Insulin sensitivity is associated with blood pressure response to sodium in older hypertensives

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Dengel, Donald R., Robert V. Hogikyan, Michael D. Brown, Scott G. Glickman, and Mark A. Supiano. Insulin sensitivity is associated with blood pressure response to sodium in older hypertensives. Am. J. Physiol. 274 (Endocrinol. Metab. 37): E403–E409, 1998.—The purpose of this study was to determine whether sodium-resistant hypertensives are more insulin resistant and whether dietary sodium restriction improves insulin sensitivity in older hypertensives. Insulin sensitivity was assessed by a frequently sampled intravenous glucose tolerance test to determine the insulin sensitivity index (SI) after 1 wk each of low- (20 mmol·l⁻¹·day⁻¹) and high- (200 mmol·l⁻¹·day⁻¹) sodium diets in 21 older (63 ± 2 yr) hypertensives. Subjects were grouped on the difference in mean arterial blood pressure (MABP) between diets (sodium sensitive [SS]: >5-mmHg increase in MABP on the high-sodium diet (n = 14); sodium resistant [SR]: ≤5-mmHg increase in MABP on the high-sodium diet (n = 7)]. There was no dietary sodium effect on fasting plasma insulin or SI. An analysis of variance indicated a significant (P = 0.0002) group effect, with SS individuals having lower fasting plasma insulin on the low- (13 ± 2 vs. 27 ± 3 µU/ml) and high- (12 ± 2 vs. 22 ± 3 µU/ml) sodium diets compared with SR individuals. Similarly, there was a significant (P = 0.0002) group effect in regard to SI, with SS individuals having significantly higher SI on the low- (3.26 ± 0.60 vs. 0.91 ± 0.31 µU × 10⁻⁴·min⁻¹·ml⁻¹) and high- (3.45 ± 0.51 vs. 1.01 ± 0.30 µU × 10⁻⁴·min⁻¹·ml⁻¹) sodium diets compared with SR individuals. We conclude that SR individuals exhibit a greater degree of insulin resistance than SS individuals and that dietary sodium restriction fails to improve insulin sensitivity regardless of sodium sensitivity status.

aging

IT HAS BEEN SUGGESTED that high dietary sodium intake may contribute to the development of hypertension (15). Although epidemiological and clinical studies support an association between dietary sodium intake and blood pressure (13), there is great variation in blood pressure responses to changes in sodium intake. This variation in the blood pressure response to the modulation of dietary sodium intake has led to the classification of individuals on the basis of their sensitivity to sodium (24, 27). Weinberger et al. (27) reported that ~25% of normotensive individuals increase their blood pressure in response to sodium loading and are classified as sodium sensitive. However, the proportion of individuals who are sensitive to the effects of sodium loading on blood pressure increases to >50% in hypertensive individuals. Although the change in blood pressure in response to increased dietary sodium intake is normally distributed, there is a shift in this distribution toward a greater increase in blood pressure in older individuals as well as those with hypertension (26).

In addition to changes in blood pressure, dietary sodium restriction has been reported to increase insulin sensitivity in young, healthy, normotensive nondiabetic Caucasian males (8). In contrast to these results, studies in young lean normotensive males (23) and older hypertensives (6, 16) have reported that dietary sodium restriction had no effect on insulin sensitivity. Additionally, Lind et al. (16) reported that insulin sensitivity, as measured when the subject was on the high-sodium diet, was significantly related to the difference in standing blood pressure between the two different sodium diets, i.e., sodium-resistant subjects had a greater degree of insulin resistance. In contrast to these observations, Rocchini et al. (19) reported that sodium-resistant young normotensive and hypertensive subjects were more insulin sensitive.

The discrepancies in studies that have examined the effect of dietary sodium restriction on insulin sensitivity may be due to differences in subject populations, especially with respect to differences in sodium sensitivity status. To date, most of these studies examined the effect of dietary sodium restriction in a young healthy normotensive population, which in general is sodium resistant (27). Such studies have not been conducted in older, overweight, sedentary hypertensives, who are more insulin resistant and might have a greater propensity for dietary sodium-exacerbated changes in glucose homeostasis. In addition, on the basis of the results of Lind et al. (16), it would appear that those individuals who are sodium resistant might also be insulin resistant compared with those who are sodium sensitive.

The purpose of the present study was to test the hypotheses that 1) sodium-resistant hypertensives would be more insulin resistant than those who are sodium sensitive, and 2) decreased dietary sodium intake would increase insulin sensitivity in older hypertensive individuals.

MATERIALS AND METHODS

Subjects. Twenty-one subjects (8 males and 13 females) with mild hypertension were recruited for study. Subjects were recruited through newspaper advertisement, from the University of Michigan Turner Geriatric Clinic, and from the Human Subjects Core of the University of Michigan Geriatrics Center. All subjects were community dwelling and in good health apart from their hypertension.

Subjects were screened before participation with a medical history and physical examination, a complete blood count,
routine chemistries, and urinalysis. Individuals were excluded from the study if they had clinically significant concomitant medical illness, such as cardiac, renal (serum creatinine > 135 mg/dL), hepatic, or gastrointestinal disease, or required medications that might affect glucose metabolism, blood pressure, or renal function. Also excluded were individuals with a recent history of smoking or drug or alcohol abuse, or clinically relevant mental disorders. Absence of diabetes mellitus, according to World Health Organization criteria (29), was confirmed in all subjects by a 2-h 75-g oral glucose tolerance test. The presence of hypertension was defined in patients who were receiving antihypertensive treatment or had a seated systolic blood pressure > 140 mmHg and/or a seated diastolic blood pressure > 90 mmHg.

General study. After a screening visit to determine their eligibility for participation as described above, subjects signed an informed consent form approved by the University of Michigan Institutional Review Board. Hypertensive subjects who were being treated with antihypertensive medications were tapered off their medications and were studied after a 4-wk period during which no antihypertensive medications were taken.

Subjects were randomized in a double-blind design to begin either a 20 or a 200 mmol·1⁻¹·day⁻¹·sodium diet, which they consumed over a 7-day period. All meals during the 7-day sodium diet period were prepared by the General Clinical Research Center Metabolic Kitchen at the University of Michigan. The two diets were identical in composition except for sodium content and consisted of 50–55% of calories as carbohydrate, 30–35% as fat, 15–20% as protein, and 300–350 mg per day of cholesterol. After completion of the first metabolic tests, the subjects consumed their own diet for a 1-wk washout period and then were switched to the alternative sodium diet, which they consumed for a second 7-day period. Compliance with the diet was monitored by 24-h urine collections for sodium.

On the 6th day of each sodium diet, intra-arterial blood pressure measurements were made while the subject rested in the supine position after a 20-min resting period. Briefly, a 20-gauge 1.25″ Insyte catheter was placed into the brachial artery of the nondominant arm. The catheter was connected to a pressure transducer (1200A quartz transducer, Hewlett-Packard, Andover, MA). Mean arterial blood pressure (MABP) was determined from the electronically integrated area under the MABP curve from the Marquette telemetry system (Marquette Electronics Series 7700, Marquette Electronics, Milwaukee, WI). Blood pressure measurements were made over a 1-h period and averaged. Subjects were classified a priori, utilizing previously published criteria, as either sodium sensitive or sodium resistant on the basis of their MABP response to the change in dietary sodium intake. Those individuals who exhibited a change in MABP ≥5 mmHg were classified as sodium sensitive, and those individuals who exhibited a change in MABP < 5 mmHg were classified as sodium resistant (21, 24).

Frequently sampled intravenous glucose tolerance test. On the 7th day of each sodium diet, a frequently sampled intravenous glucose tolerance test (FSIVGTT) was performed, as previously described by Bergman (2). In all subjects the FSIVGTT included an infusion of either tolbutamide or insulin (Humulin R, Lilly Lilly, Indianapolis, IN) to enhance precision of the estimates of insulin action (30). Subjects were studied in the supine position. Briefly, an intravenous catheter was inserted into an antecubital vein in one arm for the injection of tolbutamide or insulin and glucose. Another catheter was inserted in a retrograde manner into a dorsal hand vein of the contralateral arm, which was placed in a thermostatically controlled (60°C) warming box to arterialize venous blood samples for the measurement of glucose and insulin (12). Catheters were kept patent by a slow infusion of 0.45% saline (< 50 ml/h). Beginning 20 min after the insertion of intravenous lines, three baseline blood samples for glucose and insulin were obtained, and blood pressure and heart rate were measured at 5-min intervals. Baseline values were calculated as the mean of these three measurements for each variable.

Fifty percent glucose (300 mg/kg) was given as an intravenous push over 30 s. Blood samples (3 ml) were collected at 2, 3, 4, 5, 6, 8, 10, 12, 14, 16, 19, 22, 23, 24, 25, 27, 30, 40, 50, 70, 80, 90, 100, 120, 140, 160, and 180 min after the glucose bolus. Tolbutamide (137 mg/m² body surface area) or insulin (0.02 U/kg) was given intravenously over 30 s, 20 min after the glucose injection, to further stimulate insulin secretion.

Measurements and calculations. Blood samples for plasma glucose and insulin were collected into chilled glass tubes containing heparin sodium, stored on ice, and separated immediately after each study. Plasma was stored at −70°C until assay. Plasma glucose was measured by the automated glucose oxidase method and plasma insulin by radioimmunoassay in the Core Laboratory of the Michigan Diabetes Research and Training Center. Samples from each of the subjects’ two studies were analyzed together in the same assay.

The indexes of insulin sensitivity (SI) and glucose effectiveness (SG) were calculated from a least squares fitting of the temporal pattern of glucose and insulin throughout the FSIVGTT by use of the MINMOD program (R. N. Bergman, 1989). SI is a measure of the effect of an increment in plasma insulin to enhance the fractional disappearance of glucose. SG is a measure of the fractional glucose turnover rate at the basal insulin level. The acute insulin response to intravenous glucose (AIRG) was calculated as the mean rise in plasma insulin above baseline at 3, 4, and 5 min after intravenous glucose administration. KG, a measure of glucose tolerance, is the rate of plasma glucose disappearance calculated as the least squares slope of the natural logarithm of absolute glucose concentration between 5 and 20 min after the glucose bolus (a normal non-diabetic value for KG is > 1%/min). The reproducibility of the minimal model approach for determining insulin sensitivity has been reported to be ~ 16% (1, 10).

Body composition was determined using bioelectrical impedance (RJL Systems, Mt. Clemens, MI) on two separate occasions. Baseline values were calculated as the mean of these measurements. Body mass index (BMI, in kg/m²) was determined by the subject's weight (kg) divided by the square of his or her height (m).

Statistical analysis. Data were analyzed using Statview (Abacus Concepts, Berkeley, CA). An α-level of 0.05 was accepted for statistical significance. Characteristics of the sodium-sensitive and sodium-resistant subject groups were compared using analysis of variance (ANOVA). A two-way ANOVA with group (sodium sensitive and sodium resistant) as one variable and diet (low sodium and high sodium) as the other was utilized to examine within- and between-group differences. Comparisons of plasma glucose and insulin levels during the FSIVGTT between the sodium-sensitive and sodium-resistant subject groups on each of the sodium diets were made by use of an ANOVA with repeated measures. Simple multiple regressions and Pearson correlation coefficients were calculated between changes in MABP and changes in fasting plasma insulin levels and insulin sensitivity. To determine whether the relationship between MABP and SI was affected by age, gender, body weight, percent fat, or waist-to-hip ratio, a regression model that included a covari-
ate for each of these variables was also analyzed. All data are reported as means ± SE.

RESULTS

Subjects. Subject characteristics are presented in Table 1. Twenty-one older (63.4 ± 1.7 yr) and moderately obese (BMI: 28.2 ± 0.9 kg/m²) subjects with essential hypertension were studied. When the 21 subjects were divided into sodium-sensitive and sodium-resistant groups on the basis of their response to the dietary sodium restriction regimen, 14 individuals were categorized as sodium sensitive and 7 individuals were categorized as sodium resistant. There were no statistically significant differences in age, weight, BMI, or percent body fat between the sodium-sensitive and sodium-resistant groups. The waist-to-hip ratio tended to be higher in the sodium-resistant group, although this difference was not statistically significant. There was no significant effect of sodium status (P = 0.906) or dietary restriction (P = 0.317) on body weight (Table 2). Although there was no significant effect of sodium status on MABP, there was a significant effect of dietary restriction on MABP (P = 0.024). Additionally, there was a significant (P = 0.017) interaction effect of sodium status and dietary sodium on MABP, indicating that the sodium-sensitive individuals were able to decrease their MABP in response to the reduction of dietary sodium (116 ± 2 vs. 102 ± 2 mmHg), whereas the sodium-resistant individuals did not (113 ± 3 vs. 114 ± 4 mmHg) (Table 2).

The sodium-sensitive group had significantly lower fasting plasma glucose levels than the sodium-resistant group (Table 2). However, there was no significant diet effect on fasting plasma glucose. The sodium-sensitive group had significantly lower fasting plasma insulin levels than the sodium-resistant group (Table 2 and Fig. 1), and there was no effect of diet on fasting plasma insulin levels (Fig. 1). The change in MABP due to dietary sodium restriction tended to correlate with the fasting plasma insulin level on both the low- (r = 0.45, P = 0.04) and high- (r = 0.41, P = 0.06) sodium diets.

The S_g, as determined from modeling of the FSI V GTT results by MINMOD, was significantly lower in the

<table>
<thead>
<tr>
<th>Sodium Sensitive (n = 14)</th>
<th>Sodium Resistant (n = 7)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low sodium</td>
<td>High sodium</td>
<td></td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>76.8 ± 3.4</td>
<td>77.7 ± 3.3</td>
</tr>
<tr>
<td>Supine intra-arterial blood pressure, mmHg</td>
<td></td>
<td></td>
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<tr>
<td>Systolic</td>
<td>145 ± 3</td>
<td>165 ± 3</td>
</tr>
<tr>
<td>Diastolic</td>
<td>74 ± 2</td>
<td>83 ± 2</td>
</tr>
<tr>
<td>Mean arterial</td>
<td>102 ± 2</td>
<td>116 ± 2</td>
</tr>
<tr>
<td>Metabolic parameters of glucose kinetics</td>
<td></td>
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<tr>
<td>Fasting glucose, mmol/l</td>
<td>5.26 ± 0.08</td>
<td>5.16 ± 0.07</td>
</tr>
<tr>
<td>Fasting insulin, µU/ml</td>
<td>13.5 ± 2.4</td>
<td>12.3 ± 2.0</td>
</tr>
<tr>
<td>Insulin sensitivity index, µU × 10^{-4}·min^{-1}·ml^{-1}</td>
<td>3.26 ± 0.60</td>
<td>3.45 ± 0.51</td>
</tr>
<tr>
<td>Glucose effectiveness, min^{-1}</td>
<td>0.018 ± 0.002</td>
<td>0.016 ± 0.001</td>
</tr>
<tr>
<td>Acute insulin response, µU/ml</td>
<td>86.6 ± 12.8</td>
<td>86.6 ± 11.5</td>
</tr>
<tr>
<td>Intravenous glucose tolerance, %/min</td>
<td>2.01 ± 0.15</td>
<td>2.14 ± 0.11</td>
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Values are means ± SE; n, no. of hypertensive subjects.
Sodium-resistant than in the sodium-sensitive group (Table 2 and Fig. 2). No significant diet effect ($P < 0.807$) or order of diet effect ($P < 0.35$) on $S_I$ was identified. In addition, no order effect (sodium diet) was observed on $S_I$. When the individual plasma glucose and insulin values during the FSIVGTT were examined by ANOVA for repeated measures, a significant ($P < 0.05$) group and experimental treatment effect was observed for both the plasma glucose and insulin values on the low- and high-sodium diets (Fig. 3). In addition, a significant ($P < 0.05$) group × experimental treatment interaction was noted for the plasma glucose and insulin values on both the low- and high-sodium diets. The sodium-resistant individuals had higher glucose and insulin profiles than the sodium-sensitive individuals. There were significant correlations between $S_I$ on both the low- ($r = 0.45, P = 0.04$) and high- ($r = 0.56, P = 0.008$) sodium diets and the change in MABP (Fig. 4). In addition to the univariate linear regression analysis, the association between low- and high-sodium diet $S_I$ values was analyzed after covariance for age, gender, body weight, percent fat, and waist-to-hip ratio. These regression models indicated that a positive correlation between $S_I$ on both the low- and high-sodium diets and MABP remained significant when these variables were included as covariates.

The $K_G$ was significantly lower in the sodium-resistant than in the sodium-sensitive group (Table 2). Dietary sodium restriction did not have an effect on $K_G$ in either group. There was no difference in $S_G$ or $AIR_G$ between the two groups (Table 2), nor was there an effect of diet.

The mean 24-h urinary sodium excretion was significantly lower during the low-sodium diet in both groups, which was appropriate for the reduction in dietary...
There was a significant decrease in both plasma chloride and plasma urea levels with the reduction in dietary sodium. Plasma levels of sodium were significantly lower in the sodium-sensitive individuals (Table 3). There was no effect of sodium status or diet sodium on either plasma or urinary creatinine levels (Table 3). In addition, there was no group or diet effect on creatinine clearance calculated from the 24-h urine collections (Table 3).

DISCUSSION

The primary findings of this study are that 1) sodium-resistant hypertensive individuals exhibit a greater degree of insulin resistance than those who are sodium sensitive and 2) dietary sodium restriction in older, moderately obese hypertensives does not enhance insulin sensitivity regardless of sodium-sensitivity status.

To the best of our knowledge, this is the first study to report that sodium-resistant hypertensives are more insulin resistant than their sodium-sensitive counterparts. Lind et al. (16) previously reported a significant relationship between the difference in standing blood pressure due to changes in dietary sodium intake and insulin sensitivity measured during a high-sodium diet. The results of the present study and those of Lind et al. are in contrast to those reported by Rocchini et al. (19) and Sharma et al. (23), who reported the opposite relationship between insulin sensitivity and sodium sensitivity, namely that sodium-sensitive individuals were insulin resistant compared with individuals who were categorized as sodium resistant. A reason for the difference between results from the present study and that of Lind et al. and those of Sharma et al. and Rocchini et al. is unknown. However, it is possible that differences in subject population and classification of sodium sensitivity may explain the difference in results. In the present study, we examined the effect of dietary sodium restriction on insulin sensitivity in an older hypertensive population, whereas Rocchini et al. examined this question in young nonobese hypertensive and normotensive adults and Sharma et al. studied this same question in a young lean normotensive population. It has been demonstrated that older individuals are insulin resistant compared with younger individuals (25) and that normotensive individuals are more sensitive to insulin than a comparable group of hypertensive individuals (7). Therefore, one would expect the population in the studies of Rocchini et al. and

![Graph](image)

**Table 3. Plasma and urinary values in sodium-sensitive and sodium-resistant hypertensives on low- and high-sodium diets**

<table>
<thead>
<tr>
<th></th>
<th>Sodium Sensitive (n = 14)</th>
<th>Sodium Resistant (n = 7)</th>
<th>P Value</th>
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<tbody>
<tr>
<td></td>
<td>Low sodium</td>
<td>High sodium</td>
<td>Low sodium</td>
</tr>
<tr>
<td>Plasma variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium, mmol/l</td>
<td>4.3 ± 0.1</td>
<td>4.1 ± 0.1</td>
<td>4.0 ± 0.1</td>
</tr>
<tr>
<td>Chloride, mmol/l</td>
<td>102.4 ± 0.4</td>
<td>104.6 ± 0.4</td>
<td>102.5 ± 0.6</td>
</tr>
<tr>
<td>Sodium, mmol/l</td>
<td>137.0 ± 0.5</td>
<td>139.0 ± 0.4</td>
<td>138.0 ± 0.6</td>
</tr>
<tr>
<td>Urea, mmol/l</td>
<td>5.3 ± 0.4</td>
<td>4.6 ± 0.2</td>
<td>4.7 ± 0.3</td>
</tr>
<tr>
<td>Creatinine, µmol/l</td>
<td>89.1 ± 6.5</td>
<td>78.1 ± 5.1</td>
<td>83.8 ± 4.5</td>
</tr>
<tr>
<td>Urine variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume, ml/day</td>
<td>2,018 ± 194</td>
<td>2,184 ± 153</td>
<td>1,561 ± 197</td>
</tr>
<tr>
<td>Sodium, mmol/day</td>
<td>27.5 ± 3.5</td>
<td>202 ± 9</td>
<td>28.7 ± 5.9</td>
</tr>
<tr>
<td>Creatinine, mmol/day</td>
<td>11.5 ± 0.7</td>
<td>11.5 ± 0.6</td>
<td>11.5 ± 1.5</td>
</tr>
<tr>
<td>Creatinine clearance, ml·1.75 m⁻¹·s⁻¹</td>
<td>1.49 ± 0.09</td>
<td>1.58 ± 0.07</td>
<td>1.44 ± 0.14</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of hypertensive subjects.
Sharma et al. to be more sensitive to the effects of insulin than the older population we examined in the present study. Another possible explanation may be in the classification of sodium-sensitivity status. Rocchini et al. assessed sodium sensitivity using the Weinberger protocol, which involves the intravenous administration of 2 liters of saline followed by sodium, and volume depletion induced by a low-sodium diet and furosemide (27). A sodium-sensitive individual was defined as one with a decrease in mean blood pressure, with volume depletion ≥ 10 mmHg. In the present study, we assessed sodium sensitivity by the change in supine intra-arterial blood pressure in response to a change in dietary sodium. Although Sharma et al. used a similar dietary protocol to assess sodium sensitivity, this study used a 3-mmHg change in blood pressure measured using an automatic oscillometric blood pressure device to classify subjects as either sodium sensitive or sodium resistant. However, if the criteria of Sharma et al. for determining sodium sensitivity are applied to our subject population, only two of our subjects would switch sodium-sensitivity status, and the sodium-sensitive individuals would still have a significantly greater $S_I$ value than the sodium-resistant individuals.

The mechanism for this difference in insulin sensitivity between sodium-resistant and sodium-sensitive individuals is unclear. DeFronzo et al. (5) demonstrated that insulin has an effect to enhance renal sodium reabsorption. On the basis of this information, it might have been expected that subjects with higher insulin levels would retain more sodium on a high-sodium diet and increase their blood pressure. However, we observed that the more insulin-resistant subjects who had higher fasting plasma insulin levels exhibited the least change in blood pressure on the high-sodium diet. Previously, we have demonstrated that sodium-sensitive individuals have an increase in glomerular filtration rate in response to an increase in dietary sodium, whereas sodium-resistant individuals have no change in renal hemodynamics in response to the change in dietary sodium (28). Rocchini (18) postulated “selective” insulin resistance to explain the finding that sodium-sensitive individuals were resistant to insulin-mediated glucose uptake, yet appeared to retain the normal natriuretic effect of insulin. Perhaps given the age-related decrements in renal function (20), insulin resistance among the older hypertensive population might extend to include resistance to the effects of insulin on renal hemodynamics and sodium reabsorption. Bigazzi et al. (3) reported a decrease in renal plasma flow and an increase in filtration fraction in sensitive individuals who consumed a high-sodium diet. In the present study we observed no significant differences in creatinine clearance due to sensitivity to sodium or to the change in dietary sodium. Creatinine clearance is a crude measure of renal hemodynamics, so further studies are needed to examine the role of renal hemodynamics in explaining the differences in sensitivity to sodium and insulin. We also examined the effect of dietary sodium restriction on body weight and observed that neither sodium-sensitive nor sodium-resistant individuals had a significant change in body weight with the change in dietary sodium. Another potential explanation for the sodium-resistant group being more insulin resistant is that the sodium-resistant individuals in this study tended to have a higher waist-to-hip ratio. An increase in central adiposity has been linked to the decline in insulin sensitivity that is observed with aging (4). Therefore, the tendency for increased central adiposity in the sodium-resistant individuals might contribute to their decreased sensitivity to insulin. In the present study we did not observe any enhancement in insulin sensitivity during dietary sodium restriction in these older hypertensives, regardless of sodium sensitivity status. These results confirm our previous findings that dietary sodium restriction does not change insulin sensitivity in an older hypertensive population (6). In contrast to the lack of an effect of dietary sodium intake on insulin sensitivity in our study, Donovan et al. (8) reported a significant increase in insulin sensitivity during dietary sodium restriction in young healthy normotensive individuals. The difference between results from the present study and others (6, 11, 16, 23) and those of Donovan et al. is not clear. Potential explanations include differences in subject population, in the methods used to measure insulin sensitivity, or in the duration or sodium intake of the sodium diet periods. In the present study, the subjects consumed each diet for a 7-day period, whereas in the study by Donovan et al. the sodium diet duration was for 5 days. Recently, Fliser et al. (11) examined the effect of the duration of high- (200 mmol/day) and low- (20 mmol/day) sodium diets by comparing a 3-day vs. a 7-day diet duration with respect to insulin-mediated glucose disposal in young healthy normotensive subjects. The authors observed that there was a significant decrease in insulin-mediated glucose disposal on the low- compared with the high-sodium diet after 3 days. However, in the group that consumed the same two sodium diets for a 7-day period each, there was no difference in insulin-mediated glucose disposal rates between the two sodium diets. The results of Fliser et al. suggest that the improvement in tissue sensitivity to insulin during dietary sodium restriction may be an acute event and that studies examining the chronic effect of dietary sodium on glucose metabolism need to be carried out over a longer time.

Although previous studies have reported a change in fasting plasma insulin and glucose levels with a modulation in dietary sodium (9, 14, 17, 22, 23) similar to that of our previous study (6) and the results of Donovan et al. (8), we did not observe any significant alteration in either fasting plasma insulin or glucose levels with the change in dietary sodium. Of interest is the significantly higher fasting plasma insulin levels in the sodium-resistant individuals. These higher fasting plasma insulin levels in the sodium-resistant individuals are likely explained by their greater degree of insulin resistance. Lind et al. (16) reported that those individuals with the lowest standing blood pressure also displayed the highest fasting plasma insulin levels. However, the results of the present study and those
of Lind et al. are in contrast to those of Sharma et al. (23), who reported no difference in fasting plasma insulin levels between sodium-resistant and sodium-sensitive young normotensives.

In conclusion, our results indicate that sodium-resistant hypertensive individuals have a greater degree of insulin resistance than those with sodium-sensitive hypertension and that there is overall a positive correlation between blood pressure response to dietary sodium loading and sensitivity to insulin. Second, these results support previous studies that have reported that dietary sodium restriction does not enhance insulin sensitivity. Thus, it appears that in addition to their inability to lower their blood pressure in response to a reduction in dietary sodium, sodium-resistant individuals exhibit a greater degree of insulin resistance than their sodium-sensitive counterparts.

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