SHORT COMMUNICATION

Sex differences in blood pressure responses to mental stress are abolished after a single bout of exercise: underlying hemodynamic mechanisms

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Abstract We aimed to investigate whether the pressor responses to mental stress (MS) are exaggerated in men due to heightened cardiac responses, before and after a bout of exercise. Fifteen men and 19 women underwent a protocol consisting of blood pressure (BP), cardiac output (CO) and forearm vascular assessments at baseline and during MS, and these measurements were performed before and 60 min after a bout of exercise. Before exercise, BP response was significantly augmented in men ($\Delta 16 \pm 2$ mmHg) compared to women ($\Delta 11 \pm 1$ mmHg). This BP response was accompanied by greater increases in CO in men and similar vascular responses between sexes. After exercise, BP and CO responses to MS were attenuated in men and, consequently, no sex differences were observed. Vascular responses were not affected by exercise. The mechanism underlying the lack of sex differences in BP response to MS after exercise was found to be a marked attenuation in CO in men only.

Keywords Sex differences · Cardiovascular system · Blood pressure control · Hemodynamics · Exercise · Mental stress

Introduction

Exaggerated cardiovascular responses to acute psychological stress have been prospectively linked to subsequent increase in resting blood pressure and development of cardiovascular diseases [1, 2]. Importantly, aerobic exercise has been proposed as a coping resource for stress management. A systematic review of 15 randomized controlled trials showed significant reductions in post-exercise stress-related blood pressure responses [3], which likely have important implications for cardiovascular health. In addition, we have recently shown that this attenuation in blood pressure response to mental stress after a bout of aerobic exercise seemed to be due to a blunted cardiac response [4]. Of note, these studies recruited predominantly men and were not designed to investigate the potential existence of sex differences in post-exercise mental stress-related blood pressure responses. Yet, this becomes important to be investigated given accumulated evidence demonstrating a sex-dependent blood pressure response to a mental stressor [5], where men exhibit an augmented blood pressure response compared with women.

Despite this general consensus for a sex-dependent blood pressure response to mental stress, the underlying physiological mechanisms remain unclear. Overall, previous studies suggest that it is unlikely related to endogenous levels of sex steroids [6], sympathetic vasoconstrictor drive [5] or differences in stress-induced forearm vasodilation [7]. Given this background, the purpose of the present study was to determine whether cardiac output and vascular responses contribute to an augmented pressor response to mental stress in men compared with women, before and after a maximal aerobic exercise bout. We hypothesized that blood pressure responses to mental stress are exaggerated in men due to heightened cardiac output responses, before and after a bout of exercise.

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Methods

Thirty-four volunteers (15 men and 19 women; age 18–31 years) were studied. No subject had a history or symptoms of cardiovascular, neurologic, or respiratory diseases. Subjects arrived at the laboratory after abstaining from caffeine and exercise for at least 24 h. Subject characteristics are provided in Table 1. Women were studied between the fourth and tenth day of the menstrual cycle, during the follicular phase. All experimental procedures and protocols were consistent with the principles of the Declaration of Helsinki, and were approved by the Institutional Review Boards of the Fluminense Federal University. All subjects provided written informed consent before the study.

The experimental protocol consisted of blood pressure and forearm vascular assessments at baseline and during mental stress (3 min, Stroop color–word test), and these measurements were performed before and 60 min after a maximal cardiopulmonary exercise test, as previously described [4, 8, 9]. Briefly, the Stroop color–word test consisted of a 3-min rapid slide presentation of different names displayed in different colors, and the subject was instructed to report the color and not the written word. In addition, this test was performed with continuous auditory conflict (headphones playing three taped noises or a taped voice saying different color names). Each subject was asked to assess the difficulty of the task according to previously established levels of difficulty: 0 = not stressful; 1 = slightly stressful; 2 = stressful; 3 = very stressful; and 4 = extremely stressful. The exercise bout consisted of a standard maximal cardiopulmonary exercise test

performed on a treadmill (Master ATL; Inbrasport, Porto Alegre, RS, Brazil). This consisted of 3 min of rest standing on the treadmill, 3 min of warm-up at 3 km h^{-1} and 0 % grade, ramp protocol with linear increase in speed and grade every minute until maximal voluntary exhaustion, and 5 min of recovery at 4 km h^{-1} and 0 % grade. The ramp protocol was individualized according to predicted maximal exercise capacity to reach volitional fatigue. Subjects were verbally encouraged to exercise until exhaustion. All subjects met at least two of the following criteria to confirm that maximal effort was attained: (1) respiratory exchange ratio >1.1; (2) heart rate within ±10 beats min^{-1} of the age-predicted maximum [210−(age/0.65)]; and (3) score 10 of perceived effort on Borg 0–10 scale. Ventilation, oxygen uptake, and carbon dioxide output were measured with each breath (CPX Ultima Gas Exchange System; Medgraphics, St Paul, MN, USA). Electrocardiogram was monitored through 12 leads (Welch Allyn CardioPerfect Workstation; Welch Allyn, Skaneateles Falls, NY, USA), and perceived exertion was assessed every minute. Breath-by-breath ventilation and expired gases were averaged to 20 s to identify peak oxygen consumption (VO$_2$ peak), which was considered the highest value of oxygen uptake during exercise.

Heart rate was monitored using a standard electrocardiogram and beat-to-beat blood pressure was measured using photoplethysmography (Finometer; Finapres Medical Systems, Amsterdam, The Netherlands). Blood pressure was also intermittently monitored from a standard sphygmomanometer, specifically during the last 2 min of the mental stress test. Beat-to-beat left ventricular stroke volume was estimated by modeling flow from the arterial pressure waveform (Modelflow; TNO Biomedical Instrumentation) [10, 11]. Briefly, Modelflow is a nonlinear three-element model that uses the arterial input impedance (including continuous correction for variations in the diameter), the compliance of the aorta, and total peripheral resistance to describe the relationship between aortic flow and pressure and thus compute stroke volume [10, 11]. Cardiac output was calculated multiplying heart rate by stroke volume. In addition, the cardiac index and stroke volume index were calculated, respectively, from beat-to-beat cardiac output and stroke volume divided by body surface area [body surface area (m^2) = 0.20247 × height (m)$^{0.725}$ × weight (kg)$^{0.425}$] [12]. The rationale for deriving cardiac index and stroke volume index relates to the importance of taking into consideration differences in body size when comparing men and women. Left ventricular contractility was estimated by dP/dt$_{max}$ of finger pressure pulse. Of note, with Doppler ultrasound, it was shown that Modelflow accurately tracks changes in both cardiac output and dP/dt$_{max}$ on a beat-to-beat basis [13]. In addition, the intraclass coefficient correlation was calculated to assess

Table 1 Subject characteristics

	Men ($n = 15$)	Women ($n = 19$)
Age	25 ± 2	24 ± 1
Height (cm)	175 ± 2	166 ± 1*
Weight (kg)	79 ± 3	60 ± 1*
BMI (kg m^{-2})	26 ± 0.9	22 ± 0.4*
VO$_2$ Peak mL (kg min)$^{-1}$	42 ± 2	31 ± 1*
Time to exhaustion (min)	10 ± 0.4	9.1 ± 0.4
Fasting glucose (mg dL^{-1})	85 ± 2	78 ± 2*
Fasting insulin (μIU mL^{-1})	4.0 ± 0.5	6.8 ± 0.8*
HOMA	0.8 ± 0.1	1.3 ± 0.2*
C-Reactive Protein (mg dL^{-1})	0.34 ± 0.04	0.45 ± 0.09
Total cholesterol (mg dL^{-1})	157 ± 8	161 ± 6
LDL cholesterol (mg dL^{-1})	93 ± 5	91 ± 5
HDL cholesterol (mg dL^{-1})	46 ± 3	56 ± 2*
TG (mg dL^{-1})	90 ± 13	69 ± 6

BMI body mass index, *TG* triglycerides

* Significantly different from men ($P < 0.05$)

Table 2 Resting hemodynamics variables

	Men ($n = 15$)	Women ($n = 19$)
SBP (mmHg)		
Before	120 ± 3	110 ± 1*
After	119 ± 3	109 ± 2*
DBP (mmHg)		
Before	75 ± 2	73 ± 1
After	76 ± 2	73 ± 2
MBP (mmHg)		
Before	90 ± 2	85 ± 1*
After	91 ± 1	85 ± 2*
CI (L min^{-1} m^{-2})		
Before	3.4 ± 0.2	3.6 ± 0.1
After	3.5 ± 0.2	3.4 ± 0.1
HR (beats min^{-1})		
Before	65 ± 1	75 ± 2*
After	69 ± 3	80 ± 2*
SVI (mL m^{-2})		
Before	50 ± 2	51 ± 2
After	49 ± 3	45 ± 2
dP/dt_{max} (mmHg s^{-1})		
Before	1,173 ± 53	1,203 ± 66
After	1,113 ± 53	1,125 ± 59
TVC (mL min^{-1} mmHg^{-1})		
Before	73 ± 4	73 ± 3
After	75 ± 4	68 ± 2
FBF (mL min^{-1} 100 mL)		
Before	1.9 ± 0.2	1.3 ± 0.1*
After	2.1 ± 0.2	1.4 ± 0.2*
FVC (mL min^{-1} 100 mL^{-1} 100 mmHg)		
Before	2.2 ± 0.2	1.5 ± 0.2*
After	2.2 ± 0.2	1.6 ± 0.2*

SBP systolic blood pressure, *DBP* diastolic blood pressure, *MBP* mean blood pressure, *CI* cardiac index, *HR* heart rate, *SVI* stroke volume index, total vascular conductance, *FBF* forearm blood flow, *FVC* forearm vascular conductance

* Significantly different from men ($P < 0.05$)

the intertechnique variability and was found to be high (ICC: 0.95; $P < 0.001$). Forearm blood flow was measured by venous occlusion plethysmography [8, 14]. The right arm was supported in a comfortable position, elevated above the level of the heart at a standardized height. Two cuffs were used; one (8 cm wide) was placed around the right wrist, and one (10 cm wide) was placed around the right upper arm. The arm cuff was attached to a rapid cuff inflator (EC6; Hokanson, Bellevue, WA, USA). The mercury in silastic strain gauge (Hokanson) was placed at the widest girth of the right forearm. The diameter of the strain gauge was 1 or 2 cm smaller than the widest girth of the forearm. To measure the BF, the wrist cuff was inflated to 220 mmHg 1 min before the onset of the FBF measurement to isolate the vascular circulation of the hand, and it was kept inflated throughout the blood flow measurement. At the beginning of all measurements, the evaluator generated a standard calibration pulse of 1 mV. The FBF was measured by rapidly inflating the cuff placed around the right upper arm to 50 mmHg (in <0.5 s), maintaining this pressure for 10 s and then rapidly deflating it to 0 mmHg for 10 s, thus completing a 20-s cycle. Forearm blood flow was calculated by a semiautomatic method, which has shown a high intra- and inter-evaluator reproducibility (intraclass correlation coefficients between 0.98 and 0.99) [14]. Forearm and total vascular conductance were calculated by dividing, respectively, FBF and cardiac output by the mean blood pressure.

All data are presented as mean ± SE. Peak changes were determined for each variable on the basis of the largest changes seen after onset of mental stress. Statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS). Cardiovascular responses to mental stress were analyzed in repeated measures analyses of variance (ANOVA) with a 2 (sex: men, women) × 2 (time: before exercise, after exercise) design. A Student–

Newman–Keuls test was used post hoc to investigate main effects and interactions. An unpaired t test was used to compare subjects' characteristics. The relationship of exercise capacity (i.e., VO$_2$ peak) and post-exercise stress-related blood pressure response was evaluated by using a Pearson product moment correlation coefficient. Statistical significance was set at $P < 0.05$.

Results

As shown in Table 1, exercise capacity (i.e., peak oxygen uptake) and body mass index were higher in men, but time to exhaustion was similar between men and women. Table 2 reports resting hemodynamics variables for men and women before and 60 min after a bout of exercise. Blood pressure and forearm vascular conductance were higher in men, but resting cardiac index (i.e., cardiac output corrected for body surface area) was similar between males and females (Table 2). These resting absolute values were different 60 min after a bout of exercise (Table 2).

Before exercise, blood pressure response to mental stress was significantly exaggerated in men compared to women (Fig. 1), despite similar perceived stress score between groups (1.9 ± 0.2 vs. 2.0 ± 0.1 AU, respectively, men and women) and greater increases in total vascular conductance (Fig. 2b). This heightened pressor response to mental stress, was also accompanied by significantly greater increases in cardiac output in men compared with women (Fig. 2a) and similar forearm vasodilation between sexes (Fig. 2c). Additionally, stroke volume (Fig. 2e) and dP/dt_{max} (Fig. 2f) were also augmented in men compared with women during mental stress before exercise. Heart rate during mental stress was not different between sexes before and after exercise (Fig. 2d). After exercise, the

blood pressure, total vascular conductance, cardiac output, stroke volume, and dP/dt_{max} responses to mental stress were markedly attenuated only in men and slightly in women and, consequently, no sex differences were apparent during this period (Figs. 1, 2). The magnitude of reduction in blood pressure response to mental stress after a bout of exercise was not associated to exercise capacity exercise capacity ($r = 0.25$, $P = 0.168$). Self-reported perceived stress levels and vascular responses to mental stress were not affected by exercise.

Discussion

Sex differences in cardiovascular responses during mental stress have been studied extensively, but the extent to which sexual dimorphism in cardiac output and left ventricular performance contributes to these differences has been lacking. Furthermore, it was also unknown if the attenuation in blood pressure response to mental stress after a bout of aerobic exercise could be influenced by whether the subject is male or female. This becomes important given accumulated evidence demonstrating that an acute bout of exercise (of moderate to high intensity) attenuates stress-related blood pressure responses [3, 4, 8]. The present study reports two new findings.

First, the exaggerated pressor response to mental stress in men was associated with a significantly rise in cardiac output compared with women. In addition, this was largely mediated by changes in stroke volume. This is supported by the marked increase in dP/dt_{max} that we observed only in men and by the lack of sex differences in heart rate response to mental stress. In line with this idea, Wainstein et al. [15] showed impairments to left ventricular filling with increased heart rate by right atrial pacing in women,

Fig. 1 Summary data for men and women showing the time course of the mean blood pressure responses (*MBP*; **a**) and percent changes (*MBP*; **b**) during mental stress before and 60 min after a bout of aerobic exercise. Values are means ± SEM. *Significantly different from the response observed before exercise ($P < 0.05$). #Significantly different between men and women ($P < 0.05$)
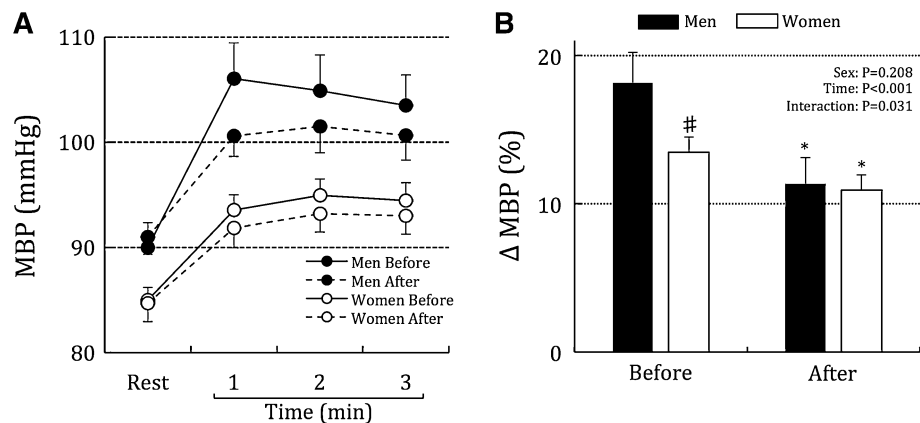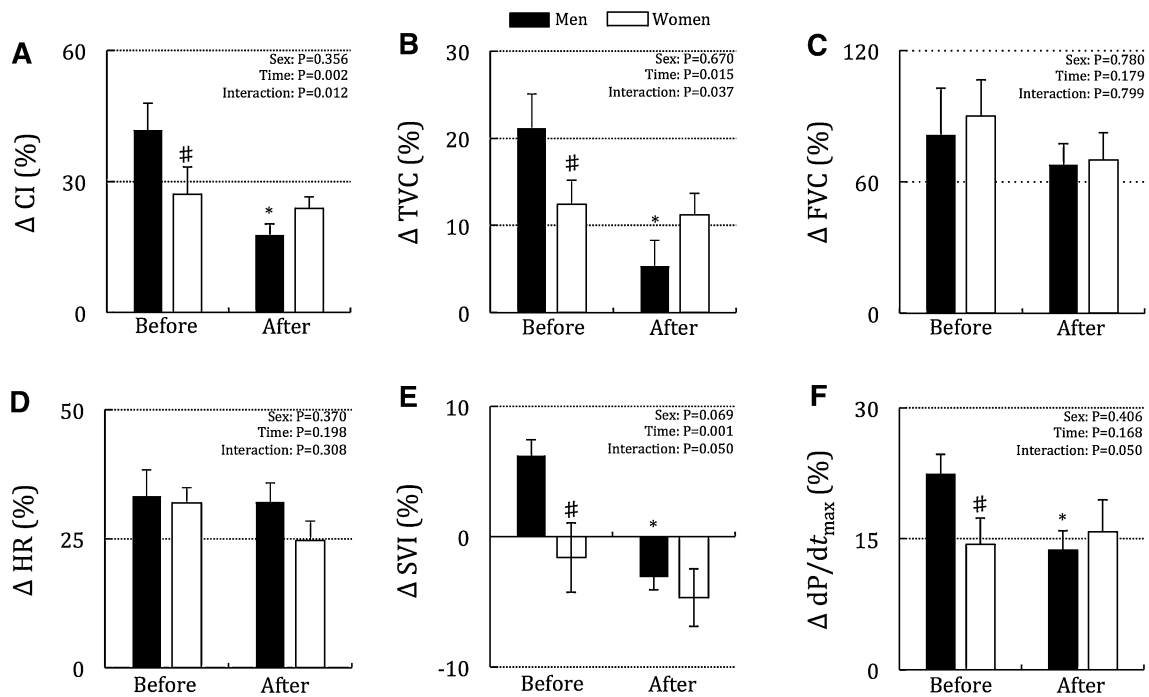
Fig. 2 Summary data for men and women showing peak changes in cardiac output corrected for body surface area (*CI*; **a**), total vascular conductance (*TVC*; **b**), forearm vascular conductance (*FVC*; **c**), heart rate (*HR*; **d**), stroke volume corrected for body surface area (*SVI*; **e**) and left ventricular performance (d*P*/d*t*$_{max}$; **f**) during mental stress before and 60 min after a bout of aerobic exercise. Values are means ± SEM. *Significantly different from the response observed before exercise ($P < 0.05$). #Significantly different between men and women ($P < 0.05$)

which appeared to limit an HR-associated rise in cardiac output in this group. Since left ventricular d*P*/d*t*$_{max}$ has been utilized as a determinant of recoil or diastolic suction [15], the current study appears to extend these findings to a more physiological stimulus by showing a reduced left ventricular performance (i.e., attenuated rise in d*P*/d*t*$_{max}$) during mental stress in young women compared with young men. Despite this, it is also possible that the left ventricular mass [16, 17] or a cardiac sympathetic mechanism contributes to our observation that cardiac responses to mental stress were augmented in men compared with women, although we acknowledge that this was not directly investigated as a part of the present study.

The second major finding is that sex differences in blood pressure reaction to mental stress were abolished following a bout of maximal exercise. Several studies have consistently shown significant reductions in post-exercise stress-related blood pressure responses [3, 4]. The present study, however, provides persuasive evidence that the attenuation in blood pressure response to mental stress after a bout of aerobic exercise in healthy young adults is markedly observed in men only. Furthermore, the hemodynamic mechanism underlying the lack of sex differences in blood pressure response to mental stress after exercise was found to be a marked attenuation in cardiac responses (i.e., cardiac output, stroke volume, and d*P*/d*t*$_{max}$) in men. Despite

the importance of this finding, it is difficult to determine which mechanism is responsible for this. One reasonable possibility is that β-adrenergic receptors are desensitized following strenuous exercise, which may explain attenuated cardiac responses to mental stress. In support of this possibility, Hart et al. [10] demonstrated in healthy male subjects that left ventricular function is attenuated at rest following a prolonged bout of rowing and in response to β-adrenergic receptor stimulation, regardless of changes in heart rate. In addition, the desensitization of the β-adrenergic receptors may also be contributing to a post-exercise reduction in total vascular conductance during mental stress, since a role for these receptors in mediating vasodilation during mental stress has previously been established [11]. Nonetheless, the investigation of these possibilities is beyond the scope of the present study and consequently remains to be determined. Of note, despite differences in exercise capacity between men and women, our main findings are unrelated to VO$_2$ peak ($r = 0.25$, $P = 0.168$), and this is in line with previous studies [3, 18, 19], indicating that fitness level does not have an effect on post-exercise stress-related blood pressure response. Collectively, our findings extend the scope of these previous studies [3, 4] by indicating that the magnitude of blood pressure stress buffering effect of acute exercise is influenced by whether the subject is male or female.

In the present study, resting blood pressure was not lower after exercise, indicating the absence of post-exercise hypotension. It is well established that the post-exercise hypotension phenomenon is quite variable and fundamentally depends on several different factors [20], such as intensity and duration of the exercise, resting pre-exercise blood pressure values, body position, and muscle mass, or may not even occur [3, 4, 8]. In the present study, this phenomenon was not observed, likely because of the characteristics of the exercise bout, i.e., progressive dynamic exercise to exhaustion of about 10-min duration. Another finding was that forearm vasodilation during mental stress was not different between sexes, regardless the moment of the mental task (i.e., before or after a bout of exercise). It is important to note that a plethora of studies have demonstrated forearm vasodilation during a mental stress, which confirms its consistence. Yet, the mechanisms mediating this response are still unresolved, but it is known that nitric oxide [21], circulating catecholamine levels [22], and β-adrenergic receptors sensitivity [23] are important contributors. Based on our results, mechanisms underlying the sex-dependent blood pressure responses to mental stress are unlikely related to stress-induced forearm vasodilation.

Several limitations of the design and interpretation of the present investigation should be considered. First, it could be argued that men are more reactive to a mental stress simply because they engage more with the Stroop color test. However, in the present study, the heightened blood pressure response in men before exercise was associated with a similar perceived stress level compared with women. In addition to this, male subjects exhibited a substantial attenuation in cardiovascular reaction to a mental stress following a bout of exercise, although reporting a similar perceived stress level compared to their values observed before exercise. Given this, it is possible that perceived stress level is not a determinant of the magnitude of cardiovascular responses to mental stress before and after exercise. In support of this idea, Carter and Ray [5] demonstrated that women perceive the mental arithmetic trial as more stressful than their male counterparts, despite their significantly reduced hypertensive response to the mental arithmetic trial. Second, the present work used a maximal exercise bout (high intensity exercise) to support the usefulness of an acute bout of exercise in buffering the cardiovascular response to a psychological stress. The rationale for using a high intensity exercise bout is based on previous studies [3, 24] that failed to support exercise as a coping resource for stress management when a relatively low to moderate intensity were used. Given this, our major findings should be extrapolated and interpreted with caution. Moreover, further studies should investigate whether a regular session of aerobic exercise training yields similar results. Third, blood flow was measured in the forearm and this variable was used as a proxy of general vascular responses to acute mental stress. Given the heterogeneity throughout the arterial tree [25], our vascular data may not represent, for example, vascular responses in the lower limbs.

Conclusion

In conclusion, these findings highlight for the first time a potential role for cardiac output and left ventricular performance in mediating the exaggerated blood pressure response to mental stress in men, as well as how exercise could benefit only male healthy adults in regards to the cardiovascular reactivity during a mental stress.

Conflict of interest None to declare.

References

1. Carroll D et al (2012) Increased blood pressure reactions to acute mental stress are associated with 16-year cardiovascular disease mortality. Psychophysiology 49(10):1444–1448
2. Carroll D et al (2011) Blood pressure reactions to acute mental stress and future blood pressure status: data from the 12-year follow-up of the West of Scotland Study. Psychosom Med 73(9):737–742
3. Hamer M, Taylor A, Steptoe A (2006) The effect of acute aerobic exercise on stress related blood pressure responses: a systematic review and meta-analysis. Biol Psychol 71(2):183–190
4. Neves FJ et al (2012) Hemodynamic mechanisms of the attenuated blood pressure response to mental stress after a single bout of maximal dynamic exercise in healthy subjects. Braz J Med Biol Res 45(7):610–616
5. Carter JR, Ray CA (2009) Sympathetic neural responses to mental stress: responders, nonresponders and sex differences. Am J Physiol Heart Circ Physiol 296(3):H847–H853
6. Carter JR, Lawrence JE (2007) Effects of the menstrual cycle on sympathetic neural responses to mental stress in humans. J Physiol 585(Pt 2):635–641
7. Harris CW et al (2000) Effects of mental stress on brachial artery flow-mediated vasodilation in healthy normal individuals. Am Heart J 139(3):405–411
8. Medeiros RF et al (2011) Impaired hemodynamic response to mental stress in subjects with prehypertension is improved after a single bout of maximal dynamic exercise. Clinics (Sao Paulo) 66(9):1523–1529
9. Nobrega AC et al (2008) Cholinergic stimulation with pyridostigmine prevents the impairment in ventricular function during mental stress in coronary artery disease patients. Int J Cardiol 125(3):418–421

10. Jansen JR et al (2001) A comparison of cardiac output derived from the arterial pressure wave against thermodilution in cardiac surgery patients. Br J Anaesth 87(2):212–222

11. Wesseling KH et al (1993) Computation of aortic flow from pressure in humans using a nonlinear, three-element model. J Appl Physiol 74(5):2566–2573

12. Du Bois D, Du Bois EF (1989) A formula to estimate the approximate surface area if height and weight be known. 1916. Nutrition 5(5):303–311; discussion 312-313

13. Kim A et al (2011) Sex differences in carotid baroreflex control of arterial blood pressure in humans: relative contribution of cardiac output and total vascular conductance. Am J Physiol Heart Circ Physiol 301(6):H2454–H2465

14. Silva BM et al (2009) Intra- and inter-tester reproducibility of venous occlusion plethysmography: comparison between a manual and a semi-automatic method of blood flow analysis. Physiol Meas 30(11):1267–1279

15. Wainstein RV, Sasson Z, Mak S (2012) Frequency-dependent left ventricular performance in women and men. Am J Physiol Heart Circ Physiol 302(11):H2363–H2371

16. Kop WJ et al (2000) Relationship between left ventricular mass and hemodynamic responses to physical and mental stress. J Psychosom Res 48(1):79–88

17. Zemva A, Rogel P (2001) Gender differences in athlete's heart: association with 24-h blood pressure. A study of pairs in sport dancing. Int J Cardiol 77(1):49–54

18. Roth DL (1989) Acute emotional and psychophysiological effects of aerobic exercise. Psychophysiology 26(5):593–602

19. Steptoe A, Kearsley N, Walters N (1993) Cardiovascular activity during mental stress following vigorous exercise in sportsmen and inactive men. Psychophysiology 30(3):245–252

20. da Nobrega AC (2005) The subacute effects of exercise: concept, characteristics, and clinical implications. Exerc Sport Sci Rev 33(2):84–87

21. Dietz NM et al (1994) Nitric oxide contributes to the rise in forearm blood flow during mental stress in humans. J Physiol 480(Pt 2):361–368

22. Lindqvist M et al (1996) Forearm vasodilator mechanisms during mental stress: possible roles for epinephrine and ANP. Am J Physiol 270(3 Pt 1):E393–E399

23. Lindqvist M, Melcher A, Hjemdahl P (1997) Attenuation of forearm vasodilator responses to mental stress by regional beta-blockade, but not by atropine. Acta Physiol Scand 161(2):135–140

24. Bartholomew JB (2000) Stress reactivity after maximal exercise: the effect of manipulated performance feedback in endurance athletes. J Sports Sci 18(11):893–899

25. Thijssen DH et al (2011) Relationship between upper and lower limb conduit artery vasodilator function in humans. J Appl Physiol 111(1):244–250