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Brief Report

Job Strain and the Risk of Stroke: An Individual-Participant Data Meta-analysis

Running head: Job strain and the risk of stroke

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Abstract

Background and Purpose: Psychosocial stress at work has been proposed to be a risk factor for cardiovascular disease. However, its role as a risk factor for stroke is uncertain.

Methods: We conducted an individual-participant-data meta-analysis of 196,380 men and women from 14 European cohort studies to investigate the association between job strain, a measure of work-related stress, and incident stroke.

Results: In 1.8 million person-years at risk (mean follow-up 9.2 years), 2023 first-time stroke events were recorded. The age- and sex-adjusted hazard ratio for job strain relative to no job strain was 1.24 (95%CI 1.05;1.47) for ischemic stroke, 1.01 (95%CI 0.75;1.36) for hemorrhagic stroke and 1.09 (95%CI 0.94;1.26) for overall stroke. The association with ischemic stroke was robust to further adjustment for socioeconomic status.

Conclusion: Job strain may be associated with an increased risk of ischaemic stroke, but further research is needed to determine whether interventions targeting job strain would reduce stroke risk beyond existing preventive strategies.

Introduction

Stroke is a major cause of morbidity, mortality and disability world-wide.^{1,2} Psychosocial stress may increase the risk of developing stroke,³ although prospective evidence to confirm this is scarce. Job strain, for example, is one of the most widely studied measures of psychosocial stress⁴ and has been linked to an increased risk of coronary heart disease.^{5,6} However, an association between job strain, or its components (i.e. high job demands and low job control), and stroke has been observed only in part⁷⁻⁹ of the studies.^{6, 10-12} To increase understanding about stress and stroke, we conducted an individual-participant-data meta-analysis examining the association between job strain, stroke and its subtypes in more than 190,000 employed men and women from 6 European countries.

Material and Methods

We used data provided by investigators from 14 prospective cohort studies (baseline examination between 1985 and 2008) of the Individual-Participant-Data meta-analysis in Working populations (IPD-Work) Consortium (**Appendix-eTable1**).⁵ Job strain at baseline was defined according to demand-control (job strain) questionnaires.⁴ Individuals exposed to job strain (i.e. reporting high job demands in combination with low control over the work situation) were compared to all others.¹³ Socioeconomic status (SES) served as a proxy marker of stroke risk factors. Data on standard stroke risk factors, such as diabetes, hypertension, smoking, and heavy alcohol consumption, were available from 3 studies (**Appendix**).

We defined incident stroke using national hospital admission and death registries (ICD-10 codes I60, I61, I63, I64, or the corresponding ICD-9 or ICD-8 codes)(for alternative definitions in 2 studies, see **Appendix**). We excluded participants with a history of stroke at baseline (transient ischemic attacks were not considered). Data on stroke subtypes, ischemic (ICD-10 I63) and hemorrhagic (I60, I61), were available from 13 studies (**Appendix**).

The participants were followed up from their assessment of job strain at baseline to the first stroke event, death, or end of follow-up – whichever came first. Using Cox proportional hazard regression we estimated hazard ratios and 95% confidence intervals (CI) to quantify the associations of job strain with overall, ischemic and hemorrhagic stroke in each study. All analyses were adjusted for age and sex, with a further adjustment for SES and, in sensitivity analyses based on 3 cohorts, standard stroke risk factors. We pooled the study-specific effect estimates in random-effects meta-analyses.

Results

A total of 196,380 participants (mean age 42.4 years, 53% female) had not experienced a stroke event before the study baseline and had complete data on age, sex, SES, job strain and incident stroke events, the analytical sample. The proportion exposed to job strain ranged from 13% to 22%, depending on the study (**Table 1**).

During 1,815,848 person-years at risk (mean follow-up 9.2 years), 2023 stroke events were recorded. The age- and sex-adjusted pooled hazard ratio of overall stroke for the job strain group compared to those not exposed to job strain was not statistically significant (1.09, 95%

CI 0.94;1.26) with little heterogeneity in estimates between the studies ($I^2=21.6\%$, $p=0.22$)(**Figure 1**).

In analysis of stroke subtypes (**Figure 1, Appendix eFigures 1-3**), job strain was associated with an increased risk of incident ischemic stroke (hazard ratio 1.24, 95% CI 1.05;1.47) but not hemorrhagic stroke (1.01, 95% CI 0.75;1.36). Further adjustment for SES yielded a hazard ratio of 1.18 (95% CI 1.00;1.39) for ischemic stroke and 0.95 (95% CI 0.72;1.27) for hemorrhagic stroke (sensitivity analyses in **Appendix**).

Discussion

In this individual-participant data meta-analysis of 190,000 working men and women in Europe, job strain was associated with an approximately 20% increased risk of acute ischemic stroke. No association with the risk of overall stroke or hemorrhagic stroke was observed.

Previous smaller-scale studies on job strain, and the risk of stroke^{6-8,10-12} were underpowered to detect a 20% elevated risk. The strength of the association between job strain and ischemic stroke found in the present study corresponds to the association observed in our previous meta-analysis on job strain and coronary heart disease.⁵ The etiology of coronary heart disease and ischemic stroke is partially overlapping, with atherosclerosis as the major common factor. Job strain might have an effect on the cardiovascular system through activation of the neuroendocrine stress response, dysregulation of the hypothalamic-pituitary-adrenal axis, the metabolic syndrome, or indirectly via unhealthy behaviors, such as physical inactivity and poor diet.¹⁴

We did not have complete data on standard stroke risk factors leaving residual confounding as a potential alternative explanation for the results. Although our sample size was large, the number of ischemic and hemorrhagic stroke events was relatively low and the diagnoses were not always confirmed by brain imaging; thus, further research is needed to confirm the findings. Additional research should also examine the mechanisms underlying the association between job strain and ischemic stroke and determine the extent to which interventions targeting job strain might reduce stroke risk beyond existing preventive strategies.

Acknowledgement

Funding for the IPD-Work Consortium is provided in **Appendix**.

Disclosures

No potential conflict of interests declared by the authors.

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Figure legends

Figure 1. Age- and sex-adjusted association between job strain and subtypes of stroke.

Stroke subtypes, adjusted for sex and age

All strokes	N=196 380, 2023 events
Ischemic	N=185 120, 1049 events
Hemorrhagic	N=179 573, 476 events

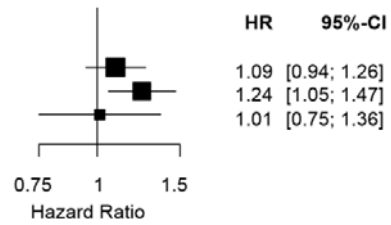


Table 1. Characteristics of participants in 14 cohort studies, IPD-Work Consortium

Study*, country	Baseline years	Number of participants	Number (%) participants with job strain	Total number of stroke events (incidence per 10,000 person-years)
Whitehall II, UK	1985-1988	10 261	1438 (14)	193 (9.9)
Still Working, Finland	1986	9137	1420 (16)	471 (24.2)
WOLF-S, Sweden	1992-1995	5648	915 (16)	104 (12.8)
IPAW, Denmark	1996-1997	2027	356 (18)	55 (21.4)
WOLF-N, Sweden	1996-1998	4683	599 (13)	95 (17.6)
COPSOQ-I, Denmark	1997	1769	361 (20)	33 (16.0)
Gazel, France	1997	11 260	1630 (14)	312 (20.5)
POLS, Netherlands	1997-2002	24 521	3911 (16)	110 (4.6)
HeSSup, Finland	1998	16 404	2875 (18)	75 (6.6)
PUMA, Denmark	1999-2000	1839	278 (15)	30 (16.4)
DWECS, Denmark	2000	5547	1231 (22)	77 (15.8)
FPS, Finland	2000	47 302	7710 (16)	351 (7.7)
NWCS, Netherlands	2005-2006	45 052	5610 (13)	62 (3.8)
SLOSH, Sweden	2006-2008	10 930	2147 (20)	55 (11.0)
Total	1985-2008	196 380	30 481 (16)	2023 (11.1)

*For study abbreviations and further details, see **Appendix**