Effects of aerobic exercise training on sympathetic and renal responses to mental stress in humans

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Ray CA, Carter JR. Effects of aerobic exercise training on sympathetic and renal responses to mental stress in humans. Am J Physiol Heart Circ Physiol 298: H229–H234, 2010. First published November 13, 2009; doi:10.1152/ajpheart.00880.2009.—The effects of aerobic exercise training (ET) on muscle sympathetic nerve activity (MSNA) and renal vascular responses to mental stress (MS) have not been determined in humans. We hypothesized that aerobic ET would reduce MSNA and renal vascular constriction during MS. MSNA, mean arterial pressure (MAP), heart rate, renal blood flow velocity (RBFV), and peak oxygen uptake (V̇O₂peak) were measured in 23 healthy adults. Fourteen subjects participated in 8 wk of aerobic ET, while nine subjects served as sedentary controls (Con). ET significantly increased V̇O₂peak (Δ18 ± 1%; P < 0.001) and decreased RBFV at rest (60 ± 4 to 48 ± 3 cm/s; P < 0.01), whereas Con did not alter V̇O₂peak or RBFV. ET did not alter resting MSNA (11 ± 1 to 9 ± 1 bursts/min) or MAP (84 ± 2 to 83 ± 2 mmHg), and these findings were similar in the Con group. MS elicited similar increases in MSNA (−Δ2 bursts/min; P < 0.05), MAP (−Δ15 mmHg; P < 0.001), and heart rate (−Δ20 beats/min; P < 0.001) before and after ET, and the responses were not different between ET and Con. Likewise, MS elicited similar decreases in RBFV and renal vascular conductance before and after ET, and the responses were not different between ET and Con. Perceived stress levels during MS were similar before and after the 8-wk study in both ET and Con. In conclusion, ET does not alter MSNA and renal vascular responses to MS in healthy humans.

SYMPATHOEXCITATION DURING mental stress has been implicated as a potential risk factor for several cardiovascular diseases, including hypertension (9), myocardial infarction (7, 26), and atherosclerosis (27, 36). Therefore, the methods for reducing sympathetic neural responses to mental stress are clinically relevant. It was recently reported that diet combined with aerobic exercise training decreased muscle sympathetic nerve activity (MSNA) during resting conditions and mental stress (34). Unfortunately, this study examined only obese women, and it was unclear whether the reductions of MSNA were due to diet, exercise training, or the combination of diet and exercise. Thus the influence of aerobic exercise training on MSNA responses to mental stress remains equivocal.

In addition to eliciting sympathoexcitation, mental stress consistently causes renal vasoconstriction in humans (13, 15, 21, 23, 33). Elevated renal vascular resistance has been associated with essential hypertension (28); thus it is important to study interventions that may blunt the reduction of renal vasoconstriction during mental stress. Aerobic exercise training has been shown to blunt the reduction of renal blood flow during mental stress in borderline hypertensive rats (19), yet no studies have examined the influence of aerobic exercise training on renal blood flow during mental stress in humans.

Therefore, the purpose of the present study was to determine the influence of aerobic exercise training on MSNA and renal blood flow responses to mental stress in men and women. We hypothesized that 8 wk of aerobic exercise training would reduce MSNA and renal vascular responses to mental stress. Reductions of MSNA and/or renal vasoconstriction during mental stress could have significant cardiovascular health benefits.

METHODS

Subjects. Twenty-three healthy subjects (11 men and 12 women) participated in the study. All subjects were nonsmokers, nondiabetics, and were not taking any medications. All subjects were instructed to abstain from exercise, alcohol, and caffeine for 12 h before laboratory testing. The experimental protocol was approved by the Institutional Review Board at the Pennsylvania State University College of Medicine, and all subjects gave written informed consent before the study. This study conformed to the provisions of the Declaration of Helsinki.

Experimental design. Heart rate, mean arterial pressure (MAP), MSNA, and renal blood flow velocity were measured during 5 min of supine rest (baseline), 5 min of mental arithmetic (mental stress), and 5 min of supine rest (recovery) in all subjects before (Pre) and after (Post) the 8-wk training study. Subjects were randomly assigned to the exercise training group (n = 14; 8 men and 6 women) or sedentary control group (n = 9; 3 men and 6 women). Subjects in the exercise training group were permitted to select either running (n = 8; 4 men and 4 women) or stationary cycling (n = 6; 4 men and 2 women) as their exercise for the 8-wk training period. Peak oxygen uptake (V̇O₂peak) was also determined before and after the 8-wk study in all subjects.

Training protocol. Exercise training consisted of running or cycling 4 times/wk for 8 wk. Subjects wore a Polar heart rate monitor (Polar S610; Polar Electro; New York, NY) during all exercising sessions to monitor peak heart rate with a recovery period between each high-intensity exercise bout. Runners performed one sprint interval and one hill interval per week. Subjects initially performed four intervals per day and were increased to seven per day as training progressed. Sprint intervals consisted of 30 s sprint, 1 min recovery, 1 min sprint, and 2 min recovery performed on a flat course. Hill intervals consisted of an uphill sprint and downhill recovery on a 0.1-mile course at 6% grade (weeks 2–5) or 10% grade (weeks 6–8). Stationary cyclists performed 2 days of bike intervals per week. Bike intervals consisted of increased power...
output for 30 s, 1 min recovery, 1 min increased power output, and 2 min recovery. All interval sessions were preceded and followed by 15 min of moderate exercise that elicited ~60% of maximum heart rate.

**Mental stress.** Mental stress was elicited by mental arithmetic. During mental stress, subjects repeatedly subtracted the number six or seven from a two- or three-digit number. Subjects answered verbally and were encouraged by the investigators to subtract as fast as possible. An investigator provided a new number to subtract from every 5–10 s. The subtraction number, six or seven, was randomized. Subjects were asked to rate their perceived stress following mental stress using a standard five-point scale of 0 (not stressful), 1 (somewhat stressful), 2 (stressful), 3 (very stressful), and 4 (very, very stressful) (2, 5). Subject-perceived stress levels were recorded after each mental stress trial.

**Measurements.** Multifiber recordings of MSNA were measured directly by inserting a tungsten microelectrode into the peroneal nerve posterior to the fibular head. A reference electrode was inserted subcutaneously 2 to 3 cm from the recording electrode. Both electrodes were connected to a differential preamplifier and then to an amplifier where the nerve signal was band-pass filtered (700–2,000 Hz) and integrated at a time constant of 0.1 s to obtain a mean voltage display of nerve activity. Satisfactory recordings of MSNA were defined by spontaneous, pulse-synchronous bursts that did not change during arousal or stroking of the skin.

Duplex ultrasound (HDI 5000, ATL Ultrasound, Bothell, WA) was used to measure renal blood flow velocity. The renal artery was scanned using the anterior abdominal approach while the subject was lying supine. To scan the arteries, a curved-array transducer (2–5 MHz) with a 2.5-MHz pulsed-Doppler frequency was used. The probe insonation angle to the renal artery was <60°. The focal zone was set at the depth of the target artery. The transducer was held in the same place to record velocity tracings during each trial, and the data were obtained in the same phase of the respiratory cycle. Each cardiac cycle Doppler tracing was analyzed using the software of the ATL machine to obtain renal blood flow velocity measurements. A minimum of five heartbeats were averaged for each minute for the whole experimental protocol. The ratio of blood flow velocity and MAP was used as an index of renal vascular conductance (RVC).

Arterial blood pressure was measured using two techniques. Resting arterial blood pressure was measured three consecutive times (separated by ~1-min intervals) using an automated sphygmomanometer and reported as a mean value. Beat-to-beat arterial blood pressure was recorded continuously via Finometer (Finapres Medical Systems, Amsterdam, The Netherlands). The Finometer allowed us to determine precise changes in blood pressure during mental stress, whereas the sphygmonomanometer allowed us to compare baseline arterial pressures. Arterial blood pressures are expressed as MAP. Heart rate was recorded using a three-lead electrocardiogram.

VO\textsubscript{2max} was determined by maximal graded exercise test on a cycle ergometer (Lode, The Netherlands; workload increased 30 W each mental stress trial. Mental stress was elicited by mental arithmetic. Resting heart rate, MAP, MSNA, and renal blood flow velocity were similar between groups before the study. VO\textsubscript{2peak} increased in the exercise training group (Δ18 ± 1%; P < 0.001) but did not in the control group (Δ1 ± 1%). Despite this significant training effect, aerobic exercise training did not alter resting heart rate, MAP, and MSNA (Table 1). However, heart rate at 120 W of the maximal-graded exercise test was significantly reduced after 8 wk of exercise training (Δ−9 ± 2 beats/min; P < 0.01); this reduction of heart rate during submaximal exercise was not observed in the control group (Δ0 ± 3 beats/min). In addition to the alteration of VO\textsubscript{2peak} and heart rate, exercise training reduced both renal blood flow velocity and conductance at rest (Table 1).

Mental stress increased heart rate and MAP in both the exercise training and control groups, and these increases were similar before and after the 8-wk study in both groups (Fig. 1). Heart rate and MAP returned to baseline levels during recovery in all trials. Mental stress elicited significant increases of MSNA in the exercise training group but not in the control group (Fig. 2). The increases in MSNA in the exercise training group were similar before and after the 8-wk exercise training regimen.

Figure 3 shows that mental stress elicited a consistent increase in renal blood flow velocity during all trials, which returned to baseline levels during recovery. Whereas the changes in renal blood flow velocity were not influenced by the time (Pre vs. Post) or group (exercise training vs. control), exercise training decreased the absolute values of renal blood flow velocity during mental stress. Mental stress elicited a similar reduction of renal vascular conductance during all trials (Fig. 3).

Perceived stress levels during mental stress were similar before and after the 8-wk study in both the exercise training groups.

**RESULTS**

Resting baseline values for the aerobic exercise training group and control group are presented in Table 1. Age, height, weight, and body mass index were similar between groups. Resting heart rate, MAP, MSNA, and renal blood flow velocity were similar between groups before the study. VO\textsubscript{2peak} increased in the exercise training group (Δ18 ± 1%; P < 0.001) but did not in the control group (Δ1 ± 1%). Despite this significant training effect, aerobic exercise training did not alter resting heart rate, MAP, and MSNA (Table 1). Howev
group (2.8 ± 0.2 vs. 2.7 ± 0.2 AU) and control group (3.0 ± 0.2 vs. 3.1 ± 0.2 AU).

DISCUSSION

This study examined the effects of aerobic exercise training on MSNA and renal blood flow responses to mental stress in humans. It is important to study nonpharmacological methods of reducing MSNA and/or renal vasoconstriction during mental stress, since mental stress is a well-recognized contributor to several cardiovascular diseases. The novel findings of this study are that aerobic exercise training does not alter MSNA and renal vascular responses to mental stress.

Several studies have attempted to determine whether aerobic exercise training reduces catecholamine responses to mental stress (1, 4, 5, 30, 31). In general, aerobic exercise training does not appear to influence catecholamine responses to mental stress, although one study reported that aerobic exercise training tended to reduce cardiovascular and catecholamine responses to mental stress (1). More recently, the effects of diet and aerobic exercise on sympathetic neural responses to mental stress are not well understood.

Fig. 1. Changes in heart rate (HR) and mean arterial pressure (MAP) during mental stress (MS) after 8 wk of exercise training or sedentary control. MS increased HR and MAP in both our exercise training and control groups, and these increases were similar before (Pre) and after (Post) the 8-wk training study in both groups. Base, baseline; Rec, recovery; bpm, beats/min. Values are reported as means ± SE; n, number of subjects.

Fig. 2. Changes in muscle sympathetic nerve activity (MSNA) during MS after 8 wk of exercise training or sedentary control. MS increased MSNA burst frequency in our exercise training group, and these increases were similar before and after training. AU, arbitrary units. Values are reported as means ± SE; n, number of subjects.
stress were examined in obese women (34). Interestingly, diet and aerobic exercise not only reduced resting MSNA but also reduced MSNA responses to mental stress. Unfortunately, the study was restricted to obese women, and the experimental design did not allow the authors to definitively determine whether the reductions of MSNA were primarily due to the diet or the exercise training. The aim of the present study was to determine whether aerobic exercise training alters sympathetic neural responses to mental stress by conducting a well-controlled study in which aerobic exercise training was the primary, and only, intervention employed.

Our results indicate that aerobic exercise training does not alter MSNA responses to mental stress. These findings are in agreement with previous studies examining catecholamine responses to mental stress and exercise training (1, 4, 5, 30, 31). Differences between our findings and Tonacio et al. (34) are likely related to differences in subject demographics (obese women vs. healthy young men and women) and the experimental design (diet combined with aerobic exercise vs. only aerobic exercise). Nevertheless, our data indicate that aerobic exercise training does not alter sympathetic neural responses to mental stress in healthy men and women.

Aerobic exercise training did not alter resting MSNA in the present study. Wallin et al. (35) have reported a significant positive correlation between MSNA and renal norepinephrine spillover in humans. This finding indicates that in healthy humans, resting renal sympathetic nerve activity (RSNA) is comparable with or proportional to MSNA. If this relation is maintained following exercise training, this would suggest that RSNA was not changed in the present study because MSNA was not altered by exercise training. This finding would diminish the likelihood of an increase in RSNA as a possible factor in mediating the change in renal blood flow velocity and conductance after exercise training. However, this does not

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**Fig. 3.** Renal blood flow velocity (RBFV) and renal vascular conductance (RVC) during MS after 8 wk of exercise training or sedentary control. Aerobic exercise training significantly reduced RBFV at rest and during MS, but the magnitude of these responses (i.e., change in RBFV and RVC) was similar before and after the 8-wk study in both groups. RVC was calculated using MAP measurements obtained from the Finometer. There was only a small difference observed between blood pressure at rest obtained using a cuff and that of the Finometer. Values are reported as means ± SE; n, number of subjects. *P < 0.05 vs. baseline; †P < 0.05 vs. corresponding pretraining value.
preclude the possibility of greater neurotransmitter release in the kidney to mediate lower renal vascular conductance following exercise training.

Additionally, it is relevant to note that the influence of aerobic exercise training on resting MSNA appears to be highly dependent on the preexisting health condition of an individual. Aerobic exercise training has been reported to decrease resting MSNA in patients with heart failure (6, 10, 25), hypertension (16), and acute myocardial infarction (22). In contrast, most (11, 24, 29, 32), but not all (12), studies performed in subjects without cardiovascular disease report that aerobic exercise training does not alter resting MSNA. Patients with cardiovascular disease (6, 10, 16, 22, 25) have much higher levels of resting MSNA compared with subjects without cardiovascular disease (11, 12, 24, 29, 32), suggesting that reductions of MSNA with aerobic exercise training may be partly dependent on the initial levels of MSNA at rest. Our data support this concept as our young, healthy subjects (with the low levels of MSNA at rest) demonstrated that aerobic exercise training did not alter resting MSNA.

Previous studies examining renal vascular responses to aerobic exercise training used whole body clearance of 131Ihippuran (8) to estimate renal plasma flow. However, these studies have led to conflicting results regarding the effects of aerobic exercise training on resting renal vascular flow and conductance. To our knowledge, the present study is the first to use ultrasound Doppler techniques to determine the effects of aerobic exercise training on renal blood flow velocity in humans. Our results indicate that aerobic exercise training leads to renal vasoconstriction. We recognize that the lower absolute resting renal blood flow velocity and conductance reported in the present study could have been a consequence of exercise training. It is important to note that the kidneys are overperfused at rest with a very low arterial-venous oxygen difference. Therefore, the apparent decrease in renal blood flow reported in the present study might not be of physiological significance because arterial-venous oxygen difference can be increased. Furthermore, reduced blood flow to the kidneys may facilitate a more rapid redistribution of blood flow to skeletal muscle. The mechanisms mediating these changes at rest are unknown. Further studies are needed to address this important finding.

It is well documented that mental stress elicits renal vasoconstriction (13, 15, 21, 23, 33), yet the influence of exercise training on renal vasoconstriction during mental stress has not been previously examined in humans. However, aerobic exercise training has been shown to blunt the reduction of renal blood flow during psychological stress in borderline hypertensive rats (19). We hypothesized that aerobic exercise training would reduce renal vasoconstriction during mental stress. Contrary to our original hypothesis, aerobic exercise training did not alter changes in renal blood flow velocity or renal vascular conductance during mental stress. This response occurred despite lower absolute values of renal blood flow velocity.

In the current study, Doppler ultrasound could not accurately measure renal artery diameter. Thus we are unable to be certain that mental stress did not elicit changes in renal diameter. However, evidence suggests that pharmacological-mediated renal vasoconstriction (18) and vasodilation (17) do not alter diameter of the renal artery. Furthermore, the vessel we examined was a conduit and not a resistance vessel. Therefore, it is unlikely that changes in renal artery diameter during mental stress influenced the results of the study. However, if differences in renal diameter do occur as the result of exercise training, this could have affected our results and subsequent interpretation.

The training period (i.e., 8 wk) and stressor (i.e., 5 min of mental arithmetic) used in the present study are commonly employed in studies examining the influence of exercise training and/or stress on neural control of the cardiovascular system. However, these interventions are relatively short in duration compared with the stress experienced over a lifetime. It is likely that chronic levels of physical activity and stress contribute importantly to neural and renal responses. The balance between chronic physical activity and stress may be a key factor in the development of cardiovascular disease. Future studies should examine neural and renal responses to stress and exercise in individuals with cardiovascular complications. Based on the ability of aerobic exercise training to reduce resting MSNA in patients with cardiovascular disease (6, 10, 16, 22, 25) and obesity (34), it is possible that aerobic training would reduce sympathoexcitation and renal vasoconstriction during mental stress in patients with cardiovascular diseases.

In conclusion, this study examined the effects of aerobic exercise training on sympathetic neural and renal blood flow responses to mental stress in humans. Our results demonstrate that aerobic exercise training does not alter MSNA or renal vascular responses to mental stress in young, healthy individuals.

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DISCLOSURES

No conflicts of interest are declared by the author(s).

REFERENCES

Mental Stress and Exercise Training


