Change in Sleep Duration and Cognitive Function: Findings from the Whitehall II Study

Jane E. Ferrie, PhD[1]; Martin J. Shipley, MSc[1]; Tasnime N. Akbaraly, PhD[1,2]; Michael G. Marmot, MD[1]; Mika Kivimäki, PhD[1,3]; Archana Singh-Manoux, PhD[1,4,5]

[1]*University College London, Department of Epidemiology and Public Health, London, UK;* [2]*INSERM U888-University Montpellier 1, Montpellier, France;* [3]*Finnish Institute of Occupational Health, Helsinki, Finland;* [4]*INSERM, U1018, Centre for Research in Epidemiology & Population Health, France;* [5]*Centre de Gérontologie, Hôpital Ste Périne, AP-HP, Paris, France*

Study Objectives: Evidence from cross-sectional studies shows that sleep is associated with cognitive function. This study examines change in sleep duration as a determinant of cognitive function.
Design: Prospective cohort.
Setting: The Whitehall II study.
Participants: 1459 women and 3972 men aged 45-69 at baseline.
Interventions: None.
Measurements and Results: Sleep duration (≤ 5, 6, 7, 8, ≥ 9 h on an average week night) was assessed once between 1997-1999, baseline for the present study, and once between 2002-2004, average follow-up 5.4 years. Cognitive function was measured (2002-2004) using 6 tests: verbal memory, inductive reasoning (Alice Heim 4-I), verbal meaning (Mill Hill), phonemic and semantic fluency, and the Mini Mental State Examination (MMSE). In analyses adjusted for age, sex, and education, and corrected for multiple testing, adverse changes in sleep between baseline and follow-up (*decrease* from 6, 7, or 8 h, *increase* from 7 or 8 h) were associated with lower scores on most cognitive function tests. Exceptions were memory, and, for a *decrease* from 6-8 h only, phonemic fluency. Further adjustment for occupational position attenuated the associations slightly. However, firm evidence remained for an association between an *increase* from 7 or 8 h sleep and lower cognitive function for all tests, except memory, and between a *decrease* from 6-8 h sleep and poorer reasoning, vocabulary, and the MMSE. The magnitude of these effects was equivalent to a 4-7 year increase in age.
Conclusions: These results suggest that adverse changes in sleep duration are associated with poorer cognitive function in the middle-aged.
Keywords: Change in sleep duration, cognitive function, white-collar, cohort study
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INTRODUCTION

Ageing appears to be accompanied by a decrease in duration of good quality nocturnal sleep and an increase in sleeplessness and sleep disturbances.[1-3] Sleep deprivation is related to worse performance on many daily tasks, such as driving and operating machinery[4] and, in laboratory settings, has been shown to have adverse consequences for contiguously measured cognitive performance.[5] Cognitive aging is characterized by heterogeneity in that not everyone experiences decline at the same rate.[6-8] It is also clear that many of the neuronal changes that accompany cognitive decline are evident in midlife.[7] There are multiple determinants of cognitive decline,[7-9] but the extent to which sleep plays a role remains unclear.

Short sleep, long sleep, and sleep problems have all been found to be associated with poorer cognitive function in cross-sectional studies,[10-19] and poor sleep is also a feature of dementia.[20] However, the few studies that have examined prospective associations between sleep assessed once at baseline and cognitive function at follow-up or cognitive decline between baseline and follow-up are inconsistent. One small laboratory-based study in the elderly that measured cognitive function once at follow-up demonstrated associations between poor sleep patterns and cognitive impairment 14 years later.[21] Similarly, a population-based study of people aged 50 and over found those who reported "any" sleep problem to have greater cognitive decline over a 3-year follow-up than those who did not report sleep problems.[22] However, in the Nurses Health Study there was no association between self-reported sleep problems and cognitive decline over a period of 2 years.[23]

Even less work has used data on sleep assessed on two occasions to examine associations between change in sleep over time and cognitive function. One exception is a large study of people aged ≥ 65 that examined associations between insomnia, depression, and cognitive decline over a 3-year period. In this study, chronic insomnia was associated with cognitive decline in men and, where conjoint with depression, in both sexes, but new onset insomnia between baseline and follow-up was associated with cognitive decline only in men with depression.[24] However, despite evidence of cross-sectional associations and widely accepted evidence that sleep duration and cognitive performance decrease with age,[1,9,25] only one small study appears to have examined change in sleep duration, as opposed to insomnia, as a determinant of cognitive function.[26] In this paper, we examine whether sleep duration and changes in sleep duration are associated with subsequent cognitive function in a large study of middle-aged women and men.

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Address correspondence to: Jane Ferrie, Senior Research Fellow, Department of Epidemiology and Public Health, University College London Medical School, 1-19 Torrington Place, London WC1E 6BT, U.K.; Tel: (+44 207) 679 5643; Fax: (+44 207) 813 0288; E-mail: j.ferrie@ucl.ac.uk

METHODS

Study Population

The target population for the Whitehall II study was all London-based office staff aged 35-55 working in 20 civil ser-

Table 1—Change in sleep duration categories

Phase 5 Sleep Duration*	Phase 7 Sleep Duration* ≤ 5	6	7	8	≥ 9
≤ 5	**188**	A (165)	A (39)	A (6)	A (0)
6	C (170)	**995**	A (535)	A (70)	A (8)
7	C (48)	C (522)	**1387**	B (376)	B (20)
8	C (7)	C (53)	C (296)	**416**	B (55)
≥ 9	D (4)	D (5)	D (7)	D (29)	**30**

*Sleep duration refers to hours sleep on an average week night; A, increase from ≤ 5 h or 6 h per night; B, increase from 7 or 8 h per night; C, decrease from 6, 7, or 8 h per night; D, decrease from ≥ 9 h per night.

vice departments in 1985. Of these, 10,308 participants (3,413 women and 6,895 men) were enrolled, a response rate of 73%. Although mostly white collar, participants covered a wide socioeconomic range with a 10-fold difference in salary across the occupational hierarchy.[27] Data collection at enrollment, Phase 1 (1985-1988) involved a clinical examination and self-administered questionnaire containing sections on demographic characteristics, health, lifestyle factors, work characteristics, social support, and life events. The clinical examination included measures of blood pressure, anthropometry, biochemistry, neuroendocrine function, and subclinical markers of cardiovascular disease. Subsequent phases of data collection have alternated between postal questionnaire alone (all even-numbered phases), and postal questionnaire accompanied by clinical examination (all odd-numbered phases). The current study uses data for 5,431 participants (1459 women and 3972 men) from Phase 5 (1997-1999) and Phase 7 (2003-2004), baseline and follow-up for the present study.

Study Design

This study examines associations between change in sleep duration (Phase 5 to Phase 7) and cognitive function at follow-up (Phase 7), in addition to presenting cross-sectional associations between sleep duration and cognitive function at Phase 7 separately by sex.

Measures

Sleep

Habitual sleep duration was measured at Phase 5 (baseline) and Phase 7 (follow-up) using a single question "How many hours of sleep do you have on an average week night?" Response categories were ≤ 5 h, 6, 7, 8, and ≥ 9 h.[28]

For the examination of changes in sleep duration between Phases 5 and 7, participants were divided into 4 categories based on whether they slept more, the same, or less hours at follow-up than at baseline. Changes in sleep duration were categorized using the following classification, as previously:[28] For increased sleep durations we hypothesized that an increase from ≤ 5 or 6 h at Phase 5 would have a beneficial effect on cognitive function, whereas an increase from 7 or 8 h would have a detrimental effect. We therefore created 2 categories; "*increase from ≤ 5 or 6 hours*" (Table 1: A) at Phase 5, and "*increase from 7 or 8 hours*" at Phase 5 (Table 1: B). Reduced sleep duration for the categories 6, 7, and 8 h, hypothesized to have a detrimental effect on cognitive function, were pooled to form the category "*decrease from 6, 7, or 8 hours*" (Table 1: C). All participants who slept ≥ 9 h at Phase 5, but less at Phase 7 were categorized as "*decrease from 9 hours or more*" (Table 1: D). In each of the 4 sleep categories we compared those sleeping less hours or more hours with the reference group, which in each case was comprised of *participants who slept the same number of hours at Phase 7 as at Phase 5*. For example, for the category "increase from 5 or 6 h," the reference group was participants who slept either 5 or 6 h at both phases.

Cognitive function

Cognitive function was assessed at Phase 7 using a battery of 6 standard tests: **Memory**—a 20-word free recall test measured short-term verbal memory. Participants were presented with a list of 20 one- or 2-syllable words at 2-sec intervals and were then asked to recall, in writing, as many of the words as possible in any order over a period of 2 min. **Reasoning**—the Alice Heim 4-I (AH4-I), consisting of 65 verbal and mathematical reasoning items of increasing difficulty with a 10-min time limit for completion, measured inductive reasoning; the ability to identify patterns and infer principles and rules.[29] **Vocabulary**—the Mill Hill Vocabulary test consists of a list of 33 stimulus words ordered by increasing difficulty, each presented with 6 multiple choice responses.[30] Verbal fluency was measured using two tests; **phonemic fluency** and **semantic fluency**. In both cases fluency was assessed by the written recall of as many words as possible in one minute; phonemic fluency by the recall of words beginning with "S," and semantic fluency by the recall of animal names.[31] Finally, the 30-item **Mini-Mental-State-Examination** (MMSE) was used to assess global cognitive status.[32]

Covariates

The covariates age, sex, education, and occupational position were derived from the Phase 7 questionnaire. We adjusted for the effects of education and occupational position due to their known association with cognitive performance.[33] Education was categorized by the highest qualification on leaving full-time education; Secondary (left school at or before age 16); Higher secondary (left school at age 18); or Tertiary (bachelor's degree, postgraduate degree). Occupational position, measured as last Civil Service employment grade, was categorized as low (clerical and administrative support staff), intermediate (professional and executive staff), or high (senior administrative staff and managers).

Ethics Approval

Ethical approval for the Whitehall II study was granted by the University College London Medical School committee on the ethics of human research.

Statistical Analysis

Of the 10,308 participants at baseline, 7830 (76%) responded at Phase 5 and 6967 (68%) responded at Phase 7. Removal of participants with missing data for variables included in the present study left 5431 participants (1459 women and 3972 men) in the analyses. Descriptive statistics for participant characteristics at Phase 7 and sleep duration at Phase 5 by sleep duration at Phase 7 are presented and tested using χ^2 tests for heterogeneity for categorical variables and analysis of variance for age. Cognitive test scores were standardized in women and men separately to a T-score, similar to a z-score, but with a mean of 50 and a standard deviation (SD) of 10, in order to allow comparison between the measures. Multiple regressions with cognitive function as the dependent variable and sleep duration categories as the independent variables were fitted, and least squares means from these regressions used to estimate means adjusted for age. Tests of heterogeneity across the sleep duration categories and tests of the difference in cognitive function compared with the ≤ 5 h category were also obtained from these regressions.

Further multiple regression models with cognitive function as the dependent variable and the changes in sleep duration as the independent variables were fitted and used to estimate means adjusted for (a) age, sex, and education; and (b) age, sex, education, and occupational position. These regression models were parameterized so as to allow each change in sleep duration category to be compared to its appropriate no change in sleep duration reference category, as described above, in a single unified model. An advantage of this unified approach is that the adjustments for the covariates come from their relationships with the outcome in the whole sample and apply to all the change in sleep duration categories.

Tests of interaction between sex and change in sleep duration in the fully adjusted models confirmed that there was no evidence of any difference in the change in sleep duration effects in women and men (all P-values > 0.16). The false discovery rate method[34] was used to take account of the multiple testing arising from comparing each change in sleep duration category with its "no change" reference group for each of the 6 cognitive function outcomes, and this correction is reflected in these tests of difference. To apply the method, the P-values for the 18 sleep duration versus "no change" comparisons were ranked by increasing magnitude. If the ranks of the P-value are denoted r, then we compare each P-value with its critical significance level defined as (r/18)*0.05, (r/18)*0.01, (r/18)*0.001. To facilitate interpretation, the adverse effects of change in duration of sleep on cognitive function were also expressed as an equivalent effect of age using the observed cognitive data and age (range 50-74 years) at Phase 7. This was estimated from the fitted regressions by dividing the coefficient for the change in sleep by the coefficient for age. All analyses were conducted using the SAS statistical program, version 9.1 (SAS Institute, Cary, NC, USA).

RESULTS

Compared to the 4877 participants enrolled in the cohort but not contributing to the analyses in the present study, the 5431 individuals included in the analyses were *more likely* to be men (73.1% vs. 59.9%), younger at baseline (44.0 vs. 44.9), have a tertiary education (36.8% vs. 31.5%), and *less likely* to be of low occupational position (12.8% vs. 33.7%). The percentage of short (≤ 5 h/night) and long (≥ 9 h/night) sleepers was higher at enrolment into the Whitehall II cohort among those not included in the analyses (Table 2). However at Phase 7, habitual sleep duration for the majority of participants was either 6 or 7 h/night (72% women, 75% men). Short sleep was reported by 10% of women and 7% of men. In both sexes 2% were long sleepers. Short and long sleep was less common in women with a university education or high occupational position. In men, education was not associated with sleep duration, but shorter sleep (≤ 5 and 6 h) durations were more prevalent among men in the lower occupational positions and longer sleep (7 and 8 h) durations in the higher positions. Sleep duration between the Phase 5 baseline and follow-up remained unchanged for about half the participants, while change in duration >1 h was observed in only 7% of the women and 4% of the men.

Sleep Duration

Table 3 shows the age-adjusted distribution of cognitive function T-scores by sleep duration at Phase 7. Ranges (observed) for the cognitive function test scores; Memory (0-18), Reasoning (12-65), Vocabulary (1-33), Phonemic fluency (3-47), Semantic fluency (2-34), and MMSE (18-30) were standardized to a mean of 50 and a standard deviation of 10 in women and men separately to allow comparison across cognitive tests. Overall associations between sleep duration and all cognitive function measures were U-shaped with poorer cognitive function scores at the short and long ends of the sleep distribution. More specifically, in women 7 h/night was associated with the highest score for every measure, followed closely by 6 h/night. Women who slept less or more had lower scores. In men, cognitive function T-scores were similar for men sleeping 6, 7, or 8 h; and only short and long sleep appeared to be associated with low scores. The pattern of the cognitive function T-scores by sleep duration remained similar after further adjustment for education and occupational position. However, differences between the sleep duration categories were attenuated, particularly in men (see supplementary Table S1).

Change in Sleep Duration

Sleep duration categories used in the analyses of change are shown in Table 4. The proportions of participants remaining in the same category at baseline and follow-up are similar in both sexes, although men are more likely to sleep 7 h at both time points. Since only 19 women and 26 men report a "decrease from 9 hours or more" and only 7 women and 23 men reported having 9 h sleep at both phases, we excluded these 75 participants from the analyses of change in sleep duration.

Table 5 shows the difference in cognitive function score at Phase 7 for each change in sleep duration category between Phases 5 and 7 relative to the appropriate reference group whose hours of sleep did not change between the 2 phases. Findings for women and men combined are shown in the upper section of the table (A) adjusted for age, sex, and education, and the lower section, (B), additionally adjusted for occupational position at Phase 7. We hypothesized that an "increase from ≤ 5 or 6 hours" sleep per night would have a beneficial effect on cognitive function, but our findings provided no evidence of any effect, either beneficial or detrimental, Table 5A. However, an "increase from 7 or 8 hours" was associated with lower scores at follow-up on all the cognitive function tests, equivalent to a 5-8 year increase in age. After correction for multiple testing, firm evidence of an association remained for all the tests except memory. In similar analyses, a "decrease from 6, 7, or

Table 2—Characteristics⁺ at Phase 7 and sleep duration at Phase 5 by number of hours of sleep at Phase 7 and sleep duration at enrolment among those included and excluded from the study analyses

	N	Hours of Sleep at Phase 7					P-value*
Women		**≤ 5 h**	**6 h**	**7 h**	**8 h**	**≥ 9 h**	
Number (%)	1459	148 (10.1)	494 (33.9)	550 (37.7)	242 (16.6)	25 (1.7)	
Age, years	1459	61.2 (0.5)	60.9 (0.3)	60.6 (0.3)	62.3 (0.4)	60.6 (1.0)	0.004
Education							
Tertiary	408	6.9	35.0	41.7	14.7	1.7	
Higher secondary	326	12.2	30.7	37.4	16.0	3.7	0.004
Secondary	725	11.0	34.6	35.6	17.9	0.8	
Occupational position							
High	725	6.2	34.3	42.4	16.6	0.8	
Intermediate	326	10.1	33.7	38.6	15.3	2.3	0.002
Low	408	14.5	33.6	30.7	19.7	1.5	
Sleep duration at Phase 5							
≤ 5 h	139	48.9	37.4	11.5	2.2	0.0	
6 h	470	11.7	51.7	32.1	4.3	0.2	
7 h	571	3.0	30.7	49.7	15.9	0.7	< 0.001
8 h	253	2.0	8.3	37.9	46.6	5.1	
≥ 9 h	26	11.5	11.5	11.5	38.5	26.9	
		Hours of Sleep at Enrolment to the Whitehall II Cohort					
		≤ 5 h	**6 h**	**7 h**	**8 h**	**≥ 9 h**	
Included in the study analyses, N (%)	1454	84 (5.8)	389 (26.8)	709 (48.8)	260 (17.9)	12 (0.8)	
Excluded from the study analyses, N (%)	1954	134 (6.9)	536 (27.5)	877 (45.0)	365 (18.8)	35 (1.8)	
		Hours of Sleep at Phase 7					
Men		**≤ 5 h**	**6 h**	**7 h**	**8 h**	**≥ 9 h**	
Number **(%)**	3972	269 (6.8)	1246 (31.4)	1714 (43.2)	655 (16.5)	88 (2.2)	
Age, years	3972	60.1 (0.4)	60.2 (0.2)	61.0 (0.1)	62.5 (0.2)	63.1 (0.6)	< 0.001
Education							
Tertiary	1593	6.8	31.2	43.6	15.9	2.4	
Higher secondary	1204	6.5	31.5	43.4	16.5	2.2	0.99
Secondary	1175	7.1	31.2	42.3	17.3	2.0	
Occupational position							
High	2238	5.3	30.7	44.2	17.7	2.2	
Intermediate	1605	8.1	31.8	42.8	15.1	2.2	< 0.001
Low	129	15.5	38.0	30.2	14.0	2.3	
Sleep duration at Phase 5							
≤ 5 h	259	46.3	43.6	8.9	1.2	0.0	
6 h	1308	8.8	57.5	29.4	3.8	0.5	
7 h	1782	1.7	19.5	61.9	16.0	0.9	< 0.001
8 h	574	0.4	5.6	34.8	51.9	7.3	
≥ 9 h	49	2.0	4.1	8.2	38.8	46.9	
		Hours of Sleep at Enrolment to the Whitehall II Cohort					
		≤ 5 h	**6 h**	**7 h**	**8 h**	**≥ 9 h**	
Included in the study analyses, N (%)	3960	135 (3.4)	1092 (27.6)	2127 (53.7)	578 (14.6)	28 (0.7)	
Excluded from the study analyses, N (%)	2903	137 (4.7)	824 (28.3)	1457 (50.2)	459 (15.8)	26 (0.9)	

⁺Figures are unadjusted means (standard errors) for age and percentages for education, occupational position and sleep duration; *P-value for heterogeneity.

8 hours" was associated with lower scores at follow-up for all cognitive tests equivalent to a 3-5 year increase in age. Firm evidence of an association remained after correction for multiple testing for reasoning, vocabulary, semantic fluency, and the MMSE. Further adjustment for occupational position, Table 5B, resulted in a slight attenuation of these associations, suggesting they are partially explained by this socioeconomic measure. However, after correction for multiple testing and, as in the education-only adjusted analyses, firm evidence remained for the association between an increase from 7 or 8 h sleep and

Table 3—Age-adjusted cross-sectional associations between sleep duration and cognitive function at Phase 7

		Hours of sleep at Phase 7					
Women	**N**	**≤ 5 h**	**6 h**	**7 h**	**8 h**	**≥ 9 h**	**P-value****
Number	1459	148	494	550	242	25	
Cognitive function T-scores†							
Memory	1455	48.7 (0.8)	50.0 (0.4)	50.3 (0.4)	50.1 (0.6)	49.0 (1.9)	0.49
AH4-I (reasoning)	1456	47.4 (0.8)	50.1* (0.4)	51.2* (0.4)	48.8 (0.6)	48.8 (1.9)	< 0.001
Mill Hill (vocabulary)	1452	46.9 (0.8)	50.2* (0.4)	51.3* (0.4)	48.7 (0.6)	48.4 (2.0)	< 0.001
Phonemic fluency	1445	48.2 (0.8)	50.0* (0.4)	50.8* (0.4)	49.7 (0.6)	47.4 (1.9)	0.03
Semantic fluency	1450	48.4 (0.8)	50.0 (0.4)	50.9* (0.4)	48.9 (0.6)	49.5 (1.9)	0.01
MMSE	1434	47.2 (0.8)	50.7* (0.4)	50.7* (0.4)	49.1 (0.6)	46.1 (2.0)	< 0.001
Men							
Number	3972	269	1246	1714	655	88	
Cognitive function T-scores†							
Memory	3965	49.3 (0.6)	49.7 (0.3)	50.5 (0.2)	49.6 (0.4)	48.6 (1.0)	0.03
AH4-I (reasoning)	3969	47.4 (0.6)	49.8* (0.3)	50.6* (0.2)	50.1* (0.4)	49.3 (1.0)	< 0.001
Mill Hill (vocabulary)	3967	48.4 (0.6)	49.6 (0.3)	50.5* (0.2)	50.2* (0.4)	49.0 (1.1)	0.006
Phonemic fluency	3957	48.5 (0.6)	50.1* (0.3)	50.2* (0.2)	50.1* (0.4)	48.5 (1.1)	0.05
Semantic fluency	3965	48.0 (0.6)	49.9* (0.3)	50.4* (0.2)	50.1* (0.4)	47.8 (1.0)	< 0.001
MMSE	3857	48.6 (0.6)	49.9 (0.3)	50.5* (0.2)	49.8 (0.4)	48.2 (1.1)	0.01

†Figures are means using T-scores (standard errors); *P < 0.05 for difference relative to ≤ 5 h (arbitrary reference category); **P-value for heterogeneity.

poorer cognitive function for all the tests except memory. In the case of a decrease from 6, 7 or 8 h sleep, firm evidence of an association with poorer cognitive function remained for reasoning, vocabulary, and the MMSE. The magnitude of these effects was equivalent to a 4-7 year increase in age.

Table 4—Sleep duration category at Phase 7 defined by change in number of hours sleep between Phase 5 and Phase 7

Sleep duration category	**Women (N = 1459)**	**Men (N = 3972)**
No change in sleep duration	% (N)	% (N)
≤ 5 h at both phases	4.7 (68)	3.0 (120)
6 h at both phases	16.7 (243)	18.9 (752)
7 h at both phases	19.5 (284)	27.8 (1103)
8 h at both phases	8.1 (118)	7.5 (298)
≥ 9 h at both phases	0.5 (7)	0.6 (23)
Total – no change in sleep duration	49.5 (720)	57.8 (2327)
Decrease from 9 hours (9 h sleep at Phase 5 and < 9 h at Phase 7)	1.3 (19)	0.7 (26)
Increase from ≤ 5 or 6 hours (≤ 5 or 6 h sleep at Phase 5 and > 5 or 6 h, respectively, at Phase 7)	16.7 (243)	14.6 (580)
Decrease from 6, 7 or 8 hours (6, 7, or 8 h sleep at Phase 5 and < 6, 7, or 8 h, respectively at Phase 7)	25.3 (369)	18.3 (727)
Increase from 7 or 8 hours (7 or 8 h sleep at Phase 5 and > 7 or 8 h, respectively, at Phase 7)	7.4 (108)	8.6 (343)

DISCUSSION

Synopsis of Findings

This study suggests that moves from a regular pattern of 6-8 hours per night to the short and long ends of the sleep distribution are associated with poorer cognitive function relative to those whose sleep duration remains unchanged. In analyses adjusted for age, sex, and education and corrected for multiple testing, a move to the long end of the sleep distribution appeared the most detrimental. An increase in sleep from 7 or 8 hours per night is associated with poorer cognitive function scores for all tests (reasoning, vocabulary, phonemic, and semantic fluency, and the mini mental state examination), except memory—equivalent to an increase in age of 5-8 years. A move to the short end of the sleep distribution, a decrease from 6, 7, or 8 h sleep per night, was also associated with poorer scores for all tests except memory and phonemic fluency—equivalent to a 3-5 year increase in age. Although these associations were partially explained by occupational position, evidence of associations between changes in sleep duration and cognitive function remained firm with the exception of that between a decrease from 6, 7, or 8 h sleep and semantic fluency.

Shape of the Associations

Most existing studies have examined cross-sectional associations between sleep problems and cognitive function.[11-13,15-19] Of those that have examined sleep duration,[10,14,19,23,35] only two appear to present data separately for men as well as women.[10,14] The present study enabled us to compare the shape of associations between sleep duration and a range of cognitive function measures separately by sex. Overall associations between sleep duration and all cognitive function measures were U-shaped, with the lowest scores consistently associated with short and long sleep. These findings are similar to those from a population

Table 5—Cognitive function at Phase 7 by change in number of hours sleep between Phase 5 and Phase 7 in women and men combined

	Change in hours of sleep between Phase 5 and Phase 7			
Cognitive Function Test#	**Increase from 5 or 6 h[a]**	**Participants with no change in sleep duration**	**Decrease from 6, 7, or 8 h[b]**	**Increase from 7 or 8 h[c]**
Number	823	3047	1096	451
A Adjusted for age, sex and education				
Memory	0.30 (-0.54, 1.14)	Ref	-0.27 (-0.96, 0.42)	-1.09 (-2.07, -0.10)
AH4-I (reasoning)	0.06 (-0.73, 0.86)	Ref	-1.44*** (-2.09, -0.79)	-1.36* (-2.29, -0.43)
Mill Hill (vocabulary)	0.26 (-0.55, 1.06)	Ref	-1.05** (-1.71,-0.39)	-1.62** (-2.56, -0.68)
Phonemic fluency	-0.21 (-1.05,0.62)	Ref	-0.59 (-1.27, 0.09)	-1.35* (-2.33, -0.38)
Semantic fluency	0.11 (-0.71, 0.93)	Ref	-0.90* (-1.57, -0.23)	-1.66** (-2.62, -0.70)
MMSE	-0.19 (-1.06, 0.68)	Ref	-1.34** (-2.05, -0.63)	-1.85* (-2.87, -0.83)
B Adjusted for age, sex, education and occupational position at Phase 7				
Memory	0.23 (-0.61, 1.06)	Ref	-0.12 (-0.80, 0.57)	-0.98 (-1.96, -0.01)
AH4-I (reasoning)	-0.13 (-0.87, 0.61)	Ref	-1.08** (-1.69, -0.47)	-1.11* (-1.98, -0.25)
Mill Hill (vocabulary)	0.09 (-0.67, 0.85)	Ref	-0.72* (-1.34, -0.10)	-1.39** (-2.28, -0.50)
Phonemic fluency	-0.34 (-1.15, 0.47)	Ref	-0.33 (-0.99, 0.33)	-1.19* (-2.14, -0.25)
Semantic fluency	-0.04 (-0.82, 0.75)	Ref	-0.62 (-1.27, 0.02)	-1.47** (-2.39, -0.55)
MMSE	-0.26 (-1.12, 0.60)	Ref	-1.19* (-1.90, -0.49)	-1.73** (-2.74, -0.72)

#Mean difference in score (95% confidence interval)
[a]≤ 5 or 6 h sleep at Phase 5 & more than 5 or 6 hours respectively at Phase 7, reference group is either ≤ 5 or 6 h at both phases (n = 1183 [68+243+120+752 - see Table 4])
[b]6, 7 or 8 h sleep at Phase 5 and < 6, 7, or 8 h, respectively, at Phase 7, reference group is either 6, 7, or 8 h at both phases (n = 2798 [243+284+118+752+1103+298 - see Table 4])
[c]7 or 8 h sleep at Phase 5 and > 7 or 8 h respectively at Phase 7, reference group is either 7 or 8 h at both phases (n = 1803 [284+118+1103+298 - see Table 4])
*P < 0.05, **P < 0.01, and ***P < 0.001 for difference from no change group
The critical values determining the significance of each test have been adjusted to allow for the multiple comparisons in this table (see methods section).

sample of adults aged 60 and over in Spain which demonstrated U-shaped associations between sleep duration and a Spanish version of the Mini-Mental state examination in both women and men, although in this sample associations were much stronger for very long sleep durations than for short sleep.[10]

Differences between the scores for memory across the sleep duration distribution were small in both sexes. However, for other measures of cognitive function; reasoning, vocabulary, fluency, and the Mini-Mental state examination, there was good evidence that short sleep and sleep durations of 8 or more hours were associated with poorer cognitive function in women, although in men such associations were observed only for short and long sleep. While differences in the cognitive scores between the sleep duration categories seem relatively small, it is now increasingly recognized that cognitive trajectories over the life course are important for late life cognitive outcomes such as dementia.[8,9] Previous work from the Whitehall II study indicates that they may be clinically relevant. Differences between sleep durations of 5 hours or less and 7 hours per night are equal to between 50% and 100% of the coronary heart disease–no coronary heart (CHD - No-CHD) disease differences in cognitive function scores observed previously in this cohort (see supplementary Table S2).[36]

Our findings for men exactly replicate findings for women aged 70 and over from the Nurses Health Study,[23] but are slightly different from those from the two other studies that have reported on the association with sleep duration in men.[10,14] Compared with 7 hours sleep per night, 6 hours or less was associated with poorer cognitive function in men aged 60+, and there were no associations between sleep durations of 8 hours or more and cognitive function. However, this smaller study had only one self-reported cognitive function measure that combined a measure of memory and general cognitive complaints.[14] Associations observed in the present study between longer sleep and poorer cognitive function, both in the cross-sectional and prospective analyses, highlight the importance of long sleep, which has tended to be overshadowed as a risk factor by insomnia and short sleep.[37]

Nature of the Association

Although education is associated with both cognitive function and sleep in these data, moves from a regular pattern of 6-8 hours per night to the short and long ends of the sleep distribution were associated with poorer cognitive function in analyses adjusted for education. Further adjustment for employment grade, a comprehensive marker of socioeconomic position in this cohort, slightly attenuated the associations observed. Thus it seems that associations between change in sleep duration and cognitive function are partially accounted for by markers of socioeconomic position. However, this attenuation falls far short of abolishing the observed associations, indicating either a direct association between change in sleep and cognitive function, or an association mediated or confounded by factors other than education and occupational position.

Adequate, good quality sleep is fundamental to human functioning and well-being. Sleep deprivation and sleepiness have such adverse effects on performance, response times, errors of commission, and attention or concentration,[38,39] that most countries have strict legislation regulating the number of hours people can work without adequate time for rest. While a direct association between sleeping for longer and adverse outcomes initially seems less plausible, a review by Grandner and Drummond[40] has suggested seven possible mechanisms underlying the association between long sleep and early death. Of these; sleep fragmentation, which can result in poor quality sleep; depression; and underlying disease processes, such as CHD, appear to be relevant to the association between long sleep and cognitive function. While poor quality sleep, analogous to sleep deprivation, could indicate a direct association; the remaining explanations suggest associations mediated or confounded by depression or disease. Depression has been shown to be associated with poor sleep, including long-sleeping,[41] and with cognitive function in this cohort.[42] CHD similarly has been shown to be associated with poor sleep,[43] and with poorer cognitive function.[36]

Reverse causality, the possibility that cognitive function determines sleep duration, cannot be ruled out in our analyses. However, the longitudinal nature of the data which permits the examination of change in sleep duration makes this explanation unlikely. Further support for this position comes from previous work that has provided no firm evidence that cognitive decline predicts sleep duration.[35]

Comparison with Other Findings

While few studies of sleep and cognitive function have used longitudinal data, our findings support those that have demonstrated prospective associations between poor sleep patterns and cognitive impairment and cognitive decline.[21,22] Our findings are also in agreement with the only previous study of change in sleep duration. In this small, population-based study a move from 7-8 hours sleep per night to ≥ 9 hours over a period of 8.5 years was associated with a doubling of the prevalence of cognitive impairment.[26]

Sleep duration has been found to be associated with a wide range of quality of life measures, such as social functioning,[44,45] health outcomes, such as poor mental health, obesity, type 2 diabetes, cardiovascular disease; and early death.[28,46-51] In common with cognitive function in the present study, this association is typically U-shaped with poorer outcomes concentrated at the short and long ends of the sleep distribution. The only work that appears to have examined change in sleep as a determinant of health is three studies on associations with mortality. While an early study found no association,[52] two subsequent studies have provided good evidence that moves to the short and long ends of the sleep distribution are associated with an excess risk of all-cause and cardiovascular mortality.[28,53]

Methodological Considerations

This study appears to be the first large study to report on the association between change in sleep duration and cognitive function and among the first to report in detail on the shape of the association between sleep duration and cognitive function in men. In addition to large numbers, the study benefits from a clinic-based measure of cognitive function comprising six tests. This gives it an advantage over the majority of other studies which either have cognitive function measured in the laboratory on small numbers or rely on self-reported measures of cognitive function. Although the cognitive function tests used did not allow us to explore specific cognitive functions with precision, the six tests provide a comprehensive evaluation of cognitive function for this population of older white-collar workers. Our findings probably represent conservative, but more realistic, estimates of the effects associated with changes in sleep duration since the reference group for each change category is participants from the same category at baseline who do not change rather than those who consistently have 7 or 8 hours sleep. This was a deliberate choice based on the understanding that habitual short or long sleep is not detrimental in all individuals.

This study has at least two main limitations. First, our measure of sleep duration is a single-item, self-reported measure that used hourly categories as responses and did not explicitly ask participants to differentiate time asleep from time in bed. Self-reports and actigraph-measured sleep duration appear to be moderately correlated in younger and older adults, with self-reports, on average, providing an overestimation of sleep duration.[54,55] Concordance between self-reported sleep duration and polysomnography, the gold standard, in older adults is low to moderate.[56] Obtaining repeat data using objective measures of sleep duration from large cohorts is expensive and time consuming, although actigraphy, the less expensive of the objective measures, is increasingly being introduced on a larger scale.[55] Nonetheless, most large cohorts with repeat data on sleep duration are still reliant on self-reports, and it is important to recognize that self-reported sleep duration is strongly associated with health outcomes.[28,46-51] Furthermore, assessments of sleep durations in the primary health care setting rely on self-reported data from patients and so our findings are likely to be ecologically valid. The other main limitation is generalizability. Findings from an occupational cohort aged 45-69 years of age at baseline and almost exclusively white-collar may not apply to wider populations.

CONCLUSIONS

The "life-long" view of dementia emphasizes the importance of risk factors across the life course from early to mid and late adulthood.[9,57,58] In the present study, we adopt this approach and apply it to sleep as a risk factor for poor cognitive function. The study describes the effects of changes in sleep over a five-year period starting in late middle age on cognitive function in later life. Our findings show that women and men who move toward the short and long ends of the sleep distribution appear to be subject to accelerated cognitive aging equivalent to a 3-8 year increase in age. Further research is needed to corroborate these findings in the general population, preferably in studies sufficient in size to examine the detriment associated with each hour of change in sleep duration. In addition, further work is needed to elucidate the mechanisms that underlie these associations.

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DISCLOSURE STATEMENT

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Table S1—Age, education and occupational position adjusted cross-sectional associations between sleep duration and cognitive function at Phase 7

	N	Hours of sleep at Phase 7					P-value**
Women		**≤ 5 h**	**6 h**	**7 h**	**8 h**	**≥ 9 h**	
Number	1459	148	494	550	242	25	
Cognitive function test scores†							
Memory	1455	49.5 (0.8)	50.0 (0.4)	50.1 (0.4)	50.2 (0.6)	49.0 (1.9)	0.92
AH4-I (reasoning)	1456	48.8 (0.6)	50.1 (0.3)	50.8* (0.3)	48.9 (0.5)	48.4 (1.5)	0.005
Mill Hill (vocabulary)	1452	48.3 (0.7)	50.2* (0.4)	50.8* (0.3)	48.9 (0.5)	48.0 (1.6)	0.001
Phonemic fluency	1445	49.2 (0.7)	50.0 (0.4)	50.5 (0.4)	49.8 (0.6)	47.0 (1.7)	0.22
Semantic fluency	1450	49.5 (0.7)	50.0 (0.4)	50.6 (0.4)	49.1 (0.5)	49.3 (1.7)	0.18
MMSE	1434	47.8 (0.8)	50.6 (0.4)	50.5 (0.4)	49.2 (0.6)	46.1 (2.0)	0.002
Men							
Number	3972	269	1246	1714	655	88	
Cognitive function test scores†							
Memory	3965	49.9 (0.6)	49.8 (0.3)	50.4 (0.2)	49.5 (0.4)	48.6 (1.0)	0.08
AH4-I (reasoning)	3969	48.8 (0.5)	49.9 (0.2)	50.3* (0.2)	49.9 (0.3)	49.2 (0.9)	0.09
Mill Hill (vocabulary)	3967	49.6 (0.5)	49.8 (0.2)	50.3 (0.2)	50.0 (0.3)	48.8 (0.9)	0.27
Phonemic fluency	3957	49.5 (0.6)	50.2 (0.3)	50.1 (0.2)	50.0 (0.4)	48.5 (1.0)	0.51
Semantic fluency	3965	49.1 (0.6)	50.0 (0.3)	50.3* (0.2)	49.9 (0.4)	47.8 (1.0)	0.05
MMSE	3857	49.1 (0.6)	49.9 (0.3)	50.4* (0.2)	49.7 (0.4)	48.2 (1.0)	0.07

†Figures are means (standard errors). *P < 0.05 for difference relative to ≤ 5 h (arbitrary reference category). **P-value for heterogeneity.

Table S2—Comparison of the cross-sectional association at Phase 7 between sleep duration and cognitive function with cognitive function differences between CHD and No-CHD*

	N	Hours of sleep at Phase 7		Standardized difference	
Women		**≤ 5 h**	**7 h**	**5 h-7 h**	**CHD-No CHD**
Number	1459	148	550		
Cognitive function T-scores†					
Memory	1455	48.7 (0.8)	50.3 (0.4)	-0.16	-0.35
AH4-I (reasoning)	1456	47.4 (0.8)	51.2* (0.4)	-0.38	-0.58
Mill Hill (vocabulary)	1452	46.9 (0.8)	51.3* (0.4)	-0.44	-0.46
Phonemic fluency	1445	48.2 (0.8)	50.8* (0.4)	-0.26	-0.47
Semantic fluency	1450	48.4 (0.8)	50.9* (0.4)	-0.25	-0.40
MMSE	1434	47.2 (0.8)	50.7* (0.4)	-0.35	-0.31
Men					
Number	3972	269	1714		
Cognitive function T-scores†					
Memory	3965	49.3 (0.6)	50.5 (0.2)	-0.12	-0.22
AH4-I (reasoning)	3969	47.4 (0.6)	50.6* (0.2)	-0.32	-0.25
Mill Hill (vocabulary)	3967	48.4 (0.6)	50.5* (0.2)	-0.21	-0.25
Phonemic fluency	3957	48.5 (0.6)	50.2* (0.2)	-0.17	-0.13
Semantic fluency	3965	48.0 (0.6)	50.4* (0.2)	-0.24	-0.14
MMSE	3857	48.6 (0.6)	50.5* (0.2)	-0.19	-0.25

†Figures are means (standard errors). *Standardized differences between CHD and No-CHD have been calculated from reference.[34]