ORIGINAL ARTICLE

Slow-Wave Sleep Is Associated With Incident Hypertension: The Sleep Heart Health Study

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We sought to quantify the association between slow-wave (stage N3) sleep and hypertension in a large cohort of middle-aged men and women. Data from 1850 participants free of baseline hypertension from the Sleep Heart Health Study were analyzed. The primary exposure was percentage of N3 sleep on baseline in-home polysomnography and the primary outcome was incident hypertension, defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, and/or use of any blood pressure lowering medications at follow-up. Multivariable logistic regression models were adjusted for study site, age, sex, race, waist circumference, tobacco use, alcohol use, apnea–hypopnea index, nocturnal oxygen desaturation, sleep duration, sleep efficiency, and arousal index. Mean age was 59.4 ± 10.1 years and 55.5% were female. The mean baseline systolic and diastolic blood pressure was 118.8 and 70.6 mm Hg, respectively. Approximately 30% of the sample developed hypertension during a mean follow-up of 5.3 years. In the multi-adjusted model, participants in quartiles 1 (<9.8%) and 2 (9.8%–17.7%) of N3 sleep had significantly greater odds of incident hypertension compared with those in quartile 3 (17.7%–25.2%) (OR 1.69, 95% CI 1.21–2.36, p = .002 and OR 1.45, 95% CI 1.04–2.00, p = .03, respectively). No significant effect modification by sex on the N3-hypertension association was observed. In conclusion, compared with intermediate levels of N3 sleep (overlapping the "normal" adult range), lower levels of percent N3 sleep are associated with increased odds of incident hypertension in both men and women, independent of potential confounders, including indices of sleep apnea and sleep fragmentation.

Keywords: slow-wave sleep, stage N3, deep sleep, hypertension, blood pressure.

Statement of Significance

This is the largest prospective study to evaluate the association between N3 sleep and the development of hypertension. The study showed that among middle-aged, community-dwelling men and women, reduced N3 sleep is independently associated with an increased likelihood of developing hypertension, and that this association persisted after adjusting for sleep disordered breathing, sleep duration, measures of sleep fragmentation, and other potential confounders. This is the first time that this association has been reported in women and in middle-aged adults. Further research is needed to assess causal mechanisms underlying this association, to better understand the dose–response relationship between N3 sleep and hypertension, and to evaluate N3 sleep as a potential target for the prevention and treatment of hypertension.

INTRODUCTION

The importance of sleep to cardiovascular health has become increasingly apparent over the past few decades. There is accumulating evidence that sleep disorders,[1–3] poor sleep quality,[4] and short sleep duration[5,6] contribute to elevated blood pressure (BP). Sleep disordered breathing has additionally been shown to be causally associated with the development of hypertension.[7] There is less evidence regarding how sleep architecture, that is, the time spent in each distinct stage of sleep, affects cardiovascular health. Discrete sleep stages are linked to variations in the neuroendocrine and autonomic systems that regulate BP. Slow-wave sleep (also referred to as stages 3 and 4 or N3 sleep) is commonly referred to as "deep sleep" and is characterized by increased vagal tone and reduced sympathetic tone, and consequently decreased heart rate and BP.[8] Experimental studies of N3-sleep suppression in humans provide support for a role of N3 sleep in glucose homeostasis[9] and fluctuations in nocturnal BP.[10] It is therefore not surprising that a prospective study demonstrated that a low proportion of N3 sleep was associated with increased odds of incident hypertension. The study by Fung et al. of older men recruited from a community cohort showed that men with levels of N3 sleep in the lowest quartile had an increased adjusted odds (OR 1.83, 95% CI 1.18–2.85) of incident hypertension compared with men in the highest quartile of N3 sleep.[11] However, the generalizability of these findings to women and younger participants is unknown. The importance of considering generalizability to women is of interest, given evidence that N3 sleep declines more significantly with age in men than in women.[12] Therefore, we sought to determine whether N3 sleep is associated with incident hypertension in a large cohort of middle-aged men and women and to assess whether this association varies by sex. We hypothesized that N3 sleep is inversely associated with incident hypertension in both men and women, although the association would be stronger in men than in women.

METHODS

Study Design and Population

The sample was derived from the Sleep Heart Health Study (SHHS), a community-based, prospective cohort study designed to evaluate the cardiovascular consequences of sleep-disordered breathing. The methodology of the SHHS has been published.[13] Briefly, 6441 women and men aged 40 or older were recruited from seven larger "parent" cohorts and underwent a baseline examination (1995–1998) including a Sleep Habits Questionnaire, anthropometric and BP measurements, and overnight unattended polysomnography (PSG). Participants underwent a second examination (2001–2003) after a mean follow-up of 5.3 years, at which time BP measurements were repeated. The present study includes 1850 participants with complete PSG and BP data who were free of hypertension at baseline, with available data for analysis (see Figure 1 for details). Institutional Review Board approval was obtained at all

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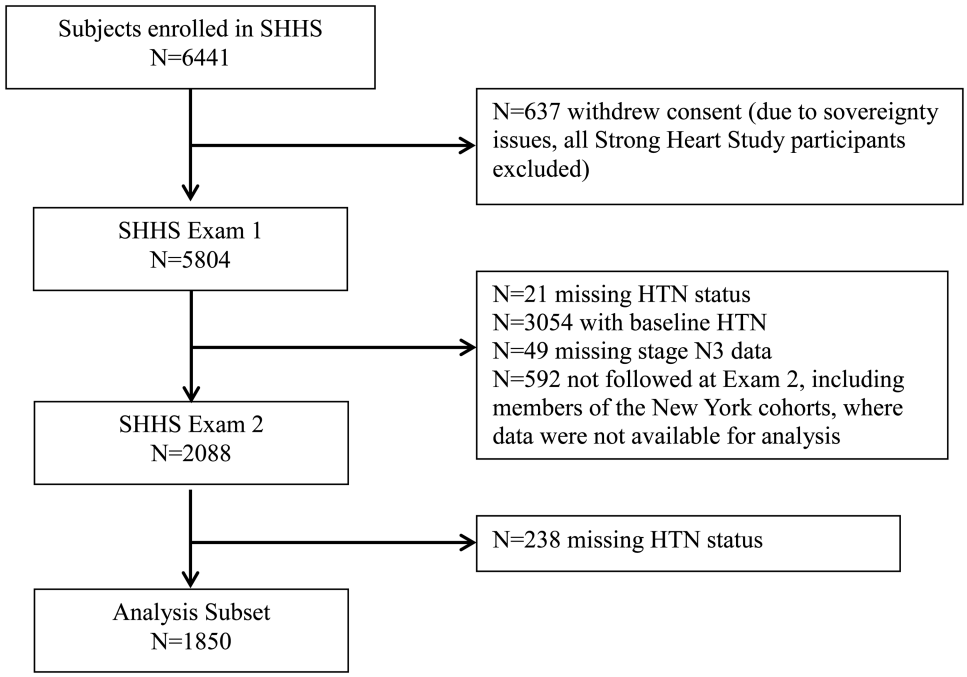

Figure 1—Flow diagram representing process from initial participant enrollment to final analytic subset.

participating institutions and all participants signed informed consent.

Outcome Definition and Covariates

At baseline and at follow-up, BP was measured manually in triplicate in a seated position after 5 minutes of rest. The average of the second and third measurements was used for this analysis. Hypertension was defined as a systolic BP ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg, and/or use of antihypertension medications. Questionnaires were administered to determine participant demographics, alcohol use, and smoking history, and medication use was ascertained by interview at each examination. Waist circumference was obtained from data collected by the parent studies.

As previously described,[13,14] in-home, single-night, unattended PSGs were performed and scored at a central reading center.[14] All sleep covariates were obtained from PSG. Percent N3 (SWS) sleep was defined as the percentage of total sleep time scored as N3 and, along with all other sleep stages, was scored using the standard criteria at that time.[15] Apnea–hypopnea index (AHI) was defined as the number of apneas and hypopneas per hour of sleep using a requirement for a 4% oxygen desaturation for hypopneas. Nocturnal hypoxemia was defined as the percentage of sleep time spent with oxygen saturation of <90%. The arousal index represents the number of EEG cortical arousals per hour of sleep. Sleep efficiency was defined as sleep duration divided by time in bed, where sleep duration was the total minutes spent sleeping as measured on PSG.

Statistical Analysis

Differences in sample characteristics across quartiles of percent N3 sleep and by incident hypertension were assessed using the Kruskal–Wallis test for continuous variables and chi-square test for categorical variables. To account for potential nonlinear associations, percent N3 sleep was categorized into quartiles. Incident hypertension was modeled using multivariable logistic regression models with N3-sleep quartile as the exposure of interest, adjusted for age, sex, race, site, waist circumference, alcohol use, and pack years of smoking. Quartile 3 was chosen as the referent as the values for the percentage of slow-wave sleep in this category overlapped the mean N3 level reported as "normal" in adults[16] and because it had the lowest incidence of hypertension. Additional models were adjusted for AHI, arousal index, percentage of time spent with oxygen saturation of <90%, sleep duration, sleep efficiency, and use of antidepressants (tricyclic and nontricyclic) or benzodiazepines. In secondary analysis, the same multivariable logistic regression models were repeated using quartiles of absolute time in slow-wave sleep as the exposure. Given our a priori hypothesis that results may vary by sex, an interaction was tested between percent N3 sleep and sex. SAS 9.4 (SAS Institute, Cary, NC) was used to conduct analyses.

RESULTS

Baseline Characteristics

The mean age of the sample was 59 ± 10.1 years; approximately 55% were female and 88% were white. At baseline, mean systolic BP was 118.8 ± 11 mm Hg and mean diastolic BP was 70.6 ± 8 mm Hg (Table 1). In univariate analysis, individuals in the lowest quartile of percent N3 sleep (<9.8%) were significantly older, more likely to be male, have a higher waist circumference, and report increased alcohol intake and pack-years smoked. Those in the lowest quartile also had a higher AHI and arousal index and a lower sleep efficiency. They also spent a greater percentage of sleep time in stages N1 and N2 sleep and

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Table 1—Baseline Sample Characteristics by Quartiles of Stage N3 Sleep.

	Overall sample *N* = 1850	Quartile 1 <9.8% *N* = 462	Quartile 2 9.8–17.7% *N* = 463	Quartile 3 17.7–25.2% *N* = 462	Quartile 4 >25.2% *N* = 463	*p*
Age	59.4 ± 10.1	61.2 ± 10.3	58.5 ± 10.1	58.1 ± 10.1	59.8 ± 9.8	<.0001
Male	824 (44.5)	333 (72)	229 (49.5)	163 (35.3)	99 (21.4)	<.0001
Race						
White	1624 (87.8)	398 (86.1)	409 (88.3)	406 (87.9)	411 (87.9)	.13
Black	81 (4.4)	31 (6.7)	20 (4.3)	17 (3.7)	13 (2.8)	
Other	145 (7.8)	33 (7.1)	34 (7.3)	39 (8.4)	39 (8.4)	
Parent Cohort						
CHS	207 (11.2)	65 (14.1)	47 (10.2)	43 (9.3)	52 (11.2)	.05
ARIC	758 (41.0)	179 (38.7)	183 (39.5)	191 (41.3)	205 (44.3)	
Framingham	472 (25.5)	100 (21.7)	123 (26.6)	130 (28.1)	119 (25.7)	
Tucson	413 (22.3)	118 (25.5)	110 (23.8)	98 (21.2)	87 (18.8)	
Body mass index, kg/m^2	27.6 ± 4.6	27.7 ± 4.0	27.6 ± 4.5	27.4 ± 4.7	27.6 ± 5.2	.15
Waist circumference, cm	94.7 ± 13.2	96.8 ± 11.8	94.7 ± 12.8	93.6 ± 13.9	93.7 ± 14.0	<.0001
Alcohol use (yes/no)	2.7 ± 5.1	3.5 ± 6.4	2.8 ± 4.9	2.6 ± 5.1	1.8 ± 3.6	.0005
Pack years smoked	11.3 ± 17.8	15.0 ± 20.4	11.1 ± 18.1	9.5 ± 15.6	9.6 ± 16.1	<.0001
Systolic BP, mm Hg	118.8 ± 11.1	119.8 ± 10.6	118.9 ± 11.3	117.6 ± 11.1	119.0 ± 11.3	.01
Diastolic BP, mm Hg	71.4 ± 8.4	72.0 ± 8.2	71.7 ± 8.7	70.9 ± 8.2	71.1 ± 8.5	.005
AHI	6.7 ± 10.0	8.5 ± 11.8	7.4 ± 10.4	5.5 ± 7.6	5.7 ± 9.6	<.0001
% N1 sleep	5.1 ± 3.5	7.0 ± 4.3	5.4 ± 3.1	4.5 ± 2.9	3.5 ± 2.4	<.0001
% N2 sleep	55.9 ± 11.0	67.5 ± 7.0	58.6 ± 6.6	53.5 ± 6.4	43.9 ± 7.9	<.0001
% REM sleep	20.8 ± 5.9	20.9 ± 6.1	21.9 ± 5.8	20.8 ± 5.8	19.6 ± 5.6	<.0001
Arousal index, events/hour	18.0 ± 9.3	21.0 ± 11.0	19.1 ± 9.6	16.6 ± 7.5	15.3 ± 7.6	<.0001
Sleep efficiency, %	87.7 ± 8.4	86.3 ± 8.8	88.3 ± 7.7	88.5 ± 8.2	87.6 ± 8.6	<.0001
% Sleep time with SaO_2 <90%	2.2 ± 6.8	2.7 ± 7.2	2.3 ± 7.4	1.9 ± 6.5	1.8 ± 5.8	.0009
Sleep duration, minutes	375.2 ± 58.2	368.5 ± 58.9	385.4 ± 53.6	378.2 ± 59.4	368.5 ± 59.2	<.0001
Benzodiazepine use	60 (3.2)	21 (4.6)	12 (2.6)	12 (2.6)	15 (3.2)	.29
Tricyclic antidepressant use	40 (2.2)	9 (2.0)	11 (2.4)	8 (1.7)	12 (2.6)	.80
Non-tricyclic antidepressant use	78 (4.2)	15 (3.2)	15 (3.2)	27 (5.8)	21 (4.5)	.15

Values are *n* (%) or mean ± *SD* unless otherwise specified.
BP indicates blood pressure; AHI = apnea–hypopnea index with 4% oxygen desaturation; ARIC = Atherosclerosis Risk in Communities Study; CHS = Cardiovascular Health Study; SaO_2 = oxygen saturation.

had greater nocturnal oxygen desaturation. Individuals in the lowest and highest quartiles of percent N3 sleep had shorter sleep duration than the middle quartiles.

A total of 550 participants (29.2%) developed hypertension at the 5-year follow-up exam. Compared with those without hypertension, those who developed hypertension were significantly older, had higher BMI and waist circumference, smoked more, and were more likely to report use of tricyclic antidepressants (Table 2). They also had higher AHI and worse sleep quality with increased arousal index, lower sleep efficiency, and total sleep duration and spent more sleep time with oxygen saturation of <90%. Incident hypertension was more common in individuals from older parent cohorts (Cardiovascular Health Study [CHS] and Atherosclerosis Risk in Communities Study [ARIC]) than the younger cohorts (Framingham Heart Study and the Tucson Epidemiologic Study of Airway Obstructive Diseases [TES] and the Tucson Health and Environment Study [H&E]).

Slow-Wave Sleep and Incident Hypertension

Participants in the lowest quartile of N3 sleep (<9.8% time in N3) had the highest incidence of hypertension (n = 166 or 36.4%), whereas those in quartile 3 (17% to 25%) had the lowest incidence of hypertension (n = 106, 22.9%) (Figure 2).

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Table 2—Baseline Sample Characteristics by Presence or Absence of Incident Hypertension.

	Incident hypertension *N* = 550	No incident hypertension *N* = 1334	*p*
Age	63.0 ± 9.6	58.0 ± 10.1	<.0001
Male	257 (46.7)	581 (43.6)	.21
Race			
White	487 (88.6)	1165 (87.3)	.03
Black	32 (5.8)	55 (4.1)	
Other	31 (5.6)	114 (8.6)	
Parent cohort			
CHS	97 (17.6)	122 (9.2)	<.0001
ARIC	252 (45.8)	516 (38.7)	
Framingham	114 (20.7)	363 (27.2)	
Tucson	87 (15.8)	333 (25.0)	
Body mass index, kg/m^2	28.7 ± 5.0	27.1 ± 4.4	<.0001
Waist circumference, cm	98.3 ± 13.4	93.1 ± 12.9	<.0001
Alcohol use (yes/no)	5.3 ± 2.9	2.6 ± 5.0	.29
Pack years smoked	14.1 ± 20.4	10.3 ± 16.6	.0004
Average systolic BP, mm Hg*	124.8 ± 9.8	116.4 ± 10.7	<.0001
Average diastolic BP, mm Hg*	72.6 ± 9.0	70.9 ± 8.1	<.0001
AHI	8.4 ± 11.9	6.1 ± 9.1	<.0001
% N1 sleep	5.3 ± 3.7	5.0 ± 3.4	.17
% N2 sleep	57.1 ± 11.4	55.4 ± 10.9	.002
% N3 sleep	16.9 ± 11.6	18.1 ± 10.9	.0007
% REM sleep	20.6 ± 5.9	20.9 ± 5.8	.25
Arousal index, events/hour	19.1 ± 10.3	17.6 ± 8.8	.012
Sleep efficiency, %	86.8 ± 8.8	88.0 ± 8.3	.001
% Sleep time with SaO_2 <90%	3.2 ± 8.1	1.7 ± 6.0	<.0001
Sleep duration, minutes	366.6 ± 62.1	378.3 ± 56.7	.0006
Benzodiazepine use	24 (4.4)	38 (2.9)	.09
Tricyclic antidepressant use	20 (3.6)	20 (1.5)	.003
Non-tricyclic antidepressant use	20 (3.6)	61 (4.6)	.36

Values are *n* (%) or mean ± *SD* unless otherwise specified.
BP indicates blood pressure; AHI = apnea–hypopnea index with 4% oxygen desaturation; ARIC = Atherosclerosis Risk in Communities Study; CHS = Cardiovascular Health Study; SaO_2 = oxygen saturation.

Table 3 demonstrates the associations between quartiles of N3 sleep with incident hypertension using quartile 3 as the reference. In the primary model, adjusting for age, sex, race, study site, waist circumference, pack years of smoking, and alcohol use, there remained a significant difference in incident hypertension across quartiles of N3 sleep (p = .017, Table 3). Post hoc tests comparing individual quartiles demonstrate that participants in quartiles 1 and 2 each had significantly higher odds of developing hypertension compared with quartile 3 such that those in quartile 1 had 69% higher odds of developing hypertension and those in quartile 2 had 45% greater odds of developing hypertension. No significant differences were observed between the highest two quartiles of N3 sleep. These associations did not substantially change after additionally adjusting for AHI, arousal index, nocturnal hypoxemia, total sleep duration, sleep efficiency, and use of antidepressants and benzodiazepines in separate models. Furthermore, after adjusting for both AHI and sleep duration in the same model, participants in the lowest quartiles of N3 sleep still had higher odds of incident hypertension compared with those in quartile 3.

Additional Analysis

Secondary analysis was conducted using absolute time in stage-N3 sleep as the exposure, again, with quartile 3 as the reference group. No differences were observed when using absolute time in stage N3 versus percentage of N3 sleep. These results are presented in Table 4.

We did not find any significant variation in self-reported habitual sleep duration across the quartiles of N3 sleep (results not shown). Given our a priori hypothesis that results may vary by sex, an interaction term between percent N3 sleep and sex was also tested but was not statistically significant (p-interaction = .50).

DISCUSSION

This large prospective cohort study of middle-aged women and men showed that relative to intermediate levels of N3 (in a range considered to be "normal"), decreased N3 sleep was associated with increased odds of developing hypertension at a mean follow-up duration of 5.3 years. Furthermore, this association persisted after considering direct measurements of sleep disordered breathing, sleep duration, measures of fragmented sleep, or other potential confounders. Together, these results suggest that reductions in N3 sleep are likely to be an independent risk factor for hypertension. Our results are consistent with the only prior study evaluating the relationship between N3 sleep and incident hypertension, which demonstrated that older men with the lowest quartile of N3 sleep had a 1.8-fold increased risk of incident hypertension compared with men with the highest quartile of N3 sleep.[11] The higher mean percent N3 sleep observed in our study compared with that of Fung et al. is in keeping with the younger age of our cohort (mean age 59.4 vs. 75.1 years), as previous studies have consistently shown percent N3 sleep to decrease with increasing age.[17] The results of this study extend the literature by confirming these findings in middle-aged men and women using the largest study sample size to date. A key difference between our study and Fung et al. is that the protective effect of N3 sleep on the development of hypertension was highest in quartile 3 and not in quartile 4 (>25.2%). In fact, participants in quartile 4 had slight, albeit nonsignificant, increased odds of incident hypertension compared with those in quartile 3 (OR 1.2, 95% CI 0.86–1.68, p = .30). This may be explained by

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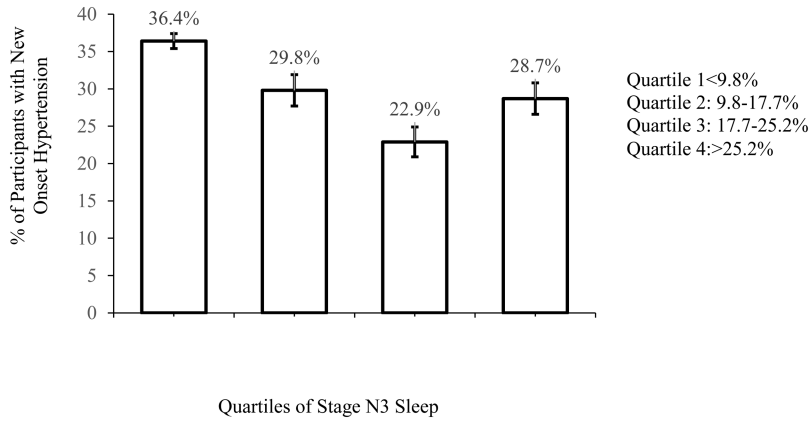

Figure 2—Bar graph demonstrating the percentage of participants who developed hypertension during a mean follow-up of 5.3 years (range of 4.7–7.1 years) among each quartile of stage N3 (slow-wave) sleep.

Table 3—Odds (95% Confidence Interval) of Incident Hypertension by Quartiles of N3 Sleep.

Model	Q1 <9.8% *N* = 462	Q2 9.8–17.7% *N* = 463	Q3 17.7–25.2% *N* = 462	Q4 >25.2% *N* = 463	Global *p*-value
Model 1[a]	1.69 (1.21–2.36) *p* = .002	1.45 (1.04–2.00) *p* = .03	Referent	1.20 (0.86–1.68) *p* = .3	.017
Model 1 + AHI 4%	1.68 (1.20–2.36) *p* = .002	1.44 (1.03–2.00) *p* = .03	Referent	1.20 (0.86–1.68) *p* = .28	.019
Model 1 + arousal index	1.69 (1.21–2.37) *p* = .002	1.45 (1.04–2.02) *p* = .03	Referent	1.20 (0.86–1.68) *p* = .28	.018
Model 1 + % sleep time with SaO_2 <90%	1.69 (1.21–2.36) *p* = .002	1.44 (1.03–2.00) *p* = .03	Referent	1.21 (0.86–1.68) *p* = .27	.018
Model 1 + sleep duration	1.70 (1.21–2.38) *p* = .002	1.49 (1.07–2.07) *p* = .02	Referent	1.18 (0.85–1.65) *p* = .3	.013
Model 1 + sleep efficiency	1.69 (1.21–2.36) *p* = .002	1.45 (1.04–2.01) *p* = .03	Referent	1.18 (0.85–1.65) *p* = .28	.018
Model 1 + antidepressants and benzodiazepines	1.65 (1.17–2.3) *p* = .004	1.43 (1.03–1.98) *p* = .03	Referent	1.18 (0.85–1.65) *p* = .30	.027
Model 1 + AHI + sleep duration	1.70 (1.21–2.38) *p* = .002	1.48 (1.07–2.10) *p* = .02	Referent	1.20 (0.86–1.68) *p* = .33	.013

[a]Model 1: adjusted for age, race, sex, waist circumference, alcohol use, pack years, and study site.
AHI indicates apnea–hypopnea index with 4% oxygen desaturation and SaO_2 = oxygen saturation.

the differences in the distributions of N3 sleep across quartiles between the two studies (quartiles 3 and 4 percent N3 sleep in Fung et al. were 10.2%–16.9% and >16.9%, respectively, compared with 17.7%–25.2% and >25.2% in the present study). Quartile 3 percent N3 sleep in the present study is comparable with the level of N3 sleep reported in healthy middle-aged adults[16,17] and is comparable with quartile 4 in the study by Fung et al. Although larger samples may be needed to evaluate whether there is an increased risk of hypertension associates with high proportions of SWS, it is of interest that the "j-shape" relationship observed parallels that between sleep duration and several cardiovascular outcomes and cardiometabolic risk factors.[18–20] It is possible that high percentage of N3 sleep may be a surrogate marker for unmeasured comorbidity that may itself predispose to the development of hypertension. In accordance with our findings, an experimental study of selective N3 sleep suppression via EEG-guided nocturnal acoustic stimuli in healthy human subjects demonstrated attenuation in mean arterial BP dipping during the first half of the night, when N3 sleep predominates.[10]

The primary mechanism underlying the relationship between reduced N3 sleep and increased nocturnal BP is probably related to alterations in autonomic nervous system activity during N3 sleep. N3 sleep is characterized by a reduction in sympathetic nervous system activity, increased parasympathetic activity, and subsequent reductions in heart rate and BP.[8,10,20] It is possible that chronically increased nocturnal elevations in BP may lead to persistent elevations of BP during the day, either through

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Table 4—Odds (95% Confidence Interval) of Incident Hypertension by Quartiles of Absolute Time in N3 Sleep.

Model	Q1 <36.5 min *N* = 462	Q2 36.5–66.5 min *N* = 463	Q3 66.5–95.0 min *N* = 462	Q4 >95 min *N* = 463	Global *p*-value
Model 1[a]	1.86 (1.33–2.62) *p* = .0003	1.46 (1.05–2.04) *p* = .02	Referent	1.13 (0.81–1.6) *p* = .46	.002
Model 1 + AHI 4%	1.86 (1.32–2. 61) *p* = .002	1.46 (1.04–2.04) *p* = .03	Referent	1.13 (0.81–1.60) *p* = 0.28	.002
Model 1 + arousal index	1.88 (1.34–2.64) *p* = .0003	1.47 (1.05–2.06) *p* = .02	Referent	1.13 (0.81–1.69) *p* = .47	.002
Model 1 + % sleep time with SaO_2 <90%	1.86 (1.33–2.62) *p* = .0003	1.45 (1.04–2.03) *p* = .03	Referent	1.13 (0.81–1.60) *p* = .45	.002
Model 1 + sleep duration	1.83 (1.3–2.58) *p* = .0004	1.46 (1.05–2.03) *p* = .03	Referent	1.16 (0.83–1.62) *p* = .4	.004
Model 1 + sleep efficiency	1.87 (1.33–2.62) *p* = .0003	1.47 (1.05–2.04) *p* = .02	Referent	1.13 (0.81–1.59) *p* = .46	.002
Model 1 + antidepressants and benzodiazepines	1.86 (1.32–2.61) *p* = .0003	1.48 (1.06–2.07) *p* = .02	Referent	1.14 (1.06–2.07) *p* = .46	.002
Model 1 + AHI + sleep duration	1.83 (1.30–2.58) *p* = .0005	1.46 (1.04–2. 03) *p* = .02	Referent	1.20 (0.83–1.63) *p* = .4	.004

[a]Model 1: adjusted for age, race, sex, waist circumference, alcohol use, pack years, study site.
AHI indicates apnea–hypopnea index with 4% oxygen desaturation and SaO_2, oxygen saturation.

sustained changes in sympathetic–parasympathetic tone or by causing vascular damage, as has been postulated for the association between nocturnal hypertension, sleep disordered breathing, and daytime hypertension.[21] To that end, Tasali et al. demonstrated that selective N3 sleep suppression during three successive nights resulted in a shift toward higher sympathetic nervous activity as measured by spectral analysis of daytime heart rate variability. However, mean plasma cortisol profiles were unchanged after selective N3 sleep deprivation.[9]

Our results do not address the question of whether it is possible to reduce the risk of hypertension in selected patients through enhancement of N3 sleep. Recently, there has been growing interest in enhancement of N3 sleep by various mechanisms, primarily to improve cognitive or memory deficits, or to improve adverse behavioral, psychological, and physiologic changes resulting from sleep deprivation. Studies assessing effects of drugs,[22,23] transcranial direct-current stimulation, transcranial magnetic stimulation, acoustic stimulation,[24] and exercise intensity[25] on stage N3 sleep suggest that this is a modifiable trait and therefore a potential therapeutic target.

Strengths of this study include the use of standardized and objective measurements of sleep parameters using PSG, reducing error and improving precision. Use of a large community sample increases generalizability and this is the first study to report these findings in women and in middle-aged men. Limitations include lack of 24-hour ambulatory BP monitoring to fully describe diurnal BP changes. We also only measured N3 sleep using one night of PSG. However, prior research has shown N3 sleep to have high night-to-night reproducibility.[26] It is possible that individuals who had poorer sleep quality during PSG also are both more sensitive to environmental changes and are at increased risk for hypertension. Lastly, we did not have information on all antipsychotic medications or antiepileptic medications, which are known to affect stage N3 sleep. However, in our community sample, it is probably that such medication use would be uncommon.

In summary, after controlling for potential confounders including indices of sleep apnea, lower levels of percent N3 sleep are associated with increased odds of incident hypertension in both men and women.

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