

Exercise Training Normalizes Vascular Changes in Aging Hypertension Involving microRNAs Profile and Target Genes

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MiRNAs profile and target genes involved in hypertension-associated vascular changes were evaluated. In addition, we checked the therapeutic role of exercise training (ET) on these parameters. Spontaneously hypertensive rats (SHR) aged 6 months and their controls Wistar Kyoto (WKY) were divided into 4 groups: SHR, trained SHR (SHR-T), WKY and trained WKY (WKY-T). Swimming ET consisted of 60 min of duration, 1x/day/10 weeks, with 4% caudal body weight workload. SHR showed an increased in systolic blood pressure (207 ± 5.5 mmHg) compared to WKY (133 ± 3.9 mmHg) analyzed by tail-cuff system, with no changes in baseline heart rate. We observed a reduction in VO_2 peak (WKY: 62 ± 1.5 ; SHR: 53 ± 2.5 mL.kg⁻¹.min⁻¹) accompanied by soleus muscle atrophy (fiber type I - WKY: 4039 ± 195 ; SHR: 2658 ± 53 ; type IIa - WKY: 2903 ± 182 , SHR: 2050 ± 68 ; Intermediate - WKY: 2663 ± 136 , SHR: 1967 ± 95 μ m²) in SHR. Vascular function of femoral artery was similar in SHR and WKY, however, wall-to-lumen ratio was increased in femoral artery (WKY: 0.17 ± 0.01 , SHR: 0.27 ± 0.01 a.u.) and muscular arteriole (WKY: 0.54 ± 0.02 , SHR: 1.14 ± 0.03 a.u.) accompanied by capillary rarefaction (WKY: 1.2 ± 0.05 , SHR: 0.6 ± 0.03 capillary-to-fiber ratio) in soleus muscle from SHR vs. WKY. In contrast, ET promoted reduction in blood pressure and resting bradycardia in trained animals. ET corrected the VO_2 peak reduction, muscle wasting, microvascular remodeling in SHR-T toward control levels. ET downregulated 8 miRNAs (-96, -205, -182, -146b-5p, -140, -328a, -665, -1) and upregulated 3 miRNAs (-499, -208b and -99b) in SHR-T when compared to SHR. Bioinformatics study for functional analysis of the predicted targets genes for the 11 miRNAs restored by ET demonstrated enrichment of different signaling pathways including cell death (p value <0.001; Fold enrichment 16.78) and vascular development (p value < 0.001; Fold enrichment 10.62). Thus, targets involved in angiogenesis and vascular integrity by the VEGF/VEGFR2/AKT/eNOS/Bcl-2 pathway were impaired in hypertension and corrected by ET. The results support the hypothesis that the structural changes arising from the progression of hypertension may be regulated by a set of miRNAs and target genes; and ET participates in restoring the vascular remodeling.

Disclosure Block:

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