



Job Strain and Cognitive Decline: A Prospective Study of the Framingham Offspring Cohort

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Abstract

Background: Workplace stress is known to be related with many behavioral and disease outcomes. However, little is known about its prospective relationship with measures of cognitive decline.

Objective: To investigate the association of job strain, psychological demands and job control on cognitive decline.

Methods: Participants from Framingham Offspring cohort (n=1429), were assessed on job strain, and received neuropsychological assessment approximately 15 years and 21 years afterwards.

Results: High job strain and low control were associated with decline in verbal learning and memory. Job strain was associated with decline in word recognition skills. Active job and passive job predicted decline in verbal learning and memory relative to low strain jobs in the younger subgroup. Active job and demands were positively associated with abstract reasoning skills.

Conclusions: Job strain and job control may influence decline in cognitive performance.

Keywords: Job strain; Cognition disorders; Work; Job demand; Active work; Passive work; Stress, psychological

Introduction

Chronic exposures to workplace psychosocial stressors, a subtle outcome of work organization, have been known to predict adverse health and behavioral outcomes such as cardiovascular diseases and depression.¹⁻⁷ The way work is organized, although anthropogenic, may expose workers to psychosocial stressors. These psychosocial stressors (stress risk

factors) lead to stress response. The stress response from these workers, when prolonged and chronic, leads to risk of diseases, regardless of the workers' awareness of the exposure and personality type.^{8,9} Although the Job Strain Hypothesis of the Demand-Control model¹⁰ has been related to a number of health outcomes,¹¹⁻¹⁴ little or no work has been done studying its association with cognitive decline.¹⁵

Cognitive decline, a hallmark of de-

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mentia,^{16,17} is a public health problem. Alzheimer's disease, the predominant subtype of dementia, and a corollary outcome of cognitive decline represents not only personal cost to the patient and their family but also a major economic burden on health care and social services.¹⁸ To date, possible etiology and pathogenesis for the cause of cognitive decline has been investigated and age and the presence of apolipoprotein (ApoE4) gene are established risk factors.¹⁹⁻²¹ Environmental factors, such as chronic psychosocial stress, might play a significant role in the development of degenerative cognitive impairment but has not been well studied.²² So far, no treatment has been found that can halt progression of Alzheimer's disease after symptoms are detected.²³ Identifying the risk factors associated with cognitive decline, and reducing or preventing exposure to these well before onset of symptoms may be the

most effective protective measure.

Chronic psychosocial stress is a suspected risk factor for various neuropsychiatric ailments, and may also contribute to the disease severity as well.²⁴⁻²⁶ Chronic psychosocial stress has been found to significantly exacerbate impairment in cognition and long-term potentiation in rat models.²⁷ A 5-year follow-up prospective study found long working hours to be associated with decline in cognitive performance.²⁸ This, however, suggests that social and psychological exposure at the workplace may be associated with incidence and severity of cognitive decline.

Considering the lack of epidemiologic studies of the relationship between workplace psychosocial stressors and cognitive decline, the high and steady increase of workplace psychosocial stressors in the American workplace over the past two decades²⁹ and the increasing incidence of Alzheimer's disease,³⁰ investigating the possible association between occupational workplace psychosocial stressors and cognitive decline is warranted. Epidemiologic evidence of association is of particular importance because it will provide insights into possible etiological factors.

The Job Strain hypothesis of the Demand-Control model developed by Karasek is based on a combination of psychological demand (job demand) and decision latitude (job control).¹⁰ The first hypothesis, the Job Strain Hypothesis, posits that adverse outcomes (diseases, fatigue, and depression) of psychological strain occur when psychological demands of the job are high and decision latitude is low. The second hypothesis, called Active Job Hypothesis, postulates that positive behavioral outcomes such as learning and growth and engagement in political and leisure activities (social participation) result when decision latitude is high and psychological demand is high. The Active quadrant is where decision latitude is high

TAKE-HOME MESSAGE

- Chronic exposures to workplace psychosocial stressors have been related to a number of health outcomes and behavioral outcomes such as cardiovascular diseases and depression.
- Chronic psychosocial stress, might play a significant role in the development of degenerative cognitive impairment, various neuropsychiatric ailments, and may also contribute to the disease severity as well.
- Exposure to some chronic workplace psychosocial stressors, measured as high job strain and low job control, at midlife is associated with decline in verbal learning and memory, which is among early symptoms of Alzheimer's disease.
- Active Job category and high psychological demand at work had a significant but protective association with abstract reason skills.
- High job strain at work has a significant association with decline in memory and learning.

and psychological demand is high. The opposite of this quadrant is the passive quadrant where both decision latitude and psychological demand is low.¹⁰ Together, these two quadrants make up the Active Job Hypothesis. The low strain quadrant is where decision latitude is high and psychological demand is low. The opposite of this is the high strain quadrant where decision latitude is low and psychological demand is high. The high and low strain quadrants make up the Job Strain hypothesis.

In the model, decision latitude refers to the worker's ability to control his or her own activities and skill usage, and not to control others. Decision latitude scales have two components: "decision authority," a socially predetermined control over detailed aspects of task performance (also called autonomy); and "skill discretion," control over use of skills by the individual, also socially determined at work (and often called variety). The latent variable (component), decision latitude (job control), is independently assessed as a primary independent variable. Psychological demand assesses mental work load (how hard a worker works) due to time pressure and role conflict (role ambiguity, concentration and mental work disruption). Psychological demand (job demand) is assessed as an independent variable. These two components (latent variables) are assessed by the items from the Job Content Questionnaire (JCQ).^{31,32}

The specific questions addressed in this paper are whether a) decision latitude (job control), psychological and psychological demand (job demand) are independently associated with decline in cognitive performance, measured by Wechsler's abstract reasoning test, Wechsler's verbal learning and memory test, visual memory tests, and premorbid intelligence tests, and b) whether job strain (a combination of low job control and high job demand) is associated with cognitive decline, and how each

category of the Demand-Control model is associated with cognitive decline with referent to low job strain category.

Materials and Methods

Study Participants

The Offspring cohort of the Framingham Heart Study (n=5124) consists of adult children (and their spouses) of the Original Cohort and were enrolled in the study in 1971 and longitudinally followed (examined) approximately every four years.³³ At each examination (Exam), participants were screened for cardiovascular and other risk factors. Occupational and demographic information were also recorded. All participants provided signed consent approved by the Boston University Institutional Review Board.

During the 3rd examination (Exam 3) of the Offspring cohort, (1984-1987), participants job strain levels were assessed by the JCQ. Following the 7th and 8th examinations, (Exams 7 and 8), participants were invited for a call back study that included administration of a neuropsychological test battery (NP test).^{34,35} The acceptance rate for the neuropsychological battery test was 72%. The number of participants who attended Exam 3 and completed the JCQ (n=3682) and both the 1st NP test (n=2571) between 1999-2005, and the 2nd NP test (n=1723) between 2001-2007 was 1527. There was at least 1.0 year difference between the 1st and 2nd NP test and the median number of years between the 1st and 2nd NP tests was 6.0 years. After excluding participants who at the 1st NP test had prevalent stroke (n=22), dementia (n=2) or other neurological disorders that could affect cognitive testing (n=21), the study sample became 1482. After eliminating participants without ApoE4 data (n=53) the study sample size was 1429 (Fig 1).

Job insecurity and strain outside the

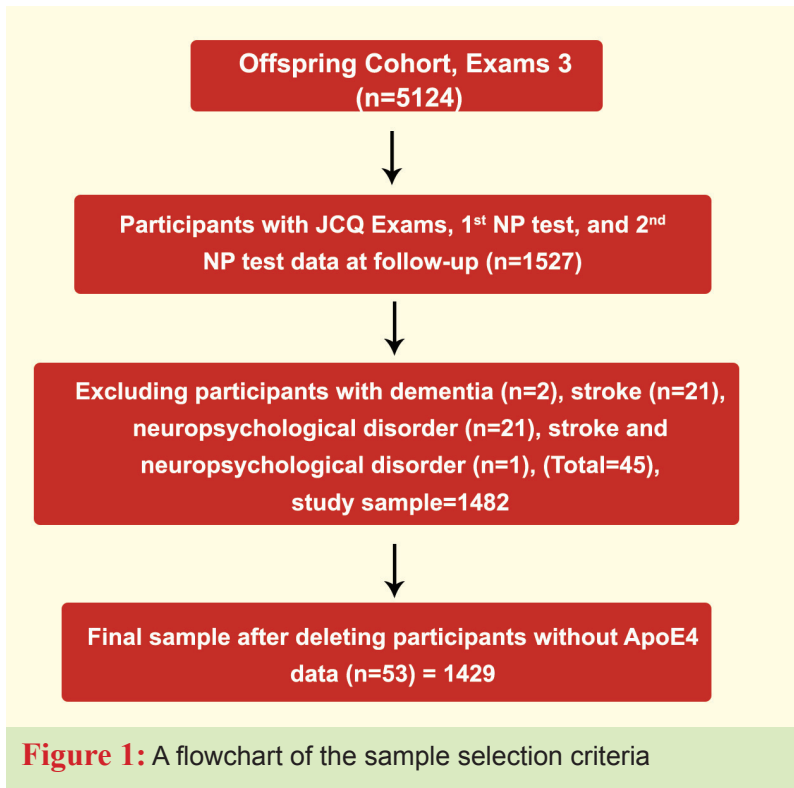


Figure 1: A flowchart of the sample selection criteria

job were, respectively, assessed using the statement “My job security is good” and the question “In general, do you find housework a big strain?” with a dichotomous response. Chronic and prolonged exposure to workplace psychosocial stressors was, in addition to the nature of the JCQ, ascertained by the number of times participants have changed their line of work and the number of times they have changed jobs in 10 years prior to the baseline assessment.

Job Strain

In measuring job strain, the psychological demand and decision latitude scales were divided into median based cut-points. Four possible combinations (groups) of job strain variables were created: a) low strain—low demands (below median) combined with high decision latitude (above median); b) active—high demands (above median) and high decision latitude (above median); c) passive—low demands (below median) and low decision latitude

(below median); and d) high strain—high demands (above median) and low decision latitude (below median). In this analysis, all participants are grouped into one of the four categories—high strain, low strain, passive, and active categories.

Cognitive Decline (primary outcome)

Table 1 lists the cognitive test administered to the Offspring participants used in this study and the presumed domains for each test measures. The tests were administered and scored by trained examiners using standardized test administration procedures.³⁶ For the primary outcomes, the variables of interest included are longitudinal annualized change (cognitive decline) in the scales in Table 1.

In all analyses, a negative relationship between psychosocial exposures and cognitive decline indicates lower performance in the 2nd NP tests in comparison with the 1st NP test.

Abstract reasoning skills are measured by similarities test, a frequently used and validated measure from the Wechsler Adult Intelligence Scale (WAIS). Abstract reasoning skills represent the ability to analyze information to solve complex problems. It is important because it has been found to be very effective in differential diagnosis of dementias through cognitive decline.³⁷ Learning and memory (including verbal memory) was measured by Wechsler Memory Scale's (WMS) subsets: Paired Associate Learning (immediate and delayed recall) test and Logical Memory (immediate and delayed recall) test. The Logical Memory test has been used extensively for measuring verbal memory. Its delayed test is in particular significantly effective in assessing long-term memory.⁴⁴ Paired Associate Learning measures the lack of ability to learn new information is a hallmark of Alzheimer's disease. The Paired Associate Learning test is accurate in measuring learning and memory to as-

Table 1: The cognitive tests administered at the 1st and 2nd NP exams and the cognitive domains they measure

Neuropsychological test	Latent cognitive ability tested
Wechsler Adult Intelligence Scale (WAIS)	
Similarities	Abstract reasoning
Wechsler Memory Scale (WMS)	
Paired Associate Learning—immediate recall (PASI) Paired Associate Learning—delayed recall (PASD)	Verbal learning
Logical Memory—immediate recall (LMI) Logical Memory—delayed recall (LMD)	Verbal memory
Visual Reproductions—immediate recall (VRI) Visual Reproductions—delayed recall (VRD)	Visual memory
Wide Range Achievement Test (WRAT)—III Word Reading Subtest	Premorbid intelligence and word recognition skills

sess cognitive decline and Alzheimer's disease, and it is particularly effective in early detection of symptoms of dementia.⁴⁴ Premorbid intelligence is the decline in intelligence attributed to cognitive decline and not old age. Wide Range Achievement test is an essential tool in accurately assessing the degree and rate of intelligence decline caused at the premorbid stage of dementia.^{38,44}

Statistical Analysis

Baseline characteristics (median and frequencies) were determined for sociodemographic and relevant variables during the 1st and 2nd NP tests.

Multivariate linear regression analysis was performed on all annualized raw change scores between the 1st and 2nd NP tests and job strain, job demand and job control separately (n=1429). For each participant, the annualized raw change was calculated as follows:

$$\text{Annualized raw change} = \frac{\text{Score of the 2}^{nd} \text{ NP test} - \text{Score of the 1}^{st} \text{ NP test}}{\text{Time interval between the 1}^{st} \text{ and 2}^{nd} \text{ test in year}}$$

Baseline performance of each cognitive performance was adjusted for in all regression analysis. Two models for adjustments were tested to control the covariates as follows:

- 1) Model 1
 - i) **For Job Demand:** $Outcome = Age + Sex + Education + Control + 1^{st} \text{ NP test}$
 - ii) **For Control:** $Outcome = Age + Sex + Education + Job demand + 1^{st} \text{ NP test}$
 - iii) **For Job Strain:** $Outcome = Age + Sex + Education + 1^{st} \text{ NP test}$
- 2) Model 2 (for demand, control and job strain): $Outcome = Age + Sex + Education + Socioeconomic status (income) + Strain outside work + Job insecurity + ApoE4 + 1^{st} \text{ NP test}$

Age stratified analysis was carried out with younger subgroup (median age at baseline ≤46 years, ie, the collection on job strain data) and elderly subgroup (median age at baseline >46 years).

ApoE, a genetic marker of risk for cognitive impairment³⁹ was adjusted for in Model 2. The process how information on ApoE was obtained is explained elsewhere.⁴⁰ A significant level of 0.05 was set

Table 2: Demographic and risk factors characteristics. Values are either median (IQR) or percentage.

Job strain, NP tests and ApoE4	All (n=1429)	Middle age (n=866)	Elderly (n=563)
Age at Exam 3 (yrs)	46 (40–54)	41 (37–45)	56 (53–60)
Age at 1 st NP test (yrs)	61 (55–69)	56 (52–60)	71 (68–74)
Time between Exam 3 and 1 st NP test (yrs)	14 (13–15)	14 (14–15)	14 (13–15)
Time between 1 st and 2 nd NP test (yrs)	6 (5–6)	6 (5–6)	6 (5–6)
Years of work experience	24 (17–31)	20 (15–25)	34 (27–40)
No. of times change job in past 10 yrs	1 (0–2)	1 (0–2)	0 (0–1)
No. of times change line of work in 10 yrs	0 (0–1)	0 (0–1)	0 (0–0)
Gender			
Men	46.1%	45.5%	46.2%
Women	53.9%	54.5%	53.8%
Educational level			
No high school	5.5%	3.8%	8.0%
High school degree	47.7%	44.2%	52.9%
Associate degree	9.7%	10.7%	8.2%
College degree and above	35.1%	39.2%	29.0%
Do you find housework a big strain			
Yes	21.1%	23.8%	16.9%
No	62.2%	61.7%	63.1%
Unknown/not applicable	16.7%	14.5%	19.0%
Income before tax at Exams 3 (per yr)			
≤ US\$ 40 000	66.7%	67.2%	65.9%
> US\$ 40 000	18.9%	19.8%	16.9%
Unknown	14.6%	12.9%	17.2%
Job security is good			
Yes	67.1%	77.5%	74.4%
No	7.5%	8.7%	6.9%
Unknown	25.4%	13.9%	18.7%
Job strain			
Low	25.5%	23.9%	27.9%
High strain	12.5%	13.1%	11.7%

Continued

Table 2: Demographic and risk factors characteristics. Values are either median (IQR) or percentage.

Job strain, NP tests and ApoE4	All (n=1429)	Middle age (n=866)	Elderly (n=563)
Job control			
High	47.0%	48.7%	40.5%
Low	53.0%	51.3%	59.5%
Active job	27.4%	32.3%	19.9%
Passive job	34.6%	30.7%	27.9%
Psychological demand			
High	46.3%	48.5%	38.2%
Low	53.4%	51.5%	61.8%
ApoE4 carrier	20.5%	22.3%	17.8%

for all analyses. SAS ver 9.3 was used for statistical analysis.

Results

Basic Characteristics

Demographics, baseline and follow-up characteristics of the 1429 study participants are provided in Table 2. The median age at baseline was 46 (IQR 40 to 54) years, and at 1st NP test was 61 (IQR 55 to 69) years. The median years of work experience at baseline was 24 (IQR 17 to 31) years. The median number of times participants changed job in the last 10 years prior to the baseline was 1 (IQR 0 to 2) and the median number of times the participants changed their line of work in 10 years was 0 (IQR 0 to 1). The median time between the 1st and 2nd NP tests was 6 (IQR 5 to 6) years. About 67% of workers said they have good job security; 27.4% of the participants were in the active job category; 53.0% had low job control; and 47% had high psychological demands in their work-

place. Sixty-two and two-tenth percent of the participants did not find housework a big strain. More than half (53.9%) of the participants were female and over 92% had a minimum of high school degree. Twenty and half percent of the participants were ApoE4 genotype carriers.

Job Strain and Cognitive Decline

There was a significant negative correlation between measures of decline in verbal learning and memory (PASI, Table 3a), and high job strain in all studied models, (Model 1: mean β -0.14 [SEM 0.06], $p=0.006$; Model 2: -0.15 [0.06], $p=0.005$). The association was significant in the younger subgroup (Model 1: -0.14 [0.06], $p=0.008$). High job strain was also associated significantly with a decline in delayed verbal memory and learning (PASD) (Model 1: -0.05 [0.02], $p=0.02$; Model 2: -0.06 [0.03], $p=0.008$).

High job strain was also significantly related with a decline in measures of premorbid intelligence (WRAT) (Model 1: -0.10 [0.05], $p=0.02$; Model 2: -0.13

Table 3a: Association of job strain with annual change in cognitive performance, n=1429. Values are mean β (SEM), and p values.

NP Test	Model 1—Job Strain			Model 2—Job Strain		
	All	<65 yrs	≥65 yrs	All	<65 yrs	≥65 yrs
ΔPASI						
High strain	−0.14 (0.06), 0.006	−0.14 (0.06), 0.008	−0.14 (0.1), 0.16	−0.15 (0.06), 0.005	−0.11 (0.06), 0.06	−0.20 (0.12), 0.06
Active	−0.06 (0.04), 0.12	−0.10 (0.04), 0.02	0.01 (0.04), 0.96	−0.07 (0.05), 0.10	−0.10 (0.05), 0.02	0.02 (0.05), 0.78
Passive	−0.06 (0.04), 0.14	−0.09 (0.04), 0.05	−0.02 (0.04), 0.77	−0.08 (0.05), 0.10	−0.08 (0.05), 0.12	−0.04 (0.05), 0.62
ΔPASD						
High strain	−0.05 (0.02), 0.02	−0.04 (0.02), 0.07	−0.07 (0.04), 0.11	−0.06 (0.03), 0.008	−0.03 (0.03), 0.14	−0.08 (0.03), 0.06
Active	0.02 (0.02), 0.25	0.03 (0.02), 0.24	0.01 (0.02), 0.74	0.02 (0.02), 0.67	0.02 (0.02), 0.23	0.03 (0.02), 0.39
Passive	−0.01 (0.02), 0.17	−0.01 (0.02), 0.51	−0.01 (0.02), 0.71	−0.03 (0.02), 0.26	−0.24 (0.02), 0.31	−0.02 (0.02), 0.66
ΔLMI						
High strain	−0.04 (0.06), 0.22	−0.002 (0.06), 0.23	−0.10 (0.06), 0.25	−0.04 (0.06), 0.29	0.003 (0.06), 0.96	−0.11 (0.06), 0.32
Active	−0.01 (0.05), 0.53	−0.01 (0.05), 0.52	−0.01 (0.05), 0.52	0.01 (0.05), 0.51	0.02 (0.05), 0.73	−0.05 (0.05), 0.57
Passive	−0.03 (0.05), 0.12	−0.10 (0.06), 0.21	0.05 (0.06), 0.35	−0.04 (0.06), 0.26	−0.05 (0.06), 0.29	0.003 (0.06), 0.33
ΔLMD						
High strain	−0.01 (0.06), 0.80	0.003 (0.06), 0.96	−0.05 (0.06), 0.54	−0.02 (0.07), 0.68	0.04 (0.07), 0.58	−0.10 (0.07), 0.52
Active	−0.03 (0.05), 0.81	0.01 (0.05), 0.86	0.04 (0.05), 0.85	0.01 (0.05), 0.57	0.03 (0.05), 0.58	−0.02 (0.05), 0.26
Passive	−0.03 (0.06), 0.23	−0.11 (0.06), 0.04	0.07 (0.06), 0.30	−0.04 (0.06), 0.31	−0.08 (0.06), 0.18	−0.03 (0.06), 0.96
ΔSimilarities						
High strain	0.03 (0.06), 0.50	0.07 (0.06), 0.21	−0.03 (0.06), 0.95	−0.01 (0.06), 0.82	−0.001 (0.06), 0.99	−0.08 (0.06), 0.58
Active	0.08 (0.04), 0.05	0.11 (0.04), 0.02	0.01 (0.04), 0.54	0.09 (0.04), 0.03	0.11 (0.04), 0.02	0.06 (0.04), 0.23

Continued

Table 3a: Association of job strain with annual change in cognitive performance, n=1429. Values are mean β (SEM), and p values.

NP Test	Model 1—Job Strain			Model 2—Job Strain		
	All	<65 yrs	≥65 yrs	All	<65 yrs	≥65 yrs
Passive	0.01 (0.04), 0.76	-0.002 (0.04), 0.96	0.03 (0.04), 0.47	0.04 (0.05), 0.35	0.01 (0.05), 0.87	0.10 (0.05), 0.52
Δ WRAT						
High strain	-0.10 (0.04), 0.02	-0.10 (0.04), 0.08	-0.10 (0.05), 0.29	-0.13 (0.05), 0.004	-0.11 (0.05), 0.04	-0.11 (0.05), 0.17
Active	-0.01 (0.03), 0.68	-0.01 (0.03), 0.86	-0.03 (0.03) 0.38	-0.02 (0.03), 0.51	-0.02 (0.03), 0.64	-0.04 (0.03), 0.71
Passive	0.001 (0.04), 0.97	0.03 (0.04), 0.23	0.04 (0.04), 0.91	0.002 (0.03), 0.99	0.02 (0.03), 0.36	0.02 (0.03), 0.63

Δ : Change in

Model 1 = age + sex + years of education + (job demand or control or job strain)

Model 2 = age + sex + education + socioeconomic status (income) + strain outside work + job insecurity

[0.05], p=0.004). The association was significant in the younger subgroup (Model 2: -0.11 [0.05], p=0.04). The remaining NP tests had no significant association with job strain (Table 3a).

Active and Passive Work and Cognitive Decline

There was a significant association between active job and decline in verbal learning and memory (PASI) in the younger subgroup (Table 3a) (Model 1: mean β -0.10 [SEM 0.04], p=0.02; Model 2: -0.10 [0.05], p=0.02). The association of passive job was marginally significant with decline in verbal learning and memory in the younger subgroup (Model 1: -0.09 [0.04], p=0.05). Passive job was significantly related to lower premorbid intelligence (WRAT) in the younger group category (Model 1: -0.10 [0.04], p=0.02; Model 2: -0.13 [0.04], p=0.01). Increase in abstract reasoning skills measured by similarities scores was significantly associated with increase active job in Model 2 (0.09 [0.04],

p=0.04), but that relationship was attenuated in Model 1 (0.08 [0.04], p=0.05). This appeared driven by the significant protective association in the younger age group (Model 1: 0.11 [0.04], p=0.02; Model 2: 0.11 [0.04], p=0.02) since there were no significant associations within the elderly group.

All the other NP tests had no significant association with passive and active work.

Demand and Cognitive Decline

Multivariate analysis revealed a significant association between increased psychological demand at work and better performance on abstract reasoning skills (Model 1: mean β 0.08 [SEM 0.03], p=0.02) (Table 3b). The association was present in the younger subgroup (Model 1: 0.08 [0.03], p=0.02; Model 2: 0.11 [0.04], p=0.004) but not the elderly group. The younger subgroup also showed a positive correlation between demand and delayed logical memory in both models (Model 1: 0.10 [0.04], p=0.01; Model 2: 0.11 [0.04],

Table 3b: Association of demand with annual change in cognitive performance, n= 1429. Values are mean β (SEM), and p values.

NP Test	Model 1			Model 2		
	All	<65 yrs	≥65 yrs	All	<65 yrs	≥65 yrs
Δ PASI	-0.05 (0.03), 0.10	-0.04 (0.03), 0.19	-0.06 (0.03), 0.32	-0.05 (0.04), 0.14	-0.03 (0.04), 0.36	-0.07 (0.04), 0.31
Δ PASD	0.01 (0.01), 0.53	0.02 (0.02), 0.29	0.005 (0.02), 0.85	0.02 (0.02), 0.27	0.03 (0.02), 0.09	-0.003 (0.04), 0.9
Δ LMI	-0.01 (0.04), 0.84	0.05 (0.04), 0.17	-0.11 (0.04), 0.08	-0.01 (0.04), 0.81	0.05 (0.04), 0.24	-0.12 (0.04), 0.08
Δ LMD	0.05 (0.04), 0.16	0.10 (0.04), 0.01	-0.05 (0.04), 0.38	0.04 (0.04), 0.30	0.11 (0.04), 0.01	-0.07 (0.04), 0.29
Δ Similarities	0.07 (0.03), 0.02	0.12 (0.04), 0.004	-0.02 (0.04), 0.74	0.06 (0.04), 0.09	0.11 (0.04), 0.004	-0.05 (0.04), 0.64
Δ WRAT	0.01 (0.03), 0.57	0.02 (0.03), 0.54	0.0001 (0.03), 0.99	-0.004 (0.03), 0.89	0.005 (0.03), 0.90	-0.02 (0.03), 0.72

Δ : Change in

Model 1 = age + sex + years of education + (job demand or control or job strain)

Model 2 = age + sex + education + socioeconomic status (income), + strain outside work + job insecurity

p=0.01). There were no other significant relationships between demand and other NP tests (Table 3b).

Control and Cognitive Decline

Multivariate analysis indicated a significant association for low control at the workplace and decline in verbal learning and memory (Table 3c), and even stronger association after adjusting for all relevant covariates (Model 1: mean β -0.08 [SEM 0.04], p=0.011; Model 2: -0.11 [0.04], p=0.003), similarly there was significant association for low control and decline in delayed verbal learning and memory even after adjustments of all covariates (Model 1: -0.03 [0.01], p=0.03; Model 2: -0.05 [0.02], p=0.001). Similar associations were found in the younger subgroup but not the elderly subgroup (Model 1: -0.05 [0.01], p=0.03; Model 2: -0.06 [0.02],

p=0.004). There was a marginal negative association between low control and WRAT (Model 2: -0.06 [0.04], p=0.05) and significant association in both Models for the younger subgroup (Model 1: -0.07 [0.03], p=0.04; Model 2: -0.08 [0.03], p=0.03). Control was not significantly associated with the remaining NP tests.

Discussion

This study indicates that the exposure to some chronic workplace psychosocial stressors, measured as high job strain and low job control, at midlife, in a sample of 1429 Caucasian residents of Framingham without dementia, stroke and/or other neurodegenerative diseases, is associated with decline in verbal learning and memory and the association appears to be driven by the younger subgroup of participants.

Table 3c: Association of Job Control with Annual Change in Cognitive Performance, n= 1429. Values are mean β (SEM), and p values.

NP Test	Model 1			Model 2		
	All	<65 yrs	≥ 65 yrs	All	<65 yrs	≥ 65 yrs
Δ PASI	-0.08 (0.04), 0.02	-0.06 (0.04), 0.08	-0.10 (0.04), 0.11	-0.11 (0.04), 0.003	-0.06 (0.04), 0.12	-0.15 (0.04), 0.03
Δ PASD	-0.03 (0.01), 0.02	-0.05 (0.01), 0.01	-0.02 (0.01), 0.35	-0.05 (0.02), 0.001	-0.06 (0.02), 0.004	-0.02 (0.04), 0.37
Δ LMI	-0.03 (0.04), 0.34	-0.03 (0.04), 0.36	-0.02 (0.04), 0.90	-0.06 (0.04), 0.10	-0.05 (0.04), 0.29	-0.05 (0.04), 0.54
Δ LMD	-0.04 (0.04), 0.22	-0.04 (0.04), 0.34	-0.04 (0.04), 0.53	-0.07 (0.04), 0.12	-0.06 (0.04), 0.41	-0.07 (0.04), 0.37
Δ Similarities	-0.01 (0.04), 0.33	0.0001 (0.04), 0.99	0.01 (0.04), 0.87	-0.001 (0.04), 0.18	-0.3 (0.04), 0.41	0.05 (0.04), 0.45
Δ WRAT	-0.03 (0.03), 0.21	-0.07 (0.03), 0.04	0.01 (0.03), 0.74	-0.06 (0.03), 0.05	-0.08 (0.03), 0.03	0.01 (0.03), 0.90

Δ : Change in

Model 1 = age + sex + years of education + (job demand or control or job strain)

Model 2 = age + sex + education + socioeconomic status (income), + strain outside work + job insecurity

Also high job strain and low job control is associated with decline in word recognition skills and word reading performance. An unexpected finding, however, was improved abstract reasoning skills associated with increasing job demands and active job category.

The study results indicate that being exposed chronically to workplace psychosocial stressors as measured by lack of job control significantly predicted a decline in verbal learning and memory, which is mainly driven by exposed middle-aged participants. Lacking the ability to learn new information is a hallmark of Alzheimer's, in its early symptoms. Lack of job control again predicted a decline in word recognition skills, which is a measure of premorbid intelligence, which again was driven mainly by the exposed middle-aged participants.

Contrary to expectation, high psychological demand at work had a significant but protective association with abstract reasoning skills as measured by WAIS Similarities test mainly driven by the middle-aged subgroup. Demand again had a significantly protective association with verbal memory. None of the other NP tests was susceptible to psychological demands due mental load due to time pressure and role conflict at the workplace.

Chronic exposure to high job strain, a combination of deleterious levels of psychological demand and job control, was a significant predictor for decline in verbal learning and memory, long-term memory and word recognition skills with respect to low job strain.

Exposure to the active job category and passive job category also predicted a decline in verbal learning and memory,

respectively, relative to low job strain category in the younger subgroup, suggesting that the best work organization design with regards to the demand-control model is the low job strain category (with respect to memory and verbal learning). A positive and significant association in abstract reasoning skills was predicted by active jobs in relation to low job strain. This could be explained by the active learning hypothesis and the concept of “flow”⁴¹ where there is a high control or wide latitude for decision making to overcome the challenges of demands and instantly receiving feedback of actions. With this concept, the employee is cognitively stimulated and has no time to brood over failures as he is moving on to the next challenge even in the upper decades of life. Active jobs therefore could improve positive outcomes such as abstract reasoning. Karasek⁴² found an association between active job category workers and leisure and popular activities off work despite their high demands at work.

Overall, abstract reasoning skills seem to increase with increase in demand and active job especially in a middle-aged worker. Reasons that could explain the effect of these positive associations between increases in demands with abstract reasoning skills may include the fact that psychological demand measures the mental load from challenges, and average psychological demand could be translated into direct actions, *ie*, problem-solving challenges, with little residual strain to cause disturbance.⁴³ A subgroup of participants with moderately high job demand, *ie*, slightly above the median cut-point, just close to the tip of the “inverse U relationship” in eustress as explained in Selye's General Adaptation syndrome,⁴⁴ could be contributing to this effect. This may also explain the positive association between job demand and logical/verbal memory.

Decline in learning ability and memory are common after chronic exposure to all

measures of job strain hypothesis: control, high job strain, active job category, and passive job category, except demand. These associations are in congruence with the stress physiological mechanism that chronic infusion of glucocorticoid to the hippocampus disrupts memory.⁹ Additionally, the lack of discretion limits the use of skills one possesses to execute the challenges of the demands, and thus the process of learning new things is inhibited.

With one exception, all the negative associations were to employees in the younger group (≤ 46 years at baseline). This result is consistent with previous studies on job strain and cardiovascular outcomes where increasing age attenuated the association between job strain and cardiovascular diseases. Reasons for this could be multifactorial. For example, it could be that only employees who remain mentally intact (due to better coping mechanism, personality type, better susceptibility, *etc*) stay at their jobs longer and this may create an over-representation of people in the high strain group at the older age group category. Furthermore, the impact of job stress on cognitive function may be temporary and whatever impact job stress has on cognition may dissipate as one grows and become adapted. Also, considering that relatively higher percentage of the younger group were in the high demand and high strain jobs (Table 2), it may be that younger professionals in the process of building their career are exposed to more stressors relative to their older counterparts who may be more settled into their maximum level and/or well versed or adapted in their job. This may therefore result in an age-restricted positive association or no significant associations in the older group. Moreover, the cognitive performance of the older group may have already been lowered and stabilized before the 1st NP test and hence resulting in minimal or no decline between the two NP tests.

For more information on the job stress among Iranian prison employees see <http://www.theijoem.com/ijoem/index.php/ijoem/article/view/403>



The association of job strain and its components to cognitive decline has not been previously reported although the demand-control model posits that adverse reactions of psychological strain occur when psychological demands of the job are high and the worker's job control is simultaneously low.¹⁰ However, recent studies have linked low cognitive performance to long working hours³³ and also low job control at old age.⁴⁵ In Virtanen, *et al*,³³ a 5-year follow-up study that explored long working hours (a workplace psychosocial stressor) and cognitive decline of middle-aged white-collar office workers, showed a decline in performance on tests of intelligence. Other human studies have resulted that stressful events and experiences have significant association with a reduction in word recall in older healthy individuals⁴⁶ and reduction in recall of words on a complex memory task.⁴⁷

In spite of the paucity of epidemiological research studies of workplace stress and cognitive performance, the physiological mechanism is quite clear. In response to threatening events, the hypothalamic-pituitary-adrenocortical axis releases glucocorticoids that affects specific areas of the brain including hippocampus, a structure critical for memory. Chronic exposure to stress would cause prolong release of glucocorticoids that results in damage to the hippocampus that adversely affects memory.⁴⁸ Exposure to chronic stress disrupts hippocampal-dependent memory in laboratory animals by a) releasing tons of glucocorticoids which activate low affinity receptors. These low affinity receptors disrupt the activities of the high affinity receptors (which enhances long-term potentiation) and consequently weaken long-term potentiation, b) chronic stress causes atrophy in the axons and dendrites and thus destroys the neural network, c) neurogenesis is also inhibited with all forms of growth during sympathetic response, d)

chronic stress also results in endangering hippocampal neurons mainly due to inhibition of glucose storage and glucocorticoid neurotoxicity.

Overall, this study is consistent with theories and epidemiological findings that chronic stress leads to a decline in some aspects of cognition that may lead to higher risk for Alzheimer's disease and other dementia subtypes. Additionally, this study has shown the significant associations between midlife exposure to workplace psychosocial stressors alone—devoid of other stressors elsewhere—and cognitive decline, over two decades later.

A number of the NP tests showed no significant association with job strain and its components, but the results is comparable to other studies that used these NP tests on even easily measurable or tangible factors. In Debette, *et al*,⁴⁹ about 17% of the six NP tests used (the present study used eight), had some form of association with either hypertension, systolic blood pressure, diabetes mellitus, smoking, hypercholesterolemia, obesity and/or waist-to-hip ratio. Bangen, *et al*,⁵⁰ reported less than 20% associations between nine NP tests with four vascular risk factors such as hypertension, cardiovascular diseases, diabetes mellitus, and smoking. This study shows 17% association between the job strain variables and the NP tests.

The strengths of this study include that it was based in a community-based sample, the comprehensive assessment of both workplace psychosocial stressors with prospective follow up for cognitive decline, and the ability to adjust for relevant confounders. This study however, has some limitations. Participants of this study were primarily of European decent, limiting the generalizability of the study results to other populations. Also, over 96% of participants had at least high school diploma, which may somewhat limit the generalizability for populations with lower educa-

tional background. Multiple analyses and comparisons were used in the study. As an exploratory study, multiple analyses were used to explore and gain ideas and insights regarding possible associations and we acknowledge these findings need to be duplicated in other studies. The approximately 6-year follow-up on the 1st and 2nd NP test may not be sufficient to detect more subtle changes in cognition, and also is not sufficient for relating to incident dementia.

In conclusion, workplace psychosocial stressors as measured as high job strain, low job control and high psychological demand at midlife independently predicts some hallmarks and measures of cognitive decline, generally considered endophenotypes of dementia and Alzheimer's disease. This finding suggests that primary prevention of workplace psychosocial stressors at midlife may reduce the incidence of old age dementia. Primary prevention is crucial in combating Alzheimer's disease since no treatment has been found to halt the disease after symptoms have begun. This is an initial exploratory study. Therefore, the importance and need for further research that could lead to confirmation of predictive associations of workplace psychosocial stressors on later life cognitive decline is warranted. Also future studies involving neuroimaging or neuropathological data will help identify the mechanisms underlying these relationships. These studies could potentially impact occupational health preventive strategies and workplace policies.

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