Augmented Cardiopulmonary Baroreflex Control of Forearm Vascular Resistance in Young Athletes

AKIRA TAKESHITA, SUMIE JINGU, TSUTOMU IMAIZUMI, YAMAMOTO KUNIHIKO, SAMON KOYANAGI, AND MOTOOMI NAKAMURA

SUMMARY The aim of this study was to examine the effect of exercise training on reflex control of vascular resistance in human males. Forearm vascular responses to lower body negative pressure (LBNP) at −10 and −40 mm Hg were compared between highly trained young athletes (21.5 ± 0.5 years old, n = 14) and age-matched nonathletes (20.7 ± 0.5 years old, n = 16). Resting heart rate was lower in athletes than in nonathletes. Resting blood pressure, central venous pressure, forearm blood flow, and forearm vascular resistance were not different between the two groups. The magnitude of reflex forearm vasoconstriction in response to LBNP at −10 mm Hg, which decreased central venous pressure but did not alter blood pressure or heart rate, was greater in athletes than in nonathletes. The slope of the regression line relating changes in central venous pressure and forearm vascular resistance was steeper in athletes than in nonathletes. Vasoconstrictive responses to intraaerally administered norepinephrine and angiotensin II did not differ between athletes and nonathletes. These results suggest that the tonic inhibitory influence of the cardiopulmonary receptors is augmented in athletes. This augmentation may contribute to some of cardiovascular and endocrine adaptations that occur with exercise training. (Circulation Research 1986;59:43-48)

KEY WORDS • lower body negative pressure • athletes • nonathletes • left ventricular diameter

ENDURANCE training induces various cardiovascular and endocrine adaptations that allow trained subjects to respond to the same stress with much less effort and to sustain the activity for a much longer period.1-3 Autonomic function is a major determinant of the acute response to exercise.4,5 However, the role of the autonomic nervous system in training effects is not well understood.2,3 In particular, there are few studies of a possible alteration in the baroreflex control of circulation with training.4 It has been shown that blood pressure and heart rate responses to the negative and positive pressure applied to the neck are flatter in trained athletes than in control subjects,6 which suggests that the gain of the carotid sinus baroreceptor reflex may be reduced in athletes. It also has been shown that trained subjects or animals have also reduced tolerance of lower-body negative pressure (LBNP)7-9 or orthostatic stress.10,11 The latter may suggest that the effectiveness of the cardiopulmonary as well as the arterial baroreceptor reflex in control of blood pressure is impaired after training. However, it is difficult to identify the effect of training on baroreflex function since few of these studies defined the level of stimulus to the receptors or considered a possible alteration in vascular responsiveness to sympathet-ic stimulation. Venous pooling in the lower body during orthostatic stress or LBNP might be greater12 and the vascular response to norepinephrine might be reduced after training.13 Furthermore, most of these studies examined the frequency of or time to the onset of syncope during LBNP or orthostatic stress. It is likely that, besides baroreflex mechanisms, other factors contribute to the development of syncope during LBNP or orthostatic stress.

The aim of this study was to examine the effect of exercise training on baroreflex control of vascular resistance in human males. In this study, we examined forearm vascular responses to LBNP at −10 and −40 mm Hg in highly trained young athletes and age-matched nonathletes. In some of the athletes and nonathletes, forearm vascular responses to LBNP at −20 mm Hg were examined also.

Subjects and Methods

Studies were done in 14 young athletes (mean age 21.5 ± 0.5 years old) and 16 nonathletes (mean age 20.7 ± 0.5 years old). All subjects were male. The athletes were members of the varsity football team, and the nonathletes were not engaged in any daily sports activity. The subjects had no past medical history of cardiovascular disease and were normotensive. The study protocol was explained to and informed consent was obtained from each subject. The study was performed with the subjects supine in the postabsorptive state in a warm and quiet room. After placing catheters and a strain-gauge plethysmo-
graph, at least 15 minutes were allowed for each subject to become accustomed to the study conditions before beginning the protocol.

Forearm blood flow was measured using a mercury-silastic strain-gauge plethysmograph with venous occlusion technique.\textsuperscript{13} The strain gauge was placed approximately 5 cm below the antecubital crease. The pressure in the venous occlusion or congesting cuff was \(-40\) mm Hg.\textsuperscript{14} Circulation to the hand was arrested by inflating a cuff around the wrist to suprasystolic pressure in the venous occlusion or congesting cuff technique.

The strain gauge was placed in-silastic strain-gauge plethysmograph with venous occlusion technique. Forexarm blood flow was taken as the average of 4 to 8 flow measurements made at 15-second intervals. Calculation of forearm blood flow was done independently by two of the authors from the copied records, and the average value was used for statistical analysis. The blood pressure was measured in the other arm with a sphygmomanometer. All blood pressure measurements were performed by one individual to minimize observer variation. Forearm vascular resistance was calculated by dividing mean arterial pressure (diastolic pressure plus one third of the pulse pressure in millimeters of mercury) by forearm blood flow (milliliters per minute per 100 ml of forearm volume); these values are expressed as "units" throughout this report. Heart rate was calculated from the electrocardiogram. Central venous pressure was obtained from a catheter introduced into an antecubital vein and advanced into an intrathoracic vein. The pressure was measured with a pressure transducer (Toyo Boldwin Limited, MPU 0.5) using the midaxillary line as a reference level.

**Baroreflex Control of Forearm Vascular Resistance**

Reflex vasoconstriction in the forearm was examined during LBNP. The subject's body below the iliac crest was enclosed in a chamber that was sealed and connected to an adjustable vacuum. Lower-body negative pressure was applied at \(-10\) and \(-40\) mm Hg or at \(-10, -20,\) and \(-40\) mm Hg, which produced graded decreases in central venous pressure and reflex increases in forearm vascular resistance. The slope of regression line relating changes in central venous pressure and forearm vascular resistance was calculated by the least square method using points at zero and, during LBNP, at \(-10\) and \(-40\) mm Hg or \(-10, -20,\) and \(-40\) mm Hg. We also calculated the slope relating absolute values of central venous pressure and forearm vascular resistance at control and during LBNP at \(-10\) and \(-40\) mm Hg or \(-10, -20,\) and \(-40\) mm Hg. Correlation coefficients were greater than 0.870.

**Forearm Vascular Responses to Norepinephrine and Angiotensin II**

Forearm blood flow was measured during intraarterial infusion of norepinephrine at a rate of 100, 200, and 500 ng/min or angiotensin II at a rate of 20 and 40 ng/min. Each dose of norepinephrine or angiotensin II was infused for 2 minutes. Forearm vascular resistance was calculated from forearm blood flow and mean arterial pressure. The arterial pressure was measured in the other arm with a sphygmomanometer.

Wall Thickness and End-Diastolic Diameter of the Left Ventricle

The end-diastolic diameter as well as the thickness of the posterior wall of the left ventricle was determined by echocardiography. Two-dimensional echocardiograms of the left ventricle were obtained in the short axis at the level of chordae tendinae, using a Toshiba SSH 11-A phased-array ultrasonograph. Then, the M mode echocardiographic cursor was oriented to sample a true diameter of the left ventricle, and an M mode echocardiogram was continuously recorded. The end-diastolic diameter of the left ventricle and the posterior wall thickness were measured at the peak of the R wave on the electrocardiogram. The diameter was measured from the septal leading edge to the posterior wall leading edge.

**Statistical Analysis**

An unpaired Student's $t$ test was used for comparisons of the results between athletes and nonathletes. Forearm vascular responses to norepinephrine and angiotensin II were compared between athletes and nonathletes by two-way analysis of variance. $p \leq 0.05$ was considered significant. All data are expressed as mean $\pm$ standard error (SE).

**Results**

Table 1 summarizes resting values and changes during LBNP in athletes and nonathletes. Resting mean blood pressure, central venous pressure, forearm blood flow, and forearm vascular resistance were not different between the two groups. However, resting heart rate was lower in athletes than in nonathletes.

Lower-body negative pressure at \(-10\) mm Hg decreased central venous pressure and forearm blood flow and increased forearm vascular resistance in athletes and nonathletes. Systolic, diastolic, and mean blood pressure and heart rate did not change significantly during LBNP \(-10\) mm Hg in either group. The decrease in central venous pressure did not differ significantly between the two groups, but the decrease in forearm blood flow and the increase in forearm vascular resistance with LBNP at \(-10\) mm Hg were greater in athletes than in nonathletes.

Lower-body negative pressure at \(-40\) mm Hg decreased systolic blood pressure, central venous pressure, and forearm blood flow and increased heart rate and forearm vascular resistance in both groups. With LBNP at \(-40\) mm Hg, the decreases in systolic blood pressure, central venous pressure, and forearm blood flow were not different between the two groups, but the increase in forearm vascular resistance was greater in athletes.

The slope of the regression line relating changes in forearm vascular resistance with LBNP at \(-10\) mm Hg and \(-40\) mm Hg was steeper ($p < 0.01$) in athletes ($-5.9 \pm 0.6$) than in nonathletes ($-2.5 \pm 0.4$) (Figure 1). The slope of the relation between absolute values of central venous pressure and those of forearm vascular resistance at
Table 1. Responses to LBNP at −10 and −40 mm Hg in Athletes and Nonathletes

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Changes during LBNP</th>
<th>Changes during LBNP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>−10 mm Hg</td>
<td>−40 mm Hg</td>
</tr>
<tr>
<td><strong>Nonathletes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>n</strong> = 16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>120 ± 2</td>
<td>0 ± 0.6</td>
<td>−7.8 ± 2.0*</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>63 ± 5</td>
<td>0.7 ± 0.6</td>
<td>1.2 ± 1.4</td>
</tr>
<tr>
<td>mBP (mm Hg)</td>
<td>82 ± 3</td>
<td>0.4 ± 0.5</td>
<td>−2.1 ± 1.1</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>62 ± 2</td>
<td>−2.0 ± 1.2</td>
<td>6.0 ± 2.2↑</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>4.3 ± 1.0</td>
<td>−1.9 ± 0.3*</td>
<td>−6.8 ± 0.6*</td>
</tr>
<tr>
<td>FoBF (ml/min/100 ml)</td>
<td>18.6 ± 2.3</td>
<td>2.7 ± 0.8↑</td>
<td>16.8 ± 2.8*</td>
</tr>
<tr>
<td>FoVR (units)</td>
<td>4.1 ± 1.2</td>
<td>−1.2 ± 0.2§</td>
<td>−2.6 ± 0.4*</td>
</tr>
<tr>
<td><strong>Athletes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>n</strong> = 14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>123 ± 2</td>
<td>0 ± 0.5</td>
<td>−9.1 ± 2.2*</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>65 ± 2</td>
<td>1.4 ± 0.8</td>
<td>3.2 ± 1.8</td>
</tr>
<tr>
<td>mBP (mm Hg)</td>
<td>50 ± 1↑</td>
<td>−2.0 ± 1.0</td>
<td>6.8 ± 1.5*</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>50 ± 1↑</td>
<td>−2.0 ± 1.0</td>
<td>6.8 ± 1.5*</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>4.4 ± 1.2</td>
<td>−0.6 ± 0.2↑</td>
<td>−2.1 ± 0.3*</td>
</tr>
<tr>
<td>FoBF (ml/min/100 ml)</td>
<td>20.9 ± 3.4</td>
<td>7.7 ± 0.5*↑</td>
<td>36.0 ± 5.1*t</td>
</tr>
</tbody>
</table>

mBP = mean blood pressure; HR = heart rate; CVP = central venous pressure; FoBF = forearm blood flow; FoVR = forearm vascular resistance; LBNP = lower body negative pressure.

*p < 0.01 vs control value. †p < 0.05 vs control value. §p < 0.01 athletes vs nonathletes. §p < 0.05 athletes vs nonathletes.

control and during LBNP at −10 and −40 mm Hg were also analyzed. The slope was steeper (p < 0.01) in athletes (5.3 ± 0.6) than in nonathletes (2.7 ± 0.4).

In 6 athletes and 6 nonathletes, reflex forearm vasoconstriction was examined during LBNP at −10, −20, and −40 mm Hg. Lower-body negative pressure at −20 mm Hg did not significantly alter systolic, diastolic, and mean blood pressure and heart rate in either group but decreased central venous pressure by −4.4 ± 0.7 mm Hg in nonathletes (p < 0.01) and −4.2 ± 0.5 mm Hg in athletes (p < 0.01) and increased forearm vascular resistance by 8.0 ± 1.1 units in nonathletes (p < 0.01 and 19.0 ± 0.6 units in athletes (p < 0.01). The decrease in central venous pressure during LBNP at −20 mm Hg was not different between the two groups, but the increase in forearm vascular resistance was greater in athletes than in nonathletes (p < 0.01). The slope of the regression line relating changes in central venous pressure and those in forearm vascular resistance with LBNP at −10, −20, and −40 mm Hg was steeper (p < 0.05) in athletes (−5.2 ± 0.6) than in nonathletes (−2.0 ± 0.6). Forearm vascular responses to intraarterial norepinephrine and angiotensin II are shown in Figure 2. Responses to norepinephrine or angiotensin II were not different between athletes and nonathletes.

The results of the echocardiographic study are summarized in Table 2. The posterior wall of the left ventricle was thicker (p < 0.01) in athletes than in nonathletes. The end-diastolic diameter of the left ventricle also tended to be greater (p < 0.1), but not significantly, in athletes. The changes in the end-diastolic diameter of the left ventricle during LBNP at −10, −20, and −40 mm Hg were not significantly different between athletes and nonathletes. However, the end-diastolic diameter of the left ventricle during LBNP at −10 mm Hg tended to be greater (p < 0.1), and that during LBNP at −20 as well as −40 mm Hg was greater (p < 0.05) in athletes.

![Figure 1](http://circres.ahajournals.org/)

**Figure 1.** Relationship between changes in central venous pressure and forearm vascular resistance under LBNP at −10 and −40 mm Hg in athletes (open circles, n = 12) and nonathletes (closed circles, n = 14). The slope of the regression line in athletes (y = 5.9x + 0.2) was steeper (p < 0.01) than that in nonathletes (y = 2.5x - 0.2).
Discussion

The major finding of this study was that reflex forearm vasoconstriction in response to LBNP at —10 mm Hg was greater and the slope of the regression line relating changes in central venous pressure and forearm vascular resistance was steeper in athletes than in nonathletes. These results suggest that exercise training augments the gain of inhibitory influence of the cardiopulmonary receptors in man.

Several questions should be addressed in interpreting the results of reflex forearm vasoconstriction during LBNP. First, we should consider the possibility that augmented forearm vasoconstriction in response to LBNP at —10 mm Hg in athletes may be related to nonspecific mechanisms such as a greater reflex stimulus or a difference in baseline central venous pressure or forearm vascular resistance. Forearm vasoconstriction during LBNP at —10 mm Hg was likely to be triggered by the decrease in central venous pressure since blood pressure and heart rate did not change at this level of LBNP. The magnitude of the decrease in central venous pressure with LBNP at —10 mm Hg did not differ between athletes and nonathletes (Table 1), which suggest that levels of reflex stimulus were not different. Baseline central venous pressure tended to be higher in athletes than in nonathletes (Table 1). Higher central venous pressure in athletes might have resulted from the increased blood volume that often occurs with training. However, in a previous study in our laboratory, changes in baseline central venous pressure caused by nitroglycerin or trapidil did not alter the slope or reflex forearm vasoconstriction with LBNP. Baseline vascular resistance may also influence vascular responses to sympathetic stimulation. However, baseline forearm vascular resistance was not different between athletes and nonathletes (Table 1).

Second, we should consider the possibility that a greater forearm vascular response to LBNP in athletes than in nonathletes might have resulted from greater vascular responses to vasoconstrictor stimuli. However, the dose–response curves with intraarterial infusion of norepinephrine or angiotensin II did not differ significantly between athletes and nonathletes.

Third, we should consider which reflex mechanisms might be involved in mediating reflex forearm vasoconstriction during LBNP at —10 mm Hg and in determining the slope of the regression line relating the changes in central venous pressure and forearm vascular resistance. Previous studies have suggested that reflex forearm vasoconstriction in response to LBNP at

Table 2. Posterior Wall Thickness and the End-Diastolic Diameter of the Left Ventricle at Rest and During LBNP

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rest</th>
<th>LBNP —10 mm Hg</th>
<th>LBNP —20 mm Hg</th>
<th>LBNP —40 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PWT</td>
<td>EDD (mm)</td>
<td>EDD (mm)</td>
<td>EDD (mm)</td>
</tr>
<tr>
<td></td>
<td>(mm)</td>
<td></td>
<td>ΔEDD (mm)</td>
<td>ΔEDD (mm)</td>
</tr>
<tr>
<td>Nonathletes (n = 6)</td>
<td>7.5 ± 0.2</td>
<td>45.6 ± 1.6</td>
<td>43.7 ± 1.6</td>
<td>—1.8 ± 0.3</td>
</tr>
<tr>
<td>Athletes (n = 6)</td>
<td>10.9 ± 0.5</td>
<td>50.9 ± 2.4</td>
<td>48.3 ± 2.7</td>
<td>—2.6 ± 0.5</td>
</tr>
<tr>
<td>p value</td>
<td>&lt; 0.01</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

PWT = posterior wall thickness; EDD = end-diastolic diameter; ΔEDD = changes in the end-diastolic diameter from value at rest.
- 10 mm Hg is largely determined by the cardiopulmonary receptors since LBNP at - 10 mm Hg does not change blood pressure or heart rate, and thus this level of LBNP presumably does not inhibit the arterial baroreceptors. In contrast, forearm vasoconstriction during LBNP at -40 mm Hg must have been mediated by deactivation of the cardiopulmonary as well as arterial baroreceptors since LBNP at -40 mm Hg decreased not only central venous pressure but also systolic blood pressure and increased heart rate. However, it has been suggested that arterial baroreceptors have only a minor role in forearm vasoconstriction during LBNP as opposed to splanchnic vasoconstriction, which is largely determined by the arterial baroreceptors. Therefore, it is likely that the slope of the regression line as well as reflex forearm vasoconstriction with LBNP at -10 mm Hg is largely determined by the cardiopulmonary baroreceptors.

On the basis of these considerations, we interpret our results to suggest that the inhibitory influence of the cardiopulmonary receptors on forearm vascular resistance is augmented in athletes. Despite the augmented inhibitory influence of the cardiopulmonary receptors, resting forearm blood flow and vascular resistance did not differ between athletes and nonathletes. However, the effects of exercise training on resting forearm blood flow and vascular resistance must be complex. After exercise training, muscles at rest as well as during submaximal exercise may need less blood flow since the capacity to extract oxygen from blood is increased. It is possible that the effect of augmented cardiopulmonary baroreflex may have been masked by such local change. Clausen et al have shown that exercise training involving large muscle groups caused the decrease in resting cardiac output and the increase in resting total peripheral vascular resistance that was accompanied by the increase in the total arterial-venous oxygen difference. It is interesting to note that they found no increase in the resting regional arterial-venous oxygen difference in the arm, suggesting that resting blood flow to the arm was not decreased. The latter results may suggest that there might have been relative vasodilation in the arm.

We do not know from our studies the mechanism by which exercise training augments the cardiopulmonary receptor reflex. We examined the possibility that the decreases in the left ventricular volume during LBNP might be greater in athletes than in nonathletes. The results indicate that the decreases in the left ventricular diameter during graded LBNP did not differ significantly between the two groups. However, the end-diastolic diameter of the left ventricle during LBNP at -20 or -40 mm Hg was greater, and also at rest or during LBNP at -10 mm Hg it tended to be greater (p < 0.1) in athletes than in nonathletes. It may be possible that the larger diastolic volume of the left ventricle at each level of LBNP in athletes could have contributed to increased firing of the ventricular receptors. However, the increased thickness of the left ventricular wall in athletes may tend to reduce receptor activation because of reduced distensibility. Thus, the mechanism by which exercise training augments the cardiopulmonary receptor reflex is unclear and further studies are needed to clarify it.

Several studies have shown that trained men and animals may have significantly lower orthostatic tolerance as judged by the frequency of or time to the onset of syncope during tilt or LBNP than normal untrained controls. The results of this study suggest that orthostatic intolerance during tilt or LBNP does not result from impaired reflex vasoconstriction mediated by the cardiopulmonary receptors. Hypotension during tilt or LBNP could be caused by multiple mechanisms, which may involve impaired arterial baroreflex, a greater venous pooling in the lower body during tilt or LBNP, or arteriolar structural changes that allow for greater dilation. An animal study has shown that training causes further impairment of orthostatic tolerance in immunosympathectomized rats as compared with nontrained immunosympathectomized rats. The latter results may be taken to suggest that orthostatic intolerance after training may be related to mechanisms other than the baroreflexes or the sympathetic nervous system.

The augmented cardiopulmonary baroreflex may contribute to some of cardiovascular and endocrine adaptations that are known to occur after training. It has been suggested that the cardiopulmonary receptor reflex contributes to the control of skin blood flow during exercise at normal as well as high temperature. The augmented inhibitory influence of the cardiopulmonary receptors may contribute to the maintenance of skin blood flow at a higher level, which may be important in temperature regulation during exercise. It has been shown that the rise in rectal temperature during exercise is lower in trained than in nontrained subjects. It also has been shown that the increase in plasma renin activity, vasopressin, and norepinephrine in response to the same work load are less after than before training which may result from the augmented cardiopulmonary baroreflex. The cardiopulmonary receptors are known to play an important role in the regulation of the release of renin and vasopressin. It also has been shown that augmentation of cardiopulmonary receptor activity attenuates the increase in sympathetic nerve activity elicited by somatic afferent stimulation. Thus, the augmented cardiopulmonary receptor reflex may contribute to altered control of sympathetic nervous activity during muscle exercise in athletes or after training. Recent observations suggest that the cardiopulmonary receptors exert surprisingly little influence on blood pressure regulation during treadmill exercise in nontrained dogs. However, it is possible that the cardiopulmonary receptors contribute to control of blood pressure during different types of exercise or to control of regional vascular resistance during exercise in some vascular beds in humans.

In summary: The results of our study suggest that the gain of cardiopulmonary receptor reflex in control of forearm vascular resistance is greater in highly trained young athletes than in age-matched nonath-
Augmented cardiopulmonary baroreflex function may contribute to some of the cardiovascular adaptations that occur with exercise training.

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Augmented cardiopulmonary baroreflex control of forearm vascular resistance in young athletes.

A Takeshita, S Jingu, T Imaizumi, Y Kunihiko, S Koyanagi and M Nakamura

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