

博士論文（要約）

Association of job stressors with panic attack and panic  
disorder in a working population in Japan: a 2-year  
prospective cohort study

日本人労働者における職業性ストレス要因とパニック発作および  
パニック障害との関連：2年間の前向きコホート研究

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## 論文の内容の要旨

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### Introduction

Panic disorder is a common anxiety disorder that causes various adverse effect in the social life of patients. Panic attack is more common than panic disorder. Panic attack is not diagnosed as a mental disorder by itself. However, panic attacks are also considerable symptoms. Various environmental risk factors also have been reported for panic disorder including age, sex, family income, and mental health problems other than panic disorder. In addition, cardiovascular disease has been reported as a risk factor for panic disorder, although less consistently.

Job stressors have been suggested to cause mental and physical health problems. Greater job strain has been associated with a risk of stroke, sleep disturbances, cardiovascular mortality, type-2 diabetes, and depressive disorder. Low workplace social support was reported to be associated with a risk of cardiovascular disease, insomnia, and depressive disorder. High effort-reward imbalance was also associated with a risk of cardiovascular disease, major depression, sleep disturbances, insomnia, and lower immunity. As these job stressors have been associated with cardiovascular disease and major depressive disorder, which are known risk factors of panic disorder, these job stressors may be associated with panic attack and panic disorder.

Job stressors may be associated also with the occurrence of panic attack and panic disorder. First, many anxiety disorders including panic disorder are closely comorbid with major depressive disorder to form a broad category of mental disorders characterized by dysphoria, anxiety, and fear, called the internalizing disorder, suggesting that these disorders may share a common psychopathology or underlying mechanism. As job stressors are associated with the occurrence of major depressive disorder, job stressors may increase the risk of panic attack and panic disorder through a common mechanism.

Second, Job stressors cause a variety of somatic symptoms. Job stressors may increase the risk of panic attack and panic disorder by triggering these conditions through altered perception of physiological changes in the body.

This study investigates a longitudinal association of greater job strain, effort-reward imbalance, and low workplace social support with panic attack and panic disorder among workers in Japan. The present study hypothesized that (1) high job strain is associated with new onset of panic attack and panic disorder, (2) low workplace social support is associated with new onset of panic attack and panic disorder, and (3) high effort-reward imbalance is associated with new onset of panic attack and panic disorder.

## Methods

A 2-year prospective cohort study was conducted of an Internet sample of 5,152 workers. Job strain, workplace social support, and effort-reward imbalance were measured by the Brief Job Stress Questionnaire and Effort-Reward Imbalance Questionnaire, and classified into tertiles. PA/PD during the follow-up were measured by a self-report scale derived from the Mini-International Neuropsychiatric Interview.

The predictive association between job stressors and incidence of PA/PD was investigated over the study period with semiparametric discrete-time Cox proportional hazard models, to estimate hazard ratio (HR), with 95% confidence intervals (CIs). Survival time was a term from baseline survey to newly occurrence PA or PD. Three types of job stressors were analyzed at the same time in model 1. In addition to model 1, model 2 was adjusted for demographic variables. In addition to model 2, model 3 was adjusted for lifestyle and health-related variables. In addition to model 3, model 4 was adjusted for time-dependent major depressive disorder. Moreover, subgroup analyses were conducted stratifying by sex.

## Results

A total of 3,706 full-time employees without a history of panic attack/panic disorder were enrolled at baseline; 1,954 participants completed follow-up for 2 years. During 52,197 person-months, 70 subjects who had new onset of panic attack were identified. The risk of panic attack was significantly lower for the group of high workplace social support after fully adjusted (HR = 0.46 [95% CI = 0.23-0.93],  $p = 0.03$ ). Among males, the groups of moderate and high job strain (HRs = 3.08 [95% CI = 1.11-8.49] and 2.93 [95% CI = 1.08-7.96];  $p = 0.03$  and  $0.04$ , respectively) and high effort reward imbalance (HR = 2.60 [95% CI = 1.02-6.63],  $p = 0.045$ ) had a significantly greater risk of panic attack. During 52,775 person-months, 30 subjects who had new onset of panic disorder were identified. The hazard ratio of panic disorder showed no significant association between three job stressors. After being fully adjusted for potential confounders, the

patterns were same.

### Discussion

In the present study, high levels of workplace social support group were associated with a significantly lower risk of PA among Japanese workers, even adjusting for all possible confounders including major depressive disorder. The findings are consistent with previous reports that workplace social support was associated with a smaller risk of insomnia and depressive disorder. The findings are inconsistent with our previous cross-sectional study showing that a group with a moderate level of workplace social support had the highest risk of PA/PD. A most likely explanation is that in the cross-sectional study, workers with low worksite social support who already had PA/PD may have left their workplace, which could underestimate the risk of PA/PD associated with low workplace social support. Also, workplace social support may reduce the risk of PA by preventing and reducing somatic symptoms, including apnea, which may trigger PA/PD. It is suggested that high workplace social support decreases the risk of PA.

High effort-reward imbalance and high job strain were significantly associated with a greater risk of PA among males. These two job stressors were significantly associated with PA in the total sample, before adjusting for major depressive disorder as a time dependent variable. The study confirmed a finding from our previous cross-sectional study indicating that high effort-reward imbalance was associated with PA. This is in line with previous findings that high effort-reward imbalance was also associated with a risk of cardiovascular diseases, major depression, sleep disturbances, and insomnia.

Effort-reward imbalance and job strain were significantly associated with PA among males, but not in the total sample, after adjusting for major depressive disorder as a time dependent variable. While a systematic review concluded that there was no gender difference in the effect of job stressors on depression, there were several studies that reported job strain and effort-reward imbalance were more associated with health outcomes among males than females. Previous studies in Japan frequently reported a greater association between job strain and health outcomes among males than females. In the traditional working culture of Japan, males have more commitment to their job. This may be a reason for the observed gender difference in the effect of job strain and effort-reward imbalance on PA.

### Limitation

First, PA/PD, as well as major depressive disorder were not diagnosed by a clinician but assessed by self-report, which might have resulted in bias because of common

response style. Moreover, the accuracy of the self-report M.I.N.I. used in the study to identify PA/PD was limited; in particular, the sensitivity was low. In addition, even when symptoms unrelated to PA/PD are caused by job stressors, these might be misinterpreted as a symptom of PA/PD even in the case of other physical or mental problems. Second, the sample size was relatively small as well as the low number of cases of PD. This may limit the statistical power of the study. Third, this study data was collected via the Internet. The socioeconomic status and educational status of the average internet user tends to be higher than that of the general population. Fourth, participants with PA/PD might drop out from the study because their panic symptoms were too severe to answer the follow-up survey. This may cause an attrition bias and may weaken the association between job stressors with PA/PD. Fifth, some risk factors for PA/PD were not adjusted. These possible confounders might affect the results in the present study. Sixth, although the effects of job stressors and the covariates on PA/PD over the follow-up did not significantly deviate from the proportional hazard assumption, the proportional hazard assumption might be violated because several Kaplan-Meier curves were crossing when I examined the curves visually. Finally, the incubation period between exposure to job stressors and the onset of PA/PD is not clear. There is a possibility that the follow-up period may be shorter for observing the onset of PA/PD associated with the exposure to job stressors.

## Conclusion

The present longitudinal study found an association between job stressors (workplace social support in the total sample, job strain and effort imbalance among males) and the risk of panic attack in a sample of Japanese workers.