Downregulation of the Vascular Renin-Angiotensin System by Aerobic Training
– Focus on the Balance Between Vasoconstrictor and Vasodilator Axes –

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Background: Hyperactivity of the renin-angiotensin system (RAS) and functional deficits in hypertension are reduced after exercise training. We evaluate in arteries, kidney and plasma of hypertensive rats the sequential effects of training on vascular angiotensinogen, Ang II and Ang (1-7) content.

Methods and Results: Spontaneously hypertensive rats (SHR) and Wistar-Kyoto rats (WKY) were trained or kept sedentary (S) for 3 months. After hemodynamic measurements (weeks 0, 1, 2, 4, 8 and 12), blood, arteries and kidneys were obtained to quantify the angiotensin content (HPLC) and angiotensinogen expression (Western Blotting). SHR-S vs. WKY-S exhibited elevated pressure, increased angiotensinogen and angiotensins’ content in the renal artery with a high Ang II/Ang (1-7) ratio (~5-fold higher than in the femoral artery, kidney and plasma, and 14-fold higher than in the aorta). Training promptly reduced angiotensinogen expression and downregulated the RAS in the renal SHR artery (1st–12th week), with a specific reduction of the vasoconstrictor axis; significant reduction of the AngII/Ang (1-7) ratio (36%, T4-T8) occurred simultaneously with significant pressure fall (5%). In other SHR arteries, plasma and kidneys and in all WKY tissues, T-induced AngII and Ang (1-7) reductions were proportional, maintaining the AngII/Ang (1-7) ratio.

Conclusions: Vascular RAS is not equally expressed in vessels, having crucial importance in the renal artery. In the renal SHR artery, training downregulates the vasoconstrictor and preserves the vasodilator axis while in other tissues and plasma training reduces both RAS axes, thus maintaining the vasoconstriction/vasodilatation balance in a lower level. (Circ J 2015; 79: 1372–1380)

Key Words: Angiotensinogen; Angiotensin II/Angiotensin (1-7) ratio; Femoral artery; Kidney; Renal artery

A ccumulating experimental evidence has shown that exercise training is an efficient and safe tool to counteract deleterious effects induced by hypertension, coronary artery disease and other cardiovascular diseases.1–3 Exercise training promotes several cardiovascular adjustments in hypertensive and normotensive individuals, such as remodeling of the heart with a simultaneous stroke volume increase and heart rate (HR) decrease,1,2,4,5 outward eutrophic remodeling of arteries and arterioles, capillary angiogenesis, and venule neoinflation in the exercised muscles.6,7 Aerobic training also restores impaired endothelial function in hypertensive animals and facilitates artery/arteriole vasodilatation.8,9 These adaptive mechanisms, by reducing vascular resistance and improving both blood flow and tissue conductance, ameliorate impaired functions in cardiovascular diseases.

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Although the use of exercise as a therapeutic tool has increased considerably, there is scarce information on the mechanisms conditioning the beneficial effects of training. Previous observations indicate the ability of training to reduce either the activity of the renin-angiotensin system (RAS), oxidative stress and inflammation.10–12 By evaluating the effects of low-intensity aerobic training on the expression of brain RAS in cardiovascular-controlling areas of spontaneously hypertensive rats (SHR), we observed a prompt and robust training-induced reduction of either angiotensinogen (Aogen)
expression, NADPH oxidase activity, reactive oxygen species formation, NF-kB translocation to the nucleus and pro-inflammatory cytokines expression, which were positively correlated with improvement of cardiovascular function and blood pressure fall.13,14 Interestingly, the effects of training on brain RAS expression were similar to those observed in hypertensive rats after chronic AT1 receptor blockade,15 suggesting the potenti-ality for aerobic training to block RAS hyperactivity. Previous studies in heart failure and hypertensive animals also indicated that training reduced the overactivity of the vasoconstrictor arm while preserving the RAS vasodilator axis in the heart, kidney, skeletal muscle and aorta.16-19 There is no information on the effects of training on the RAS activity in resistance arteries that are crucial to maintain blood pressure and flow at rest and during exercise. It is our working hypothesis that training might promptly alter the expression/content of vascular ACE-Ang II-AT1 receptor and ACE2-Ang (1-7)-Mas recep-tor axes and that this change might differ between arteries and between hypertensive and normotensive vessels.

Therefore we sought to investigate in SHR the sequential effects of aerobic training on Aogen expression and on Ang II and Ang (1-7) content in resistance arteries that respond to exercise with vasoconstriction (renal), vasodilation (femoral and carotid), or no change (thoracic aorta). For comparison, exercise with vasoconstriction (renal), vasodilation (femoral and angioplasty cytokines expression, which were positively correlated with improvement of cardiovascular function and blood pressure fall.13,14 Interestingly, the effects of training on brain RAS expression were similar to those observed in hypertensive rats after chronic AT1 receptor blockade,15 suggesting the potenti-ality for aerobic training to block RAS hyperactivity. Previous studies in heart failure and hypertensive animals also indicated that training reduced the overactivity of the vasoconstrictor arm while preserving the RAS vasodilator axis in the heart, kidney, skeletal muscle and aorta.16-19 There is no information on the effects of training on the RAS activity in resistance arteries that are crucial to maintain blood pressure and flow at rest and during exercise. It is our working hypothesis that training might promptly alter the expression/content of vascular ACE-Ang II-AT1 receptor and ACE2-Ang (1-7)-Mas recep-tor axes and that this change might differ between arteries and between hypertensive and normotensive vessels.

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excitation and 465nm of emission) in a Tecan infinity F200 system (Switzerland). Serum ACE2 activity was determined by spectrofluorimetry (Tecan, Switzerland), using the synthetic fluorogenic substrate, Mca-APK-Dnp (10umol/L), as previously described, but with some modifications. To each well, 10μl of each sample was added, along with 90μl of buffer and 25μl of RIPA lysis buffer, centrifuged at 12,000 rpm for 10 min at 4°C, and the supernatant was collected. The protein levels were measured using a BCA protein kit assay (Thermo Scientific). The samples were treated with Laemmli buffer containing dithiothreitol (Bio-Rad) and boiled for 5 min. Similarly aliquots (35μg) were resolved under denaturating conditions in a 8% SDS-PAGE gel and electroblotted onto a nitrocellulose membrane for 2 h at 100 volts (constant) in a Bio-Rad miniaturized apparatus. Non-specific protein binding to the nitrocellulose membrane was reduced by pre-incubation of the nitrocellulose membrane with 5% non-fat milk in TBS-T for 1 hour, with shaking. The samples were then incubated overnight at 4°C with primary antibodies against Aogen (1:1,000 Epitomics). After 3-times washing, the membrane was incubated with horseradish peroxidase-conjugated anti-rabbit secondary antibody (Amersham Pharmacia, UK) for 1h. The reactive bands were visualized using an ECL kit (Super Signal West Pico) according to the manufacturer’s instructions.

Table 1. Sequential Changes on Treadmill Performance and Resting MAP and HR in WKY and SHR Submitted to Sedentary (S) or Training (T) Protocols

<table>
<thead>
<tr>
<th>Treadmill speed (km/h)</th>
<th>WKY-S</th>
<th>WKY-T</th>
<th>SHR-S</th>
<th>SHR-T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>1.11±0.04 (n=45)</td>
<td>1.10±0.03 (n=108)</td>
<td>1.53±0.05*(n=38)</td>
<td>1.53±0.03*(n=84)</td>
</tr>
<tr>
<td>Week 4</td>
<td>1.08±0.05 (n=25)</td>
<td>1.47±0.04* (n=52)</td>
<td>1.25±0.07* (n=24)</td>
<td>2.07±0.07*** (n=46)</td>
</tr>
<tr>
<td>Week 8</td>
<td>1.01±0.07 (n=26)</td>
<td>1.80±0.07** (n=40)</td>
<td>1.09±0.08† (n=25)</td>
<td>2.34±0.09*** (n=26)</td>
</tr>
<tr>
<td>Week 12</td>
<td>1.01±0.01 (n=15)</td>
<td>2.04±0.11*** (n=23)</td>
<td>1.26±0.10† (n=17)</td>
<td>2.50±0.18** (n=11)</td>
</tr>
</tbody>
</table>

Performance gain (km/h) −0.10±0.06 (n=15) +0.98±0.30* (n=23) −0.30±0.12† (n=17) +1.00±0.20** (n=11)

MAP (mmHg)

<table>
<thead>
<tr>
<th>Week 0</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>123±1 (n=15)</td>
<td>122±3 (n=7)</td>
<td>121±1 (n=15)</td>
<td>122±2 (n=14)</td>
<td>122±1 (n=15)</td>
<td>127±1 (n=13)</td>
</tr>
<tr>
<td>177±2* (n=15)</td>
<td>179±3* (n=7)</td>
<td>175±2* (n=12)</td>
<td>177±2* (n=12)</td>
<td>169±3*† (n=10)</td>
<td>180±2*† (n=16)</td>
</tr>
</tbody>
</table>

HR (beats/min)

<table>
<thead>
<tr>
<th>Week 0</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>320±8 (n=15)</td>
<td>320±8 (n=15)</td>
<td>309±8 (n=15)</td>
<td>308±9 (n=14)</td>
<td>287±9 (n=15)</td>
<td>313±5 (n=16)</td>
</tr>
<tr>
<td>379±13* (n=15)</td>
<td>379±13* (n=15)</td>
<td>347±13*† (n=12)</td>
<td>346±7* (n=12)</td>
<td>344±13*† (n=10)</td>
<td>373±7* (n=16)</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SEM. Performance gain was calculated by the difference in attained velocity between weeks 12 and 0. Significances (P<0.05) are *vs. WKY; †vs. week 0; ‡Denotes a significant change. HR, heart rate; MAP, mean arterial pressure; SHR, spontaneously hypertensive rats; WKY, Wistar-Kyoto rats.

Different membranes were compared by loading a standard reference sample in all gels; results were corrected to membrane’s Ponceau red staining (0.5% w:v). Band intensities were quantified by optical densitometry (Image J) of the developed autoradiographs.

Statistical Analysis

Results are expressed as mean ± SEM. Differences in running distance between groups (WKY and SHR) and conditions (S and T) were analyzed by a 3-way ANOVA for repeated measurement (time). A factorial ANOVA was used to compare the sequential effects of training on mean AP (MAP), HR and RAS components in WKY and SHR groups. The comparison of RAS components at the beginning (week 0) and at the end of the protocols (week 12) in both groups was made by using a 2-way ANOVA. Fischer was used as the post-hoc test. Differences were considered significant at P<0.05.

Results

Efficacy of Training Protocol and Functional Measurements in SHR and WKY

SHR exhibited a better performance on the treadmill than age-matched WKY controls from the beginning of the experiment (Table 1). In the T groups, running velocity was significantly increased at weeks 4, 8 and 12, with parallel increases in WKY-T and SHR-T. At the end of the protocols, the performance gain was similar between trained groups. In contrast, SHR-S exhibited a small performance loss (P<0.05), while effective running velocity was unchanged in WKY-S during the 12-week period (Table 1).

Hemodynamic measurements showed that SHR-S exhibited higher resting MAP and HR than age-matched WKY (at week 0, Table 1). T was effective to cause resting bradycardia in
and Ang (1-7) concentration was much higher in the renal than in the femoral, carotid and thoracic aorta (Figure 1C). Except for the femoral, SHR arteries exhibited a higher Ang II/Ang (1-7) ratio than that in WKY; the largest difference (3.1-fold) being observed in the renal arteries.

Interestingly, only 1 week of exercise training was effective to normalize Ang II content in the renal artery of the SHR (a 54% reduction at T1; Figure 2A), which was accompanied by a significant, although small reduction, of Ang (1-7) content (Figure 2C). Both the Ang II and Ang (1-7) content were maintained at these levels up to the end of the training protocol. Training also reduced angiotensins' content in the renal artery of the WKY, but the effect on Ang II was smaller than that observed in the SHR group (Figures 2A, C). Except for a small Ang II decrease in the renal artery, there was no change in Ang II or Ang (1-7) content of sedentary time-controls. Training also reduced angiotensins' content in the femoral artery of the SHR (Figures 2B, D): Ang II reduction was progressive (–29% at T2) and normalized only after 8 weeks of

Effects of Hypertension and Training on Vascular, Renal and Plasma RAS Components
The expression of vascular Aogen, the RAS precursor, differed between SHR and WKY and among arteries; it was higher in the renal artery (SHR: +16% at week 0, P<0.05, Figures 1A,B) but unchanged in the femoral artery of SHR-S when compared to WKY-S. Training promptly reduced and normalized Aogen expression in the renal artery of the SHR (average decrease of 15% from the first up to the eighth week of training), without changing its expression in the WKY group (Figure 1A). Training did not change femoral Aogen expression in both groups. Accordingly, the vascular Ang II and Ang (1-7) concentration was much higher in the renal than in the femoral, carotid and thoracic aorta (Figure 1C). Except for the femoral, SHR arteries exhibited a higher Ang II/Ang (1-7) ratio than that in WKY; the largest difference (3.1-fold) being observed in the renal arteries.

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SHR-S vs. WKY-S exhibited higher Ang II and Ang (1-7) levels in the kidney and elevated plasma Ang (1-7) content (Table 2). It also shows that training in the SHR markedly reduced Ang II content in all arteries analyzed, in the kidney as well as in the plasma, with proportional reductions in Ang (1-7) content in the femoral and carotid arteries and kidney (Table 2). There was no significant change of Ang (1-7) content in the plasma, and a reduction of similar magnitude in the thoracic aorta, due to the high variability, did not attain significance. Therefore, the Ang II/Ang (1-7) ratio of the SHR-S (vs. WKY-S) was significantly elevated in the renal and carotid arteries, but reduced in plasma and renal tissue (Figure 3).

Evaluation of serum ACE activity (Figure 4) showing reduced values in SHR-S vs. WKY-S but unaltered ACE2 activity, confirmed the smaller plasma Ang II/Ang (1-7) ratio in SHR-S when compared to WKY. It is interesting to note that, in the SHR group, training reduced the Ang II/Ang (1-7) ratio only in the renal artery, with minor not significant changes in the other arteries, kidney and plasma (Figure 3). In the WKY group, except for unchanged plasma and kidney Ang (1-7), trained-induced Ang II and Ang (1-7) reductions were of
Table 2. Ang II and Ang (1–7) Content in the Renal, Femoral and Carotid Arteries, Thoracic Aorta, Kidney and Plasma in Trained (T) and Sedentary (S) WKY and SHR at the End of Protocols

<table>
<thead>
<tr>
<th></th>
<th>WKY-S</th>
<th>WKY-T</th>
<th>SHR-S</th>
<th>SHR-T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal artery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ang II (pmol/g)</td>
<td>21.68±4.01</td>
<td>12.31±1.68</td>
<td>32.78±2.67*</td>
<td>17.36±3.74#</td>
</tr>
<tr>
<td>Ang (1–7) (pmol/g)</td>
<td>19.73±1.98</td>
<td>6.40±1.04*</td>
<td>6.80±1.27*</td>
<td>5.66±1.78</td>
</tr>
<tr>
<td>Femoral artery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ang II (pmol/g)</td>
<td>0.088±0.006</td>
<td>0.050±0.009</td>
<td>0.199±0.024*</td>
<td>0.061±0.010#</td>
</tr>
<tr>
<td>Ang (1–7) (pmol/g)</td>
<td>0.107±0.009</td>
<td>0.048±0.006*</td>
<td>0.195±0.017*</td>
<td>0.061±0.009#</td>
</tr>
<tr>
<td>Carotid artery</td>
<td></td>
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<tr>
<td>Ang II (pmol/g)</td>
<td>0.120±0.012</td>
<td>0.062±0.006*</td>
<td>0.331±0.041*</td>
<td>0.138±0.017*#</td>
</tr>
<tr>
<td>Ang (1–7) (pmol/g)</td>
<td>0.157±0.072</td>
<td>0.080±0.046</td>
<td>0.107±0.008</td>
<td>0.037±0.003#</td>
</tr>
<tr>
<td>Thoracic aorta</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ang II (pmol/g)</td>
<td>0.066±0.004</td>
<td>0.014±0.002#</td>
<td>0.051±0.005</td>
<td>0.020±0.007#</td>
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<tr>
<td>Ang (1–7) (pmol/g)</td>
<td>0.641±0.128</td>
<td>0.123±0.024*</td>
<td>0.331±0.110*</td>
<td>0.135±0.047</td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
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</tr>
<tr>
<td>Ang II (pmol/g)</td>
<td>16.10±3.73</td>
<td>9.72±1.60</td>
<td>69.52±15.97*</td>
<td>28.81±3.21*#</td>
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<tr>
<td>Ang (1–7) (pmol/g)</td>
<td>6.90±1.28</td>
<td>5.46±1.74</td>
<td>74.02±7.80*</td>
<td>39.93±3.35*#</td>
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<tr>
<td>Plasma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ang II (pg/ml)</td>
<td>270±32</td>
<td>156±10#</td>
<td>285±60</td>
<td>131±27#</td>
</tr>
<tr>
<td>Ang (1–7) (pg/ml)</td>
<td>120±19</td>
<td>117±16</td>
<td>311±53*</td>
<td>240±21*</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SEM. Angiotensins’ content in renal, femoral, carotid and thoracic vessels was quantified in 6–9 arteries/group; 5–6 kidneys/group and 7–9 plasma samples/group. Significances (P<0.05) are * vs. WKY; vs. respective S controls. Abbreviations as in Table 1.
The present study confirmed the beneficial effects of training to reduce AP and the vasoconstrictor axis of the RAS in hypertensive rats, showing additionally that these effects are progressive, with a marked reduction and normalization of the Ang II/Ang (1-7) ratio in the renal artery occurring at the eighth week of training, simultaneously with a significant pressure decrease. This set of data also revealed other new observations: (1) vascular RAS is not equally expressed in arteries, having a crucial importance in the renal artery and lumbar sympathetic nerve activity were not changed by hypertension. It was also shown that hypertension in female SHR was maintained mainly by hypertrophy of the renal arterioles.

The vasculature also expresses the vasodilator, anti-throphic and anti-inflammatory ACE2-Ang (1-7)-Mas receptor axis, mainly in the presence of ACE and AT1 receptor inhibition. The present set of data showed a minor contribution of the vasodilator, anti-throphic and anti-inflammatory ACE2-Ang (1-7)-Mas receptor axis in the reactivity of the renal and carotid arteries of the SHR (Ang II/Ang (1-7) ratio=4.04±0.47 and 3.08±0.28, respectively), whereas the contribution of both axes was almost the same in resistance arteries of the WKY and in the thoracic aorta of both strains, which showed a very small ratio (0.04 to 0.07±0.01). Interestingly, the Ang II/Ang (1-7) ratio in the kidney and plasma as well as the serum ACE activity of the SHR group, were significantly lower than those exhibited by WKY. Indeed, differential expression of ACE and ACE2, Ang II and Ang (1-7), AT1, AT2 and Mas receptors, as well as differential responses to RAS stimulation were observed in vessels, kidney and plasma.

Discussion

The vasculature also expresses the vasodilator, anti-throphic and anti-inflammatory ACE2-Ang (1-7)-Mas receptor axis, mainly in the presence of ACE and AT1 receptor inhibition. The present set of data showed a minor contribution of the vasodilator, anti-throphic and anti-inflammatory ACE2-Ang (1-7)-Mas receptor axis in the reactivity of the renal and carotid arteries of the SHR (Ang II/Ang (1-7) ratio=4.04±0.47 and 3.08±0.28, respectively), whereas the contribution of both axes was almost the same in resistance arteries of the WKY and in the thoracic aorta of both strains, which showed a very small ratio (0.04 to 0.07±0.01). Interestingly, the Ang II/Ang (1-7) ratio in the kidney and plasma as well as the serum ACE activity of the SHR group, were significantly lower than those exhibited by WKY. Indeed, differential expression of ACE and ACE2, Ang II and Ang (1-7), AT1, AT2 and Mas receptors, as well as differential responses to RAS stimulation were observed in vessels, kidney and plasma.

One of the most important observations of the present study is that aerobic training promptly downregulates vasoconstrictor and vasodilator RAS axes in vessels of both normotensive and hypertensive animals, with a specific reduction of the vasoconstrictor axis in the renal artery of the SHR. The downregulation was an early response in both strains (significant changes were observed since the first week of training), being more pronounced in hypertensive individuals. Unlike some studies showing that training augments the expression/activity of vasodilator RAS axis in the heart, kidney, skeletal muscle and aorta of hypertensive and/or chronic heart failure rats, our data revealed a proportional reduction of both Ang II and Ang (1-7) content in the femoral, carotid and thoracic aorta of the trained SHR, indicating that training did not alter normal balance of vascular RAS, but adjusts it to a lower level. In contrast, the robust Ang II reduction simultaneously with the smaller decrease in Ang (1-7) in the renal artery of the SHR indicates that training alters the vasoactive profile of this vessel to favor vasodilator, anti-throphic and anti-inflammatory responses. Indeed, training-induced normalization of the Ang II/Ang (1-7) ratio in the renal artery occurred simultaneously with training-induced pressure reduction, suggesting that this response contributes to the pressure fall observed only in hypertensive rats. Since hypertrophic structural remod-

![Figure 4](https://example.com/figure4.png)

**Figure 4.** Effects of training (T) and sedentary (S) protocols on serum ACE and ACE2 activities in normotensive (WKY) and spontaneously hypertensive rats (SHR) at the end of protocols. Values were obtained in 6–9 rats/group. *Significance (P<0.05) vs. respective WKY groups.

Similar magnitude in all vessels analyzed (some responses were significant, others were not) in such way that no significant changes were observed in the Ang II/Ang (1-7) ratio (Table 2, Figure 3). Exercise training did not change serum ACE and ACE2 activities in the WKY group (Figure 4).
eling of the renal arteries/arterioles, increased renal sympathetic activity, and increased the Ang II/Ang (1-7) ratio (present set of data) are important contributors to the maintenance of hypertension, we propose that training-induced reduction of vascular Ang II content in the renal artery could facilitate blood pressure reduction in the trained SHR.

Technical limitations (the small amount of protein extracted and the non-specific selectivity of many commercially available AT1 receptor antibodies) precluded the quantification of sequential training effects on angiotensins’ receptors in the renal artery. Although we did not measure the expression/activity of different RAS components, the decreased Aogen content in the renal artery of trained SHR suggests that reduced activity of the vasconstrictror axis was mainly due to the reduced synthesis of angiotensins’ precursor. Indeed, previous studies have shown that the angiotensinogen gene plays a pivotal role in setting blood pressure levels and that angiotensinogen is involved in both intrarenal RAS activation and development of hypertension. Therefore, it is likely that training-induced angiotensinogen reduction in the renal artery is one important mechanism contributing to smaller vasoconstriction and blood pressure fall. Similar observations were previously made in trained vs. sedentary SHR: cardiovascular effects of Ang II were directly correlated with the reduction of Aogen mRNA expression in brain areas involved in cardiovascular control, an effect similar to that observed after chronic losartan treatment. Fernandes et al also showed that swimming training decreased RAS activity in the heart by reducing Aogen expression in the left ventricle. These results, together with the present observation of specific training-induced Ang II reduction in the renal artery, indicate a strong effect of exercise training to oppose the overactivity of the local vasoconstrictor RAS axis.

Our results in the WKY group also showed a high Ang II and Ang (1-7) content in the renal vs. other arteries, and that aerobic training was effective to proportionally reduce both Ang II and Ang (1-7) content in all arteries studied. It is interesting to note that in all WKY arteries, as well as in the femoral, carotid and aorta of the SHR and plasma and kidney content of both groups, training did not change the normal balance of vasoconstrictor/vasodilator axes, but adjusted it to a lower level.

In summary, the present set of data shows that RAS and its counter-regulatory axes are differentially expressed in the vasculature. Data also provides strong evidence that low-intensity aerobic training downregulates both arms of RAS in vessels, kidney and plasma of normotensive and hypertensive rats, but it specifically reduces Ang II and preserves Ang (1-7) content/activity in the renal artery of the SHR. The improvement of the vasodilator, anti-proliferative and anti-inflammatory axis in the renal artery is a protective training-induced adjustment that contributes to blood pressure reduction observed in hypertensive individuals. These observations improve our knowledge on mechanisms triggered by RAS in a strategic area for blood pressure control, and opens new research perspectives for a more efficient treatment of hypertension.

Disclosures

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