

## Impaired Muscarinic Receptor-Mediated Vasodilation in Young, Black Men is Not Influenced by Oxidative Stress

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### ABSTRACT

The black population (BL) presents an elevated risk for hypertension and cardiovascular disease relative to other populations. While the cause is multifactorial, vascular dysfunction is indicated as a key contributing factor. Young BL men exhibit microvascular dysfunction across a variety of stimuli including local heating and muscarinic receptor-mediated dilation (MRMD) of the cutaneous circulation. Previously, our group has noted that increased NADPH oxidase (NOX) and xanthine oxidase (XO)-derived oxidative stress impairs local heating-mediated dilation in BL men. However, whether oxidative stress from these sources or from uncoupled endothelial nitric oxide synthase (eNOS) contributes to blunted MRMD in BL men is currently unknown. **PURPOSE:** The present study aimed to test the hypothesis that blunted MRMD in BL men will be ameliorated following inhibition of oxidative stress from NOX, XO, or uncoupled eNOS via apocynin, allopurinol, and tetrahydrobiopterin (BH4; an essential eNOS cofactor), respectively.

**METHODS:** To test this hypothesis, four intradermal microdialysis membranes were placed in the dorsal forearm of 11 BL men (mean±SD; age: 23±4 y) and red blood cell flux (RBF) responses to 100µM methacholine (MCh) infusions were observed. This dose has been shown in preliminary testing to elicit approximately a 50% blunted increase in cutaneous vascular conductance (CVC) in BL compared to whites. Following trauma resolution, each site received one of four infusions for 30-min: lactated Ringer's, 100µM apocynin, 10µM allopurinol, or 10mM BH4. Each site was then locally heated to 33°C for 10-min to establish baseline RBF. MCh (MCh<sub>1</sub>) was then co-infused with either lactated Ringer's (control) or each site's respective treatment for 6-min. Following MCh infusion, 20mM N(ω)-nitro-L-arginine methyl ester (L-NAME) was administered for 60-min to inhibit NOS activity. During co-infusions either lactated Ringer's (control) or each site's respective treatment were continued. After 60-min, MCh (MCh<sub>2</sub>) co-infusion was administered as before. While at 33°C, 28mM sodium nitroprusside (SNP) was infused for 10-min to determine endothelium-independent vasodilatory responsiveness. Local temperature was then raised to 43°C while SNP infusion continued for 25-min to determine maximal dilatory capacity. CVC was calculated as RBF/mean arterial pressure and normalized to maximal conductance (%CVC<sub>max</sub>). MCh responses are reported as the increase from baseline and L-NAME for MCh<sub>1</sub> and MCh<sub>2</sub>, respectively. Nitric oxide contribution was calculated as the difference between MCh<sub>1</sub> and MCh<sub>2</sub>. **RESULTS:** No difference was observed during MCh<sub>1</sub> at the apocynin, allopurinol, or BH4 sites ( $P > 0.05$ ). Further, no differences were observed between sites for the NO-contribution to dilation ( $P > 0.05$ ) or maximal dilatory response ( $P > 0.05$ ). **CONCLUSION:** These data suggest that attenuated MRMD in BL men is not related to elevated oxidative stress. However, further research is warranted as high- and low-responders to MCh were observed, each group producing seemingly divergent responses to the treatment drugs.