

# The Association between Work-Related Stress and Autonomic Imbalance among Call Center Employees in Japan

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There is little epidemiological evidence linking subjective stress to objective etiologic indicators. To clarify an association between work-related stress and autonomic nervous function, we examined call center employees (167 males and 371 females) undergoing electrocardiography (ECG) at the time of annual health checkups. The questionnaire was composed of the Brief Job Stress Questionnaire based on the demand-control-support model and the Social Readjustment Rating Scale including detailed contents of home stress. The Bazett's corrected QT (QTc) interval, QT index, and heart rate were obtained from the ECG data. The male employees showed significantly higher scores of job demand, job control, and supervisor support than the female ones. In the male employees, QT index indicating the extent of autonomic imbalance and heart rate were associated with high score of supervisor support and low score of coworker support ( $P < 0.05$ ), but no significant relationships were seen between QTc interval and either job strain (i.e., job demand and job control) or home stress. By contrast, the female employees showed no significant links between any autonomic indicators and either work-related stress or home stress. These data suggest that work-related stress affected QT index in male employees suffering specific occupational stressors such as emotional abuse from unsatisfied customers. Specifically, supports from supervisors and coworkers were paradoxically associated with QT index, implying that supervisors may have failed to effectively support such male employees. Also, autonomic nervous function in male employees appears to be more vulnerable to work-related stress than that in female ones.

**Keywords:** autonomic nervous function; call center employees; demand-control-support model; electrocardiography; subjective job stress

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## Introduction

With regard to the epidemiological evidence linking work-related stress to cardiovascular disease, the stress and cardiovascular disease are not directly tied but mediated by a certain etiologic mechanism. However, there is less research on the etiological pathways of the disease causation (Schnall et al. 1994). Collins et al. (2005) examined electrocardiographic QT intervals for 36 healthy men wearing 48-h Holter-monitor, and one mechanism suggested by them was the disturbed cardiovascular regulatory pattern associated with job strain in a pathogenic manner. In this case, it may not be easy to examine a large number of workers with 48-h monitor. Another mechanism was concerning autonomic imbalance induced by home stress (Maeda et al. 2015), but not work-related stress. For the earlier prevention of work-related cardiovascular events and a better understanding of the pathophysiology, it is important to investigate the association between work-

related stress and autonomic outcomes by using simpler tools.

As a measure of work-related stress, the job demand-control-support (DCS) model with three dimensions (i.e., job demand, job control, and social supports), focusing on self-reported features of the work environment that can trigger disease (Karasek 1979), has been widely used all over the world (Schnall et al. 1994; Karasek et al. 1998). A number of studies have related these data to job performance, job satisfaction, presenteeism, and depressive status (Kawada and Otsuka 2011; Inoue et al. 2016; Saijo et al. 2016, 2017; Sugawara et al. 2017; Oh et al. 2017), but most of them were done by use of subjective outcome variables resulting from a questionnaire method. In this sense, there are few reports using objective outcomes (Collins et al. 2005; Otsuka et al. 2009; Maeda et al. 2015). QT intervals, as well as heart rate variability (HRV) and heart rate, have been considered as an objective marker of the development of ventricular arrhythmia or of the susceptibility to sudden

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death (El-Sherif and Turitto 2003; Jouven et al. 2005), because QT intervals represent the duration between ventricular depolarization and subsequent repolarization (Yun et al. 2015) while the corrected QT interval (Bazett 1920), by comparison with QT index (Rautaharju et al. 2009), tends to depend on heart rate (Arai et al. 2013). In this study, we investigated the impact of work-related stress, as well as home stress, on autonomic nervous function among call center employees undergoing electrocardiography (ECG) at the time of their annual health checkups. Moreover, sex and industry-type differences of such an effect were discussed in light of the literature, because the above employees frequently suffer specific occupational stressors such as emotional abuse from unsatisfied customers (Deery et al. 2002; Oh et al. 2017).

## Methods

### *Study population*

In August–September 2015, a self-reported questionnaire was distributed to approximately 1,400 employees of a telephone call center in northeast Japan. They were engaged in call center work, and some had shift work. Of them, 244 male and 565 female employees, not including persons in a managerial position, consented to participate in this study and returned the questionnaire form to the health care nurse of the company (response rate = 61% and 69%, respectively). We excluded some respondents who did not undergo the annual health checkup conducted in September 2015 under the Industrial Safety and Health Law in Japan, those who suffered from stroke, heart disease including obvious pathological ECG, diabetes mellitus, chronic renal failure, and alcoholic dependency diagnosed by psychiatrist, and those whose forms of the questionnaire were not completed. On the other hand, we included 45 males and 118 females who had taken medicine as long as they did not have a history of diseases mentioned above. Finally, a total of 167 males aged 22–60 years and 371 females aged 20–61 years were enrolled. The institutional ethics committee for epidemiological studies of Akita University Graduate School of Medicine reviewed and approved the procedures of this study. All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

### *Measurement*

The questionnaire included the Brief Job Stress Questionnaire (BJSQ) (Shimomitsu et al. 2000) based on the Job Content Questionnaire (JCQ) (Karasek 1979), the Social Readjustment Rating Scale (SRRS) (Holmes and Rahe 1967), and information about possible confounders such as age, height, body weight, employment status (i.e., permanent or precarious employment), smoking and drinking habits (yes/no), regular exercise (yes/no), sleep duration, and blood pressure (BP). Body mass index (BMI, kg/m<sup>2</sup>) was calculated from height and body weight. Regular exercise was defined as at least one 30-min session at least once per week. Sleep duration (min) was computed as the difference between bedtime and wake time on workdays.

*Job stress and home stress:* The BJSQ was employed to evaluate job demand, job control, and social supports (i.e., supervisor and coworker supports), and has been widely used in Japan for practical occupational health evaluation and occupational health research

(Fukuoka et al. 2005; Harada et al. 2005; Otsuka et al. 2009). Each dimension comprised three questions with responses being scored on a 4-point Likert scale (1 = “agree”; 2 = “somewhat agree”; 3 = “somewhat disagree”; and 4 = “disagree”) (Saijo et al. 2016): Concerning job demand, i) you have to do an enormous amount of work, ii) you cannot complete all your work in the allotted time, and iii) you have to work very hard. Concerning job control, i) you can work at your own pace; ii) you can decide the order in which you do your work and the way you do it; and, iii) you can provide your opinions on the work strategy of your workplace. Concerning supervisor support (or coworker support), i) you can often communicate with supervisors (or coworkers); ii) you can strongly rely on supervisors (or coworkers) when you have problems; and, iii) your supervisors (or coworkers) are prepared to spend their time on your personal problems. The reversed total score for the job-demand or social-support questions and the total score for the job-control questions were used to evaluate them, and higher scores denoted higher job demand, job control, and social supports. Home stress, selected from the SRRS, included all kinds of events (i.e., divorce, marital separation, death of close family member, personal injury or illness, change in health of family member, gain of new family member, son or daughter leaving home, entrance examination of son or daughter, matrimonial quarrel, home mortgage of JP¥ 3,000,000 and over, mortgage or loan of less than JP¥ 3,000,000) that participants had for past one year (Natsume et al. 1988), and the response was scored as 0 = “absence” or 1 = “presence” of more than one event.

*ECG QT-related indicators:* The ECG test was conducted by trained nurses of Sendai General Medical Checkup Clinic, using ECG-9130 electrocardiograph (Nihon Koden Co., Tokyo, Japan) after the subjects rested in the supine position for 2 min (Maeda et al. 2015). Since QT intervals are known to be affected by heart rate (beats/min), corrected QT (QTc) interval was calculated from the RR and QT intervals on the ECG according to the Bazett’s formula:  $QTc \text{ (ms}^{1/2}\text{)} = (\text{QT interval}) / \sqrt{(\text{RR interval})}$  (Bazett 1920; Murata et al. 1999a, b). QT index defined by Rautaharju et al. (2009) also was calculated as  $(\text{measured QT} / \text{predicted QT}) \times 100$ , where the predicted  $QT = 656 / (1 + 0.01 \times \text{heart rate})$ .

### *Statistical analysis*

The significance of sex differences was tested by Student *t* test for the BJSQ scores and autonomic outcomes (i.e., QTc interval, QT index, heart rate, and systolic and diastolic BP), along with age, BMI, and sleep duration, and by  $\chi^2$  test for home stress, regular exercise, smoking and drinking habits, shift work, and employment status. Multiple regression analysis was used to examine the relations of work-related stress (job demand, job control, and social supports), home stress, and possible confounders to the autonomic indicators. Likewise, multiple logistic regression analysis was done to calculate the odds ratio (OR) and 95% confidence interval (CI) of work-related stress and home stress on autonomic indicators after adjusting for the confounders. As a cutoff value, asymptotically abnormal QT was defined as QTc interval  $\geq 420 \text{ ms}^{1/2}$  and QT index  $> 110$  (Murata et al. 1999a; Maeda et al. 2015). High heart rate was defined as heart rate  $\geq 75$  beats/min according to the report on a predictor of sudden death (Jouven et al. 2005). In addition, hypertension was defined as systolic BP  $\geq 140$  mmHg or diastolic BP  $\geq 90$  mmHg at the time of annual health checkups. All analyses, with two-side *P* value, were performed using the Statistical Package for the Biosciences (SPBS Ver. 9.68) (Murata and Yano 2002), and the significance level was set

at  $P < 0.05$ .

## Results

Background characteristics of 167 male and 371 female employees with complete data, as well as 244 male and 565 female respondents including incomplete data, are shown in Table 1. There was no significant difference in age or drinking habit between both sexes, while most of the characteristics showed significant sex differences. Concerning work-related stress scores, job demand, job control, and supervisor support were significantly higher in the males than in the females; likewise, the proportion of hypertension was 18.6% for the males and 7.5% for the females, and significantly higher in the former ( $P < 0.001$ ). On the contrary, QTc interval was significantly longer in the female employees than in the male ones.

Since there were no significant relationships between the BJSQ scores and systolic/diastolic BPs in the male and female employees ( $P > 0.05$  by the Pearson product-moment correlation coefficients), the BPs were excluded from a series of outcome variables. The associations of work-related stress and possible confounders with autonomic indicators are presented in Table 2. Although no significant relationships between work-related stress and autonomic indicators were seen in the female employees, supervisor support was positively related to QT index and heart rate and coworker support was negatively related to QT index in the male employees. Of possible confounders,

BMI was positively related to all autonomic indicators except for QTc interval in the female employees; likewise, age was positively related to QTc interval in the males and females and QT index in the males. By contrast, regular exercise was negatively related to heart rate in the males and females. In addition, permanent/precarious employment was associated with long QTc interval in the males; in fact, age-adjusted QTc intervals in the permanent males ( $402 \pm 18 \text{ ms}^{1/2}$ ) was longer than those in the precarious males ( $397 \pm 15 \text{ ms}^{1/2}$ ) (analysis of covariance,  $P = 0.036$ ). When adding the presence/absence of taking medicine in independent variables of Table 2, it was not significantly related to any autonomic indicators and did not affect the above results (data not shown).

The proportions of elevated QTc interval ( $\geq 420 \text{ ms}^{1/2}$ ) were 9.6% for the males and 18.6% for the females, and the significant difference was seen between both sexes ( $\chi^2 = 6.378$ ,  $P = 0.012$ ). Also, the proportions of higher QT index ( $> 110$ ) and heart rate ( $\geq 75$ ) were 17.4% and 32.9% for the males and 22.1% and 27.2% for the females, respectively, but there were no significant sex differences ( $P > 0.05$ ). When the ORs of work-related stress and home stress after adjustment for possible confounders were surveyed (Table 3), supervisor support and coworker support were significantly associated with QT index of more than 110 only in the male employees.

Table 1. Basal characteristics, work-related and home stress, and autonomic indicators of call center employees.

	Males <sup>a</sup> (N = 167)	Females <sup>a</sup> (N = 371)	<i>P</i> value <sup>b</sup>	Male respondents including incomplete data <sup>a</sup> (N)		Female respondents including incomplete data <sup>a</sup> (N)	
Basal characteristics							
Age (years)	40.4 ± 7.9	40.5 ± 8.0	0.930	37.4 ± 9.2	(244)	36.8 ± 9.9	(565)
Body mass index (kg/m <sup>2</sup> )	24.1 ± 4.9	22.9 ± 5.0	0.006	24.1 ± 5.0	(244)	22.6 ± 5.1	(565)
Sleep duration (min)	397 ± 71	379 ± 73	0.009	402 ± 76	(226)	391 ± 75	(544)
Regular exercise (%)	19.8	10.5	0.006	21.7	(244)	11.2	(565)
Smoking habit (%)	54.5	33.4	< 0.001	51.2	(244)	30.8	(565)
Drinking habit (%)	56.9	50.7	0.170	54.1	(244)	46.9	(565)
Shift worker (%)	28.1	9.7	< 0.001	40.6	(239)	16.4	(550)
Permanent employee (%)	47.9	21.6	< 0.001	47.9	(188)	19.8	(415)
Work-related stress and home stress							
Job demand (score)	8.5 ± 2.2	8.1 ± 2.1	0.041	8.6 ± 2.2	(241)	7.6 ± 2.1	(555)
Job control (score)	7.1 ± 1.9	6.7 ± 2.0	0.014	7.0 ± 1.9	(239)	6.8 ± 2.0	(554)
Supervisor support (score)	7.3 ± 2.3	6.9 ± 2.2	0.017	7.5 ± 2.2	(240)	7.2 ± 2.2	(552)
Coworker support (score)	7.5 ± 2.1	7.7 ± 2.1	0.500	7.8 ± 2.0	(240)	8.3 ± 2.3	(555)
Home stress (presence, %)	25.2	51.5	< 0.001	23.0	(244)	45.3	(565)
Objective outcome variables							
QTc interval (ms <sup>1/2</sup> )	400 ± 17	406 ± 15	< 0.001	400 ± 18	(189)	406 ± 15	(416)
QT index	104.1 ± 8.5	105.3 ± 7.0	0.117	104.4 ± 8.6	(189)	105.2 ± 7.0	(416)
Heart rate (beats/min)	70.8 ± 11.7	70.3 ± 9.6	0.572	71.2 ± 11.6	(189)	70.1 ± 9.5	(416)
Systolic blood pressure (mmHg)	125 ± 17	116 ± 16	< 0.001	125 ± 17	(244)	115 ± 16	(565)
Diastolic blood pressure (mmHg)	79 ± 12	72 ± 11	< 0.001	78 ± 12	(244)	70 ± 11	(565)

<sup>a</sup>Mean ± SD or %; <sup>b</sup>Student *t* test or  $\chi^2$  test.

Table 2. Factors affecting objective outcome variables in call center employees: results of multiple regression analysis.

	QTc interval		QT index		Heart rate	
	$\beta^a$	<i>P</i> value	$\beta^a$	<i>P</i> value	$\beta^a$	<i>P</i> value
<i>Male employees (N = 167)</i>						
Work-related stress						
Job demand	-0.119	0.150	-0.032	0.701	0.041	0.622
Job control	0.029	0.720	-0.088	0.285	-0.125	0.130
Supervisor support	0.053	0.572	0.233	0.015	0.251	0.009
Coworker support	-0.162	0.086	-0.257	0.007	-0.200	0.035
Home stress	-0.017	0.821	0.067	0.379	0.089	0.252
Possible confounders						
Age	0.226	0.004	0.157	0.042	0.047	0.546
Body mass index	0.232	0.003	0.262	< 0.001	0.164	0.035
Sleep duration	-0.011	0.886	-0.005	0.951	0.009	0.914
Regular exercise	0.058	0.464	-0.123	0.123	-0.192	0.018
Smoking habit	0.015	0.840	0.066	0.394	0.068	0.381
Drinking habit	0.057	0.465	-0.008	0.917	-0.049	0.535
Shift work	0.037	0.632	0.070	0.365	0.056	0.467
Permanent employment	0.230	0.010	0.066	0.460	-0.073	0.414
<i>R</i> <sup>b</sup>	0.422	0.003	0.420	0.004	0.410	0.006
<i>Female employees (N = 371)</i>						
Work-related stress						
Job demand	-0.067	0.223	0.009	0.867	0.055	0.312
Job control	0.063	0.291	0.029	0.631	-0.008	0.887
Supervisor support	0.034	0.625	0.113	0.109	0.117	0.090
Coworker support	-0.076	0.263	-0.056	0.415	-0.025	0.707
Home stress	-0.031	0.563	-0.074	0.168	-0.073	0.164
Possible confounders						
Age	0.165	0.003	0.036	0.511	-0.063	0.245
Body mass index	0.040	0.470	0.151	0.006	0.159	0.004
Sleep duration	0.036	0.512	0.085	0.119	0.074	0.169
Regular exercise	0.081	0.128	-0.049	0.355	-0.112	0.034
Smoking habit	0.002	0.971	-0.013	0.803	-0.014	0.797
Drinking habit	0.012	0.818	-0.034	0.533	-0.053	0.328
Shift work	0.030	0.584	-0.031	0.574	-0.061	0.261
Permanent employment	-0.043	0.420	0.010	0.853	0.043	0.416
<i>R</i> <sup>b</sup>	0.208	0.245	0.201	0.309	0.252	0.033

<sup>a</sup>Standardized regression coefficient; <sup>b</sup>Multiple correlation coefficient.

## Discussion

We employed QT-related parameters as objective outcome variables for subjective stress, whereas call center employees in our study had significantly lower BJSQ scores than Japanese nurses (65 males and 992 females) living in Hokkaido, Japan ( $P < 0.001$  by Student *t* test) whose scores were  $9.2 \pm 1.9$  (mean  $\pm$  SD) for job demand,  $7.3 \pm 1.9$  for job control,  $7.4 \pm 2.1$  for supervisor support, and  $8.3 \pm 2.0$  for coworker support (Saijo et al. 2016). The main finding was that subjective supports from supervisors and coworkers were associated with QT index and heart rate in a sta-

tionary state among the male employees. Collins et al. (2005) demonstrated a significant association between job strain (i.e., job demand and job control) and sympathetic control during working hours. The different stressors seen in these two studies would have been due to the job type (i.e., community health planners and call center employees) as well as the measurement method. On the other hand, another study with 1,809 male employees, belonging to a health insurance union of automobile dealerships in Japan, failed to find a significant relation of work stress to QT index or QTc interval (Maeda et al. 2015), probably because of one question of whether the subject felt any stress at the

Table 3. Effects of work-related and home stress on autonomic abnormalities in call center employees: Odds ratio (OR) and 95% confidence interval (CI) after adjustment for possible confounders by multiple logistic regression analysis<sup>a</sup>.

	QTc interval $\geq 420$		QT index $> 110$		Heart rate $\geq 75$	
	OR	95% CI	OR	95% CI	OR	95% CI
<i>Male employees (N = 167)</i>						
Work-related stress						
Job demand	0.81	0.61-1.07	0.96	0.76-1.22	1.05	0.88-1.27
Job control	0.92	0.66-1.26	0.97	0.75-1.27	0.85	0.69-1.05
Supervisor support	1.01	0.72-1.42	1.34	1.01-1.78	1.19	0.96-1.46
Coworker support	0.90	0.63-1.28	0.72	0.54-0.97	0.87	0.70-1.09
Home events	1.03	0.32-3.32	0.90	0.35-2.30	1.56	0.75-3.25
<i>Female employees (N = 371)</i>						
Work-related stress						
Job demand	0.97	0.84-1.11	0.99	0.87-1.12	1.03	0.92-1.17
Job control	1.09	0.94-1.26	0.98	0.85-1.12	1.02	0.90-1.16
Supervisor support	1.03	0.87-1.22	1.08	0.92-1.26	1.10	0.95-1.27
Coworker support	0.90	0.76-1.06	1.01	0.86-1.18	1.00	0.86-1.17
Home events	1.10	0.63-1.90	1.03	0.62-1.71	1.01	0.63-1.63

<sup>a</sup>Confounders used were age, BMI, sleep duration, regular exercise, smoking and drinking habits, shift work, and permanent employment.

workplace (yes/no), but not a multidimensional questionnaire like the JCQ. Individuals with effort-reward imbalance at work have an increased risk of coronary heart disease (Kivimäki et al. 2012; Dragano et al. 2017), and QTc prolongation has been reported to be associated with all-cause mortality and cardiovascular events (Yap et al. 2016). Therefore, such autonomic imbalance resulting from work-related stress may represent a high-risk state leading to cardiovascular events, though the effects of work-related stress appear to differ among the industry types.

To our knowledge, this may be the first study to suggest contradictory effects of two social supports on autonomic imbalance. In other words, high supervisor support and low coworker support were associated with high QT indices, respectively. Nagami et al. (2010) also reported similar results in relation to job performance, but they seemed to avoid the decisive conclusion. Social supports are thought to be a key influencing factor on health (Blanch 2016). Most of the studies based on the DCS model reported that supervisor support had a buffering effect on depressive symptoms (Saijo et al. 2016; Weigl et al. 2016) and that higher coworker support showed a protective effect on job satisfaction and productivity (Baruch-Feldman et al. 2002) and absenteeism (Saijo et al. 2017). Consequently, coworker support appears to control autonomic imbalance in male employees. With regard to supervisor support, by contrast, two following explanations are possible: Supervisors of this study might have failed to alleviate the stress of male employees effectively due to the atypical working environment, in which employees had to engage in one-to-one phone conversation with their customers; next, higher supervisor support might reflect higher morale and

performance of the employees, followed by a grave responsibility and a great burden for them. In any way, additional research with a large number of male workers is required to reconfirm the paradoxical effects of supervisor/coworker supports on autonomic imbalance.

The male employees of our study showed higher scores of all work-related stressors except for coworker support than the female ones. Also, the way to link work-related stress to autonomic imbalance seemed to differ between the male and female employees (Table 2); i.e., the significant associations of social supports with autonomic indicators were observed only in the male employees, nevertheless the females were twice the size of the males. Likewise, job control and social supports were significantly related to job performance in male employees of a manufacturing company in Japan (Nagami et al. 2010), but there were no significant relationships between them in female employees of the same company. Apart from the work-related stress, QTc prolongation due to shift work has been reported in male workers (Murata et al. 1999a, b, 2005) but not female nurses in Japan (Ishii et al. 2004, 2005). In this study, the presence/absence of shift work was used as a confounder of our multivariate model, but we could not find any significant relationship between shift work and autonomic indicators. Thus, limited evidence suggests that autonomic imbalance resulting from work-related stress may emerge more readily in male workers than in female workers. Future research on occupational stress should be carried out for males and females separately. In addition, what affects autonomic imbalance in female workers awaits further study.

As other factors excluding work-related stress, age and



BMI were suggested to affect QT-related indicators for male and female employees (Table 2), which is consistent with previous reports (Murata and Araki 1996; Arai et al. 2013). In addition, permanent employment, compared with precarious employment, was associated with prolonged QTc interval only for male employees. Although precarious employment has been reported to be associated with increased depressive symptoms (Virtanen et al. 2005; Kim et al. 2016), our result seems to be contradictory. However, the male permanent employees of call center bore a heavier responsibility than other employees within the company, which would be associated with autonomic imbalance as a result. In any study, special attention should be paid to employment status and industry type (Tanaka et al. 2017), as well as confounders such as age and BMI.

The proportions of smoking and drinking habits among call center employees of this study, excluding that of male drinker, were higher than those of the national representatives (30.1% for male smoking, 7.9% for female smoking, 61.9% for male drinking, and 30.6% for female drinking) (Ministry of Health, Labour and Welfare 2017). These proportions were similar to those obtained from salesmen residing in the same region (Dakeishi et al. 2004; Iwata et al. 2013). That is, the proportions of such habits may have differed between workers and the general population. In addition, drinking habit was not significantly related to any autonomic nervous indicators in young adults (Arai et al. 2013), and smoking and drinking habits also were not significantly associated with QT intervals in an initial cohort with normal QT interval or without hypertension (Murata et al. 1999a). For that reason, the characteristics of the present participants would not affect the external validity greatly.

This study may have some limitations, together with strength. Of the 244 male and 565 female respondents in the current study, 271 (33.5%) had some incomplete data (Table 1), but their data did not significantly differ from those of the current 538 participants except for two confounders of age and shift work in both sexes ( $P < 0.01$ ), and sleep duration and scores of job demand and social supports in females ( $P < 0.05$ ). The main reason for incomplete data was that some young employees with night work could not undergo ECG test at the time of the annual health checkups; whereas, such employees did so at the time of special medical examination for workers engaged in night work. The sample size of the study population might not have been large enough to have a potent power, but we could find some significant associations between work-related stress and autonomic indicators in the 167 male employees after adjustment for possible confounders. We did not have socioeconomic and educational data which might distort our results (Saijo et al. 2016; Loerbroeks et al. 2017), but the employees were in a homogenous condition because of the same company. Due to the cross-sectional design, the directions of associations should be interpreted carefully. Autonomic indicators employed in the current study are

objective measures and thought to reflect a function in a stationary state; for this reason, it is unlikely that QT-related indicators caused work-related stress unless the subject had a heart disease. Regarding the assessment of autonomic nervous function, since we developed a new method to examine the averaged QTc interval and QT index of 30-sec ECG data, as well as the HRV with frequency-domain analysis, totally in 10 minutes (Arai et al. 2013; Tatsuta et al. 2015), its use would have been more desirable than the ECG test of the current study. In any case, our data appear not to be heavily influenced by measurement bias and/or confounders.

In conclusion, high supervisor support and low coworker support in male employees were associated with increased QT index, suggesting that autonomic imbalance due to such stressors may enhance an cardiovascular risk in a neurogenic manner. QT index of ECG obtained from individual health checkups, as well as a stress checklist like the BJSQ, will be useful for the primary prevention of cardiovascular disease in workers. In addition, male employees appear to be more susceptible to the autonomic effect of work-related stress than female ones.

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## Conflict of Interest

The authors declare no conflict of interest.

## References

- Arai, K., Nakagawa, Y., Iwata, T., Horiguchi, H. & Murata, K. (2013) Relationships between QT interval and heart rate variability at rest and the covariates in healthy young adults. *Auton. Neurosci.*, **173**, 53-57.
- Baruch-Feldman, C., Brondolo, E., Ben-Dayan, D. & Schwartz, J. (2002) Sources of social support and burnout, job satisfaction and productivity. *J. Occup. Health Psychol.*, **7**, 84-93.
- Bazett, H.C. (1920) An analysis of the time-relations of electrocardiograms. *Heart*, **7**, 353-370.
- Blanch, A. (2016) Social support as a mediator between job control and psychological strain. *Soc. Sci. Med.*, **157**, 148-155.
- Collins, S.M., Karasek, R.A. & Costas, K. (2005) Job strain and autonomic indices of cardiovascular disease risk. *Am. J. Ind. Med.*, **48**, 182-193.
- Dakeishi, M., Iwata, T., Ishii, N. & Murata, K. (2004) Effects of alcohol consumption on hepatocellular injury in Japanese men. *Tohoku J. Exp. Med.*, **202**, 31-39.
- Deery, S., Iverson, R. & Walsh, J. (2002) Work relationships in telephone call centers: understanding emotional exhaustion and employee withdrawal. *J. Manage. Stud.*, **39**, 471-496.
- Dragano, N., Siegrist, J., Nyberg, S.T., Lunau, T., Fransson, E.I., Alfredsson, L., Björner, J.B., Borritz, M., Burr, H., Erbel, R., Fahlen, G., Goldberg, M., Hamer, M., Heikkilä, K., Jöckel, K.H., et al. (2017) Effort-reward imbalance at work and incident coronary heart disease: a multi-cohort study of 90,164 individuals. *Epidemiology*, **28**, 619-626.

- El-Sherif, N. & Turitto, G. (2003) Torsade de pointes. *Curr. Opin. Cardiol.*, **18**, 6-13.
- Fukuoka, Y., Dracup, K., Forelicher, E.S., Ohno, M., Hirayama, H., Shina, H. & Kobayashi, F. (2005) Do Japanese workers who experience an acute myocardial infarction believe their prolonged working hours are a cause? *Int. J. Cardiol.*, **100**, 29-35.
- Harada, H., Suwazono, Y., Sakata, K., Okubo, Y., Oishi, M., Uetani, M., Kobayashi, E. & Nogawa, K. (2005) Three-shift system increases job-related stress in Japanese workers. *J. Occup. Health*, **47**, 397-404.
- Holmes, T.H. & Rahe, R.H. (1967) The social readjustment rating scale. *J. Psychosom. Res.*, **11**, 213-218.
- Inoue, N., Otsui, K., Yoshioka, T., Suzuki, A., Ozawa, T., Iwata, S. & Takei, A. (2016) A simultaneous evaluation of occupational stress and depression in patients with lifestyle-related diseases. *Intern. Med.*, **55**, 1071-1075.
- Ishii, N., Dakeishi, M., Sasaki, M., Iwata, T. & Murata, K. (2005) Cardiac autonomic imbalance in female nurses with shift work. *Auton. Neurosci.*, **122**, 94-99.
- Ishii, N., Iwata, T., Dakeishi, M. & Murata, K. (2004) Effects of shift work on autonomic and neuromotor functions in female nurses. *J. Occup. Health*, **46**, 352-358.
- Iwata, T., Arai, K., Saito, N. & Murata, K. (2013) The association between dietary lifestyles and hepatocellular injury in Japanese workers. *Tohoku J. Exp. Med.*, **231**, 257-263.
- Jouven, X., Empana, J.P., Schwartz, P.J., Desnos, M., Courbon, D. & Ducimetière, P. (2005) Heart-rate profile during exercise as a predictor of sudden death. *N. Engl. J. Med.*, **352**, 1951-1958.
- Karasek, R.A. (1979) Job demands, Job decision latitude, and mental strain: implication for job resign. *Adm. Sci. Q.*, **24**, 285-309.
- Karasek, R.A., Brisson, C., Kawakami, N., Houtman, I., Bongers, P. & Amick, B. (1998) The Job Content Questionnaire (JCQ): an instrument for internationally comparative assessment of psychosocial job characteristics. *J. Occup. Health Psychol.*, **3**, 322-355.
- Kawada, T. & Otsuka, T. (2011) Relationship between job stress, occupational position and job satisfaction using a brief job stress questionnaire (BJSQ). *Work*, **40**, 393-399.
- Kim, W., Park, E.C., Lee, T.H. & Kim, T.H. (2016) Effect of working hours and precarious employment on depressive symptoms in South Korean employees: a longitudinal study. *Occup. Environ. Med.*, **73**, 816-822.
- Kivimäki, M., Nyberg, S.T., Batty, G.D., Fransson, E.L., Heikkilä, K., Alfredsson, L., Bjorner, J.B., Borritz, M., Burr, H., Casini, A., Clays, E., De Bacquer, D., Dragano, N., Ferrie, J.E., Geuskens, G.A., et al. (2012) Job strain as a risk factor for coronary heart disease: a collaborative meta-analysis of individual participant data. *Lancet*, **380**, 1491-1497.
- Loerbroeks, A., Ding, H., Han, W., Wang, H., Wu, J.P., Yang, L., Angerer, P. & Li, J. (2017) Work stress, family stress and asthma: a cross-sectional study among women in China. *Int. Arch. Occup. Environ. Health*, **90**, 349-356.
- Maeda, E., Iwata, T. & Murata, K. (2015) Effect of work stress and home stress on autonomic nervous function in Japanese male workers. *Ind. Health*, **53**, 132-138.
- Ministry of Health, Labour and Welfare (2017) The National Health and Nutrition Survey in Japan, 2015. [Cited: October 1, 2017]. <http://www.mhlw.go.jp/bunya/kenkou/eiyoudl/h27-houkoku.pdf> [Accessed: October 1, 2017].
- Murata, K. & Araki, S. (1996) Assessment of autonomic neurotoxicity in occupational and environmental health as determined by ECG R-R interval variability: a review. *Am. J. Ind. Med.*, **30**, 155-163.
- Murata, K. & Yano, E. (2002) *Medical statistics for evidence-based medicine with SPBS user's guide*, Nankodo Publisher, Tokyo.
- Murata, K., Yano, E., Hashimoto, H., Karita, K. & Dakeishi, M. (2005) Effects of shift work on QTc interval and blood pressure in relation to heart rate variability. *Int. Arch. Occup. Environ. Health*, **78**, 287-292.
- Murata, K., Yano, E. & Shinozaki, T. (1999a) Impact of shift work on cardiovascular functions in a 10-year follow-up study. *Scand. J. Work Environ. Health*, **25**, 272-277.
- Murata, K., Yano, E. & Shinozaki, T. (1999b) Cardiovascular dysfunction due to shift work. *J. Occup. Environ. Med.*, **41**, 748-753.
- Nagami, M., Tsutsumi, A., Tsuchiya, M. & Morimoto, K. (2010) Job control and coworker support improve employee job performance. *Ind. Health*, **48**, 845-851.
- Natsume, M., Murata, H., Sugimoto, K., Nakamura, A., Asao, H. & Jujii, H. (1988) The method for stress assessment of workers (Part 1). Stress score by self-rating method. *Sangyo Igaku*, **30**, 266-279.
- Oh, H., Park, H. & Boo, S. (2017) Mental health status and its predictors among call center employees: a cross-sectional study. *Nurs. Health Sci.*, **19**, 228-236.
- Otsuka, T., Kawada, T., Ibuki, C. & Kusama, Y. (2009) Relationship between job strain and radial arterial wave reflection in middle-aged male workers. *Prev. Med.*, **49**, 260-264.
- Rautaharju, P.M., Surawicz, B., Gettes, L.S., Bailey, J.J., Childers, R., Deal, B.J., Gorgels, A., Hancock, E.W., Josephson, M., Kligfield, P., Kors, J.A., Macfarlane, P., Mason, J.W., Mirvis, D.M., Okin, P., et al. (2009) AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram. Part IV: the ST segment, T and U waves, and the QT interval: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. *Circulation*, **119**, e241-250.
- Saijo, Y., Yoshioka, E., Kawanishi, Y., Nakagi, Y., Itoh, T. & Yoshida, T. (2016) Relationships of job demand, job control, and social support on intention to leave and depressive symptoms in Japanese nurses. *Ind. Health*, **54**, 32-41.
- Saijo, Y., Yoshioka, E., Nakagi, Y., Kawanishi, Y., Hanley, S.J.B. & Yoshida, T. (2017) Social support and its interrelationships with demand-control model factors on presenteeism and absenteeism in Japanese civil servants. *Int. Arch. Occup. Environ. Health*, **90**, 539-553.
- Schnall, P.L., Landsbergis, P.A. & Baker, D. (1994) Job strain and cardiovascular disease. *Annu. Rev. Public Health*, **15**, 381-411.
- Shimomitsu, T., Iwata, N. & Nakamura, K. (2000) The final development of the Brief Job Stress Questionnaire mainly used for assessment of the individuals. In *Ministry of labour sponsored grant for the prevention of work-related illness: the 1999 Report*, edited by Kato, M., Tokyo Medical College, Tokyo, pp. 126-164.
- Sugawara, N., Danjo, K., Furukori, H., Sato, Y., Tomita, T., Fujii, A., Nakagami, T., Kitaoka, K. & Yasui-Furukori, N. (2017) Work-family conflict as a mediator between occupational stress and psychological health among mental health nurses in Japan. *Neuropsychiatr. Dis. Treat.*, **13**, 779-784.
- Tanaka, O., Maeda, E., Fushimi, M., Iwata, T., Shimizu, T., Saito, S. & Murata, K. (2017) Precarious employment is not associated with increased depressive symptoms: a cross-sectional study in care service workers of Japan. *Tohoku J. Exp. Med.*, **243**, 19-26.
- Tatsuta, N., Nakai, K., Satoh, H. & Murata, K. (2015) Impact of the Great East Japan earthquake on child's IQ. *J. Pediatr.*, **167**, 745-751.
- Virtanen, M., Kivimäki, M., Joensuu, M., Virtanen, P., Elovainio,

- M. & Vahtera, J. (2005) Temporary employment and health: a review. *Int. J. Epidemiol.*, **34**, 610-622.
- Weigl, M., Stab, N., Herms, I., Angerer, P., Hacker, W. & Glaser, J. (2016) The associations of supervisor support and work overload with burnout and depression: a cross-sectional study in two nursing settings. *J. Adv. Nurs.*, **72**, 1774-1788.
- Yap, J., Jin, A.Z., Nyunt, S.Z., Ng, T.P., Richards, A.M. & Lam, C.S.P. (2016) Longitudinal community-based study of QT interval and mortality in Southeast Asians. *PLoS One*, **11**, e0154901.
- Yun, J., Hwangbo, E., Lee, J., Chon, C.R., Kim, P.A., Jeong, I.H., Park, M., Park, R., Kang, S.J. & Choi, D. (2015) Analysis of an ECG record database reveals QT interval prolongation potential of famotidine in a large Korean population. *Cardio-vasc. Toxicol.*, **15**, 197-202.
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