YOUNG NORMOTENSIVE BLACKS demonstrate greater arterial blood pressure reactivity to laboratory stressors than young whites (2, 3, 16). Arterial blood pressure reactivity to laboratory stressors is an independent risk factor for future hypertension development (9). Consistent with these observations, blacks demonstrate a greater prevalence of hypertension than whites (6, 7). Thus greater levels of stress reactivity in young normotensive blacks may explain, in part, their greater risk of hypertension development.

Laboratory stressors increase muscle sympathetic nerve activity (MSNA) and arterial blood pressure in humans (1, 24). Transduction of increases in MSNA into vascular resistance is a determinant of arterial blood pressure reactivity. Whether this process of sympathetic vascular transduction is augmented in young normotensive blacks compared with age-matched normotensive whites is uncertain. In this context, it has been demonstrated that α1-adrenergic receptor sensitivity may be elevated in young blacks compared with whites (20). Thus, for a given increase in vasoconstrictor nerve traffic, greater pressor responses may be observed in blacks compared with whites. However, simultaneous measurements of MSNA and regional vascular resistances are currently unavailable in black and white humans. Accordingly, we determined forearm vascular responses to elevations in MSNA in young normotensive blacks and whites. We hypothesized that blacks would demonstrate augmented forearm vascular responses to elevations in MSNA in young normotensive blacks and whites. The results provide experimental support for racial differences in sympathetic vascular transduction. These findings may provide a mechanism underlying augmented arterial blood pressure reactivity in young normotensive blacks.

METHODS

Subjects. Twenty-one healthy (12 black and 9 white), young (age = 20–33 yr), normotensive, nonobese subjects volunteered for the present study. Written, informed consent was obtained from subjects after verbal explanation of the study protocol, and approval was obtained from the Institutional Review Board of the University of Georgia.

Experimental design. Studies were performed in supine subjects seated in a lower body negative pressure (LBNP) chamber at the levels of the iliac crest. After subject instrumenta-
tion and a 10-min baseline period, LBNP was applied at −5 mmHg for 4 min followed consecutively by 4 min at both −15 mmHg and −40 mmHg. During these periods,

MSNA, arterial blood pressure, heart rate, and forearm blood flow were measured. LBNP was used in the present study for several reasons. First, LBNP allows for steady-state data acquisition of MSNA and forearm blood flow. Second, LBNP is a sympathetically maneuvers with minimal competitive vasodilatory influences (e.g., epinephrine and nitric oxide). Third, LBNP was used to examine possible racial differences in MSNA response to cardiopulmonary and arterial baroreceptor unloading, which has not been previously documented.

Measurements. Multifiber recordings of MSNA were made with a tungsten microelectrode inserted in the peroneal nerve lateral to the knee. A reference electrode was inserted subcutaneously in close proximity (~2–3 cm) to the recording electrode. The recording electrode was adjusted until a site with clear spontaneous sympathetic bursts was established. Standard criteria for acceptable recordings of MSNA were applied (23). Raw nerve recordings were amplified (20,000–90,000×) and filtered at a bandwidth of 700–2,000 Hz. These signals were then rectified and integrated at a 0.1-s time constant to obtain mean voltage neurograms. MSNA has been demonstrated to be similar in the arms and legs during LBNP (18).

Resting arterial blood pressure was measured by using an automatic arterial pressure device (ACCUTORR 3, Datascop). Continuous measurements of arterial blood pressure and heart rate during the experimental intervention were made by using a Finapres blood pressure monitor (Ohmeda, Englewood, CO). Forearm blood flow was measured with venous occlusion plethysmography (Hokanson, Bellevue, WA). A mercury-in-Silastic strain gauge was placed around the maximal circumference of the forearm. Forearm blood flow was measured four times per minute. During blood flow measurements, a wrist cuff in an air occlusion plethysmography (Hokanson, Bellevue, WA). A mercury-in-Silastic strain gauge was placed around the maximal circumference of the forearm. Forearm blood flow was measured four times per minute. During blood flow measurements, a wrist cuff in 220 mmHg arrested circulation to the hand. Venous collecting cuff pressure was applied (23). Raw nerve recordings were amplified (20,000–90,000×) and filtered at a bandwidth of 700–2,000 Hz. These signals were then rectified and integrated at a 0.1-s time constant to obtain mean voltage neurograms. MSNA was expressed as burst frequency and total MSNA (sum of burst area) as measured from baseline or during LBNP in blacks and whites (42 ± 4 min).

Fig. 1. Responses of heart rate (A) and mean arterial blood pressure (MAP, B) during lower body negative pressure (LBNP) in black (B; ●) and white (W; ○) adults. Heart rate increased (P < 0.05) and MAP was unchanged during LBNP. No differences existed between black and white subjects. Values are means ± SE.
Despite similar levels of MSNA at rest, blacks demonstrated less increase in total MSNA compared with whites during LBNP (28 ± 7 vs. 55 ± 18%, 81 ± 21 vs. 137 ± 42%, 174 ± 81 vs. 556 ± 98% for −5, −15, and −40 mmHg, respectively; \( P < 0.001 \)). Burst frequency increased (\( P < 0.05 \)) during LBNP in blacks and whites (18 ± 3 vs. 17 ± 4; 24 ± 4 vs. 22 ± 4; 35 ± 6 vs. 35 ± 5 bursts/min) (Fig. 3). Because the increases in burst frequency were similar in blacks and whites, whites relied on a greater increase in burst area to increase total MSNA more than blacks. Blacks demonstrated elevated sympathetic vascular transduction (%FVR/%MSNA) compared with whites during LBNP at −5 (0.95 ± 0.07 vs. 0.82 ± 0.07; \( P < 0.01 \)), −15 (0.82 ± 0.11 vs. 0.64 ± 0.09; \( P = 0.09 \)), and −40 mmHg (0.95 ± 0.37 vs. 0.35 ± 0.09; \( P < 0.03 \)) (Fig. 4).

**DISCUSSION**

These data provide direct experimental support for racial differences in vascular responsiveness to increases in MSNA. This conclusion is supported by at least two novel findings. First, blacks demonstrate elevated sympathetic vascular transduction during LBNP, such that, for a given increase in MSNA, there is a greater increase in FVR. Second, during LBNP, MSNA responses are greater in young normotensive whites than age-matched normotensive blacks.

At rest, arterial blood pressure, forearm blood flow, and FVR did not differ in blacks and whites. Despite similarities at rest, LBNP elicited greater increases in FVR per unit increase in MSNA in blacks. The mechanism(s) responsible for this augmented sympathetic vascular transduction in blacks is unclear. Because FVR responses were similar in the face of augmented MSNA responses in whites, it is reasonable to suspect several potential mechanisms for augmented vascular responses in blacks. Potential candidates include augmented \( \alpha \)-adrenergic receptor sensitivity or number and/or altered norepinephrine kinetics within the neurovascular junction.

Augmented \( \alpha_1 \)-adrenergic receptor sensitivity and/or number could amplify vascular responses to increases in MSNA. This conclusion is supported by at least two novel findings. First, blacks demonstrate elevated sympathetic vascular transduction during LBNP, such that, for a given increase in MSNA, there is a greater increase in FVR. Second, during LBNP, MSNA responses are greater in young normotensive whites than age-matched normotensive blacks.

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in MSNA and subsequent norepinephrine release. Consistent with this potential mechanism, forearm vascular responses to an intrabrachial $\alpha_1$-adrenergic agonist (i.e., phenylephrine hydrochloride) produce greater vasoconstriction in young blacks than in young whites (20). However, recent evidence suggests that phenylephrine hydrochloride can induce $\beta$-adrenergic receptor-mediated vasodilation (22). In this regard, it is important to point out that blacks demonstrate blunted $\beta$-adrenergic-mediated vasodilation (19). Thus it is unclear whether augmented $\alpha_1$-adrenergic receptor sensitivity and/or a blunted antagonistic $\beta$-adrenergic vasodilation mediated the augmented responses to intrabrachial phenylephrine hydrochloride in the study by Stein et al. (20). Current data do not allow us to determine whether this is the case, but it appears important that these previous findings be confirmed under conditions of forearm $\beta$-adrenergic blockade. Our data are consistent with elevated $\alpha$-adrenergic receptor sensitivity in young normotensive blacks compared with whites. An important question now becomes how might $\alpha$-adrenergic receptor sensitivity be augmented in the forearms of blacks? In this context, endothelin is elevated in normotensive blacks compared with age-matched whites (8), and endothelin is known to increase contractile responses to norepinephrine (25). Thus augmented forearm vascular responses to increases in MSNA in blacks may be mediated by amplified vasoconstriction during norepinephrine release secondary to elevated levels of endothelin. Because endothelin was not measured in the present study, we can only speculate that it may have played a role in the augmented forearm vascular responses to increases in MSNA in blacks in the present study. Confirming the present findings under conditions of endothelin-receptor blockade may provide useful insight into this hypothesis. Furthermore, either an increased number of $\alpha$-adrenergic receptors or an increased affinity for norepinephrine by $\alpha$-adrenergic receptors may explain elevated sympathetic vascular transduction in blacks.

Greater norepinephrine release and/or reduced clearance/reuptake of norepinephrine could result in a greater release of norepinephrine and subsequent exposure to postjunctional $\alpha$-adrenergic receptors. We are not aware of any data examining racial differences in norepinephrine release from sympathetic nerve terminals. However, polymorphisms in the $\alpha_2$-adrenergic receptor have been identified, which are associated with hypertension in blacks (14). On the basis of the functional role of presynaptic $\alpha_2$-adrenergic receptors in modulating norepinephrine release from sympathetic nerve endings, it appears important to determine whether differences are present in blacks compared with whites. If differences are present between blacks and whites, it may suggest that, per unit increases in MSNA, greater levels of norepinephrine are exposed to postjunctional $\alpha$-adrenergic receptors. Furthermore, the norepinephrine transporter pathway is important in disposing of norepinephrine from sympathetic nerve terminals. Reduced norepinephrine transporter mechanisms in blacks could lead to higher concentrations of synaptic norepinephrine and greater vascular responses to increases in sympathetic nerve traffic in lieu of a change in postjunctional $\alpha$-adrenergic receptor sensitivity. We are aware of no data examining this issue in blacks or whites, but both clearance rates (26) and venous plasma norepinephrine levels (10) appear similar in blacks and whites. Thus elevated synaptic levels of norepinephrine probably do not mediate racial differences in the vascular responses to increases in MSNA.

Data suggest that normotensive blacks demonstrate greater cardiovascular reactivity to laboratory stressors such as the cold pressor test (5) and psychological stress (13, 15). If vascular responses to MSNA increases are augmented in blacks, it may, in part, explain augmented pressor responses to laboratory stressors. Our data support the concept that sympathetic vascular transduction is augmented in blacks. As such, sympathetic vascular transduction may play an important role in determining the augmented level of stress reactivity noted in blacks. Furthermore, the facts that blacks are more prone to developing hypertension and demonstrate enhanced arterial blood pressure reactivity to laboratory stressors suggest a possible mechanistic link. In this context, enhanced arterial blood pressure reactivity is an independent predictor of future hypertension development (9). As such, understanding mechanisms underlying augmented stress/arterial blood pressure reactivity, such as sympathetic vascular transduction, should be of widespread clinical and physiological interest.

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A separate, but equally provocative question is what explains the greater increase in MSNA during LBNP in whites compared with blacks? Stein et al. (20) suggested that during LBNP there was no evidence of altered sympathetic responses in blacks. The conclusion by Stein and colleagues that sympathetic responses to LBNP did not differ in blacks and whites was based on the finding that forearm norepinephrine spillover did not differ between blacks and whites. Close inspection of the data reveals that norepinephrine spillover did not increase from baseline levels during LBNP in either blacks or whites. These findings are inconsistent with those of others who have demonstrated increased forearm norepinephrine spillover during LBNP (11, 12). MSNA is elevated under even low levels of LBNP (21) and supports the contention that direct measurements of MSNA are essential in these types of studies. Our results clearly demonstrate an increased but attenuated MSNA response to graded LBNP in blacks compared with whites.

In the current study, racial differences in response to LBNP became larger as the level of LBNP was increased. It is possible that reductions in central venous pressure during application of similar levels of LBNP were greater in whites, suggesting a greater level of baroreflex unloading. However, it is unlikely that the magnitude of baroreceptor unloading explains our findings. First, greater reductions in forearm blood flow would be expected in whites to maintain arterial blood pressure at baseline levels if this were the case, which was not observed. Second, greater increases in heart rate would be expected during LBNP in whites if the baroreflexes were unloaded to a greater degree because baroreflex control of cardiac period is similar across the races (17). However, both of these responses were not found. Thus these findings suggest similar baroreceptor unloading in whites and blacks. Why whites demonstrate greater increases in MSNA during similar levels of LBNP than blacks remains unknown.

Conversely, the blunted MSNA responses to LBNP in young normotensive blacks appear to be opposite to that found during cold pressor testing, in which blacks demonstrated greater MSNA responses (5). The reason for these differences can likely be attributed to differences in the stressors themselves. Specifically, baroreceptor unloading during LBNP and increased activity of cutaneous afferents during cold pressor testing likely explain the differential responses. Thus MSNA response to baroreceptor unloading cannot be equated directly to responses noted during other laboratory stressors (i.e., cold pressor test). However, these differences do not preclude group comparisons of the ability of MSNA to modify vascular resistance (i.e., sympathetic vascular transduction), as done in the present study.

Limitations. It is unknown whether either white or black subjects had a family history of hypertension. Many subjects could not state definitively whether hypertension was present in their families. Sympathetic and cardiovascular responses to laboratory stressors may differ based on the presence of familial history (4). Additionally, gender does not appear to have affected our conclusions. First, the experimental groups had a similar composition of women. Second, there were no apparent trends evident in the data when subjects were analyzed separately by gender. Collectively, these observations suggest that gender did not influence the results of this study.

The microneurographic technique does not permit comparison of absolute total activity between two groups because this measurement is strongly determined by the number of nerve fibers recorded from by the microelectrode. However, in the current study, total MSNA at baseline was similar between the two groups (314 ± 56 vs. 317 ± 100 U for blacks and whites, respectively). This finding indicates that the smaller percentage increase in total MSNA in blacks observed during LBNP was not a mathematical artifact due to baseline differences.

In summary, these data, to the best of our knowledge, provide the first direct experimental support for the hypothesis that sympathetic vascular transduction during LBNP is augmented in young normotensive blacks compared with whites. These results may be important in the context of augmented arterial blood pressure reactivity in young normotensive blacks. Additionally, these data indicate greater sympathetic activation to baroreceptor unloading in normotensive whites than in blacks.

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