Overweight and Sympathetic Overactivity in Black Americans


Abstract—A large body of clinical investigation implicates an important role for the sympathetic nervous system in linking obesity with hypertension. However, the experimental support for this hypothesis is derived from strictly white cohorts. The goal of this study was to determine whether being overweight begets sympathetic overactivity in black Americans, the ethnic minority at highest risk for hypertension. We recorded postganglionic sympathetic nerve discharge with microelectrodes in muscle nerve fascicles of the peroneal nerve in 92 normotensive young adult black men and women within a wide range of body mass index. The same experiments were performed in a control group of 45 normotensive white men and women of similar ages and body mass indices. The major new findings are 2-fold. First, in young, normotensive, overtly healthy black women, being overweight begets sympathetic overactivity ($r=0.45$, $P=0.0009$), a putative intermediate phenotype for incident hypertension. Second, in black men, sympathetic nerve discharge is dissociated from body mass index ($r=0.03$, $P=NS$). This dissociation is explained in part by a 20% to 40% higher rate of sympathetic nerve discharge in lean black men compared with lean white men and lean black and white women (28±3 versus 18±2, 21±2, and 17±2 bursts/min, respectively; $P<0.05$). Sympathetic nerve discharge in lean black men is comparable to that of overweight black men and women as well as white men and women. These data provide the first microneurographic evidence for tonic central sympathetic overactivity in blacks, both adiposity-related sympathetic overactivity in black women and adiposity-independent sympathetic overactivity in black men.

Key Words: obesity ■ sympathetic nervous system ■ blacks ■ blood pressure

Obesity is firmly established to be a major risk factor for hypertension, and a large body of clinical investigation implicates an important role for the sympathetic nervous system in linking adiposity with hypertension.1–6 In numerous studies of normotensive young adults, increasing adiposity is accompanied by increased sympathetic nerve discharge (SND) to skeletal muscle, a major site of energy expenditure.3–7 Overweight-related sympathetic overactivity is hypothesized to be a compensatory mechanism to burn fat and minimize weight gain but at the cost of increased sympathetic discharge to the peripheral vasculature, which could predispose to hypertension.2,8 However, the experimental support for this hypothesis is derived from strictly white cohorts.5,6

The importance of inclusion of minority subjects in this field of clinical investigation is underscored by recent studies of Pima Indians, an ethnic minority with a high prevalence of obesity but a comparatively low prevalence of hypertension.4 Basal levels of skeletal muscle SND are lower in normotensive male Pima Indians than in whites and do not track with adiposity. This relative sympathetic underactivity constitutes a potential explanation for the surprisingly low prevalence of hypertension in this population.4,5

The goal of the present study was to explore the relationship between adiposity and SND in black Americans, the ethnic minority with the highest risk for hypertension. In the United States, hypertension and obesity are both more prevalent among black women than white women.10 Therefore, we hypothesized that adiposity begets sympathetic overactivity in black women as well as in white women. On the other hand, the prevalence of hypertension is strikingly higher in black men than in white men, despite comparable levels of obesity.11,12 In a longitudinal study of initially normotensive black male medical students, a remarkably high incidence of hypertension was observed even among the physicians who remained lean throughout adult life.13 Taken together, these epidemiological data led us to hypothesize a major gender difference in the relationship between adiposity and SND in blacks. Specifically, we sought to determine whether sympathetic overactivity is present in lean black men; such overactivity would constitute a potential explanation for a high risk of hypertension independent of obesity. To test these
hypotheses, we used intraneural microelectrodes to record skeletal muscle SND in 92 normotensive young adult African American men and women within a wide range of body mass index (BMI). The same experiments were performed in a control group of 45 normotensive white men and women of similar ages and BMIs.

Methods

General Methods

We studied a total of 137 overtly healthy volunteers age 18 to 39 years. The protocol was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center, and all subjects gave their written informed consent to participate. All subjects were free of any history of cardiovascular disease or of substance abuse. Specifically, all subjects were normotensive and had normal fasting blood glucose concentrations at the time of study.

All experiments were performed after an overnight fast with the subjects in the supine position. Heart rate (ECG), blood pressure (Welch-Allyn oscillometric sphygmomanometry), and postganglionic SND were recorded continuously by using intraneural microelectrodes. The analog signals were recorded by using Gould ES1000 electrostatic signal conditioners and routed to a MacLab A-D board for data collection and analysis.

Muscle SND

Multunit recordings of postganglionic sympathetic action potentials were obtained with unipolar tungsten microelectrodes inserted selectively into muscle nerve fascicles of the peroneal nerve posterior to the fibular head according to the technique of Valbo et al. This technique provides a reproducible measure of sympathetic vasoconstrictor drive targeted to the skeletal muscle bed, which is an important component of peripheral vascular resistance and blood pressure. Briefly, the neural signals were amplified, filtered (bandwidth 700 to 2000 Hz), rectified, and integrated to obtain a mean voltage display of muscle SND. A recording of muscle SND was considered acceptable when the neurograms revealed spontaneous pulse synchronous bursts of neural discharge, with the largest bursts showing a minimal signal-to-noise ratio of 3:1. The interobserver variability in identifying bursts are showing a minimal signal-to-noise ratio of 3:1. The interobserver variability in identifying bursts are showing a minimal signal-to-noise ratio of 3:1. The interobserver variability in identifying bursts are showing a minimal signal-to-noise ratio of 3:1.

Anthropometric Measurements

Body weight, height, and waist and hip circumferences were measured by standard procedures. Skinfold thicknesses were measured at 9 different anatomic sites (subscapular, chest, midauxiliary, abdominal, suprailliac, triceps, biceps, thigh, and calf) by use of Lange skinfold calipers (Cambridge Scientific Instruments Inc). The means of 3 repeat measurements at each site were used for calculations. Percentage body fat was calculated by using the nomogram of Baum et al.

Twenty-Four-Hour Ambulatory Blood Pressure Monitoring

In the black subjects, 24-hour ambulatory blood pressure was monitored according to standard methods, with use of a Space Labs model 90207 monitor. The monitor was programmed to measure blood pressure once every 20 minutes for the entire 24-hour period.

Statistical Methods

Two sample t tests were used to compare genders within each ethnic group. A linear model was used to assess the effect of gender while adjusting for covariates such as age, arterial pressure, heart rate, and family history of hypertension, focusing on the relationship between sympathetic nerve discharge and different measures of adiposity. Because none of the covariates significantly affected the results, Pearson correlation coefficients are reported. A value of $P\leq0.05$ was considered to indicate significance.

Results

In the black subjects (Table 1), there were no gender differences in age, BMI, or fasting plasma concentrations of glucose. As expected, 24-hour heart rates estimated body fat and triceps skinfold thickness; all were higher in the women. In contrast, 24-hour systolic blood pressures were slightly but significantly higher in the men. For the group as a whole, sympathetic discharge in bursts per 100 heartbeats (a heart rate–independent measure of nerve discharge) was higher in black men than women (Table 1). In the 12 black subjects (6 women, 6 men) who were studied twice (10±4 months between studies), the correlation coefficient of reliability in the measurement of SND was 0.91.

The major new findings are 2-fold. First, in the black women, sympathetic discharge was closely correlated with BMI (Table 2 and Figures 1 and 2). This correlation persisted after adjustment for age, arterial pressure, or family history of hypertension (data not shown). We also found a significant correlation between BMI and sympathetic discharge in both white women and men (Figure 2), which confirms previous reports.

### Table 1. Baseline Characteristics of Black Subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Black Women (n=52)</th>
<th>Black Men (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>32±1</td>
<td>29±1</td>
</tr>
<tr>
<td>24-h systolic blood pressure, mm Hg</td>
<td>119±2*</td>
<td>124±2</td>
</tr>
<tr>
<td>24-h diastolic blood pressure, mm Hg</td>
<td>73±1</td>
<td>74±1</td>
</tr>
<tr>
<td>24-h mean arterial pressure, mm Hg</td>
<td>88±2</td>
<td>90±1</td>
</tr>
<tr>
<td>24-h heart rate, bpm</td>
<td>82±2*</td>
<td>76±2</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.6±1</td>
<td>26.7±1</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>85.4±2</td>
<td>87.7±2</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.81±0.02</td>
<td>0.85±0.01</td>
</tr>
<tr>
<td>Triceps skinfold thickness, mm</td>
<td>32.7±2*</td>
<td>17.5±3</td>
</tr>
<tr>
<td>Total body fat, %</td>
<td>33.4±2*</td>
<td>18.5±2</td>
</tr>
<tr>
<td>Fasting blood glucose, mmol/L</td>
<td>2.23±0.05</td>
<td>2.19±0.1</td>
</tr>
<tr>
<td>SND, bursts/min</td>
<td>24±2</td>
<td>27±2</td>
</tr>
<tr>
<td>SND, bursts/100 heartbeats</td>
<td>32±2*</td>
<td>40±2</td>
</tr>
</tbody>
</table>

*P<0.05 vs black men.

Values are mean±SE.
Second, in black men, sympathetic discharge was (1) overall higher than that in white men (27 ± 62 versus 22 ± 61 bursts/min, respectively; P<0.02) and (2) dissociated from BMI and numerous other indices of adiposity (Table 2 and Figure 2). The lack of correlation between adiposity and SND was attributed in part to a significantly higher rate of sympathetic discharge seen in lean (BMI < 25) black men compared with lean white men and lean black and white women (28 ± 3 versus 18 ± 2, 21 ± 2, and 17 ± 2 bursts/min, respectively; P<0.05; Figures 2 and 3). In the lean black men, sympathetic discharge was comparable to that of overweight (BMI ≥ 25) black men and women as well as overweight white men and women (28 ± 3 versus 27 ± 2, 26 ± 2, 25 ± 2, and 30 ± 3 bursts/min, respectively; Figure 3).

Unlike sympathetic discharge, 24-hour heart rates were correlated with adiposity in both black men and women (Table 2). No correlation was found between 24-hour blood pressures and BMI.

Discussion

This is the first study to explore the relationship between adiposity and SND in blacks. The major new findings are 2-fold: (1) In normotensive overtly healthy young US black women, overweight begets sympathetic overactivity. (2) In contrast, in normotensive young black men, sympathetic discharge is dissociated from adiposity, in part, because in the lean black men, the discharge rates are 20% to 40% higher than those in lean black women or in lean white men and women of comparable BMI.

![Figure 2. Scatterplots showing the relationship between individual values of BMI and SND for the 4 ethnic/gender groups. Significant correlations were evident for all groups except black men. The average age, mean arterial pressure, heart rate, and BMI are 30 ± 2 years, 80 ± 2 mm Hg, 67 ± 3 bpm, and 28 ± 2 kg/m², respectively, for white women and 28 ± 1 years, 84 ± 2 mm Hg, 65 ± 2 bpm, and 26 ± 1 kg/m², respectively, for white men.](image-url)
Although the mechanism linking overweight and sympathetic overactivity is unknown, several hormonal signals have been postulated. These include (1) insulin, which has been shown in humans to increase muscle SND during euglycemic insulin clamp; (2) free fatty acids, which have been shown in rats to increase blood pressure by stimulation of excitatory hepatic afferent nerves; and (3) leptin, the ob gene product, which has been shown in rats to increase sympathetic discharge to several tissues, including skeletal muscle. However, these observations are based on acute exogenous infusions or correlational studies, and the role played by endogenous production of these or other hormones in causing the chronic sympathetic overactivity in overweight individuals remains to be determined.

In addition, subclinical sleep apnea leading to chemoreflex sensitization recently has been proposed as an important neurogenic mechanism causing obesity-related sympathetic overactivity in whites. Because sleep apnea appears to be more prevalent in blacks than in whites, further studies are needed to determine whether this mechanism mediates obesity-related sympathetic overactivity in black women.

Regardless of the precise mechanistic explanation, the new data in black women are consistent with the hypothesis first proposed by Landsberg, who suggested that sympathetic activation is a compensatory autonomic adjustment to weight gain. In contrast, black men constitute an exception to the Landsberg hypothesis, because sympathetic discharge rates are dissociated from BMI and numerous other measures of adiposity. To document the ethnic specificity of this gender difference, we performed the same experiments on a cohort of white men and women, and in both genders, we found strong correlations between sympathetic discharge and BMI, confirming previous reports. From these cross-sectional data, however, we cannot exclude any possibility that in black men a relationship between SND and adiposity was obscured by factors that are more important than adiposity in governing basal sympathetic discharge.

In this regard, the situation in black men also differs from that described in Pima Indian men, in whom basal sympathetic discharge rates are not only dissociated from adiposity but also lower than those in similar white cohorts. In the Pima Indian men, the disproportionate sympathetic underactivity constitutes a potential explanation for the low prevalence of hypertension despite the high prevalence of obesity. In contrast, in black men, the basal sympathetic discharge rates are not only dissociated from adiposity but also higher than those in white men of comparable age and BMI. This is, in part, because of 20% to 40% higher sympathetic discharge rates in lean black men compared with lean white men and lean black and white women. Although the environmental and genetic factors driving this disproportionate increase in sympathetic discharge are unknown, sympathetic overactivity constitutes a potential explanation for the remarkably high incidence of hypertension in lean black men.

Because there can be marked heterogeneity in the regulation of regional autonomic outflow, these data should not be extrapolated to make general statements about ethnic/gender differences in the regulation of sympathetic outflow to tissues other than the skeletal muscle vasculature. Unlike skeletal muscle sympathetic discharge, mean 24-hour heart rates increased with increasing adiposity in both black men and women, presumably reflecting both increased sympathetic and decreased parasympathetic drive to the sinus node. Unlike skeletal muscle sympathetic discharge and heart rate, mean 24-hour blood pressures were not found to be correlated with adiposity in our normotensive young adult black men or women. In general, much larger population-based studies are needed to demonstrate a robust cross-sectional correlation between blood pressure and BMI. We speculate that in normotensive populations, including blacks, increased sympathetic discharge, such as heart rate, will turn out to be an early independent predictor of increased risk for the future development of hypertension.

The traditional thinking is that the sympathetic nervous system plays little role in the pathogenesis of hypertension in...
blacks, with the latter being assumed to be mainly volume-dependent/low-renin hypertension. More recently, however, there is evidence to suggest that peripheral vascular α-adrenergic receptor sensitivity to norepinephrine is greater in young black men than in white men, whereas β-adrenergic receptor–mediated vasodilation is reduced in blacks. The only previous microneurographic studies in blacks indicated a heightened sympathetic response to cold pressor stimulation in normotensive blacks compared with normotensive whites; however, the apparent ethnic difference disappeared when adjustments were made for family history of hypertension. Thus, the present study is the first to provide microneurographic evidence of tonic central sympathetic overactivity in blacks, both adiposity-related sympathetic overactivity in black women and adiposity-independent sympathetic overactivity in lean black men. Because heightened sympathetic activity portends a poor prognosis in patients with cardiovascular diseases, we speculate that central sympathetic activation may be a factor explaining why black men suffer the highest overall cardiovascular mortality rates of any ethnic/gender group in this country.

Acknowledgments

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References

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