The Association between Stressful Life Event and Resting Heart Rate in Korean Adults

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The Association between Stressful Life Event and Resting Heart Rate in Korean Adults

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ABSTRACT

The Association between Stressful Life Event and Resting Heart Rate in Korean Adults

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Objectives: Stress is associated with various cardiovascular conditions. However the direct association between stressful life events and resting heart rate has not been fully studied. Thus, we evaluated the association of stressful life events and resting heart rate in Korean adults.

Methods: We performed cross-sectional analysis of baseline data of 1703 males and 2730 females (aged 27 to 87) who participated in baseline examinations of the Korean Genome and Epidemiology Study- Kanghwa study. We measured both objective stress and perceived stress by Korean version of life experience survey questionnaire. Heart rate and blood pressure were measured twice with at least 5 minutes intervals using an automatic sphygmomanometer and if the difference between the first and second measurement was more than 10 mmHg, repeated measurements were done. The average of the last two measurements was used for analysis. The association between life events and heart rate was assessed using ß coefficient by multiple linear regressions.

Results: According to the number of stressful life events from 0 to 1, 2, and 3 or more, means of resting heart rate decreased from 67.30 ± 9.99 bpm to 64.65 ± 10.09 bpm (β=-1.655, p=0.002), 63.73 ± 9.13 bpm (β=-3.568, p<0.001), and 64.17 ± 9.39 bpm (β=-3.133, p<0.001), respectively. After the adjustment for age, body mass index, hypertension treatment, oral contraceptive use (only in female), postmenopausal hormone therapy (only in female), past medical history of thyroid disease, past medical history of liver disease, cigarette smoking, alcohol drinking, and blood urea nitrogen creatinine ratio, this association was remained (β= -1.485, -3.718, -3.176 and p=0.005, <0.001, <0.001, respectively).

Conclusions: Our findings suggest that stressful life events had association with low resting heart rate.

Key words: Stress, Life Change Events, Heart rate

I. INTRODUCTION

Stress is associated with various cardiovascular conditions such as cardiovascular disease (Iso et al., 2002, Mostofsky et al., 2012), metabolic syndrome (Rosmond, 2005, Fabre et al., 2012) , blood pressure (Melamed et al., 1997, Fallo et al., 2002) and heart rate variability (Lucini et al., 2005, Bernatova et al., 2002). Heart rate is associated with future cardiovascular conditions such as cardiovascular mortality (Kannel et al., 1987). Despite of diverse literatures on the association between stress and various cardiovascular conditions, whether direct associations of stressful life event and resting heart rate has not been fully studied.

The aim of this study was to evaluate the association of stressful life event and resting heart rate in a rural adult population of Korea.

II. METHODS

1. Participants

This study is a cross-sectional analysis of a community-based prospective cohort named Korean Genome and Epidemiologic Study (KoGES) - Kangwha study. The KoGES - Kangwha study started in 2006 in Kangwha Island, South Korea. This analysis enrolled participants who completed baseline health examinations in 2006 to 2010. Among the total 4446 participants, we excluded eight participants because their answers were inconsistent with presence of stressful life events and each life event's perceptive scores. An additional five participants were excluded for the following reasons: absence of systolic blood pressure (SBP) or <60 mmHg, absence of diastolic blood pressure (DBP) or <40 mmHg, and absence of heart rate or <30 beats/min.

Finally, 4433 participants (male 1703, female 2730; aged 27-87 years) were used for this analysis. All participants signed written informed consents and the study protocol was approved by the Institutional Review Board.

2. Life experiences survey questionnaire

Detailed methods for measurement in KoGES - Kangwha study were previously reported elsewhere (Lee et al., 2009, Oh et al., 2010). We measured both objective stress and perceived stress. Objective stress was measured by the number of stressful life events. Perceived stress was measured by the points scale that power of influence of each stressful life event to individuals. Extremely negative is minus 3 point, moderately negative is minus 2 point, somewhat negative is minus 1 point, no impact is 0 point, slightly positive is plus 1 point, moderately positive is plus 2 point, and extremely positive is plus 3 point. These were measured by Korean version (Lee, 1993.8) of life experiences survey questionnaire (appendix 1) which were originally developed and validated by Sarason, Johnson, and Siegel (Sarason et al., 1978). We measured stressful life events in the last 3 months to minimize recall bias (Dohrenwend, 2006, Raphael et al., 1991). Trained interviewers obtained the information including medical and family history, health behavior, stressful life events and diet with a standardized questionnaire. In case of self administered questionnaires, interviewers checked and confirmed missing or irrelevant item(s), if any (Oh et al., 2010). There are five stressful life events indices from life experiences survey questionnaire: total number of stressful life events, total score of stressful life events, total negative score of stressful life events, total positive score of stressful life events, and balance which is defined as total negative score minus total positive score.

3. Resting heart rate and other variables

Resting heart rate and blood pressure

Participants were required to refrain from smoking or ingesting caffeine for eight hours preceding the health examination. Before heart rate and blood pressure measurements were acquired, subjects were asked to sit and rest in a room for at least five minutes. With participants seated, an appropriate-sized cuff was applied snugly around the upper right arm at the heart level. Appropriate cuff size was chosen for each subject according to mid-arm circumference. Heart rate and blood pressure were measured twice with at least 5 minutes intervals using an automatic sphygmomanometer (Dinamap 1846 SX/P; GE Healthcare, Waukesha, Wisconsin, USA). If the difference between the first and second measurement was more than 10 mmHg, repeated measurements were done. The average of the last two measurements was used for the analysis. Bradycardia was defined as heart rate less than 6o bpm.

Electrocardiogram

The standard 12-lead electrocardiogram with a recording speed of 25 mm/sec (Page Writer Trim III, Philips Medical Systems M1707A) was taken for all participants. Electrocardiogram recordings were carried out in a quiet, separated room and subjects were maintained in the supine position. Participants were asked to avoid rigorous exercise, caffeine, nicotine, and alcohol for at least eight hours before testing. Heart rate and QT intervals were analyzed automatically by Phillips software program (Phillips 12-lead Algorithm, Netherlands). All electrocardiogram measurements were confirmed

by a cardiologist. Sphygmomanometer heart rates were compared with ventricular rate in electrocardiogram.

Other variables

Blood samples were collected from antecubital vein after at least eight hours fasting. Blood samples were sent to the centralized research laboratory. Enzymatic methods were applied to measure fasting plasma glucose, serum uric acid, triglycerides, total cholesterol, and high-density lipoprotein cholesterol (ADVIA 1650, Simens Healthcare Diagnostics INC., Deerfield, Illinois, USA). Complete blood counts test was measured by impedance method using automatic analyzers (ADVIA 120, Bayer Corp, USA). Fasting plasma insulin was measured by radioimmunoassay using a commercial kit (Biosource, Belgium). Blood urea nitrogen (BUN) and creatinine (Cr) were measured by colorimetric methods using automatic analyzers (ADVIA 1650, Bayer Corp, USA).

Standing height was measured to the nearest 0.1 cm on a stadiometer (SECA-225, Germany). Participants moved or removed hair ornaments from the top of their heads in order to measure stature properly. They stood on the floor with the heels of both feet together and toes pointed slightly outward at approximately a 60^{o} angle. The position of the heels, buttocks, shoulder blades, and back of the head was checked for contact with the vertical backboard. Once correctly positioned, participants took a deep breath and the headboard was lowered and positioned firmly on top of the head with sufficient pressure to compress the hair and height was recorded by the examiners. Body weight was measured to the nearest 0.1 kg on a digital scale (GL-60000-20, Korea) with

participants wearing underwear and examination clothes. Subjects stood still in the center of the scale platform with their hands at their sides and looked straight ahead. When the digital readout was stable, weight was recorded by the examiners. Body mass index was calculated as weight (kg) divided by height squared (m^2).

Total body water was derived from bioelectrical impedance measurement. Bioelectrical impedance was measured standard procedures for the technique (Gil Woo Trading Company, GIF-891DX, Seoul, Korea). The method involved the use of a tetra polar lead system in which an 800 micro amp constant current source at a 50 kHz signal was introduced into subjects via distal electrodes on the hands and feet and bioelectrical impedance was detected by the proximal electrodes. Measurements were performed in a fasting state without previous exercise.

4. Statistical analysis

Prior to statistical analysis, total number of stressful life events divided into people without stressful life events and people with stressful life events. And then people with stressful life events divided into 3 categories because of the skewed distribution (Table 1). The differences between investigated variable's means according to the life events were tested by the Chi-square test and ANOVA. The relationships between life events and other variables were assessed by the Pearson's correlation coefficients. The association between life events and heart rate were tested by multiple linear regression analysis. We calculated the unadjusted and adjusted ß coefficient using the people without stressful life events as the reference. In adjusted model, we controlled age, body mass index, hypertension treatment, oral contraceptive

use (only in female), postmenopausal hormone therapy (only in female), past medical history of thyroid disease, past medical history of liver disease, cigarette smoking (never, former, current), alcohol drinking (never, former, current), and BUN/Cr ratio.

Controlled variables are selected by following reasons. First, age, BMI, hypertension treatment status, contraceptive use, hormone therapy after menopause, past medical history of thyroid disease, past medical history of liver disease, smoking status were selected after the literature review, whereas sex was stratified. Second, smoking status and drinking status were selected because stressful life events could influence these behaviors. Third, BUN/Cr ratio was additionally adjusted as a marker of kidney function.

All statistical analyses were performed using SAS version 9.2.0 (SAS Institute, Cary, NC, USA). We considered two tailed test and a value of $p<0.05$ was taken to be statistically significant.

Table 1. Distributions of total number of stressful life events

Total number of life events (No. events)	Frequency (N)	Percentage (%)	Cumulative frequency (N)	Cumulative Percentage (%)
0	3638	82.07	3638	82.07
1	402	9.07	4040	91.13
2	171	3.86	4211	94.99
3	76	1.71	4287	96.71
4	44	0.99	4331	97.70
5	39	0.88	4370	98.58
6	24	0.54	4394	99.12
7	8	0.18	4402	99.30
8	7	0.16	4409	99.46
9	4	0.09	4413	99.55
10	4	0.09	4417	99.64
11	7	0.16	4424	99.80
12	1	0.02	4425	99.82
13	1	0.02	4426	99.84
14	2	0.05	4428	99.89
15	1	0.02	4429	99.91
18	1	0.02	4430	99.93
21	1	0.02	4431	99.95
22	2	0.05	4433	100.00

III. RESULTS

1. Life experiences survey questionnaire descriptive analysis

The result of the life experiences survey questionnaire in study participants were summarized in Appendix 2. According to the percentage of people, ranked in descending order are as follows. Major change in sleeping habits was reported by 183 people (4.1 %). Major change in eating habits was reported by 158 people (3.6 %). Trouble with in-laws, and relatives was reported by 89 people (2.0 %). Major change in the number of arguments with spouse was reported by 87 people (2.0 %). Major change in closeness of family members was reported by 82 people (1.8 %). According to the severe events using life change units more than 50 in Holmes and Rahe stress scale are described in Appendix 3.

Table 2. Characteristics according to the total number of life events in 1703 males

Characteristics	Total number of stressful life events				p
	0 (N=1418)	1 (N=142)	2 (N=64)	≥3 (N=79)	
Age (y)	57.1 ± 8.8	60.6 ± 9.8	59.8 ± 9.1	56.9 ± 8.9	<.001
BMI (kg/m^2)	24.3 ± 2.9	24.4 ± 3.0	23.9 ± 2.8	24.1 ± 3.2	0.701
SBP (mmHg)	122.0 ± 17.1	123.3 ± 16.2	120.0 ± 16.6	122.8 ± 16.4	0.616
DBP (mmHg)	77.7 ± 10.0	77.0 ± 9.6	76.5 ± 10.8	78.0 ± 10.7	0.687
HR (bpm)	66.3 ± 10.5	64.4 ± 9.5	61.8 ± 7.9	64.2 ± 10.2	0.001
HR on ECG (bpm)	62.5 ± 10.3	60.2 ± 8.4	59.1 ± 8.3	61 ± 9.5	0.003
PR interval on ECG (ms)	172.9 ± 23.2	174.9 ± 21.6	174.8 ± 28.5	172.0 ± 23.8	0.700
QRS duration on ECG (ms)	94.5 ± 12.5	91.3 ± 19.0	92.5 ± 23.7	90.0 ± 17.4	0.005
Bradycardia	391 (27.6)	51 (35.9)	23 (35.9)	28 (35.4)	<.001
BUN/Cr ratio	15.4 ± 4.1	15.8 ± 4.4	15.5 ± 3.9	15.7 ± 4.7	0.558
Hematocrit (%)	44.4 ± 3.4	44.8 ± 4.3	44.2 ± 4.0	44.6 ± 3.8	0.532
Total body water (kg)	39.0 ± 6.4	40.6 ± 7.8	39.9 ± 6.9	39.4 ± 6.6	0.030
Thyroid disease history	17 (1.2)	0 (0.0)	0 (0.0)	1 (1.3)	0.474*
Liver disease history	5 (0.4)	0 (0.0)	0 (0.0)	1 (1.3)	0.456*
Hypertension	498 (35.1)	62 (43.7)	23 (35.9)	30 (38.0)	0.238
Hypertension treatment					
Yes	325 (22.9)	43 (30.3)	16 (25.0)	16 (20.3)	0.217
No	1093 (77.1)	99 (69.7)	48 (75.0)	63 (79.8)	
Cigarette smoking					
Never	452 (31.9)	36 (25.4)	22 (34.4)	29 (36.7)	0.006
Former	508 (35.8)	73 (51.4)	28 (43.8)	31 (39.2)	
Current	458 (32.2)	33 (23.2)	14 (21.9)	19 (24.1)	
Alcohol drinking					
Never	359 (25.3)	41 (28.9)	22 (34.5)	23 (29.1)	0.345
Former	163 (11.5)	22 (15.5)	8 (12.5)	8 (10.1)	
Current	896 (63.2)	79 (55.6)	34 (53.1)	48 (60.8)	
Exercise status					
Yes	517 (36.5)	49 (34.5)	20 (31.3)	31 (39.2)	0.750
No	901 (63.5)	93 (65.5)	44 (68.8)	48 (60.8)	

Data were expressed as mean ± SD or number (%)

* Results may not be accurate because frequency is smaller than five

Table 3. Characteristics according to the total number of life events in 2730 females

Characteristics	Total number of stressful life events				p
	0 (N=2220)	1 (N=260)	2 (N=107)	≥3 (N=143)	
Age (y)	55.7 ± 8.6	58.6 ± 10.2	59.1 ± 9.6	54.8 ± 8.9	<.001
BMI (kg/m^2)	24.8 ± 3.3	24.8 ± 3.6	25.2 ± 3.2	25.0 ± 2.8	0.540
SBP (mmHg)	119.6 ± 18.2	122.9 ± 19.0	122.4 ± 18.5	118.8 ± 17.5	0.020
DBP (mmHg)	72.2 ± 10.2	71.7 ± 10.2	71.3 ± 9.3	71.3 ± 10.0	0.539
HR (bpm)	68.0 ± 9.6	66.3 ± 10.4	64.9 ± 9.6	64.2 ± 8.9	<.001
HR on ECG (bpm)	64.3 ± 9.1	62.8 ± 9.3	61.7 ± 8.6	62.1 ± 11.3	<.001
PR interval on ECG (ms)	164.4 ± 21.0	166.8 ± 21.0	169.3 ± 25.5	166.3 ± 21.1	0.038
QRS duration on ECG (ms)	87.5 ± 14.7	85.6 ± 19.9	84.7 ± 23.6	82.6 ± 18.5	0.005
Bradycardia	406 (18.3)	59 (22.7)	29 (27.1)	44 (30.8)	<.001
BUN/Cr ratio	17.2 ± 4.9	18.2 ± 5.1	17.3 ± 4.5	17.4 ± 4.6	0.017
Hematocrit (%)	39.3 ± 3.0	40.0 ± 2.9	39.9 ± 3.2	39.1 ± 3.2	0.001
Total body water (kg)	29.7 ± 4.5	30.3 ± 5.6	31.0 ± 6.5	31.4 ± 6.02	<.001
Thyroid disease history	98 (4.4)	14 (5.4)	7 (6.5)	4 (2.8)	0.473
Liver disease history	10 (0.5)	0 (0.0)	0 (0.0)	1 (0.7)	0.589*
Hypertension	753 (33.9)	100 (38.5)	41 (38.3)	52 (36.4)	0.390
Hypertension treatment					
Yes	524 (23.6)	72 (27.7)	29 (27.1)	42 (29.4)	0.201
No	1696 (76.4)	188 (71.3)	78 (72.9)	101 (70.6)	
Use oral contraceptive					0.744*
Yes	6 (0.3)	1 (0.3)	0 (0.0)	1 (0.7)	
No	2214 (99.7)	259 (99.6)	107 (100.0)	142 (99.3)	
Postmenopausal Hormone Tx					
Yes	117 (5.3)	6 (2.3)	2 (1.9)	7 (4.9)	0.087
No	2103 (94.7)	254 (97.7)	105 (98.1)	136 (95.1)	
Cigarette smoking					0.976*
Never	2134 (96.1)	252 (96.9)	104 (97.0)	139 (97.2)	
Former	35 (1.6)	3 (1.1)	1 (0.9)	2 (1.4)	
Current	51 (2.3)	5 (1.9)	2 (1.9)	2 (1.4)	

(Continued)

Alcohol drinking					0.006*
Never	1560 (70.3)	185 (71.8)	79 (73.8)	88 (61.5)	
Former	70 (3.2)	18 (6.9)	3 (2.8)	9 (6.3)	
Current	590 (26.6)	57 (21.9)	25 (23.4)	46 (32.2)	
Exercise status					
Yes	724 (32.6)	95 (36.5)	34 (31.8)	53 (37.1)	0.438
No	1496 (67.4)	165 (63.5)	73 (68.2)	90 (62.9)	

Data were expressed as mean ± SD or number (%)

* Results may not be accurate because frequency is smaller than five

2. Characteristics of the participants

The characteristics of the study participants were summarized in Table 2 and Table 3 according to the total number of stressful life events. Age, heart rate, heart rate on electrocardiogram, QRS duration on electrocardiogram, prevalence of bradycardia, and total body water distribution was statistically different in both sexes. Cigarette smoking status was statistically different only in males, whereas systolic blood pressure, pulse pressure ($p<0.01$, data were not shown), PR interval on electrocardiogram, BUN/Cr ratio, hematocrit, and alcohol drinking was statistically different only in females. People with stressful life events tended to have longer PR intervals on electrocardiogram, higher BUN/Cr ratio in females. People with stressful life events tended to have fewer current cigarette smokers in male. People with three or more stressful life events had more current alcohol drinkers in female.

3. Relationship between life events and investigated variables

Age and all of stressful life events indices had positive correlations with total number of stressful life events in both sexes (Table 4). Heart rate, electrocardiogram on heart rate, and QRS duration on electrocardiogram had inverse correlations with total number of stressful life events in both sexes. Total number of stressful life events had positive correlations with total score of stressful life events. Therefore total number of stressful life events could be the surrogate of total score of stressful life events. PR interval on electrocardiogram, pulse pressure, and total body water had positive correlations with total number of stressful life events only in female.

4. Association between stressful life events and heart rate

People with stressful life events had lower heart rate than people without stressful life events (Table 5). Among people with stressful life events, higher number of stressful life events was associated with lower heart rate. These associations were same after adjustment for age, body mass index, hypertension treatment, oral contraceptive use (only in female), postmenopausal hormone therapy (only in female), past medical history of thyroid disease, past medical history of liver disease, cigarette smoking, alcohol drinking, and BUN/Cr ratio.

Table 4. Correlation between total number of stressful life events and investigated variables

Variables	Total (4433)		Male (1703)		Female (2730)	
	Pearson's coefficient	p	Pearson's coefficient	p	Pearson's coefficient	p
Age (y)	0.044	0.004	0.053	0.029	0.041	0.033
BMI (kg/m^2)	0.010	0.507	-0.018	0.463	0.022	0.246
SBP (mmHg)	0.013	0.386	0.004	0.855	0.020	0.304
DBP (mmHg)	-0.025	0.092	-0.009	0.698	-0.027	0.154
PP (mmHg)	0.039	0.009	0.015	0.540	0.049	0.011
HR (bpm)	-0.098	<.001	-0.084	0.001	-0.111	<.001
HR on ECG (bpm)	-0.076	<.001	-0.079	0.001	-0.077	<.001
PR interval on ECG (ms)	0.026	0.090	0.008	0.754	0.044	0.022
QRS duration on ECG (ms)	-0.075	<.001	-0.085	0.001	-0.073	<.001
BUN/Cr ratio	0.031	0.039	0.026	0.294	0.029	0.132
Hematocrit (%)	0.004	0.808	0.015	0.543	0.023	0.230
body water (kg)	0.041	0.006	0.043	0.081	0.093	<.001
TSSLE (point)	0.769	<.001	0.815	<.001	0.756	<.001
NSSLE (point)	0.650	<.001	0.715	<.001	0.633	<.001
PSSLE (point)	0.589	<.001	0.579	<.001	0.594	<.001
Balance (point)	0.165	<.001	0.137	<.001	0.179	<.001

BMI; Body mass index, SBP; systolic blood pressure, DBP; diastolic blood pressure, PP; pulse pressure, HR; heart rate, ECG; electrocardiogram, BUN; blood urea nitrogen, Cr; creatinine, TSSLE; total score of stressful life events, NSSLE; negative score of stressful life events, PSSLE; positive score of stressful life events

Table 5. Association between total number of stressful life events and resting heart rate

Total number of	Unadjusted		Adjusted*	
stressful life events	β coefficient	p	β coefficient	p
Total (N=4433)				
0 (N=3638)	Reference	–	Reference	–
1 (N=402)	-1.655	0.002	-1.485	0.005
2 (N=171)	-3.568	<.001	-3.718	<.001
3 or more (N=222)	-3.133	<.001	-3.176	<.001
Male (N=1703)				
0 (N=1418)	Reference	–	Reference	–
1 (N=142)	-1.820	0.045	-1.790	0.050
2 (N=64)	-4.483	0.001	-4.469	0.001
3 or more (N=79)	-2.066	0.084	-2.009	0.092
Female (N=2730)				
0 (N=2220)	Reference	–	Reference	–
1 (N=260)	-1.662	0.009	-1.395	0.028
2 (N=107)	-3.063	0.001	-3.278	0.001
3 or more (N=143)	-3.812	<.001	-3.742	<.001

*****Adjusted by age, body mass index, hypertension treatment, oral contraceptive use (only in female), postmenopausal hormone therapy (only in female), past medical history of thyroid disease, past medical history of liver disease, cigarette smoking (never, former, current), alcohol drinking (never, former, current), and BUN/Cr ratio.

IV. DISCUSSION

In this rural adult population of Korea, people with stressful life events had lower heart rate than people without stressful life events. More stressful life events had lower heart rate compared with people without stressful life events as reference.

There were few studies that directly showed the associations between stress and resting heart rate. Instead, there were findings that stress was associated with heart rate variability (Lucini et al., 2005, Bernatova et al., 2002, Mezzacappa et al., 2001, Schmidt et al., 2010, Servant et al., 2009), cardiac reactivity (Ginty and Conklin, 2011), and cardiac arrhythmia (Lynch et al., 1977). These studies very differ from our study in participants, study design, and measured variables. First, they used animal model commonly (Bernatova et al., 2002, Schmidt et al., 2010, Sarenac et al., 2011). In human studies participants were special people such as posttraumatic disorder patients (Sahar et al., 2001), or shifting workers (Furlan et al., 2000). Studies were rare in general community based population. Second, these studies conducted experiments commonly and comparing before and after the stress intervention. Third most studies used vague stress or relied on stress tests. However, in the real world, people are exposed to various stressors such as stressful life events rather than few stress tests in laboratory. Also there is a need of focusing on observable and quantifiable stress. Therefore we measured stressful life events using life experiences survey questionnaire instead of measuring vague stress level. Heart rate is frequently and noninvasively measured in various settings. Many people regularly check blood pressure with heart rate at hospital, clinic, or community health center. Therefore the results of this study would apply easily and widely.

The association between recent stressful life events and lower heart rate could be explained by three mechanisms. One of the possible explanations could be the vagal rebound effect after psychological stress (Mezzacappa et al., 2001). Partial data which were decreased heart rate after stress were reported in previous articles (Lucini et al., 2005, Bernatova et al., 2002, Mezzacappa et al., 2001, Smeets, 2010). Also stress situation induced hyperactivity of vagus nerve were reported (Alboni et al., 2011). In our study, QRS duration on electrocardiogram trends support this mechanism. QRS duration on electrocardiogram decreased as total number of stressful life events increased in both sexes (Table 4). Conduction from atrioventricular node to ventricles and ventricle contraction went faster as total number of stressful life events increased although heart rate in electrocardiogram (measured from RR interval) is decreased. Therefore lowering heart rate is not due to muscle weakness and it is not same as aging process. This supports the effect of parasympathetic nerve (vagus nerve) on sinoatrial node directly.

Second possible mechanism is adaptation process that maintains homeostasis. Our study measured stressful life events within three months which might contain recovery state after the stress. Partial data which were decreased heart rate after stress were reported in previous articles (Smeets, 2010, Lucini et al., 2005, Bernatova et al., 2002, Mezzacappa et al., 2001). At the recovery state this vagal rebound may be crucial in restoring cardiovascular homeostasis (Mezzacappa et al., 2001). In the cardiopulmonary physical training (physical stress) after the certain duration our heart adapts the situation and athlete's heart showed decreased heart rates. Similarly stressful life events (mental, psychological stress) after the certain duration our heart adapts the situation and showing decreased heart rates might be possible.

Third possible explanation could be the aldosterone effect. Stress such as emotion (anxiety, fear, and hostility), pain, and surgical stress could directly influence aldosterone production via nervous control (Wikipediaeditors, 2012). Furthermore there is an indirect way that stress influence aldosterone production. It is part of Hypothalamic-pituitary-adrenal axis. Adrenocorticotropic hormone is secreted by the anterior pituitary gland in response to stress via neurosecretion of corticotropin releasing factor in the hypothalamus (Walters, 1986). This increasing adrenocorticotropic hormone could increase aldosterone production. And aldosterone functions as water retention in vivo thereby plasma volume increased and preload of the heart increased. As a result same volume status could reach via less energy so heart rate decreased. Clinical meaning of heart rate is a part of vital sign, and it is considered as systematic volume status. Our study could not measure plasma volume directly. Therefore we used available surrogate indices to evaluate volume status such as body water from bioelectrical impedance, hematocrit, and BUN/Cr ratio (Table 2, 3). In our data higher total number of stressful life events had more total body water in both sexes. Although total body water contains both extracellular and intracellular fluid (include Plasma, interstitial, and transcelluar fluid), BUN/Cr ratio at people with stressful life events is slightly higher in females. This might suggest the aldosterone effect. And these participants were relatively healthy community people and functioning well therefore their volume statuses were normal. Hence stressful life events reduced heart rate means beneficial to heart health lowering cardiac loading.

Our study is the first to examine associations between stressful life events and heart rate in a well constructed cohort study in Korea as far as we know. We measured stressful life events only within 3 months and it might help to reduce the recall bias

(Raphael et al., 1991, Dohrenwend, 2006). If someone has to recall long periods, it is only feasible to focus on major events. Assessment of more easily forgotten minor events is not even remotely feasible unless recall periods are as short as possible (Dohrenwend, 2006). Also this might help the intracategory variability problem.

Limitations of the present study were discussed here. One of the limitations is cross-sectional study design. Therefore we could not assess temporal relationships between stressful life events and resting heart rate. Other limitation is intracategory variability (Dohrenwend, 2006) inside Life Experience Survey questionnaire itself. Instead of measuring vague stress, we measured observable and quantifiable stressful life events and its influence. The problem with this questionnaire is that the one to which all of the others are in some way and to some degree related, so the actual experiences that lead a respondent to make a positive response to a given checklist category vary greatly (Dohrenwend, 2006). For imaginary example, person who had had cancer (event 1; Major personal illness or injury) could lead to trouble with employer because of absence (event 2; Trouble with employer). Thereby he lost his job (event 3; Being fired from job) could lead to financial crisis (event 4; Major change in financial status). However this problem is inherently exists in the data similar to the Food Frequency Questionnaire. Nevertheless we want to minimize this limitation by measuring within 3 months. If measuring period elongates, this effect might be increased. The other limitation is that residual or unmeasured confounding variables may exist. We could not rule out mediated effect of individual characteristics. The association could be bidirectional. For example, some people regard marriage as a very positive event, but others consider marriage as a very negative event. Even inside the one person, ambivalent is also possible. We want to minimize this limitation by using each life

event's individual perceptive score and analyzed several times using total score of stressful life events, positive score of stressful life events, negative score of stressful life events and Balance which is difference between negative score and positive score. However there was not so much difference using these indices. Also emotional stressors such as anger, anxiety, and hostility or personal characteristics like optimistic or pessimistic might be one of the unmeasured confounding variables.

In conclusion our findings suggest that stressful life events were associated with lower heart rate. However further investigations are required to examine the temporal relationship between stressful life events and resting heart rate. Further investigations are also required to examine the cardiovascular protective effect related to the lower heart rate due to stressful life events.

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Appendix 1. Life experiences survey questionnaire

생활경험조사

* 다음은 생활에 변화를 가져오고 우리에게 재적응을 하도록 하는 여러 가지 사건들이 나열되어 있습니다. 이 사건들 중에서 귀하가 **최근 3개월 동안 경험했던 사건들을 골라 ( )안에 "○"표** 하여 주십시오. 아울러 귀하가 경험했던 사건이 당신의 생활에 얼마나 좋은(긍정적인) 영향을 미쳤는지 아니면 얼마나 나쁜(부정적인) 영향을 미쳤는지를 평가해 주십시오. 즉 **극단적으로 나쁜 영향을 미쳤다고 생각되면 -3에 "○"표 하시고, 극단적으로 좋은 영향을 미쳤다면 +3에 "○"표** 하시면 됩니다. **긍정적이거나 부정적인 영향을 미치지 않았다고 생각되면 0에 "○"표** 하시면 됩니다. 경험하지 않은 사건들에 대해서는 답하실 필요가 없습니다.

		영 향						
	경험 여부	매우 나쁜	상당히 나쁜	약간 나쁜	영향 없음	약간 좋은	상당히 좋은	매우 좋은
1) 결혼	( )	-3	-2	-1	0	1	2	3
2) 유치장이나 수용기관에 수용	( )	-3	-2	-1	0	1	2	3
3) 배우자의 죽음	( )	-3	-2	-1	0	1	2	3
4) 잠자는 습관의 변화 (잠이 늘거나 줄어듬)	( )	-3	-2	-1	0	1	2	3
5) 가족의 죽음								
(1) 어머니	( )	-3	-2	-1	0	1	2	3
(2) 아버지	( )	-3	-2	-1	0	1	2	3
(3) 형제자매	( )	-3	-2	-1	0	1	2	3
(4) 할머니	( )	-3	-2	-1	0	1	2	3
(5) 할아버지	( )	-3	-2	-1	0	1	2	3
(6) 기타	( )	-3	-2	-1	0	1	2	3
6) 먹는 습관의 변화 (먹는 양이 늘거나 줄어듬)	( )	-3	-2	-1	0	1	2	3
7) 대부나 저당에 의한 재산손실	( )	-3	-2	-1	0	1	2	3
8) 가까운 친구의 죽음	( )	-3	-2	-1	0	1	2	3
9) 개인적인 일을 성취함	( )	-3	-2	-1	0	1	2	3
10) 가벼운 법률위반(교통위반, 경범죄 등)	( )	-3	-2	-1	0	1	2	3
11) 남자: 부인이나 여자친구의 임신	( )	-3	-2	-1	0	1	2	3
12) 여자: 임신	( )	-3	-2	-1	0	1	2	3
13) 직장의 여건 변화								
(새로운 책임, 작업조건이나 시간의 변동)	( )	-3	-2	-1	0	1	2	3
14) 새로운 직업을 얻음	( )	-3	-2	-1	0	1	2	3
15) 가족들이 심한 질병이나 상처를 입게 됨								
(1) 어머니	( )	-3	-2	-1	0	1	2	3
(2) 아버지	( )	-3	-2	-1	0	1	2	3
(3) 형제자매	( )	-3	-2	-1	0	1	2	3
(4) 할아버지	( )	-3	-2	-1	0	1	2	3
(5) 할머니	( )	-3	-2	-1	0	1	2	3
(6) 배우자	( )	-3	-2	-1	0	1	2	3
(7) 기타	( )	-3	-2	-1	0	1	2	3
16) 성적인 곤란이나 문제	( )	-3	-2	-1	0	1	2	3
17) 경영주와의 갈등								
(실직의 위험, 임금문제, 직위문제 등)	( )	-3	-2	-1	0	1	2	3
18) 친척과의 갈등	( )	-3	-2	-1	0	1	2	3
19) 경제상태의 중요한 변화								
(형편이 아주 좋아 지거나 나빠짐)	( )	-3	-2	-1	0	1	2	3
20) 가족들 간의 사이가 더 가까워지거나 더 멀어짐	( )	-3	-2	-1	0	1	2	3
21) 새로운 가족이 생김								
(출생, 입양 또는 이사에 의해)	( )	-3	-2	-1	0	1	2	3

22) 주거의 변화	( )	-3	-2	-1	0	1	2	3
23) 갈등으로 배우자와 별거	( )	-3	-2	-1	0	1	2	3
24) 종교 활동의 중요한 변화 (참석 횟수의 변화)	( )	-3	-2	-1	0	1	2	3
25) 배우자와의 화해	( )	-3	-2	-1	0	1	2	3
26) 배우자와 다투는 횟수의 변화 (자주 다투거나 덜 다투게 됨)	( )	-3	-2	-1	0	1	2	3
27) 남자: 부인 직장의 변동 (새로 일을 시작하거나, 그만두거나, 직장을 옮김)	( )	-3	-2	-1	0	1	2	3
28) 여자: 남편 직장의 변동 (실직하거나, 새직장을 갖거나, 퇴직을 하게 됨)	( )	-3	-2	-1	0	1	2	3
29) 취미.오락 생활의 중요한 변화 (유형이나 횟수의 변화)	( )	-3	-2	-1	0	1	2	3
30) 700만원 이상을 빌림	( )	-3	-2	-1	0	1	2	3
31) 700만원 이하를 빌림	( )	-3	-2	-1	0	1	2	3
32) 직장에서 해고를 당함	( )	-3	-2	-1	0	1	2	3
33) 남자: 부인이나 애인이 유산을 하게 됨	( )	-3	-2	-1	0	1	2	3
34) 여자: 유산을 하게 됨	( )	-3	-2	-1	0	1	2	3
35) 큰 질병이나 상처를 입음	( )	-3	-2	-1	0	1	2	3
36) 모임이나 방문 등과 같은 사교활동의 중요한 변화 (참여횟수가 줄거나 늘게 됨)	( )	-3	-2	-1	0	1	2	3
37) 생활여건의 중요한 변화 (집을 짓고 개축하거나, 실내장식을 바꾸거나, 지역이 바뀜)	( )	-3	-2	-1	0	1	2	3
38) 이혼을 하게 됨	( )	-3	-2	-1	0	1	2	3
39) 친한 친구가 심한 병이나 상처를 입게 됨	( )	-3	-2	-1	0	1	2	3
40) 직장에서 퇴직하게 됨	( )	-3	-2	-1	0	1	2	3
41) 아이들이 집을 떠나게 됨 (결혼이나 학교문제 등)	( )	-3	-2	-1	0	1	2	3
42) 학교를 졸업하게 됨	( )	-3	-2	-1	0	1	2	3
43) 배우자와 떨어져 있게 됨 (여행이나 직장 때문에)	( )	-3	-2	-1	0	1	2	3
44) 약혼	( )	-3	-2	-1	0	1	2	3
45) 이성친구와 절교	( )	-3	-2	-1	0	1	2	3
46) 처음으로 집을 떠나게 됨	( )	-3	-2	-1	0	1	2	3
47) 이성친구와 화해를 함	( )	-3	-2	-1	0	1	2	3
48) 대학이나 대학원 생활의 시작	( )	-3	-2	-1	0	1	2	3
49) 학교를 옮김	( )	-3	-2	-1	0	1	2	3
50) 정학 또는 근신	( )	-3	-2	-1	0	1	2	3
51) 기숙사에서 나오게 됨	( )	-3	-2	-1	0	1	2	3
52) 중요한 시험을 망침	( )	-3	-2	-1	0	1	2	3
53) 전공을 바꿈	( )	-3	-2	-1	0	1	2	3
54) 과목낙제를 함	( )	-3	-2	-1	0	1	2	3
55) 수강과목을 취소함	( )	-3	-2	-1	0	1	2	3
56) 친목써클에 가입함	( )	-3	-2	-1	0	1	2	3
57) 경제적인 곤란 (학업을 계속하기 힘들 정도의)	( )	-3	-2	-1	0	1	2	3
최근 3개월 동안에 귀하에게 일어났던 중요한 사건들 중 위에서 열거되지 않은 것이 있으면 아래에 적어 주십시오.								
58)	( )	-3	-2	-1	0	1	2	3
59)	( )	-3	-2	-1	0	1	2	3
60)	( )	-3	-2	-1	0	1	2	3

Appendix 2. Descriptive analysis of life experiences survey questionnaire

Event name	Presence	Impact						
		-3	-2	-1	0	1	2	3
1) Marriage	17	1	0	2	3	5	3	3
2) Detention in jail or comparable institution	3	0	2	0	1	0	0	0
3) Death of spouse	2	0	0	0	1	0	0	1
4) Major change in sleeping habits (much more or much less sleep)	183	13	11	83	42	22	6	6
5) Death of close family member:								
(1) mother	27	16	2	5	3	0	1	0
(2) father	15	4	4	3	4	0	0	0
(3) brother and sister	18	11	4	2	1	0	0	0
(4) grandmother	3	0	2	0	1	0	0	0
(5) grandfather	5	0	2	1	2	0	0	0
(6) other (specify)	47	9	6	15	17	0	0	0
6) Major change in eating habits (much more or much less food intake)	158	9	13	47	37	38	5	9
7) Foreclosure on mortgage or loan	43	14	8	16	4	1	0	0
8) Death of close friend	55	19	8	15	13	0	0	0
9) Outstanding personal achievement	66	1	0	3	7	16	11	28
10) Minor law violations (traffic tickets, disturbing the peace, etc.)	52	5	5	23	18	0	0	1
11) Male: Wife/girlfriend's pregnancy	0	0	0	0	0	0	0	0
12) Female: Pregnancy	0	0	0	0	0	0	0	0
13) Changed work situation (different work responsibility, major change in working conditions, working hours, etc.)	29	1	2	8	3	11	3	1
14) New job	22	1	1	2	5	4	4	5
15) Serious illness or injury of close family member:								
(1) mother	30	11	5	11	1	1	0	1

(2) father	10	1	4	3	2	0	0	0
(3) brother and sister	20	8	2	5	4	0	1	0
(4) grandfather	1	0	0	1	0	0	0	0
(5) grandmother	0	0	0	0	0	0	0	0
(6) spouse	35	17	7	7	2	0	2	0
(7) other (specify)	33	18	2	9	4	0	0	0
16) Sexual difficulties	30	6	3	15	5	0	0	1
17) Trouble with employer (in danger of losing job, being suspended, demoted, etc.)	19	3	3	9	4	0	0	0
18) Trouble with in-laws and relatives	89	27	15	37	8	1	1	0
19) Major change in financial status (a lot better oil or a lot worse off)	73	4	15	28	13	9	3	1
20) Major change in closeness of family members (increased or decreased closeness)	82	14	3	25	8	7	8	17
21) Gaining a new family member (Through birth, adoption, family ember moving in, etc.)	52	1	0	2	3	0	11	35
22) Change of residence	43	0	1	0	8	13	5	16
23) Marital separation from mate (due to conflict)	8	2	1	2	2	0	1	0
24) Major change in church activities (increased or decreased attendance)	68	2	2	13	12	11	9	19
25) Marital reconciliation with mate	31	1	0	4	5	10	6	5
26) Major change in number of arguments with spouse (a lot more or a lot less arguments)	87	14	7	33	12	11	8	2
27) Married male: Change in wife's work outside the home (beginning work, ceasing work, changing to a new job, etc.)	5	0	0	0	3	1	0	1
28) Married female: Change in husband's work (loss of job,	18	3	1	1	7	4	2	0

beginning new job, retirement, etc.)								
29) Major change in usual type and/or amount of recreation	73	2	1	4	1	22	11	32
30) Borrowing more than 7,000,000 KR₩ (buying home, business, etc.)	38	3	2	11	16	3	2	1
31) Borrowing less than 7,000,000 KR₩ (buying car, TV, getting school loan, etc.)	16	4	0	4	4	3	1	0
32) Being fired from job	3	2	0	1	0	0	0	0
33) Male: Wife/girlfriend having abortion	0	0	0	0	0	0	0	0
34) Female: Having abortion	0	0	0	0	0	0	0	0
35) Major personal illness or injury	43	18	6	7	6	1	4	1
36) Major change in social activities, e.g., parties, movies, visiting (increased, decreased participation)	74	1	0	8	11	25	8	21
37) Major change in living conditions of family (building new home, remodeling, deterioration of home, neighborhood, etc.)	43	0	0	1	2	16	7	17
38) Divorce	3	1	1	0	0	0	0	1
39) Serious injury or illness of close friend	25	8	6	5	6	0	0	0
40) Retirement from work	4	0	0	2	2	0	0	0
41) Son or daughter leaving home (due to marriage, college, etc.)	49	3	1	14	21	4	2	4
42) Ending of formal schooling	4	0	1	0	2	0	0	1
43) Separation from spouse (due to work, travel, etc.)	13	2	2	6	0	1	0	2
44) Engagement	0	0	0	0	0	0	0	0
45) Breaking up with boyfriend/ girlfriend	1	0	1	0	0	0	0	0
46) Leaving home for the first time	0	0	0	0	0	0	0	0
47) Reconciliation with boyfriend/ girlfriend	0	0	0	0	0	0	0	0

48) Beginning a new school experience at a higher academic level (college, graduate school, professional school, etc.)	3	0	0	0	0	0	2	1
49) Changing to a new school at same academic level (undergraduate, graduate, etc.)	1	0	0	0	0	0	1	0
50) Academic probation	1	0	0	1	0	0	0	0
51) Being dismissed from dormitory or other residence	0	0	0	0	0	0	0	0
52) Failing an important exam	0	0	0	0	0	0	0	0
53) Changing a major	0	0	0	0	0	0	0	0
54) Failing a course	0	0	0	0	0	0	0	0
55) Dropping a course	0	0	0	0	0	0	0	0
56) Joining a fraternity/sorority	2	0	0	0	0	2	0	0
57) Financial problems concerning school (in danger of not having sufficient money to continue)	4	0	1	2	1	0	0	0
58) Others (open question)	17	6	5	1	1	0	0	4
59) Others (open question)	4	3	0	1	0	0	0	0
60) Others (open question)	3	1	1	1	0	0	0	0

Data were expressed as number

Appendix 3. Life experiences survey questionnaire descriptive analysis according to the severe events using life change units more than 50 in Holmes and Rahe Stress Scale

Event name	Presence	Impact						
		-3	-2	-1	0	1	2	3
1) Marriage	17	1	0	2	3	5	3	3
2) Detention in jail or comparable institution	3	0	2	0	1	0	0	0
3) Death of spouse	2	0	0	0	1	0	0	1
5) Major change in sleeping habits (much more or much less sleep)								
(1) mother	27	16	2	5	3	0	1	0
(2) father	15	4	4	3	4	0	0	0
(3) brother and sister	18	11	4	2	1	0	0	0
(4) grandmother	3	0	2	0	1	0	0	0
(5) grandfather	5	0	2	1	2	0	0	0
(6) other (specify)	47	9	6	15	17	0	0	0
23) Marital separation from mate (due to conflict)	8	2	1	2	2	0	1	0
38) Divorce	3	1	1	0	0	0	0	1
43) Separation from spouse (due to work, travel, etc.)	13	2	2	6	0	1	0	2

Data were expressed as number