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Hypertension published online Sep 4, 2007;
DOI: 10.1161/HYPERTENSIONAHA.107.095471
Hypertension is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0194-911X. Online ISSN: 1524-4563

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Abstract—Sleep deprivation (≤5 hour per night) was associated with a higher risk of hypertension in middle-aged American adults but not among older individuals. However, the outcome was based on self-reported diagnosis of incident hypertension, and no gender-specific analyses were included. We examined cross-sectional and prospective associations of sleep duration with prevalent and incident hypertension in a cohort of 10 308 British civil servants aged 35 to 55 years at baseline (phase 1: 1985–1988). Data were gathered from phase 5 (1997–1999) and phase 7 (2003–2004). Sleep duration and other covariates were assessed at phase 5. At both examinations, hypertension was defined as blood pressure ≥140/90 mm Hg or regular use of antihypertensive medications. In cross-sectional analyses at phase 5 (n=5766), short duration of sleep (≤5 hour per night) was associated with higher risk of hypertension compared with the group sleeping 7 hours, among women (odds ratio: 2.01; 95% CI: 1.13 to 3.58), independent of confounders, with an inverse linear trend across decreasing hours of sleep (P=0.003). No association was detected in men. In prospective analyses (mean follow-up: 5 years), the cumulative incidence of hypertension was 20.0% (n=740) among 3691 normotensive individuals at phase 5. In women, short duration of sleep was associated with a higher risk of hypertension in a reduced model (age and employment) (6 hours per night: odds ratio: 1.56 [95% CI: 1.07 to 2.27]; ≤5 hour per night: odds ratio: 1.94 [95% CI: 1.08 to 3.50] versus 7 hours). The associations were attenuated after accounting for cardiovascular risk factors and psychiatric comorbidities (odds ratio: 1.42 [95% CI: 0.94 to 2.16]; odds ratio: 1.31 [95% CI: 0.65 to 2.63], respectively). Sleep deprivation may produce detrimental cardiovascular effects among women. (***Hypertension*. 2007;50:694-701.**)

Key Words: sleep duration ■ blood pressure ■ hypertension ■ gender differences ■ confounders ■ comorbidities

Sleep-disordered breathing (SDB) has been linked to elevated blood pressure and risk of hypertension in several epidemiological observational studies.[1–5] Growing evidence indicates that sleep deprivation is also associated with a number of health outcomes, including hypertension.[6–14] For example, in a recent longitudinal analysis of the first National Health And Nutrition Examination Survey (NHANES-I), short sleep duration (≤5 hours per night) was associated with a 60% higher risk of incident hypertension in middle-aged (32 to 59 years) American adults without apparent sleep disorders during a mean follow-up of 8 to 10 years.[13] No association was found in individuals ≥60 years of age. However, the outcome was based on self-reported diagnosis of incident hypertension, and no gender-specific analyses were included. Furthermore, a cross-sectional analysis from the Sleep Heart Health Study on a sample of ≈6000 US adults showed a significant higher prevalence of hypertension among individuals with usual sleep duration above or below the median of 7 to <8 hours per night.[14] The association was stronger, ie, a 66% higher risk of hypertension, among short sleepers (<6 hours per night). Although this study attempted to account for a number of potential confounders, including psychiatric and cardiovascular comorbidities, the cross-sectional design did not allow inference on the temporal relationship between sleep duration and hypertension.

Several studies in humans indicate potential pathophysiological mechanisms supporting the biological plausibility of the association between sleep deprivation and hypertension. For example, acute curtailments of sleep may induce an overactivity of the sympathetic nervous system leading to higher blood pressure in both normotensive and hypertensive individuals.[15–17] Other contributing mechanisms may include overactivity of the renin-angiotensin-aldosterone system,

Received May 30, 2007; first decision June 24, 2007; revision accepted August 3, 2007.

From the Clinical Sciences Research Institute (F.P.C., S.S., N-B.K., M.A.M., F.M.T.), Warwick Medical School, Coventry, United Kingdom; and the International Centre for Health and Society (M.K., J.E.F., M.J.S., E.J.B., M.G.M.), University College London Medical School, London, United Kingdom.

Correspondence to Francesco P. Cappuccio, Clinical Sciences Research Institute, Warwick Medical School, UHCW Campus, Clifford Bridge Rd, Coventry CV2 2DX, United Kingdom. E-mail sleepresearch@warwick.ac.uk

Hypertension **is available at http://hyper.ahajournals.org** **DOI: 10.1161/HYPERTENSIONAHA.107.095471**

proinflammatory responses, endothelial dysfunction, and renal impairment.[18,19] On the other hand, intervention studies to improve duration and quality of sleep have been effective in reducing both daytime and nighttime blood pressures.[19,20] However, there is concern that sleep habits may represent a marker of health status and quality of life rather than a casual factor for hypertension and other health outcomes.[21]

In the present analysis, we sought to examine both the cross-sectional and prospective associations of sleep duration with prevalent and incident hypertension in the Whitehall II Study, a prospective cohort of 10 308 white-collar British civil servants aged 35 to 55 at baseline (phase 1: 1985–1988). Because reduced durations of sleep might be associated with more detrimental effects on cardiovascular outcomes among women,[6–9] unlike previous investigations, we conducted gender-specific analyses with the inclusion of a number of potential confounding variables.

Methods

Study Population

The Whitehall II Cohort was recruited in 1985–1988 (phase 1) from 20 London-based civil service departments. The rationale, design, and methods of the study have been described in detail elsewhere.[22] Briefly, the initial response rate was 73%, and the final cohort consisted of 10 308 participants; 3413 women and 6895 men. Follow-up screening examinations took place in 1991–1993 (phase 3), 1997–1999 (phase 5), and 2003–2004 (phase 7), whereas postal questionnaires were sent to participants in 1989 (phase 2), 1995 (phase 4), and 2001 (phase 6). The participation rates of the original cohort (n=10 308) were 83%, 76%, and 68% at phases 3, 5, and 7, respectively. In this report, we used data from phases 5 and 7. The total sample at phase 5 consisted of 7204 participants. The present analyses were restricted to white individuals (n=6592), given the low numbers of other ethnic groups (n=612). For the cross-sectional analyses, only participants with a complete set of data at phase 5 were included (n=5766; 4199 men and 1567 women). Their characteristics were comparable to the overall sample (see Appendix). For the longitudinal analyses, the incidence of hypertension at phase 7 was assessed among participants who were normotensive at phase 5 (n=3691: 2686 men and 1005 women).

Sleep Duration

At phases 5 and 7, sleep duration was elicited by the question, "How many hours of sleep do you have on an average week night?" Response categories were ≤5 hours, 6 hours, 7 hours, 8 hours, and ≥9 hours.

Covariates

For the present analyses, age and other covariates were derived from the questionnaires at phase 5. Employment grade was determined from the participant's last known civil service grade title (19% had retired by phase 5) and divided into 3 categories in order of decreasing salary: administrative, professional/executive, and clerical/support. Participants were allocated to 1 of 4 smoking categories: never, ex-smoker, pipe and/or cigar only, or current cigarette smoker (manufactured or hand-rolled cigarettes). Alcohol consumption in the previous week was recorded (units per week). Leisure-time physical activity was categorized by energy use in 2 categories: "vigorous" (subjects who reported ≥1.5 hour of vigorous activity per week) and no vigorous activity. General health status was assessed using the physical and mental health component summaries of the Short Form-36 (SF-36) health survey questionnaire[23]: low scores indicate low functioning. Psychiatric morbidity, including depression, was assessed with a modified General Health Questionnaire score. Participants taking sleep medication (hypnotics) or cardiovascular drugs were identified through a questionnaire item on current medication. At both phase 5 and 7 screening examinations, anthropometric measures were recorded, including height, weight, and waist circumference; body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Blood pressure was measured 3 times using a standard mercury manometer by trained and certified technicians in both examinations. The onsets of the first-phase (systolic) and fifth-phase (diastolic) Korotkoff sounds were recorded. The mean of the second and third measures were used in the analyses. At both examinations, hypertension was defined as blood pressure ≥140/90 mm Hg or regular use of antihypertensive medications.

Ethical Approval

Ethical approval for the Whitehall II Study was obtained from the University College London Medical School committee on the ethics of human research.

Statistical Analysis

For continuous and categorical variables, respectively, Kruskal Wallis and χ^2 tests were used to determine the statistical significance of any difference in the distribution of baseline variables at phase 5 across categories of sleep duration. The statistical significance of the interaction between each baseline characteristic and sleep duration, adjusted for other important baseline variables, was tested in multivariate logistic regression models that included this interaction and the corresponding main effect terms. The interaction between sleep duration and gender was significant (P<0.05); therefore, all of the analyses were stratified by gender. No significant interactions were found between sleep duration and age or other relevant covariates. Univariate and multivariate regression analyses were conducted to test the association between categories of sleep duration and prevalent hypertension at phase 5 (cross-sectional analyses), as well as the association between sleep duration at phase 5 and incident hypertension at phase 7 (prospective analyses). Covariates included the following: baseline age, employment, alcohol consumption, smoking, physical activity, BMI, cardiovascular disease (CVD) drugs (other than antihypertensive medications), the SF-36 mental and physical health component scores, depression, and use of hypnotics. In these analyses, 7 hours of sleep was selected as the reference category. All of the techniques were implemented using Stata 9.0.

Results

Descriptives

Characteristics for both male and female participants (Table 1) at phase 5 (baseline) are reported by categories of sleep duration. Among men, participants sleeping ≥9 hours were, on average, older than other participants; in addition, they were less likely to be physically active and more likely to be on medication for CVD drugs. On the other hand, male participants sleeping ≤5 hours had a lower employment status, higher mean levels of BMI and waist circumference, were more likely to be depressed and on medication for hypnotics, and reported lower scores for mental and physical health than other participants. No significant differences in drinking and smoking habits were reported across categories of sleep duration. For blood pressures, no consistent pattern of association was noted; however, the mean levels of systolic blood pressure (and pulse pressure) and the prevalence of hypertension were significantly higher among participants sleeping 8 hours than in other participants.

Among women, participants at the 2 extreme categories of sleep duration (ie, ≤5 hours and ≥9 hours) were characterized, in general, by a poorer health status and lifestyle profile. In particular, they had a lower employment status, were less likely to be physically active, more likely to be on medication

TABLE 1. Baseline Characteristics (Phase 5: 1997–1999) Across Categories of Sleep Duration: The Whitehall II Study (n=5766)

	Sleep Duration					
Characteristics	≤5 h	6 h	7 h	8 h	≥9 h	*P**
Men (n=4199)						
No. of subjects	265	1383	1886	620	45	
Age, y	54.6 (5.6)	54.6 (5.7)	55.5 (6.1)	57.5 (6.1)	57.7 (5.4)	<0.001
DBP, mm Hg	79.2 (10.9)	78.2 (10.4)	78.6 (10.5)	79.0 (10.9)	78.1 (10.6)	0.57
SBP, mm Hg	124.0 (16.7)	122.3 (15.4)	123.9 (15.8)	125.1 (17.3)	122.5 (16.6)	0.009
Pulse pressure, mm Hg	44.7 (11.5)	44.1 (10.7)	45.3 (11.0)	46.1 (12.4)	44.4 (11.1)	0.003
Lowest employment, n (%)	26 (9.8)	66 (4.8)	62 (3.3)	18 (2.9)	3 (6.7)	<0.001
BMI, kg/m^2	27.0 (4.1)	26.4 (3.5)	25.9 (3.4)	25.4 (3.3)	25.7 (3.3)	<0.001
Waist, cm	94.9 (11.6)	92.8 (10.2)	91.6 (9.7)	90.2 (9.9)	91.5 (8.5)	<0.001
Weekly alcohol, units	18.0 (21.2)	16.9 (15.9)	16.5 (15.9)	16.3 (17.1)	17.7 (20)	0.58
CVD drugs, n (%)	49 (18.6)	185 (13.4)	259 (13.8)	111 (18.0)	9 (20.0)	0.013
Physical activity, n (%)	108 (40.8)	687 (49.7)	930 (49.3)	320 (51.6)	17 (37.8)	0.022
SF-36 mental (score)	47.1 (12.2)	50.5 (9.2)	52.5 (8.2)	53.7 (7.5)	52.0 (9.9)	<0.001
SF-36 physical (score)	50.2 (8.8)	52.1 (7.1)	52.4 (6.4)	51.9 (6.8)	50.9 (8.5)	0.019
Use of hypnotics, n (%)	7 (2.7)	8 (0.6)	4 (0.2)	2 (0.3)	0 (0.0)	<0.001
Depression cases, n (%)	62 (23.8)	178 (13.1)	173 (9.3)	55 (9.0)	4 (8.9)	<0.001
Current smoking, n (%)	30 (11.5)	123 (8.9)	154 (8.2)	49 (7.9)	4 (8.9)	0.45
Hypertensive, n (%)	84 (31.7)	358 (25.9)	533 (28.3)	205 (33.1)	14 (31.1)	0.014
No medication	45 (17.0)	218 (15.8)	323 (17.1)	115 (18.6)	9 (20.0)	...
Medication	38 (14.3)†	140 (10.1)	208 (11.0)‡	90 (14.5)	5 (11.1)	...
Women (n=1567)						
No. of subjects	157	511	597	272	30	
Age, y	56.4 (5.9)	56.1 (6.1)	55.7 (6.1)	56.8 (6.1)	54.7 (5.7)	0.07
DBP, mm Hg	75.7 (10.4)	74.9 (10.1)	74.4 (9.8)	74.2 (10.0)	74.0 (10.0)	0.50
SBP, mm Hg	124.2 (18.3)	121.2 (16.8)	120.3 (17.1)	121.4 (16.8)	118 (17.2)	0.07
Pulse pressure, mm Hg	48.5 (13.8)	46.3 (12.3)	45.9 (12.3)	47.2 (11.6)	44.0 (10.9)	0.07
Lowest employment, n (%)	52 (33.1)	143 (28.1)	162 (27.2)	67 (25.0)	11 (36.7)	0.003
BMI, kg/m^2	27.1 (5.8)	26.2 (5.1)	25.9 (4.4)	26.3 (5.0)	25.8 (4.6)	0.31
Waist, cm	82.5 (14.3)	80.2 (11.8)	80.1 (11.2)	80.4 (11.9)	81.5 (12.0)	0.66
Weekly alcohol, units	7.3 (10.8)	8.0 (8.5)	8.2 (9.5)	8.4 (10.0)	9.8 (9.4)	0.10
CVD drugs, n (%)	36 (23.1)	58 (11.4)	94 (15.8)	46 (16.9)	4 (13.3)	0.007
Physical activity, n (%)	38 (24.2)	169 (33.1)	215 (36)	108 (39.7)	6 (20.0)	0.006
SF-36 mental (score)	42.9 (13.1)	49.0 (10.3)	50.8 (9.2)	52.6 (8.8)	46.9 (15.0)	<0.001
SF-36 physical (score)	46.0 (12.5)	50.2 (8.4)	49.8 (9.0)	49.9 (8.8)	45.2 (10.1)	<0.001
Use of hypnotics, n (%)	2 (1.3)	5 (1.0)	4 (0.7)	2 (0.7)	1 (3.3)	0.60
Depression cases, n (%)	50 (32.5)	72 (14.4)	66 (11.2)	20 (7.4)	5 (16.7)	<0.001
Current smoking, n (%)	20 (12.9)	79 (15.5)	76 (12.8)	31 (11.4)	1 (3.3)	0.22
Hypertensive, n (%)	58 (36.9)	124 (24.3)	152 (25.5)	66 (24.3)	7 (23.3)	0.024
No medication	27 (17.2)	72 (14.1)	69 (11.6)	29 (10.7)	5 (16.7)	...
Medication	31 (19.7)	52 (10.2)	83 (13.9)	37 (13.6)	2 (6.7)	...

Data are expressed as the mean (SD) or as n (%). DBP indicates diastolic blood pressure; SBP, systolic blood pressure.

*P value for comparison across sleep duration groups using the χ^2 analysis for categorical variables and Kruskal-Wallis test for continuous variables.

†One value is missing.

‡Two values are missing.

for CVD drugs or hypnotics, more likely to be depressed, and reported lower scores for mental and physical health than other categories. No significant differences in drinking and smoking habits were reported across categories of sleep duration. For blood pressures, there was a consistent pattern of association among female participants sleeping ≤5 hours, who reported higher mean levels of systolic blood pressure (and pulse pressure), as well as a significantly higher preva-

TABLE 2. OR (95% CI) of Prevalent Hypertension Across Categories of Sleep Duration at Phase 5 (1997–1999): The Whitehall II Study (n=5766)

	Sleep Duration													P*	
Sample Models	≤5 h			6 h			7 h	8 h			≥9 h			Linear	Nonlinear
Men (n=4199)															
No.	265			1383			1886	620			45			...	...
Cases, n	84			358			533	205			14			...	...
Model 1‡	1.18	0.89	1.55	0.89	0.76	1.04	1	1.25†	1.03	1.52	1.15	0.61	2.17	0.06	0.015
Model 2§	1.23	0.92	1.63	0.93	0.79	1.09	1	1.11	0.91	1.36	0.99	0.52	1.90	0.70	0.09
Model 3¶	0.88	0.63	1.23	0.86	0.72	1.03	1	1.12	0.89	1.41	0.92	0.44	1.92	0.05	0.54
Women (n=1567)															
No.	157			511			597	272			30			...	
Cases, n	58			124			152	66			7			...	
Model 1‡	1.72†	1.18	2.49	0.94	0.71	1.23	1	0.94	0.67	1.31	0.89	0.37	2.12	0.13	0.06
Model 2§	1.64†	1.11	2.42	0.90	0.68	1.19	1	0.83	0.58	1.17	0.98	0.40	2.40	0.12	0.15
Model 3¶	1.72†	1.07	2.75	0.92	0.67	1.28	1	0.74	0.50	1.11	0.70	0.21	2.37	0.037†	0.31

*P value for test of linear and nonlinear trends.
†P<0.05.
‡Model 1: unadjusted.
§Model 2: adjusted for age and employment.
¶Model 3: model 2+alcohol consumption, smoking, physical activity, BMI, SF-36 mental, SF-36 physical, depression cases, hypnotics use, and CVD drugs.

lence of hypertension than other participants (in both treated and untreated individuals).

Cross-Sectional Analysis

Table 2 displays the odds ratios (ORs) and 95% CIs of prevalent hypertension across categories of sleep duration at phase 5, using 7 hours of sleep as the reference category. Among men, no consistent pattern of association was noted. Among women, in fully adjusted analyses, short duration of sleep (≤5 hours per night) was associated with a significantly higher risk of hypertension compared with the group sleeping 7 hours (OR: 2.01; 95% CI: 1.13 to 3.58), independent of several potential confounders, with a significant inverse linear trend across decreasing hours of sleep ($P=0.003$).

Prospective Analysis

Table 3 displays the ORs (and 95% CIs) of incident hypertension at phase 7 among participants who were normotensive at phase 5. During a mean follow-up of 5 years, the cumulative incidence of hypertension was 20.0% (740 of

TABLE 3. OR (95% CI) of Incident Hypertension at Phase 7 (2002–2003) Across Categories of Sleep Duration at Phase 5 (1997–1999): The Whitehall II Study (n=3691)

	Sleep Duration													P*	
Sample Models	≤5 h			6 h			7 h	8 h			≥9 h			Linear	Nonlinear
Men (n=2686)															
No.	160			900			1224	372			30				
Cases, n	29			179			243	85			3				
Model 1‡	0.89	0.58	1.37	1.00	0.81	1.24	1	1.20	0.90	1.58	0.45	0.13	1.49	0.60	0.53
Model 2§	0.96	0.62	1.48	1.07	0.86	1.34	1	1.07	0.80	1.42	0.36	0.11	1.19	0.51	0.42
Model 3¶	0.89	0.55	1.43	1.02	0.80	1.31	1	1.11	0.80	1.53	0.13†	0.02	0.98	0.55	0.18
Women (n=1005)															
No.	75			330			394	186			20				
Cases, n	20			77			64	37			3				
Model 1‡	1.88†	1.05	3.34	1.56†	1.08	2.27	1	1.28	0.82	2.01	0.91	0.26	3.20	0.029†	0.38
Model 2§	1.94†	1.08	3.50	1.56†	1.07	2.27	1	1.17	0.74	1.86	0.92	0.26	3.27	0.015†	0.42
Model 3¶	1.31	0.65	2.63	1.42	0.93	2.16	1	0.99	0.59	1.69	1.07	0.29	3.94	0.12	0.61

*P value for test of linear and nonlinear trends.
†P<0.05.
‡Model 1: unadjusted.
§Model 2: adjusted for age and employment.
¶Model 3: model 2+alcohol consumption, smoking, physical activity, BMI, SF-36 mental, SF-36 physical, depression cases, hypnotics use, and CVD drugs.

3691 total: 539 of 2686 in men and 201 of 1005 in women). Among men, no consistent pattern of association was seen across categories of sleep duration. Among women, short duration of sleep was associated with significantly higher risks of hypertension compared with the group sleeping 7 hours in unadjusted analyses, as well as in a reduced model (age and employment; 6 hours per night: OR: 1.56 [95% CI: 1.07 to 2.27], ≤5 hours per night: OR: 1.94 [95% CI: 1.08 to 3.50]). However, these associations were attenuated after accounting for cardiovascular risk factors and psychiatric comorbidities (OR: 1.42 [95% CI: 0.94 to 2.16]; OR: 1.30 [95% CI: 0.65 to 2.62], respectively). The proportion of the variance of the risk of developing hypertension explained by the age- and employment-adjusted model was 2.95%. In the fully adjusted model it was 6.14%. The major contributor in the full multivariate model was body mass index (explaining 2.23% of the added variance), whereas the remaining covariates all accounted for <1% of the remaining difference. Results were virtually unchanged after further adjustment for the baseline values of systolic blood pressure (data not shown).

Other Analyses

We also carried out linear regression analyses to test the association between sleep duration and blood pressures (systolic, diastolic, and pulse pressures) at phase 5 (cross-sectional analyses), as well as the association between sleep duration at phase 5 and changes in blood pressures between the 2 phases (prospective analyses), among participants not taking antihypertensive medications. In cross-sectional analyses, there were consistent, significant inverse associations ($P<0.05$) between duration of sleep and either systolic blood pressure ($\beta=-1.24$ mm Hg per hour of sleep; 95% CI: −2.23 to −0.24 mm Hg per hour of sleep) or pulse pressure ($\beta=-0.91$ mm Hg per hour of sleep; 95% CI: −1.63 to −0.20 mm Hg per hour of sleep), only among women, in fully adjusted models. In prospective analyses, no significant associations were found for any of the blood pressure measures among either male or female participants (data not shown).

Discussion

Findings from the Whitehall II cohort showed gender-specific associations between sleep duration and hypertension. Spe-

APPENDIX. Baseline Characteristics (Phase 5: 1997–1999): The Whitehall II Study

	n=6592*		n=5766†		n=612‡	
Characteristics	Men	Women	Men	Women	Men	Women
No. of subjects	4724	1868	4199	1567	329	283
Age, y	55.6 (6.0)	56.3 (6.1)	55.4 (6.0)	56.1 (6.1)	57.7 (5.9)	56.2 (5.4)
DBP, mm Hg	78.6 (10.6)	74.6 (10.0)	78.6 (10.6)	74.6 (10.0)	79.2 (10.8)	78.5 (10.2)
SBP, mm Hg	123.5 (16.0)	121.1 (17.1)	123.6 (16.0)	121.1 (17.1)	125.6 (17.3)	127.5 (19.1)
Pulse pressure, mm Hg	44.9 (11.2)	46.5 (12.4)	45.0 (11.2)	46.5 (12.3)	46.4 (12.6)	49.0 (14.1)
Sleep duration, n (%)						
≤5 h	296 (6.4)	190 (10.4)	265 (6.3)	157 (10.0)	43 (13.6)	34 (12.8)
6 h	1521 (32.8)	602 (32.9)	1383 (32.9)	511 (32.6)	121 (38.2)	94 (35.3)
7 h	2090 (45.0)	687 (37.6)	1886 (44.9)	597 (38.1)	95 (30.0)	101 (38.0)
8 h	683 (14.7)	310 (17.0)	620 (14.8)	272 (17.4)	45 (14.2)	31 (11.7)
≥9 h	53 (1.1)	40 (2.2)	45 (1.1)	30 (1.9)	13 (4.1)	6 (2.3)
Lowest employment grade, n (%)	207 (4.4)	545 (29.5)	175 (4.2)	435 (27.9)	65 (19.8)	181 (64.4)
BMI, kg/m^2	26.1 (3.5)	26.2 (4.9)	26.0 (3.5)	26.2 (4.9)	25.7 (3.2)	28.1 (5.1)
Waist, cm	92.1 (10.1)	80.4 (11.9)	92.0 (10.1)	80.5 (11.9)	90.6 (9.0)	85.1 (11.4)
Weekly alcohol, units	16.7 (16.6)	7.8 (9.5)	16.7 (16.5)	8.1 (9.6)	10.3 (18.3)	2.7 (5.4)
CVD drugs, n (%)	719 (15.3)	299 (16.1)	613 (14.6)	238 (15.2)	89 (27.2)	93 (32.9)
Physical activity, n (%)	2277 (48.2)	601 (32.2)	2062 (49.1)	536 (34.2)	99 (30.1)	47 (16.6)
SF-36 mental, score	51.6 (9.0)	49.7 (10.4)	51.7 (8.9)	49.7 (10.4)	50.0 (10.4)	49.1 (10.8)
SF-36 physical, score	60.0 (7.1)	49.1 (9.6)	52.1 (6.9)	49.5 (9.3)	49.2 (8.7)	44.5 (10.4)
Use of hypnotics, n (%)	26 (0.55)	17 (0.9)	21 (0.5)	14 (0.9)	2 (0.6)	0 (0.0)
Depression cases, n (%)	545 (11.8)	255 (14.1)	472 (11.4)	213 (13.8)	66 (21.4)	57 (22.2)
Current smoking, n (%)	436 (9.3)	266 (14.3)	360 (8.6)	207 (13.3)	40 (12.3)	13 (4.63)
Male hypertensive, n (%)	1194 (25.3)	407 (21.8)	1194 (28.4)	407 (26.0)	110 (33.4)	117 (41.3)
No medication	630 (13.3)	153 (8.2)	713 (17.0)	202 (12.9)	35 (10.6)	32 (11.3)
Medication	564 (11.9)	254 (13.6)	481 (11.5)	205 (13.1)	75 (22.8)	85 (30.0)

Data are expressed as the mean (SD) or as n (%).
*n=6592 for all white participants.
†n=5766 for white participants with complete data on blood pressure.
‡n=612 for ethnic minorities excluded from the analysis.

cifically, short duration of sleep was associated with higher risks of prevalent and incident hypertension only among women. We could not detect consistent associations among men or for long duration of sleep. For the latter finding, it should be noted, however, that there were very few individuals (≈1.3% of the overall sample) in our study who reported sleeping ≥9 hours per night, thus yielding a limited statistical power to examine the association between sleep duration and hypertension in this subgroup. Furthermore, our findings point to the importance of a comprehensive scrutiny of potential confounders and mediators when examining the associations between durations of sleep and health outcomes. In fact, the observed associations among women were attenuated after accounting for a number of cardiovascular risk factors, measures of general health, and psychiatric comorbidities.

A substantial amount of evidence exists about the link between SDB and hypertension.[1–5] The epidemiological data have been corroborated by findings of mechanistic studies emphasizing the critical role of sympathetic overactivity in the etiology of SDB-related hypertension,[24,25] although other mechanisms are likely to be involved.[19] More recently, sleep deprivation has been indicated as a risk factor for several chronic health outcomes in individuals without overt sleep disorders.[6–12] However, we are aware of only 2 population-based studies so far, both coming from the United States, that have attempted to examine the association between self-reported durations of sleep and risk of hypertension.[13,14] Specifically, in a longitudinal analysis of the NHANES-I (n=4810), short sleep duration (≤5 hours per night) was associated with a 60% higher risk of incident hypertension, in fully adjusted models, among middle-aged (32 to 59 years) American adults without apparent sleep disorders.[13] No association was found in individuals ≥60 years of age. However, in this study, the diagnosis of incident hypertension was based on self-report with a potential of misclassification (underdiagnosis), as suggested by a lower cumulative incidence (647 of 4810 [≈13.5%]) as compared with that observed in our study (740 of 3691 [20.0%]), despite comparable age ranges between the 2 studies and a longer follow-up period in the NHANES-I (8 to 10 years versus 5 years, respectively). In addition, no gender-specific analyses were included in the NHANES-I. Moreover, in a cross-sectional analysis of the large sample of the Sleep Heart Health Study (≈6000 US adults), a significantly higher prevalence of hypertension was reported among either short (<6 hours per night) or long sleepers (≥9 hours per night) as compared with the median duration of sleep of 7 to <8 hours per night.[14] However, the association was stronger among short sleepers than in long sleepers (ie, 66% versus 30% higher risk of hypertension, respectively). Although this study accounted for a number of potential covariates, including psychiatric and cardiovascular comorbidities, the cross-sectional design does not allow us to exclude the possibility of residual confounding by unknown variables, as well as to exclude the potential of reverse causality. In addition, the Sleep Heart Health Study sample cohort was, on average, older than those in both NHANES-I and Whitehall II, thus with a higher likelihood of geriatric comorbidities potentially affecting sleep patterns.[26]

Strengths

Unlike these earlier investigations, our study examined both cross-sectional and prospective gender-specific associations between sleep duration and hypertension with the inclusion of a number of potential confounding variables. Our findings suggest a potential role of sleep deprivation in the etiology of hypertension and other adverse health outcomes.

First, the observation that reduced duration of sleep may be associated with a higher risk of hypertension only among women is a novel finding. Indeed, although previous investigations have emphasized the potential impact of both short and long durations of sleep on chronic disease risk among women,[6–9] the mechanisms underlying the gender-specific association between sleep deprivation and hypertension, observed in our study, are unknown. Given the mean age of our female participants falling around the menopausal period (≈55 years), we can speculate that the periods marking shifts in the reproductive stages, such as menopause, are particularly vulnerable times for women, because they are associated with major hormonal turmoil and psychosocial stresses that may, in turn, lead to adverse health outcomes.[27] For example, in our sample of female participants, the prevalence of depression cases was higher among women reporting short duration of sleep (≤5 hours per night) than in other subgroups. In addition, as shown in our descriptive analyses, the distribution of correlates of short sleep duration that have the potential to affect hypertension risk was different between genders and may have partially contributed to the observed associations. Finally, we cannot rule out the possibility of differential self-reporting of sleep habits between men and women, as suggested in a previous analysis from the Sleep Heart Health Study examining the relationship of gender to subjective measures of sleepiness.[28]

Second, although findings from cross-sectional analyses consistently showed a strong, significant association between short sleep duration and risk of hypertension among women, in prospective analyses, the risk estimates were attenuated after accounting for cardiovascular risk factors, measures of general health, and psychiatric comorbidities. Thus, these findings emphasize the importance of a comprehensive examination of correlates that are likely to confound or may be on the causal pathway between sleep deprivation and adverse health outcomes. Nevertheless, recent prospective analyses from the Monitoring Trends Determinants in Cardiovascular Disease Augsburg survey indicate a modest but significant association between short sleep duration and incident myocardial infarction in middle-aged women, but not men, from the general population.[29]

Third, our descriptive analyses clearly demonstrate that both short and long duration of sleep may indeed identify population subgroups with a distinct cluster of sociodemographic characteristics, lifestyle behaviors, and disease conditions that are likely to be affected by the cultural setting in which the research is being conducted.[30–33] In this regard, the study of health consequences related to curtailments of sleep seems to be epidemiologically relevant in the general population, given the downward trends in the average duration of sleep and the increasingly higher prevalence of "short sleepers" in many Western countries.[34,35] Conversely, it may be

difficult for epidemiological studies to examine the health consequences of long durations of sleep in middle-aged, healthy populations considering the relatively low prevalence of "long sleepers" in the absence of overt psychiatric comorbidities.[36]

Limitations

There are limitations in this study. First, the population under investigation is an occupational cohort of white-collar workers and limited to whites, which may reduce the generalizability of our findings to other populations. However, this would not affect the internal validity of our results with respect to the prospective analyses. Second, information about sleep duration was self-reported by the participants. Nevertheless, self-report assessments of sleep have been shown to be valid measures compared with quantitative sleep assessments with actigraphy.[37,38] Moreover, because the outcome was also assessed prospectively, any misclassification of sleep duration would be nondifferential with respect to incident hypertension, thus resulting in underestimation of the true effects. A further limitation of this study is the relatively short time of follow-up (5 years), which may have precluded us from detecting larger and significant effects of sleep deprivation on subsequent hypertension incidence. The strengths of this study include the simultaneous inclusion of a number of covariates known to be related to both sleep patterns and hypertension. A further strength is that the diagnosis of incident hypertension was also based on directly measured blood pressures at both examinations, thus minimizing the potential of misclassification that occurs when using self-report alone.

Conclusions

In summary, findings from the Whitehall II cohort suggest gender-specific associations between sleep duration and hypertension risk. Specifically, cross-sectional analyses showed a significant, consistent association between short sleep duration (≤5 hours per night) and risk of hypertension only among women, which was attenuated in prospective analyses after multivariate adjustment.

Perspectives

Sustained sleep curtailment, ensuing excessive daytime sleepiness, and the higher cardiovascular risk are causes for concern. Emerging evidence also suggests a potential role for sleep deprivation as a predictor or risk factor for conditions like obesity, diabetes, and metabolic syndrome not only in adults[39] but also in children.[40] Further prospective studies with improved assessment of long-term exposure (repeated self-reported sleep duration or repeated actigraphy) and better control for confounders are needed before causality can be determined.

Acknowledgments

We thank all of the participating civil service departments and their welfare, personnel, and establishment officers; the Occupational Health and Safety Agency; the Council of Civil Service Unions; all of the participating civil servants in the Whitehall II Study; and all members of the Whitehall II Study team.

Sources of Funding

The Whitehall II Study has been supported by grants from the Medical Research Council; British Heart Foundation; Health and Safety Executive; Department of Health; National Heart Lung and Blood Institute (HL36310), National Institutes of Health; National Institute on Aging (AG13196), National Institutes of Health; Agency for Health Care Policy Research (HS06516); and the John D. and Catherine T. MacArthur Foundation Research Networks on Successful Midlife Development and Socioeconomic Status and Health. J.E.F. is supported by the Medical Research Council (grant G8802774), M.J.S. by a grant from the British Heart Foundation, and M.G.M. by a Medical Research Council research professorship.

Disclosures

F.P.C. holds the Cephalon Chair, an endowed post at Warwick Medical School, the result of a donation from the company. The appointment to the chair was made entirely independent of the company, and the postholder is free to devise his own program of research. Cephalon do not have any stake in intellectual property associated with the postholder, and the chair has complete academic independence from the company. The remaining authors report no conflicts.

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