Training-Induced, Pressure-Lowering Effect in SHR
Wide Effects on Circulatory Profile of Exercised and Nonexercised Muscles

Ronaldo Meira Melo, Eduardo Martinho, Jr, Lisete Compagno Michelini

Abstract—We showed that the training-induced, pressure-lowering effect correlates with decreased arteriole wall/lumen ratio and venule growth in the gracilis muscle. To investigate whether these beneficial changes are tissue-specific or occur in other muscles and tissues, we analyzed the effects of hypertension and training on microcirculatory profile of locomotor/nonlocomotor muscles and another nonmuscular tissue. Spontaneously hypertensive rats (SHR) and Wistar-Kyoto rats were submitted to low-intensity training (50% to 60% maximal exercise capacity, 13 weeks); age-matched control rats were kept sedentary. Trained and sedentary rats were instrumented for pressure and heart rate measurements at rest. Morphometric analyses (arterioles, capillaries, venules) were performed in all tissues. Training attenuated pressure and heart rate only in SHR. Arterioles (inner diameter <30 μm) were markedly hypertrophied in sedentary SHR, but wall/lumen ratio was equally reduced (~30%) and normalized by training in locomotor (soleus, gastrocnemius, gracilis) and nonlocomotor skeletal muscles (temporalis) in the myocardium and diaphragm, without changes in the renal cortex. Training also increased venule density (~2-fold) only in locomotor and nonlocomotor muscles of SHR. Capillary density was similarly increased in all exercised muscles of both groups, with no change in temporalis and kidneys. Data suggest that growth/proliferation of small venules and regression of hypertrophied arteriole wall/lumen ratio are generalized tissue-specific (skeletal muscle) and group-specific (SHR) adjustments to training to reduce local resistance and augment physical capacity of circulation, thus contributing to training-induced pressure-lowering effect. They are accompanied by remodeling of myocardium (cardiac output) and diaphragm arterioles (ventilatory adjustments), stressing the importance of training as a nonpharmacological therapy to control pressure levels in hypertension. (Hypertension. 2003;42[part 2]:851-857.)

Key Words: life style ▪ hypertension, chronic ▪ arterioles ▪ capillaries ▪ myocardium ▪ kidney

Chronic hypertension is a highly prevalent disease (affecting 20% of adults and ~50% of elderly) and a common risk factor for different cardiovascular diseases. The search for efficient pharmacological and nonpharmacological antihypertensive therapies is a goal pursued by many researchers and clinicians.1–3 Experimental evidence has shown that regular physical activity reduces pressure in hypertensive patients, contributing to the decrease cardiovascular morbidity and mortality rates.3,4 However, very little information on the mechanisms underlying the beneficial effects of repetitive exercise is available.

In two recent well-controlled studies on male spontaneously hypertensive rats (SHR),5,6 we confirmed the efficacy of low-intensity aerobic training to reduce pressure levels, showing in addition that pressure reduction was significantly correlated with both hind limb resistance decrease and normalization of the enlarged arteriole wall-to-lumen ratio, presented by the gracilis muscle in hypertensive sedentary control animals.5 We were also able to show in the trained SHR that pressure fall as well as the large hind limb blood inflow during dynamic exercise were both significantly correlated with venular growth in the gracilis.6 These responses were specific for the trained SHR group and not observed in trained normotensive control rats (Wistar-Kyoto rats, WKY).5,6 It is our working hypothesis that these training-induced changes in the circulatory profile, by reducing vascular resistance and increasing parallel conductance of muscle circulation, could effectively contribute to decrease pressure and increase reactive hyperemia in hypertensive subjects. It was necessary to determine if these responses are characteristic of the gracilis muscle or occur in other locomotor and nonlocomotor skeletal muscles as well as other muscles actively participating in the exercise such as the myocardium (cardiac output adjustments) and diaphragm (ventilatory responses).

Therefore, with the use of male SHR and age-matched WKY, we compared the effects of hypertension and training on (1) baseline blood pressure and heart rate and (2) simul-
nonlocomotor muscle), of myocardium and diaphragm (exercised but not locomotor), and of renal cortex (not locomotor, not exercised) were obtained from WKY\textsubscript{S}, WKY\textsubscript{T}, SHR\textsubscript{S}, and SHR\textsubscript{T}.

**Morphometric Evaluations**

All samples were cut into small pieces and immersed in the same fixative for 24 hours. Tissue samples were dehydrated in a graded series of ethanol (70%, 95%, 100%), embedded in resin (2-hydroxyethylmethacrylat, dissolved in 4% paraformaldehyde), and polymerized at 70°C. The resin blocks were cut with glass knives, with the use of a microtome (Pyramike LKB 1800, 2-μm sections). The sections were heat-mounted on glass slides and stained with 0.25% toluidine blue. From each tissue sample, 3 slides were made (initial, middle, and final part of the block) with 9 slices each; 2 microscopic fields were analyzed in each slice, amounting to 18 areas per slide.

Morphometric analysis was made in transversal tissue sections with a light microscope (Leica DML, Germany, ×200 magnification). Arterioles were identified and respective images were acquired (color video camera Sony CCD IRIS/RGB, model DXC-151A), digitized, and analyzed off-line (Media Cybernetics, Pro-Series 128 Capture Kit software). Analysis included determination of inner and outer diameter ($D=2r$, where $r$ is the inner or the outer radius) and the calculation of both wall thickness ($\delta$=outer $r$–inner $r$) and wall-to-lumen ratio (wall/lumen=δ/inner $D$). Arteriole inner mean diameter was determined as the average of maximal and minimal measured radii and used as a criterion to classify arterioles according to its size. Only the arterioles of similar size occurring in all groups were included in the statistical analysis. With the exception of myocardium in which larger arterioles were easily found (inner $D$ up to 60 μm), the statistics in other tissues only included smaller arterioles (inner $D$ in the range of 8 to 10 up to 25 to 30 μm).

Morphometric analysis also included quantification of capillaries, muscle fibers, and small venules in WKY\textsubscript{S}, WKY\textsubscript{T}, SHR\textsubscript{S}, and SHR\textsubscript{T} groups. Occurrence of these structures in the different tissues (determined in microscopic field measuring 0.0697 mm$^2$) were randomly determined in at least 18 slices per rat. Capillaries were identified as small vessels, lined by a single layer of endothelial cells with a diameter of <12 μm.$^5$ To avoid possible mistakes with lymphatic capillaries, small vessels with irregular profiles were excluded from the counting. In the kidneys, capillary occurrence was determined in the glomeruli. In all tissues, both muscular and nonmuscular venules were analyzed. Nonmuscular venules were identified as vessels lined by a single layer of endothelial cells and surrounded by reticular fibers and pericytes.$^9$ They had maximal internal diameter slightly larger than capillaries (12 up to 25 to 30 μm) and differed from capillaries because of the nonuniform lumen. Muscular venules were easily identified by the presence of a well-defined smooth muscle coat. Since venules with internal diameter >40 μm were not equally found among the 4 groups, comparison of venule density was based only on those with inner diameter <40 μm. To avoid misidentification (due to toluidine blue staining of the renal cortex, venules and renal tubules showed a close similar appearance), renal venules were not included in the statistical analysis. Values for venule and capillary densities, always obtained in 0.0697 mm$^2$, were expressed as number per mm$^2$.

**Statistical Analysis**

All data are reported as mean±SEM. Two-way ANOVA (strain×condition) was used to compare basal values of MAP and HR, and the morphometric parameters (densities, vascular dimensions, capillary/fiber, and wall/lumen ratios). Significant differences were further investigated by using Newman-Keuls as the post hoc test. The level of significance was $P<0.05$.

**Results**

**Control Values of Pressure and Heart Rate**

At the beginning of T or S protocol, SHR had elevated tail pressure (175±6 versus 110±2 mm Hg in the WKY group) but similar body weight (~216±7 g). Weight gain during the
had a thicker wall than normotensive arterioles of similar size.

As expected, hypertensive arterioles had a thicker wall than normotensive arterioles of similar size.

Figure 1. Upper panels: MAP and HR values in conscious sedentary (S) and trained (T) WKY and SHR at rest; n=6 to 8 rats per group. Bottom panels: Effects of hypertension and training on arteriole wall/lumen ratio in different tissues; n=3 to 4 rats per group. *P<0.05 vs †WKY, ‡sedentary.

13-week period was slightly lower in the WKY compared with the other groups (+98±8 versus +106±5 to +123±6 g, respectively). After the 13-week period, tail pressure was similar in WKY and WKY (119±1 mm Hg) but significantly reduced in SHR versus SHT (176±1 versus 190±1 mm Hg). Direct measurement of arterial pressure in the conscious state confirmed an 8.3% reduction on MAP in the SHR group (166±9 versus 181±9 mm Hg in SHRS, Figure 1, upper panel), without any pressure change in the trained WKY versus WKY (116±3 mm Hg). Low-intensity training also attenuated baseline HR in the SHR group (355±15 versus 395±13 bpm, with a smaller reduction in the WKY group: from 387±10 to 368±12 bpm, P>0.05, Figure 1).

Microcirculatory Changes Induced by Training in Hypertensive and Normotensive Animals

After the control measurements, WKYS, WKYT, SHR, and SHR were deeply anesthetized for transcardiac perfusion and tissue sampling. Morphometric analysis after histological processing revealed profound changes in microcirculatory profile of skeletal muscle circulation induced by training in hypertensive animals. As expected, hypertensive arterioles had a thicker wall than normotensive arterioles of similar size (see Figure 2). Quantitative data in all tissues analyzed revealed that arterioles with mean internal diameter in the range of 7 to 8 up to 24 to 26 μm had increased wall thickness (average of +28% up to +95%, Table) and enlarged wall/lumen ratio (average of +41% up to +102% in the myocardium and gastrocnemius, respectively, over the normotensive values in the range of 0.32±0.03 up to 0.43±0.05, Figure 1). Despite this, training was effective to normalize SHR arteriole wall/lumen ratio in all tissues analyzed, with the exception of the renal arterioles (Figure 1). Interestingly, as depicted in Figure 2B, low-intensity training was able to correct the enlarged wall/lumen ratio of the control, not exercised, skeletal muscle (temporalis muscle). The reversion of wall/lumen ratio of SHR arterioles back to control normotensive values was due to a significant decrease in wall thickness (as observed in the gastrocnemius and temporalis muscles, Table) or by a slighter decrease simultaneous to a persisted enlargement of the inner diameter (as observed in the soleus, gracilis, diaphragm, and myocardium arterioles). Consistently, training did not change thickness and/or inner diameter of kidney SHR arterioles as well as those of normotensive rats (Table and Figure 1). Of interest was the myocardium response. One observes that it depends on the arteriole size: When larger arterioles (inner diameter up to 60 μm) are included in the statistical analysis, the effect of hypertension was persistent (SHRT=0.45±0.02, WKYS=0.32±0.04, <0.05), but training was not able to completely correct the enlarged wall/lumen ratio of these arterioles (SHRT=0.41±0.02, >0.05 versus SHRS).

The effect of hypertension on venule occurrence (inner diameter <40 μm) changed according to the tissue analyzed: Reduction or a tendency to reduction (gastrocnemius, gracilis, diaphragm, and myocardium), increase (soleus), and no change (temporalis) were observed. Low-intensity training consistently caused a marked increase in venule density of all skeletal muscles, exercised or not (increases of 1.8-fold up to 2.5-fold were observed in the soleus, gracilis, and gastrocnemius as well as in the temporalis muscle, Table). No significant venular changes were observed after training in the diaphragm and myocardium of the SHR group as well as in all tissues of normotensive animals.

Mean values of capillary density confirmed that hypertension induced rarefaction (average reduction of 20%, SHR,

Figure 2. Comparison of photomicrographs taken from soleus (A) and temporalis muscles (B). In each set are shown transverse sections from arterioles of WKY (upper panels) and SHR (lower panels) submitted to training program (T, right panels) or kept sedentary (S, left panels). Double arrows indicate wall thickness. Bar=25 μm.
Capillary, Venular, and Arteriolar Microcirculatory Changes Induced by Hypertension and Training in the Tissues Analyzed

<table>
<thead>
<tr>
<th>Vessel Measurement, Tissue</th>
<th>WKY₀</th>
<th>WKY₁</th>
<th>SHR₀</th>
<th>SHR₁</th>
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<tbody>
<tr>
<td>Capillary density, n/mm²</td>
<td></td>
<td></td>
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<tr>
<td>Soleus</td>
<td>377±14</td>
<td>576±22†</td>
<td>366±9</td>
<td>521±12†*</td>
</tr>
<tr>
<td>Gracilis</td>
<td>463±18</td>
<td>688±6†</td>
<td>366±8*</td>
<td>507±8†*</td>
</tr>
<tr>
<td>Gastrocnemius</td>
<td>429±13</td>
<td>569±24†</td>
<td>349±24</td>
<td>473±47†*</td>
</tr>
<tr>
<td>Temporalis</td>
<td>497±6</td>
<td>501±7</td>
<td>368±21*</td>
<td>376±22*</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>497±9</td>
<td>752±18†</td>
<td>413±6</td>
<td>644±76†*</td>
</tr>
<tr>
<td>Myocardium</td>
<td>908±3</td>
<td>1117±12†</td>
<td>788±13*</td>
<td>918±10*</td>
</tr>
<tr>
<td>Kidney</td>
<td>3723±205</td>
<td>4015±251</td>
<td>3110±34*</td>
<td>3392±109*</td>
</tr>
<tr>
<td>Capillary/fiber ratio, n/fiber</td>
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<td></td>
</tr>
<tr>
<td>Soleus</td>
<td>1.89±0.07</td>
<td>3.00±0.11†</td>
<td>1.90±0.04</td>
<td>2.68±0.07†*</td>
</tr>
<tr>
<td>Gracilis</td>
<td>2.03±0.04</td>
<td>3.08±0.08†</td>
<td>1.75±0.06*</td>
<td>2.30±0.04†*</td>
</tr>
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<td>Gastrocnemius</td>
<td>2.00±0.10</td>
<td>2.75±0.12†</td>
<td>1.80±0.18*</td>
<td>2.45±0.13†*</td>
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<tr>
<td>Temporalis</td>
<td>2.40±0.14</td>
<td>2.43±0.17</td>
<td>1.58±0.21*</td>
<td>1.95±0.17*</td>
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<tr>
<td>Diaphragm</td>
<td>2.40±0.15</td>
<td>2.65±0.09†</td>
<td>1.60±0.21*</td>
<td>2.13±0.12†</td>
</tr>
<tr>
<td>Venule density, n/mm²</td>
<td></td>
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<tr>
<td>Soleus</td>
<td>5.5±0.5</td>
<td>5.9±0.2</td>
<td>7.7±0.6*</td>
<td>13.7±2.2*</td>
</tr>
<tr>
<td>Gracilis</td>
<td>5.9±0.4</td>
<td>5.9±0.4</td>
<td>4.7±0.8</td>
<td>10.0±1.1*</td>
</tr>
<tr>
<td>Gastrocnemius</td>
<td>7.7±1.0</td>
<td>9.4±1.3</td>
<td>3.7±0.5*</td>
<td>9.3±1.8*</td>
</tr>
<tr>
<td>Temporalis</td>
<td>4.8±1.3</td>
<td>5.4±0.6</td>
<td>4.8±1.0</td>
<td>9.8±1.0†*</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>7.1±1.2</td>
<td>6.9±0.9</td>
<td>4.7±0.1</td>
<td>7.1±0.8</td>
</tr>
<tr>
<td>Myocardium</td>
<td>46.1±3.2</td>
<td>36.1±4.9</td>
<td>41.4±1.2</td>
<td>49.6±5.1</td>
</tr>
<tr>
<td>Arterioles</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soleus (8–23 μm)</td>
<td>23.2±1.4/13.2±0.8</td>
<td>20.1±1.6/12.1±0.9</td>
<td>24.0±1.1/10.5±0.7</td>
<td>26.9±1.4/14.0±0.8</td>
</tr>
<tr>
<td>Gracilis (8–22 μm)</td>
<td>20.2±1.4/11.9±1.0</td>
<td>22.6±1.8/13.1±1.2</td>
<td>27.8±1.7/12.0±0.9</td>
<td>32.6±2.9/17.3±1.5</td>
</tr>
<tr>
<td>Gastrocnemius (8–21 μm)</td>
<td>23.9±3.0/13.3±2.7</td>
<td>24.5±3.1/13.9±2.9</td>
<td>27.8±1.5/10.7±0.7</td>
<td>23.3±1.3/12.3±0.8</td>
</tr>
<tr>
<td>Temporalis (8–26 μm)</td>
<td>33.7±4.9/19.2±3.2</td>
<td>28.1±2.0/14.4±0.7</td>
<td>37.5±2.7/14.7±1.3</td>
<td>24.9±1.1/12.8±0.7</td>
</tr>
<tr>
<td>Diaphragm (7–24 μm)</td>
<td>20.1±2.4/11.1±1.6</td>
<td>30.2±3.5/17.0±2.4</td>
<td>24.1±1.0/10.5±0.7</td>
<td>29.2±2.8/15.9±1.9†</td>
</tr>
<tr>
<td>Myocardium (10–24 μm)</td>
<td>25.5±1.7/15.6±1.3</td>
<td>26.3±1.6/15.3±1.0</td>
<td>28.8±1.3/14.8±0.8</td>
<td>26.9±1.1/15.3±0.6</td>
</tr>
<tr>
<td>Kidney (12–26 μm)</td>
<td>29.9±1.9/17.4±1.0</td>
<td>25.0±1.9/14.8±0.7</td>
<td>45.2±0.8/20.7±0.7*</td>
<td>44.1±1.5/19.1±0.9*</td>
</tr>
</tbody>
</table>

Values (mean±SEM) refer to 3 to 4 rats/group. Arterioles are presented as number analyzed/group (in parenthesis), respective outer/inner diameter, wall thickness (between brackets), and the minimum-maximal inner diameter of all arterioles analyzed (bold, below the indication of the tissue).

*P<0.05 vs WKY; †P<0.05 vs sedentary (S).
Performance to Maximal Exercise Test and Efficacy of Training Protocol

Performance of rats to the maximal exercise test on the treadmill differed between SHR and WKY groups since the beginning of the protocols (1.83 ± 0.07 versus 0.97 ± 0.04 km/h, respectively), at week zero). On the other hand, adjustment of the exercise protocol to 50% to 60% of respective maximal exercise capacity produced similar training effects on both groups. After 13 weeks, SHR_T and WKY_T maintained unaltered treadmill performance (1.70 ± 0.07 and 0.88 ± 0.03 km/h, respectively), whereas sedentary control animals showed a marked decrease in the exercise intensity attained at maximal exercise test (0.96 ± 0.11 and 0.54 ± 0.06 km/h, respectively). Therefore at the end of protocols, low-intensity training was effective to similarly increase exercise performance on treadmill: +77% in SHR_T and +63% in WKY_T (increments did not differ between groups).

Discussion

Data of the present study confirmed the efficacy of training to lower pressure and to reduce heart rate in hypertensive animals, showing in addition that the training-induced, pressure-lowering effect was accompanied by (1) normalization of arteriole wall/lumen ratio in all muscles (locomotor or not, exercised or not) without changing renal arterioles, a nonmuscular tissue, and (2) marked increase in venule density of all skeletal muscle analyzed, with no change in the myocardium and diaphragm. These adjustments are shown to be specific for the trained SHR group. In addition, our data also showed training-induced enlargement of the capillary bed in both SHR and WKY groups but only in tissues actively participating in the exercise.

It is well recognized that regular physical activity reduces blood pressure in hypertensive individuals, without significant pressure changes in normotensive individuals.2–6,10–14 It has also been suggested that exercise intensity influences the pressure-lowering effect, with larger reductions being observed with lower exercise intensities.12–14 We did not analyze the effect of training intensity, but our results clearly show that exercise protocol used (50% to 60% of maximal physical activity) caused an important MAP decrease (average reduction of 15 mm Hg, only in the SHR group). Pressure reduction was accompanied by both resting bradycardia and specific training-induced adjustment in hypertensive arterioles of all muscles analyzed.

The cause-effect relation between hypertension and arteriolar hypertrophy is well established.15–18 Currently, it is recognized that an efficient antihypertensive therapy should aim not only to reduce blood pressure but also to correct lesions associated with hypertension, such as the altered vascular structure.1,15,17,18 Several pharmacological treatments have been shown to reduce arteriolar hypertrophy,17–19 but with exception of one previous study by us,6 there is no information on training-induced changes of arteriole wall/lumen ratio. In the previous study with trained/sedentary SHR, we documented the efficacy of training to normalize gracilis arteriole wall/lumen ratio, showing in addition that arteriolar response as well as hind limb resistance reduction after training were significantly correlated with blood pressure reduction.5 What we show now is that the arteriolar adjustment is a generalized response of the hypertensive skeletal muscle arterioles to training, present in locomotor and nonlocomotor muscles, exercised or not. This is a potentially important response, considering the relative extension of the skeletal muscle tissue. Although not a main objective of the present study, we could observe in several tissues that arteriole wall/lumen ratios were reduced by increases of inner and/or outer diameter, with no changes in vessel thickness (data in the Table), which is a characteristic pattern for vascular remodeling.18 Of importance is the demonstration that training, by reversing lumen encroachment, does normalize enlarged wall/lumen ratio of small arterioles in hypertensive muscles, even though pressure was not normalized. Probably the absence of similar effects in other tissues harboring vasoconstriction to repetitive dynamic exercise (such as the kidneys) and/or in larger arterioles or arteries could explain why pressure decreases but is not normalized after training. Independent of the pressure effect, the broad normalization of arteriolar structure in active/inactive muscles is an important adaptive response to training, considering both the high proportion of muscle mass/body weight and the strong opposition to a pressor mechanism involving mainly the smaller vessels. In this regard, our present and previous data,5 showing a complete normalization of arteriolar structure in the skeletal muscle (arterioles < 30 μm) as well as myocardium and diaphragm, stressed the potential therapeutic power of the exercise training as a nonpharmacological tool to correct vascular changes leading to hypertension.

Our data also showed in the trained SHR a marked increase in venular growth, specific for small venules (up to 40 μm in diameter), which indicates vessel neoformation.20 Previous works have shown increased capillary density as a result of exercise training in normotensive5,21–23 and hypertensive animals.5 In a recent study, we have shown that low-intensity training was effective to induce venular growth in the gracilis muscle of SHR, without any change in the WKY group.6 It was also observed that venule density increase was significantly correlated with both the larger blood inflow during dynamic exercise and the pressure decrease observed in the SHR group.6 The present results extended this observation to other exercised and nonexercised skeletal muscles but not to the diaphragm and myocardium, indicating that training-induced venular growth is a more general phenomenon than previously described but is specific for skeletal muscle circulation of hypertensive individuals.
Although venous capacitance does not directly contribute to pressure levels, venular growth is an interesting adjustment to training. Venules and veins contain \( \approx 70\% \) of the total blood volume.\(^{24}\) The increased skeletal muscle venular bed in SHR\(_T\), by further augmenting the vascular capacity of an already-large tissue, contributes to reducing blood volume/vascular capacity ratio and to accommodating larger blood inflow during reactive hyperemia. This response may be of interest if one considers that blood volume/vascular capacity ratio (as indicated by mean circulatory filling pressure) is significantly increased in several models of hypertension.\(^{16}\) According to Guyton’s theory, mean circulatory filling pressure increase does contribute to pressure elevation in hypertension. Actually, the relevance of vascular capacity changes to reduce pressure in hypertensive individuals has been noted before.\(^{6,25}\) In addition, venules could also sense locally produced metabolites and release endothelial vasoactive factors, which, reaching adjacent arterioles, can affect vascular tone and local flow.\(^{26–28}\) In this regard, training-induced venular growth could be another functional benefit of training in the SHR group, since a large endothelial surface favors the production/release of endothelium-derived factors.

The observation that training-induced venule enlargement and arteriole wall/lumen ratio reduction were observed only in the SHR group (that underwent opposite vascular changes during the establishment of hypertension) pointed to the potential role of repetitive exercise to correct hypertensive mechanisms. On the other hand, capillary growth and increased capillary/fiber ratio were observed in both SHR\(_T\) and WKY\(_T\) groups when compared with respective sedentary controls. Generalized capillary rarefaction in hypertensive\(^{29–30}\) and increased capillary supply of skeletal muscle and myocardium in exercised normotensive\(^{20–23,31}\) and hypertensive\(^{6}\) animals and human beings were already described. It was also shown that electrical stimulation increased local capillary density.\(^{32,33}\) The present data confirmed these observations showing significant rarefaction or a clear tendency to rarefaction in different tissues of SHR\(_T\) (versus WKY\(_S\)) and significant capillary growth only in the exercised tissues of SHR\(_T\) and WKY\(_T\) (versus respective sedentary control animals). These results associated with the absence of capillary growth in both temporal muscle (not exercised) and renal cortex (disclosing reduced flow during repetitive exercise) reinforce the observation that large capillary supply in exercised skeletal muscles reflects mainly the increased oxygen uptake of active muscles, being an adaptive response to augmented local flow during dynamic exercise.\(^{20,34}\)

Although this study did not address the mechanisms responsible for training-induced effects, one might speculate that changes in capillary supply are not group-specific, being mediated through local factors released or activated by the exercise in active tissues. On the other hand, arteriole and venule adjustments are group-specific (SHR) and probably not dependent on paracrine/autocrine, metabolic, and/or myogenic factors, since similar alterations were observed in the temporals as well as the other locomotor (presenting venule and arteriole adaptive responses) and nonlocomotor muscles (presenting only arteriolar adaptive response). The identity of these mechanisms remains to be studied.

In conclusion, growth and proliferation of small venules and regression of hypertrophied arteriole wall/lumen ratio are anatomic responses of exercised and nonexercised muscles, specific to the SHR group. These compensatory adjustments, by reducing local resistance and augmenting physical capacity of skeletal muscle circulation, contribute to the training-induced, pressure-lowering effect observed in hypertensive subjects. They are accompanied by anatomic remodeling of myocardium and diaphragm arterioles, with important improvement of cardiac output and ventilation.

**Perspectives**

Although classic pharmacological therapies have led to good control of pressure levels with reasonable reversion of arteriole hypertrophy (mainly by converting enzyme inhibitors and angiotensin receptor blockers), the problem still persists. In the last decade, exercise training has been used as an important additional therapeutic tool, helping to lower blood pressure mainly in borderline/moderate hypertensive subjects. The findings of this study proving the great and wide impact of low exercise training to normalize and improve microcirculatory profile in different tissues (representing a large proportion of the body) reinforce the importance of low-intensity training as a complementary nonpharmacological therapy to obtain a more efficient control of pressure levels in moderate as well as severe hypertension.

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**References**


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