Acute endurance exercise induces changes in vasorelaxation responses that are vessel-specific

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Muiras JM, Grise KN, Jiang M, Kowalchuk H, Melling CWJ, Noble EG. Acute endurance exercise induces changes in vasorelaxation responses that are vessel-specific. Am J Physiol Regul Integr Comp Physiol 304: R574–R580, 2013. First published December 12, 2012; doi:10.1152/ajpregu.00508.2012.—The dynamic adjustment and amplitude of the endothelium-dependent vasorelaxation of the carotid, aorta, iliac, and femoral vessels were measured in response to acute low-(LI) or high-intensity (HI) endurance exercise. Vasorelaxation to 10^-4 M ACh was evaluated in 10 control, 10 LI, and 10 HI rats. Two-millimeter sections of carotid, aorta, iliac, and femoral arteries were mounted onto a myography system. Vasorelaxation responses were modeled as a monoeXponential function. The overall (average of four vessel-type) % vasorelaxation was larger in LI (73 ± 16%) and HI (75 ± 16%) than in control (66 ± 19%) (P < 0.05). The overall rate of vasorelaxation was greater in LI (1.9 ± 0.9%·s^-1) and HI (1.1 ± 1.1%·s^-1) compared with control (1.0 ± 0.7%·s^-1) (P < 0.05). The vessel-specific responses (average response for the three conditions) showed that carotid displayed a slower adjustment (τ, 18.9 ± 5.4 s; time-to-steady-state, 30.4 ± 18.4 s) compared with the aorta (τ, 10.3 ± 3.8 s; time-to-steady-state, 46.3 ± 15.2 s), the iliac (τ, 6.2 ± 2.1 s; time-to-steady-state, 30.3 ± 9.0 s), and the femoral (τ, 6.0 ± 1.9 s; time-to-steady-state, 29.3 ± 8.4 s). The % vasorelaxation was larger in the carotid (82 ± 14%) than in the aorta (67 ± 16%), iliac (61 ± 13%), and femoral (71 ± 19%) (P > 0.05). The rate of vasorelaxation was carotid (1.1 ± 0.2%·s^-1), aorta (1.5 ± 0.4%·s^-1), iliac (2.2 ± 0.8%·s^-1), and femoral (2.6 ± 1.0%·s^-1). In conclusion, an acute bout of endothelium-dependent vasorelaxation exercise increased vascular responsiveness. The dynamic and percent adjustments were vessel-specific with vessel function likely determining the response.

endothelium-dependent vasorelaxation; vessel myography; vascular responsiveness; vascular kinetics

THE MATCHING OF BLOOD FLOW to the metabolic demands for oxygen and other nutrients throughout different organs is of critical importance to maintain cellular energetics and homeostasis (2). In this regard, relaxation of the vascular smooth muscle through diffusion of nitric oxide (NO) produced in the endothelial cells through the activation of endothelial NO synthase (e-NOS) has been shown to be fundamental (6, 9, 29). Although the positive effects of endurance exercise training on vascular responsiveness (and more specifically endothelium-dependent vasodilatation) have been demonstrated (12, 13, 15, 28), the effects of an acute bout of exercise on vascular responsiveness are poorly understood. For instance, an early study by Delp and Laughlin (5) showed no changes in the vasorelaxation response to a given dose of ACh in the aorta of rats 24 h after a single, 1-h bout of high-intensity endurance exercise. On the other hand, Haram et al. (15) demonstrated improved endothelium-dependent vasodilatation that peaked between 12 and 24 h following a single bout of high-intensity endurance exercise. Even though higher intensities of exercise are supposed to result in higher levels of shear stress [which is considered the most important stimulus for the continuous formation of NO (6)], and thus, have become obvious interventions for testing potential changes in vascular responsiveness, the effects of lower intensities of exercise [which are often the choice in different populations (11)] on vasorelaxation responses are unknown.

Modifications in vascular responsiveness to different types of interventions are often measured as changes in the dose-response to vasoactive substances as absolute and percent vasorelaxation (15, 20, 26, 31). We have recently described those changes examining the rate of adjustment of the vasorelaxation response to a given dose of ACh (23). This analysis, in addition to the determination of the percent vasorelaxation and the rate of vasorelaxation of a given vessel, provides information not only on the amplitude of the changes but also on the dynamic component of the vessel’s adjustment. In that study, we also demonstrated that the time course of the vasorelaxation response was vessel-specific, with the aorta artery displaying a slower adjustment compared with the iliac and femoral arteries. These data derived from conduit arteries located in different sections of the vascular tree, supported previous studies showing that more distal arterioles (AS) adjusted faster compared with the more proximal ones (1As) (27) and confirmed the idea that the responsiveness of the vessels might be affected by their morphology and/or location within the vasculature. As such, the use of the thoracic aorta (which has been prevalent in the literature during in vitro experimental setups) might limit the interpretation of the data as, in fact, it does not vasodilate significantly in vivo (32).

Hence, the main goals of this study were 1) to determine the rate of adjustment and amplitude of the endothelium-dependent vasorelaxation response to a single bout of low- or high-intensity endurance exercise; and 2) to compare the endothelium-dependent rate of adjustment in different arteries through-out the vascular tree: carotid, aorta, iliac, and femoral. An additional goal of this study was to explore potential mechanisms controlling the vasorelaxation response. As such, we measured e-NOS and heat shock protein 90 (Hsp90) [a protein responsible for the proper coupling of e-NOS (11)] content in each vessel segment. We hypothesized that a single bout of high-intensity endurance exercise (HI) would result in faster and larger responsiveness compared with the control group and the single bout of low-intensity endurance exercise (LI) group and that the iliac and the femoral vessels (located nearer the...
active muscles) would be more responsive than the carotid and aorta arteries. Additionally, we hypothesized that e-NOS and Hsp90 protein content would be elevated in the HI compared with the control and LI groups.

METHODS

Animal characteristics. This study was approved by the University of Western Ontario Council on Animal Care and was performed in accordance with the guidelines of the Canadian Council on Animal Care. Thirty male 8-wk-old Sprague-Dawley rats were obtained from Charles River Laboratories (St. Constant, QC, Canada) and housed in standard rat cages with a 12:12-h light-dark cycle at a constant temperature (20 ± 1°C) and relative humidity (50%) for 1 wk. Food and water were provided ad libitum.

Experimental protocol. Rats were randomly assigned to a control (n = 10; 306 ± 22 g), LI (n = 10; 317 ± 16 g), or HI (n = 10; 314 ± 17 g) group. To minimize the stress generated by treadmill running, the animals undertook two familiarization sessions of 10 min each that consisted of progressive running speeds at 15 m/min for 2 min, 24 m/min for 4 min, 30 m/min for 2 min, and 15 m/min for the last 2 min. The familiarization sessions were separated by 48 h and were performed 48 h prior to the acute bout of exercise. LI and HI exercised for 1 h on a motorized treadmill with a 2% grade at the speed of 15 m/min and 30 m/min, respectively. The exercise intensities were determined on the basis of earlier research that investigated oxygen uptake in rats at various treadmill running speeds, suggesting ~70–80 and 50–60% of VO2 max for the HI and LI groups, respectively (1). Because of the potential temperature effect on Hsp90, resting and end-exercise rectal temperatures were collected and recorded. Rats were killed 24 h after their last bout of exercise, as previous studies have demonstrated endothelium-dependent vasodilation to peak between 12 and 24 h after an acute bout of endurance exercise (15).

Vessel collection. Rats were anesthetized via an intraperitoneal injection of 65 mg/kg pentobarbital sodium and were killed via heart excision. The carotid, aorta, iliac, and femoral arteries were excised and immediately placed into ice-cold modified Krebs-Henseleit buffer (118.1 mM NaCl, 4.7 mM KCl, 1.5 mM CaCl2, 1.2 mM KH2PO4, 1.2 mM MgSO4, 11.1 mM D-glucose, and 25 mM NaHCO3, at pH 7.4). The vessels were cautiously cleaned of adjacent connective and adipose tissue. A portion of the carotid, abdominal aorta, iliac, and femoral artery was partitioned into ~2-mm-long rings, and following cautious removal of blood clots in the lumen, vessel rings were used for in vitro isometric tension studies. The remains of the vessels were segmented at arbitrary lengths, blood clots were detached, and the sections were snap-frozen in liquid nitrogen and successively stored at −70°C for additional analysis.

In vitro isometric tension analysis. Each vessel ring was mounted onto a GlobalTown Microtech EZ-bath system (GobalTown Microtech, Sarasota, FL) and immersed in 5 ml of modified Krebs-Henseleit buffer (37°C). The buffer was constantly oxygenated (gas mixture, 95% O2 and 5% CO2). The initial tension in the rings was manually adjusted to ~2 g in the aorta, ~1.5 g in the carotid and iliac, and ~1.0 g in the femoral artery. Pilot testing from our laboratory determined that these values were optimal for maintaining baseline tensions for each vessel section. Rings equilibrated at these tensions for ~40 min. The tension of each vessel was measured using force transducers that were calibrated before each experiment. Fresh buffer (5 ml) was added to organ baths at the end of the equilibration period. Isometric contractions and relaxations were measured with PowerLab (ML856 26T; ADInstruments, Colorado Springs, CO). Data were recorded using LabChart v7.0 (ADInstruments) at a sampling rate of 1,000 Hz. The vessels were preconstricted with 10−5 M phenylephrine (PE). When a steady-state level of constriction was achieved, vasorelaxation of the vessels was induced using a single dose of 10−4 M ACh (ACh condition) (23). The single-dose response was selected, as the main purpose of the analysis was to examine the kinetics of the vasorelaxation as opposed to curve shifts to a dose-response curve.

Data analysis. The on-transient vasorelaxation profiles were modeled using the following equation:

\[ Y(t) = Y_{\text{bsln}} - A(1 - e^{-(t-\tau)/Y_{\text{bsln}}}) \]

where \( Y_{\text{bsln}} \) represents the tension (g) at any given time; \( Y_{\text{bsln}} \) is the steady-state baseline value of \( Y \) before a decrease in the tension as a consequence of the vasorelaxation; \( A \) is the amplitude of the decrease in \( Y \) above \( Y_{\text{bsln}} \); \( \tau \) (time constant of the response) represents the time required to attain 63% of the steady-state amplitude; and TD represents the mathematically generated time delay through which the exponential model is predicted to intersect \( Y_{\text{bsln}} \). Vasorelaxation responses were modeled to ~2 min because the relaxation effects following ACh infusion are known to be transient due to the chemical instability of endothelium-derived relaxing factors (16). The model parameters were estimated by least-squares nonlinear regression (Origin, OriginLab, Northampton, MA), in which the best fit was defined by minimization of the residual sum of squares and minimal variation of residuals around the y-axis (\( \gamma = 0 \)). The 95% confidence interval (CI95) for the calculated time constant was calculated after preliminary fit of the data with \( Y_{\text{bsln}}, A, \text{and TD} \) constrained to the best-fit values and the \( \tau \) allowed to vary. The calculated time delay for the vasorelaxation response (TD) was estimated using second-by-second data and was associated to the time, after ACh infusion, at which the signal started a systematic decrease from its steady-state constriction value. The time-to-steady-state represented the CTD + 4\( \tau \) (with 4\( \tau \) being ~98% of the total adjustment) represents the total time for the vasorelaxation response to be completed. It is acknowledged that the physiological CTD is composed of a diffusion time of ACh to the endothelium and the time taken for the response to develop once the muscarinic receptors were activated. Although it cannot be determined which one of these components contributes more to the CTD, ACh was consistently applied in the same place in the organ bath (as close as possible to the vessel). As such, the diffusion time was kept consistent across experimental conditions, and it was reduced to its minimum expression under the experimental conditions. The rate of vasorelaxation was calculated as percent vasorelaxation/time-to-steady-state (−%/s) and represented the interaction between the kinetics and the % vasorelaxation component. Baseline constriction values were calculated as the mean value in the 30 s prior to a transition.

Western blotting. Sections of vessels that were not used for myography measurements were minced and homogenized in 100 μl of homogenizing buffer [25 mM Tris, 137 mM NaCl, 1% Triton X-100 (pH 7.4–7.5)] that included a cocktail of protease and phosphatase inhibitors (Sigma P8340, P0044, and P5726) using a glass Dounce homogenizer and then transferred into 1.5 ml microcentrifuge tubes. Samples were kept on ice for the entire protocol. The microcentrifuge tubes were later centrifuged at 14,000 g for 10 min at 4°C. Supernatants were removed and placed into new microcentrifuge tubes for storage at −70°C. Sample protein content was determined using a Bradford assay, and 30–50 μl of protein homogenate was equally loaded into each well (depending on the protein content, such that each vessel type had the same amount of total protein loaded, as subsequently corroborated by Ponceau S staining). A human endothelial cell lysate (BD 611450) was used as the positive control. Electrophoresis was performed, and proteins were separated by running through a 6% polyacrylamide gel for 1 h at 100 V. Proteins were electrophoretically transferred to a nitrocellulose membrane for ~2 h at 100 V. They were blocked with 5% nonfat dry milk (Bio-Rad, Hercules, CA; 170–6404) in Tween-Tris buffered saline (TTBS; 10 mM Tris, 100 mM NaCl, 0.1% Tween-20, pH 7.5) for 1 h at room temperature. Subsequently, they were washed in TTBS (3 × 10 min) and then incubated with primary antibody specific for e-NOS (mouse monoclonal anti-e-NOS IgG, BD 610297; 1:2,000) overnight at 4°C.
The next day, membranes were incubated with horseradish peroxidase-conjugated secondary antibody specific for mouse IgG (goat anti-mouse IgG-HRP conjugate, Bio-Rad 170-6516; 1:5,000). Protein bands were visualized and captured on digital camera using a Bio-Rad Chemidoc XRS imager, and optical density was quantified using Bio-Rad Quantity One software. Optical density was normalized to the appropriate standards. The Western blots used for the immunodetection of e-NOS protein were subsequently stripped by incubation in stripping buffer [62.5 mM Tris·HCl (pH 6.7)-100 mM 2-mercaptoethanol-0.2% SDS] for 30 min. The membranes were then washed with Tris-buffered saline-1% Tween 20, blocked with 5% milk, and reblotted with Hsp90 antibody (mouse monoclonal anti-Hsp90 IgG, BD 610418, 1:2,000) for the detection of Hsp90 protein. The next day, they were incubated with horseradish peroxidase-conjugated secondary antibody specific for mouse IgG (goat anti-mouse IgG-HRP conjugate, Bio-Rad 170-6516; 1:5,000).

Statistics. Data are presented as means ± SD. A two-way repeated-measures ANOVA was used to determine statistical significance for the dependent variables. The ANOVA model was described as G3 × V4 such that groups (G; control, LI, and HI) were crossed with condition vessels (V; carotid, aorta, iliac, and femoral). A Tukey post hoc analysis was used when significant differences were found for the main effects of each dependent variable. The ANOVA was analyzed by SPSS version 15.0. (SPSS, Chicago, IL). Statistical significance was declared when P < 0.05.

RESULTS

Figure 1, A–D depicts typical responses observed in each vessel. Kinetics parameters, the rate of vasorelaxation, and the percent relaxation for each vessel in each condition are presented in Fig. 2, A–C. Analysis by vessel type revealed that the carotid displayed a slower rate of adjustment (τ, 18.9 ± 4.4 s; time-to-steady-state, 80.4 ± 18.4 s) compared with the aorta (τ, 10.3 ± 3.8 s; time-to-steady-state, 46.3 ± 15.2 s), the iliac (τ, 6.3 ± 2.1 s; time-to-steady-state, 30.3 ± 9.0 s), and the femoral (τ, 6.0 ± 1.9 s; time-to-steady-state, 29.3 ± 8.4 s). Similarly, the responsiveness of the aorta was slower than that of the iliac and femoral arteries. The % vasorelaxation was larger in the carotid (82 ± 14%) than in the aorta (67 ± 16%), iliac (61 ± 13%), and femoral (71 ± 19%) (P < 0.05). Additionally, the % vasorelaxation of the femoral was larger than the iliac (P < 0.05). As a consequence, the rate of vasorelaxation was progressively greater in each vessel type: carotid (1.1 ± 0.2%·s⁻¹), aorta (1.5 ± 0.4%·s⁻¹), iliac (2.2 ± 0.8%·s⁻¹), and femoral (2.6 ± 1.0%·s⁻¹). There was no main effect for the CTD (carotid, 4.8 ± 1.5 s; aorta, 5.3 ± 1.4 s; iliac, 5.1 ± 1.5 s; femoral, 5.2 ± 2.4 s) for vessel type (P > 0.05). The CI95 differed between vessels such that the carotid (0.6 ± 0.2 s) was larger than the aorta (0.5 ± 0.1 s), iliac (0.4 ± 0.2 s), and femoral (0.3 ± 0.1 s) (P < 0.05). Similarly, the CI95 for the aorta was larger than that of the iliac and femoral.

The overall τ (control, 10.5 ± 6.0 s; LI, 10.4 ± 5.7 s; HI, 11.0 ± 6.9 s), and time-to-steady-state (control, 47.6 ± 24.0 s; LI, 46.2 ± 22.8 s; HI, 49.1 ± 28.3 s) of the vasorelaxation response was similar in all groups (control, 2.9 ± 1.1 g; LI, 2.8 ± 1.0 g; HI, 2.8 ± 1.0 g), the % vasorelaxation was larger in LI (73 ± 16%) and HI (73 ± 16%) than in control (66 ± 19%) (P < 0.05), and the rate of vasorelaxation was also greater in LI (1.9 ± 0.9%·s⁻¹) and HI (1.9 ± 1.1%·s⁻¹) compared with control (1.6 ± 0.7%·s⁻¹; Fig. 3) (P < 0.05). Neither the CTD (control, 5.5 ± 1.9 s; LI, 4.6 ± 1.2 s; HI, 5.2 ± 1.7 s) nor the CI95 (control, 0.4 ± 0.2 s; LI, 0.5 ± 0.2 s; HI, 0.4 ± 0.2 s) were affected by condition. Although no main effect for vessel type was observed for e-NOS protein content, there was a trend toward lower e-NOS content in the femoral (34 ± 28%) compared with the carotid (57 ± 49%). The e-NOS protein content was significantly lower in HI (35 ± 32% standard) compared with control (55 ± 45%) (P < 0.05) but not LI (49 ± 46%) (P > 0.05; Fig. 4).

Fig. 1. Model fits for a representative carotid (A), aorta (B), iliac (C), and femoral (D).
Resting rectal temperatures were similar in all groups (control, 35.0 ± 0.5°C; LI, 35.2 ± 0.3°C, and HI; 35.3 ± 0.6°C) (P > 0.05). End-exercise rectal temperatures were significantly higher during exercise (LI, 37.1 ± 0.7°C; HI, 38.1 ± 0.7°C) compared with resting conditions and in HI compared with LI (P < 0.05).

**DISCUSSION**

This study examined the dynamic adjustment and amplitude changes of the endothelium-dependent vasorelaxation in different conduit arteries throughout the vascular tree in response to a single bout of low- or high-intensity endurance exercise. The main findings were that 1) although the % vasorelaxation was the largest in the carotid artery, the dynamic adjustment rate of vasorelaxation were faster in the femoral and iliac vessels compared with the aorta and the carotid. This suggests that the amplitude and the dynamic adjustment of the vascular responses may be under differential control. 2) In the absence of changes in dynamic adjustment per se, HI and LI resulted in a larger % vasorelaxation and thus in a greater rate of vasorelaxation compared with the control condition.

An important finding from the present investigation was the vessel-specific vasorelaxation response to similar concentrations of ACh. This differential response might be determined by function and/or location and/or morphology of each individual vessel. The iliac and femoral, which are closest to the active muscles during locomotion and play an important functional role for distribution of “bulk” blood flow to the sites in highest metabolic demand, displayed the fastest rate of adjustment (τ, and time-to-steady-state) compared with the aorta and the carotid. We have previously reported similar responses in the femoral, iliac, and aorta arteries of control and diabetic animals (23). This is relevant because the majority of previous myography studies limited the analysis to the aorta, likely because of the simplicity of the experimental preparation. However, it is known that the aorta relaxes only marginally compared with other distal vessels (32). One of the novel aspects of the present investigation is the addition of the responses in the carotid artery. Interestingly, the carotid had the slowest rate of adjustment compared with all the other vessels. Considering the morphological characteristics (diameter, lumen-to-wall ratio, surrounding tissue) and location of the carotid, a response more similar to the iliac vessel could be

Hsp90 analysis by vessel type showed a larger protein content in the aorta (292 ± 102%) compared with the carotid (150 ± 70%), iliac (155 ± 69%), and femoral (109 ± 51%) (P < 0.05). The femoral also displayed a lower Hsp90 content compared with the iliac (P < 0.05). The Hsp90 protein content was the same in control (178 ± 92%), LI (171 ± 118%), and HI (181 ± 94%) (P > 0.05; Fig. 5).
expected; however, this was not the case. We have previously noted that more distal vessels display a faster adjustment compared with the aorta (23) and suggested that this was in line with studies showing progressively faster vasoresponsiveness in the more distal arterioles (τ values of ~6 s and ~3 s for 1As and 3As arterioles, respectively) (2, 27). The fact that a somewhat distal artery as the carotid shows the slowest dynamic responsiveness contradicts this idea. As such, function and not location or morphological characteristics per se might be the main determinant in the responsiveness of the vessels. Indeed, large extracerebral vessels, such as the carotid, have been shown to be a major site of resistance to blood flow in the brain circulation and to contribute significantly to the total vascular resistance of that area (7).

Contrary to our expectations, the e-NOS and Hsp90 data did not provide further insight into the mechanisms responsible for the vessel type-related vascular responsiveness. The e-NOS protein expression was similar among different vessels. However, other factors that could not be measured in this study, such as the concentration of e-NOS regulators, or morphological characteristics, such as the lumen-to-wall ratio, might influence the responses so that the same total e-NOS protein content in different vessels still results in differential responses throughout the vascular tree. The vessel-specific difference in Hsp90 protein expression (larger in the aorta and smaller in the femoral) may simply reflect the abundance of this protein in the smooth muscle, which is more predominant in larger vessels. Regardless of the inability to identify the mechanisms respon-

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**Fig. 4.** e-NOS protein content for each vessel in control, LI, and HI groups. LI, low-intensity exercise; HI, high-intensity exercise; C, carotid; A, aorta; I, iliac; F, femoral.

**Fig. 5.** Hsp90 protein content for each vessel in control, LI, and HI groups. C, carotid; A, aorta; I, iliac; F, femoral; †Significantly different from aorta. ‡Significantly different from iliac.
sible for the observed differences, it is plausible that different signaling pathways are controlling the dynamic and the % adjustment of the vasorelaxation response.

In the present study, no differences were observed in the τ or the time-to-steady-state of the vessels in response to LI and HI; however, the % vasorelaxation and the rate of vasorelaxation were significantly greater in LI and HI compared with the control group. While dose-response changes in the % vasorelaxation have been previously described (15), this study is the first to describe improvements in the dynamic vasorelaxation response to a single bout of exercise. Although for this study, we were unable to test the vasorelaxation response under NO inhibition, data from six different sets of experiments in our laboratory [(23) and unpublished observations] and other (15, 19, 22) laboratories have established that this improved vasoresponsiveness is endothelium-dependent upon release of NO, and likely due to increased expression of e-NOS protein (19).

The e-NOS protein expression progressively declined in the LI and HI groups compared with control (albeit only statistically lower in HI). This finding was unexpected. Interestingly, in trained female (30) and more acutely exercised male (17) animals, exercised at intensities similar to the HI group in the present study, a reduction in e-NOS expression under NO and likely due to increased expression of e-NOS protein (19). The e-NOS protein expression progressively declined in the LI and HI groups compared with control (albeit only statistically lower in HI). This finding was unexpected. Interestingly, in trained female (30) and more acutely exercised male (17) animals, exercised at intensities similar to the HI group in the present study, a reduction in e-NOS expression under NO inhibition, data from six different sets of experiments in our laboratory [(23) and unpublished observations] and other (15, 19, 22) laboratories have established that this improved vasoresponsiveness is endothelium-dependent upon release of NO, and likely due to increased expression of e-NOS protein (19).

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Regarding the mechanisms responsible for the observed responses, our data showed that acute endurance exercise improved the % vasorelaxation (amplitude component) and rate of vasorelaxation (with the vessel producing a larger relaxation in the same period of time). Recently, we have shown larger rates of vasorelaxation in control compared with diabetic animals (23). The present findings extend those previously reported showing that exercise affects not only the amplitude but also the rate of change of the response. Importantly, these changes in the responsiveness of the vessels were observed to a single bout of exercise, and they may even be amplified by training. In regard to the acute changes in vascular responsiveness, results are still conflicting. One previous study has shown no changes in the % vasorelaxation response to a single dose of ACh in the aorta of rats 24 h following a single bout of high-intensity endurance exercise (5), while another study (15) has shown a right shift in the dose-dependent curve to ACh for the % vasorelaxation endothelium-dependent vasodilation that peaked between 12 and 24 h following a single bout of high-intensity endurance exercise. This is relevant because, collectively, these data suggest that the type of analysis performed for determination of vascular responsiveness might determine whether or not significant differences are observed.

The greater % vasorelaxation and rate of vasorelaxation observed in response to endurance training may have important functional implications from an exercise prescription perspective. For instance, a slower rate of adjustment of the oxidative phosphorylation has been shown to be partly determined by impairments in blood flow distribution (24, 25) and has been proposed to disturb cellular homeostasis and reduce exercise tolerance due to an increase in metabolic by-products associated with nonoxidative metabolism (4). This rapid improvement in vascular responses might improve O2 provision to the active tissues and thus reduce exercise-related fatigue. Additionally, the finding that a single bout of exercise is enough to improve the % vasorelaxation response and the rate of vasorelaxation adds to the knowledge that acute exercise offers vascular protection and that repeated acute bouts or chronic exercise results in larger and more durable improvements in vascular responses (15).

In conclusion, this study demonstrated that an acute bout of endurance exercise induces increases in vascular responsiveness. Additionally, these data showed that the rate of vasorelaxation and the percent adjustments of the responses are vessel-specific and suggested that the function of the vessel plays a critical role in determining this response.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS


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