TACSM Abstract

The Effect of Age and Exercise Training on Endothelial Function and Protein:Protein Interactions Among eNOS and Its Regulatory Proteins in Rat Aortas

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Category: Doctoral

ABSTRACT

Previous studies indicate that nitric oxide (NO)-mediated endothelium-dependent dilation declines with age. **PURPOSE:** The purpose of this study was to test the hypothesis that impaired NO-mediated, endothelium-dependent dilation in aged arteries is due to age-related alterations in protein:protein interactions among endothelial nitric oxide synthase (eNOS) and its regulatory proteins, resulting in reduced NO production in aged arteries. The regulatory proteins of interest in this study are Caveolin-1 (Cav1), an inhibitor of eNOS enzyme activity, and Heat-shock protein 90 (Hsp90), which enhances eNOS activity. **METHODS:** Young (2 mo) and Old (22 mo) male Fischer 344 rats were endurance exercise trained on a motorized treadmill or remained sedentary for 10wks yielding four groups of rats: 1)Young Sed (4 mo; n = 10), 2)Young Ex (4 mo; n = 10), 3) Old Sed (24 mo; n = 10), and 4) Old Ex (24 mo; n = 10). After the 10 week training period, rats were anesthetized; aortas were removed, cut into rings, and mounted on a wire myograph for assessment of endothelial function. Endothelium-dependent relaxation was assessed in aortic rings using acetylcholine (ACh). Endothelium-independent relaxation was assessed with sodium nitroprusside (SNP). Additional segments of aortas were isolated and snap frozen for use in co-immunoprecipitation experiments to assess Cav1:eNOS and Hsp90:eNOS protein:protein interactions. **RESULTS:** ACh-induced relaxation was impaired in aged aortic rings. Exercise training improved endothelium-dependent relaxation in old aortic rings such that ACh-induced relaxation in Old Ex aortas did not differ from Young Sed. Results from co-immunoprecipitation experiments revealed no significant age differences in the Cav1:eNOS interactions. Additionally, there was no significant training effect on Cav1:eNOS interaction in either young or old aortas. However, the Hsp90:eNOS interaction revealed a trend toward reduced interaction between the two proteins in the Old Sed group compared to the Young Sed group ($p = 0.087$). There was no significant training effect on Hsp90:eNOS interaction in young or old aortas. **CONCLUSION:** Ten weeks of exercise training improves endothelium-dependent relaxation in aortas from old rats. This improvement does not appear to be due to exercise-induced alterations in protein:protein interactions among eNOS and its regulatory proteins.

TEXAS CHAPTER
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