

## **Cumulative exposure to high-strain and active jobs as predictors of cognitive function: the Whitehall II study.**

Marko Elovainio, Jane Ferrie, Archana Singh-Manoux, David Gimeno, Roberto de Vogli, Martin Shipley, Jussi Vahtera, Eric Brunner, Michael Marmot, Mika Kivimaki

► **To cite this version:**

Marko Elovainio, Jane Ferrie, Archana Singh-Manoux, David Gimeno, Roberto de Vogli, et al.. Cumulative exposure to high-strain and active jobs as predictors of cognitive function: the Whitehall II study.. Occup Environ Med, 2009, 66 (1), pp.32-7. 10.1136/oem.2008.039305 . inserm-00327325

**HAL Id: inserm-00327325**

**<https://www.hal.inserm.fr/inserm-00327325>**

Submitted on 8 Oct 2008

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

**Cumulative exposure to high strain and active jobs as predictors of cognitive function: The Whitehall II study**

Marko Elovainio, Jane E. Ferrie, Archana Singh-Manoux, David Gimeno, Roberto De Vogli, Martin J. Shipley, Jussi Vahtera, Eric J. Brunner, Michael G. Marmot, Mika Kivimäki

Elovainio et al. Strain and cognitive function

**Word count text:** 4454

**Word count abstract:** 255

**Number of figures:** 0

**Number of tables:** 4

Affiliations: University College London, UK (M.E., J.E.F., A. S-M. D.G., R.D.V., M.J.S., E.J.B., M.G.M., M.K.); National Research and Development Centre for Welfare and Health, Helsinki, Finland (M.E.); INSERM U697-IFR69 (A.S-M); Finnish Institute of Occupational Health, Helsinki, Finland (M.K., J.V.)

**Correspondence to:**

Marko Elovainio, National Research and Development Centre for Welfare and Health, PO Box 220, Fi-00370 Helsinki, Finland.

marko.elovainio@stakes.fi

## ABSTRACT

**Objectives:** A high strain job (a combination of high job demands and low job control) is expected to increase the risk of health problems, whereas an active job (high demands and high control) can be hypothesized to be associated with a greater capacity to learn. We tested associations between high strain and active jobs and cognitive function in middle-aged men and women.

**Methods:** Data on 4146 British civil servants (2,989 men and 1,157 women) aged 35 - 55 years at baseline came from the Whitehall II study. Cumulative exposure to both high strain and active jobs was assessed at Phases 1 (1985-1988), 2 (1989-1990) and 3 (1991-1993). Cognitive performance was assessed at Phases 5 (1997-1999) and 7 (2003-2004) using the following tests: verbal memory, inductive reasoning (Alice Heim), verbal meaning (Mill Hill), phonemic and semantic fluency. Analyses were adjusted for age, sex, and employment grade.

**Results:** Longer exposure to high job strain and shorter exposure to active jobs were associated with lower scores in most of the cognitive performance tests. However, these associations disappeared on adjustment for employment grade. Phonemic fluency was an exception to this pattern. Associations between exposure to an active job and phonemic fluency at both follow-up phases were robust to adjustment for employment grade. However, there was no association between exposure to active jobs and change in phonemic fluency score between the follow-up phases after adjustment for employment grade.

**Conclusions:** In these data associations between cumulative exposure to high strain or active jobs and cognition are largely explained by socioeconomic position.

**Key words:** Job strain, cognitive function, memory, psychosocial factors, longitudinal

### Main messages:

Very few studies have tested the fundamental learning hypothesis of job demands-control model

Our results did not offer strong support for the cumulative learning possibilities and following cognitive capacity of active work

High strain work did not seem to be strong predictor of low learning capacity measured by cognitive tests

### Policy implications:

Further research is needed to determine the possible interventions in reducing socioeconomic inequalities in learning capacity in terms of cognitive functions

## INTRODUCTION

The job strain model (also known as, the demand-control model) proposes that high strain jobs, a combination of high job demands and low job control, are hazardous to employee health. This proposition has received extensive endorsement in the literature [1-8]. The model also suggests that high strain inhibits learning and may thus have an adverse effect on cognitive capabilities in the long run. Another fundamental, but less explored hypothesis relates to active jobs. These jobs combine the chance to control the main parameters of one's job with high and challenging job demands. It is possible that active jobs contribute to learning new skills and/or coping strategies which [9, 10] in turn, may improve cognitive function and protect against cognitive decline. Yet, to our knowledge, only two longitudinal studies have assessed the association between components of the job strain model and cognitive functioning. One found that learning-like outcomes such as self-efficacy mediated the effect of job control on depression and the authors concluded that high job strain inhibits learning [11]. Another study found that high levels of job strain had adverse effects on learning among new employees [12]. Both studies were based on small samples, short follow-up periods and self-reported outcomes.

Adverse effects on learning and memory, following intense stress have repeatedly been found [13-17]. It has been reported, for instance, that intense stress results in marked inaccuracies in memory [18-20]. Also chronic stress has been shown to affect memory and other cognitive functions. Öhman and others [21] found performance deficits for episodic memory and for tasks requiring divided attention during either encoding or retrieval of words among chronic stress patients. Poor performance was also found in mental tempo, prospective memory and semantic access.

In this study, we examined whether shorter exposure to active jobs and longer exposure to high job strain was associated with poorer cognitive function in the Whitehall II study, a cohort of British civil servants. The advantage of using Whitehall II data is the opportunity to examine cumulative exposure to high strain and active jobs as predictors of cognitive function in a large, longitudinal occupational cohort with a wide range of cognitive function measures, such as memory functions, inductive reasoning, verbal meaning, semantic fluency and phonemic fluency.

## METHODS

### Participants and design

The target population for the Whitehall II Study was all office staff aged 35 to 55 years based in 20 civil service departments in London, England. With a 73% participation rate, the cohort included 6,895 men and 3,413 women at study entry in 1985-1988. The present study focused on the 2,989 men (43% of all men participants) and 1,157 women (34% of all women participants) who responded to a survey on job strain at Phases 1 (the baseline of this study, 1985-1988), 2 (1989-1990) and 3 (1991-1993), and completed the cognitive function test at Phases 5 (1997-99) and 7 (2003-2004).

## High strain jobs and active jobs

Components of the job strain model were measured using the Job Strain Questionnaire [22]. Job demands were measured using 4 items (internal consistency, Cronbach's  $\alpha=0.67$ ), and job control using 15 items (internal consistency, Cronbach's  $\alpha=0.84$ ). All questions were answered on a four point scale from "often" to "never/almost never". Responses were combined and then divided into high and low based on the median split for the respective component. Four job categories were created based on the demand-control model: active (high control and high demands), low strain (high control and low demands), passive (low control and low demands) and high strain (low control and high demands) [23]. The accumulation of exposure to high strain and active jobs over the three measurement periods (phases 1, 2, and 3) was computed by adding together the number of times the participant had been working in high strain or active jobs.

## Cognitive function

Cognitive data are drawn from Phases 5 and 7, when cognitive testing was performed on all participants attending the Whitehall II medical examination. Cognitive function was measured using the following five standard tests:

(a) Verbal memory was 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.

(b) The Alice Heim intelligence test (AH4) [24] is composed of a series of 65 items (32 verbal and 33 mathematical reasoning items) of increasing difficulty. This is a test of inductive reasoning that measures the ability to identify patterns and infer principles and rules. Participants had 10 minutes to complete this section.

(c) The Mill Hill vocabulary test [25] assesses knowledge of verbal meaning and encompasses the ability to recognize and comprehend words. We used the test in its multiple format, which consists of a list of 33 stimulus words ordered by increasing difficulty, and six response choices per word.

(d) Two measures of verbal fluency: phonemic and semantic, were used [26]. 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. High scores on all tests denote better performance.

Change scores in cognitive function between Phase 5 and Phase 7 were defined by taking the difference in the cognitive function score between Phase 5 and Phase 7. As previously [27, 28] decline was defined as performance in the worst quintile of change. Because the interval between Phases 5 and 7 was not equal for everybody (mean 5.4 years, range 3.2 to 7.2 years) further adjustments were made by including the time interval as a covariate in the regression models.

## Potential Confounding Factors

Potential confounding factors measured at Phase 5 included sex, age, employment grade, smoking, alcohol consumption, body mass index (BMI), depression and hypertension. Socioeconomic position was measured as civil service employment grade (administrative, professional, clerical/support). Health behaviour measures were smoking (self-reported cigarette smoking classified as never smoker, former smoker and current smoker), alcohol consumption (units/week, classified as: none, 1–14 units, 15–21 units, 22 + units with the highest two categories combined in women), and body mass index (BMI, kg/m<sup>2</sup>, classified as under 18.5, 18.5 -25, 25 -30 over 30). Depressive symptoms in the Whitehall II study were measured using a four item depression subscale (Cronbach  $\alpha=0.88$ ). Derived from the General Health Questionnaire-30 (GHQ-30), the subscale was based on principal component analysis and compared with the depression subscale items from the GHQ-28. The four items requested whether the participant had recently:

- (a) been thinking of him/herself as a worthless person;
- (b) felt that life is entirely hopeless;
- (c) felt that life isn't worth living; and,
- (d) found at times he/she couldn't do anything because his/her nerves were too bad.

Response options were on a Likert scale from 0 to 3 ("not at all", "no more than usual", "rather more than usual", and "much more than usual") [29]. The items were summed up and those scoring 3 or more were classified as depressive. Subjects with systolic blood pressure (SBP)  $\geq 140$  mmHg and diastolic blood pressure (DBP)  $\geq 90$  mmHg or on antihypertensive treatment were classified as hypertensive [30].

### **Statistical analysis**

Relationships between cumulative exposure to (1) a high strain job and (2) an active job and cognitive function at Phases 5 and 7 were analyzed using least squares regression with continuous measures of the cognitive tests as the outcome. Least squares means were used to present the age-adjusted cognitive function means from these analyses. We additionally tested the associations using repeated analyses of variance. Statistical models were sequentially adjusted for age, sex, and employment grade, and then additionally for alcohol consumption, smoking status, BMI, physical activity, depression, and hypertension. Most of these factors have been shown to be associated with cognitive functioning previously [27, 31-33]. Associations between cumulative exposure to (a) a high strain job and (b) an active job and subsequent change in cognitive function between Phases 5 and 7 were examined using logistic regression with the worst quintile of change as the outcome. In comparing included participants with those excluded, a t-test for the continuous variables and a chi-squared test for the categorical variables were used. The statistical tests were performed using Statistical Analysis System (SAS) version 9.01, and statistical significance was inferred from a 2-tailed p-value  $<0.05$ .

## **RESULTS**

Participants who were excluded from the current analyses were, at Phase 1, older (45.1 years compared to 43.4 years,  $p < 0.001$ ), more likely to be women (38% vs. 28%,  $p < 0.001$ ), and from the lowest employment grade (24% vs. 11%,  $p < 0.001$ ). Additionally they had both higher job demands (mean 59.1 vs. 56.7,  $p = 0.043$ ) and job control level (mean 67.0 vs. 63.1,  $p < 0.001$ ) at baseline.

**Table 1. Sample characteristics (N=4,146) <sup>+</sup>**

	<b>n</b>	<b>%</b>	<b>Mean (SD)</b>
<b>Age (years)</b>	4,146		54.8 (5.69)
<b>Sex</b>			
Male	2,989	72	
Female	1,157	28	
<b>Employment grade level (Phase 5/ Phase 7)</b>			
1 Senior administrators (highest grade)	889/1073	22/26	
2	996/889	24/22	
3	592/629	14/15	
4	693/641	17/15	
5	508/491	12/12	
6 Clerical/support (lowest grade)	463/397	11/10	
Missing	5/26	-/1	
<b>Smoking</b>			
Never or former smokers	3,770	91	
Current smokers	342	8	
Missing	34	1	
<b>Alcohol consumption (units of alcohol/week)</b>			
None	567	14	
1-14 units/week	2,053	50	
15 –21 units/week	595	14	
22 units/week or over	825	20	
Missing	106	2	
<b>Body mass index (kg/m<sup>2</sup>)</b>	4,141		26.2 (8.50)

under 18.5	61	2
18.5 - 25	2,610	63
25 - 30	1,272	32
over 30	198	5
<b>Depression</b>		
No	3,360	81
Yes	786	19
<b>Hypertension</b>		
No	2,521	61
Yes	1,623	39
Missing	2	

---

**Table 1 continued**

**Phases 1 to 3**

**High strain job over 3 phases**

No exposure	2,513	61
One exposure	1,013	24
Two exposures	458	11
Three exposures	162	4

**Active job over 3 phases**

No exposure	1,804	44
One exposure	940	23
Two exposures	718	17
Three exposures	684	16

**Phase 5 Cognitive functions**

Verbal memory	4,146	7.0 (2.39)
Inductive reasoning (AH4)	4,146	47.5 (10.67)
Verbal meaning (Mill Hill)	4,146	25.2 (4.33)



Phonemic fluency	4,146	17.1 (4.43)
Semantic fluency	4,146	16.7 (4.19)
<b>Phase 7 Cognitive functions</b>		
Verbal memory	4,146	6.9 (2.41)
Inductive reasoning (AH4)	4,144	44.7 (10.87)
Verbal meaning (Mill Hill)	4,136	25.1 (4.32)
Phonemic fluency	4,126	16.0 (4.17)
Semantic fluency	4,138	15.9 (3.87)

<sup>+</sup> Characteristics as at Phase 5, unless otherwise stated

Characteristics of the study participants at Phase 5 are shown in Table 1. Their mean age was 54.8 years, the majority worked in the highest grade. Only 8% were current smokers, less than one fifth were classified as depressed and 39% were hypertensive. Four percent of the participants were in high strain jobs and 16% in active jobs at Phases 1, 2 and 3. There was a slight decline in the average test score for each cognitive function measure between Phase 5 and Phase 7.

Mean scores for the cognitive function measures at Phases 5 and 7 by exposure to high strain jobs are shown in Table 2. Although the age and sex adjusted analyses showed declines in cognitive function with cumulative exposure to high strain jobs, further adjustment for employment grade attenuated all the associations such that cumulative exposure to a high strain job was not associated with any of the cognitive function tests at Phase 5 or 7. Adjusting for smoking, alcohol consumption, BMI, depression and hypertension did not change the results and repeated analyses of variance did not produce any statistically significant exposure X time interactions (not shown).

Table 2. Association between high strain job and cognitive functions at Phases 5 and 7 (means and 95% CI).

High strain job Phases 1, 2 and 3	Memory		Inductive reasoning (AH4)		Verbal meaning (Mill Hill)		Phonemic fluency		Semantic fluency	
	Model 1 <sup>+</sup>	Model 2 <sup>~</sup>	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
	Outcomes measured at Phase 5									
No exposure	7.1 (7.0 - 7.2)	7.1 (6.9 - 7.1)	46.9 (46.4 - 47.3)	46.1 (45.7 - 46.4)	24.8 (24.6 - 25.0)	25.5 (24.3 - 24.7)	17.3 (17.1 - 17.5)	17.1 (16.9 - 17.3)	16.8 (16.7 - 17.0)	16.6 (16.4 - 16.8)
1 exposure	6.9 (6.8 - 7.1)	7.0 (6.8 - 7.1)	45.3 (44.6 - 45.9)	45.7 (45.1 - 46.3)	24.4 (24.1 - 24.7)	24.6 (24.4 - 24.8)	16.7 (16.5 - 17.0)	16.8 (16.6 - 17.1)	16.2 (15.9 - 16.4)	16.3 (16.1 - 16.6)
2 exposures	6.8 (6.6 - 7.1)	6.8 (6.6 - 7.1)	44.7 (43.7 - 45.6)	45.4 (44.6 - 46.2)	24.7 (24.3 - 25.1)	24.9 (24.6 - 25.2)	16.8 (16.4 - 17.2)	17.0 (16.6 - 17.4)	16.3 (16.0 - 16.7)	16.6 (16.2 - 16.9)
3 exposures	6.9 (6.5 - 7.2)	7.0 (6.6 - 7.3)	45.1 (43.6 - 46.7)	45.9 (44.5 - 47.2)	24.3 (23.7 - 25.0)	24.7 (24.1 - 25.2)	17.0 (16.3 - 17.7)	17.2 (16.6 - 17.9)	16.1 (15.4 - 16.7)	16.3 (15.7 - 16.9)
p-value for linear trend	0.003	0.127	<0.001	0.163	0.064	0.073	0.002	0.678	<0.001	0.203
Outcomes measured at Phase 7										
No exposure	7.1 (7.0 - 7.2)	7.0 (6.9 - 7.1)	44.0 (43.5 - 44.4)	42.7 (42.3 - 43.1)	24.9 (24.7 - 25.0)	24.3 (24.1 - 24.5)	16.2 (16.1 - 16.4)	15.8 (15.6 - 16.0)	15.9 (15.8 - 16.1)	15.5 (15.3 - 115.7)
1 exposure	6.9 (6.7 - 7.0)	6.9 (6.7 - 7.0)	42.4 (41.8 - 43.0)	42.4 (41.8 - 42.9)	24.4 (24.1 - 24.6)	24.4 (24.1 - 24.5)	15.7 (15.5 - 16.0)	15.7 (15.5 - 16.0)	15.4 (15.2 - 15.6)	15.4 (15.1 - 15.6)
2 exposures	6.9 (6.7 - 7.2)	7.0 (6.7 - 7.2)	42.3 (41.3 - 43.2)	42.3 (41.5 - 43.1)	24.7 (24.3 - 25.1)	24.6 (24.3 - 24.9)	15.6 (15.3 - 15.9)	15.6 (15.3 - 16.0)	15.5 (15.1 - 15.8)	15.5 (15.2 - 15.7)
3 exposures	6.8 (6.4 - 7.2)	6.8 (6.5 - 7.2)	43.2 (41.6 - 44.8)	43.3 (42.0 - 44.7)	24.3 (23.6 - 24.9)	24.3 (23.7 - 24.9)	15.4 (14.7 - 16.1)	15.5 (14.9 - 16.1)	15.2 (14.7 - 15.8)	15.3 (14.8 - 115.8)
p-value for linear trend	0.006	0.395	<0.001	0.806	0.024	0.313	<0.001	0.176	<0.001	0.277

<sup>+</sup> Model 1 is adjusted for age and sex (at Phase 5).

<sup>~</sup> Model 2 is adjusted for age, sex and employment grade (at Phase 5).

Associations between exposure to an active job and cognitive function are presented in Table 3. Increasing exposure to an active job over Phases 1, 2 and 3 was associated with higher performance on all the cognitive function tests at Phase 5 in analyses adjusted for age and sex. However, only the associations with verbal meaning at Phase 5 and phonemic fluency at Phase 5 and 7 were robust to additional adjustment for employment grade. Adjusting for smoking, alcohol consumption, BMI, depression and hypertension had no effect on these associations. There were no statistically significant exposure X time interactions between active job and phonemic fluency (not shown).

Table 3. Association between cumulative exposure to active job and cognitive functions at Phases 5 and 7 (means and 95% CI).

Active job Phases 1, 2 and 3	Memory		Inductive reasoning (AH4)		Verbal meaning (Mill Hill)		Phonemic fluency		Semantic fluency	
	Model 1 <sup>+</sup>	Model 2 <sup>-</sup>	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
<b>Outcomes measured at Phase 5</b>										
No exposure	6.8 (6.7 - 6.9)	7.0 (6.9 - 7.1)	43.4 (42.9 - 43.8)	45.9 (45.5 - 46.3)	23.8 (23.6 - 23.9)	24.8 (24.7 - 25.0)	16.2 (16.0 - 16.4)	16.9 (16.7 - 17.1)	15.7 (15.5 - 15.9)	16.4 (16.2 - 16.6)
1 exposure	7.2 (7.0 - 7.3)	7.1 (7.0 - 7.3)	47.1 (46.5 - 47.7)	45.8 (45.3 - 46.4)	24.8 (24.6 - 25.1)	24.3 (24.1 - 24.6)	17.2 (16.9 - 17.5)	16.9 (16.6 - 17.2)	17.0 (16.8 - 17.3)	16.6 (16.4 - 16.9)
2 exposures	7.2 (6.9 - 7.3)	6.8 (6.7 - 7.0)	49.1 (48.3 - 49.8)	45.8 (45.1 - 46.5)	25.7 (25.4 - 26.1)	24.4 (24.1 - 24.7)	18.1 (17.7 - 18.4)	17.2 (16.9 - 17.6)	17.4 (17.1 - 17.7)	16.5 (16.2 - 16.8)
3 exposures	7.4 (7.2 - 7.6)	6.9 (6.8 - 7.2)	50.5 (49.7 - 51.2)	46.0 (45.3 - 46.7)	26.3 (25.9 - 26.6)	24.5 (24.2 - 24.8)	18.5 (18.2 - 18.8)	17.3 (16.9 - 17.6)	18.0 (17.7 - 18.3)	16.7 (16.3 - 17.0)
p-value for linear trend	<0.001	0.403	<0.001	0.894	<0.001	0.022	<0.001	0.017	<0.001	0.192
<b>Outcomes measured at Phase 7</b>										
No exposure	6.7 (6.6 - 6.8)	6.9 (6.8 - 7.0)	40.8 (40.4 - 41.3)	42.5 (42.0 - 43.9)	23.7 (23.5 - 23.9)	24.4 (24.3 - 24.6)	15.1 (14.9 - 15.3)	15.5 (15.4 - 15.7)	15.0 (14.8 - 15.1)	15.4 (15.3 - 15.6)
1 exposure	7.1 (6.9 - 7.3)	6.9 (6.8 - 7.1)	44.3 (43.7 - 44.9)	42.6 (42.0 - 43.2)	24.9 (24.7 - 25.2)	24.2 (23.9 - 24.4)	16.2 (15.9 - 16.4)	15.7 (15.5 - 16.0)	16.0 (15.7 - 16.2)	15.4 (15.2 - 15.7)
2 exposures	7.4 (7.2 - 7.5)	7.0 (6.8 - 7.2)	46.2 (45.5 - 47.0)	42.8 (42.1 - 43.6)	25.8 (25.5 - 26.1)	24.4 (24.1 - 24.7)	17.1 (16.7 - 17.4)	16.1 (15.8 - 16.5)	16.6 (16.3 - 16.9)	15.6 (15.3 - 15.9)
3 exposures	7.4 (7.2 - 7.6)	6.9 (6.7 - 7.1)	47.2 (46.5 - 48.0)	42.9 (42.1 - 43.6)	26.2 (25.9 - 26.6)	24.4 (24.1 - 24.7)	17.2 (16.9 - 17.6)	16.1 (15.7 - 16.4)	17.0 (16.7 - 17.3)	15.7 (15.4 - 16.0)
p-value for linear trend	<0.001	0.812	<0.001	0.276	<0.001	0.998	<0.001	0.001	<0.001	0.118

<sup>+</sup> Model 1 is adjusted for age and sex (at Phase 5).

<sup>-</sup> Model 2 is adjusted for age, sex and employment grade (at Phase 5).

Further analyses of change in cognitive function test scores between Phases 5 and 7 were conducted only for verbal meaning and phonemic fluency as these were the measures associated with an active job (Table 3, Model 2). As can be seen in Table 4, there was an association between a high strain job, and an inverse association between exposure to an active job, and a declining verbal meaning score between Phase 5 and Phase 7. However, these associations were not robust to adjustment for employment grade. Correspondingly, the inverse associations observed between an active job and phonemic fluency attenuated after adjustment for employment grade and did not remain statistically significant.

Table 4. Association between exposure to high strain or active job during 3 study phases and verbal meaning and phonemic fluency change score (belonging to the worst quintile) between Phases 5 and 7 (Odds Ratios, OR and 95% CI). All models are also adjusted for time interval between Phases 5 and 7.

	Verbal meaning / Mill Hill (the worst quintile)				Phonemic fluency change (the worst quintile)								
	N/cases	OR	95% CI	Adjusted for ages and sex	OR	95% CI	N/cases	Adjusted for age and sex	OR	95% CI	Adjusted for age, sex and employment grade	OR	95% CI
High strain job over 3 phases													
No exposure	2503/505	1		1			2485/522	1			1		
1 exposure	1011/215	1.08	0.90, 1.29	1.03	0.86, 1.24	1.02	1006/215	1.02	0.85, 1.22	1.05	0.87, 1.26		
2 exposures	453/95	1.06	0.82, 1.36	1.02	0.80, 1.31	0.98	452/94	0.98	0.77, 1.26	1.02	0.79, 1.31		
3 exposures	161/43	1.48	1.03, 2.13	1.42	0.98, 2.05	1.29	160/41	1.29	0.89, 1.87	1.34	0.92, 1.95		
p-value for trend		0.795		0.188		0.432		0.246					
Active job over 3 phases													
No exposure	1796/414	1		1			1785/358	1			1		
1 exposure	934/184	0.81	0.78, 0.99	0.90	0.73, 1.11	1.12	927/199	1.12	0.92, 1.37	1.10	0.86, 1.35		
2 exposures	715/121	0.68	0.53, 0.86	0.79	0.61, 1.00	1.14	710/155	1.14	0.92, 1.42	1.09	0.86, 1.38		
3 exposures	682/139	0.83	0.67, 1.04	1.00	0.77, 1.28	1.25	681/160	1.25	1.00, 1.55	1.18	0.90, 1.51		
p-value for trend		0.012		0.524		0.038		0.197					

No exposure is the reference category

Because it is possible that the excluded subjects represented a more susceptible population (e.g., lower cognitive reserve), the restriction criteria might have introduced attrition bias into our analyses. In order to rule out that possibility, we additionally tested the association between baseline exposure to high strain or active jobs and cognitive functions at both study phases. Exposure to a high strain job at baseline was associated with a lower verbal meaning (Mill Hill) score at Phase 5 ( $p=0.002$ ) and at Phase 7 ( $p=0.019$ ) when adjusted for employment grade. None of the other tested associations were statistically significant.

## DISCUSSION

In this study of a middle-aged population there were dose-response associations between cumulative exposure to high strain or active jobs and several cognitive performance test scores before but not after adjustment for socioeconomic position. Only the association between an active job and phonemic fluency was robust to adjustment for employment grade at both follow-up periods which were, on average, 6 and 12 years after assessment of the exposure. However, no independent relationships were found between cumulative exposure to high strain or active jobs and change in cognitive performance between the follow-ups.

Numerous studies have observed adverse effects on learning and memory following intense stress or glucocorticoid treatment [13-17]. The release of stress hormones, for example, epinephrine and glucocorticoids from the adrenal glands during or after emotionally stressful experiences, has been shown to affect the consolidation of lasting memories [18]. Additionally, extensive evidence suggests that the amygdalae, and specifically the basolateral amygdalae, mediate stress hormone effects on memory functions [19]. In previous investigations it has also been reported that chronic stress results in poor performance in many cognitive tests [21].

Chronic psychological stress would have been a plausible explanation of our findings had we observed an association between high job strain and low cognition function. The failure to observe such an association in the present study suggests that high job strain may be a psychological stressor of insufficient intensity to result in long-term impairment of cognitive function. Indeed, the adverse effect of high job strain on cardiovascular outcomes is expected to result from long-lasting exposure to moderate rather than high intensity stress [34].

In the few previous studies on this issue, it has been suggested that high strain jobs inhibit learning [12], or have adverse effects on learning-like outcomes [11]. Several issues may explain why our results are not in line with these longitudinal studies. First, our findings were based on a cohort of over 4,000 employees whereas previous studies had much smaller samples. Second, our study is the only one to use cumulative exposure to the job strain categories to determine the long-term effects of work environment stressors. Although repeat measures may result a more reliable assessment, there is a possibility that the effect of exposure to high strain or active jobs may wear off due to habituation. A considerable proportion of the Whitehall II participants had already retired from the civil service by Phases 5 and 7 and so were no longer exposed to the negative effects of a high strain job or the benefits of an active job, a factor that may lead to 'dilution' of the effects.

We used a large variety of cognitive tests to determine learning outcomes. Previous studies have used self-determined or perceived sense of learning, such as sense of mastery and self-efficacy. These measures may be open to common-method bias that can artificially inflate associations. Furthermore, such self-assessment scales may reflect coping rather than cognition. Indeed, people may learn how to master or to cope with the demands of their job without any improvement in general cognitive capacity.

The nearly ubiquitous associations observed between high strain or active jobs and cognitive performance in this study, were substantially reduced after adjustment for employment grade. A clear socioeconomic gradient has been found in both components of high strain and active jobs. High job control and high demands are more common in higher socioeconomic groups [35]. It is possible that the relationship between an active job in the high employment grades and cognitive performance is reciprocal. That is, active jobs may lead to better cognitive functioning in people who get the better jobs i.e. those with high psychological demands combined with high job control. While this cannot be ruled out, socioeconomic position is also a marker of myriad other risk factors that may affect cognition, such as early life conditions, education, and cardiovascular diseases.

### **Study strengths and weaknesses**

This study has certain strengths that reduce the possibility of false negative conclusions. The study benefits from using data from Whitehall II, a well-characterized cohort with sufficient power to detect effects, and repeated measures of the key factors: job strain components, and cognitive function tests. Furthermore, cognitive function was tested using a wide variety of well-characterized validated tests. Nonetheless, it is important to note some limitations. First, the final analyses were conducted using participants with complete data on cognitive function at Phases 5 and 7 and work characteristics at Phases 1, 2 and 3. This meant that more than half the original population was excluded. There were some differences in baseline characteristics between included and excluded civil servants even in the exposure variables suggesting over-representation of those belonging to the active category. Although selective processes may have resulted in some underestimation of the association between the job strain categories and cognitive function, they are unlikely to have completely masked an association. Second, our analysis of change in cognitive scores is based on only two waves of data. It is recognized that such analyses are subject to ceiling and floor effects, regression to the mean, and measurement error. However, data from two waves are a distinct improvement on cross-sectional analysis even though robust causal inferences are best obtained from multi-wave studies [36]. Third, our data come from a cohort of older, white-collar civil servants and cannot be assumed to represent the general population. However, participants cover a good proportion of the socioeconomic spectrum. Given the increased representation of workers employed in white-collar occupations, our sample may be more representative than initially thought. In addition, the longitudinal changes in cognitive function measures between Phase 5 and Phase 7 were small, probably partly as a result of the relatively short follow-up time, limiting the statistical power to detect significant associations. However, there were statistically significant associations between exposure to an active job and two of the cognitive function



measures, but those associations were not robust to adjustments for employment grade.

## **Conclusions**

Although we found an association between active job and some measures of cognition, verbal meaning and verbal fluency, there was no evidence that an active job predicts change in these measures, independent of socioeconomic position. Our results do not offer strong support for the hypothesis that active work is causally associated, through cumulative learning experiences, with enhanced cognitive function or lower risk of cognitive decline. We also failed to obtain consistent support for job strain as a determinant of cognitive function.

## **ACKNOWLEDGEMENTS / 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), US, NIH: National Institute on Aging (AG13196), US, NIH; Agency for Health Care Policy Research (HS06516); and the John D and Catherine T MacArthur Foundation Research Networks on Successful Midlife Development and Socio-economic Status and Health. J.E.F. is supported by the MRC (Grant number G8802774), M.J.S. by a grant from the British Heart Foundation, M.G.M. by an MRC Research Professorship, MK by the Academy of Finland (project 117604, 124322 and 124271), ME by the WEF (project 203533) and A S-M by EURYI award from the European Science Foundation. We thank all participating Civil Service departments and their welfare, personnel, and establishment officers; the Occupational Health and Safety Agency; the Council of Civil Service Unions; all participating civil servants in the Whitehall II study; all members of the Whitehall II study team.

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd and its Licensees to permit this article (if accepted) to be published in Occupational and Environmental Medicine editions and any other BMJPG products to exploit all subsidiary rights, as set out in our licence (<http://oem.bmjournals.com/misc/ifora/licenceform.shtml>).

**Competing interests:** none

## REFERENCES

1. Theorell T, Perski A, Akerstedt T, et al. Changes in job strain in relation to changes in physiological state. A longitudinal study. *Scand J Work Environ Health*, 1988, **14**:189-96.
2. Theorell T, Karasek RA, Eneroth P: Job strain variations in relation to plasma testosterone fluctuations in working men--a longitudinal study. *J Intern Med*, 1990, **227**:31-6.
3. Theorell T, Tsutsumi A, Hallquist J, et al. Decision latitude, job strain, and myocardial infarction: a study of working men in Stockholm. The SHEEP Study Group. Stockholm Heart epidemiology Program. *Am J Public Health* 1998, **88**:382-8.
4. Vahtera J, Kivimaki M, Pentti J, Theorell T: Effect of change in the psychosocial work environment on sickness absence: a seven year follow up of initially healthy employees. *J Epidemiol Community Health*, 2000, **54**:484-93.
5. Bosma H, Marmot MG, Hemingway H, et al. Low job control and risk of coronary heart disease in Whitehall II (prospective cohort) study. *Bmj.*, 1997. **314**:558-65.
6. Karasek R, Baker D, Marxer F, et al. Job decision latitude, job demands, and cardiovascular disease: a prospective study of Swedish men. *Am J Public Health*, 1981, **71**:694-705.
7. Landsbergis PA, Schnall PL, Deitz DK, et al. Job strain and health behaviors: results of a prospective study. *American Journal of Health Promotion*, 1998, **12**:237-45.
8. Karasek RA, Theorell T, Schwartz JE, et al. Job characteristics in relation to the prevalence of myocardial infarction in the US Health Examination Survey (HES) and the Health and Nutrition Examination Survey (HANES). *Am J Public Health*, 1988, **78**:910-8.
9. Johnson JV, Hall EM: Job strain, work place social support, and cardiovascular disease: a cross-sectional study of a random sample of the Swedish working population. *Am J Public Health*, 1988, **78**:1336-42.
10. Amick BC, 3rd, Kawachi I, Coakley EH, et al. Relationship of job strain and iso-strain to health status in a cohort of women in the United States. *Scand J Work Environ Health*, 1998, **24**:54-61.
11. Holman DJ, Wall TD: Work characteristics, learning-related outcomes, and strain: a test of competing direct effects, mediated and moderated models. *Journal of Occupational Health Psychology*, 2002, **7**:283-301.
12. Taris TW, Feij JA: Learning and strain among newcomers: a three wave study on the effects of job demands and job control. *Journal of Psychology*, 2004, **138**:543-563.
13. McGaugh JL, Roozendaal B: Role of adrenal stress hormones in forming lasting memories in the brain. *Curr Opin Neurobiol.*, 2002, **12**:205-210.
14. McEwen BS: Allostasis and allostatic load: implications for neuropsychopharmacology. *Neuropsychopharmacology*, 2000, **22**:108-24.
15. Roozendaal B, Hahn EL, Nathan SV, de Quervain DJ, McGaugh JL: Glucocorticoid effects on memory retrieval require concurrent noradrenergic activity in the hippocampus and basolateral amygdala. *J Neuroscience*, 2004, **15**:8161-9.
16. de Kloet ER, Oitzl MS, Joels M: Stress and cognition. Are corticosteroids good or bad guys? *T Neuroscience*, 1999, **22**:422-426.
17. Lupie SJ, King S, Meaney MJ, et al. Can poverty get under your skin? basal cortisol levels and cognitive function in children from low and high socioeconomic status. *Dev Psychopathol*, 2001, **13**:653-76.
18. Roozendaal B: Stress and memory: opposing effects of glucocorticoids on memory consolidation and memory retrieval. *Neurobiol Learning and Memory*, 2002, **78**:578-95.
19. Dudai Y: Molecular basis of long-term memories: a question of persistence. *Curr Opin Neurobiol.*, 2002, **12**:211-216.
20. Morgan CAr, Hazlett G, Doran A, et al. Accuracy of eyewitness memory for persons encountered during exposure to highly intense stress. *Int J Law Psychiatry*, 2004, **27**:265-79.

21. Ohman J, Nordin S, Bergdahl J, et al. Cognitive function in outpatients with perceived chronic stress. *Scand J Work Environ Health*, 2007, **33**: 223-232.
22. Karasek RA: Job demands, job decision latitude and mental strain: Implications for job redesign. *Administrative Science Quarterly*, 1979, **24**:285.
23. Chandola T, Brunner E, Marmot M: Chronic stress at work and the metabolic syndrome: prospective study. [see comment]. *BMJ*, 2006, **332**:521-5.
24. Heim AW: *AHA4 group test for general intelligence ASE*, NFER-Nelson Publishing Co.Ltd., 1970
25. Raven JC: *Guide to using the Mill Hill vocabulary scale with progressive matrices.*, HK Lewis, 1965
26. Borkowski JG, Benton AL, Spreen O: Word fluency and brain damage. *Neuropsychologia*, 1967, **5**:135-140.
27. Singh-Manoux A, Hillsdon M, Brunner E, et al. Effects of physical activity on cognitive functioning in middle age: evidence from the Whitehall II prospective cohort study. *Am J Public Health*, 2005, **95**:2252-8.
28. Anstey KJ, Luszcz MA, Giles LC: Demographic, health, cognitive and sensory variables as predictors of mortality in very old adults. *Psychology of Ageing*, 16:3-11, 2001
29. Goldberg DP, Gater R, Sartorius N, et al. The validity of two versions of the GHQ in the WHO study of mental illness in general health care. *Psychological Medicine*, 1997, **27**:191-7.
30. Kivimaki M, Ferrie J, Brunner E, et al. Justice at work and reduced risks of coronary heart disease among employees: the Whitehall II study. *Archives of Internal Medicine*, 2005, **24**:2245-2251.
31. Singh-Manoux A, Richards M, Marmot M: Socioeconomic position across the lifecourse: how does it relate to cognitive function in mid-life? *Annals of Epidemiology*, 2005, **15**:572-8.
32. Singh-Manoux A, Britton AR, Marmot M: Vascular disease and cognitive function: evidence from the Whitehall II Study. *Journal of the American Geriatrics Society*, 2003, **51**:1445-50.
33. Kivipelto M, Helkala EL, Hanninen T, et al. Midlife vascular risk factors and late-life mild cognitive impairment: A population-based study. *Neurology*, 2001, **56**:1683-9.
34. McEwen BS: Protective and damaging effects of stress mediators. *N Engl J Med*, 1998, **338**:171-9.
35. Kuper H, Marmot M: Job strain, job demands, decision latitude, and risk of coronary heart disease within the Whitehall II study. *J Epidemiol Community Health*, 2003, **57**:147-53.
36. Clarke PS: Causal analysis of individual change using the difference score. *Epidemiology*, 2004, **15**:414-21.