Twenty-four-Hour Blood Pressure Profiles in Normotensive Sons of Hypertensive Parents

Gary L. Schwartz, Stephen T. Turner, and Charles F. Sing

We investigated whether blood pressures are higher in normotensive offspring of hypertensive parents than in normotensive offspring of normotensive parents outside the physician's office and, if so, whether these higher blood pressures are dependent on the level of dietary sodium intake. We compared 24-hour ambulatory blood pressure profiles between 11 normotensive sons of two hypertensive parents and 11 normotensive sons of two normotensive parents; profiles were recorded after 1 week of a low sodium diet (10 meq/day) and after 1 week of a high sodium diet (200 meq/day). The sons of hypertensive parents were on average 6 years older than the sons of normotensive parents (47 ± 5 [SD] versus 41 ± 4 years, p < 0.05). The shift from low to high sodium diet did not significantly change the magnitude of differences in office or ambulatory blood pressures between the groups (i.e., no group-by-diet interaction); thus, we assessed group effects by contrasting blood pressure means for each group pooled across diets. Age-adjusted office blood pressure was higher in sons of hypertensive parents than in sons of normotensive parents (116 ± 7/80 ± 6 versus 111 ± 7/75 ± 6 mm Hg; p = 0.020 for systolic and p = 0.003 for diastolic blood pressure). The mean for age-adjusted systolic blood pressure was significantly higher in sons of hypertensive parents than in sons of normotensive parents while sons were awake (9 mm Hg higher, p = 0.011) but not while asleep (2 mm Hg higher, p = 0.494), whereas the mean for age-adjusted diastolic blood pressure was significantly higher in sons of hypertensive parents than in sons of normotensive parents both while sons were awake (10 mm Hg higher, p = 0.010) and while asleep (7 mm Hg higher, p = 0.045). This study demonstrates that higher office blood pressures in normotensive offspring of hypertensive parents than in normotensive offspring of normotensive parents reflect persistent differences in blood pressure that are independent of the low (10 meq/day) and high (200 meq/day) dietary sodium intakes imposed for 1-week periods. (Hypertension 1992;20:834–840)

Key Words • blood pressure monitoring, ambulatory • hypertension, genetic • heart rate
were measured with a random zero sphygmomanometer. Office blood pressures and screening laboratory tests, including a chemistry profile, hematologic profile, urinalysis, chest x-ray, and electrocardiogram. Office blood pressures were measured with a random zero sphygmomanometer.

Values are mean±SD for variables measured within 1 month before study participation. bpm, Beats per minute; HDL, high density lipoprotein.

Experimental Protocol

The experimental protocol lasted 2 weeks. During the first week, subjects ate a low sodium diet containing 10 meq sodium per day; during the second week, they ate a high sodium diet containing 200 meq sodium per day. Both diets contained the same amounts of protein (79 g), potassium (100 meq), calcium (900 mg), phosphorus (1,200 mg), and magnesium (345 mg). Supplementation of the low sodium diet with calcium carbonate (Tums, Norcliff Thayer, Tarrytown, N.Y.) was required to match its calcium content to that of the high sodium diet. The amounts of carbohydrate and fat were adjusted to maintain each individual's usual caloric intake. All meals were prepared and eaten in the Clinical Research Center. Adherence to the diet was confirmed by measuring the amount of sodium, potassium, and creatinine excreted in the urine each day. On day 6 of the low sodium diet, 24-hour urinary excretion of sodium was 13±6 meq/day in the SONT and 13±6 meq/day in the SOHT group (contrast of means between groups, p=0.93); 24-hour urinary excretion of potassium was 102±16 meq/day in the SONT and 94±16 meq/day in the SOHT group (contrast of means between groups, p=0.22). On day 6 of the high sodium diet, 24-hour urinary excretion of sodium was 197±25 meq/day in the SONT and 200±27 meq/day in the SOHT group (contrast of means between groups, p=0.82); 24-hour urinary excretion of potassium was 94±21 meq/day in the SONT and 95±15 meq/day in the SOHT group (contrast of means between groups, p=0.99).9

On the sixth day of each diet, i.e., on days 6 and 13 of the experimental protocol, subjects underwent 24-hour ambulatory monitoring of blood pressure and heart
Laboratory Methods

Screening laboratory tests that preceded the experimental protocol were carried out in the clinical laboratories of the Mayo Clinic. Sodium and potassium concentrations in plasma and urine samples collected during the experimental protocol were measured by flame photometer (model 1943, Instrumentation Laboratories, Lexington, Mass.).

The raw blood pressure and heart rate readings from the ambulatory recordings were processed by computer software that applied previously established criteria to identify readings that might indicate machine malfunction. The mean percentage of readings excluded from analysis was 9±6% per ambulatory recording.

Statistical Analyses

The variables measured at the screening visit before the study protocol were summarized as group means±SD (Table 1). Student's t test was used to assess the statistical significance of differences in means between the groups.

Because the SOHT were on average 6 years older than the SONT group (Table 1), we assessed the differences in office blood pressure on days 6 and 13 of the study protocol after adjustment for age by linear regression. An overall adjustment for age that ignored strata was justified because an analysis of covariance demonstrated no statistically significant heterogeneity of the regression of office systolic or diastolic blood pressure on age among the four offspring and diet strata. With the adjusted data, a repeated measures analysis of variance was used to assess the statistical significance of the difference between group means, the difference between means of the low and high sodium diets, and the interaction between effects of group classification and dietary sodium intake (Table 2).

After assessing differences between the groups in office blood pressure, we next used the ambulatory monitoring data to assess whether blood pressure differences persisted outside the office and whether the differences in ambulatory blood pressures were influenced by dietary sodium intake. For each hour of the ambulatory recording on each diet, we calculated group means±SD for systolic blood pressure, diastolic blood pressure, and heart rate. For all hours in which means were available for all subjects, we carried out a profile analysis to assess whether the profiles on each diet were parallel in the two groups. Because the profiles on each diet were parallel during the period 6 AM to 10 PM and during the period 10 PM to 6 AM, we summarized each individual's ambulatory recording by calculating average levels of systolic blood pressure, diastolic blood pressure, and heart rate for the hours when the subject was awake and when he was asleep. No subject reclined or slept between 6 AM and 10 PM, and the average number of hours subjects reported sleeping between 10 PM and 6 AM was 6.9±0.6 (SD). The awake and asleep means for each of the three measures were then adjusted for age by linear regression. A global adjustment of each of these six variables was justified because in no case did an analysis of covariance indicate statistically significant heterogeneity of the regression of the waking or sleeping means on age among the four offspring and diet strata. After adjusting each variable for age, we carried out a repeated measures analysis of variance with group stratification to assess the statistical significance of differences between group means, the difference between means of the low and high sodium diets, and the interaction between effects of group classification and dietary sodium intake (Table 3).

Results

Description of the Sample

Compared with the SONT, the SOHT group was on average 6 years older (p=0.015) and, at the screening visit before the study protocol, had higher mean unadjusted systolic blood pressure (p=0.202), diastolic blood pressure (p=0.093), fasting levels of serum glucose
Ambulatory Blood Pressure and Heart Rate

Table 3. Age-Adjusted Awake and Asleep Means for Ambulatory Blood Pressure and Heart Rate With Subjects on Low and High Sodium Diets

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Low sodium diet</th>
<th>High sodium diet</th>
<th>Diets pooled</th>
<th>Group × diet</th>
<th>Group</th>
<th>Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure awake (mm Hg)</td>
<td>SOHT</td>
<td>131±7</td>
<td>131±8</td>
<td>131±8</td>
<td>0.313</td>
<td>0.011</td>
<td>0.159</td>
</tr>
<tr>
<td></td>
<td>SONT</td>
<td>124±9</td>
<td>121±5</td>
<td>122±8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pooled</td>
<td>128±9</td>
<td>126±8</td>
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<td></td>
</tr>
<tr>
<td>Systolic blood pressure asleep (mm Hg)</td>
<td>SOHT</td>
<td>112±6</td>
<td>111±9</td>
<td>111±8</td>
<td>0.460</td>
<td>0.494</td>
<td>0.239</td>
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<tr>
<td></td>
<td>SONT</td>
<td>111±11</td>
<td>107±7</td>
<td>109±9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pooled</td>
<td>111±2</td>
<td>109±8</td>
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<tr>
<td>Diastolic blood pressure awake (mm Hg)</td>
<td>SOHT</td>
<td>88±7</td>
<td>82±9</td>
<td>85±8</td>
<td>0.599</td>
<td>0.010</td>
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<tr>
<td></td>
<td>SONT</td>
<td>79±9</td>
<td>72±8</td>
<td>75±9</td>
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<td></td>
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<tr>
<td></td>
<td>Pooled</td>
<td>83±9</td>
<td>77±10</td>
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<tr>
<td>Diastolic blood pressure asleep (mm Hg)</td>
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<td>73±6</td>
<td>72±9</td>
<td>73±8</td>
<td>0.778</td>
<td>0.045</td>
<td>0.186</td>
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<td>SONT</td>
<td>68±8</td>
<td>65±7</td>
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<td>Pooled</td>
<td>71±8</td>
<td>68±9</td>
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<tr>
<td>Heart rate awake (bpm)</td>
<td>SOHT</td>
<td>82±8</td>
<td>75±7</td>
<td>79±8</td>
<td>0.875</td>
<td>0.107</td>
<td>&lt;0.001</td>
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<td>SONT</td>
<td>77±11</td>
<td>70±6</td>
<td>73±9</td>
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<tr>
<td></td>
<td>Pooled</td>
<td>80±9</td>
<td>73±7</td>
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<tr>
<td>Heart rate asleep (bpm)</td>
<td>SOHT</td>
<td>70±7</td>
<td>62±6</td>
<td>66±7</td>
<td>0.185</td>
<td>0.005</td>
<td>&lt;0.001</td>
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<td>57±4</td>
<td>59±5</td>
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<tr>
<td></td>
<td>Pooled</td>
<td>66±7</td>
<td>60±5</td>
<td></td>
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</tbody>
</table>

Values are mean±SD for 11 sons of normotensive parents (SONT) and 11 sons of hypertensive parents (SOHT). Values of p are for significance of differences in means between groups, differences in means between low and high sodium diets, and interactions between effects of group classification and dietary sodium intake. bpm, Beats per minute.

(\(p=0.005\)), plasma total cholesterol (\(p=0.026\)), and triglycerides (\(p=0.054\)) (Table 1). Both groups had means for systolic and diastolic blood pressures that were within the normal range (<140/90 mm Hg).

Office Blood Pressure

During the study protocol, differences between the groups in the means for age-adjusted office systolic and diastolic blood pressures did not change significantly with the shift from a low to a high sodium diet (i.e., no group-by-diet interaction) (Table 2). Because these results suggest that group differences are independent of dietary sodium intake, we assessed the group and diet effects by contrasting pooled group and pooled diet means. The means for age-adjusted systolic and diastolic blood pressures pooled across diets were significantly higher in the SOHT than in the SONT group (5 mm Hg higher for both systolic and diastolic blood pressure; \(p=0.020\) for systolic blood pressure; \(p=0.003\) for diastolic blood pressure) (Table 2). With the transition from low to high sodium diet, the means for both systolic and diastolic blood pressures pooled across groups decreased 3 mm Hg; however, these decreases were not statistically significant at the 0.05 level of probability.

Table 3. Age-Adjusted Awake and Asleep Means for Ambulatory Blood Pressure and Heart Rate With Subjects on Low and High Sodium Diets

Ambulatory Blood Pressure and Heart Rate

Hourly means. For both diets, hourly means for systolic blood pressure, diastolic blood pressure, and heart rate unadjusted for differences in age (Figure 1) were higher in the SOHT than in the SONT group throughout most of the 24-hour period. Higher systolic blood pressures persisted throughout all daytime hours but not all nighttime hours. Higher diastolic blood pressures persisted throughout the entire 24-hour period. Higher heart rates persisted throughout the 24-hour period with the exception of a few daytime hours. Despite the occasional convergence of hourly means (Figure 1), separate profile analyses for each trait on each diet failed to reject the null hypothesis of parallelism during the daytime and nighttime periods (\(p>0.05\) for each analysis). Because the profiles were parallel during these periods, we summarized each subject's ambulatory recording by calculating the average levels of systolic blood pressure, diastolic blood pressure, and heart rate for the hours when the subject was awake and when he was asleep as described in "Methods." This allowed a global adjustment of the waking and sleeping data for age before further analyses were performed.

Awake and asleep means. There was no statistically significant evidence that the differences between the SOHT and SONT groups in mean age-adjusted systolic blood pressure, diastolic blood pressure, or heart rate, either awake or asleep, depended on dietary sodium intake. That is, for none of these traits was the test of group-by-diet interaction statistically significant at a level of probability <0.185 (Table 3). Thus, we assessed the group and diet effects on these traits by contrasting the pooled group and diet means.

The mean for age-adjusted systolic blood pressure pooled across diets was significantly higher in the SOHT than in the SONT group while awake (9 mm Hg higher, \(p=0.011\)) but not while asleep (2 mm Hg higher, \(p=0.494\)) (Table 3). With the shift from low to high sodium diet, awake and asleep means for systolic blood pressure pooled across groups decreased slightly (2 mm Hg) but not significantly (Table 3, Figure 2).

The mean for age-adjusted diastolic blood pressure pooled across diets was significantly higher in the SOHT
than in the SONT group, both while awake (10 mm Hg higher, \( p=0.010 \)) and while asleep (7 mm Hg higher, \( p=0.045 \)) (Table 3). With the shift from low to high sodium diet, awake and asleep means for diastolic blood pressure pooled across groups decreased (Table 3, Figure 2), but only the decrease in the awake mean for diastolic blood pressure was statistically significant (6 mm Hg decrease, \( p<0.001 \)).

The mean for age-adjusted heart rate pooled across diets was significantly higher in the SOHT than in the SONT group while asleep (7 beats per minute higher, \( p=0.005 \)) but not while awake (6 beats per minute higher, \( p=0.107 \)) (Table 3). With the shift from low to high sodium diet, awake and asleep means for heart rate pooled across groups decreased significantly (7 beats per minute decrease for awake heart rate; 6 beats per minute decrease for asleep heart rate; 6 beats per minute decrease for awake heart rate; 6 beats per minute decrease for asleep heart rate).
SYSTOLIC BLOOD PRESSURE

AWAKE

ASLEEP

DIASTOLIC BLOOD PRESSURE

AWAKE

ASLEEP

HEART RATE

AWAKE

ASLEEP

FIGURE 2. Graphs show effect of dietary sodium intake on age-adjusted awake and asleep means for systolic blood pressure (top panel), diastolic blood pressure (middle panel), and heart rate (bottom panel). ○, Mean +1 SD for sons of hypertensive parents; ●, mean -1 SD for sons of normotensive parents. *p < 0.05 low sodium vs. high sodium diet.

Discussion

The results of the present study demonstrate that higher blood pressures in normotensive individuals with a familial predisposition for the development of essential hypertension persist outside the physician’s office, and that these higher blood pressures do not depend on the level of dietary sodium intake. The first conclusion is supported by the finding that the hourly means for systolic and diastolic blood pressures were higher in the SOHT than in the SONT group throughout most of the 24-hour period (Figure 1) and that the awake and asleep means for systolic and diastolic blood pressures were higher in the SOHT than in the SONT group (Table 3). The second conclusion is supported by the finding that the magnitude and direction of differences in blood pressure between the SOHT and the SONT group were not significantly different with subjects on low and on high sodium diets (Table 3, Figure 2).

Persistence of differences in blood pressure level between SOHT and SONT, especially while asleep, suggests that higher office blood pressures in people predisposed to essential hypertension are not solely a reflection of increased blood pressure responsivity to environmental stimuli. Although a difference between the groups in blood pressure responsivity might account for persistent blood pressure differences while awake, it is an unlikely explanation for blood pressure differences while asleep when environmental stimulation was minimal and was comparable in the two groups. A study by Ravogli and colleagues also demonstrated that higher blood pressure levels persist outside the physician’s office in the offspring of hypertensive parents. In contrast to the findings of others, these investigators found the blood pressure response to a variety of laboratory stressors (mental arithmetic, mirror image drawing, cold pressor, hand grip) was not increased in the offspring of hypertensive parents, leading them to conclude that higher blood pressure levels in this group could not be explained by hyperresponsivity. Regardless of the issue of increased blood pressure responsivity to the office environment or to laboratory stressors, our study and that of others using ambulatory blood pressure monitoring over a 24-hour period indicate that higher blood pressure levels are established in the offspring of hypertensive parents before the diagnosis of hypertension is made and that the differences in blood pressure between the groups persist outside the physician’s office. Thus, we believe that the higher office blood pressures observed in the SOHT group in this study are more a reflection of persistently higher levels than of transient increases in response to the office environment.

The finding that the magnitude of difference in blood pressure between the groups did not change significantly when subjects shifted from a low to a high sodium diet indicates that the average blood pressure response to changes in dietary sodium was similar in both groups. Unexpectedly, the response was a decrease in blood pressure, not an increase (Figure 2). Previous studies have demonstrated that the blood pressure response to acute dietary sodium loading is heterogenous, both in normotensive and in hypertensive subjects; but in most studies, the average response was an increase in blood pressure in both groups. We also observed a heterogenous response of blood pressure within each group to the change from a low to a high sodium diet. Why the average response in each group was a decrease, not an increase, in blood pressure is uncertain. A possible explanation is that the extremely low sodium diet in the first week of this study (10 meq/day) stimulated physiological mechanisms to defend against a potential fall in blood pressure due to volume depletion. In this setting,
the major effect of initiating a high sodium diet (200 meq/day) may have been to inhibit these pressor stimuli, resulting in a fall in blood pressure. This logic would imply that blood pressure increased from baseline in response to the low sodium diet used initially. Although we did not assess this possibility by also measuring ambulatory blood pressure at study entry before initiation of the low sodium diet, others have observed an increase in blood pressure in response to acute sodium restriction.16-17 With larger groups, longer periods on each sodium intake, or a different sequence of the diets, significant differences in the response of blood pressure may have been observed between these groups. Notwithstanding these caveats, our findings suggest that differences in the familial predisposition to hypertension do not predict differences in the magnitude or direction of blood pressure responses to acute dietary sodium loading.

Additional findings in this study were that the heart rate was faster in the SOHT than in the SONT group and that the difference in heart rate between the groups was not dependent on the level of dietary sodium intake. Studies reviewed by Julius and Esler18 have demonstrated that an increase in basal activity of the sympathetic nervous system, manifested in part by a faster resting heart rate, is a characteristic of individuals with borderline blood pressure elevations who are at increased risk for the development of hypertension. More recently, Reaven19 has drawn attention to the association between increased activity of the sympathetic nervous system and resistance to insulin-stimulated glucose uptake, a cellular abnormality hypothesized to contribute to the pathogenesis of hypertension. Other metabolic abnormalities that contribute to or are associated with insulin resistance include obesity and hypertriglyceridemia. Faster heart rates in the SOHT in our present study, particularly while asleep, and the finding that the SOHT group was heavier and had higher fasting levels of serum glucose and plasma triglycerides than the SONT group (Table 1) suggest that increased basal sympathetic tone and insulin resistance may also be characteristics of the familial predisposition to hypertension.

In conclusion, the present study demonstrates that higher office blood pressures in normotensive offspring of hypertensive parents than in normotensive offspring of normotensive parents reflect persistent, not transient, differences in blood pressure level between these groups. In the Dutch Hypertension Offspring Study, blood pressure differences between such groups were detectable at birth and became statistically significant as early as age 13 years.20 Because the biochemical, physiological, and structural alterations that are causative of higher blood pressures must also be present at an early age, studies comparing these groups have the potential to provide valuable insights into the pathogenesis of essential hypertension. However, because adaptations to elevated blood pressure may also occur at an early age, sorting out which alterations are causes rather than effects of elevated blood pressure remains a challenge.

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References

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