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THE CONTRIBUTION OF NITRIC OXIDE AND ENDOTHELIUM-DERIVED HYPERPOLARIZING FACTOR TO RESTING AND STIMULATED VASODILATOR TONE IN AFRICAN AMERICAN AND WHITES

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Whether impaired endothelial function in African Americans (AA) compared to Whites is due to alterations in nitric oxide (NO) or endothelium-derived hyperpolarizing factor (EDHF) activity is unknown. We hypothesized that there is a differential racial contribution of these two agonists to vasodilator tone.

Methods: In 45 White and 36 AA healthy subjects, we measured forearm blood flow (FBF) using strain gauge plethysmography at rest and after infusions of bradykinin (BK, 100, 200, 400ng/min), acetylcholine (ACH 7.5, 15, 30 µg/min) and sodium nitroprusside (1.6 and 3.2 µg/min). Measurements were repeated after NO blockade with L-NMMA, calcium-dependent potassium channel blockade with tetraethylammonium (TEA, inhibiting EDHF activity), and combined blockade.

Results: Both L-NMMA and TEA reduced resting FBF in both groups indicating similar contribution of NO and EDHF to resting tone; Whites vs. AA with L-NMMA: -22% and -18%, p=0.01; with TEA: -23% and -24%, p=0.001; with L-NMMA + TEA: -42% and -35%, p=0.001, respectively, compared to baseline.

BK-mediated vasodilation was greater in Whites than AA (p=0.04). L-NMMA attenuated BK responses in Whites (-30%, p=0.0005) but not in AA (-18%, p=0.11), indicating a greater contribution of NO in Whites. TEA reduced blood flow (23% and 22% in Whites and AA, respectively, p<0.001), indicating similar contribution of EDHF in both groups.

ACH-mediated vasodilation was greater in Whites than AA (p=0.001). TEA did not change flow in either group, but L-NMMA attenuated ACH-mediated dilation only in Whites and not in AA (-18%, p<0.01 vs -2%, p=NS), indicating a reduced NO in AA.

Sodium nitroprusside-mediated dilation was greater in Whites than AA (p=0.006), indicating reduced sensitivity of the smooth muscle cells to NO in AA.

Conclusions: Although NO and EDHF contribute equally to resting blood flow, there is reduced availability and sensitivity to NO during pharmacologic stimulation even in healthy AA compared to Whites. In contrast, EDHF activity is preserved in AA. Preserved EDHF but reduced NO activity in AA may underlie the increased risk of hypertension and cardiovascular disease in AA, and may have therapeutic implications that need to be explored.