Sympathetic Activity and Cardiovascular Risk Factors in Young Men in the Low, Normal, and High Blood Pressure Ranges

Arnljot Flaa, Håvard H. Mundal, Ivar Eide, Sverre Kjeldsen, Morten Rostrup

Abstract—We hypothesized that resting blood pressure is related to sympathetic activity in young men who are unaware of their blood pressure status in high, normal, and low ranges and that there is a relationship between sympathetic activity and coronary risk factors. Forty-three healthy, young men from the 1st [group 1, 106/52±2/2 mm Hg (±SEM), n=15], 50th (group 2, 129/79±2/1 mm Hg, n=15), and 98th to 99th percentile (group 3, 166/97±3/1 mm Hg, n=13) at a blood pressure screening were studied with intraarterial blood pressure, heart rate, and arterial plasma catecholamine responses to a mental, cold pressor, and orthostatic stress test. At baseline, group 3 had significant higher blood pressure (137/74±3/2 mm Hg) than group 2 (126/66±3/2 mm Hg; P<0.01) and group 1 (116/62±2/1 mm Hg; P<0.001). Group 1 had lower systolic blood pressure than group 2 (P=0.007). Baseline epinephrine and norepinephrine showed a clear positive linear trend (P<0.05), with the lowest values being in group 1 and highest in group 3. High-density lipoprotein was negatively related to epinephrine (r=-0.387; P=0.010). Mental stress was the only test that showed significant differences in cardiovascular and sympathetic responses among the groups, where group 3 had a more pronounced response in systolic and diastolic blood pressure and heart rate compared with group 1 (P<0.001) and group 2 (P<0.01). Furthermore, we found significant positive linear trends for Δcatecholamines during mental stress across the groups (Δepinephrine P=0.001 and Δnorepinephrine P=0.026, ANOVA). We conclude that resting blood pressure reflects both variation in resting arterial catecholamines and variation in cardiovascular and sympathetic responses specifically to mental stress. (Hypertension. 2006;47:396-402.)

Key Words: blood pressure ★ catecholamines ★ epinephrine ★ stress ★ norepinephrine

W e have demonstrated previously that pure knowledge of being hypertensive may increase blood pressure (BP), heart rate (HR), plasma catecholamines, and cardiovascular and sympathetic responses to laboratory stressors, thereby being a confounding factor in hypertension research. Thus, pathophysiologic studies in hypertension should ideally be carried out in subjects unaware of their BP status. In a previous study,4 we examined plasma catecholamines in 3 groups of 19-year-old men with different screening BPs while keeping them unaware of their BP level. In our laboratory, the group with the highest screening BP had normal BP and plasma catecholamines after 30 minutes of supine rest. Thus, in this former study, we were not able to examine sympathetic activity in unaware subjects with high resting BP. We found, however, that subjects from the highest percentile of screening BP were characterized by cardiovascular hyperreactivity specifically to mental stress. Furthermore, important coronary risk factors seemed to be catecholamine dependent in this group.

Based on our previous observations, we hypothesized in the present study that resting BP was related to arterial plasma catecholamines, cardiovascular and sympathetic reactivity to laboratory stressors and coronary risk factors, and adaptation to and recovery from mental stress. The young men were kept unaware of their BP status, eliminating possible confounding effects of awareness of hypertension. BP, as well as plasma catecholamines, were measured and sampled intraarterially. We also aimed to additionally investigate associations between sympathetic activity and coronary risk factors, including indicators of insulin resistance and blood lipids.

Methods

Subjects

All 19-year-old men in Norway have to attend a medical examination for the military draft procedure. The draft procedure takes a whole day and includes a psychological test, a test of physical strength and endurance, and a medical examination. BP measurements on all 19-year-old men attending in Oslo (N=4137) during 1 year were undertaken standardized by a trained physician once after 5 minutes sitting by means of an automatic auscultatory device with a hidden printer (Boso-digital II S, Bosh & Sohn GmbH u Co), as described earlier. Mean BP (MBP) was thereafter calculated as diastolic BP (DBP)+pulse pressure/3. Neither physicians nor subjects could read

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the results of the BP recordings. Therefore, the subjects got their final military physical fitness score and medical evaluation independent of the BP recording.

We selected a total of 130 subjects from the screening. The selection process is illustrated in Figure 1. Twenty subjects belonged to the 1st percentile (group 1, 62 ± 2 mm Hg, mean ± SEM), 25 to the 50th percentile (group 2, 90 ± 4 mm Hg), and 80 to the 98th to 99th percentile of MBP (group 3, 123 ± 5 mm Hg). Six months after the draft procedure, they were all sent an identical letter asking them to take part in a study of cardiovascular risk factors. In order to secure and reassess differences in resting BP, the subjects were reexamined in our laboratory on a separate day before final inclusion by the same auscultatory device as that used at the screening. Subjects belonging to the 98th to 99th percentile of screening MBP were included if the MBP at reexamination exceeded the population MBP (95.6 ± 8.7 mm Hg). Subjects of the 50th percentile were included if their MBP was within mean screening BP (95 ± 1 SD). Subjects of the 1st percentile were included if their MBP was lower than mean screening BP (95 ± 2 SD). Because of a clear tendency to normalization at the second examination, we finally identified 15 subjects in group 1, 15 subjects in group 2, and 13 subjects in group 3. All were previously healthy without any history of diabetes, renal disease, elevated BP, or other cardiovascular disease, including a normal physical examination, ECG, routine blood tests, and urinalysis. None was on medical treatment or abused drugs or alcohol. There were no group differences in smoking habits. The subjects were asked for diseases among their parents, including hypertension, and no significant difference was found (data not given).

**Protocol**

The study was approved by the local ethics committee, and the procedures followed were in accordance with institutional guidelines. Informed consent was obtained from each subject. The protocol is described in detail elsewhere.4

A short Teflon catheter (Venflon, 19G, Viggo AB) was introduced under local anesthesia without epinephrine (Xylocain, AstraZeneca) into the left brachial artery for blood sampling and intraarterial pressure monitoring (as described previously).1 The catheter was connected to a transducer (EMT 35, Elema-Schönander) by a 60-cm manometer connecting tube (Portex Ltd). Pressure recordings and ECGs were obtained using a mingograph (Mingograph 34, Elema-Schönander). The instrument was calibrated and checked for linearity by a mercury sphygmomanometer. The pressure values presented were obtained using a computer for area measurements (Cardio 80, Kontron Medical).

The participants rested supine for 30 minutes in the presence of the examining physician only. At the end of this 30-minute period, they were informed about a cold pressor test (CPT). The right hand was then completely immersed in ice water (0°C) for 1 minute. Thereafter, the subjects rested for 30 minutes before the mental arithmetic challenge test (MST) was announced. The subjects were asked to subtract the number “13” repetitively for 5 minutes starting from “1079,” while a metronome making noise at a frequency of 2 Hz was used to distract the subjects. They were informed about any miscalculation. After MST, the subjects rested for 30 minutes before an orthostatic stress test (ORT) was announced, where they were asked to stand up for 2 minutes. Arterial blood for catecholamine assay was collected into polypropylene syringes after 30 minutes of supine rest, during announcement of the MST and CPT, 2 times during the CPT, 3 times during the MST, 1 time during the ORT, and during the recovery periods, with a total of 12 samples in each subject.

**Assays**

Blood for the platelet-free catecholamine assay was drawn in 10-mL glass tubes containing glutathione and EGTA, and platelet number and size were determined by a 147 C Compact Thrombocyte Analyzer (Analys Instrument AB). Platelet and plasma catecholamines were measured by a radioenzymatic technique according to Peuler and Johnson,5 as reported previously.1,6 All of the samples were analyzed by the same technician who did not have any knowledge of the BP status of the participants.
Statistics
The data were analyzed using the statistical package SPSS version 12.0 for Windows (SPSS Inc.). Parametric tests were used for normally distributed data and nonparametric when normality was not achieved by log-normal transformation. One-way ANOVA with trend analysis or Kruskall–Wallis test was used to compare baseline variables, Δ values (from baseline to mean stress), adaptation to stress (percentage change from the first to the last measurement during MST), and recovery (percentage change from baseline to posttest measurement). The 3 groups were selected based on their differences across the groups. Subsequent Student posttest measurement. The 3 groups were selected based on their differences were analyzed by effect of stress tests on BP and plasma catecholamines were additionally analyzed by repeated-measures ANOVA, and group differences were analyzed by effect of group interaction, with subse-
quent t tests.

Groups were assessed using Pearson’s correlation coefficients (r) or Spearman’s rank correlation coefficients (rs). Forward stepwise multiple regression analysis was used to test for dependence on other variables. Null hypotheses were rejected if 2-tailed P value was <0.05. Data are presented as mean±SEM unless indicated otherwise.

Results
Baseline
The baseline characteristics are presented in Table 1. The 3 groups differed in resting catecholamines, where epinephrine (P = 0.010) and norepinephrine (P = 0.043) showed a positive linear trend, with the highest levels in group 3 and the lowest in group 1. The platelet catecholamines did not show any significant differences between the groups. There was a more favorable cardiovascular profile in groups 1 and 2, with a negative linear trend for high-density lipoprotein (HDL; P = 0.034) and HDL:total cholesterol ratio (P = 0.011) and a positive linear trend for triglycerides (P = 0.002), fructosamine (P = 0.005), and waist:hip ratio (P = 0.026).

Stress Tests
Cardiovascular and Arterial Catecholamine Responses
All 3 of the stress tests had significant effects on BP, HR, and arterial catecholamines in all 3 of the groups (CPT: P = 0.05; MST: P < 0.02; ORT: P < 0.01, repeated measures ANOVA). When comparing the stress effects between the groups, MST was the only stress test that showed significant group differences, and linear trend analysis revealed highly significant differences in ΔMBP (P < 0.001), ΔHR (P = 0.003), Δepinephrine (P = 0.001), and Δnorepinephrine (P = 0.025), where group 3 had the most and group 1 the least pronounced response from baseline to mean stress (Figure 2).

Resting DBP and SBP correlated significantly with ΔDBP (r = 0.416; P = 0.006) and ΔSBP (r = 0.331; P = 0.032) during MST. In addition, ΔHR during CPT correlated negatively with resting HR (r = -0.361; P = 0.019).

In a multiple stepwise regression analysis of the BP measured at military screening using the mean pressures during rest and stress tests as independent variables, SBP during MST (R² = 0.459; P < 0.001), and DBP during ORT (R² = 0.418; P < 0.001) turned out to be the only explanatory variables for SBP and DBP, respectively, at screening.

MST Adaptation and Recovery
There were significant group differences in percentage changes from the first to the last measurement during MST for DBP (P = 0.011, Kruskal–Wallis), where group 3 increased most and group 1 increased least. Recovery showed significant group differences in norepinephrine, where group

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group 1 (n=15)</th>
<th>Group 2 (n=15)</th>
<th>Group 3 (n=13)</th>
<th>P Value for Linear Trend (ANOVA)</th>
<th>P Value Between Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>116.4±2.0</td>
<td>126.2±2.7</td>
<td>136.6±2.7</td>
<td>&lt;0.001</td>
<td>0.007 0.006</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>62.1±1.3</td>
<td>66.2±1.1</td>
<td>74.1±2.0</td>
<td>&lt;0.001</td>
<td>n.s. 0.003</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>56.2±2.1</td>
<td>60.2±2.5</td>
<td>63.2±2.9</td>
<td>n.s. (0.059)</td>
<td>n.s. n.s. (0.051)</td>
</tr>
<tr>
<td>E, pg/mL</td>
<td>30.8±5.6</td>
<td>43.0±8.6</td>
<td>62.4±10.2</td>
<td>0.010</td>
<td>n.s. n.s.</td>
</tr>
<tr>
<td>NE, pg/mL</td>
<td>98.9±11.5</td>
<td>100.2±13.4</td>
<td>136.1±12.1</td>
<td>0.043</td>
<td>n.s. n.s. (0.051)</td>
</tr>
<tr>
<td>Platelet E, pg/mL</td>
<td>100.4±20.3</td>
<td>87.8±5.8</td>
<td>106.2±13.3</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Platelet NE, pg/mL</td>
<td>953.5±184.2</td>
<td>918.4±97.3</td>
<td>989.7±149.5</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Tot.chol, mmol/L</td>
<td>3.90±0.22</td>
<td>4.14±0.27</td>
<td>4.13±0.24</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>HDL, mmol/L</td>
<td>1.26±0.06</td>
<td>1.07±0.08</td>
<td>1.05±0.06</td>
<td>0.034</td>
<td>n.s. (0.051) n.s.</td>
</tr>
<tr>
<td>HDL-chol ratio</td>
<td>0.34±0.02</td>
<td>0.27±0.02</td>
<td>0.26±0.02</td>
<td>0.011</td>
<td>0.020 n.s.</td>
</tr>
<tr>
<td>Trigl, mmol/L</td>
<td>0.69±0.08</td>
<td>0.85±0.08</td>
<td>1.12±0.11</td>
<td>0.002</td>
<td>n.s. n.s. (0.067)</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>4.50±0.12</td>
<td>4.47±0.10</td>
<td>4.48±0.18</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Insulin, pmol/L</td>
<td>74.3±9.2</td>
<td>81.1±7.7</td>
<td>79.3±11.3</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Glu-ins ratio</td>
<td>0.07±0.01</td>
<td>0.06±0.01</td>
<td>0.06±0.01</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Fruct, mmol/L</td>
<td>2.16±0.04</td>
<td>2.14±0.06</td>
<td>2.36±0.04</td>
<td>0.005</td>
<td>n.s. 0.002</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>21.9±0.7</td>
<td>24.2±1.0</td>
<td>22.7±0.8</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Waist:hip ratio</td>
<td>0.83±0.01</td>
<td>0.86±0.01</td>
<td>0.88±0.02</td>
<td>0.026</td>
<td>n.s. n.s.</td>
</tr>
</tbody>
</table>

Mean±SEM. E/NE indicates arterial plasma epinephrine/norepinephrine; Tot.chol, total serum cholesterol; HDL-chol ratio, HDL:total cholesterol ratio; Trigl, serum triglycerides; Glu-ins ratio, glucose:insulin ratio; Fruct, fructosamine; BMI, body mass index; n.s., not significant.
2 had the slowest recovery \((P=0.030, \text{ANOVA})\), and DBP, where group 3 had the slowest recovery \((P=0.042, \text{Kruskal–Wallis})\).

### Correlations Between Sympathetic Activity and Coronary Risk Factors

Table 2 summarizes the correlations between cardiovascular risk factors and catecholamines during rest and stress. Baseline epinephrine was related to resting SBP and correlated negatively with HDL. Norepinephrine at baseline did not show any significant correlations. Epinephrine and norepinephrine during mental stress were positively related to baseline serum fructosamine. During CPT, epinephrine correlated with serum triglycerides. There were no significant correlations during ORT, and HR, glucose, or body mass index did not correlate with plasma catecholamines.

### Discussion

We compared young, healthy men in the low, normal, and high BP ranges who were all unaware of their BP status. The differences in resting BP were reflected by a similar difference in arterial epinephrine and norepinephrine at rest, but no such difference in platelet catecholamines. The 3 stress tests evoked significant cardiovascular and catecholamine responses in all of the groups. However, the mental stress test was the only test that induced differential responses between the groups, where the high BP group showed the most and the low BP group the least pronounced response in BP, HR, and plasma catecholamines. The present study also showed that low BP was associated with a better lipoprotein profile than both normal and high BP. In addition, we found that arterial adrenaline levels were negatively related to serum HDL and that adrenaline and noradrenaline were related to serum fructosamine. This may suggest that the better cardiovascular profile observed in those with low BP is partly explained by lower arterial adrenaline concentration.

The present study was designed to compare men with low, normal, and high resting BP. By examining subjects with low BP, we are able to bring new elements into explaining the variation of BP rather than just considering a hypertensive and normotensive population. This is an analogue to Lewington et al., who did a metaanalysis of individual data for 1 million adults and found that BP at least down to 115/75 mm Hg is positively related to vascular mortality risk. Thus, there is no threshold level. Although significant differences in BP could be measured at rest in laboratory, the differences were smaller than

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Rest</th>
<th>CPT</th>
<th>MST</th>
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<tbody>
<tr>
<td></td>
<td>E (44.6±5.0)</td>
<td>NE (110.6±7.4)</td>
<td>E (57.1±5.5)</td>
</tr>
<tr>
<td>SBP (125.9±1.9)</td>
<td>0.431†</td>
<td>0.208</td>
<td>0.468†</td>
</tr>
<tr>
<td>DBP (67.2±1.2)</td>
<td>0.137</td>
<td>0.204</td>
<td>0.329*</td>
</tr>
<tr>
<td>Tot.chol (4.05±0.14)</td>
<td>-0.108</td>
<td>-0.053</td>
<td>0.178</td>
</tr>
<tr>
<td>HDL (1.13±0.04), mmol/L</td>
<td>-0.387*</td>
<td>-0.251</td>
<td>-0.144</td>
</tr>
<tr>
<td>Trigl (0.88±0.06)</td>
<td>0.124</td>
<td>0.181</td>
<td>0.356*</td>
</tr>
<tr>
<td>Fruct (2.22±0.03)</td>
<td>0.101</td>
<td>0.209</td>
<td>0.250</td>
</tr>
</tbody>
</table>

E/NE indicates arterial plasma epinephrine/norepinephrine (pg/mL); DBP/SPB, resting diastolic/systolic blood pressure (mm Hg); Tot.chol, total serum cholesterol (mmol/L); Trigl, serum triglycerides (mmol/L); Fruct, fructosamine (mmol/L). Triglycerides and epinephrine during MST were log transformed. Epinephrine during CPT was not normally distributed after log transformation.

The table shows correlation coefficients: *\(P<0.05\); †\(P<0.01\).
in the military draft screening. This may be a “regression toward the mean” phenomenon. On the other hand, as discussed previously, military draft is to be considered as an unspecified stress test rather than a resting baseline situation. This is supported by the fact that screening BP in our study was mostly explained by stress BP and not resting BP in a stepwise multiple regression analysis. Thus, our participants were selected based partly on their BP reactivity to stress and not merely on resting BP. However, because the military draft procedure in Norway is compulsory, we have a unique opportunity to obtain data from individuals unaware of their BP in the lowest, middle, and highest percentiles of the BP distribution.

We believe that confounding factors were eliminated to a minimum in our study, because all of the subjects were white men at the same age with no medication and similar body mass index. The population in Oslo, as in Norway in general, is stable, thus reflecting a genetically homogenous population. However, one may bear in mind that genetic studies have revealed associations between gene polymorphisms and cardiovascular risk factors like BP, BP reactivity, cholesterol levels, and hyperglycemia.

To assess sympathetic activity, we measured arterial catecholamines, which have been reported previously to be better than venous catecholamines when comparing hypertensive and normotensive groups. An increased level of norepinephrine in hypertension may predominantly reflect an increased sympathetic tone to the heart and kidneys, and muscle contributes to ≈50% of peripheral venous norepinephrine. Thus, arterial samples would reflect the sympathetic tone from heart and kidney better than venous samples. Furthermore, it has been stated previously that laboratory stress induces relatively small increases in sympathetic nerve firing in skeletal muscles, and, as a consequence, antecubital venous plasma norepinephrine measurements may be misleading and interpretation difficult.

Our study supports the hypothesis that resting BP is related to arterial plasma catecholamines. This is in accordance with Beilin et al, who has demonstrated previously that young subjects with high normal BP have increased renal medullary activity and altered autonomic tone. Our data additionally support the hypothesis that subjects with low pressure have decreased sympathetic tone compared with normotensives, and, as far as we know, this is a novel observation. Clausen et al studied the influence of the adrenergic system, fasting serum insulin level, and insulin sensitivity on BP in young subjects of both sexes who were unaware of their BP status. Multiple regression analysis showed that, after sex, plasma epinephrine level was the most important determinant of SBP, whereas there were no correlations between SBP and norepinephrine. There are several studies demonstrating that hypertensive subjects have increased plasma epinephrine, and these subjects are characterized by an increased sensitivity to epinephrine as well.

Blood platelets lack enzymes for catecholamine synthesis, and concentration of free catecholamines in platelets has been used as a marker of longstanding sympathetic activation. We found that the groups did not differ, perhaps suggesting that their plasma catecholamine differences are mainly determined by the present situation at the examining day and not a constant finding in the every day life. On the other hand, the statistical power to detect differences was limited because of the relatively small groups.

MST was the only stress test that induced significant group differences in cardiovascular and catecholamine responses. This was additionally supported by the finding that there were positive correlations between BP responses only to MST and baseline BP. One reason can be that the subjects with high BP were partly preselected to respond vigorously to a psychological stress situation, similar to MST. However, there is evidence that hypertension and high normal BP is associated with increased cardiovascular and sympathoadrenal reactivity to mental stress compared with physical stress, such as orthostatic and CPT.

One may speculate whether the duration of CPT and ORT was too short to compare with 5-minute mental stress. CPT lasted for 1 minute in accordance with Hines and Brown, who introduced the test. The peak response usually occurs within 30 s. Gehring et al have demonstrated a sensitivity of 88% for 1 minute and 99% for 2 minutes of head-up tilt for detecting orthostatic hypotension. Furthermore, all 3 of the stress tests had significant effects on BP, HR, and catecholamines, indicating a satisfactory duration. However, we cannot by certainty exclude group differences if the tests had lasted longer. The sample groups were rather small, which raises the question of whether the power was sufficient to detect possible differences in CPT and ORT. The statistical power to detect a similar difference during CPT and ORT as during MST was >80% for Δepinephrine, Δnorepinephrine, ΔMBP, and ΔHR between groups 1 and 3 and Δepinephrine and ΔHR between groups 2 and 3. This indicates that our findings are trustworthy.

There are several possible mechanisms behind a hyperreactivity to MST among subjects in our study. One explanation is that structural changes in the vascular wall or increased receptor sensitivity may amplify the pressor effect of catecholamines. As mentioned, gene polymorphisms in twin studies are shown to influence not only on resting but also on stress-related BP during MST and CPT. Thus, one would have expected a similar hyperreactivity to ORT and CPT if vascular wall or receptor properties were the only explanation. Some authors have proposed that there is a U-shaped relationship between pressor sensitivity and BP, where borderline hypertensives have a reduced sensitivity and an increased sympathetic activity and reactivity. Persons with established hypertension may show normal sympathetic activity assessed by arterial plasma catecholamines, but the receptor sensitivity and vascular hypertrophy are raised. We found differences not only in BP and HR responses, but also in catecholamine responses. This indicates that the mechanism behind our finding may be located in the central brain structures and leads us to the second possible explanation, namely that changes in the subcortical structures (hypothalamus and brain stem) can induce exaggerated impulses.

More recently, evidence has accumulated to suggest that the dorsomedial hypothalamic nucleus plays a key role in integrating the cardiovascular response to acute stress. Observations in rats indicate that this area is crucial in integrating the cardiovascular and autonomic responses to
emotional stress. The third option is that the mechanism underlying hyperreactivity is located in the cortical areas, because each subject has a different perception and reaction pattern. Some have described a “hypertensive personality,” with a tendency to be submissive, to avoid confrontations and to suppress anger. Gianaros et al.46 have done functional brain MRI of individuals who differ in BP reactivity to mental stress and found an increased activity of the posterior cingulate cortex in the hyperreactive persons during stress.

Although there is diversity in the prospective studies regarding reactivity and hypertension,21,25,26 several studies have demonstrated hyperreactivity to CPT, ORT, and different forms of mental stress as a risk marker of future hypertension.25–30 This supports the reactivity hypothesis, which states that exaggerated physical or psychological stress responses identify subgroups with increased cardiovascular risk.31 However, we do not know whether this relation is causal or not. One possible explanation is that intermittent pressure elevations could lead to structural vascular changes, but attempts to produce irreversible, sustained BP elevations purely as a consequence of transient elevations in dogs have not succeeded.32,33 Although evidence does not indicate that transient BP elevations are the cause of hypertension development per se, there is evidence that sympathetic tone is a trophic factor for vascular hypertrophy.34,35 Because we have demonstrated that hyperresponsive subjects have increased resting catecholamine levels, this is one possible explanation for why there is a positive relationship between BP reactivity and future hypertension. The fact that this cross-sectional study did not demonstrate any relationship between reactivity to ORT or CPT and BP level does not exclude the possibility that a selection of hyperreactors to these tests may develop hypertension over time.

We found that young men with high resting BP increased more in DBP within the mental stress test. Furthermore, the same group also seemed to have an impaired recovery. The normotensives had the slowest recovery in plasma norepinephrine levels, a somewhat surprising finding, which may have occurred by chance. Schneider et al.36 have documented that healthy, young men with parental history of hypertension have enhanced reactivity, blunted adaptation, and delayed recovery. Several authors have found a connection between impaired poststress cardiovascular recovery and future hypertension.37–40

Reims et al.41 have recently reported a negative relationship between epinephrine and HDL, that is, the opposite of our finding. It is, however, doubtful whether the studies are comparable, as we measured arterial epinephrine samples in contrast to the venous samples of Reims et al.41 In addition, our population was somewhat leaner.

One may speculate whether group 3 had a low-grade form of the metabolic syndrome. However, although there was a negative linear trend for HDL and HDL:total cholesterol ratio and a positive linear trend for triglycerides, fructosamine, and waist:hip ratio, group 3 did not show significant differences compared with the normotensives, except for fructosamine, and nearly significant differences for triglycerides levels. In addition, there were no differences in triceps or subscapularis skin-fold thickness (data not presented). Thus, we do not have supporting data that can classify group 3 as having metabolic syndrome.

Fasting serum insulin and glucose were similar in the 3 groups, indicating that hyperinsulinism most likely is not a cause of high-sympathetic activity in these young men, but this observation may also be partly explained by lack of statistical power. Fructosamine increased significantly, corresponding to the BP, and, as a measure of total serum glycated proteins and marker of blood glucose levels in the previous 3 weeks, this suggests that the subjects with higher BP have sustained higher glucose levels. This is in accordance with our previous finding that 1 screening BP measurement in healthy young men predicts insulin resistance and elevated fasting glucose.42 The mechanism between hypertension and insulin resistance is still unknown.43 There is substantial evidence that hypertension occurs more frequently among diabetic patients,44 and hyperglycemia has been reported to stimulate the sympathetic nervous system.45 Villafana et al.46 have done experiments on rats, demonstrating the pressor effect of glucose, mainly caused by increased efferent sympathetic activity and activation of the renin–angiotensin system. On the other hand, it is a well-known fact that epinephrine inhibits insulin and stimulates glucagon secretion, thereby increasing the blood glucose level. We found that arterial catecholamine levels during mental stress are related to baseline fructosamine, which is in accordance with the hypothesis that hyperreactive persons respond to stress in the everyday life by increased catecholamine release and, hence, a greater release of glucose.

The present study suggests that resting BP reflects the underlying sympathetic activity. The fact that the groups had similar levels of platelet catecholamine levels may indicate that the difference in sympathetic activity among young men is present only in stressful situations. Because men with higher BP showed a cardiovascular and catecholamine hyperreactivity to mental stress only, we conclude that sympathetic and cardiovascular responses to mental stress seem to differentiate better between categories of BPs than physical tests.

Perspectives

Although there are several reports of increased catecholamine levels in subjects with high BP,13,42,47,48 this is the first study to demonstrate that there is an association between plasma catecholamines and BP within the whole range of resting BP. Subjects with high-screening BP are furthermore characterized by a hyperreactivity to MST. All of the subjects were unaware of their BP status, shown previously to be a confounding factor.1–3 To get additional insight into the underlying mechanisms and the significance of the hyperreactivity demonstrated in the current study, longitudinal studies will be of crucial significance.

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References


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