Passive triceps surae stretch inhibits vasoconstriction in the nonexercised limb during posthandgrip muscle ischemia

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Tokizawa, Ken, Masaki Mizuno, Yoshio Nakamura, and Isao Muraoka. Passive triceps surae stretch inhibits vasoconstriction in the nonexercised limb during posthandgrip muscle ischemia. J Appl Physiol 97: 1681–1685, 2004. First published July 23, 2004; doi: 10.1152/japplphysiol.00312.2004.—We investigated whether selective muscle mechanoreceptor activation in the lower limb opposes arm muscle metaboreceptor activation-mediated limb vasoconstriction. Seven subjects completed two trials: one control trial and one stretch trial. Both trials included 2 min of handgrip and 2 min of posthandgrip exercise muscle ischemia (PEMI). In the stretch trial, a 2-min sustained triceps surae stretch, by brief passive dorsiflexion of the right foot, was performed simultaneously during PEMI. Mean arterial pressure, heart rate, and forearm blood flow (FBF) in the nonexercised arm and forearm vascular conductance (FVC) in the nonexercised arm were measured. During PEMI in the control trial, mean arterial pressure was significantly greater and FBF and FVC were significantly lower than baseline values (P < 0.05 for each). In contrast, FBF and FVC during PEMI in the stretch trial exhibited different responses than in the control trial. FBF and FVC were significantly greater in the stretch trial than in the control trial (FBF, 5.5 ± 0.4 vs. 3.8 ± 0.4 ml·100 ml⁻¹·min⁻¹; FVC, 0.048 ± 0.004 vs. 0.033 ± 0.003 unit, respectively; P < 0.05). These results indicate that passive triceps surae stretch can inhibit vasoconstriction in the nonexercised forearm mediated via muscle metaboreceptor activation in the exercised arm. 

EXERCISE CAUSES INCREASES in blood pressure, heart rate (HR), and vasoconstriction in nonactive tissues. Two neural mechanisms have been implicated in these responses. One is central command, which refers to activation of the cardiovascular centers by descending central neural pathways involved in initiation of somatomotor activity (6). The second is a feedback mechanism via thin slow-conducting (group III and group IV) afferents arising from mechanically (mechanoreceptor) and chemically sensitive (metaboreceptor) nerve endings located within the muscle (15). The cardiovascular responses to exercise performed by several limbs simultaneously equal less than the algebraic sum of the responses produced separately by each limb (3, 18, 21). The responses of muscle sympathetic nerve activity (MSNA) exhibit a similar relationship (20). This suggests that cardiovascular responses elicited during exercise of separate limbs exhibit an “inhibitory interaction” (20). However, the mechanisms for this interaction have not been identified. In a recent study from our laboratory (22), we observed that venous occlusion to the lower limb, which we assume activates the group III and group IV afferents in response to the mechanical distension of the venular structures in muscle (8), attenuates vasoconstriction in the nonexercised forearm during posthandgrip exercise muscle ischemia (PEMI). Ray et al. (14) reported that increases in MSNA produced by PEMI were attenuated with contralateral rhythmic handgrip. Consequently, inhibitory effects on cardiovascular responses could arise from the combined muscle afferent activation from different limbs.

In our laboratory’s previous study, we targeted the muscle afferent activation involved in mechanical stimulation of peripheral blood vessels (22). In our present study, we focused on the effects of mechanical stimulation of myofiber structures. The proportion of activated group III and group IV muscle afferents involved in mechanical stimulation of blood vessels (8) differs from that of myofiber structures (10). Ray et al. (14) used sensory nerve blockade to study the underlying mechanism of MSNA during PEMI with focus on central command. They suggested that it is unlikely that the attenuation of increased MSNA results from central command and that it appears to be a result of muscle mechanoreceptor activation. It has been reported that passive triceps surae stretch selectively activates muscle mechanoreceptor (2, 7). Therefore, using triceps surae stretch permits us to more directly examine the interactive effects of muscle mechanoreceptor activation on cardiovascular responses.

The purpose of this study was to determine whether muscle mechanoreceptor activation in the lower limb acts to oppose arm muscle metaboreceptor activation-mediated limb vasoconstriction. We presumed that the application of passive triceps surae stretch would attenuate the reduction in vascular conductance in the nonexercised limb during PEMI.

METHODS

Subjects. Seven men volunteered to participate in this study, which was approved by the local ethics committee; all work conformed to the Declaration of Helsinki. Before the experiment, the subjects were informed of all aspects of the study, and each signed an informed consent document. The subjects’ mean (±SD) age, height, and weight were 24.1 ± 1.4 yr, 170.7 ± 3.9 cm, and 70.6 ± 9.6 kg, respectively. Proc. Maximal voluntary handgrip (HG) contraction was assessed in the right hand using a HG dynamometer. The average of three attempts was taken as the subject’s maximal voluntary contraction. On separate days after the preliminary test, the subjects performed two trials on different days in a random order: one control trial and one stretch trial. The experimental setup is shown schematically in Fig. 1. Both trials included a baseline measurement with the subject in a supine position, followed by 2 min of HG exercise and 2 min of...
PEMI. In the stretch trial, triceps surae stretch was performed during PEMI to activate muscle mechanoreceptor activation in the lower limb. HG was performed as a static contraction at 30% of maximal voluntary contraction (16.6 ± 2.1 kg) with the right hand. PEMI was applied using a cuff placed around the upper right arm and inflated to 200 mmHg at 5 s before the end of exercise. Triceps surae stretch was accomplished by brief passive dorsiflexion of the right foot starting from an ankle joint of 90° to an angle slightly less than where the subject reported discomfort. The foot secured to a metal plate was passively and rapidly rotated around the subject’s ankle joint axis and locked into position to obtain a sustained stretch in the triceps surae. It takes ~2 s for the rotation. For all subjects, mean ankle joint angle was 72.3 ± 4.4° during triceps surae stretch. On a separate day from the two trials described above, a trial was performed with only triceps surae stretch to confirm the cardiovascular changes when muscle mechanoreceptor activation in only the lower limb was elicited.

Measurements. Blood pressure was measured with a finger cuff using an optomechanical photoplethysmographic method (2300 Finapres, Ohmeda, Englewood, CO). The monitoring finger cuff was placed around the middle finger of the left hand and supported at the heart level. HR was determined using standard ECG leads (model OEC-8108, Nihon Kohden, Tokyo, Japan). Forearm blood flow (FBF) in the nonexercised arm was measured by venous occlusion plethysmography (23) using a mercury-in-Silastic strain gauge (model EC-5R, Hokanson, Bellevue, WA). The strain gauge was placed around the largest area of the left forearm. The arm was supported at the level of the heart, and a venous occlusion pressure of 60 mmHg was used. The average of three measurements was taken as the baseline value. In HG and PEMI, FBF was measured at 30-s intervals. FBF value was calculated from the rate of increase of forearm volume during venous occlusion and expressed as milliliters per minute per 100 ml of forearm volume. Forearm vascular conductance (FVC) in the nonexercised arm was calculated as FBF (in ml·100 ml⁻¹·min⁻¹)/mean arterial pressure (MAP; in mmHg), and it was expressed in "units" (actual units, ml·100 ml⁻¹·min⁻¹·mmHg⁻¹). Although the target limb is slightly elevated above heart level to ensure venous drainage in venous occlusion plethysmography in general, we measured at the heart level because blood pressure was measured simultaneously in the same arm. We conducted an additional experiment on five subjects to examine effect of the arm position on the FBF value during resting condition. The result showed that the FBF value measured at heart level was significantly correlated with that measured above heart level (regression line: y = 1.04x − 0.17; r² = 0.98, P < 0.01).

In an additional experiment on four subjects, myoelectric activity of medial gastrocnemius and vastus lateralis muscles during passive triceps surae stretch was detected using surface electromyography (EMG) and recorded using bipolar 5-mm-diameter Ag-AgCl electrodes with an interelectrode distance of 40 mm. Signals were amplified by a bioelectric amplifier (model AB-621G, Nihon-Kohden, Tokyo, Japan) and collected by MacLab (ADInstruments, Castle Hill, Australia).

**RESULTS**

A typical EMG recording during passive triceps surae stretch in one subject is shown in Fig. 2. There was no EMG activity detected in medial gastrocnemius and vastus lateralis muscles in all subjects. Figure 3 shows the changes in the cardiovascular responses during the triceps surae stretch-only trial. There were no significant changes in MAP, FBF, and FVC in response to the 2-min triceps surae stretch. In contrast, HR increased significantly above baseline immediately after triceps sura stretch and subsequently declined to baseline values.

MAP and HR responses in both trials are shown in Fig. 4. In both trials, MAP was increased significantly during HG and was maintained at a significantly higher level during PEMI. Although HR tended to increase during HG, there was no significant change from baseline. No significant differences were observed between trials during HG and PEMI in these responses.

FBF and FVC responses in both trials are shown in Fig. 5. During HG, FBF and FVC did not change significantly in either trial and did not differ significantly between trials. During PEMI in the control trial, FBF and FVC were significantly lower than the baseline value (FBF, 3.8 ± 0.4 vs. 5.0 ± 0.3 ml·100 ml⁻¹·min⁻¹, except for 3.5 min after the onset of exercise, P = 0.09; FVC, 0.033 ± 0.003 vs. 0.055 ± 0.004 unit). In contrast, during PEMI in the stretch trial, FBF and FVC were similar to the preexercise baseline values and differed significantly from those observed in the control trial. FBF and FVC were significantly greater in the stretch trial than in the control trial (FBF, 5.5 ± 0.4 vs. 3.8 ± 0.4 ml·100 ml⁻¹·min⁻¹; FVC, 0.048 ± 0.004 vs. 0.033 ± 0.003 unit).
Fig. 3. Changes from baseline in mean arterial pressure (ΔMAP; A), heart rate (ΔHR; B), forearm blood flow (ΔFFB; C), and forearm vascular conductance (ΔFVC; D) during triceps surae stretch. MAP and HR are represented in 5-beat intervals (5b, 10b, 15b) immediately after triceps surae stretch and at each 30-s interval during triceps surae stretch. Values are means ± SE. *P < 0.05 vs. baseline.

Fig. 4. Changes in MAP (A) and HR (B) during handgrip (HG) and posthandgrip exercise muscle ischemia (PEMI) in each control and stretch trial. Values are means ± SE. There were no significant differences between trials.

Fig. 5. Changes in FBF (A) and FVC (B) during HG and PEMI in each control and stretch trial. Values are means ± SE. *P < 0.05 vs. baseline. #P < 0.05 vs. control.
DISCUSSION

The major finding of our study is that decreases in FVC during PEMI in the control trial were not seen with passive triceps surae stretch. This suggests that passive triceps surae stretch inhibits the vasoconstriction in the nonexercised forearm mediated by exercised arm muscle metaboreceptor activation.

This study was designed to evaluate the peripheral limb vascular response to activation of both muscle metaboreceptor and mechanoreceptor in different limbs. Using PEMI and triceps surae stretch, we attempted to selectively activate muscle metaboreceptor and mechanoreceptor. The external cuff pressure of PEMI causes accumulation of metabolites in the exercised limb (1), which activates muscle metaboreceptor in the absence of central command and muscle mechanoreceptor activation. Our results in the control trial during PEMI are consistent with results from previous studies (1, 16) showing activation. Our results in the control trial during PEMI are the absence of central command and muscle mechanoreceptor activation. MAP was significantly greater and that FBF and FVC were significantly lower than baseline values. Our results indicate that the PEMI model fully activated muscle metaboreceptor. MSNA should be increased during this phase (11). Baum et al. (2) reported that passive calf stretch in a sitting position for 10 min has no significant effects on MAP and HR. However, they confirmed that MAP in the early phase (~1 min) increased slightly to the level induced by voluntary calf contraction. Gladwell and Coote (7) reported that passive triceps surae stretch in a semisupine position for 1 min significantly increased HR without affecting blood pressure. Although these two studies reported inconsistent results, they both suggest that passive stretch evokes muscle mechanoreceptor activation. We confirmed that HR was significantly increased in the triceps surae stretch-only trial. Therefore, it was thought that the triceps surae stretch model used in our study activated muscle mechanoreceptor. Consistent with earlier studies (2, 7), we observed no EMG activity during passive triceps surae stretch in the subjects (Fig. 2, see RESULTS); thus we believe it unlikely that reflexogenic muscle contractions in triceps surae affected the cardiovascular responses. Triceps surae stretch during PEMI did not increase HR. The downward transition of HR from exercise to the postexercise period might have counteracted the increase in HR with triceps surae stretch.

Ray et al. (14) reported that increases in MSNA produced by PEMI were attenuated with contralateral rhythmic HG. Central command (11) and the baroreflex (19) inhibit MSNA during exercise. In the study by Ray et al., blood pressure did not change significantly during PEMI with or without contralateral rhythmic HG, suggesting that attenuation of MSNA during PEMI with contralateral rhythmic HG was not mediated by the baroreflex. They also confirmed that performing contralateral rhythmic HG under sensory nerve blockade of muscle afferent fails to attenuate MSNA during PEMI, suggesting that central command does not attenuate MSNA during PEMI. Consequently, they suggested that muscle metaboreceptor activation-mediated increases in MSNA could be inhibited by muscle mechanoreceptor activation produced by contralateral rhythmic HG. In our study, MAP was similar in both trials during PEMI, suggesting that attenuation of the decreased FVC by application of triceps surae stretch during PEMI is not directly mediated by the baroreflex. In addition, it is unlikely that central command would mediate any change in FVC. Therefore, attenuation of the decreased FVC during PEMI observed in our study could have arisen from withdrawal of MSNA related to the activation of muscle mechanoreceptor in the lower limb. However, the sensing limbs in which muscle mechanoreceptor activation was assessed differed between our study and that of Ray et al.

It was reported that muscle mechanoreceptor activation increases MSNA (9, 12). McClain et al. (12) demonstrated that external compression of the exercising forearm during static HG caused MSNA to increase significantly above levels observed during control conditions. Because MSNA was unaffected by external compression during PEMI and thus muscle metaboreceptor activation would not have differed between trials, they concluded that muscle mechanoreceptor activation increases MSNA. In contrast to the study by McClain et al., which elicited muscle mechanoreceptor activation in exercising muscle, the study by Ray et al. (14) elicited muscle mechanoreceptor activation in the contralateral limb during PEMI. In our study, muscle mechanoreceptor activation was elicited in a different limb from that eliciting muscle metaboreceptor activation in the forearm. We suggest that combinedafferent activation from each limb, but not from the same limb, may contribute to inhibitory effects of muscle mechanoreceptor activation on MSNA and vasoconstriction in the peripheral limb.

In the stretch-only trial, triceps surae stretch elicited significant increases in HR over 15 beats, followed by a return to baseline values. In contrast, triceps surae stretch during PEMI attenuated the decrease in FBF and FVC for 2 min in the stretch trial. Although we can only speculate on the possible mechanisms, these uncoupled responses might reflect differences between the control of sympathetic outflow to each of the tissues (4) and cardiac vagal and sympathetic outflow (13). Additionally, emotional stress could be involved during triceps surae stretch. We also observed uncoupling between MAP and FVC to triceps surae stretch during PEMI. MAP was unchanged despite an increase in FVC. It is possible that attenuation of the decreased FVC elicited by triceps surae stretch may not have been of sufficient magnitude to change MAP and that sympathetic outflow to other vascular beds may have increased. The attenuated decrease in FVC may be a tissue-specific response (e.g., cholinergic vasodilation), because there is a different response of forearm and calf vascular resistance to contralateral limb exercise (5, 16).

Besides sympathetic vasocontrol, other mechanisms are involved in limb vascular regulation. Shear stress and cholinergic nerve vasodilation have been suggested as two possible mechanisms. MAP was the same in both trials during PEMI, and there was no difference in FBF during PEMI in the stretch trial relative to the baseline in our study. Therefore, it is unlikely that shear stress causes the attenuated decrease in FVC in the stretch trial. Direct evidence for the existence of sympathetic cholinergic fibers in humans is still lacking. However, pharmacological antagonism of vasodilation is thought to arise from cholinergic stimulation in response to exercise. For example, Sanders et al. (17) demonstrated that forearm vasodilation during contralateral HG exercise was abolished by atropine but was not affected by propranolol. They concluded that sympathetic cholinergic vasodilation was implicated in humans. We can only speculate on the effect of cholinergic vasodilation with triceps surae stretch during PEMI on the
FVC in our study. To clarify the mechanism, further investigations are needed.

Finally, our results do not exclude the possibility that triceps surae stretch activates mechanoreceptor other than in muscle. The mechanical muscle deformation by triceps surae stretch may have activated mechanoreceptor in blood vessel. The mechanical distention of the peripheral blood vessel via increasing blood volume activates group III and IV muscle afferents (8). Additionally, triceps surae stretch may have activated mechanoreceptor in skin and joint.

In conclusion, our data show that application of triceps surae stretch during PEMI did not decrease FVC. This finding suggests that muscle mechanoreceptor activation in the lower limb could attenuate vasoconstriction in the nonexercised limb when muscle metaboreceptor activation is activated in the upper limb.

REFERENCES