TACSM Abstract

Aging impairs ACh-induced dilation in skeletal muscle feed arteries: role of Akt-dependent phosphorylation of eNOS.

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ABSTRACT

We tested the hypothesis that impaired nitric oxide (NO)-mediated, endothelium-dependent dilation in aged soleus muscle feed arteries (SFA) is due to an age-related decrement in PI3-kinase(PI3K)/protein kinase B (Akt)-dependent phosphorylation of endothelial NO synthase (eNOS) on serine residue 1177 (p-eNOS^{ser1177}). SFA from young (4 mo) and old (24 mo) Fischer 344 rats were cannulated for examination of endothelium-dependent vasodilator responses to acetylcholine (ACh). To determine the mechanism by which aging affected vasodilation to ACh, vasodilator responses were assessed in the absence and presence of *N*^{w}-nitro-L-arginine (L-NNA, to inhibit NOS), LY-294002 (to inhibit PI3K), or 1L6-hydroxymethyl-chiro-inositol-2-(R)-2-O-methyl-3-O-octadecyl-sn-glycerocarbonate (AktI, to inhibit Akt). Results indicate that ACh-induced vasodilation was significantly blunted in old SFA, whereas dilation to sodium nitroprusside (a NO donor) was not compromised. The age-group difference in ACh-induced dilation was abolished in the presence of L-NNA, LY-294002, or AktI. In a separate set of experiments, ACh-induced vasodilation was assessed in SFA from young and old rats. SFA were subsequently removed from the pipettes, snap frozen, and immunoblot analysis was used to assess p-Akt^{Ser473}, p-eNOS^{ser1177}, total Akt and total eNOS protein content. ACh-induced vasodilation was blunted in old SFA; however, the p-Akt^{Ser473}/Akt and p-eNOS^{ser1177}/eNOS ratios were similar in young and old SFA. Collectively, these results indicate that NO-mediated dilation is impaired in old SFA; however, the decrement in endothelial function is not due to reduced PI3K/Akt-dependent phosphorylation of eNOS on serine residue 1177. Research supported by AHA 0765043Y (CRW), AHA 4150031 (CRW), and Sydney and J.L. Huffines Institute of Sports Medicine Graduate Student Research Grants (MJL, JWS, and DWT).