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Research Article

Sleep Mediates the Association Between Stress at Work and Incident Dementia: Study From the Survey of Health, Ageing and Retirement in Europe

Xiao Tan, PhD,[1,2,*] Aleksandra Lebedeva, MD, PhD,[3] Torbjörn Åkerstedt, PhD,[1,3] and Hui-Xin Wang, PhD[3,*]

[1]Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden. [2]Department of Neuroscience, Uppsala University, Uppsala, Sweden. [3]Stress Research Institute, Department of Psychology, Stockholm University, Stockholm, Sweden.

*Address correspondence to: Xiao Tan, PhD, Department of Clinical Neuroscience, Karolinska Institutet, Nobels Väg 9, 171 77 Stockholm, Sweden. E-mail: xiao.tan@ki.se; and Hui-Xin Wang, PhD, Stress Research Institute, Department of Psychology, Stockholm University, Albanovägen 12, 106 91 Stockholm, Sweden. E-mail: huixin.wang@su.se

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Abstract

Background: Both psychosocial stress at work and sleep disturbance may predispose impaired cognitive function and dementia in later life. However, whether sleep plays a mediating role for the link between stress at work and subsequent dementia has yet to be investigated.

Methods: Data from the Survey of Health, Ageing and Retirement in Europe were used for the study. A cohort of 7 799 dementia-free individuals (aged 71.1 ± 0.2 years) were followed up for a median of 4.1 years for incident dementia. Job demand and control were estimated using questions derived from the Karasek's Job Content Questionnaire. Sleep disturbance was ascertained by a question in the EURO-Depression scale. Cox proportional hazard models adjusted for age, sex, education, cognitive test score, and other potential covariates were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of dementia in relation to different job strain levels.

Results: An interaction between job demand and sleep disturbance regarding the risk of dementia was detected. Data suggested a protective role of high-level job demand for dementia in individuals with sleep disturbance (HR [95% CI]: 0.69 [0.47, 1.00]) compared with low job demand. A 4-category job strain model based on the combination of job demand and job control levels suggested that among individuals with sleep disturbance, passive job (low demand, low control) was associated with a higher risk of dementia (1.54 [1.01, 2.34]), compared to active job (high demand, high control).

Conclusion: The link between work-related stress and risk of dementia is limited to individuals suffering sleep disturbance.

Keywords: Dementia, Psychosocial stress, Sleep

Occupation covers a long period of life course for the vast majority of people. Psychosocial stress at work, hallmarked by job demand (eg, workload and pressure) and job control (eg, freedom to make decision), is a considerable phenomenon and has been identified a risk factor for various adverse health outcomes such as cardiovascular diseases and depression (1,2). In recent years, mounting evidence supports that stress at work in midlife is related to an increased risk of cognitive impairment and dementia in later life (3,4). Specifically, compared to those who had high job control in their occupational life, individuals who had low job control were at higher risk of developing dementia and Alzheimer's disease (AD) in their older age (3).

Sufficient, high-quality sleep is essential for brain health. Sleep disturbances, such as insomnia symptoms and sleep-disordered breathing, induce nocturnal awakenings, and may underlie the pathogenesis of AD and dementia through alteration of amyloid-beta dynamics (5–8). Given the close link between psychosocial stress and sleep quality, job stress is of particular concern due to its chronic, repetitive nature, and its possible long-term effect on sleep (9). One study has suggested that job stress, regardless of stressful experiences at home, is associated with poor sleep quality (10). In a separate study, work overload was associated with the frequency of poor sleep quality, role conflict was associated with difficulty

initiating sleep and nonrestorative sleep, and job autonomy was negatively associated with nonrestorative sleep (11).

Despite the parallel links between job stress and sleep disturbance with the risk of dementia, it is not clear whether an interactive relationship exists between these 2 dementia risk factors. More specifically, could sleep serve as a mediator between work-related stress and development of dementia (Supplementary Figure S1)? Disentangling the job stress–sleep complexity may thus facilitate the prevention of dementia in real-life settings. Hence, we hypothesize that dimensions of job stress, such as job demand and control, as well as job reward, may differently associate with sleep disturbance regarding the risk of dementia in later life.

Method

Study Population

The study population was derived from the Survey of Health, Ageing and Retirement in Europe (SHARE). SHARE is an ongoing longitudinal study initiated in 2004, which focuses on health, economic, and social conditions in Europe. Eligible participants were people aged 50 years or older and their partners, regardless of age. Participants have been followed up every 2 years using computer-assisted personal interviewing technique, with 7 waves of data collected until up to the present analysis. Data collection and follow-up procedures of SHARE have been described elsewhere (12–17). SHARE was approved by the University of Mannheim's internal review board and Ethics Council of the Max Planck Society. Written consent form has been obtained from each participant.

Information about sleep disturbance and dementia status following the assessment of psychosocial stress at work was available from Wave 4. Thus, we set Wave 4 as the baseline of the present investigation, with observational period lasting throughout Waves 5–7. Among 10 605 participants with available work-related stress measurement results at baseline, 10 385 were free from dementia. Participants with inconsistent report of dementia (ie, answered "yes" in an earlier wave followed with "no" in any of the later waves, n = 89), not attended any follow-up surveys (Wave 5 to Wave 7, n = 1 671), had missing information in any potential confounders (n = 818), and aged <50 years at baseline (n = 8) were further excluded, leaving 7 799 participants (aged 50–101 years at baseline) for the analysis.

Assessments of Job Demand, Control, and Reward

Job demand, control, and reward circumstances regarding participants' main (longest-hold) job were assessed by SHARE Work Quality questionnaire. The demand–control model including 5 items was derived from the Job Content Questionnaire (18). Job demand was assessed by 3 items: "work had heavy time pressure," "work was emotionally demanding," and "work involved conflicts." Job control was assessed with 2 items: "freedom to decide how to do my work" and "opportunity to develop new skills." Job reward was assessed by 2 selected items from the Effort–Reward Imbalance model: "work gave recognition" and "work had adequate salary" (19). The items were quantified by 4-Likert scale with a score from 1 (strongly agree) to 4 (strongly disagree). The scores were summed up for each of the dimensions and dichotomized according to the tertile cutoffs as ≤8 versus >8 of a range 3–12 for demand; ≤3 versus >3 of 2–8 for control; and ≤5 versus >5 of 2–8 for reward. Individuals with scores above or below the cutoffs were regarded as low/high job demand, high/low job control, and high/low job reward, respectively (Chronbach's alpha between the 3 dimensions = 0.238).

Karasek's job strain model was introduced based on the dichotomization of the job demand and job control scores (18). The 4-category job strain model further stratified the study population into: (a) active job (high job demand + high control); (b) low strain (low job demand + high control); (c) high strain (high job demand + low control); (d) passive job (low job demand + low control).

Incident Dementia

The incidence of dementia was ascertained according to self-report or proxy respondent's (eg, guardian of the participant) report in each follow-up survey. If physical and/or cognitive limitations made it too difficult for a respondent to complete the interview her-/himself, the respondent was assisted by a proxy respondent to complete the interview. The question was asked as "Has a doctor ever told you that you had/Do you currently have any of the conditions on this card? With this we mean that a doctor has told you that you have this condition, and that you are either currently being treated for or bothered by this condition." Dementia was defined by the answer: "Alzheimer's disease (AD), dementia, organic brain syndrome, senility or any other serious memory impairment."

Assessment of Sleep Disturbance

Sleep disturbance was assessed by a question in the EURO-Depression (EURO-D) scale at baseline. The question was asked as "Have you had trouble sleeping recently? (Trouble with sleep or recent change in pattern)" with responding options of "Yes" or "No." Participants with an answer "Yes" were regarded as having sleep disturbance.

Confounding Factors

Selection of the potential confounders at baseline was based on the *Lancet* Commission's 2020 report on dementia prevention, intervention, and care (20). These include age, sex, duration of education, country of residence, body mass index (BMI), current smoking status, alcohol intake frequency, level of physical activity, number of chronic diseases, depression, and cognitive test score. Participants' duration of education was reported in years. BMI was defined as mass (kg)/height $(m)^2$ and treated as a continuous variable in the analyses. Current smoking status was dichotomized as "yes" and "no." Alcohol intake frequency was dichotomized into "taking alcohol drinks 5 or more days per week" and "taking alcohol drinks less than 5 days per week." Physical activity was dichotomized as physically active (vigorous or moderate physical activity more than once a week, or 1–3 times a month) and inactive (hardly ever or never in vigorous or moderate physical activity). Number of chronic diseases was ascertained by the question "Do you currently have any conditions …" and the answers to the listed chronic diseases (including heart diseases, hypertension, high blood cholesterol, stroke, diabetes, chronic lung diseases, arthritis, cancer, etc.) in the questionnaire. Status of depression was derived from the answers to the question "Have you been sad (depressed, miserable, in low spirits, blue) recently?" in the EURO-D scale. The cognitive score was calculated as a sum of numeric test score, immediate recall score, and delayed recall score which were conducted at the baseline investigation.

Statistical Analysis

Comparisons of baseline characteristics between participants who developed dementia and nondementia counterparts were conducted using analysis of variance for continuous variables and Pearson chi-square test for categorical variables. Cox regression analysis was performed to investigate the association between job demand, control, reward, job strain, and dementia. The interaction term between the abovementioned exposure variables and sleep disturbance regarding hazard ratio (HR)

for dementia was further included into the Cox regression models. Time at risk was calculated from the date of the study baseline to the date of dementia diagnosis, death, or last follow-up survey, whichever came first. For participants who developed dementia, time at risk was calculated as the length of nondementia period plus half of the time (in months) between the survey at which they first had the dementia and the previous examination (21). All analyses were performed using Stata 15.1 (StataCorp LLC, College Station, TX). A 2-sided *p* value of less than .05 was regarded as statistically significant.

Results

Characteristics of the Cohort

During the entire observational period, 297 participants developed dementia (3.8% of the total cohort). The median censoring time for dementia was 3.12 years. Baseline characteristics of the cohort are summarized in Table 1. Compared to the participants who did not develop dementia, those who developed dementia during the follow-up were older, with fewer years of education, and had lower BMI at baseline. In addition, participants who developed dementia showed lower prevalence of smoking, but were more likely to be physically inactive or suffer from depression and sleep disturbance, and had more chronic diseases than participants free from dementia.

Interaction Between Sleep Disturbance With Job Demand Regarding Incident Dementia

In total, the investigated cohort was 38 011 years at risk of being censored with dementia. As shown by multivariable Cox regression analyses, levels of job demand, control, or reward were not independently associated with the risk of dementia (Table 2). Having

Table 1. Baseline Characteristics of the Study Population in Relation to Incident Dementia

Characteristic	**Mean (95% CI)/*n* (%)**			
	Total Population (*n* = 7 799)	Nondementia (*n* = 7 502)	Incident Dementia (*n* = 297)	*p* Value*
Age, years	71.1 (70.9, 71.3)	70.8 (70.6, 71.0)	78.1 (77.3, 79.0)	<.001
Years of education	10.6 (10.5, 10.7)	10.6 (10.5, 10.7)	9.4 (8.9, 9.9)	<.001
Body mass index, kg/m^2	26.9 (26.8, 27.0)	26.9 (26.9, 27.0)	26.2 (25.7, 26.6)	.002
Cognitive score	12.9 (12.8, 13.0)	13.0 (13.0, 13.1)	9.1 (8.6, 9.6)	<.001
Sex, *n* (%)				.486
Women	4 075 (52.2)	3 918 (52.2)	149 (50.2)	
Men	3 732 (47.1)	3 584 (47.8)	148 (49.8)	
Country of residence, *n* (%)				<.001
Austria	342 (4.4)	323 (4.3)	19 (6.4)	
Belgium	1 038 (13.3)	996 (13.3)	42 (14.1)	
Czechia	353 (4.5)	342 (4.6)	11 (3.7)	
Switzerland	667 (8.6)	643 (8.6)	24 (8.1)	
Germany	515 (6.6)	492 (6.6)	23 (7.7)	
Denmark	655 (8.4)	633 (8.4)	22 (7.4)	
Spain	561 (7.2)	521 (6.9)	40 (13.5)	
France	745 (9.6)	723 (9.6)	22 (7.4)	
Italy	985 (12.6)	942 (12.6)	43 (14.5)	
The Netherlands	666 (8.5)	657 (8.8)	9 (3.0)	
Poland	682 (8.7)	659 (8.8)	23 (7.7)	
Sweden	590 (7.6)	571 (7.6)	19 (6.4)	
Smoking currently, *n* (%)				.006
Yes	1 236 (15.9)	1 206 (16.1)	30 (10.1)	
No	6 563 (84.2)	6 296 (83.9)	267 (89.9)	
Alcohol intake frequency, *n* (%)				.318
5 days or more per week	2 141 (27.5)	2 067 (27.6)	223 (75.1)	
Less than 5 days per week	5 658 (72.6)	5 435 (72.4)	74 (24.9)	
Level of physical activity, *n* (%)				<.001
Inactive	2 266 (29.1)	2 142 (28.6)	124 (41.8)	
Active	5 533 (70.9)	5 360 (71.4)	173 (58.2)	
Number of chronic diseases, *n* (%)				.003
0	1 493 (19.1)	1 451 (19.3)	42 (14.1)	
1	2 362 (30.3)	2 274 (30.3)	88 (29.6)	
2	1 882 (24.1)	1 819 (24.2)	63 (21.2)	
3 or more	2 062 (26.4)	1 958 (26.1)	104 (35.0)	
Depression, *n* (%)				.008
Yes	2 898 (37.2)	2 766 (36.9)	132 (44.4)	
No	4 901 (62.8)	4 736 (63.1)	165 (55.6)	
Sleep disturbance, *n* (%)				.013
Yes	2 581 (33.1)	2 463 (32.8)	118 (39.7)	
No	5 218 (66.9)	5 039 (67.2)	179 (60.3)	

Notes: CI = confidence interval.

*Comparison between nondementia and dementia groups, 1-way analysis of variance or Pearson chi-square test.

sleep disturbance at baseline was associated with a higher subsequent risk of dementia when adjusted for age, sex, and years of education (HR [95% confidence interval {CI}]: 1.38 [1.09, 1.75], p = .008).

In the Cox regression analysis, an interaction effect has been detected between sleep disturbance and job demand on the risk of dementia (HR [95% CI]: 0.61 [0.38, 0.97], p = .036, adjusted for age, sex, years of education; HR [95% CI]: 0.63 [0.40, 1.01], p = .057, fully adjusted for age, sex, years of education, cognitive test score, country of residence, smoking, alcohol intake, level of physical activity, BMI, number of chronic diseases, and depression). A further multivariable Cox regression conducted on data split by the prevalence of sleep disturbance suggested that the association between low job demand and risk of dementia only existed among those suffering sleep disturbance (HR [95% CI]: 0.69 [0.47, 1.00], p = .049, low vs high job demand, fully adjusted model; Figure 1). No interactions have been detected between job control and sleep disturbance (HR [95% CI]: 0.93 [0.54, 1.60], p = .789, adjusted for age, sex, years of education; HR [95% CI]: 0.83 [0.48, 1.44], p = .516, fully adjusted model), or job reward and sleep disturbance (HR [95% CI]: 1.10 [0.61, 1.96], p = .758, adjusted for age, sex, years of education; HR [95% CI]: 1.07 [0.60, 1.91], p = .825, fully adjusted model) regarding the subsequent risk of dementia.

Interaction Between Sleep Disturbance With Job Strain Regarding Incident Dementia

Results of the tests between categories of job strain and incident dementia in the multivariable Cox regression model are shown in Table 3. No significant links between the 4 job strain categories and risk of dementia were detected. A strain model × sleep disturbance interaction was detected regarding the risk of dementia (HR [95% CI]: 1.73 [1.11, 2.70], p = .015, adjusted for age, sex, years of education; HR [95% CI]: 1.59 [1.02, 2.49], p = .041, fully adjusted model). Further stratification of the data by prevalence of sleep disturbance demonstrated that among participants with sleep disturbance, having a passive job was associated with an increased risk of dementia, compared to those having an active job (Table 4).

Sensitivity Analyses

A set of sensitivity analysis has been conducted. Survival analysis taking death (n = 720, 9.2% of the total cohort) as a competing risk factor for dementia did not change the main finding of the study (subdistribution hazard ratio (sHR) [95% CI] in Fine-Gray proportional hazards regression for interaction term between job demand and sleep disturbance: sHR [95% CI]: 0.61 [0.38, 0.98], p = .041, adjusted for age, sex, and years of education; sHR [95% CI]: 0.63 [0.39, 1.02], p = .061, fully adjusted model). Similar results were demonstrated when using median cutoffs for dichotomizing job demand, control, and reward variables (data shown in Supplementary Tables S1 and S2). In addition to the previously mentioned 2 items for job reward, we further added "work had adequate support" as an extra item in this domain; no association has been found between job reward and incident dementia (HR [95% CI]: 1.00 [0.95, 1.08], low vs high job reward in fully adjusted Cox regression model). Neither was a job reward–sleep interaction detected in this model (p = .63).

Other potential confounding factors have also been considered in the additional analyses. Status of retirement (retired n = 6 910, 88.6% of the total population) and type of main occupation (physical- or mental-demanding job) were reported by the participant or the proxy respondent. Similar interaction between job demand and sleep disturbance, or strain model and sleep disturbance, regarding the risk of dementia was detected by adding status of retirement and type of occupation into the Cox regression model. Job demand × sleep disturbance HR [95% CI]: 0.61 [0.38, 0.98], p = .041, adjusted for age, sex, years of education, retirement status, and type of occupation; HR [95% CI]: 0.64 [0.40, 1.03], p = .064, fully adjusted model. Strain model × sleep disturbance HR [95% CI]: 1.72 [1.11, 2.69], p = .016, adjusted for age, sex, years of education, retirement status, and type of occupation; HR [95% CI]: 1.54 [0.98, 2.41], p = .060, fully adjusted model. Finally, the potential impact of leisure-time activities (participating charity work, caring for the disabled, helping others, training course, club activities, and religious

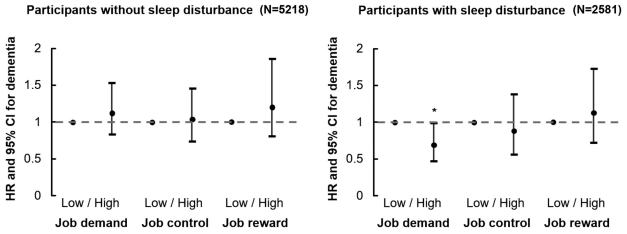

Figure 1. Job demand, control, reward and risk of incident dementia, split by prevalence of sleep disturbance (HR = hazard ratio; CI = confidence interval; *p < .05, fully adjusted Cox proportional hazards model).

Table 2. Association of Demand, Control, and Reward With Incident Dementia

	Model 1		Model 2		Model 3	
	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Demand						
Low (n = 3 135)	Reference		Reference		Reference	
High (n = 4 664)	0.99 (0.78, 1.24)	.906	0.93 (0.74, 1.18)	.558	0.93 (0.74, 1.18)	.548
Control						
Low (n = 2 171)	Reference		Reference		Reference	
High (n = 5 628)	1.17 (0.89, 1.53)	.266	0.97 (0.74, 1.28)	.831	0.97 (0.74, 1.27)	.816
Reward						
Low (n = 6 238)	Reference		Reference		Reference	
High (n = 1 561)	0.92 (0.68, 1.22)	.562	1.17 (0.87, 1.58)	.306	1.18 (0.87, 1.59)	.285

Notes: CI = confidence interval; HR = hazard ratio. Model 1: adjusted for age, sex, and years of education; Model 2: adjusted for Model 1 + cognitive test score, country of residence, smoking, alcohol intake, level of physical activity, body mass index, number of chronic diseases, and depression; Model 3: adjusted for Model 2 + sleep quality.

Table 3. Risk of Dementia Relation to Job Strain Status According to Karasek Model

	Model 1		Model 2		Model 3	
	HR (95% CI)	*p* Value	HR (95% CI)	*p* Value	HR (95% CI)	*p* Value
Active (*n* = 3 480)	Reference		Reference		Reference	
Low strain (*n* = 2 148)	0.81 (0.55, 1.20)	.293	1.01 (0.68, 1.50)	.944	1.02 (0.69, 1.52)	.916
High strain (*n* = 1 184)	0.97 (0.68, 1.38)	.853	1.15 (0.81, 1.65)	.433	1.15 (0.80, 1.65)	.431
Passive (*n* = 987)	1.10 (0.84, 1.43)	.506	1.14 (0.87, 1.50)	.327	1.14 (0.87, 1.50)	.331
p for trend		.375		.641		.625

Notes: CI = confidence interval; HR = hazard ratio. Model 1: adjusted for age, sex, and years of education; Model 2: adjusted for Model 1 + cognitive test score, country of residence, smoking, alcohol intake, level of physical activity, body mass index, number of chronic diseases, and depression; Model 3: adjusted for Model 2 + sleep quality.

Table 4. Risk of Dementia in Relation to Job Strain Status According to Karasek Model, Stratified by Prevalence of Sleep Disturbance

	Participants Without Sleep Disturbance			Participants With Sleep Disturbance		
	N of Incidence (dementia/no dementia)	HR (95% CI)	*p* Value	*N* of Incidence (dementia/no dementia)	HR (95% CI)	*p* Value
Active	81/2 169	Reference		46/1 184	Reference	
Low strain	52/1 368	0.82 (0.50, 1.36)	.447	45/683	1.50 (0.78, 2.86)	.223
High strain	26/802	1.07 (0.68, 1.68)	.772	15/341	1.26 (0.70, 2.29)	.443
Passive	20/700	0.94 (0.66, 1.34)	.736	12/255	1.54 (1.01, 2.34)	.045*

Notes: CI = confidence interval; HR = hazard ratio. Cox proportional hazards model adjusted for age, sex, years of education, country of residence, smoking, alcohol intake, level of physical activity, body mass index, number of chronic diseases, and depression.

*$p < .05$.

activities for at least once a week) and social support (receiving personal care or practical household help from anyone outside the household in last 12 months) of the participants have been tested. Similar interactions between job demand/strain model and sleep disturbance for the risk of dementia were found in the Cox regression analyses. Job demand × sleep disturbance, HR [95% CI]: 0.60 [0.37, 0.96], $p = .032$, adjusted for age, sex, years of education, frequency of leisure-time activity, and social support; HR [95% CI]: 0.63 [0.40, 1.02], $p = .058$, fully adjusted model. Strain model × sleep disturbance HR [95% CI]: 1.73 [1.11, 2.70], $p = .015$, adjusted for age, sex, years of education, frequency of leisure-time activity, and social support; HR [95% CI]: 1.59 [1.02, 2.49], $p = .041$, fully adjusted model.

Discussion

In this longitudinal study among adults living in 12 different European countries, we observed that the association between psychosocial stress at work and incident dementia was mediated by sleep disturbance. Specifically, job demand, control, reward, as well as different combinations of demand and control in Karasek's job strain model were not linked to an altered risk of subsequent dementia among individuals without sleep disturbance. In contrast, both high demand and passive job were associated with an altered risk of incident dementia among persons reported sleep disturbance. It is worth noting that for persons with sleep disturbance, being exposed under high job demand attenuated their future risk of getting dementia. Moreover, among individuals with sleep disturbance, those who fulfilled both low job demand and low job control in their occupation were particularly prone to dementia in later life, compared to those who experienced high levels in both job demand and job control.

The link between psychosocial stress at work and incident dementia in our study was only discovered among those who reported sleep disturbance. This indicates a potential role of sleep for bridging the psychosocial stress at work and the development of dementia, and also emphasizes the prominence of maintaining a healthy sleep pattern among those who work under a suboptimal psychosocial environment. Prevalence of sleep disturbance increases with advancing age (22); in the present analysis nearly one third of the participants reported sleep disruptions at baseline. Sleep disturbance such as insufficient sleep, insomnia symptoms, sleep-disordered breathing, and other disorders have been associated with dementia in later life, particularly caused by AD. A 25-year longitudinal study carried out on 7 959 British adults reported a 30% higher risk of dementia diagnosis among participants who had persistent short sleep duration (6 hours or less per night) at age 50, 60, and 70, compared to those with a 7-hour sleep duration in all 3 time points (7). Another longitudinal study with 1 574 men from Sweden at baseline found that insomnia complaints at age 70 increased subsequent risk of dementia and AD by 114% and 192%, respectively (23). On the other hand, proper treatment of obstructive sleep apnea—the most common cause of sleep-disordered breathing—lowered the risk of incident AD by about 22% in older Medicare beneficiaries (24). Sleep disturbance may contribute to the pathogenesis of AD and dementia through different mechanisms. These include but are not limited to a malfunctioning glymphatic system due to reduced slow-wave sleep (25,26), hypoxia due to apnea–hypopnea events (27), and neuroinflammation (28).

Findings from previous studies regarding job demand and risk of dementia are inconsistent. In a recent study among 1 277 adults aged 60 years and older, no association between mental demand at work and incidence of dementia was suggested following a 14-year mean observation period. However, a meta-analysis incorporating 4 relevant studies suggested that higher work complexity led to a reduced risk for dementia (29). Specific types of job demand characteristics may relate to dementia outcome. For instance, a previous

study demonstrated greater risk for AD when mental occupational demands were lower and physical occupational demands were higher (30). Another study found that higher social demands, but not intellectual demands were associated with reduced risk of AD (31). It must be kept in mind that the potential interaction with sleep disturbance was not investigated in the abovementioned studies. In our study, high job demand was protective for the development of dementia among individuals with disturbed sleep. This may seem contradictory because high job demand itself is often associated with sleep complaints (32). We assume that most of the high demand jobs may involve in high work complexity, which has a protective effect against dementia and may counterbalance the detrimental impact of sleep disturbance on the brain structure and cognitive functions in later life (29,33–35). Another possible explanation could be that participants in this study were over 50 years old and they were in the later stages of their working life. People with extremely high levels of job demand in earlier career stage might have left the relevant job due to heavy psychosocial burden, while those who stayed might either have relatively lower levels of high job demand or become psychologically adapted to such work environment. However, further evidence is warranted to confirm the observation in our study.

The association between low job control and dementia has been well established by earlier studies. A Swedish twin cohort involving more than 10 000 participants identified lower job control as a risk factor for any dementia and vascular dementia (36). Another study in 913 older community dwellers showed a 120% increased adjusted HR for AD among those having low-level job control (3). We observed in individuals with sleep disruption that passive job strain (ie, low demand and low control) was associated with a 54% increased risk for subsequent dementia, compared to active job (high demand, high control). This is in line with a recent multicohort study (n = 107 896) (37). In that study, cognitively low-stimulating jobs include low-demanding tasks and low job decision latitude was associated with an elevated subsequent risk for dementia. Additional analyses found that individuals with low cognitive stimulation at work had higher levels of plasma proteins related to neurodegeneration (eg, slit homologue 2, carbohydrate sulfotransferase 12, and peptidyl-glycine α-amidating monooxygenase) (37). Separate evidence has shown that sleep deprivation may facilitate such pathways and further inhibit neurogenesis and memory consolidation (38,39). Thus, a combination of passive jobs and sleep disturbance should be of particular concern in terms of prevention of dementia.

Given the observed relationship between sleep disturbance and subsequent risk of dementia, it is of importance to investigate whether worksite interventions, as a part of holistic occupation wellness programs, could have a positive impact on sleep quality. A systemic review focusing on workplace intervention to promote sleep health reported preliminary evidence supporting the effectiveness of sleep hygiene and fatigue management on self-reported outcomes of sleep (40). This encourages the employers to provide aid on sleep in order to mitigate the burden on cognitive health caused by job stress.

The present study contains a relatively large sample size. Data were collected by a standard survey from European countries in different regions and with different socioeconomic status. In the analyses, several important potential confounders, such as cognitive function at baseline and depressive symptoms, have been taken into account. Nevertheless, the study is subject to a number of limitations. Sleep disturbance was ascertained by a single question reflecting participant's current situation without scopes of its duration and frequency in the past; thus, the study could not reveal whether sleep disturbance as a chronic problem has an interaction with job strain regarding the risk of dementia. We were also unable to disclose whether a particular pattern of sleep disturbance, such as insufficient sleep or fragmented sleep, played the mediating role in the interaction. Furthermore, dementia incidence was extracted from follow-up surveys of SHARE which carried out every 2 years; hence, censoring period cannot be narrowed down according to the exact date of dementia initiation. Finally, in addition to the cognitive function assessed at baseline, future studies may consider controlling cognitive trajectory before the onset of dementia which can reflect the process of cognitive deterioration.

In conclusion, results of this study suggest that dementia risk induced by psychosocial stress at work could be mediated by sleep disturbance. In addition to the beneficial impact of high demand job on the occurrence of dementia, our findings support strengthening job control for curbing the risk of dementia in late life, especially among individuals with sleep disturbance.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

None declared.

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References

1. Kivimäki M, Leino-Arjas P, Luukkonen R, Riihimäki H, Vahtera J, Kirjonen J. Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees. *BMJ*. 2002;325(7369):857. doi:10.1136/bmj.325.7369.857
2. Mausner-Dorsch H, Eaton W. Psychosocial work environment and depression: epidemiologic assessment of the demand–control model. *Am J Public Health*. 2000;90(11):1765–1770. doi:10.2105/ajph.90.11.1765
3. Wang HX, Wahlberg M, Karp A, Winblad B, Fratiglioni L. Psychosocial stress at work is associated with increased dementia risk in late life. *Alzheimers Dement*. 2012;8(2):114–120. doi:10.1016/j.jalz.2011.03.001
4. Sindi S, Hagman G, Håkansson K, et al. Midlife work-related stress increases dementia risk in later life: the CAIDE 30-year study. *J Gerontol B Psychol Sci Soc Sci*. 2017;72(6):1044–1053. doi:10.1093/geronb/gbw043
5. Xie L, Kang H, Xu Q, et al. Sleep drives metabolite clearance from the adult brain. *Science*. 2013;342(6156):373–377. doi:10.1126/science.1241224
6. Kang JE, Lim MM, Bateman RJ, et al. Amyloid-beta dynamics are regulated by orexin and the sleep–wake cycle. *Science*. 2009;326(5955):1005–1007. doi:10.1126/science.1180962
7. Sabia S, Fayosse A, Dumurgier J, et al. Association of sleep duration in middle and old age with incidence of dementia. *Nat Commun*. 2021;12(1):2289. doi:10.1038/s41467-021-22354-2
8. Yaffe K, Laffan AM, Harrison SL, et al. Sleep-disordered breathing, hypoxia, and risk of mild cognitive impairment and dementia in older women. *JAMA*. 2011;306(6):613–619. doi:10.1001/jama.2011.1115.

9. Kim EJ, Dimsdale JE. The effect of psychosocial stress on sleep: a review of polysomnographic evidence. *Behav Sleep Med*. 2007;5(4):256–278. doi:10.1080/15402000701557383
10. Burgard SA, Ailshire JA. Putting work to bed: stressful experiences on the job and sleep quality. *J Health Soc Behav*. 2009;50(4):476–492. doi:10.1177/002214650905000407
11. Knudsen HK, Ducharme LJ, Roman PM. Job stress and poor sleep quality: data from an American sample of full-time workers. *Soc Sci Med*. 2007;64(10):1997–2007. doi:10.1016/j.socscimed.2007.02.020
12. Börsch-Supan A, Brandt M, Hunkler C, et al.; SHARE Central Coordination Team. Data resource profile: the Survey of Health, Ageing and Retirement in Europe (SHARE). *Int J Epidemiol*. 2013;42(4):992–1001. doi:10.1093/ije/dyt088
13. Börsch-Supan A. *Survey of Health, Ageing and Retirement in Europe (SHARE) Wave 3—SHARELIFE. Release Version: 7.1.0. SHARE-ERIC. Data Set*. 2020. doi:10.6103/SHARE.w3.710
14. Börsch-Supan A. *Survey of Health, Ageing and Retirement in Europe (SHARE) Wave 4. Release Version: 7.1.0. SHARE-ERIC. Data Set*. 2020. doi:10.6103/SHARE.w4.710
15. Börsch-Supan A. *Survey of Health, Ageing and Retirement in Europe (SHARE) Wave 5. Release Version: 7.1.0. SHARE-ERIC. Data Set*. 2020. doi:10.6103/SHARE.w5.710
16. Börsch-Supan A. *Survey of Health, Ageing and Retirement in Europe (SHARE) Wave 6. Release Version: 7.1.0. SHARE-ERIC. Data Set*. 2020. doi:10.6103/SHARE.w6.710
17. Börsch-Supan A. *Survey of Health, Ageing and Retirement in Europe (SHARE) Wave 7. Release version: 7.1.1. SHARE-ERIC. Data Set*. 2020. doi:10.6103/SHARE.w7.711
18. Karasek R, Brisson C, Kawakami N, Houtman I, Bongers P, Amick B. The Job Content Questionnaire (JCQ): an instrument for internationally comparative assessments of psychosocial job characteristics. *J Occup Health Psychol*. 1998;3(4):322–355. doi:10.1037//1076-8998.3.4.322
19. Siegrist J, Starke D, Chandola T, et al. The measurement of effort–reward imbalance at work: European comparisons. *Soc Sci Med*. 2004;58(8):1483–1499. doi:10.1016/S0277-9536(03)00351-4
20. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet*. 2020;396(10248):413–446. doi:10.1016/S0140-6736(20)30367-6
21. Wu JJ, Wang HX, Yao W, Yan Z, Pei JJ. Late-life depression and the risk of dementia in 14 countries: a 10-year follow-up study from the Survey of Health, Ageing and Retirement in Europe. *J Affect Disord*. 2020;274:671–677. doi:10.1016/j.jad.2020.05.059
22. Miner B, Kryger MH. Sleep in the aging population. *Sleep Med Clin*. 2017;12(1):31–38. doi:10.1016/j.jsmc.2016.10.008
23. Benedict C, Byberg L, Cedernaes J, et al. Self-reported sleep disturbance is associated with Alzheimer's disease risk in men. *Alzheimers Dement*. 2015;11(9):1090–1097. doi:10.1016/j.jalz.2014.08.104
24. Dunietz GL, Chervin RD, Burke JF, Conceicao AS, Braley TJ. Obstructive sleep apnea treatment and dementia risk in older adults. *Sleep*. 2021;44(9):zsab076. doi:10.1093/sleep/zsab076
25. Dijk D. Slow-wave sleep deficiency and enhancement: implications for insomnia and its management. *World J Biol Psychiatry*. 2010;11(suppl 1):22–28. doi:10.3109/15622971003637645
26. Hablitz LM, Vinitsky HS, Sun Q, et al. Increased glymphatic influx is correlated with high EEG delta power and low heart rate in mice under anesthesia. *Sci Adv*. 2019;5(2):eaav5447. doi:10.1126/sciadv.aav5447
27. Tan X, Sundström J, Lind L, Franzon K, Kilander L, Benedict C. Reverse dipping of systolic blood pressure is associated with increased dementia risk in older men: a longitudinal study over 24 years. *Hypertension*. 2021;77(4):1383–1390. doi:10.1161/HYPERTENSIONAHA.120.16711
28. Leng Y, Musiek ES, Hu K, Cappuccio FP, Yaffe K. Association between circadian rhythms and neurodegenerative diseases. *Lancet Neurol*. 2019;18(3):307–318. doi:10.1016/S1474-4422(18)30461-7
29. Huang LY, Hu HY, Wang ZT, et al. Association of occupational factors and dementia or cognitive impairment: a systematic review and meta-analysis. *J Alzheimers Dis*. 2020;78(1):217–227. doi:10.3233/JAD-200605
30. Smyth KA, Fritsch T, Cook TB, McClendon MJ, Santillan CE, Friedland RP. Worker functions and traits associated with occupations and the development of AD. *Neurology*. 2004;63(3):498–503. doi:10.1212/01.wnl.0000133007.87028.09
31. Andel R, Crowe M, Pedersen NL, et al. Complexity of work and risk of Alzheimer's disease: a population-based study of Swedish twins. *J Gerontol B Psychol Sci Soc Sci*. 2005;60(5):P251–P258. doi:10.1093/geronb/60.5.p251
32. Portela LF, Kröning Luna C, Rotenberg L, et al. Job strain and self-reported insomnia symptoms among nurses: what about the influence of emotional demands and social support? *Biomed Res Int*. 2015;2015:820610. doi:10.1155/2015/820610
33. Wang HX, MacDonald SW, Dekhtyar S, Fratiglioni L. Association of lifelong exposure to cognitive reserve-enhancing factors with dementia risk: a community-based cohort study. *PLoS Med*. 2017;14(3):e1002251. doi:10.1371/journal.pmed.1002251
34. Dekhtyar S, Wang HX, Fratiglioni L, Herlitz A. Childhood school performance, education and occupational complexity: a life-course study of dementia in the Kungsholmen Project. *Int J Epidemiol*. 2016;45(4):1207–1215. doi:10.1093/ije/dyw008
35. Karp A, Andel R, Parker MG, Wang HX, Winblad B, Fratiglioni L. Mentally stimulating activities at work during midlife and dementia risk after age 75: follow-up study from the Kungsholmen Project. *Am J Geriatr Psychiatry*. 2009;17(3):227–236. doi:10.1097/JGP.0b013e318190b691
36. Andel R, Crowe M, Hahn EA, et al. Work-related stress may increase the risk of vascular dementia. *J Am Geriatr Soc*. 2012;60(1):60–67. doi:10.1111/j.1532-5415.2011.03777.x
37. Kivimäki M, Walker KA, Pentti J, et al. Cognitive stimulation in the workplace, plasma proteins, and risk of dementia: three analyses of population cohort studies. *BMJ*. 2021;374:n1804. doi:10.1136/bmj.n1804.
38. Delorme J, Wang L, Kuhn FR, et al. Sleep loss drives acetylcholine- and somatostatin interneuron-mediated gating of hippocampal activity to inhibit memory consolidation. *Proc Natl Acad Sci USA*. 2021;118(32):e2019318118. doi:10.1073/pnas.2019318118
39. Kostin A, Alam MA, McGinty D, Alam MN. Adult hypothalamic neurogenesis and sleep–wake dysfunction in aging. *Sleep*. 2021;44(2):zsaa173. doi:10.1093/sleep/zsaa173
40. Redeker NS, Caruso CC, Hashmi SD, Mullington JM, Grandner M, Morgenthaler TI. Workplace interventions to promote sleep health and an alert, healthy workforce. *J Clin Sleep Med*. 2019;15(4):649–657. doi:10.5664/jcsm.7734