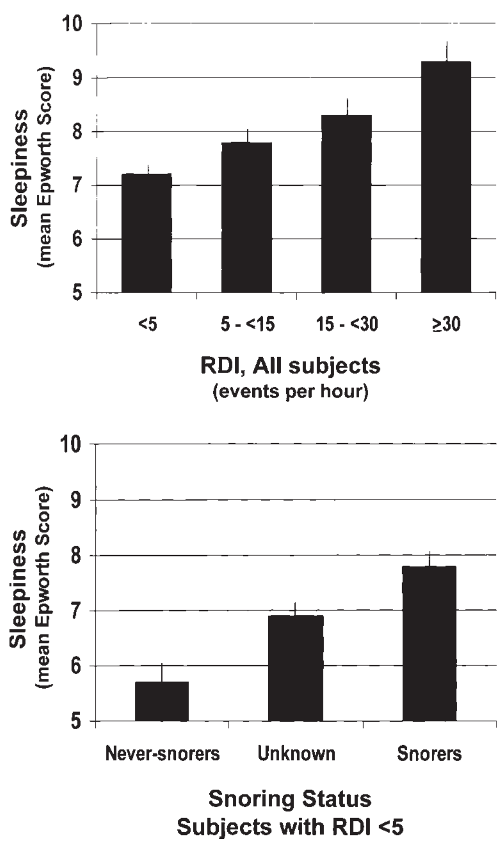

Figure 1. The relation of sleepiness to respiratory disturbance index (*top panel*), among all 1,824 subjects, and to snoring status (*bottom panel*), among 898 subjects with RDI < 5. Error bars are standard error. RDI = respiratory disturbance index.

On the basis of their responses to the questions "Have you ever snored?" and "How often do you snore?", the group with RDI < 5 was further divided into never-snorers (responding "No" to the first question), snorers (responding "Yes" to the first question and able to estimate frequency of snoring), and unknown (responding "Don't know" to the first question, or responding "Yes" but unable to estimate frequency of snoring). Never-snorers with RDI < 5 had a mean ESS score of 5.7 (SD 3.6), and 9.5% had an ESS score ≥ 11; snorers with RDI < 5 had a mean ESS score of 7.8 (4.5), and 25% had an ESS score ≥ 11 (Figure 1, *bottom panel*). Subjects whose snoring status was unknown were intermediate between snorers and never-snorers: mean ESS score was 6.9 (4.2), 25% with ESS score ≥ 11. Differences between snorers and never-snorers were significant for mean ESS score ($p < 0.001$) and prevalence of ESS score ≥ 11 ($p = 0.001$).

DISCUSSION

Excessive sleepiness is a common condition, reported by 5 to 12% of adult subjects in population surveys (1, 9, 22). The prevalence of moderate sleepiness is probably much higher: 25% of our subjects had an ESS score ≥ 11, the mean ESS score in a previously reported group of patients in whom mild OSAS had been diagnosed (8) and a level that is considered to represent abnormal daytime sleepiness. Sleepiness is associated with substantial morbidity, including adverse effects on job performance (2, 23), family relationships (3), and quality of life (3, 5). Sleepiness is also an important cause of motor vehicle accidents, which occur with greatest frequency in the early morning hours, with a secondary peak in the midafternoon, corresponding to the normal biphasic circadian rhythm of sleepiness (2). In a random sample of licensed drivers in the state of New York, 25% reported having fallen asleep at the wheel, and more than 4% reported having had a motor vehicle accident while asleep or drowsy (24). When evidence of sleepiness was systematically obtained after motor vehicle accidents, sleepiness was found to be a causal factor in more than 15% of these accidents (25). The annual cost of sleepiness-related motor vehicle and occupational accidents in the United States has been estimated to be as high as $56 billion (4).

Obstructive sleep apnea syndrome, an important cause of excessive sleepiness, has a prevalence commonly estimated at 1 to 4% of adults middle-aged and older (9, 10, 13). A much larger percentage of the population experiences nocturnal apneas and hypopneas without reporting excessive sleepiness. For example, in the study of Wisconsin state employees conducted by Young and colleagues (13), 9% of women and 24% of men 30 to 60 yr of age had a RDI ≥ 5, although only 2% of women and 4% of men had both a RDI ≥ 5 plus self-reported excessive sleepiness, defined as a report that ≥ 2 days per week the subject felt excessively sleepy during the daytime, woke up unrefreshed no matter how long he or she had slept, and had uncontrollable daytime sleepiness that interfered with daily living. Although the prevalence of hypersomnolence was approximately twice as great in subjects with RDI ≥ 5 than in those with RDI < 5, the investigators suggest that the use of a dichotomous variable to assess hypersomnolence may have underestimated the actual prevalence of excessive sleepiness.

In the present study, we employed an instrument that measures sleepiness on a 25-point scale, permitting the evaluation of more subtle differences in sleepiness. We have demonstrated that SDB, quantified by polysomnographic measurement of the RDI, is associated with excess sleepiness in a population of community-dwelling middle-aged and older adults recruited independent of the presence of sleep disorders. Moreover, this association is apparent even at very mild levels of elevation of RDI. The strength of this association is similar in men and women, and similar in those ⩽ 65 and those > 65 yr of age. Sleepiness was increased in those who reported sleeping for fewer hours per night, who had evidence of chronic restriction of sleep time as evidenced by a longer sleep period on weekends than on weekdays, or who had questionnaire evidence of periodic limb movement disorder or nocturnal leg cramps. The effect of RDI on sleepiness was, however, independent of these other causes of sleepiness.

The observed association between RDI and sleepiness is of a potentially important magnitude. Relative to subjects with RDI < 5, those with minimal (5 to < 15), mild (15 to < 30), and moderate to severe (⩾ 30) elevations of RDI had mean ESS scores that were increased by 8%, 15%, and 29%, respectively. When excessive daytime sleepiness was defined as an ESS score ⩾ 11, subjects with minimal to mild elevation of RDI were 33% more likely to have excessive sleepiness, whereas those with moderate to severe elevation of RDI were 67% more likely to have excessive sleepiness, when compared with subjects with RDI < 5. In patients with OSAS, sleep fragmentation by repeated arousals in response to apneas and hypopneas is the apparent cause of excessive sleepiness (26). It is likely that arousal from sleep in response to respiratory events also explains the association of RDI with sleepiness in our subjects.

The 21% prevalence of excessive sleepiness (ESS score ⩾ 11) in subjects with RDI < 5 is high, although it is similar to the frequency with which subjects having RDI < 5 report excessive daytime sleepiness ⩾ 2 days per week in the Wisconsin Sleep Cohort Study (13). Although there are many possible causes of sleepiness in these subjects, those with a low RDI may have mild SDB as evidenced by the presence of snoring. Young and colleagues (13) have shown that snorers with RDI < 5 are more likely than nonsnorers with RDI < 5 to report excessive sleepiness. Similarly, we found that among subjects with RDI < 5, snorers had a significantly higher mean ESS score than did never-snorers and were similar to subjects with minimally elevated RDI. This confirms the finding of the Wisconsin study that even among subjects with RDI < 5, SDB as indicated by snoring is associated with excess sleepiness.

Several potential limitations of this study should be considered. The study sample was recruited from among community-dwelling adult participants in ongoing longitudinal cohort studies. The sample differs from the adult U.S. population in its racial and ethnic composition, and may differ in other, unmeasured, characteristics; however, the sample was not selected on the basis of sleepiness, RDI, or known sleep disorders, and there is no reason to suspect that the selection methods would have introduced a bias in the RDI-ESS association. Adjustment by analysis of covariance for the parent cohort from which the subject had been recruited into the SHHS confirmed that center effects did not bias the relation between RDI and ESS score.

The RDI was measured using unattended, in-home PSG. Despite the lack of attendance by a trained technician during the night, all studies included in the analysis were of sufficient quality to perform both sleep staging and respiratory event scoring. Twenty-two percent of subjects had a RDI ⩾ 15. This figure appears high when compared with the 4% of women and 9% of men with RDI ⩾ 15 in the Wisconsin Sleep Cohort Study, although those subjects were considerably younger (30 to 60 yr of age) than our subjects (13). In contrast, Ancoli-Israel and colleagues (12) found that 44% of subjects 65 to 99 yr of age had RDI ⩾ 20. Direct comparisons of RDI across studies may be inappropriate, as differences in recording and scoring methods may influence the absolute magnitude of the RDI. More important, we found that RDI showed the expected relations to BMI and sex, two of the most important predictors of RDI in previous studies. Although it is accepted that RDI increases with age through at least age 60, it is controversial whether the RDI increases further beyond age 60. Our observation that RDI increases with age through our oldest age stratum (⩾ 75 yr) is consistent with the findings of Ancoli-Israel and colleagues of a statistically nonsignificant increase with age in the frequency of elevated RDI among subjects 65 to 89 yr of age. Thus, the unattended, in-home PSG performed in this study appears to provide a valid measurement of RDI.

Sleepiness was measured using a self-completion questionnaire, the Epworth Sleepiness Scale. This instrument provides a subjective measure of sleepiness based on the subject's perception of his or her likelihood of falling asleep rather than a measure of the actual time that is required for the subject to fall asleep, as in the Multiple Sleep Latency Test (MSLT), or the amount of time that they are able to stay awake in a soporific environment, as in the Maintenance of Wakefulness Test (MWT); however, the ESS is a well validated questionnaire that has been shown to reliably measure persistent daytime sleepiness in adults (19, 20). The ESS score has been shown to be inversely correlated with sleep latency on both the MSLT ($r = -0.42$) and the MWT ($r = -0.48$) (21, 27), and is higher in patients with OSAS, narcolepsy, or idiopathic hypersomnia than in apparently healthy control subjects (19). In patients with OSAS, the ESS score is positively correlated with RDI (8, 19) and falls significantly with effective treatment of the sleep apnea (20). Moreover, in a general population sample, the ESS score has been found to be significantly related to the likelihood of falling asleep while driving (28).

Sleepiness is multifactorial, and an elevated RDI is but one among many causes, including common nonmedical factors such as shift work and insufficient total sleep time, common illnesses such as insomnia, depression, and those conditions associated with chronic pain or dyspnea, as well as the less common disorders of excessive sleepiness such as narcolepsy and periodic limb movement disorder. Although the lack of a direct measure of limb movements is a limitation of this study, several consistent lines of reasoning suggest that the relation of RDI to sleepiness is not due to confounding by periodic limb movement disorder. First, we excluded apneas and hypopneas that appeared to follow an arousal. Second, questionnaire evidence of periodic limb movement disorder was associated with increased sleepiness, but it did not influence the relation of RDI to sleepiness. Third, periodic limb movement disorder is more common in the elderly, whereas the relation of RDI to sleepiness was similar in younger and older subjects. Similarly, questionnaire evidence of chronic restriction of sleep time was associated with increased sleepiness, but it did not influence the relation of RDI to sleepiness.

Measurements of both RDI and sleepiness are known to be somewhat imprecise. Night-to-night variability in RDI has been clearly demonstrated, and appears to be greatest in those with mildly elevated RDI (29). No "gold standard" for the measurement of sleepiness exists, and the various validated measures of sleepiness (MSLT, MWT, ESS) are only modestly correlated with one another, with correlation coefficients between 0.4 and 0.5 (21, 27, 30). The imprecision inherent in their measurement would therefore lead to a modest correlation between RDI and sleepiness even if there was a perfect correlation between "true" RDI and "true" sleepiness. This suggests that the present study may underestimate the true strength of the association between RDI and sleepiness. There is also substantial individual variation in the relation of sleep-related breathing disturbance to the physiologic arousal that results in sleepiness. This is exemplified by the condition known as the upper airways resistance syndrome, in which repetitive arousals occur in response to partial collapse of the upper airway, despite minimal if any detectable decrease in airflow (31). Conversely, some subjects with very high RDI will report only a normal degree of daytime sleepiness.

The magnitude of the relation between RDI and sleepiness observed in this study is nonetheless of potentially important public health impact, as fully half of our subjects are exposed to a level of RDI that is associated with increased sleepiness. Increased baseline sleepiness has been shown to increase the level of sleepiness experienced in response to shift work (32), and among the 25% of employees engaged in shift work (23) those with mildly elevated RDI may be at increased risk of poor job performance and occupational accidents. Baseline sleepiness is also known to potentiate the performance decrements associated with moderate alcohol consumption (33), and a mildly elevated RDI may therefore act synergistically with alcohol consumption to increase the risk of motor vehicle accidents. Persons with mildly elevated RDI may also be at increased risk for accidents after acute sleep restriction, as is quite common prior to long automobile trips (34). Consistent with this interpretation, it has recently been reported that among subjects participating in the Wisconsin Sleep Cohort Study, those with an RDI of 5 to 15 had a threefold increased odds of experiencing multiple motor vehicle accidents during the preceding 5 yr than were subjects with no evidence of SDB (35).

In summary, we have shown that in a sample of community-dwelling adults there is a significant association between sleepiness and polysomnographically measured RDI. Although the magnitude of the association between RDI and sleepiness appears modest, this study suggests that as much as half of the middle-aged and older adult population may be exposed to levels of RDI that are associated with increased sleepiness. Sleep-disordered breathing may therefore contribute substantially to the population burden of excessive sleepiness, an important cause of accidents, impaired social performance, and reduced quality of life.

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APPENDIX

Participating Institutions and SHHS Investigators

Field Centers

Framingham, MA: *Boston University*: George T. O'Connor, Sanford H. Auerbach, Emelia J. Benjamin, Ralph B. D'Agostino, Rachel J. Givelber, Daniel J. Gottlieb, Philip A. Wolf; *University of Wisconsin*: Terry B. Young.

Minneapolis, MN: *University of Minnesota*: Eyal Shahar, Conrad Iber, Mark W. Mahowald, Paul G. McGovern, Lori L. Vitelli.

New York, NY: *New York University*: David M. Rapoport, Joyce A. Walsleben; *Cornell University*: Thomas G. Pickering, Gary D. James; *State University of New York, Stonybrook*: Joseph E. Schwartz; *Columbia University (Harlem Hospital)*: Velvie A. Pogue, Charles K. Francis.

Sacramento, CA/Pittsburgh, PA: *University of California, Davis*: John A. Robbins, William H. Bonekat; *University of Pittsburgh*: Anne B. Newman, Mark Sanders.

Tucson, AZ/Strong Heart Study: *University of Arizona*: Stuart F. Quan, Michael D. Lebowitz, Paul L. Enright, Richard R. Bootzin, Anthony E. Camilli, Bruce M. Coull, Russell R. Dodge, Gordon A. Ewy, Steven R. Knoper, Linda S. Snyder; *Medlantic Research Institute–Phoenix Strong Heart*: Barbara V. Howard; *University of Oklahoma–Oklahoma Strong Heart*: Elisa T. Lee, J. L. Yeh; *Missouri Breaks Research Institute–Dakotas Strong Heart*: Thomas K. Welty.

Washington County, MD: *The Johns Hopkins University*: F. Javier Nieto, Jonathan M. Samet, Joel G. Hill, Alan R. Schwartz, Philip L. Smith, Moyses Szklo.

Coordinating Center

Seattle, WA: *University of Washington*: Patricia W. Wahl, Bonnie K. Lind, Coralyn W. Whitney, Richard A. Kronmal, Bruce M. Psaty, David S. Siscovick.

Sleep Reading Center

Cleveland, OH: *Case Western Reserve University*: Susan Redline, Carl E. Rosenberg, Kingman P. Strohl.

NHLBI Project Office

Bethesda, MD: James P. Kiley, Richard R. Fabsitz.