Elderly Blacks Have a Blunted Sympathetic Neural Responsiveness But Greater Pressor Response to Orthostasis Than Elderly Whites

Yoshiyuki Okada, M. Melyn Galbreath, Sara S. Jarvis, Tiffany B. Bivens, Wanpen Vongpatanasin, Benjamin D. Levine, Qi Fu

Abstract—Neural control of blood pressure (BP) has been reported to differ between young blacks and whites. We hypothesized that elderly blacks have enhanced sympathetic neural responses during orthostasis compared with elderly whites. Muscle sympathetic nerve activity, arm-cuff BP, and heart rate were recorded continuously, and cardiac output, stroke volume, and total peripheral resistance were measured intermittently during supine and 5-minute 60° upright tilt in 10 blacks (65 [SD, 4] years; 4 women) and 20 whites (68 [6] years; 8 women). We found that muscle sympathetic nerve activity burst frequency was similar between blacks and whites in the supine position (44 [10] versus 42 [7] bursts per minute) and during upright tilt (59 [11] versus 60 [9] bursts per minute; P=0.846 for race, P<0.001 for posture, and P=0.622 for interaction). However, upright total muscle sympathetic nerve activity was smaller in blacks than in whites (162 [39] versus 243 [112]% ; P=0.003). Systolic BP, heart rate, cardiac output, and stroke volume were not different between groups. Diastolic BP was similar in the supine position, increased in all of the subjects during tilting; upright diastolic BP was greater in blacks than in whites (80 [10] versus 71 [7] mmHg; P=0.008). Total peripheral resistance did not differ between blacks and whites in the supine position or during upright tilt (P=0.354 for race, P<0.001 for posture, P=0.825 for interaction). Thus, elderly blacks have a blunted sympathetic neural responsiveness but enhanced pressor response to orthostasis compared with elderly whites, which may be attributable to an augmented sympathetic vascular transduction and/or nonadrenergic vasoconstrictor mechanisms (ie, angiotensin II or the venoarteriolar response).

Key Words: muscle sympathetic nerve activity  sympathetic vascular transduction  aging  race  vasoconstriction

Higher age-specific blood pressure (BP) and greater prevalence of hypertension have been reported in blacks compared with whites.1–4 BP control rates, however, remain low among antihypertensive drug-treated blacks,5 and pressure-related cardiovascular and renal complications occur excessively.4,6 These epidemiological observations suggest possible racial differences in BP regulation.

Numerous studies have shown enhanced responses in peripheral vascular resistance in young blacks. It was found that physiological or psychological stressors increased sympathetic nerve activity more in blacks than in whites,7,8 especially in those with a family history of hypertension,9 suggesting that racial differences in sympathetic neural reactivity may contribute to the enhanced peripheral vascular resistance. On the other hand, forearm vascular resistance in young blacks was higher during the cold pressor test than age-matched whites, but the sympathetic neural response was not different between groups.10 In addition, Ray and Mo-nahan11 reported that forearm vascular resistance was similar in blacks and whites during orthostatic stress despite a lower muscle sympathetic nerve activity (MSNA) in blacks. These results suggest that transduction of the MSNA signals into vascular resistance may be greater in young blacks than in young whites. Thus, an enhanced sympathetic neural reactivity or an increase in vasoconstrictor sensitivity may account for the high occurrence of hypertension in young blacks.

There is no information available regarding racial differences in sympathetic neural control and vascular sensitivity in seniors. Because both MSNA12 and BP1 increase with age, and a higher MSNA was shown in hypertensive patients than in normotensive individuals,13 we speculated that the augmented sympathetic neural reactivity would be more predominant in elderly blacks compared with whites. Therefore, we hypothesized that elderly blacks have enhanced sympathetic neural responses to orthostatic stress compared with elderly whites. Furthermore, it was reported recently that the baro-
reflex, through which the autonomic nervous system regulates BP, was less effective in response to hypotensive and hypertensive stimuli in young blacks, at least for heart rate (HR) regulation. However, because of previous reports suggesting possible racial differences in sympathetic vascular control, baroreflex regulation of MSNA needs to be evaluated. In this context, we compared sympathetic baroreflex sensitivity (BRS) between elderly blacks and whites.

Methods

Subjects
Thirty sedentary elderly volunteers (age range, 60–74 years; 10 blacks and 20 whites) participated in this study. Power and sample size calculation were based on the study of Calhoun et al (see the online-only Data Supplement). All of the subjects were screened with a careful medical history, physical examination, 12-lead ECG, echocardiogram, and 24-hour ambulatory BP monitoring (screening ABPM). They were nonsmokers and had no overt history of chronic diseases except for stage 1 hypertension. They were excluded if they exercised at moderate-to-high intensity levels for >30 min/day for >3 times per week. Women taking hormone replacement treatment were excluded. Subjects gave their written informed consent to a protocol approved by the institutional review boards of University of Texas Southwestern Medical Center and Texas Health Presbyterian Hospital Dallas.

After screening, subjects who had been taking antihypertensive medications were weaned from these drugs to avoid any effects of the drug on MSNA and cardiovascular response (see Table S1 in the online-only Data Supplement for drug information). All of the subjects underwent a 3-week run-in period before testing, and they were instructed to maintain a healthy lifestyle according to the seventh report of the Joint National Committee standard guidelines. Then, 24-hour ABPM was measured at the end of the run-in period (run-in ABPM).

Measurements

Muscle Sympathetic Nerve Activity
MSNA signals were obtained with microneurography. Briefly, a recording electrode was placed in the peroneal nerve at the popliteal fossa, and a reference electrode was placed subcutaneously 2 to 3 cm apart from the recording electrode. The nerve signals were amplified (70000–160000-fold), band-pass filtered (700–2000 Hz), full-wave rectified, and integrated with a resistance-capacitance circuit (time constant, 0.1 second). Criteria for adequate MSNA recording include the following: (1) pulse synchrony; (2) facilitation during hypotension phase of the Valsalva maneuver and suppression during the hypertensive overshoot phase after release; (3) increase in response to breath holding; and (4) insensitivity to emotional stimuli.

Hemodynamics
HR was determined from lead II of the ECG (Hewlett-Packard), and beat-by-beat BP was derived from finger photoplethysmography (Nexfin). Arm cuff BP was measured by electrophysiomyomanometry (SunTech) with a microphone placed over the brachial artery to detect Korotkoff sounds. Cardiac output (Qc) was measured via the following: (1) pulse synchrony; (2) facilitation during hypotension phase of the Valsalva maneuver and suppression during the hypertensive overshoot phase after release; (3) increase in response to breath holding; and (4) insensitivity to emotional stimuli.

Protocol
Before testing, all of the subjects consumed a 3-day isocaloric constant diet consisting of 100 mEq of sodium, 100 mEq of potassium, and 1000 mg of calcium daily. Fluid intake was ad libitum and assessed by 24-hour urine output the day before testing to verify dietary compliance.

The experiment was performed in the morning ≥2 hours after a light breakfast, ≥72 hours after the last caffeinated or alcoholic beverage, and ≥24 hours after strenuous physical activity in a quiet, environmentally controlled laboratory with an ambient temperature of ~25°C. The subject was placed in the supine position, and an intravenous catheter was inserted into the antecubital vein of the left arm for blood samples. At least 10 minutes after a satisfactory nerve recording site had been found, baseline data were recorded for 6 minutes during spontaneous breathing. Subsequently, the subject was tilted passively to 60° for 5 minutes, followed by 3 minutes of recovery in the supine position. Arm BP and Qc were measured and blood samples were taken for assessment of plasma catecholamine concentration, direct renin, aldosterone, and vasopressin concentration during supine and at the fifth minute of 60° upright tilt. Throughout the entire procedure, beat-by-beat BP, HR, respiratory waves, and MSNA were recorded continuously.

Data Analysis
Data were sampled at 625 Hz and stored on a personal computer with a commercial data acquisition system (Biopac). Off-line data analyses were performed using signal-processing software (LabView). Beat-by-beat HR was calculated from the R-R interval measured by ECG. Beat-by-beat SBP and DBP were obtained from the arterial pressure waveform. Sympathetic bursts were identified by a computer program and then confirmed by an experienced microneurographer. The integrated neurogram was normalized by assigning a value of 100 to the largest amplitude of a sympathetic burst during the 6-minute baseline. Burst area was measured as the area under the curve of each sympathetic burst of the normalized integrated neurogram on a beat-by-beat basis. Total MSNA was defined as the burst area per minute, and the value in the upright posture was expressed as the percentage of the baseline value. Changes in total MSNA (Δtotal MSNA, arbitrary units) from supine to upright were calculated. The number of bursts per minute (burst frequency) and total MSNA were used as quantitative indices. We also estimated the efficacy of MSNA for vasoconstriction from the percentage change of TPR divided by a given change of total MSNA. We used the spontaneous breathing method for assessment of sympathetic BRS (see the supplementary Methods section in the online-only Data Supplement).

Statistical Analysis
Values are expressed as means (SDs). MSNA indices and beat-by-beat hemodynamics were collected for 6-minute supine baseline and from the second to the fifth minute of 60° upright tilt. Subject characteristics, ABPM results, and Δtotal MSNA between groups were compared by using unpaired t-tests if normality tests passed and using Mann-Whitney rank-sum tests if normality tests failed. MSNA, hemodynamic, and hormonal responses to upright tilt between groups were analyzed using 2-way repeated-measures ANOVA with factors for race, posture, and the interaction (race×posture). The Holm-Sidak method was used for the post hoc multiple comparisons. A P value of <0.05 was considered statistically significant.

Results

Subject Characteristics
As shown in Table 1, there were no differences in physical characteristics between groups. The ratios of men:women (3:2) and hypertensives:normotensives (1:1) were the same for both groups. Twenty-four-hour BP were similar between groups except for higher 24-hour DBP in blacks than in whites after the run-in period (P=0.048).

Hemodynamic Responses
Both supine and upright SBPs were not different between groups (Figure 1A). Although DBP and mean BP were...
similar in the supine position, the increases were greater in blacks than in whites during tilting; upright DBP and mean BP were higher in blacks than in whites (Figure 1B and 1C). HR increased and stroke volume decreased during upright tilt without any differences between blacks and whites (Figure 1D and 1E). Therefore, Qc showed a similar reduction during tilting between groups (Figure 1F). TPR did not differ between groups in both supine and upright postures (Figure 1G).

**Neural and Hormonal Responses**

MSNA burst frequency was similar between blacks and whites in the supine position and during upright tilt (Figure 1H). However, the percentage of total MSNA response to upright tilt was smaller in blacks than in whites (162 [39] versus 243 [112]%; Figure 1I). There was no difference in absolute total MSNA between groups in the supine position, whereas the increase during tilting was smaller in blacks than in whites (Δtotal MSNA, 400 [289] versus 765 [546] units; \( P < 0.041 \)). Meanwhile, blacks demonstrated a greater response in TPR for a given change in MSNA than whites during upright tilt, because this efficacy of MSNA for TPR decreased in whites but was maintained in blacks during tilting (Figure 2A). Sympathetic BRS increased (more negative) during upright tilt in whites but not in blacks (Figure 2B). Plasma norepinephrine and epinephrine concentrations similarly increased during tilting in blacks and whites, whereas direct renin, aldosterone, and vasopressin concentra-

![Figure 1. Responses of systolic blood pressure (SBP; A), diastolic blood pressure (DBP; B), mean blood pressure (MBP; C), heart rate (HR; D), stroke volume (SV; E), cardiac output (Qc; F), total peripheral resistance (TPR; G), and muscle sympathetic nerve activity (MSNA) burst frequency (H) and total MSNA (I) during supine rest and 60° head-up tilt (HUT) in blacks and whites. Values are means (SDs). *Blacks vs whites at \( P < 0.05 \).](http://hyper.ahajournals.org/)}
tion responses during upright tilt were not different between groups (Table 2).

**Discussion**

The major findings from this study are as follows: (1) MSNA burst frequency responses to upright tilt were similar between groups, but the percentage increase in total MSNA and \( \Delta \text{total MSNA} \) were smaller in elderly blacks than in elderly whites; (2) sympathetic BRS remained unchanged in blacks but increased in whites during tilting; (3) during upright tilt, increases in mean BP and DBP were greater in blacks compared with whites, but the increase in SBP was similar between groups; and (4) elderly blacks had a greater response in TPR for a given change in total MSNA during tilting. These results suggest that elderly blacks have a blunted sympathetic neural responsiveness but enhanced pressor response to orthostasis compared with elderly whites, which may be attributable to an augmented sympathetic vascular transduction and/or nonadrenergic vasoconstrictor mechanisms (ie, angiotensin II or the venoarteriolar response).

**Table 2. Hormonal Responses to Upright Tilt**

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<th>Variables</th>
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<tr>
<td>Norepinephrine, pg/mL</td>
<td>341 (126)</td>
<td>380 (237)</td>
</tr>
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<td>Supine</td>
<td>526 (210)*</td>
<td>583 (243)*</td>
</tr>
<tr>
<td>60° HUT</td>
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<td></td>
</tr>
<tr>
<td>Epinephrine, pg/mL</td>
<td>19 (11)</td>
<td>18 (9)</td>
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<tr>
<td>Supine</td>
<td>33 (17)*</td>
<td>33 (22)*</td>
</tr>
<tr>
<td>60° HUT</td>
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<td></td>
</tr>
<tr>
<td>Direct renin, pg/mL</td>
<td>n=7</td>
<td>n=13</td>
</tr>
<tr>
<td>Supine</td>
<td>12 (7)</td>
<td>11 (5)</td>
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<tr>
<td>60° HUT</td>
<td>13 (9)</td>
<td>10 (5)</td>
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<td>Aldosterone, ng/dL</td>
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<td>6.9 (7.3)</td>
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<td>60° HUT</td>
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<td>Vasopressin, pg/mL</td>
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<td>60° HUT</td>
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Values are means (SDs). HUT indicates head-up tilt. *Versus supine at *P* < 0.05.

**Racial Differences in Sympathetic Neural Control During Orthostasis**

Consistent with previous reports from young individuals, we found that elderly blacks also had an enhanced pressor response without any racial differences in HR during upright posture. Because MSNA modulates vasoconstriction in the arterioles, we expected that this enhanced pressor response would be caused by a greater increase in MSNA. Contrary to our expectation, the current data showed that the increase in burst frequency during upright tilt was similar between groups, whereas the increase in total MSNA was actually smaller in elderly blacks than in whites. It could be argued that the blunted upright total MSNA could be explained by displacement of the recording electrodes during tilting. However, we cannot think of any reasons that such a displacement only occurred in one group but not the other group. Although both groups were well matched for sex ratios, it is possible that similar responses within one sex may have obscured existing racial differences within the other. Kienbaum et al have proposed that there are 2 sites for modulation of sympathetic activity by arterial baroreceptors; one determines whether or not a burst will occur (site 1) and another determines the strength of the discharge, expressed as burst area (site 2). It is possible that blacks have a blunted site 2. These results suggest that, rather than MSNA control, vascular function may be responsible for the enhanced pressor response in elderly blacks.

It has been found that cardiovagal BRS is similar or lower in young blacks than in whites. However, there is no information about racial difference in the sympathetic baroreflex-regulating BP through TPR at the vasculature. We observed an increase in sympathetic BRS during upright tilt in whites but not blacks, suggesting an impairment of sympathetic baroreflex function for orthostasis in elderly blacks. Previous reports consistently demonstrated that sympathetic BRS was increased despite a reduced distensibility of the barosensory artery during upright posture. This could be the net outcome of impaired transduction of intravessel BP into distortion of the artery (mechanical component of the sympathetic baroreflex) and improved transduction of the distortion into sympathetic nerve activity (neural component; Figure 3). The unchanged sympathetic BRS
The higher efficacy of MSNA on TPR in elderly blacks than whites suggests that sympathetic vascular transduction at the arterioles and/or other nonadrenergic mechanisms concurrently responsible for vasoconstriction may be enhanced in blacks. The enhanced sympathetic vascular transduction may be attributed to a higher concentration of norepinephrine at the neurovascular junction and/or a greater sensitivity/density of postsynaptic adrenergic receptors. Both supine and upright plasma norepinephrine concentrations were similar between groups despite the lower total MSNA response during tilting in blacks. We recognize that plasma norepinephrine is not a direct index of the synaptic level of norepinephrine; however, the change in plasma norepinephrine concentration has been found to correlate well with the interindividual response in MSNA. Therefore, the greater sympathetic vascular transduction in elderly blacks may be attributable to a higher synaptic norepinephrine release per unit increase of MSNA. This may also be the case in young blacks. This notion is supported by the findings that young blacks had a smaller increase in total MSNA during orthostasis, but greater norepinephrine release, as well as greater orthostatic tolerance, was observed in young black women. Thus, the mechanisms involved in the high prevalence of hypertension in elderly blacks may already exist in healthy young blacks, especially in women. Racial differences in α-adrenergic vasoconstriction were investigated previously, and the results were inconsistent; similar or enhanced adrenergic vasoconstriction in blacks compared with whites was reported. These inconsistent findings seem to be affected by not only vasoconstrictor sensitivity but also systemic reflexes (eg, the baroreflex). Conversely, it was found that blacks demonstrated a blunted β2-adrenergic–mediated vasodilation. Therefore, the greater vasoactivity in elderly blacks may be attributed to an offset by a lower β2-adrenergic sensitivity. To evaluate the contributions of α-adrenergic vasoconstriction and β2-adrenergic vasodilatation to racial differences of vasoreaction, future studies will be required. Nonetheless, the interaction between α- and β2-adrenergic receptor sensitivities may explain the augmented sympathetic vascular transduction in elderly blacks.

Several nonadrenergic mechanisms may also be considered. First, endothelium-dependent NO–mediated vasodilation was found to be attenuated in blacks compared with whites. A previous study suggested that NO-mediated vasodilation increased during orthostatic stress, and it is possible that the attenuation of NO-mediated vasodilation in blacks contributed to the greater vasoactivity during upright tilt. Second, the renin-angiotensin-aldosterone system releases powerful vasoconstrictor hormones, as well as antidiuretic hormone from the pituitary–vasopressin, which may be associated with greater vasoconstriction in blacks during orthostasis, because it was reported that plasma renin activity
increased during orthostasis in young blacks but not whites. However, the levels of these hormones during upright tilt did not differ between groups, at least within 5 minutes of tilting. Because we did not measure angiotensin II, we cannot completely exclude the possibility that upright angiotensin II was greater in elderly blacks than whites. Third, blacks may have an enhanced vasoconstrictor response (ie, a local axon reflex), which causes nonbaroreflex, nonadrenergically mediated regional vasoconstriction triggered by venous distension and is believed to contribute to ≈45% of the increase in systemic vascular resistance during orthostasis. To our knowledge, there is no information available on racial differences in the vasoconstrictor response. Future research is necessary in this regard.

Limitations
First, sympathetic neural activity was assessed with micro-neurography. It is possible that elderly blacks and whites have similar or different neural responses in other vascular beds, such as renal and splanchnic vascular beds. Second, despite elderly blacks and whites being well matched for physical characteristics, we did not match the groups for socioeconomic status. Although the racial difference in adrenergic responsiveness has been observed even after controlling for social class, this leaves the perennial question of “nature versus nurture” still open. Third, we studied healthy normotensive and mild hypertensive individuals. It is possible that sympathetic neural control may be different in patients with moderate and severe hypertension. Fourth, because we did not measure limb blood flow to the muscular bed to which we recorded MSNA, we cannot provide direct evidence regarding vasoconstrictor responsiveness. Finally, there are some limitations associated with the spontaneous breathing method for assessment of sympathetic BRS (see discussions in the online-only Data Supplement).

Perspectives
Enhanced vasoconstrictor responsiveness despite a lower reaction of sympathetic activity seems to make BP higher during orthostasis in senior blacks. Conversely, it is possible that, during baroreceptor loading (ie, excessive rise in BP and nocturnal recumbency when central blood volume increases), elderly blacks may have a smaller reduction of MSNA compared with elderly whites. The synergistic behavior may contribute importantly to the high prevalence of hypertension in the US adult population. Results from the third national health and nutrition examination survey, 1988–1991. Hypertension. 1995;25:305–313.


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Disclosures
None.

References
4. T."
Enhanced pressor response in elderly blacks was accompanied by a blunted sympathetic neural responsiveness and an unaltered sympathetic baroreflex sensitivity during orthostasis.

What Is Relevant?
- Enhanced vasoconstrictor responsiveness despite a lower reaction of sympathetic activity seems to make BP higher during orthostasis.
- This may be one of the causes of the high prevalence of hypertension in blacks.
Elderly Blacks Have a Blunted Sympathetic Neural Responsiveness But Greater Pressor Response to Orthostasis Than Elderly Whites
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Hypertension. 2012;60:842-848; originally published online July 9, 2012;
doi: 10.1161/HYPERTENSIONAHA.112.195313

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ELDERLY BLACKS HAVE A BLUNTED SYMPATHETIC NEURAL RESPONSIVENESS BUT GREATER PRESSOR RESPONSE TO ORTHOSTASIS THAN ELDERLY WHITES

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Running head: Racial differences in orthostatic responses

Supplementary Introduction

Calhoun et al1 previously evaluated the responses in muscle sympathetic nerve activity (MSNA) to the cold stress in young blacks and whites, and found that an enhanced pressor response in normotensive blacks was attributable to a greater increase in MSNA. They, however, showed that this racial difference disappeared in hypertensives.2 Thereafter, a detailed determination was performed between race and family history of hypertension within normotensive subjects, and it was found that the greater sympathetic response to the cold pressor test was true only in blacks with a family history of hypertension.3 Based on these findings, one would speculate that racial differences in sympathetic neural control may not be the same in elderly normotensive and hypertensive individuals. Thus, we evaluated the hemodynamic and sympathetic neural responses to orthostatic stress (60° upright tilt for 5 min) in elderly hypertensive and normotensive blacks and whites, separately.

Total MSNA has the factors of burst occurrence (i.e., burst frequency and burst incidence) and burst strength (i.e., burst area). Ray et al.4 demonstrated the racial difference in MSNA response to orthostasis only in total MSNA but not MSNA burst frequency in the young population, which was similar to our observations in the elderly. These data suggest that racial differences of MSNA responses may be derived from burst strength. Accordingly, we evaluated responses of sympathetic baroreflex sensitivity (BRS) calculated with burst incidence and mean burst area, separately, as well as that with total MSNA in the main manuscript.

Supplementary Data Analysis

Sympathetic baroreflex sensitivity

Sympathetic BRS was assessed by using the slope of the linear correlation between MSNA and DBP.5-7 To perform a linear regression, values for total MSNA were calculated over a 2-mmHg DBP bin increment covering the lowest to highest DBP.5, 6, 8, 9 This pooling procedure reduces the statistical impact of inherent beat-by-beat variability in nerve activity attributable to non-baroreflex influences (e.g. respiration).7 Moreover, a statistical weighting procedure was adopted to minimize the effect of minor variation of bin width and bin position on the slope with respect to the number of cardiac cycle in the bins.10 The sensitivity was determined from the slope in each subject after confirming that r value was >0.5 as described previously.9
Supplementary Statistical Analysis

Power and sample size calculation was based on the study of Calhoun et al. The differences in group means of increases in burst frequency and total MSNA were 10 bursts/min and 173%. The within group standard deviations were 9 bursts/min and 84%, and the ratio of blacks to whites was 1:2 (= 0.5). Thus, we will need to study 10 elderly blacks and 20 elderly whites to be able to reject the null hypothesis that the population means of blacks and whites are equal with probability (power) 0.80, and the Type I error probability associated with this test of this null hypothesis is 0.05.11

Values are expressed as means (SD). MSNA indices and beat-by-beat blood pressure (BP) and heart rate (HR) were collected for 6-min supine baseline and from the 2nd to the 5th min of 60° upright tilt. Subject characteristics and ambulatory BP monitoring (ABPM) results between groups were compared using 2-way ANOVA (blacks vs whites and hypertensives vs normotensives). MSNA, hemodynamic, efficacy of MSNA, and sympathetic BRS responses during upright tilt between groups were analyzed using 2-way repeated measures ANOVA with factors for race, posture, and the interaction (race × posture) within hypertensives and normotensives. Sympathetic BRS calculated with mean burst area and burst incidence were also analyzed using 2-way repeated measures ANOVA with factors for race, posture, and the interaction (race × posture). The Holm-Sidak method was used as post hoc for multiple comparisons. A P value of < 0.05 was considered statistically significant.

Supplementary Results

Subject characteristics

Table S1 shows drug information of the hypertensive patients. Table S2 depicts similar physical characteristics between racial groups as well as subgroups divided into hypertensives and normotensives. 24-h ABPM was higher in hypertensives than normotensives, while blacks had a higher ABPM-diastolic BP (DBP) than whites within hypertensives.

Hemodynamic responses

Both DBP and mean BP (MBP) were greater in normotensive blacks than normotensive whites during upright tilt, whereas these two variables showed similar trends in hypertensive blacks and whites (Figure S1A-F). The HR response, the reductions in stroke volume (SV) and cardiac output (Qc), and the increase in total peripheral resistance (TPR) were similar between blacks and whites both in normotensives and hypertensives (Figure S1G-N).

Sympathetic neural responses

MSNA burst frequency increased during upright tilt and the increase was similar between blacks and whites both within hypertensives and normotensives (Figure S1O&P). On the other hand, an increase in % total MSNA by tilting was seen only in whites within both hypertensives and normotensives (Figure S1Q&R). Changes in absolute total MSNA from supine to HUT (Δtotal MSNA) in whites and blacks were 914 (671) and 414 (248) units (P=0.137) in hypertensives and 669 (334) and 387(355) units (P=0.155) in normotensives. The efficacy of MSNA for vasoconstriction decreased and sympathetic BRS increased during upright tilt in hypertensive whites but not in hypertensive blacks (Figure S2A&C). Similar responses were observed for normotensives but were not statistically significant in reduction of the efficacy of MSNA for vasoconstriction in normotensive whites (Figure S2B&D).
Sympathetic baroreflex sensitivity responses

Sympathetic BRS calculated with mean burst area increased (more negative) during upright tilt in whites but remained unchanged in blacks (Figure S3A), which was similar to the result of sympathetic BRS calculated with total MSNA reported in the main manuscript. Conversely, sympathetic BRS calculated with burst incidence decreased in whites but was unchanged in blacks (Figure S3B).

Supplementary Discussion

Racial differences in the pressor response and sympathetic baroreflex sensitivity within normotensives and hypertensives

An enhanced pressor response in blacks compared with whites was observed more clearly in normotensives. Compared to normotensive whites, hypertensive whites appeared to have an increase in systolic pressure during upright tilt, which enhanced the pressor response in hypertensive whites. Compared to normotensive blacks, hypertensive blacks appeared to have higher baseline BPs, which reduced the pressor response in hypertensive blacks. Therefore, the racial difference in the pressor response may be weakened in hypertensives. Conversely, the unchanged sympathetic BRS and efficacy of MSNA on vasoconstriction during upright posture in blacks along with increased sympathetic BRS and decreased efficacy in whites were shown both within normotensives and hypertensives. These results are consistent with the findings reported in the main manuscript when hypertensives and normotensives were combined within the same racial group. It is suggested that hypertension in elderly blacks may be associated with the higher sympathetic vascular transduction and impaired sympathetic baroreflex sensitivity, while elderly whites may have different mechanism(s) underlying their hypertension.

Racial differences in MSNA burst occurrence and burst strength

The response in sympathetic BRS was similar when calculated with mean burst area (Figure S3B) and total MSNA (Figure 2B in the main manuscript), but not with burst incidence. Thus, the racial difference of the sympathetic baroreflex response to orthostasis is likely to be derived from burst strength (burst area per MSNA burst) rather than burst occurrence.

Supplementary Limitations

We used the spontaneous method with total MSNA, which includes both burst strength and burst occurrence to evaluate sympathetic BRS in the main manuscript. Hart et al recently reported that sympathetic BRS assessed with burst incidence was correlated more with that assessed by the modified Oxford method, and it was less affected by non-baroreflex influences during supine rest. Whether similar results can be obtained during upright posture is unclear. Since in this study, the racial difference of the change in MSNA during upright tilt (baroreceptor unloading) seemed to be derived from different control of burst area rather than burst occurrence, sympathetic BRS evaluated with burst incidence did not show any racial difference of baroreflex control during tilting (Figure S3). However, sympathetic BRS assessed with mean burst area showed similar results as those reported in the main manuscript. There remains debate as to whether burst incidence or total MSNA should be used in the assessment of sympathetic BRS during orthostasis in humans.
References

Table S1. Anti-hypertensive drug information on the screening day

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<th>Groups</th>
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ARB indicates angiotensin II AT1 receptor blocker. ACE, angiotensin-converting enzyme.
## Table S2. Subject characteristics

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<th>Variables</th>
<th>Hypertensives</th>
<th>Normotensives</th>
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<tr>
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<td>Blacks n=5</td>
<td>Whites n=10</td>
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<tr>
<td>Age, years</td>
<td>66 (6)</td>
<td>67 (4)</td>
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<tr>
<td>Height, cm</td>
<td>169 (10)</td>
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<tr>
<td>Weight, kg</td>
<td>81 (13)</td>
<td>78 (11)</td>
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<td>1.9 (0.2)</td>
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<tr>
<td>BMI, kg/m²</td>
<td>28.6 (3.9)</td>
<td>26.9 (2.7)</td>
</tr>
</tbody>
</table>

**ABPM (run-in)**

| SBP, mmHg | 151 (10)†      | 142 (7)†       | 124 (9)       | 126 (7)     |
| DBP, mmHg | 88 (4)‡‡       | 79 (8)‡        | 75 (6)        | 72 (5)      |

Values are means (SD). BSA indicates body surface area; BMI, body mass index; ABPM, ambulatory blood pressure monitoring; SBP, systolic blood pressure; DBP, diastolic blood pressure. *, vs whites within hypertensives; †, vs normotensives within the same race at \( P<0.05 \).
Continued
(Continued)
(Continued)
**Figure S1:** Responses of systolic blood pressure (SBP, A & B), diastolic blood pressure (DBP, C & D), mean blood pressure (MBP, E & F), heart rate (HR, G & H), stroke volume (SV, I & J), cardiac output (Qc, K & L), total peripheral resistance (TPR, M & N), and muscle sympathetic nerve activity (MSNA) burst frequency (O & P), and % total MSNA (Q & R), during supine rest and 60° head-up tilt (HUT) in hypertensive and normotensive blacks and whites, respectively. Values are means (SD). *, blacks vs whites; †, supine vs 60° HUT within the same race at P<0.05.
Figure S2: Change in total peripheral resistance (TPR) for a given change in total muscle sympathetic nerve activity (MSNA) calculated as %TPR/%total MSNA (A, hypertensives; B, normotensives) and sympathetic baroreflex sensitivity (BRS) (C, hypertensives; D, normotensives) in the supine position and during 60° head-up tilt (HUT) in blacks and whites. Values are means (SD). *, supine vs 60° HUT within whites at P<0.05.
Figure S3: Sympathetic baroreflex sensitivity (BRS) calculated with mean burst area (burst strength; $A$) and sympathetic BRS calculated with burst incidence ($B$) in the supine position and during 60° head-up tilt (HUT) in blacks and whites. Values are means (SD). *, supine vs 60° HUT within whites at $P<0.05$. 