Overweight and Sympathetic Overactivity in Black Americans

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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. **(*Hypertension*. 2001;38:379-383.)**

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.[5–7] 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.[4,9]

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

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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

Multiunit 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.[14] 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.[14] 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 and intraobserver variability in identifying bursts are $<$10% and 5%, respectively. Nerve traffic was expressed as both the number of bursts per minute and the number of bursts per 100 heartbeats; the latter is a heart rate–independent measure of sympathetic discharge.

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, suprailiac, 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 Baun et al.[15]

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.[16] 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 $P \leq 0.05$ was considered to indicate significance.

TABLE 1. Baseline Characteristics of Black Subjects

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

Values are mean±SE.
*$P<0.05$ vs black men.

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.[4–6,17]

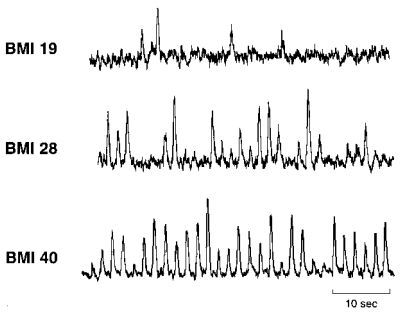

Figure 1. Illustrative recordings of SND in 3 young black women, who are lean (top), obese (middle), and very obese (bottom). The narrow-based peaks are spontaneous bursts of postganglionic SND targeted to the skeletal muscle vasculature. The rate of nerve firing increases progressively with increasing BMI.

TABLE 2. Correlation Between Measures of Adiposity and 24-Hour Blood Pressure, 24-Hour Heart Rate, and SND

	BMI (kg/m^2)		Body Fat (%)		Triceps Fold Thickness (mm)		Waist Circumference (cm)		Waist-to-Hip Ratio	
Variables	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Black women										
SND (bursts/min)	0.45	0.0009	0.52	0.0001	0.51	0.0002	0.37	0.009	0.33	0.02
SND (bursts/100 heartbeats)	0.33	0.02	0.42	0.003	0.41	0.004	0.3	0.03	0.34	0.02
24-h mean arterial pressure (mm Hg)	0.3	0.06	0.13	0.43	0.17	0.29	0.17	0.31	0.06	0.7
24-h heart rate (bpm)	0.39	0.01	0.3	0.06	0.33	0.04	0.31	0.05	0.11	0.53
Black men										
SND (bursts/min)	0.03	0.9	0.09	0.9	0.04	0.8	0.05	0.7	0.17	0.3
SND (bursts/100 heartbeats)	−0.05	0.8	0.05	0.8	−0.09	0.6	0.05	0.7	0.09	0.6
24-h mean arterial pressure (mm Hg)	0.06	0.77	0.13	0.49	0.13	0.5	0.009	0.96	0.08	0.66
24-h heart rate (bpm)	0.51	0.004	0.54	0.003	0.47	0.01	0.57	0.001	0.28	0.14

Second, in black men, sympathetic discharge was (1) overall higher than that in white men (27±2 versus 22±1 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.

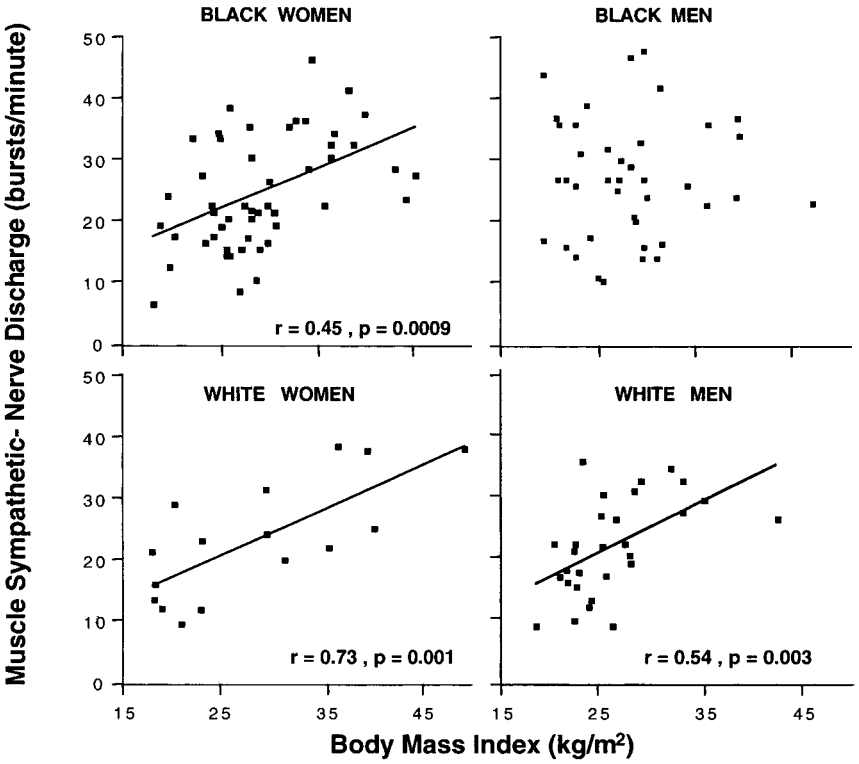

Figure 2. Scatterplots showing the relationship between individual values of BMI and SND for the 4 ethnic/gender groups. Significant correlations were evident for all groups except black men. The average age, mean arterial pressure, heart rate, and BMI are 30±2 years, 80±2 mm Hg, 67±3 bpm, and 28±2 kg/m^2, respectively, for white women and 28±1 years, 84±2 mm Hg, 65±2 bpm, and 26±1 kg/m^2, respectively, for white men.

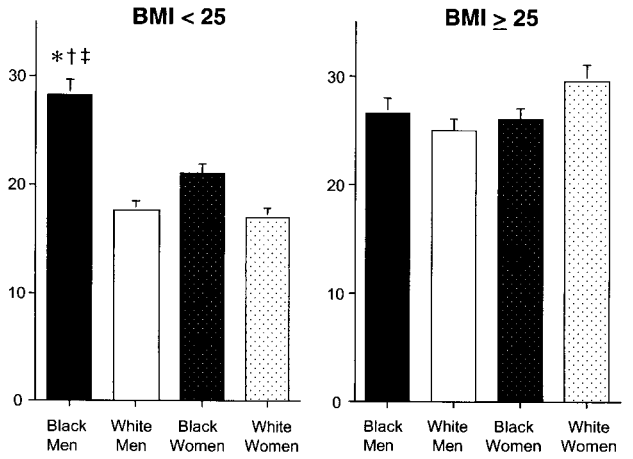

Figure 3. Summary data showing SND (bursts per minute) for the lean (BMI <25, left) and overweight (BMI≥25, right) subjects from the 4 ethnic/gender groups. Lean black men (n=13) had a significantly higher SND than did lean white men (n=13), lean black women (n=20), and lean white women (n=8), despite a similar BMI (22.4 versus 22.2, 21.7, and 20.1, respectively). *P<0.01 vs lean white men; †P=0.02 vs lean black women; and ‡P=0.01 vs lean white women. In contrast, SND of overweight black men (n=27) was similar to that of overweight white men, black women, and white women (n=16, 32, and 8, respectively). With use of a BMI cutoff of 25, overweight white men had a significantly higher SND than did lean white men (P=0.006), and overweight white women had a significantly higher SND than did lean white women (P=0.004). In contrast, the threshold for the effect of adiposity on SND in black women was higher than in whites. With use of a BMI cutoff of 25, there was a tendency for SND to be higher in overweight black women than in lean black women, but this tendency did not reach statistical significance (P=0.07). When we defined overweight in black females by a higher BMI cutoff, the difference became statistically significant (P=0.03 for BMI ≥27.8, P=0.000003 for BMI ≥30).

Thus, sympathetic overactivity in young adulthood constitutes one potential explanation for both the high incidence of obesity-related hypertension in black women and the disproportionately high incidence of hypertension in lean black men.[18]

In the black women, adiposity was a major determinant of sympathetic discharge, by univariate analysis, accounting for one third of the interindividual variability in discharge rates. This finding was robust, because adiposity remained a strong predictor of sympathetic discharge in multivariate analyses that accounted for possible covariates such as age, blood pressure, and family history of hypertension. The strength of the relationship between sympathetic discharge rates and numerous indices of adiposity in black women is very similar to that observed in previous studies of white subjects.[4–6,17]

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[19]; (2) free fatty acids, which have been shown in rats to increase blood pressure by stimulation of excitatory hepatic afferent nerves[20]; and (3) leptin, the ob gene product, which has been shown in rats to increase sympathetic discharge to several tissues, including skeletal muscle.[21] However, these observations are based on acute exogenous infusions or correlational studies,[9,19,22] 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.[23] Because sleep apnea appears to be more prevalent in blacks than in whites,[24] 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,[2,8] 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.[4–6,17] 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.[4] 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.[25]

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.[26,27] 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.[28] We speculate that in normotensive populations, including blacks, increased sympathetic discharge, such as heart rate,[29] 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.[30] More recently, however, there is some 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.[31] The only previous microneurographic studies in blacks indicated a heightened sympathetic response to cold pressor stimulation in normotensive blacks compared with normotensive whites[32]; however, the apparent ethnic difference disappeared when adjustments were made for family history of hypertension.[33] 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,[34] we speculate that central sympathetic activation may be 1 factor explaining why black men suffer the highest overall cardiovascular mortality rates of any ethnic/gender group in this country.[25]

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References

1. Anderson EA, Hoffman RP, Balon TW, Sinkey CA, Mark AL. Hyperinsulinemia produces both sympathetic neural activation and vasodilation in normal humans. *J Clin Invest*. 1991;87:2246–2252.
2. Landsberg L. Hyperinsulinemia: possible role in obesity-induced hypertension. *Hypertension*. 1992;19(suppl I):I-61. Abstract.
3. Victor RG, Mark AL. The sympathetic nervous system in human hypertension. In: Laragh JH, Brenner BM, eds. *Hypertension: Pathophysiology, Diagnosis, and Management*. New York, NY: Raven Press; 1995:863–878.
4. Spraul M, Ravussin E, Fontvvielle AM, Rising R, Larson DE, Anderson EA. Reduced sympathetic nervous activity: a potential mechanism predisposing to body weight gain. *J Clin Invest*. 1993;92:1730–1735.
5. Scherrer U, Randin D, Tappy L, Vollenweider P, Jequier E, Icod P. Body fat and sympathetic nerve activity in healthy subjects. *Circulation*. 1994;89:240–263.
6. Grassi G, Seravelle G, Cattaneo BM, Bolla GB, Lanfranchi A, Colombo M, Giannattasio C, Brunani A, Cavagnini F, Mancia G. Sympathetic activation in obese normotensive subjects. *Hypertension*. 1995;25:560–563.
7. Levine JA, Eberhardt NL, Jensen MD. Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science*. 1999;283:212–214.
8. Landsberg L. Obesity. In: *Hypertension Primer*. Baltimore, Md: Williams & Wilkins; 1999.
9. Weyer C, Pratley RE, Snitker S, Spraul M, Ravussin R, Tataranni PA. Ethnic differences in insulinemia and sympathetic tone as links between obesity and blood pressure. *Hypertension*. 2000;36:531–537.
10. Burt VL, Cutler JA, Higgins M, Horan MJ, Labarthe D, Whelton P, Brown C, Roccella EJ. Trends in the prevalence, awareness, treatment, and control of hypertension in the adult US population: data from the health examination surveys, 1960 to 1991. *Hypertension*. 1995;26:60–69.
11. Winkleby MA, Kraemer HC, Ahn DK, Varady AN. Ethnic and socioeconomic differences in cardiovascular disease risk factors: findings for women from the Third National Health and Nutrition Examination Survey, 1988–1994. *JAMA*. 1998;280:356–362.
12. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: prevalence and trends, 1960–1994. *Int J Obesity*. 1998;22:39–47.
13. Neser W, Thomas J, Semenya K, Thomas D, Gillum R. Obesity and hypertension in a longitudinal study of black physicians. *J Chronic Dis*. 1986;39:105–113.
14. Valbo AB, Hagbarth K-E, Toreebjork HE, Wallin BG. Somatosensory proprioceptive and sympathetic activity in human peripheral nerves. *Physiol Rev*. 1979;59:919–957.
15. Baun W, Baun M, Raven P. A nomogram for the estimate of percent body fat from generalized equations. *Res Q Exerc Sport*. 1981;52:380–384.
16. Appel LJ, Stason WB. Ambulatory blood pressure monitoring and blood pressure self-measurement in the diagnosis and management of hypertension. *Ann Intern Med*. 1993;118:867–882.
17. Gudbjornsdottir S, Lonnroth P, Sverrisdottir YB, Wallin BG, Elam M. Sympathetic nerve activity and insulin in obese normotensive and hypertensive men. *Hypertension*. 1996;27:276–280.
18. Johnson AL, Cornoni JC, Cassel JC, Tyroler HA, Heyden S, Hames CG. Influence of race, sex and weight on blood pressure behavior in young adults. *Am J Cardiol*. 1975;35:523–530.
19. Vollenweider P, Randin D, Tappy L, Jequier E, Nicod P, Scherrer U. Impaired insulin-induced sympathetic neural activation and vasodilation in skeletal muscle in obese humans. *J Clin Invest*. 1994;93:2365–2371.
20. Grekin RJ DC, Vollmer AP, Watts SW, Webb RC. Mechanism in the pressor effect of hepatic portal venous fatty acid infusion. *Am J Physiol*. 1997;273:R324–R330.
21. Haynes WG MD, Walsh SA, Mark AL, Sivitz WI. Receptor-mediated regional sympathetic nerve activation by leptin. *J Clin Invest*. 1997;100:270–278.
22. Haastrup AT, Stepniakowski KT, Goodfriend TL, Egan BM. Intralipid enhances alpha adrenergic receptor-mediated pressor sensitivity. *Hypertension*. 1998;32:693–698.
23. Narkiewicz K, van de Borne PJ, Cooley RL, Dyken ME, Somers VK. Sympathetic activity in obese subjects with and without obstructive sleep apnea. *Circulation*. 1998;98:772–776.
24. Redline S, Tishler PV, Hans MG, Tosteson TD, Strohl KP, Spry K. Racial differences in sleep-disordered breathing in African-Americans and Caucasians. *Am J Respir Crit Care Med*. 1997;155:186–192.
25. American Heart Association. *Heart and Stroke Statistical Update*. Dallas, Tex: American Heart Association; 2001:1–32.
26. Peterson HR, Rothschild M, Weinberg CR, Fell RD, McLeish KR, Pfeifer MA. Body fat and the activity of the autonomic nervous system. *N Engl J Med*. 1988;318:1077–1083.
27. Grassi G, Vailati S, Bertinieri G, Seravalle G, Stella ML, Dell'Oro R, Mancia G. Heart rate as marker of sympathetic activity. *J Hypertens*. 1998;16:1635–1639.
28. Liu K, Ballew C, Jacobs DR, Sidney S, Savage PJ, Dyer A, Hughes G, Blanton MM. Ethnic differences in blood pressure, pulse rate, and related characteristics in young adults: the CARDIA study. *Hypertension*. 1989;14:218–226.
29. Palatini P. Elevated heart rate as a predictor of increased cardiovascular morbidity. *J Hypertens*. 1999;17:S3–S10.
30. Lang CC, Stein CM, He HB, Belas FJ, Blair IA, Wood M, Wood AJ. Blunted blood pressure response to central sympathoinhibition in normotensive blacks: increased importance of nonsympathetic factors in blood pressure maintenance in blacks. *Hypertension*. 1997;30:157–162.
31. Lang CC, Stein CM, Brown RM, Deegan R, Nelson R, He HB, Wood M, Wood AJ. Attenuation if isoproterenol mediated vasodilatation in blacks. *N Engl J Med*. 1995;333:155–160.
32. Calhoun DA, Mutinga ML, Wyss JM, Oparil S. Normotensive blacks have heightened sympathetic response to cold pressor test. *Hypertension*. 1993;22:801–805.
33. Calhoun DA, Mutinga ML. Race, family history of hypertension, and sympathetic response to cold pressor testing. *Blood Press*. 1997;6:209–213.
34. Cohn JN, Levine TB, Olivari MT, Garberg V, Lura D, Francis GS, Simon AB, Rector T. Plasma norepinephrine as a guide to prognosis in patients with chronic congestive heart failure. *N Engl J Med*. 1984;311:819–823.