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Epigenome-wide meta-analysis of PTSD across 10 military and civilian cohorts identifies methylation changes in AHRR

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Association of Psychological Stress with Physical Fitness in a Military Cohort: The CHIEF Study

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ABSTRACT

Introduction

Psychological stress is associated with sedentary behavior, which may impair exercise performance. The aim of our study was to examine the association between psychological stress and physical fitness in military personnel.

Method

A military cohort of 4080 subjects in Taiwan was used for the analysis. The Brief Symptoms Rating Scale (BSRS-5) includes items of anxiety, depression, hostility, interpersonal sensitivity, and insomnia measured by a five-point Likert-type scale of 0–4. Psychological stress was defined as normal ($n = 3657$), slight ($n = 314$), and great ($n = 109$) by BSRS-5 score ≤ 5 , 6–9, and ≥ 10 , respectively. Aerobic fitness and anaerobic fitness were evaluated by the time of 3000-meter running and the numbers of 2-min sit-ups and 2-min push-ups, respectively. Multiple linear and logistic regression analyses were used to determine the relationship.

Results

As compared with normal stress, slight and great stress were positive dose-dependently correlated with 3000-meter running time ($\beta = 9.09$ and 14.44 ; $P = 0.0032$ and 0.048 , respectively) after adjusting for age, sex, service specialty, body mass index, systolic blood pressure, cigarette smoking, alcohol intake, hemoglobin levels, and exercise frequency. Similarly, those with slight stress were more likely to be the worst 10% performers in the 3000-meter run test relative to the normal individuals (odds ratio and 95% confidence intervals: 1.50, 1.00–2.24). By contrast, there was no relationship of psychological stress with the numbers of 2-min sit-ups and 2-min push-ups.

Conclusions

Our findings suggest that the presence of higher psychological stress on military personnel may reduce their cardiorespiratory fitness but not affect the anaerobic fitness.

INTRODUCTION

Military personnel who have to take multiple deployments, heavier training, and responsibility are vulnerable to greater psychological stress and at higher risk of mental disorders.¹ According to a meta-analysis of 37 studies in the U.S. military, the prevalence of major depression ranges from 2.0 to 37.4%.¹ Similarly, the one-year prevalence of major depression of the Canadian Armed Forces is about 8%, much higher than 4% of the matched Canadian civilians.² In addition, the prevalence of posttraumatic stress disorder among the military returning from the Iraq war is estimated from 4 to 17% in the United States and from 3 to 6% in the United Kingdom.^{3,4} A meta-analysis also revealed consistent results that the pooled prevalence of posttraumatic stress disorder among rescue workers was about 10%.⁵

Previous studies have demonstrated a relationship between physical activity and psychological stress.⁶ The American College of Sports Medicine (ACSM) suggested that regular

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exercise improves stress-related psychiatric symptoms including depression and anxiety.⁷ This recommendation was made mainly based on the results from a number of studies consistently showing beneficial influence of aerobic exercise on mental health.^{8–10} Aerobic training improves both cardiovascular and autonomic nervous systems functions, and modulates hypothalamic-pituitary-adrenal axis, which lead to a reduction of heart rate and plasma epinephrine and norepinephrine concentrations during exercise.^{11,12} The altering physiological activity with aerobic training may thus reduce the severity of psychosomatic symptoms. However, a few studies investigated the effect of anaerobic exercise on mental health and inconsistently showed null or beneficial results.^{13–15}

In contrast, acute psychological stress transiently enhances muscle strength by activating sympathetic neurohormonal axis and elevating blood pressure.¹⁶ When the stress persists, pro-inflammatory cytokines such as interleukin-6 and NF-kappa¹⁷ and oxidative stress are produced, which may result in skeletal muscle wasting.^{18,19} A systemic review of observational studies has shown that greater psychological stress is associated with more sedentary behavior or less exercise, possibly reducing physical fitness further.^{20,21} Prior studies only confirmed an inverse relationship between depressive symptom severity and aerobic fitness.⁷ However, the effect of mental stress on anaerobic fitness was unknown. Therefore, we aimed to examine the association of mental stress severity with aerobic and anaerobic fitness in a large military cohort in Taiwan.

METHOD

Study Population

The present study used a historical cohort of 4080 military men and women, with an average of 29.2 years of age from the cardiorespiratory fitness and hospitalization events in armed forces (CHIEF) study performed in Taiwan during 2014. All participants self-reported a questionnaire for the experience of substance use and their mental status. In addition, the participants carried out a formal health examination in Hualien Armed Forces General Hospital, and underwent at least one of the annual three exercise tests including 3000-meter non-weight-bearing running, 2-min sit-ups, and 2-min push-ups at Military Physical Training and Testing Center of eastern Taiwan. The study design of CHIEF study has been described in detail previously.^{22–24}

Physical and Laboratory Assessment

All participants were measured for their anthropometric parameters including height and weight assessed in a standing position. Body mass index (BMI) was defined as body weight (kg) divided by square of height (m²), and waist size was measured at the midpoint between the last palpable rib and the top of the iliac crest by a stretch-resistant tape. Hemodynamic

data including pulse rate and blood pressure were measured once over right upper arm by the FT-201 automated blood pressure monitor (Parama-Tech Co Ltd, Fukuoka, Japan) in a sitting position after a rest for at least 15 min. Laboratory data including blood routine and biochemical tests for serum total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and fasting plasma glucose were obtained after a 12-hour fast.

Psychological Stress Assessment

The Brief Symptom Rating Scale (BSRS-5) was used to evaluate the severity of psychological stress of the military in the past weeks in Taiwan. The BSRS-5 is composed of five psychopathology domains, ie, feeling tense (anxiety), feeling blue (depression), feeling easily annoyed or irritated (hostility), feeling inferior to others (interpersonal sensitivity), and trouble falling asleep (insomnia). The scoring of each domain ranges from 0 to 4 in severity: 0, not at all; 1, a little bit; 2, moderately; 3, quite a bit; 4, extremely.²⁵ Normal, slight, and great mental stress was defined by the sum of BSRS-5 scores ≤ 5 , 6–9, and ≥ 10 , respectively.^{26,27} Internal consistency (Cronbach alpha) coefficients of the BSRS-5 ranged from 0.77 to 0.90. The test-retest reliability coefficient was 0.82.²⁵

Physical Fitness Assessment

Aerobic fitness was evaluated by the execution time of 3000-meter running,²⁸ which is a strong indicator of the velocity at lactate (anaerobic) threshold.²⁹ All runs were performed only when the risk coefficient of heat stroke (the product of outdoor temperature (°C) and relative humidity (%) $\times 0.1$) was less than 40 and no raining. Anaerobic fitness was respectively evaluated by the numbers of 2-min sit-ups and push-ups. The procedures of 2-min push-ups and sit-ups were standardly and respectively performed on a sponge pad and scored by two kinds of computer infrared sensing systems. All testing courses of each participant were video recorded and monitored by the observing officers. The anaerobic exercise tests were performed from 2:00 PM to 3:00 PM and there would be a break between the 2-min push-up and sit-up exercises. After an hour of rest, the aerobic exercise test was performed at 4:00 PM. Since the annual exercise tests are related to the military award and rank promotion, the performance of each participant is reasonably regarded as their best fitness. This study was reviewed and approved by the Institutional Review Board of the Mennonite Christian Hospital (No. 16-05-008) in Hualien of Taiwan, and written informed consent was obtained from all participants.

Statistical Analysis

Continuous variables in the baseline characteristics were presented as mean \pm standard deviation (SD) and compared by two-tailed t test if the normality test, Kolmogorov-Smirnov test, was fulfilled. Otherwise, Wilcoxon signed rank test was

used. In addition, categorical variables were presented as numbers and percentages and compared by chi square test.

The difference in each exercise performance among those with normal, slight, and great stress was estimated by using analysis of covariance (ANCOVA), and the results were presented as mean \pm standard error (SE). Moreover, multiple linear regression was used to determine the correlation of slight and great stress with each exercise performance when normal stress was treated as the reference. In addition, multiple logistic regression was used to determine the odds ratio of the best (top 10 percentile) and the worst (last 10 percentile) performances in each exercise with slight and great mental stress relative to normal mental stress.

In model 1, age, sex, and service specialty were adjusted. In model 2, BMI was additionally adjusted. In model 3, cigarette smoking status, alcohol use status, systolic blood pressure, hemoglobin concentrations, and exercise frequency were additionally adjusted. These potential confounders were chosen for the models according to prior published associations with psychological stress and physical fitness.^{30–32} A 2-tailed value of $P < 0.05$ was considered significant. SAS statistical software (SAS System for Windows, version 9.4; SAS Institute, Cary, NC, United States) was used for all statistical analyses.

RESULTS

Baseline Group Characteristics

The baseline characteristics of each mental stress group are shown in Table I. The cases of normal, slight, and great mental stress were 3657, 314, and 109, respectively. Those with slight or great mental stress had higher proportions of female sex, current cigarette smoking, and current alcohol intake, but had lower levels of systolic blood pressure and exercise frequency compared with those with normal stress. There were no significant differences regarding service specialty, BMI, and waist size among groups. In addition, although there were statistical differences in the means of age and hemoglobin concentrations between the normal and mental stress groups, the differences might not be clinically significant.

Group Mean Comparisons

Table II demonstrates the results of ANCOVA for testing the difference in each exercise performance between groups. There were differences in 3000-meter running time between those with slight or great mental stress and those with normal stress in models 1–3. Although there was no difference in 3000-meter running time between those with slight stress and those with great stress, there was a trend of higher stress with longer running time (P -value for trend < 0.001). In addition, there were no differences in the numbers of 2-min sit-ups and push-ups among groups in models 1–3.

Multiple Linear Regressions

The results of multiple linear regression of each exercise performance, with slight and great mental stress relative to normal mental stress, in models 1–3 are shown in Table III. The relationships of slight and great mental stress with each exercise performance are in line with the findings presented in Table II. In model 1, slight and great mental stress were dose-dependently correlated with 3000-meter running time ($\beta = 13.66$ and 22.09 , respectively). In addition, the associations remained significant in model 2 ($\beta = 13.63$ and 19.80 , respectively) and model 3 ($\beta = 9.09$ and 14.44 , respectively). However, the correlations of slight or great mental stress with 2-min sit-ups and push-ups were null.

Multiple Logistic Regressions

Table IV reveals the results of multiple logistic regressions of the best 10% and the worst 10% performance in each exercise, with slight and great mental stress in reference to normal mental stress. In models 1 and 2, those with great mental stress had a lower possibility of being the best 10% performers in the 2-min sit-ups as compared with those with normal stress (OR = 0.34 and 0.35, respectively). However, the association became marginally significant in model 3 (OR = 0.41). Similarly, slight mental stress was marginal inversely associated with the best 10% performance in the 3000-meter run test as well (OR: 0.76). By contrast, those with slight mental stress had a higher possibility of being the worst 10% performers in the 3000-meter run test as compared with those with normal stress in models 1–3 (OR: 1.58, 1.58, and 1.50, respectively). In addition, the association of great mental stress with the worst 10% performance in the 3000-meter run test was marginally significant in model 1 (OR: 1.77), but was reduced in models 2 and 3 (OR: 1.69 and 1.57, respectively).

DISCUSSION

On the basis of our findings, psychological stress was associated with worse aerobic fitness but did not influence anaerobic fitness in the military members in Taiwan. The severity of psychological stress was positive dose-dependently correlated with the execution time of 3000-meter running after adjusting for age, sex, body mass index, cigarette smoking, alcohol consumption, systolic blood pressure, hemoglobin levels, and exercise frequency. In addition, those with mental stress were likely to have an increased 1.50-fold possibility being the worst 10% performers in the 3000-meter run test.

Our findings were consistent with the Stress in AmericaTM survey report conducted by the American Psychological Association that higher exercise frequency in leisure time was related to better mental status.³³ We found that those feeling less stress (BSRS ≤ 5) and with a habit of frequent exercises ≥ 3 times per week accounted for 37% of the overall military cohort compared with the U.S. survey report that 35% staying in good mood and 30% feeling less stressed following exercise of the general population.³³ In addition, our military personnel

TABLE I. Basic Characteristics of the Military Cohort Based on BSRS Scores ($n = 4080$)

	BSRS ≤ 5 N = 3657		BSRS 6–9 N = 314		BSRS ≥ 10 N = 109		P value
Age (year)	29.15	± 5.97	30.04	± 5.82	29.22	± 5.57	0.039
Sex							0.032
Men	3304	(90.35)	271	(86.31)	94	(86.24)	
Women	353	(9.65)	43	(13.69)	15	(13.76)	
Service specialty							0.46
Air Force	1016	(27.78)	86	(27.39)	22	(20.18)	
Army	1879	(51.38)	163	(51.91)	65	(59.63)	
Navy	762	(20.84)	65	(20.70)	22	(20.18)	
BMI (kg/m^2)	24.63	± 3.18	24.66	± 3.01	24.88	± 2.98	0.71
Waist size (cm)	82.33	± 8.48	82.59	± 8.31	83.25	± 8.32	0.48
SBP (mmHg)	117.41	± 13.55	114.91	± 13.36	116.29	± 12.21	0.0057
DBP (mmHg)	70.11	± 10.25	69.14	± 9.13	69.96	± 9.43	0.26
Hb (g/dL)	14.96	± 1.18	14.84	± 1.21	15.19	± 1.16	0.030
Cigarette smoking	1252	(34.24)	128	(40.76)	46	(42.20)	0.033
Alcohol drinking	1457	(39.84)	170	(54.14)	59	(54.13)	<.0001
Exercise frequency							<.0001
< 1 time/wk	759	(20.75)	97	(30.89)	39	(35.78)	
1–2 times/wk	1367	(37.38)	138	(43.95)	49	(44.95)	
≥ 3 times/wk	1531	(41.86)	79	(25.16)	21	(19.27)	

Continuous variables are expressed as mean \pm SD and categorical variables as n (%). BSRS: brief symptom rating scale; BMI: body mass index; DBP: diastolic blood pressure; Hb: hemoglobin; SBP: systolic blood pressure.

TABLE II. Relationship of BSRS Scores with Physical Performances

	3000-m run (seconds)			2-min sit-up (numbers)			2-min push-up (numbers)		
	N	Mean (SE)	P-value	N	Mean (SE)	P-value	N	Mean (SE)	P-value
Model 1			<0.001 ¹			<0.001 ¹			<0.001 ¹
BSRS ≤ 5	3254	871.07(1.28)		3638	46.62(0.14)		3614	47.72(0.19)	
BSRS 6–9	275	888.20(4.40)	<0.001 ²	303	45.65(0.46)	0.02 ²	313	46.30(0.66)	0.094 ²
BSRS ≥ 10	87	894.60(7.81)	<0.001 ³	108	45.26(0.79)	0.08 ³	105	46.37(1.13)	0.23 ³
Model 2			<0.001 ¹			<0.001 ¹			<0.001 ¹
BSRS ≤ 5	3247	871.50(1.19)		3630	46.57(0.13)		3605	47.70(0.18)	
BSRS 6–9	275	885.13(4.11)	<0.001 ²	303	45.99(0.44)	0.21 ²	313	46.56(0.64)	0.089 ²
BSRS ≥ 10	87	891.30(7.30)	<0.001 ³	108	45.29(0.75)	0.094 ³	105	46.53(1.10)	0.30 ³
Model 3			<0.001 ¹			<0.001 ¹			<0.001 ¹
BSRS ≤ 5	3200	872.02(1.18)		3580	46.54(0.13)		3555	47.64(0.19)	
BSRS 6–9	275	881.12(4.01)	0.032 ²	303	46.36(0.44)	0.69 ²	313	46.99(0.64)	0.33 ²
BSRS ≥ 10	87	886.46(7.20)	0.048 ³	108	45.86 (0.75)	0.37 ³	105	46.29 (1.10)	0.75 ³

¹Overall P value;

²BSRS 6–9 vs. BSRS ≤ 5 ;

³BSRS ≥ 10 vs. BSRS ≤ 5

Model 1: Adjusted for sex, age, and service specialty; Model 2: Adjusted for sex, age, service specialty, and body mass index; Model 3: Adjusted for sex, age, service specialty, body mass index, systolic blood pressure, diastolic blood pressure, current smoking, alcohol intake, hemoglobin, and exercise frequency.

reporting slight or great stress were less likely than those reporting normal psychological stress to mention they exercise more than once weekly (67.8% vs. 79.3%), similar to the U.S. survey report (54.0% vs. 64.0%).³³ Furthermore, the military members exercising less than once a week reported mental stress levels in the past weeks higher than those exercising once a week or more as well.

As is known, psychological stress is reciprocally related to physical activity. In a prospective U.S. cohort of 300 enlisted military personnel, those who had a lower summation score of

physical fitness at baseline exhibited more depressive symptoms at the end of an eight-week combat training course.¹⁰ However, the differential effects between aerobic and anaerobic fitness on the depressive symptoms were not approached. In contrast, a meta-analysis of 16 studies with a pooled 4,039 participants showed an inverse correlation of depressive symptom severity with cardiorespiratory fitness measured by maximal oxygen consumption in treadmill exercise.⁸ To our knowledge, the present study was the first one using a quantified self-report to evaluate mental stress severity

TABLE III. Multiple Linear Regression of Slight and Great Mental Stress Groups with Exercise Performances

	BSRS 6–9				BSRS ≥10			
	β	(SE)	95% CI	P value	β	(SE)	95% CI	P value
Model 1								
3000 m run	13.66	(4.42)	(4.99–22.33)	0.0020	22.09	(7.64)	(7.12–37.06)	0.0038
2-min sit-up	−0.59	(0.46)	(−1.50–0.32)	0.2029	−1.34	(0.77)	(−2.84–0.16)	0.0796
2-min push-up	−1.13	(0.68)	(−2.46–0.19)	0.0943	−1.38	(1.14)	(−3.61–0.85)	0.2254
Model 2								
3000 m run	13.63	(4.28)	(5.23–22.03)	0.0015	19.80	(7.40)	(5.29–34.30)	0.0075
2-min sit-up	−0.58	(0.46)	(−1.48–0.33)	0.2118	−1.28	(0.76)	(−2.78–0.22)	0.0936
2-min push-up	−1.14	(0.67)	(−2.44–0.17)	0.0886	−1.17	(1.12)	(−3.36–1.03)	0.2974
Model 3								
3000 m run	9.09	(4.25)	(0.76–17.42)	0.0324	14.44	(7.30)	(0.12–28.76)	0.0481
2-min sit-up	−0.19	(0.46)	(−1.09–0.72)	0.6875	−0.69	(0.76)	(−2.18–0.80)	0.3666
2-min push-up	−0.65	(0.67)	(−1.97–0.66)	0.3309	−0.35	(1.12)	(−2.55–1.84)	0.7532

Model 1: Adjusted for age and service specialty; Model 2: Adjusted for age, service specialty, and body mass index; Model 3: Adjusted for age, service specialty, body mass index, systolic blood pressure, diastolic blood pressure, heart rate, current smoking, alcohol intake, hemoglobin, and exercise frequency.

TABLE IV. Correlation of Slight and Great Mental Stress with Best 10% and Worst 10% of Exercise Performances

	BSRS 6–9			BSRS ≥10		
	OR	(95% CI)	P value	OR	(95% CI)	P value
For the best 10% performance level						
Model 1						
3000 m run ≤ 786 seconds	0.77	(0.57–1.05)	0.1038	1.16	(0.74–1.83)	0.5164
2-min sit-up ≥ 57 numbers	1.09	(0.74–1.60)	0.6603	0.34	(0.13–0.94)	0.0380
2-min push-up ≥ 60 numbers	0.87	(0.58–1.30)	0.4960	0.76	(0.38–1.53)	0.4453
Model 2						
3000 m run ≤ 786 seconds	0.77	(0.57–1.05)	0.1038	1.15	(0.73–1.82)	0.5368
2-min sit-up ≥ 57 numbers	1.09	(0.74–1.61)	0.6527	0.35	(0.13–0.95)	0.0399
2-min push-up ≥ 60 numbers	0.87	(0.58–1.31)	0.5017	0.79	(0.39–1.58)	0.5017
Model 3						
3000 m run ≤ 786 seconds	0.76	(0.56–1.04)	0.0863	1.12	(0.71–1.78)	0.6173
2-min sit-up ≥ 57 numbers	1.22	(0.83–1.82)	0.3148	0.41	(0.15–1.13)	0.0844
2-min push-up ≥ 60 numbers	0.98	(0.65–1.48)	0.9143	0.96	(0.47–1.94)	0.8992
For the worst 10% performance level						
Model 1						
3000 m run ≥ 984 seconds	1.58	(1.07–2.34)	0.0213	1.77	(0.95–3.31)	0.0734
2-min sit-up ≤ 39 numbers	1.25	(0.84–1.86)	0.2782	1.42	(0.74–2.73)	0.2970
2-min push-up ≤ 33 numbers	1.02	(0.71–1.46)	0.9150	1.29	(0.74–0.74)	0.3668
Model 2						
3000 m run ≥ 984 seconds	1.58	(1.06–2.35)	0.0243	1.69	(0.90–3.19)	0.1028
2-min sit-up ≤ 39 numbers	1.26	(0.84–1.89)	0.2629	1.41	(0.73–2.73)	0.3044
2-min push-up ≤ 33 numbers	1.01	(0.70–1.45)	0.9538	1.24	(0.71–2.18)	0.4488
Model 3						
3000 m run ≥ 984 seconds	1.50	(1.00–2.24)	0.0489	1.57	(0.83–2.97)	0.1702
2-min sit-up ≤ 39 numbers	1.10	(0.72–1.66)	0.6678	1.14	(0.58–2.23)	0.7072
2-min push-up ≤ 33 numbers	0.92	(0.64–1.33)	0.6575	1.07	(0.61–1.89)	0.8156

Model 1: Adjusted for age and service specialty; Model 2: Adjusted for age, service specialty, and body mass index; Model 3: Adjusted for age, service specialty, body mass index, systolic blood pressure, diastolic blood pressure, heart rate, current smoking, alcohol intake, hemoglobin, and exercise frequency.

from five psychopathology domains rather than only based on the aspect of depression. In addition, our study also confirmed an inverse association of psychological stress severity with aerobic fitness as the previous meta-analysis for the adverse effect of depression displayed. Moreover, we further demonstrated a novel finding that the relationship of

psychological stress severity with anaerobic fitness might not be present in the military personnel.

Our study had several strengths. First, all exercise tests and laboratory examinations were performed in a strict manner and the procedures were standardized. Second, large numbers of military participants were enrolled in this study provid-

ing sufficient power to detect the difference between those with and those without mental stress. Third, since the daily life of military such as diet, training, and stress source was unified in the county, many unmeasured confounders had been controlled at baseline. By contrast, there were some limitations in our study. First, women accounted for only one tenth of the military cohort, making it difficult to perform sex-specific analyses. Second, response bias in self-report measures might exist because of personal considerations to being good in the military personnel. Objective measures for mental stress such as plasma levels of stress-related hormones like testosterone, estrogen, and thyroid functions as well as the brain study of electroencephalography or functional magnetic resonance imaging would be helpful to confirm the association with physical fitness in advance. Third, the fitness tests would impose stress on military personnel, possibly influencing the results of the tests. The psychological impact of the fitness per se was not measured in this study. Fourth, even though a number of covariates were adjusted, we could not avoid the presence of other potential confounders that lead to a bias completely. Fifth, there seemed to have an inverse relationship that those who had slight psychological stress were more likely to be the best 10% performers in the 2-min sit-up test despite statistical insignificance. This paradoxical finding should be an area for further exploration.

In conclusion, our findings suggest that higher severity of psychological stress on military personnel may reduce their cardiorespiratory fitness but not affect the anaerobic fitness. As the first report to reveal the relationship of mental stress severity with aerobic and anaerobic fitness, further studies should be performed to examine the association by other psychological scoring systems.

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