

# Effects of work stress and home stress on autonomic nervous function in Japanese male workers

Eri MAEDA<sup>1-3</sup>, Toyoto IWATA<sup>1</sup> and Katsuyuki MURATA<sup>1\*</sup>

<sup>1</sup>Department of Environmental Health Sciences, Akita University Graduate School of Medicine, Japan

<sup>2</sup>Department of Public Health, Graduate School of Medicine, The University of Tokyo, Japan

<sup>3</sup>Research Fellow of Japan Society for the Promotion of Science, Japan

Received July 30, 2014 and accepted October 27, 2014

Published online in J-STAGE November 8, 2014

**Abstract:** Autonomic imbalance is one of the important pathways through which psychological stress contributes to cardiovascular diseases/sudden death. Although previous studies have focused mainly on stress at work (work stress), the association between autonomic function and stress at home (home stress) is still poorly understood. The purpose was to clarify the effect of work/home stress on autonomic function in 1,809 Japanese male workers. We measured corrected QT (QTc) interval and QT index on the electrocardiogram along with blood pressure and heart rate. Participants provided self-reported information about the presence/absence of work/home stress and the possible confounders affecting QT indicators. Home stress was related positively to QT index ( $p=0.040$ ) after adjusting for the possible confounders, though work stress did not show a significant relation to QTc interval or QT index. The odds ratio of home stress to elevated QT index ( $\geq 105$ ) was 2.677 (95% CI, 1.050 to 6.822). Work/home stress showed no significant relation to blood pressure or heart rate. These findings suggest that autonomic imbalance, readily assessed by QT indicators, can be induced by home stress in Japanese workers. Additional research is needed to identify different types of home stress that are strongly associated with autonomic imbalance.

**Key words:** Corrected QT (QTc) interval, QT index, Home stress, Work stress, Workmen

## Introduction

The association between autonomic imbalance and increased cardiovascular disease (CVD) risks has been emphasized by earlier studies<sup>1, 2</sup>. A relative or absolute decrease in vagal activity or an increase in sympathetic activity influences heart rate and beat-to-beat rhythm<sup>3</sup>. Autonomic imbalance increases arrhythmias involved in coronary occlusion and lowers ventricular fibrillation threshold resulting in sudden death<sup>4</sup>. Electrocardiographic

(ECG) QT intervals, as well as heart rate variability (HRV)<sup>5</sup>, blood pressure<sup>6, 7</sup> and heart rate<sup>8</sup>, have been considered as a biomarker of the development of ventricular arrhythmia or of the susceptibility to sudden death<sup>9, 10</sup>, because QT intervals represent the duration between ventricular depolarization and subsequent repolarization<sup>11</sup>. Nonetheless, little is known about lifestyles affecting the QT or corrected QT (QTc) intervals, except for shift work<sup>12–14</sup>.

Altered autonomic imbalance is one of the important pathways through which psychological stress contributes to CVD<sup>15–17</sup>. Although stress includes some uncomfortable emotional experience accompanied by predictable biochemical, physiological, and behavioral changes<sup>18</sup>, such as stress at workplace or school, stress concerning

\*To whom correspondence should be addressed.

E-mail: winestem@med.akita-u.ac.jp

©2015 National Institute of Occupational Safety and Health

family and relationship, and stress accompanied by health problems<sup>19)</sup>, previous studies have focused mainly on chronic psychological stress at work and its relevance to CVDs<sup>16)</sup>. Only a few studies have examined stress at home, demonstrating the influence of marriage, having children, or doing housework on CVD risks<sup>20–22)</sup>. Furthermore, experimental mental stress like a 1-min mental arithmetic has been reported to induce QT prolongation<sup>23)</sup>, but little research has been done to address an association between chronic psychological stress and QT indicators. For promoting the primary prevention of CVD or sudden death, therefore, it is crucial to clarify an association between psychological stress not only at work (hereafter, work stress) but also at home (home stress), and asymptomatic autonomic failure.

The objective of this study was to examine the effects of work stress and home stress on autonomic function. HRV and QT-related indicators at rest have been utilized in epidemiological studies<sup>5, 12–14, 24–27)</sup>, and the standardization and interpretation have been established<sup>28, 29)</sup>. However, HRV measurement requires not only specific equipment, but also a longer administration compared to QT measurement<sup>30)</sup>. For this reason, we used QT-related indicators, which can be obtained from annual health checkups, as the present main outcomes. We also investigated the association with other physiological indicators, such as blood pressure and heart rate, which are consistent with the previous studies<sup>6–8)</sup>.

## Materials and Methods

### Study sample

In February–March 2012, a self-reported questionnaire was distributed to approximately 2,200 employees belonging to a health insurance union of motor vehicle dealerships in northeast Japan. They were male aged between 19 and 59 yr old, being engaged in non-supervisory sales task, machinery maintenance, or clerical job. Of them, 1,857 men consented to participate in the present study and returned the questionnaire form to the occupational health nurse of the union (response rate =84%). Forty-eight respondents were excluded; those who did not undergo an annual health checkup conducted under the Industrial Safety and Health Law in Japan in April–July 2012, those who suffered from stroke, heart disease including obvious pathological ECG, diabetes mellitus, alcoholic dependency diagnosed by psychiatrist, and those whose forms were not completed. The institutional ethics committee of the Akita University Graduate School of Medicine reviewed and ap-

proved the procedures of this study.

### Measurement

Participants reported whether they felt any stress at the workplace (yes/no) and at home (yes/no). Home stress included all kinds of stress that participants could have at home (e.g., marital stress, stress concerning parent-child relation, care-giving stress, or housework stress). Participants also indicated whether they smoked (yes/no) and whether they exercised regularly (yes/no). Regular exercise was categorized according to whether or not they exercised for more than 30 min at least once per week. Nighttime sleep duration (min) was computed as the difference between bedtime and wake time on workdays<sup>31)</sup>. They stated their weekly amount of each type of alcoholic beverage consumed. A total of 100% ethanol equivalent dose (g/day) was calculated according to our previous report<sup>32)</sup>.

The ECG test during the annual health checkup was conducted by trained public health nurses of Akita Health Promotion Center, using the ECG-9202 electrocardiograph (Nihon Kohden Co., Japan) after the subjects rested in the supine position for 2 min. Since QT intervals are known to be affected by heart rate<sup>23, 29)</sup>, QTc interval was calculated from the RR and QT intervals on the ECG according to the Bazett's formula<sup>12, 13, 33)</sup>:  $QTc \text{ (msec}^{1/2}\text{)} = (\text{QT interval}) / \sqrt{\text{RR interval}}$ . QT index defined by Rautaharju *et al.*<sup>34)</sup> also was calculated as  $(\text{measured QT} / \text{predicted QT}) \times 100$ , where the predicted QT =  $656 / (1 + 0.01 \text{ heart rate})$ . At the same time, systolic and diastolic blood pressure (SBP and DBP) and heart rate were measured by trained public health nurses, using the BP-103i blood pressure monitor (Omron Healthcare Co., Japan), 2 min after sitting in a chair with their backs supported and their arms bared and supported at heart level. Hypertension was defined as SBP  $\geq 140$  mmHg or DBP  $\geq 90$  mmHg.

### Statistical analysis

The significance of differences between the subjects with and without work stress or home stress in QT-related indicators, blood pressure and heart rate, along with possible confounders (age, body mass index (BMI, kg/m<sup>2</sup>), sleep duration, regular exercise, smoking habit, and ethanol ingestion) was analyzed by Student *t* test or Fisher exact probability. Multiple regression analysis was done to examine the relations of work/home stress and the above confounders with the QT and cardiovascular indicators. Likewise, multiple logistic regression analysis was used to calculate the odds ratio (OR) and 95% confidence

**Table 1. Basal characteristics of 1,809 male workers stratified by work stress or home stress**

	Work stress			Home stress		
	Presence (N=1,154)	Absence (N=655)	<i>p</i> value <sup>a</sup>	Presence (N=331)	Absence (N=1,478)	<i>p</i> value <sup>a</sup>
Age (yr)	35.9 ± 8.7	34.6 ± 9.9	0.003	35.4 ± 8.3	35.4 ± 9.4	0.940
Body mass index (kg/m <sup>2</sup> )	23.4 ± 3.8	23.0 ± 9.9	0.031	23.3 ± 3.9	23.3 ± 3.7	0.881
Sleep duration (min)	416 ± 56	425 ± 52	<0.001	412 ± 59	421 ± 54	0.016
Regular exercise (%)	18.0	17.9	0.949	16.0	18.4	0.342
Smoking habit (%)	60.1	60.8	0.803	66.2	59.0	0.018
Drinking habit (%)	70.4	64.4	0.010	72.2	67.3	0.090
Ethanol ingestion (g/day)	21.8 ± 30.6	19.1 ± 28.8	0.071	23.4 ± 32.1	20.2 ± 29.5	0.080
Systolic blood pressure (mmHg)	119 ± 14	118 ± 14	0.615	118 ± 14	119 ± 14	0.280
Diastolic blood pressure (mmHg)	71 ± 11	70 ± 11	0.043	70 ± 11	71 ± 11	0.202
Heart rate (beats/min)	68 ± 10	68 ± 10	0.510	68 ± 10	68 ± 10	0.554
QTc interval (msec <sup>1/2</sup> )	393 ± 20	391 ± 20	0.048	395 ± 20	392 ± 20	0.040
QT index (%)	94.7 ± 4.4	94.3 ± 4.5	0.067	95.0 ± 4.4	94.4 ± 4.4	0.032

<sup>a</sup> Student *t* test or Fisher exact probability

interval (CI) of the stress on autonomic nervous and cardiovascular functions after adjusting for the confounders<sup>30</sup>). Asymptomatically abnormal QT was defined as QTc interval  $\geq 420$  msec<sup>1/2</sup> and QT index  $\geq 105$ <sup>13</sup>). In addition, high heart rate was defined as heart rate  $\geq 75$  beats/min according to one report on a predictor of sudden death<sup>8</sup>). All analyses with two-sided *p* values were performed using the Statistical Package for Biosciences Ver. 9.65<sup>35</sup>), and the significance level was set at *p*<0.05.

## Results

Basal characteristics of 1,809 workers stratified by work stress and home stress are summarized in Table 1. The proportion of those who experienced work stress was 63.8%. The workers with work stress were significantly older than those without work stress; similarly, the former had higher BMI, shorter sleep duration, higher DBP, and longer QTc interval compared to the latter. A significantly higher proportion of those with work stress developed drinking habits. Next, the proportion of those who had home stress was 18.3%. The workers with home stress had shorter sleep duration, longer QTc interval, and higher QT index than those without home stress. A significantly higher proportion of those with home stress smoked.

The association between stress and cardiovascular or autonomic nervous function after adjusting for possible confounders is represented in Table 2. Home stress was associated positively with QT index, though work/home stress did not show any significant relation to blood pressure or heart rate. Regarding possible confounders, QTc

interval was significantly related to age, BMI, and ethanol ingestion, while QT index was significantly connected with age, regular exercise, and ethanol ingestion.

Table 3 represents ORs of work/home stress for hypertension, high heart rate, and abnormal QT after adjusting for possible confounders. In stress model 1, the OR of home stress for elevated QT index was 2.677 (*p*=0.039), but no significant associations were seen between work/home stress and hypertension, heart rate or prolonged QTc. In stress model 2, two kinds of stresses were divided into four as shown in Table 3. Given the same confounders as in Table 2 in the multiple logistic model, the OR of work stress (-)/home stress (+) for elevated QT index was 9.949 (*p*=0.012), and the OR of work stress (+)/home stress (+) for elevated QT index was 3.585 (*p*=0.053).

## Discussion

The principal finding of our study was that psychological stress was associated with abnormal QT among Japanese male workers. Especially, the OR of home stress to elevated QT index ( $\geq 105$ ) was statistically significant. In other words, home stress affected autonomic nervous function assessed by QT indicators. This result is similar to those addressing the clinical relationship between home stress and cardiovascular risks, indicating that unhappy marriage was associated with increased risks for recurrent coronary events<sup>20</sup>) and cardiovascular mortality<sup>21</sup>). Likewise, marital concerns have been reported to affect saliva cortisol levels and to elevate blood pressures regardless of gender<sup>36</sup>). On the other hand, the asymptomatic effect

**Table 2. Psychological stress and confounders relating to blood pressure, heart rate, and QT indicators in 1,809 male workers: results of multiple regression analysis**

	Systolic blood pressure		Diastolic blood pressure		Heart rate		QTc interval		QT index	
	Standard regression coefficient	<i>p</i> value	Standard regression coefficient	<i>p</i> value	Standard regression coefficient	<i>p</i> value	Standard regression coefficient	<i>p</i> value	Standard regression coefficient	<i>p</i> value
Psychological stress										
Work stress	-0.016	0.462	0.010	0.602	0.006	0.808	0.017	0.465	0.013	0.577
Home stress	-0.020	0.335	-0.030	0.119	0.011	0.653	0.044	0.062	0.048	0.040
Possible confounders										
Age	0.186	<0.001	0.418	<0.001	0.052	0.031	0.239	<0.001	0.251	<0.001
Body mass index	0.416	<0.001	0.327	<0.001	0.156	<0.001	0.051	0.027	0.010	0.669
Sleep duration	0.077	<0.001	0.083	<0.001	0.063	0.007	0.031	0.183	0.019	0.408
Regular exercise	-0.025	0.236	-0.018	0.333	-0.077	0.001	0.021	0.352	0.053	0.020
Smoking habit	-0.060	0.004	-0.081	<0.001	0.030	0.204	-0.001	0.958	-0.014	0.546
Ethanol ingestion	0.096	<0.001	0.120	<0.001	0.031	0.190	0.055	0.019	0.053	0.024
<i>R</i> <sup>a</sup>	0.497	<0.001	0.601	<0.001	0.195	<0.001	0.273	<0.001	0.278	<0.001

<sup>a</sup> Multiple correlation coefficient

**Table 3. Odds ratios of psychological stress for hypertension, high heart rate, and raised QT indicators in 1,809 male workers after adjusting for possible confounders<sup>a</sup>: results of multiple logistic regression analysis**

	Hypertension <sup>b</sup>		Heart rate $\geq 75$		QTc interval $\geq 420$		QT index $\geq 105$	
	Odds ratio	95% CI <sup>c</sup>	Odds ratio	95% CI <sup>c</sup>	Odds ratio	95% CI <sup>c</sup>	Odds ratio	95% CI <sup>c</sup>
Stress model 1								
Work stress(+)	0.993	0.675–1.460	0.937	0.740–1.186	0.974	0.679–1.397	1.230	0.452–3.351
Home stress(+)	0.979	0.605–1.586	1.066	0.797–1.425	1.460	0.968–2.202	2.677	1.050–6.822
Stress model 2								
Work(-)/Home(-) ( <i>N</i> =613)	1.000		1.000		1.000		1.000	
Work(+)/Home(-) ( <i>N</i> =865)	0.959	0.643–1.432	0.876	0.684–1.122	0.929	0.635–1.359	1.855	0.571–6.025
Work(-)/Home(+) ( <i>N</i> =42)	0.611	0.121–3.076	0.524	0.214–1.279	0.954	0.279–3.267	9.949	1.651–59.94
Work(+)/Home(+) ( <i>N</i> =289)	0.993	0.579–1.703	1.040	0.751–1.441	1.445	0.904–2.310	3.585	0.981–13.11

<sup>a</sup> Possible confounders were age, body mass index, sleep duration, regular exercise, smoking habit, and ethanol ingestion (Table 2). <sup>b</sup> Hypertension (*N*=160) was defined as systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg; the number of workmen with heart rate  $\geq 75$  beats/min was 429; that with QTc interval  $\geq 420$  msec<sup>1/2</sup> was 162; and, that with QT index  $\geq 105$  was 22. <sup>c</sup> 95% confidence interval

on autonomic nervous function is still limited. Previous works focused on HRV changes to evaluate the autonomic nervous influences of psychological factors such as depression<sup>37</sup>), anxiety disorder<sup>38</sup>), and psychological stress<sup>39, 40</sup>). Thus, this may be the first study to demonstrate the effect of psychological stress on QT-related indicators in relation to its pathophysiology. This implication is that elevated QT index (e.g., more than 105), readily assessed by annual health checkups of workers<sup>12–14</sup>), can predict the presence of home stress to some degree, if the worker does not show obvious pathological ECG.

In the present study, although a significant association between work stress and prolonged QTc interval is shown in Table 1, QT index appears to be a more useful indica-

tor of detecting home stress than QTc interval (Table 3). This supports a recent result, suggesting that QTc index, unaffected by heart rate<sup>34</sup>), reflected autonomic nervous function rather than QT interval<sup>30</sup>). By contrast, we failed to find any significant relation of work stress with QT indicators or cardiovascular functions, though earlier studies using work stress classification, such as the job strain model<sup>41</sup>) and the effort-reward model<sup>42</sup>), demonstrated close associations of work stress with both high blood pressure<sup>43, 44</sup>) and autonomic nervous activities<sup>45</sup>). Two possible reasons for this disagreeable result on work stress are as follows. First, we employed self-reported binary variables to assess work stress. Second, work stress in the Japanese workers, possibly different from Caucasian

workers, may have been less serious than home stress according to the result of stress model 2 in Table 3, though Karoshi (death from overwork) has been suggested to be associated with work stress<sup>46, 47</sup>. In either case, our study with QT-related indicators emphasized the importance of home stress in Japanese workers. Further research with continuous data rather than binary data is required to detect such potent associations.

The current study indicated that larger BMI, shorter sleep duration, and overdrinking were significantly connected with work stress in Japanese workers, as shown in Table 1; similarly, shorter sleep duration and smoking habit were associated with home stress. These findings are consistent with the previous reports showing negative links between psychological distress and both sleep duration<sup>48</sup> and smoking cessation<sup>49</sup>. In addition, sleep duration had a close relation to autonomic nervous function even in children<sup>31</sup>. Thus, sleep duration, along with age, BMI, and drinking and smoking habits, should be considered as possible confounders in the assessment of psychological stress, whereas the temporal sequence between the psychological stress and change in sleep duration should also be scrutinized.

There may have been some limitations to be noted in this study. First, it is difficult to infer causal relationships because of the cross-sectional study design. Nevertheless, there was a temporal difference of 1–6 months between the stress assessed by the questionnaire and autonomic endpoints. Second, we addressed overall stress at home; for this reason, we could not specify what type of stress experience at home (e.g., marital stress, care-giving stress, and housework stress) led to QT abnormality. Third, although a self-reported questionnaire might introduce bias, its effect in this study would be limited because this study used a large number of subjects in the same occupational setting and the outcomes were measured objectively<sup>29, 30</sup>. Finally, potential confounders such as age, BMI, sleep duration, regular exercise, ethanol ingestion, and smoking habit, were considered in the data analysis. Thus, it appears that measurement bias and confounders did not heavily influence our data.

In conclusion, our finding suggests that home stress, as well as job stress<sup>45, 50</sup>, can affect autonomic nervous function in Japanese male workers. Moreover, QT index appears to be a more useful indicator of autonomic imbalance compared to QTc interval. Using the Japanese samples also added new evidence to the previously less surveyed populations; in fact, the majority of works exploring the link between work/home stress and CVDs

employed Caucasian samples. In future studies, female participants should be included because both genders perceive home stress differently.

## Acknowledgements

This work was supported partly by a grant-in-aid for Scientific Research (C) from the Japan Society for the Promotion of Science (Grant Number 23590772). The authors thank Ms. Yumiko Kato from the health insurance union of motor vehicle dealerships, for her assistance in data collection.

## References

- 1) Charkoudian N, Rabbitts JA (2009) Sympathetic neural mechanisms in human cardiovascular health and disease. *Mayo Clin Proc* **84**, 822–30.
- 2) Thayer JF, Yamamoto SS, Brosschot JF (2010) The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *Int J Cardiol* **141**, 122–31.
- 3) Collins SM, Karasek RA, Costas K (2005) Job strain and autonomic indices of cardiovascular disease risk. *Am J Ind Med* **48**, 182–93.
- 4) Schwartz PJ, Wolf S (1978) QT interval prolongation as predictor of sudden death in patients with myocardial infarction. *Circulation* **57**, 1074–7.
- 5) 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**, 155–63.
- 6) Kondo H, Kawamura T, Hirai M, Tamakoshi A, Wakai K, Terazawa T, Sugi S, Ohno M, Okamoto N, Tsuchida T, Ohno Y, Toyama J (2001) Risk factors for sudden unexpected death among workers: a nested case-control study in central Japan. *Prev Med* **33**, 99–107.
- 7) Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr Roccella EJ, National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure National High Blood Pressure Education Program Coordinating Committee (2003) The 7th report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA* **289**, 2560–72.
- 8) Jouven X, Empana JP, Schwartz PJ, Desnos M, Courbon D, Ducimetière P (2005) Heart-rate profile during exercise as a predictor of sudden death. *N Engl J Med* **352**, 1951–8.
- 9) El-Sherif N, Turitto G (2003) Torsade de pointes. *Curr Opin Cardiol* **18**, 6–13.
- 10) Straus SM, Kors JA, De Bruin ML, van der Hoof

- CS, Hofman A, Heeringa J, Deckers JW, Kingma JH, Sturkenboom MC, Stricker BH, Witteman JC (2006) Prolonged QTc interval and risk of sudden cardiac death in a population of older adults. *J Am Coll Cardiol* **47**, 362–7.
- 11) Yun J, Hwangbo E, Lee J, Chon CR, Kim PA, Jeong IH, Park M, Park R, Kang SJ, Choi D (2014) Analysis of an ECG record database reveals QT interval prolongation potential of famotidine in a large Korean population. *Cardiovasc Toxicol* (in press) .
  - 12) Murata K, Yano E, Shinozaki T (1999) Cardiovascular dysfunction due to shift work. *J Occup Environ Med* **41**, 748–53.
  - 13) Murata K, Yano E, Shinozaki T (1999) Impact of shift work on cardiovascular functions in a 10-year follow-up study. *Scand J Work Environ Health* **25**, 272–7.
  - 14) Ishii N, Dakeishi M, Sasaki M, Iwata T, Murata K (2005) Cardiac autonomic imbalance in female nurses with shift work. *Auton Neurosci* **122**, 94–9.
  - 15) Iso H, Date C, Yamamoto A, Toyoshima H, Tanabe N, Kikuchi S, Kondo T, Watanabe Y, Wada Y, Ishibashi T, Suzuki H, Koizumi A, Inaba Y, Tamakoshi A, Ohno Y, JACC Study Group (2002) Perceived mental stress and mortality from cardiovascular disease among Japanese men and women: the Japan Collaborative Cohort Study for Evaluation of Cancer Risk Sponsored by Monbusho (JACC Study). *Circulation* **106**, 1229–36.
  - 16) Everson-Rose SA, Lewis TT (2005) Psychosocial factors and cardiovascular diseases. *Annu Rev Public Health* **26**, 469–500.
  - 17) Tsutsumi A, Kayaba K, Ishikawa S (2011) Impact of occupational stress on stroke across occupational classes and genders. *Soc Sci Med* **72**, 1652–8.
  - 18) Baum A (1990) Stress, intrusive imagery, and chronic distress. *Health Psychol* **9**, 653–75.
  - 19) American Psychological Association (2014) Understanding chronic stress. <https://www.apa.org/helpcenter/understanding-chronic-stress.aspx>. Accessed July 30, 2014.
  - 20) Orth-Gomér K, Wamala SP, Horsten M, Schenck-Gustafsson K, Schneiderman N, Mittleman MA (2000) Marital stress worsens prognosis in women with coronary heart disease: the Stockholm female coronary risk study. *JAMA* **284**, 3008–14.
  - 21) Matthews KA, Gump BB (2002) Chronic work stress and marital dissolution increase risk of posttrial mortality in men from the Multiple Risk Factor Intervention Trial. *Arch Intern Med* **162**, 309–15.
  - 22) Non AL, Rimm EB, Kawachi I, Rewak MA, Kubzansky LD (2014) The effects of stress at work and at home on inflammation and endothelial dysfunction. *PLoS ONE* **9**, e94474.
  - 23) Andrassy G, Szabo A, Ferencz G, Trummer Z, Simon E, Tahy A (2007) Mental stress may induce QT-interval prolongation and T-wave notching. *Ann Noninvasive Electrocardiol* **12**, 251–9.
  - 24) de Bruyne MC, Kors JA, Hoes AW, Klootwijk P, Dekker JM, Hofman A, van Bommel JH, Grobbee DE (1999) Both decreased and increased heart rate variability on the standard 10-second electrocardiogram predict cardiac mortality in the elderly: the Rotterdam study. *Am J Epidemiol* **150**, 1282–8.
  - 25) Grandjean P, Murata K, Budtz-Jørgensen E, Weihe P (2004) Cardiac autonomic activity in methylmercury neurotoxicity: 14-year follow-up of a Faroese birth cohort. *J Pediatr* **144**, 169–76.
  - 26) Gruden G, Giunti S, Barutta F, Chaturvedi N, Witte DR, Tricarico M, Fuller JH, Cavallo Perin P, Bruno G (2012) QTc interval prolongation is independently associated with severe hypoglycemic attacks in type 1 diabetes from the EURODIAB IDDM complications study. *Diabetes Care* **35**, 125–7.
  - 27) Soliman EZ, Howard G, Cushman M, Kissela B, Kleindorfer D, Le A, Judd S, McClure LA, Howard VJ (2012) Prolongation of QTc and risk of stroke: The REGARDS (REasons for Geographic and Racial Differences in Stroke) study. *J Am Coll Cardiol* **59**, 1460–7.
  - 28) Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) Heart rate variability: standards of measurement, physiological interpretation and clinical use. *Circulation* **93**, 1043–65.
  - 29) Rautaharju PM, Surawicz B, Gettes LS, Bailey JJ, Childers R, Deal BJ, Gorgels A, Hancock EW, Josephson M, Kligfield P, Kors JA, Macfarlane P, Mason JW, Mirvis DM, Okin P, Pahlm O, van Herpen G, Wagner GS, Wellens H, American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology American College of Cardiology Foundation Heart Rhythm Society (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**, e241–50.
  - 30) 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**, 53–7.
  - 31) Sampei M, Murata K, Dakeishi M, Wood DC (2006) Cardiac autonomic hypofunction in preschool children with short nocturnal sleep. *Tohoku J Exp Med* **208**, 235–42.
  - 32) Dakeishi M, Murata K, Tamura A, Iwata T (2006) Relation between benchmark dose and no-observed-adverse-effect level in clinical research: effects of daily alcohol intake on blood pressure in Japanese salesmen. *Risk Anal* **26**, 115–23.
  - 33) Bazett HC (1920) An analysis of the time-relations of electrocardiograms. *Heart* **7**, 353–70.
  - 34) Rautaharju PM, Warren JW, Calhoun HP (1990) Estimation

- of QT prolongation. A persistent, avoidable error in computer electrocardiography. *J Electrocardiol* **23** Suppl, 111–7.
- 35) Murata K, Yano E (2002) Medical statistics for evidence-based medicine with SPBS user's guide. Nankodo Publisher, Tokyo.
- 36) Barnett RC, Steptoe A, Gareis KC (2005) Marital-role quality and stress-related psychobiological indicators. *Ann Behav Med* **30**, 36–43.
- 37) Carney RM, Saunders RD, Freedland KE, Stein P, Rich MW, Jaffe AS (1995) Association of depression with reduced heart rate variability in coronary artery disease. *Am J Cardiol* **76**, 562–4.
- 38) Kawachi I, Sparrow D, Vokonas PS, Weiss ST (1995) Decreased heart rate variability in men with phobic anxiety (data from the Normative Aging Study). *Am J Cardiol* **75**, 882–5.
- 39) Chandola T, Heraclides A, Kumari M (2010) Psychophysiological biomarkers of workplace stressors. *Neurosci Biobehav Rev* **35**, 51–7.
- 40) Eller NH, Kristiansen J, Hansen ÅM (2011) Long-term effects of psychosocial factors of home and work on biomarkers of stress. *Int J Psychophysiol* **79**, 195–202.
- 41) Karasek R, Baker D, Marxer F, Ahlbom A, Theorell T (1981) Job decision latitude, job demands, and cardiovascular disease: a prospective study of Swedish men. *Am J Public Health* **71**, 694–705.
- 42) Siegrist J (1996) Adverse health effects of high-effort/low-reward conditions. *J Occup Health Psychol* **1**, 27–41.
- 43) Matthews KA, Cottington EM, Talbott E, Kuller LH, Siegel JM (1987) Stressful work conditions and diastolic blood pressure among blue collar factory workers. *Am J Epidemiol* **126**, 280–91.
- 44) Schlüssel YR, Schnall PL, Zimble M, Warren K, Pickering TG (1990) The effect of work environments on blood pressure: evidence from seven New York organizations. *J Hypertens* **8**, 679–85.
- 45) Jarczok MN, Jarczok M, Mauss D, Koenig J, Li J, Herr RM, Thayer JF (2013) Autonomic nervous system activity and workplace stressors—a systematic review. *Neurosci Biobehav Rev* **37**, 1810–23.
- 46) Uehata T (1991) Long working hours and occupational stress-related cardiovascular attacks among middle-aged workers in Japan. *J Hum Ergol (Tokyo)* **20**, 147–53.
- 47) Uehata T (2005) [Karoshi, death by overwork]. *Nihon Rinsho* **63**, 1249–53.
- 48) Hsieh SD, Muto T, Murase T, Tsuji H, Arase Y (2011) Association of short sleep duration with obesity, diabetes, fatty liver and behavioral factors in Japanese men. *Intern Med* **50**, 2499–502.
- 49) Holm KE, LaChance HR, Bowler RP, Make BJ, Wamboldt FS (2010) Family factors are associated with psychological distress and smoking status in chronic obstructive pulmonary disease. *Gen Hosp Psychiatry* **32**, 492–8.
- 50) Kobayashi Y, Hirose T, Tada Y, Tsutsumi A, Kawakami N (2005) Relationship between two job stress models and coronary risk factors among Japanese part-time female employees of a retail company. *J Occup Health* **47**, 201–10.