

Long Working Hours and Cognitive Function: the Whitehall II Study

Marianna Virtanen¹, PhD
Jane E. Ferrie², PhD
Archana Singh-Manoux^{2,3,4}, PhD
David Gimeno², PhD
Michael Marmot², MD, PhD
Marko Elovainio⁵, PhD
Markus Jokela¹, PhD
Jussi Vahtera¹, MD, PhD
Mika Kivimäki², PhD

¹ Finnish Institute of Occupational Health, Topeliuksenkatu 41 a A, FIN-00250 Helsinki, Finland

² Department of Epidemiology and Public Health, University College London, UK

³ INSERM U687-IFR69, France

⁴ Centre de Gérontologie, Hôpital Ste Péline, AP-HP, France

⁵ National Research and Development Centre for Welfare and Health, Helsinki, Finland

Word count: 181 in Abstract, 3978 in text, 60 references, 4 tables, 1 figure

ABSTRACT

This study examined the association between long working hours and cognitive function in middle age. Data were collected in 1997-1999 (baseline) and 2002-2004 (follow-up) from a prospective study of 2214 British civil servants who were in full time employment at baseline and had data on cognitive tests and covariates. A battery of cognitive tests (short-term memory, Alice Heim 4-I, Mill Hill vocabulary, phonemic fluency and semantic fluency) were measured at baseline and at follow-up. Compared with working 40 hours per week at most, working more than 55 hours per week was associated with lower scores in the vocabulary test both at baseline and at follow-up. Long working hours also predicted decline in performance on the reasoning test. Similar results were obtained using working hours as a continuous variable; the associations between working hours and cognitive function were robust to adjustments for several potential confounding factors including age, sex, marital status, education, occupation, income, physical diseases, psychosocial factors, sleep disturbances, and health risk behaviors. This study shows that long working hours may have a negative effect on cognitive performance in middle age.

Long working hours are common worldwide; for example in the European Union member states 12%-17% of employees worked overtime in 2001 (1). Long working hours have been found to be associated with cardiovascular and immunological reactions, reduced sleep duration, unhealthy life style,²⁻⁸ and adverse health outcomes, such as cardiovascular disease, diabetes, subjective health complaints, fatigue (2-7), and depression (8). There is increasing evidence to suggest the importance of midlife risk factors for later dementia (9). Furthermore, the link between cognitive impairment and later life dementia is clearly established (10-11). Thus, it is important to examine risk factors for poor cognition in midlife, and there is little research on the potential effects of long working hours on cognition among middle-aged.

A cross sectional study of 248 automotive workers found an association between overtime work and impaired performance on tests of attention and executive function (12). This finding was in agreement with other studies that focused on different forms of shift work or work schedule rather than on long working hours (13-14). For example, deterioration in cognitive performance, including impaired grammatical reasoning and alertness, has been found in post vs pretest conditions among employees working 9 to 12-hour shifts compared with a traditional 8-hour shift (13). However, little is known about the health effects of long total working hours as opposed to long hours of shift work.

This study examined the relationship between long working hours and cognitive function over a five year follow-up period in a large-scale, prospective occupational cohort of British Civil Servants (the Whitehall II Study)(15). We were able to take into account several factors that may act as confounders or mediators of this association, such as education, occupational position, physical health status, psychological and psychosocial factors, sleep problems, and health risk behaviors (2).

MATERIALS AND METHODS

Participants and procedure

The Whitehall II study sample recruitment (Phase 1) took place between late 1985 and early 1988 among all office staff, aged 35 to 55, from 20 London based Civil Service departments (15). The response rate was 73% (6895 men and 3413 women). Since Phase 1 there have been seven further data collection phases. Informed consent was gained from all participants. The University College London Medical School Committee on the Ethics of Human Research approved the protocol.

As cognitive performance was measured on the whole sample for the first time at Phase 5, this Phase is used as baseline for the present study. We included all 2214 participants (1694 men and 520 women) who were employed and responded to the questions on working hours and for whom the covariates and cognitive test scores were available at Phase 5 (1997-1999) and Phase 7 (2002-2004). A flow chart of sample selection is shown in Figure 1. The mean age of the 2214 participants at Phase 5 was 52.1 (SD 4.2, range 45 to 66) years. There were no major differences between the participants and all full-time employees who participated in phase 5 (n=3597) in terms of age (52.1 vs 52.4 years), sex (77% vs 75% male), occupational grade (18% with the lowest occupational grade, vs 22%), and prevalence of coronary heart disease, CHD (10% vs 11%). However, employees who participated in our study at phases 5 and 7 differed from the cohort at recruitment to the Whitehall II study (n=10,308), in that they were younger (mean age 40.6 vs 44.5 at phase 1), more likely to be male (77% vs 67%); from the higher socioeconomic groups (10% with the lowest grade vs 23%) and less likely to have pre-existing CHD at phase 1 (2.7% vs 4.1%).

Tests of cognitive function

The cognitive function test battery at phases 5 and 7 consisted of five standard tasks chosen to evaluate cognitive functioning in middle-aged adults. The first was verbal memory assessed by a 20-word free recall test of short-term memory. Participants were presented a list of 20 one or two syllable words at 2-second intervals and were then asked to recall in writing as many of the words in any order within 2 minutes. The Alice Heim-I (AH 4-I)(16) is a test of inductive reasoning that measures fluid intelligence, i.e. the ability to identify patterns and infer principles and rules. This test is composed of a series of 65 items (32 verbal and 33 mathematical reasoning items) of increasing difficulty. The participants had 10 min to complete this section. The Mill Hill vocabulary test (17) assesses crystallized intelligence, i.e. knowledge of verbal meaning and encompasses the ability to recognize and comprehend words. We used this test in its multiple-choice format which consists of a list of 33 stimulus words ordered by increasing difficulty, and six response choices per word. The final two tests were measures of verbal fluency: phonemic and semantic (18). Phonemic fluency was assessed via “S” words and semantic fluency via “animal” words. Subjects were asked to recall in writing as many words beginning with “S” and as many animal names as they could. One minute was allowed for each test of verbal fluency. A higher score indicated better performance in each test.

The change score was calculated for each measure of cognitive function as Phase 7 score minus Phase 5 score. As the time interval between clinical examination at Phases 5 and 7 varied between 3.9 and 7.1 years (mean 5.5 years), the difference in cognitive score was divided by the time in years between the two measures for each individual and multiplied by 5 to give everyone the same (5-year) time period between the two phases of cognitive data collection.

Working hours and other baseline characteristics

Working hours were determined at Phase 5 from the following two questions: “How many hours do you work per average week in your main job, including work brought home?”, and “How many hours do you work in an average week in your additional employment?” Participants were divided into the following three groups: a total of 35-40 hours; 41-55 hours; more than 55 hours per week (5-7). In addition, analyses were conducted using the scale as a continuous variable. Participants in the Whitehall II study are almost exclusively white-collar civil servants. The most common weekly working hours correspond to 36 hours per week net although various flexible working arrangements can also be arranged. In the present cohort, the mean working hours was 45.2 hours/week (S.D. 8.0, range 35 to 120).

Altogether 20 socio-demographic characteristics, behavioral, psychological, psychosocial and medical conditions known to be associated with cognitive function and/or working hours, were included as covariates in the analysis (2-9,12,19-38). In addition to sex and age, marital status, indicators of socioeconomic position, i.e. occupational grade (6 levels from which the lowest two levels were collapsed to obtain sufficient numbers), education (post graduate, graduate, higher secondary school, lower secondary school, or no academic qualifications), and the participant's report of his/her annual gross salary were assessed. Employment status (working vs. not working) at follow-up was obtained from the Phase 7 questionnaire.

The physical functioning component score of the SF36(39) was used as a measure of global physical health status and divided into quartiles separately for men and women. Prevalent CHD at phase 5 included cases of non-fatal myocardial infarction (MI) and angina. In addition to definite non-fatal MI and definite angina our total non-fatal CHD events outcome included self-reported cases in the absence of any clinical record evidence of coronary disease. Systolic blood

pressure and diastolic blood pressure were measured using the Hawksley random-zero sphygmomanometer. In keeping with standard definitions, subjects with systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg or on antihypertensive treatment were considered to be hypertensive (40).

Psychological distress was assessed using the 30-item General Health Questionnaire (GHQ-30)(41). The GHQ-30 has been validated in a number of diverse populations and has been validated specifically against the Clinical Interview Schedule in Whitehall II data, giving a cut-off point of 4/5 positive responses for dividing non-cases from cases (42). In addition, a 5-item subscale of anxiety (e.g. feelings of constant strain, panic, nervousness) was derived from the General Health Questionnaire (GHQ-30)(41). Scores in the top decile were used to define anxiety cases, corresponding to the prevalence of anxiety disorders in the general population (43).

Sleep was assessed in two ways; the first was a measure of duration with respondents identified as short sleepers if they reported sleeping less than 6 hours on an average week night (44). Sleep quality was assessed using the Jenkins Scale (45) which assesses sleep disturbances during the past 4 weeks. The mean response score for all four questions was divided into tertiles.

Of the health behaviors, alcohol consumption (units/week) was classified into three categories: none; >0 to 14 (women) / 21 (men) units; more than 14/21 units (46). Smoking was assessed by a single question of whether the respondent was a current smoker or not. For the physical activity score the participants were asked about the frequency and duration of their participation in physical activity (47). The amount of time spent in activities with MET values ranging from 0 to 6 or above was summed to allow calculation of total number of hours per week of physical activity and divided into three categories low, moderate and high.

Social support was measured by the 15-item Close Persons Questionnaire (48) which includes questions about confiding/emotional support, practical support, and negative aspects of close relationships. The mean of all responses was divided into tertiles. Strain in family relations was measured with a single-item question of how often the participant had any worries or problems with other relatives e.g. parents or in-laws (always/often vs sometimes/seldom/never/not applicable). Job strain was formulated by splitting the job demands score and decision latitude score at their medians. High demands and low decision latitude indicated high job strain and other combinations indicated low job strain (49).

Statistical analysis

All analyses were carried out using SAS statistical software, version 9.1, except missing-data analysis which was done using STATA 9.0 statistical software. First, we compared baseline characteristics of the participants by working hours and compared the longer-hours group (>55 hours per week) with the employees with normal working hours (35-40 hours a week) using χ^2 tests. We used multiple analysis of covariance (MANCOVA) to examine whether work hours had an overall association with cognitive function, as checking for each measure of cognitive function separately increases the chance of Type 1 error. Subsequently, ANOVA was used to assess the association between work hours and individual measures of cognitive function. When a significant difference was found in cognitive function tests at baseline and/or at follow-up between groups additional analyses were carried out with the change score to assess temporal order and examine whether the change was statistically significant. Sequential analyses were undertaken to see whether adjustment for covariates attenuated the association between long working hours and change in cognitive function. Age was entered into the models as a continuous variable and all other covariates were entered as categorical variables. As

recommended by Glymour et al. (50) we used baseline-unadjusted change scores for cognitive change. In order to examine linear trend in the association between working hours and cognitive function, we repeated the analysis using working hours as a continuous variable.

To explore whether selection bias might have occurred due to loss to follow-up we undertook a sensitivity analysis in which we used multiple multivariate imputation (51) using working hours, all covariates, cognition variables to impute values for missing values in any variables with some missing data, amongst all 3163 participants free of stroke and TIA at baseline. We used switching regression in Stata as described by Royston (51), and carried out 20 cycles of regression switching and generated 20 imputation datasets. The multiple multivariate imputation approach creates a number of copies of the data (in this case we generated 20 copies) each of which has values that are missing imputed with an appropriate level of randomness using chained equations. The estimates are obtained by averaging across the results from each of these 20 datasets using Rubin's rules. The procedure takes account of uncertainty in the imputation as well as uncertainty due to random variation, as undertaken in all multivariable analyses.

RESULTS

Characteristics of the study participants by working hours at baseline are shown in Table 1. 853 (39%) participants reported 35 to 40 hours of work per week, 1180 (53%) reported 41 to 55 hours, and 181 (8%) reported more than 55 hours of work per week. Compared to employees with 35-40 hours, a higher percentage of those who worked more than 55 hours were men and were married or cohabited, had a higher occupational grade, higher education, higher income, more psychological distress, shorter sleep, higher alcohol use and more social support.

MANCOVA analysis revealed an overall association of working hours with cognitive function at baseline ($p=0.002$) and follow-up ($p=0.037$) cognitive function as well as change in cognitive function scores between baseline and follow-up ($p=0.044$). Table 2 shows the associations between working hours at baseline and each cognitive function measure at baseline and at follow-up after adjustment for all covariates measured at baseline. Compared to employees working ≤ 40 hours per week, employees working more than 55 hours had lower vocabulary scores at baseline and at follow-up. At follow-up they had lower scores also on the reasoning test. No significant difference between groups was found in any other measures of cognitive function at follow-up. Repeating these analyses with working hours treated as a continuous variable largely replicated the findings, and additionally showed an association between working hours and better phonemic fluency at baseline but not at follow-up.

Table 3 examines the mean difference in the change in reasoning score between those working normal hours and those working long hours. Successive models show the effects of step-by-step adjustments. The stepwise adjustments show that various adjustments produced little attenuation of the effect of working hours on decline in reasoning score and a clear dose-response pattern was revealed between exposure and outcome. Again the findings were replicated in models replacing categories with a continuous measure of working hours.

Sensitivity analyses

To further examine whether the findings are robust, we ran a sensitivity analysis in a sub-group of participants still employed at follow-up ($n=1672, 1677$). In line with the main analyses, working >55 hours vs ≤ 40 hours was associated with a greater decline in the

reasoning score (difference -1.47, $p=0.002$) and lower scores in the vocabulary test at baseline and at follow-up (difference -0.77, $p=0.009$ at baseline; -0.60, $p=0.046$ at follow-up). Corresponding p-values for the continuous working hours were $p=0.009$, $p=0.004$, and $p=0.023$.

To examine sex differences, we conducted altogether 15 tests of interaction between sex and continuous working hours on cognitive function outcomes and found two statistically significant interactions; for the vocabulary test at baseline ($p=0.015$) and at follow-up ($p=0.003$). Sex-stratified analysis showed a significant negative association between working hours and vocabulary score at baseline and at follow-up among men (p-values <0.001) but not among women (p-values 0.899 and 0.339).

Finally, table 4 repeats the analyses on those associations which were found to be robust in tables 2 and 3, except that the results were obtained from the multiple multivariate imputation analysis for the baseline population, a total of 3163 participants. To simplify comparison of cohorts before and after imputations, we present effects of working hours as per 10 hours increase in a continuous measure. Imputation had little effect on the associations with vocabulary at baseline and follow-up and reasoning at follow-up. The association with reasoning at baseline was strengthened considerably but the association with change in reasoning was slightly attenuated ($p=0.053$). Corresponding p-values for categorical working hours variable were as follows: between the groups of >55 hours vs ≤ 40 hours, $p<0.001$ for vocabulary score at baseline and follow-up; $p=0.068$ for reasoning score at baseline; $p=0.002$ for reasoning at follow-up; and $p=0.025$ for the change score in reasoning (data not shown), thus replicating the original findings.

DISCUSSION

In this study of middle-aged men and women, working more than 55 hours per week was associated with lower scores on two of the five tests of cognitive function. Long working hours at baseline were related to poorer performance in the vocabulary test both at baseline and at follow-up. Furthermore, long working hours predicted decline in performance on the reasoning test over a 5-year follow-up period. These effects were robust to adjustments for 20 potential confounding factors, such as education, occupational position, physical diseases (cardiovascular dysfunction), psychosocial stress factors, sleep problems, and health risk behaviors.

We found an association between long working hours and decline in the scores for the AH 4-I reasoning test and associations with the Mill Hill Vocabulary tests at baseline and at follow-up. AH 4-I is also recognised as a measure of fluid intelligence, i.e. executive function or “meta” cognitive ability as it integrates other cognitive processes like memory, attention, and speed of information processing. Fluid intelligence is seen to be intrinsically associated with information processing and involves short-term memory, abstract thinking, creativity, ability to solve novel problems, and reaction time. It is the aspect of intelligence most affected by aging, biological factors, diseases, and injuries (52,53). Fluid intelligence usually increases up to the mid-20s after which it gradually declines until the 60s when a more rapid decline takes place.

The Mill Hill vocabulary test measures crystallized intelligence which is assumed to accumulate during the lifespan through education, occupational and cultural experience and exposure to culture and intellectual pursuits (52,53). Crystallized abilities usually increases up to the sixth or seventh decade of age and may not decrease until after 80 years of age. We found the Mill Hill scores to remain relatively stable as expected for this middle aged cohort. However, the Mill Hill scores were lower among employees with long working hours both at baseline and at

follow-up. This consistency with two separate measures with a 5-year interval suggests not only a plausible finding but also stability of the far-reaching effect of long working hours on vocabulary. We did not find an interaction effect between follow-up employment status and working hours on significant outcomes which suggests that the associations found are not dependent on employment status at follow-up. However, people who work long hours might be exposed to a narrower variation of intellectual pursuits i.e. only to those that are related to their work tasks and therefore might not be able to develop a wide variety of functions in crystallized intelligence measured in the test. However, reversed causality is also possible: employees with lower cognitive ability may be more prone to work overtime than workers with good cognitive ability in order to get their work done.

Previous literature, mostly cross sectional, suggests that long working hours are associated with various health outcomes, the strongest effects observed for cardiovascular diseases, fatigue, and sleep disturbances (2-8). These can also be hypothesized to be mediating mechanisms for the association between long working hours and cognitive decline. Hypertension is associated with cognitive dysfunction by producing subtle disturbances in cerebral perfusion and affecting brain cell metabolism (19-20). However, we found no evidence of an association between long working hours and hypertension or CHD suggesting that the effect of long hours on cardiovascular dysfunction, if any, is unlikely to explain cognitive decline in this study.

Another hypothesis on mediating mechanisms links long working hours with psychological stress and poor recovery from work as indicated by sleeping problems and reduced sleep. Psychological stress has been suggested as affecting the brain via two neuroendocrine systems; the sympathetic adrenomedullary system with the secretion of epinephrine and norepinephrine, and the hypothalamic pituitary adrenocortical (HPA) system with the secretion of cortisol (54). Of the few studies in the field, only one study has found an association between

long working hours and neuroendocrinological stress markers (55). We found that long working hours were associated with short sleep duration and psychological distress but not with sleep disturbances. Further adjustment for these factors did not provide support for the hypothesis that psychological distress and poor recovery act as mediating mechanisms.

The third hypothesis suggests that long working hours may affect cognitive function through health risk behaviors. Evidence on the association between long working hours and unhealthy behaviors is weak, but there is stronger evidence for the relationship between health behaviors and cognitive function (22-24,26). We found that adjustment for all these health risk behaviors had no effect on the association between long working hours and cognitive function, suggesting that health risk behaviors may not be an important mediating or confounding variable.

When working hours was entered into the model as a continuous variable, we found an association between long hours and better phonemic fluency at baseline but not at follow-up. This inconsistency is also reflected in the lack of an association between the categorical working hours and phonemic fluency. More research is needed to determine whether employees with long working hours do better than other employees on tests of verbal fluency. Out of 15 analyses, we found two statistically significant interaction effects between working hours and sex and sex-stratified analysis showed that long working hours were associated with poorer vocabulary performance among men but not among women. However, further research with larger samples is needed to examine potential sex differences in the association between working hours and cognition.

Strengths and limitations

The strengths of this study include large sample size and the possibility to explore prospectively the association between long working hours and a possible change in cognitive function over a 5-year interval which has not been feasible in earlier studies. Furthermore, we used five separate measures of cognitive function, allowing associations with specific aspects of cognition to be observed, and we were able to adjust for a large number of covariates as potential confounding or mediating factors between the exposure and outcome.

There are also important limitations in this study. First, the period of 5 years for cognitive decline might not be sufficient to detect a significant decline in cognitive function in general. Second, the Whitehall II cohort is based on civil servants and not representative of the entire working population, limiting the generalisability of our results. Third, we used self-reported working hours, with inherent problems of recall. Fourth, middle-aged occupational cohorts, such as ours, are subject to a healthy survivor effect as the study design involves participants being employed and gradually excludes those who develop work disability. However, all cohort studies focusing on work-related exposures at midlife are open to health-related selection because participants need to be employed. Because poor health is linked with worse cognition, healthy survivor effect is likely to lead to conservative estimates of the associations found. The baseline of the present study was approximately 15 years after inclusion into the Whitehall II study; men, employees in the higher occupational grades, and those free from CHD were slightly over-represented. However, the associations between work hours, vocabulary and reasoning were robust to adjustments for sex, occupational grade and health. Furthermore, similarity of these associations in the complete case and multiple imputation analyses suggests that loss-to-follow-up after the baseline is an unlikely source of bias in this study.

Conclusions

Decline in cognitive function has already been shown to be present among the middle-aged (9). As mild cognitive impairment predicts dementia (10,11) and mortality (56-58), the identification of risk factors for mild cognitive impairment in middle age is important. The results of this study show that long working hours may be one of the risk factors that have a negative effect on cognitive performance in middle age. Our findings can have clinical significance as the 0.6 to 1.4-unit difference in aspects of cognitive functioning between employees working long hours and those working normal hours is of the similar magnitude as smoking, a risk factor for dementia (59), has been found to have on cognition in the Whitehall II study (60). However, further research is needed to identify potential underlying factors for the relationship between long working hours and cognitive function and to examine generalisability of our findings.

REFERENCES

1. Vaguer C, Van Bastelaer A. Working overtime. *Statistics in Focus, Population and Social Conditions, European Communities* 11, 2004.
2. van der Hulst M. Long workhours and health. *Scand J Work Environ Health* 2003;29:171–88.
3. Caruso CC, Hitchcock EM, Dick RB, et al. Overtime and extended work shifts: Recent findings on illnesses, injuries, and health behaviors. NIOSH: Department of Health and Human Services, 2004.
4. Johnson JV, Lipscomb J. Long working hours, occupational health and the changing nature of work organization. *Am J Ind Med* 2006;49:921–9.
5. Sokejima S, Kagamimori S. Working hours as a risk factor for acute myocardial infarction in Japan: case-control study. *BMJ* 1998;317:775–80.
6. Liu Y, Tanaka H, The Fukuoka Heart Study Group. Overtime work, insufficient sleep, and risk of non-fatal acute myocardial infarction in Japanese men. *Occup Environ Med* 2002;59:447–51.
7. Sekine M, Chandola T, Martikainen P, Marmot M, Kagamimori S. Work and family characteristics as determinants of socioeconomic and sex inequalities in sleep: The Japanese Civil Servants Study. *Sleep* 2006;29:206–16.
8. Shields M. Long working hours and health. *Health Rep* 1999;11:33-48.
9. Kivipelto M, Ngandu T, Laatikainen T, et al. Risk score for the prediction of dementia risk in 20 years among middle aged people: a longitudinal, population-based study. *Lancet Neurol* 2006;59:735–41.
10. Chertkow H. Mild cognitive impairment. *Curr Opin Neurol* 2002;15:401-7
11. Morris JC, Storandt M, Miller JP, et al. Mild cognitive impairment represents early-stage Alzheimer disease. *Arch Neurol* 2001;58:397–405.
12. Proctor SP, White RF, Robins TG, et al. Effect of overtime work on cognitive function in automotive workers. *Scand J Work Environ Health* 2006;22:124–32.
13. Lockley SW, Cronin JW, Evans EE, et al. Effect of reducing interns' weekly work hours on sleep and attentional failures. *N Engl J Med* 2004;351:1829–37.
14. Knauth P. Extended work periods. *Ind Health* 2007;45:125–36.

15. Marmot M, Brunner E. Cohort profile: The Whitehall II Study. *Int J Epidemiol* 2005;34:251–6.
16. Heim AW. AH 4 group test of general intelligence ASE. Windsor, UK: NFER-Nelson Publishing Company Ltd, 1970.
17. Raven JC. Guide to using the Mill Hill vocabulary scale with progressive matrices. London: HK Lewis, 1965.
18. Borkowski JG, Benton AL, Spreen O. Word fluency and brain damage. *Neuropsychologica* 1967;5:135–40.
19. Launer LJ, Masaki K, Petrovich H, et al. The association between mid-life blood pressure levels and late-life cognitive function: the Honolulu-Asia Aging Study, *JAMA* 1995;274:1846–51.
20. Breteler MM. Vascular involvement in cognitive decline and dementia. Epidemiologic evidence from the Rotterdam Study and the Rotterdam Scan Study. *Ann N Y Acad Sci* 2000;903:457–65.
21. Singh-Manoux A, Sabia S, Lajnef M, et al. History of coronary heart disease and cognitive performance in midlife: the Whitehall II study. *Eur Heart J* 2008;29:2100–7.
22. Swan G, Lessow-Schlaggar CN. The effects of tobacco smoke and nicotine on cognition and the brain. *Neuropsychol Rev* 2007;17:259–73.
23. Silvers JM, Tokunaga S, Berry RB, et al. Impairments in spatial learning and memory: ethanol, allopregnanolone, and the hippocampus. *Brain Res Brain Res Rev* 2003;43:275–84.
24. Espeland MA, Gu L, Masaki KH, et al. Association between reported alcohol intake and cognition: results from the Women's Health Initiative Memory Study. *Am J Epidemiol* 2005;161:228–38.
25. Britton A, Singh-Manoux A, Marmot M. Alcohol consumption and cognitive function in the Whitehall II Study. *Am J Epidemiol* 2004;160:240–7.
26. Colcombe S, Kramer AF. Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychol Sci* 2003;14:125–30.
27. Bassuk SS, Berkman LF, Wypij D. Depressive symptomatology and incident cognitive decline in an elderly community sample. *Arch Gen Psychiatry* 1998;55:1073–81.
28. Yaffe K, Blackwell T, Gore R, et al. Depressive symptoms and cognitive decline in nondemented elderly women: a prospective study. *Arch Gen Psychiatry* 1999;56:425–30.

29. Philibert I. Sleep loss and performance in residents and nonphysicians: a meta-analytic examination. *Sleep* 2005;28:1392–1402.
30. Singh-Manoux A, Richards M, Marmot M. Socioeconomic position across the lifecourse: how does it relate to cognitive function in mid-life? *Ann Epidemiol* 2005;15:572–8.
31. Lee S, Buring JE, Cook NR, et al. The relation of education and income to cognitive function among professional women. *Neuroepidemiology* 2006;26:93–101.
32. Koster A, Penninx BW, Bosma H, et al. Socioeconomic differences in cognitive decline and the role of biomedical factors. *Ann Epidemiol* 2005;15:564–71.
33. Glymour MM, Weuve J, Fay ME, et al. Social ties and cognitive recovery after stroke: does social integration promote cognitive resilience? *Neuroepidemiology* 2008;31:10–20.
34. Bassuk SS, Glass TA, Berkman LF. Social disengagement and incident cognitive decline in community-dwelling elderly persons. *Ann Intern Med* 1999;131:165–73.
35. Lee S, Kawachi I, Grodstein F. Does caregiving stress affect cognitive function in older women? *J Nerv Ment Dis* 2004;192:51–7.
36. Crowe M, Andel R, Pedersen NL, et al. Personality and risk of cognitive impairment 25 years later. *Psychol Aging* 2006;21:573–80.
37. Lupien SJ, Maheu F, Tu M, et al. The effects of stress and stress hormones on human cognition: Implications for the field of brain and cognition. *Brain Cognition* 2007;65:209–37.
38. Potter GG, Helms MJ, Plassman BL. Association of job demands and intelligence with cognitive performance among men in late life. *Neurology* 2008;70:1803–8.
39. Ware JE, Kosinski M, Bayliss MS, et al. Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: Summary of results from the medical outcomes study. *Med Care* 1995;33:264–79.
40. Kivimäki M, Head J, Ferrie JE, et al. Hypertension is not the link between job strain and coronary heart disease in the Whitehall II Study. *Am J Hypertension* 2007;20:1146–53.
41. Goldberg DP. *The detection of psychiatric illness by questionnaire*. London, UK: Oxford University Press, 1972.
42. Stansfeld SA, Marmot MG. Social class and minor psychiatric disorder in British Civil Servants: a validated screening survey using the General Health Questionnaire. *Psychol Med* 1992; 22:739–49.

43. Jenkins R, Lewis G, Bebbington P, et al. The National Psychiatric Morbidity Surveys of Great Britain - initial findings from the Household Survey. *Psychol Med* 1997;27:775–89.
44. Ferrie JE, Shipley MJ, Cappuccio FP, et al. A prospective study of change in sleep duration: associations with mortality in the Whitehall II cohort. *Sleep* 2007;30:1659–66.
45. Jenkins D, Stanton BA, Niemcryk S, et al. A scale for the estimation of sleep problems in clinical research. *J Clin Epidemiol* 1988;41:313–21.
46. White I, Altmann DR, Nanchahal K. Mortality in England and Wales attributable to any drinking, drinking above sensible limits and drinking above lowest risk level. *Addiction* 2004;99:749–56.
47. Kujala UM, Sarna S, Kaprio J, et al. Hospital care in later life among former world-class Finnish athletes. *JAMA* 1996;276:216–20.
48. Stansfeld SA, Marmot MG. Deriving a survey measure of social support: The reliability and validity of the close persons questionnaire. *Soc Sci Med* 1992;35:1027–35.
49. Karasek RA. Job demands, job decision latitude and mental strain: implications for job redesign. *Admin Sci Quart* 1979;24:285–308.
50. Glymour M, Weuve J, Berkman LF, et al. When is baseline adjustment useful in analyses of change? An example with education and cognitive function. *Am J Epidemiol* 2005;162:267–78.
51. Royston P. Multiple imputation of missing values. *Stata Journal* 2004;4:227–41.
52. Christensen H. What cognitive changes can be expected with normal ageing? *Aust N Z J Psychiatry* 2001;35:768–75.
53. Blair C. How similar are fluid cognition and general intelligence? A developmental neuroscience perspective on fluid cognition as an aspect of human cognitive ability. *Beh Brain Sci* 2006;29:109–60.
54. Lundberg U. Stress hormones in health and illness: The roles of work and gender. *Psychoneuroendocrinology* 2005;30:1017–21.
55. Garde AH, Faber A, Persson R, et al. Concentrations of cortisol, testosterone and glycosylated haemoglobin (HbA1c) among construction workers with 12-h workdays and extended workweeks. *Int Arch Occup Environ Health* 2007;80:404–11.

56. Sabia S, Guéguen A, Marmot MG, et al. Does cognition predict mortality in midlife? Results from the Whitehall II cohort study. *Neurobiol Aging* 2008 Jun 7 [Epub ahead of print].
57. Pavlik VN, Alves de Moraes S, Szklo M, et al. Relation between cognitive function and mortality in middle-aged adults. The Atherosclerosis Risk in Communities Study. *Am J Epidemiol* 2003;157:327–34.
58. Portin ML, Muuriaisniemi M, Joukamaa S, et al. Cognitive impairment and the 10-year survival probability of a normal 62-year-old population. *Scand J Psychol* 2001;42:359–66.
59. Anstey KJ, von Sanden C, Salim A, et al. Smoking as a risk factor for dementia and cognitive decline: a meta-analysis of prospective studies. *Am J Epidemiology* 2007;166:367–78.
60. Sabia S, Marmot M, Dufouil C, et al. Smoking history and cognitive function in middle-age in Whitehall II study. *Arch Intern Med* 2008;168:1165–73.

Figure 1. Sample selection.

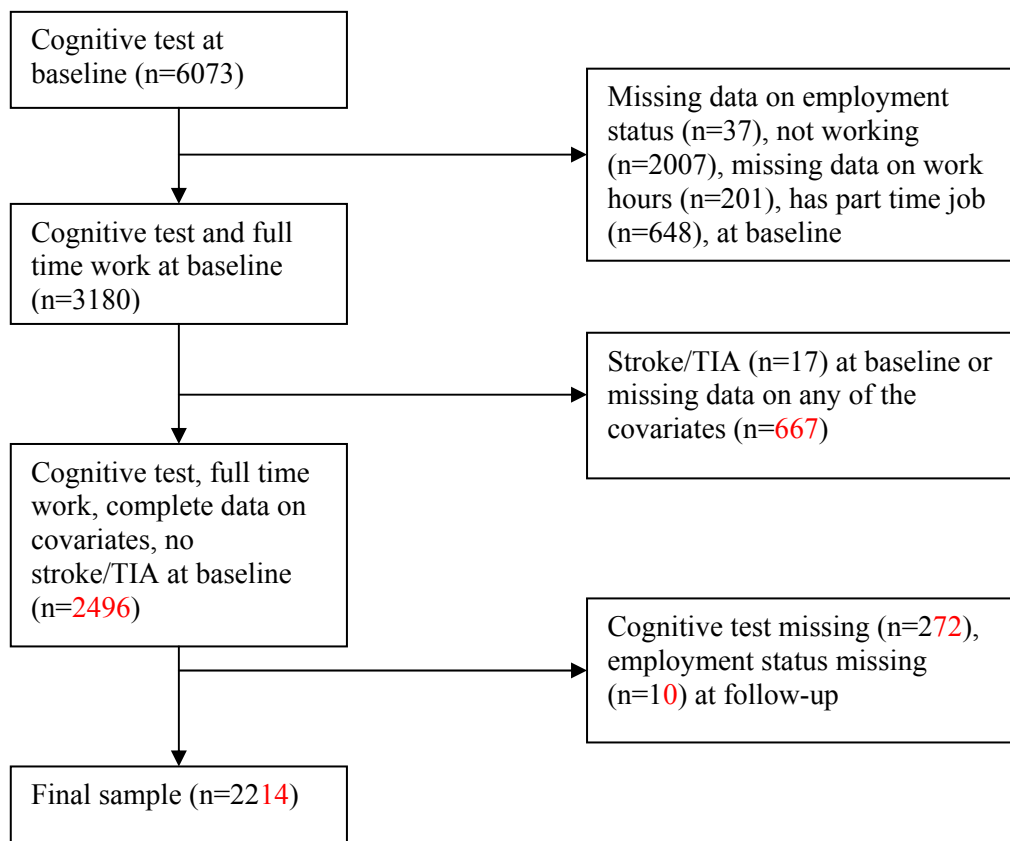


TABLE 1. Characteristics of the participants by working hours at baseline, the Whitehall II Study 1997-2004

	All	Working hours per week			<i>p</i> *
		≤ 40	41-55	> 55	
Sex					<0.001
Men	1694 (77)	607 (71)	936 (79)	151 (83)	
Women	520 (23)	246 (29)	244 (21)	30 (17)	
Age (years); Mean (S.E.)	52.1 (0.09)	52.4 (0.14)	51.8 (0.12)	52.5 (0.31)	0.741
Marital status					<0.001
Married/cohabited	1749 (79)	624 (73)	969 (82)	156 (86)	
Non-married / co-habited	465 (21)	229 (27)	211 (18)	25 (14)	
Occupational grade level					<0.001
1 highest	495 (22)	75 (9)	328 (28)	92 (51)	
2	569 (26)	164 (19)	356 (30)	49 (27)	
3	359 (16)	161 (19)	180 (15)	18 (10)	
4	400 (18)	231 (27)	160 (14)	9 (5)	
5-6 lowest	391 (18)	222 (26)	156 (13)	13 (7)	
Educational level					<0.001
Post graduate	378 (17)	93 (11)	238 (20)	47 (26)	
Graduate	551 (25)	200 (23)	294 (25)	57 (31)	
Higher secondary	657 (30)	251 (29)	356 (30)	50 (28)	
Lower secondary	499 (23)	240 (28)	235 (20)	24 (13)	
No academic qualifications	129 (6)	69 (8)	57 (5)	3 (2)	
Income (£/year)					<0.001
≥ 50,000	358 (16)	46 (5)	232 (20)	80 (44)	
25,000 < 50,000	1176 (53)	393 (46)	703 (60)	80 (44)	
15,000 < 25,000	579 (26)	351 (41)	214 (18)	14 (8)	
< 15,000	101 (5)	63 (7)	31 (3)	7 (4)	
Physical health status					0.137
I lowest	404 (18)	148 (17)	215 (18)	41 (23)	
II	551 (25)	219 (26)	298 (25)	34 (19)	
III	589 (27)	234 (27)	301 (26)	54 (30)	
IV highest	670 (30)	252 (30)	366 (31)	52 (29)	
CHD					0.478
No	1988 (90)	769 (90)	1059 (90)	160 (88)	
Yes	226 (10)	84 (10)	121 (10)	21 (12)	
Hypertension					0.368
No	1801 (81)	682 (80)	969 (82)	150 (83)	
Yes	413 (19)	171 (20)	211 (18)	31 (17)	
Psychological distress					<0.001
No	1674 (76)	678 (79)	880 (75)	116 (64)	
Yes	540 (24)	175 (21)	300 (25)	65 (36)	

Table 1 cont.

Table 1 cont.

Anxiety					0.230
No	1972 (89)	770 (90)	1044 (88)	158 (87)	
Yes	242 (11)	83 (10)	136 (12)	23 (13)	
Short sleep (<6 hrs)					0.013
No	2043 (92)	799 (94)	1084 (92)	160 (88)	
Yes	171 (8)	54 (6)	96 (8)	21 (12)	
Sleeping problems					0.375
Low	707 (32)	292 (34)	360 (31)	55 (30)	
Intermediate	836 (38)	316 (37)	455 (39)	65 (36)	
High	671 (30)	245 (29)	365 (31)	61 (34)	
Alcohol use					0.018
No	259 (12)	118 (14)	127 (11)	14 (8)	
Moderate	1382 (62)	553 (65)	714 (61)	115 (64)	
High	573 (26)	182 (21)	339 (29)	52 (29)	
Smoking					0.611
No	2020 (91)	777 (91)	1076 (91)	167 (92)	
Yes	194 (9)	76 (9)	104 (9)	14 (8)	
Physical activity					0.819
Low	352 (16)	153 (18)	164 (14)	35 (19)	
Intermediate	780 (35)	326 (38)	389 (33)	65 (36)	
High	1082 (49)	374 (44)	627 (53)	81 (45)	
Social support					0.008
Low	763 (34)	312 (37)	406 (34)	45 (25)	
Intermediate	764 (35)	306 (36)	386 (33)	72 (40)	
High	687 (31)	235 (28)	388 (33)	64 (35)	
Strain in family relations					0.192
No	1792 (81)	700 (82)	951 (81)	141 (78)	
Yes	422 (19)	153 (18)	229 (19)	40 (22)	
Job strain					0.937
No	1671 (75)	648 (76)	886 (75)	137 (76)	
Yes	543 (25)	205 (24)	294 (25)	44 (24)	
Employment status at follow-up					0.052
Employed	1680 (76)	624 (73)	911 (77)	36 (80)	
Non-employed	534 (24)	229 (27)	269 (23)	145 (20)	

* *P*-value for difference between the groups working ≤ 40 hours and > 55 hours per week.

TABLE 2. Association between working hours at baseline and cognitive function at baseline and at follow-up, fully adjusted models*, the Whitehall II Study 1997-2004

Weekly working hours at baseline	Memory		Reasoning		Vocabulary		Phonemic fluency		Semantic fluency	
	Range 0-18 (1-18)		Range 12-65 (10-65)		Range 1-33 (6-32)		Range 3-47 (2-34)		Range 2-34 (2-33)	
	Mean (SE)	<i>p</i> †	Mean (SE)	<i>p</i> †	Mean (SE)	<i>p</i> †	Mean (SE)	<i>p</i> †	Mean (SE)	<i>p</i> †
Cognitive function at baseline										
≤ 40	6.94 (0.18)	Ref.	46.14 (0.63)	Ref.	24.80 (0.25)	Ref.	16.95 (0.33)	Ref.	16.83 (0.30)	Ref.
41-55	7.12 (0.17)	0.081	46.02 (0.60)	0.744	24.38 (0.24)	0.005	17.25 (0.31)	0.117	16.87 (0.29)	0.810
> 55	7.14 (0.23)	0.306	45.93 (0.79)	0.763	23.96 (0.32)	0.002	17.62 (0.41)	0.056	17.08 (0.38)	0.441
Test for linear trend‡	<i>p</i> = 0.835		<i>p</i> = 0.206		<i>p</i> < 0.001		<i>p</i> = 0.031		<i>p</i> = 0.874	
Cognitive function at follow-up										
≤ 40	7.11 (0.18)	Ref.	44.17 (0.65)	Ref.	24.97 (0.25)	Ref.	15.66 (0.31)	Ref.	16.20 (0.28)	Ref.
41-55	7.18 (0.18)	0.547	43.53 (0.62)	0.099	24.62 (0.24)	0.020	15.95 (0.29)	0.111	16.18 (0.26)	0.912
> 55	6.93 (0.23)	0.359	42.74 (0.81)	0.040	24.39 (0.32)	0.032	16.00 (0.38)	0.302	16.08 (0.35)	0.680
Test for linear trend‡	<i>p</i> = 0.118		<i>p</i> = 0.010		<i>p</i> = 0.003		<i>p</i> = 0.088		<i>p</i> = 0.430	

Note. In each cognitive test higher score indicates better cognitive performance.

*Adjusted for age, sex, marital status, follow-up employment status, occupational grade, education, income, physical health indicators, psychological distress, anxiety, sleep problems, health risk behaviors, social support, family stress, and job strain.

† *P* for difference with the reference group with ≤40 working hours per week.

‡ Total working hours entered into the model as a continuous variable.

TABLE 3. Stepwise adjustments of the association between working hours at baseline and change in reasoning score between baseline and follow-up, the Whitehall II Study 1997-2004

	Change in reasoning score											
	Model I		Model II		Model III		Model IV		Model V		Model VI	
Weekly working hours at baseline	Mean diff. (SE)	<i>p</i> *	Mean diff. (SE)	<i>p</i> *	Mean diff. (SE)	<i>p</i> *	Mean diff. (SE)	<i>p</i> *	Mean diff. (SE)	<i>p</i> *	Mean diff. (SE)	<i>p</i> *
≤ 40	-1.90 (0.19)	Ref.	-1.95 (0.24)	Ref.	-1.71 (0.28)	Ref.	-1.94 (0.25)	Ref.	-1.87 (0.21)	Ref.	-1.77 (0.39)	Ref.
41-55	-2.36 (0.18)	0.033	-2.41 (0.23)	0.035	-2.18 (0.27)	0.030	-2.37 (0.24)	0.049	-2.34(0.20)	0.031	-2.23 (0.37)	0.046
> 55	-2.97 (0.38)	0.006	-2.98 (0.41)	0.009	-2.80 (0.42)	0.006	-2.99 (0.41)	0.008	-2.96 (0.39)	0.006	-2.90 (0.49)	0.007
Mean difference†	-1.08		-1.04		-1.09		-1.05		-1.09		-1.13	
Test for linear trend‡	<i>p</i> = 0.020		<i>p</i> = 0.026		<i>p</i> = 0.018		<i>p</i> = 0.026		<i>p</i> = 0.018		<i>p</i> = 0.036	

Model I: adjusted for age, sex, marital status and follow-up employment status.

Model II: Model I + additionally adjusted for physical health indicators.

Model III: Model I + additionally adjusted for psychological distress, anxiety, and sleep problems.

Model IV: Model I + additionally adjusted for health risk behaviors.

Model V: Model I + additionally adjusted for social support, family stress and job strain.

Model VI: Adjusted for all covariates in models I, II, III, IV, V + occupational grade, education, and income.

**P* for difference with the reference group working ≤40 hours per week.

† Difference in mean between the group working >55 hours and the group working ≤40 hours per week.

‡ Total working hours entered into the model as a continuous variable.

TABLE 4. Multivariable-adjusted* associations between working hours, vocabulary and reasoning for participants before and after imputation of missing data imputed, the Whitehall II Study 1997-2004

Cohort	Vocabulary score				Reasoning score					
	Baseline		Follow-up		Baseline		Follow-up		Change	
	Beta (SE)	<i>p</i>	Beta (SE)	<i>p</i>	Beta (SE)	<i>p</i>	Beta	<i>p</i>	Beta	<i>p</i>
Weekly working hours at baseline										
Before imputation (n = 2210 - 2204)										
Per 10-hour increase†	-0.38 (0.09)	<0.001	-0.27 (0.09)	0.003	-0.28 (0.23)	0.206	-0.60 (0.23)	0.010	-0.30 (0.14)	0.036
After imputation (n = 3163)‡										
Per 10-hour increase†	-0.42 (0.08)	<0.001	-0.36 (0.08)	<0.001	-0.52 (0.19)	0.005	-0.77 (0.20)	<0.001	-0.24 (0.13)	0.053

*Adjusted for age, sex, marital status, follow-up employment status, occupational grade, education, income, physical health indicators, psychological distress, anxiety, sleep problems, health risk behaviors, social support, family stress, job strain.

†Continuous variable for working hours

‡Based on multiple multivariate imputations.