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ORIGINAL ARTICLE

# **Observational Study**

# Psychological stress and long-term blood pressure variability of military young males: The cardiorespiratory fitness and hospitalization events in armed forces study

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### Informed consent statement:

Written informed consent was obtained from all participants.

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# **Abstract**

# **BACKGROUND**

Acute stress might increase short-term heart rate variability and blood pressure variability (BPV); however, chronic stress would not alter short-term BPV in animal models.

### **AIM**

To examine the association of psychological stress with long-term BPV in young male humans.

### **METHODS**

We prospectively examined the association of chronic psychological stress with long-term BPV in 1112 healthy military males, averaged 32.2 years from the cardiorespiratory fitness and hospitalization events in armed forces study in Taiwan. Psychological stress was quantitatively evaluated with the Brief Symptom Rating Scale (BSRS-5), from the least symptom of 0 to the most severe of

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Received: July 3, 2020 Peer-review started: July 3, 2020 First decision: October 6, 2020 Revised: October 10, 2020 Accepted: November 4, 2020 Article in press: November 4, 2020 20, and the five components of anxiety, insomnia, depression, interpersonal sensitivity, and hostility (the severity score in each component from 0 to 4). Longterm BPV was assessed by standard deviation (SD) for systolic and diastolic blood pressure (SBP and DBP), and average real variability (ARV), defined as the average absolute difference between successive measurements of SBP or DBP, across four visits in the study period from 2012 to 2018 (2012-14, 2014-15, 2015-16, and 2016-18).

### RESULTS

The results of multivariable linear regressions showed that there were no correlations of the BSRS-5 score with  $SD_{SBP}$ ,  $SD_{DBP}$ ,  $ARV_{SBP}$ , and  $ARV_{DBP}$  after adjusting for all the covariates [ $\beta$ (SE): -0.022 (0.024), -0.023 (0.026), -0.001 (0.018), and 0.001 (0.020), respectively; P > 0.05 for all]. In addition, there were also no correlations between each component of the BSRS score and the long-term BPV indexes.

### CONCLUSION

Our findings suggest that chronic psychological stress might not be associated with long-term BPV in military young male humans.

Key Words: Long-term blood pressure variability; Military; Psychological stress; Young males; Brief Symptom Rating Scale; Average real variability

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**Core Tip:** This study investigated the relationship of psychological stress evaluated using the Brief Symptom Rating Scale (BSRS-5) with long-term blood pressure variability (BPV) in 1112 military young male adults across four visits during a 7-year period. We found that there were no correlations of the BSRS-5 score and related components with systolic and diastolic BPV indexes in the fully adjusted model. Although previous studies have demonstrated that there was an association between psychological stress and elevated blood pressure, our study suggested no association of psychological stress and long-term BPV in young male adults.

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### INTRODUCTION

Psychological stress is related to activation of the sympathetic nervous system and production of norepinephrine and epinephrine from the adrenal glands, leading to elevated blood pressure. Previous studies have shown that psychological stress, particularly chronic stress, may cause the development of hypertension<sup>[1]</sup>. To our knowledge, psychological stress is subjective and complicated in human beings. An experiment in mice demonstrated that acute stress might result in increased short-term heart rate variability and blood pressure variability (BPV); however, chronic stress would not alter short-term BPV<sup>[2]</sup>. Whether chronic mental stress is associated with long-term BPV remains unclear in human beings. Therefore, we investigated such association in a military cohort of young male adults.

# MATERIALS AND METHODS

### Study population

We prospectively examined the association of chronic psychological stress with long-



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term BPV in 1112 healthy military males aged 18-40 years (32 years on average) from the cardiorespiratory fitness and hospitalization events in armed forces study in Taiwan<sup>[3-10]</sup>. All participants visited the Hualien Armed Forces General Hospital for a comprehensive health examination including the survey of demographics, anthropometrics, hemodynamics, mental stress, and behaviors and laboratory studies at least at two-year intervals from 2012 to 2018 (2012-14, 2014-15, 2015-16, and 2016-

### Psychological stress measurements

The chronic psychological stress severity of military males in Taiwan was assessed using the Brief Symptom Rating Scale (BSRS-5) in the past 3 mo. There were five psychological domains included in BSRS-5, i.e., depression (feeling blue), anxiety (feeling tense), interpersonal sensitivity (feeling inferior to others), hostility (feeling easily annoyed or irritated), and insomnia (trouble falling asleep). The scoring scale of each domain is Likert-type, ranging from 0 to 4 in severity: 0, nothing; 1, a little; 2, moderately; 3, quite a bit; 4, extremely<sup>[11,12]</sup>. The BSRS-5 scores ≤ 5, 6-9, and ≥10 were defined as normal, slight, and great stress, respectively[11]. The test-retest reliability coefficient of the BSRS-5 score was 0.82, and the internal consistency (Cronbach alpha) coefficients ranged from 0.77 to 0.90<sup>[12,13]</sup>.

### BPV measurements

Caffeine or theophylline-containing materials were banned for all participants in a 12h fast before each hospital visit. Systolic and diastolic blood pressure (SBP and DBP, respectively) was measured with an automated blood pressure monitor (FT-201; Parama-Tech Co. Ltd., Fukuoka, Japan), once over right upper arm of each participant in a sitting position after a rest for 15 min or more at each visit. Long-term BPV was assessed across four visits in the study period by standard deviation (SD) and average real variability (ARV) for SBP and DBP variability. For instance, SD and ARV for SBP variability denoted as SD<sub>SBP</sub> and ARV<sub>SBP</sub> are respectively presented by dotted and solid lines in Figure 1. ARV was defined as the average absolute difference between successive measurements of blood pressure, and it takes the order of measurements into account  $[(|\Delta 1| + |\Delta 2| + |\Delta 3|)/3]^{[14]}$ .

### Statistical analysis

The characteristics of those who had a BSRS-5 score ≤ 5 and BSRS-5 score > 5 are expressed as the mean ± SD for continuous data, and categorical data are expressed as numbers and percentages. In model 1, a multivariable linear regression model adjusted for age, body mass index, baseline SBP and DBP, alcohol intake status, and physical activity (exercise frequency) was used to determine the relationship. The statistic power calculated was 0.85. A value of P < 0.05 was considered significant. SAS statistical software (SAS version 9.4; SAS Institute, Cary, NC, United States) was used for all statistical analyses.

### RESULTS

Table 1 shows the baseline profiles of the study participants. The age, body stature, hemodynamic status, and serum lipid profiles were similar between the normal subjects and those with stress. Those who had chronic mental stress were found with a lower level of physical activity and higher prevalence of alcohol drinking. Table 2 shows the results of multivariable linear regressions. In the unadjusted model, there were no correlations between the BSRS score and each component with SD and ARV for SBP and DBP variability, except that interpersonal sensitivity was borderline significantly and negatively correlated with  $SD_{SBP}[\beta(SE): -0.010 (0.005), P = 0.07]$ . After adjusting for the covariates in model 1, the associations of the BSRS score and each component with the long-term BPV indexes did not change a lot and remained insignificant. The correlation between interpersonal sensitivity and SD<sub>SBP</sub> was just mildly reduced [ $\beta$ (SE): -0.009 (0.005), P = 0.09].

### DISCUSSION

We found that young military male adults with chronic psychological stress had a higher prevalence of alcohol drinking and less physical activity, reflecting that the



Table 1 Baseline characteristics of the study cohort (n = 1112)							
Characteristic	BSRS ≤ 5 ( <i>n</i> = 983)	BSRS > 5 (n = 129)	P value				
Age (yr)	32.21 ± 3.87	32.22 ± 4.02	0.99				
Body mass index (kg/m²)	25.14 ± 2.93	25.18 ± 2.71	0.89				
SBP (mmHg)	118.45 ± 13.45	117.60 ± 12.98	0.49				
DBP (mmHg)	71.58 ± 10.12	$71.83 \pm 9.95$	0.78				
Heart rate (beats per min)	$74.96 \pm 10.48$	75.51 ± 11.54	0.58				
Fasting plasma glucose (mg/dL)	94.42 ± 13.17	95.09 ± 15.33	0.59				
Total cholesterol (mg/dL)	180.27 ± 36.62	179.30 ± 34.01	0.75				
High-density lipoprotein (mg/dL)	47.97 ± 9.78	48.30 ± 11.15	0.72				
Physical activity							
Never or occasionally	147 (15.0)	38 (29.5)	< 0.01				
1-2 times/wk	365 (37.1)	62 (48.1)					
≥ 3-5 times/wk	471 (47.9)	29 (22.5)					
Current drinkers (%)	441 (44.9)	76 (58.9)	< 0.01				
Current smokers (%)	376 (38.3)	55 (42.5)	0.33				

Continuous variables are expressed as the mean ± SD, and categorical variables as n (%). BSRS: Brief Symptom Rating Scale; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

> BSRS score may be reliable for the evaluation of mental stress[15,16]. The principal finding was that there was no association of chronic psychological stress and its pivotal domains with long-term BPV in young military male adults. A prior study in mice has revealed that acute stress but not chronic stress was associated with shortterm BPV (within an hour measurement)[2]. In addition, acute stressors on human beings could lead to an elevation of blood pressure levels and the effect persisted for a while<sup>[17]</sup>. This finding may make short-term BPV less sensitive to stress as compared with heart rate variability in human beings and similarly in the mouse model<sup>[2,18]</sup>. Notably, this study was the first one providing the evidence for a null association between chronic psychological stress and long-term BPV.

> The results from the mouse experiment also demonstrated that acute stress could increase short-term BPV, which was likely due to sympathetic nervous system activation and baroreflex control impairment<sup>[2]</sup>. On the contrary, chronic stress might reduce short-term BPV due to the coordination of sympathetic activation and physiological response to the vascular alterations in hypertension<sup>[19,20]</sup>. Our findings also revealed that the BSRS-5 score was inversely correlated to almost all of the longterm BPV indexes in young male adults despite insignificance. This tendency of inverse association might differ by the components of BSRS-5 score, which was in line with anxiety, depression, and interpersonal sensitivity but contradicted to insomnia.

> There were some strengths in this study. First, the questionnaire for BSRS-5, physical examinations, and blood pressure measurements were all performed standardly and in a strict manner at the clinic visit. Second, many unmeasured confounders had been controlled at baseline since daily life of the military such as deployment, physical activity, and stress sources were similar across troops. On the contrary, there were several limitations in this study. First, the results were obtained from the male subjects and might be inappropriately applied for the female subjects. Second, the study had a follow-up period for merely 7 years when the prevalence of hypertension remained low, possibly reducing the degree of association between psychological stress and BPV. Third, we used only a single measurement of blood pressure on each visit, which might be susceptible to change by cigarettes, coffee, and indoor temperature. Although the objective environment and the detailed preparations for blood pressure assessment have been regulated, other confounders such as white coat hypertension might be present in some subjects, possibly resulting in a bias. Lastly, there were only four occasions (every two years in interval) for blood pressure measurement, which would cause wide variations of SD and ARV, resulting in reduced associations for psychological stress. The interval of blood pressure

Table 2 Association of the Brief Symptom Rating Scale score and the components with the long-term blood pressure variability indexes in multivariable liner regressions

	Unadjusted			Model 1		
	β(SE)	P value	R <sup>2</sup> , %	β(SE)	P value	R <sup>2</sup> , %
BSRS scores						
$ARV_{SBP}$	-0.005 (0.019)	0.80	0.0	-0.001 (0.018)	0.94	7.2
$\mathrm{ARV}_{\mathrm{DBP}}$	-0.003 (0.020)	0.88	0.0	0.001 (0.020)	0.96	7.2
$\mathrm{SD}_{\mathrm{SBP}}$	-0.028 (0.025)	0.26	0.1	-0.022 (0.024)	0.36	7.2
$\mathrm{SD}_{\mathrm{DBP}}$	-0.032 (0.027)	0.23	0.1	-0.023 (0.026)	0.38	7.2
Anxiety						
$ARV_{SBP}$	-0.005 (0.005)	0.31	0.1	-0.003 (0.005)	0.51	6.2
$ARV_{DBP}$	-0.003 (0.005)	0.53	0.0	-0.001 (0.005)	0.83	6.1
$SD_{SBP}$	-0.009 (0.006)	0.17	0.2	-0.006 (0.006)	0.32	6.2
$SD_{DBP}$	-0.007 (0.007)	0.29	0.1	-0.003 (0.007)	0.66	6.1
Depression						
$ARV_{SBP}$	-0.002 (0.004)	0.62	0.0	-0.001 (0.004)	0.71	5.6
$ARV_{DBP}$	0.000 (0.004)	0.93	0.0	0.000 (0.004)	0.93	5.6
$\mathrm{SD}_{\mathrm{SBP}}$	-0.007 (0.005)	0.16	0.2	-0.006 (0.005)	0.21	5.7
$\mathrm{SD}_{\mathrm{DBP}}$	-0.005 (0.006)	0.40	0.1	-0.003 (0.006)	0.58	5.6
Hostility						
$ARV_{SBP}$	0.002 (0.004)	0.66	0.0	0.003 (0.004)	0.55	6.1
$ARV_{DBP}$	0.001 (0.005)	0.88	0.0	0.001 (0.005)	0.83	6.0
$SD_{SBP}$	-0.003 (0.006)	0.54	0.0	-0.002 (0.006)	0.67	6.1
$\mathrm{SD}_{\mathrm{DBP}}$	-0.006 (0.006)	0.31	0.1	-0.005 (0.006)	0.40	6.1
Interpersonal sensitivity						
$ARV_{SBP}$	-0.002 (0.004)	0.55	0.0	-0.002 (0.004)	0.60	6.1
$ARV_{DBP}$	-0.001 (0.004)	0.76	0.0	0.000 (0.004)	0.90	6.1
$SD_{SBP}$	-0.010 (0.005)	0.07	0.3	-0.009 (0.005)	0.09	6.3
$SD_{DBP}$	-0.008 (0.006)	0.18	0.2	-0.006 (0.006)	0.29	6.2
Insomnia						
$ARV_{SBP}$	0.003 (0.004)	0.49	0.0	0.003 (0.004)	0.41	3.9
$ARV_{DBP}$	0.001 (0.004)	0.80	0.0	0.001 (0.004)	0.74	3.8
$SD_{SBP}$	0.001 (0.005)	0.84	0.0	0.002 (0.005)	0.72	3.8
$SD_{DBP}$	-0.003 (0.005)	0.58	0.0	-0.002 (0.005)	0.71	3.8

 $\beta$  means standardized regression coefficient;  $R^2$  means a measure for model prediction. The covariates adjusted in model 2 include age, systolic and  $diastolic \ blood \ pressure, \ physical \ activity, \ and \ current \ alcohol \ intake. \ BSRS: \ Brief \ Symptom \ Rating \ Scale; \ ARV_{SBP}: \ Average \ real \ variability \ for \ systolic \ properties \ and \ properties \ propertie$  $blood\ pressure\ variability;\ ARV_{DBP}:\ Average\ real\ variability\ for\ diastolic\ blood\ pressure\ variability;\ SD_{SBP}:\ Standard\ deviation\ for\ systolic\ blood\ pressure\ variability\ pressure\ variability\ pressure\ pressu$ variability;  $\mathrm{SD}_{\mathrm{DBP}}\!.$  Standard deviation for diastolic blood pressure variability.

> measurement had a long time scale (years instead of months). Therefore, it may promote further studies to either confirm or dispute the conclusions.

# CONCLUSION

In conclusion, our findings suggest that chronic psychological stress is not associated



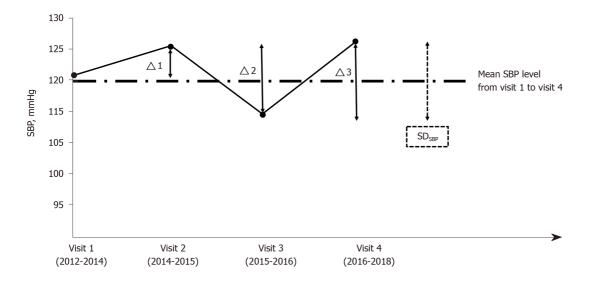


Figure 1 Standard deviation and average real variability for systolic blood pressure variability denoted as SD<sub>SBP</sub> and ARV<sub>SBP</sub> respectively presented by dotted and solid lines. Average real variability was defined as the average absolute difference between successive measurements of blood pressure, and it takes the order of measurements into account  $[(|\Delta 1| + |\Delta 2| + |\Delta 3|)/3]$ . SBP: Systolic blood pressure; SD<sub>SRP</sub>: Standard deviation for systolic blood pressure variability.

with long-term BPV in young males. In addition, this study is the first one revealing a null association between each chronic stress component and long-term BPV in human beings. It is necessary to see whether there might be a change for the relationship with long-term BPV in a longer follow-up when the prevalence of hypertension increases with ageing.

# ARTICLE HIGHLIGHTS

### Research background

An experiment in mice demonstrated that acute stress might result in increased shortterm heart rate variability and blood pressure variability (BPV); however, chronic stress would not alter short-term BPV.

### Research motivation

Whether chronic mental stress is associated with long-term BPV remains unclear in human beings.

### Research objectives

To examine the association of psychological stress with long-term BPV in young male adults.

### Research methods

The association between chronic psychological stress and long-term BPV was examined in 1112 healthy military males, averaged 32.2 years in Taiwan. Psychological stress was quantitatively evaluated using the Brief Symptom Rating Scale (BSRS-5), from the least symptom of 0 to the most severe of 20, and the five components of anxiety, insomnia, depression, interpersonal sensitivity, and hostility (the severity score in each component from 0 to 4). Long-term BPV was assessed by standard deviation (SD) for systolic and diastolic blood pressure (SBP and DBP), and average real variability (ARV), defined as the average absolute difference between successive measurements of SBP or DBP, across four visits in the study period from 2012 to 2018 (2012-14, 2014-15, 2015-16, and 2016-18).

### Research results

The results of multivariable linear regressions showed that there were no correlations of the BSRS-5 score with  $SD_{SBP}$ ,  $SD_{DBP}$ ,  $ARV_{SBP}$ , and  $ARV_{DBP}$  after adjusting for all the covariates  $[\beta(SE): -0.022 (0.024), -0.023 (0.026), -0.001 (0.018), and 0.001 (0.020),$ respectively; P > 0.05 for all]. In addition, there were also no correlations between each component of the BSRS score and the long-term BPV indexes.

### Research conclusions

Our findings suggest that chronic psychological stress might not be associated with long-term BPV in military young males.

### Research perspectives

Future studies should focus on the association between chronic mental stress and longterm BPV which is assessed by a smaller interval of blood pressure measurement (i.e., from years to months).

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