A Quantitative Study of Muscle Nerve Sympathetic Activity in Resting Normotensive and Hypertensive Subjects

B. Gunnar Wallin, M.D., and Göran Sundlöf, M.D.

SUMMARY Recordings of multi-unit sympathetic activity were made from muscle branches of the peroneal or median nerves in 33 healthy and 12 hypertensive subjects resting in the recumbent position. Simultaneous recordings of intra-arterial blood pressure were made on 17 normotensive and all hypertensive subjects. The neural activity, quantified by counting the number of sympathetic pulse-synchronous impulse bursts in the mean voltage neurogram (burst incidence) was plotted against the age and the arterial blood pressure level of the subjects. Between different subjects there were marked differences in mean burst incidence, from less than 10 to more than 90 bursts/100 heart beats and there was a tendency for increasing values with increasing age. Taking the age differences into account there was no significant correlation between the amount of activity and the blood pressure level. The effect of spontaneous temporary blood pressure fluctuations was studied by correlating different pressure parameters of individual heart beats to the probability of occurrence of a sympathetic burst and to the mean voltage amplitude of the occurring burst. Irrespective of the mean burst incidence, the occurrence of the bursts and their mean voltage amplitudes were determined mainly by fluctuations of the diastolic blood pressure. The diastolic blood pressure threshold for sympathetic outflow was found to be reset to higher blood pressure values in the hypertensive subjects and the variability of their thresholds was also greater than for the normotensive controls. At a given diastolic blood pressure, more sympathetic activity occurred if diastolic blood pressure was falling than if it was rising, and this directional dependence was more pronounced in the hypertensive subjects. We suggest that the increased directional dependence accounts for the greater variability of the blood pressure threshold for sympathetic outflow in the hypertensive subjects. The differences can be explained on the basis of findings in animals with experimental hypertension, and it appears that they are secondary to the hypertension. Hypertension 1:67-77, 1979.

KEY WORDS • pathophysiology of hypertension • microneurography • vasoconstrictor activity • muscle nerves • baroreflex control

Although overactivity in the sympathetic nervous system often has been considered an important factor in the pathogenesis of arterial hypertension in man, the supporting evidence is still incomplete. In early (or labile) hypertension there are signs of a net increase of adrenergic influence on the heart but at least in established hypertension this seems to be due more to a withdrawal of parasympathetic rather than to an increase of sympathetic tone. In early hypertension total peripheral resistance is too high in relation to the elevated cardiac output, and in established essential hypertension there is an absolute increase in total peripheral resistance. In neither case, however, is it clear whether this is due only to structural alterations of the blood vessel walls or if there is also an increased sympathetic drive. The concentration of noradrenaline in plasma has been used as an index of total sympathetic activity and there are several reports of increased noradrenaline levels in essential hypertension. Recently, however, these results have been contested by Lake et al., who, in a large series, found no differences between normal and hypertensive subjects when differences in age between the groups were taken into account. With the introduction of the microneurographic technique, it became possible to make direct recordings of sympathetic action potentials in human peripheral nerves, and in a study of sympathetic outflow in skin and muscle nerves no qualitative differences were found between normal and hypertensive subjects. Recently, we devised methods for quantitating muscle nerve sympathetic activity (MSA) and showed that there are large reproducible differences in the amount of activity between different normal subjects resting in the recumbent posture.
In each individual transient variations in the strength of the MSA correlated intimately to transient diastolic blood pressure fluctuations but there was no correlation between the average amount of activity and the average blood pressure level. In the present study resting MSA has been recorded in a group of subjects with arterial hypertension and the results are compared with those of normal controls. The aim has been to search for possible differences either in the relationship between blood pressure and sympathetic activity or in the average amount of sympathetic activity.

Material and Methods

Subjects

Normotensive Subjects

Recordings of MSA were made in 33 healthy subjects, 25 men and eight women aged 18-54 (mean 32.1) years. The recordings were made either in the peroneal nerve at the fibular head (28 subjects) or in the median nerve at the elbow level (five subjects). Intra-arterial blood pressure was recorded together with the sympathetic activity in 17 subjects aged 18-54 (mean 29.6) years.

Hypertensive Patients

Simultaneous recordings of MSA (recorded in the peroneal nerve at the fibular head) and intra-arterial blood pressure were made in 12 subjects (nine men and three women) with arterial hypertension, aged 18-59  
(mean 39.4) years. The most important clinical and experimental data on these subjects are presented in table 1. Based on routine clinical investigation for hypertension, 10 patients were classified as hypertensive and two as borderline. Although clinically classified as hypertensive, one patient (Case 5, table 1) had normal blood pressure during the experiment. The routine examination included ECGs, which showed suspected left ventricular hypertrophy in four subjects (Cases 8, 9, 10 and 11) and was normal in all others. The heart volume, determined by chest x-ray, was moderately increased in two subjects (Cases 11 and 12) and normal in all others. Renal arteriography was carried out in eight patients. One patient (Case 8) had a hypoplastic left kidney with five times higher plasma renin activity (PRA) in venous blood from that kidney compared with blood from the other kidney. This subject became normotensive after nephrectomy and was classified as having renovascular hypertension. Another patient (Case 5) had a hypoplastic right kidney but no side-difference in renin activity. Signs of renal artery stenosis were found in four other patients (Cases 6, 7, 9 and 11). One patient (Case 9) had twice as high PRA in venous blood from the affected kidney and was also considered having renovascular hypertension. In three patients (Cases 6, 7 and 11) the arterial stenosis was considered of no clinical significance. Seven subjects had taken antihypertensive drugs at some previous time. At the time of the investigation three had been off medication for 5 weeks.

Table 1. Clinical and Experimental Data on 12 Subjects with Arterial Hypertension

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Sex/ Age (yrs)</th>
<th>Resting BP before experiment (mm Hg)</th>
<th>Known duration of hypertension</th>
<th>Degree of hypertensive retinal changes</th>
<th>Renal arteriography</th>
<th>Resting BP during experiment (mm Hg)</th>
<th>Heart rate/min</th>
<th>Sympathetic bursts/100 heart beats</th>
<th>Sympathetic bursts/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/18</td>
<td>150/90-160/110</td>
<td>20 mos</td>
<td>0</td>
<td></td>
<td>102/101</td>
<td>66.5</td>
<td>54.6</td>
<td>36.3</td>
</tr>
<tr>
<td>2</td>
<td>M/24</td>
<td>140/80-160/105</td>
<td>3 wks</td>
<td>0</td>
<td></td>
<td>138/91</td>
<td>62.6</td>
<td>32.1</td>
<td>20.1</td>
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<tr>
<td>3</td>
<td>F/31</td>
<td>120/80-160/115</td>
<td>6 mos</td>
<td>0</td>
<td></td>
<td>152/92</td>
<td>74.6</td>
<td>49.7</td>
<td>37.0</td>
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<td>F/35</td>
<td>150/110-220/130</td>
<td>2 wks</td>
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<td></td>
<td>188/122</td>
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<td>50.3</td>
<td>42.5</td>
</tr>
<tr>
<td>5</td>
<td>M/36</td>
<td>130/80-160/130</td>
<td>6 yrs</td>
<td>0</td>
<td>Hypoplastic rt kidney</td>
<td>130/88</td>
<td>75.7</td>
<td>76.2</td>
<td>57.7</td>
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<td>6</td>
<td>M/43</td>
<td>150/95-180/115</td>
<td>2 mos</td>
<td>0</td>
<td>Stenosis rt renal artery</td>
<td>189/118</td>
<td>68.3</td>
<td>57.6</td>
<td>39.4</td>
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<td>7</td>
<td>M/43</td>
<td>140/90-185/120</td>
<td>8 yrs</td>
<td>I-II</td>
<td>Bilateral renal artery stenosis</td>
<td>180/106</td>
<td>74.8</td>
<td>64.3</td>
<td>48.0</td>
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<tr>
<td>8</td>
<td>M/44†</td>
<td>150/100-160/115</td>
<td>3 mos</td>
<td>0</td>
<td>Hypoplastic lt kidney</td>
<td>180/105</td>
<td>85.6</td>
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<td>9</td>
<td>M/44†</td>
<td>180/120-210/145</td>
<td>1 yr</td>
<td>I-II</td>
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<td>I</td>
<td></td>
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<td>78.5</td>
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<tr>
<td>11</td>
<td>M/49</td>
<td>180/120-220/150</td>
<td>5 yrs</td>
<td>I</td>
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<td>187/116</td>
<td>69.5</td>
<td>62.6</td>
<td>43.5</td>
</tr>
<tr>
<td>12</td>
<td>F/58</td>
<td>210/130-220/140</td>
<td>1 mo</td>
<td>I-II</td>
<td></td>
<td>231/120</td>
<td>70.9</td>
<td>60.8</td>
<td>43.1</td>
</tr>
</tbody>
</table>

*Subject with borderline hypertension.
†Subject with renal hypertension.

Abbreviation: BP = blood pressure.
or more, two (Cases 6 and 9) had been without drugs (hydralazine and a thiazide diuretic) for 16 and 10 days, respectively, another patient (Case 8) for 14 days (propranolol) and the last patient (Case 9) for 5 days (methyldopa).

Procedures

Nerve electrodes, recording technique and display system have been described in detail previously. Neural recordings were made with insulated tungsten microelectrodes that were manually inserted through intact skin into a muscle nerve fascicle. The electrode was adjusted until a position was found in which sympathetic impulses could be recorded. After amplification the neural activity was fed through a RC-integrating network (time constant 0.1 sec) to obtain a mean voltage neurogram. Both the original neural record and mean voltage neurogram were stored on an 8-channel FM tape recorder (PI 6200, Precision Instruments, Palo Alto, CA).

Arterial blood pressure was monitored through a catheter in the brachial artery connected to a pressure transducer EMT 35 and electromanometer EMT 31 (Siemens-Elema Ltd., Stockholm, Sweden) and stored on the tape recorder. Electrocardiograms were recorded by surface chest electrodes. Respiratory movements were recorded by a strain gauge strapped around the chest with a rubber band.

Analyses

The mean voltage neurogram together with ECG, arterial blood pressure and respiratory movements were displayed from the tape on an inkjet recorder (Mingograph 800, Siemens-Elema Ltd., Sweden) with a paper speed of 3-5 mm/sec. The records were divided into analysis periods of approximately 3 minutes (range 2-4 minutes) duration and all the pulse synchronous sympathetic bursts that could be identified by inspection were marked. The analog signals of the mean voltage neurogram and the blood pressure were then converted into digital form (sampling frequency 100 Hz) and fed into a computer (PDP 11/40, Digital Equipment, Maynard, MA). In previous recordings of MSA a reflex delay was demonstrated between blood pressure and neural events and appropriate compensation for this delay was made by the computer, using a standard value of 1.45 seconds for all subjects. For each heart beat the computer determined systolic, diastolic, mean and pulse pressure, and marked which beats were preceded by beats with higher blood pressure, and one of heart beats preceded by lower pressure. Beat-to-beat analyses were then performed separately for each population of heart beats.

Experimental Procedure

Subjects were in a comfortable recumbent position. The microelectrode was manually inserted into the nerve and small electrode adjustments were then made until a recording site with optimal signal-to-noise ratio for sympathetic impulses was found. Details of the identification procedure and evidence that the impulses derived from sympathetic vasoconstrictor fibers have been described previously. The spontaneous multi-unit sympathetic activity was then recorded during a number of 3-minute rest periods. On the average seven rest periods (range 2-14) were recorded in each subject and the different periods often were separated by maneuvers such as deep breathing, fist clenchings, and mental arithmetic. The effects of these maneuvers will be described separately. The first 20 seconds after a maneuver were excluded from the quantitative analyses.

Results

Relationship Between Transient Blood Pressure Variations and Sympathetic Bursts

In agreement with previous results the general character of the MSA was similar in normal and hypertensive subjects. The sympathetic impulses were grouped in pulse synchronous bursts, which usually occurred in irregular sequences separated by periods of more or less total neural silence. This is illustrated in figure 1, which shows examples of the MSA at rest in one normal and one hypertensive subject. The figure also illustrates that in both types of subjects there was an inverse relationship between the occurrence of bursts and spontaneous blood pressure fluctuations. The bursts occurred most frequently during temporary blood pressure reductions and disappeared during peaks in the blood pressure curve. This type of relationship suggests that for each individual there is a characteristic blood pressure threshold below which the bursts occur and above which they disappear. The threshold can be expressed quantitatively by means of "threshold variability diagrams" as we described earlier. Figure 2A shows examples of such diagrams for diastolic and systolic pressures from a single rest period in one normal and one hypertensive subject. For both subjects there is a close negative correlation to diastolic blood pressure, but there is no apparent correlation to systolic pressures for any of the subjects. The results were similar in all recordings, i.e. the occurrence of bursts regularly correlated as described previously.
Figure 1. Examples of the relationship between arterial blood pressure and muscle nerve sympathetic activity at rest in one normotensive and one hypertensive subject. Tracings from above: Mean voltage neurogram (time constant 0.1 sec), blood pressure, instantaneous heart rate.

Figure 2. The occurrence of sympathetic bursts in relation to diastolic and systolic blood pressures. A: Examples of relationship during a 3-minute rest period from one normotensive (solid circle) and one hypertensive (open circle) subject. Correlation coefficients for linear regression are: -0.95 and +0.21 for the normotensive subject and -0.93 and -0.07 for the hypertensive subject. B: Distribution of correlation coefficients for 170 rest periods in 17 normotensive subjects (open columns) and 85 periods in 12 hypertensive subjects (hatched columns).
better to diastolic than to systolic pressures and there was no difference in the degree of correlation between normal and hypertensive subjects. This is illustrated in figure 2B which summarizes the correlation coefficients from the threshold variability diagrams from 170 rest periods in 17 normotensive subjects and 85 rest periods in 12 hypertensive and borderline patients.

Similar analyses were also made for mean and pulse pressures and pulse interval. In most cases there was a negative correlation to mean blood pressure with the correlation coefficients falling between those of diastolic and systolic pressures. To pulse pressure and pulse interval, on the other hand, the correlation was usually positive, that is, the higher the pulse pressure and the longer the pulse interval the higher the probability for the occurrence of a burst. When comparing the results from the normal and hypertensive groups, correlation coefficients for mean blood pressure and pulse interval were similar in both groups, whereas correlation coefficients for pulse pressure were often lower in the hypertensive group. Table 2 summarizes mean correlation coefficients in the two groups for all pressure parameters and the pulse intervals during all rest periods.

The threshold variability diagrams are conveniently characterized by the blood pressure value at which 50% of the heart beats were associated with a burst (T_m) and by the slope of the regression line which gives a measure of the variability of the threshold. In the patients with established hypertension, T_m was 116.3 ± 10.2 (mean ± SD); in those with borderline hypertension, 89.9; and in the normal subjects, 78.0 ± 8.1 mm Hg. These figures indicate that the blood pressure threshold for sympathetic outflow of the hypertensive subjects was positioned higher up on the blood pressure axis than in normal subjects (fig. 2A).

The steepness of the slope for the threshold variability diagrams varied considerably between different rest periods and between different subjects, but as illustrated in figure 3 there was a systematic difference between normotensive and hypertensive subjects, mean values being -4.70 in the normotensive and -3.48 in the hypertensive (including borderline) group (p < 0.001, Student's t test). For both the normo- and hypertensive subjects a correlation was found between the steepness of the slope (the degree of threshold variability) and the amount of variation of the diastolic blood pressure. As illustrated in figure 4, the smaller the threshold variability the smaller the blood pressure variations. In view of this finding the question arose whether the greater threshold variability in the hypertensive subjects was associated with a greater instability of their diastolic blood pressure as compared to the control subjects. When comparing the variations in diastolic pressure between the two groups there was, however, only a small and insignificant difference (mean observed standard deviation of diastolic blood pressure/rest period, 3.70 ± 1.60 mm Hg in normotensive subjects and 4 ± 2.03 in hypertensive subjects; p > 0.1).

<table>
<thead>
<tr>
<th>Table 2. Mean Correlation Coefficients for the Relationship Between Burst Incidence and Different Blood Pressure (BP) Parameters</th>
<th>Mean correlation coefficient</th>
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<td>Patient group</td>
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<td>Normotensive</td>
<td>-0.81</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>-0.78</td>
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</table>

Figure 3. Distribution of slopes of the regression lines for all threshold variability diagrams in normotensive (open columns, n = 170), hypertensive (hatched columns, n = 76) and borderline (filled columns, n = 9) subjects.

Figure 4. Relationship between slope of regression line for threshold variability diagram and diastolic blood pressure variability (expressed as the standard deviation) during the same rest period. Each point represents the mean diastolic pressure variability for all rest periods within a slope interval of 0.5. The figure is based on all rest periods in both normotensive and hypertensive subjects (n = 255).
Relationship Between Transient Blood Pressure Variations and Burst Amplitude

In addition to burst incidence, burst amplitude also increased during temporary blood pressure reductions both in normo- and hypertensive subjects. This was shown by plotting burst amplitudes against corresponding blood pressure values and calculating regression lines and correlation coefficients for each rest period in both groups of subjects. Figure 5A shows examples of such plots for diastolic and systolic pressures from a single rest period in one normotensive and one hypertensive subject. For both subjects there is a close negative correlation to diastolic and no correlation to systolic pressures. The results were similar in all recordings and as illustrated in Figure 5B and table 3 there was no appreciable difference in the degree of correlation between the normo- and the hypertensive groups.

Since the absolute burst amplitude depends on the position of the electrode tip in relation to the active fibers, a factor which cannot be controlled with the present recording technique, no attempt was made to compare absolute burst amplitudes between different subjects.

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Mean correlation coefficient</th>
</tr>
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<td></td>
<td>Diastolic BP</td>
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<td>-0.72</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>-0.84</td>
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</table>

Direction of Blood Pressure Changes

Burst Incidence

In normal subjects, Sundlöf and Wallin\textsuperscript{18} showed that at a given diastolic blood pressure, sympathetic bursts were more likely to occur if pressure was falling than if it was rising. To test whether this was true also for hypertensive subjects, the rest periods were divided into two fractions, one consisting of heart beats preceded by beats with lower diastolic pressure and one consisting of beats preceded by beats with higher pressure. For each fraction burst incidence and mean diastolic blood pressure were compared. The 132 rest periods from normotensive subjects and 83 periods...
from hypertensive subjects were analyzed in this way (40 periods had to be excluded for technical reasons). In both groups burst incidence was virtually always higher during decreasing than during increasing blood pressure, the mean difference being 30.8 bursts/100 heart beats in the normotensive and 27.2 bursts/100 heart beats in the hypertensive group. However, in both groups mean diastolic blood pressure was always lower during the fraction of decreasing pressure and therefore it was questioned whether this could explain the difference in burst incidence. This was tested for each rest period by using the threshold variability diagram as illustrated in the upper right corner of figure 6. From the observed difference in mean diastolic blood pressures between the fractions (a), the “expected” difference in burst incidence (b) was determined, and “expected” and “observed” differences were then plotted against each other. As shown in figure 6 the observed differences were greater than the expected in almost all rest periods, indicating that both in normo- and hypertensive subjects a given diastolic blood pressure is more likely to be associated with a sympathetic burst if pressure is falling than if it is rising.

The directional dependence was also expressed in pressure terms. This was done by using the difference in burst incidence between rising and falling pressure and the slope of the threshold variability diagram to calculate an “expected” difference in diastolic blood pressure. The “directional dependence” was then determined by subtracting the observed pressure difference from the expected. For the normal subjects the difference was $4.8 \pm 3.5$ mm Hg (mean ± SD), i.e. burst incidences would be equal if mean rising diastolic blood pressure was 4.8 mm lower than mean falling diastolic blood pressure. For the hypertensive group corresponding figures were $6.5 \pm 5.5$ mm Hg (difference between groups was significant at the $p < 0.01$ level). The question arose whether this difference in directional dependence was associated with the difference in threshold variability between normo- and hypertensive subjects demonstrated in figure 4. For this reason the slope of the threshold variability diagram for each rest period was related to the directional dependence of the same period. The results were similar in both the normo- and hypertensive group and therefore data from all subjects are summarized in figure 7. The diagram shows that there

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**FIGURE 6.** Expected versus observed differences in burst incidence between fractions of decreasing and increasing blood pressure in normotensive (closed circles) and hypertensive (open circles) subjects. Line at 45° denotes line of identity. Threshold variability diagram shown in upper right corner illustrates method of calculating expected difference in burst incidence (b) from observed difference in mean diastolic blood pressure (a) between fractions of decreasing and increasing blood pressure.
was an approximately exponential relationship between the variables so that the steeper the slope the smaller the directional dependence.

**Burst Amplitudes**

Burst amplitudes were also compared between fractions of decreasing and increasing pressure. In each rest period the difference in mean diastolic blood pressure between the fractions were compensated for by a procedure similar to that used for burst incidence. The result was that the "observed" difference in burst amplitude between the fractions was greater than the "expected" in approximately 93% of the rest periods in both groups. When the directional dependence was expressed in blood pressure terms it was $4.9 \pm 5.4$ mm Hg (mean ± SD) in the normotensive and $8.5 \pm 9.1$ mm Hg in the hypertensive group (significant difference $p < 0.01$, Student's $t$ test).

In normal subjects we compared the regression lines for the relationship between diastolic blood pressure and burst amplitude for decreasing and increasing pressures. We found that the slope of the line from the "decreasing fraction" in general was steeper than that from the "increasing fraction," suggesting that for a given blood pressure change, sympathetic activity changes more if pressure is falling than if it is rising. A similar comparison was made for the hypertensive subjects. Due to the low number of bursts (especially in the "increasing fraction") and the large amplitude variability, significant regression lines (slope of line tested with Student's $t$ test, $p < 0.01$) for both fractions were obtained only in 35 rest periods in 11 normotensive and 28 periods in 11 hypertensive subjects. Figure 8A shows individual examples of the comparisons of the lines from one period in each group in which the lines from the "decreasing fraction" were steeper than those from the "increasing fraction." In figure 8B the results from the two groups are summarized. In both groups the "decreasing slopes" were steeper than the "increasing" ones ($p < 0.01$ in the normotensive, and $p < 0.05$ in the hypertensive group, Student's $t$ test). There was, on the other hand, no significant difference in the degree of asymmetry between normo- and hypertensive subjects (tested by comparing the ratios of the slopes in the two groups, $p > 0.1$, Student's $t$ test).

**Relationship Between the Mean Amount of Sympathetic Activity and the Static Blood Pressure Level**

In agreement with our earlier findings, burst incidence usually showed only small variations between different rest periods in the same individual. For each subject in the two groups on whom simultaneous recordings of MSA and blood pressure were made, mean burst incidence and mean diastolic blood pressure for all rest periods were calculated. As illustrated in figure 9, there were marked differences between individuals in both blood pressure and sympathetic activity. When the amount of activity was expressed as both bursts/100 heart beats (fig. 9A) and bursts/min (fig. 9B) there was a slight tendency for increasing activity at higher blood pressure levels (slope of regression line different from 0 at the $p < 0.1$ level in A, and at the $p < 0.05$ in B).

**Relationship Between Mean Amount of Sympathetic Activity and Age**

Figure 10 shows the relationship between the mean amount of sympathetic activity (expressed as mean number of sympathetic bursts/100 heart beats) and age for all subjects. In both the normotensive and hypertensive group there was a wide scatter of the experimental points and in both groups there was a tendency for increasing amount of activity with increasing age (slope of regression line different from 0 at the $p < 0.05$ level for normotensive and at the $p < 0.1$ level for hypertensive subjects, respectively, Student's $t$ test). If all subjects are treated as one group the significance increases to $p < 0.01$.
FIGURE 8. The differences in slope of the regression lines for the relationship between diastolic blood pressure and burst amplitude between fractions of decreasing and increasing blood pressure. A: Example from a 3-minute rest period in one normotensive and one hypertensive subject with decreasing (solid circles and line) and increasing (open circles, dotted line) pressure fractions analyzed separately. B: Comparison of the slopes in 35 rest periods from 11 normotensive and 28 rest periods from 11 hypertensive subjects. Lines at 45° denote lines of identity.

FIGURE 9. Relationship between mean diastolic blood pressure and amount of muscle nerve sympathetic activity expressed as bursts/100 heart beats (A) and bursts/min (B). Each point represents mean values from all rest periods in one subject. Solid circle = normotensive subjects; open circle = hypertensive subjects. Correlation coefficients for linear regression: 0.34 in A, and 0.41 in B.
We recently showed that in normotensive subjects there was a tendency for increasing amounts of MSA with increasing age.18 For hypertensive subjects the data show a similar trend. Although the exact reason for the age dependency is unknown it may be related to a reduction of baroreceptor activity. This may occur both because of baroreceptor degeneration15,19 or because of reduced distensability of the vessel walls in the baroreceptor regions in higher ages.20

Blood Pressure Variations

As discussed by Wallin et al.13 the pulse synchrony and the inverse relationship between variations in blood pressure and MSA indicate that baroreflex modulation of the sympathetic outflow still occurs in hypertensive subjects. The elevated blood pressure threshold for sympathetic outflow, found in the present investigation, in all probability reflects the well-known static resetting of the operating range of the baroreflex, secondary to the hypertension.11-12 In addition, the present study shows that qualitatively the dynamic characteristics of the reflex are preserved. The variations in strength of the MSA were determined mainly by diastolic blood pressure fluctuations and, at a given blood pressure, more sympathetic activity occurred if pressure was falling than if it was rising (directional dependence). Consequently, in hypertensive subjects the baroreflex defends the elevated blood pressure level in a way similar to that found in normal subjects.

However, quantitatively there were two differences between normo- and hypertensive subjects: 1) the slopes of the threshold variability diagrams were less steep, and 2) when determined from both burst incidence and burst amplitude the directional dependence was greater in the hypertensive than in the normotensive group. The two differences are probably related to each other. The less steep slopes in the threshold variability diagrams indicate that the blood pressure threshold for sympathetic outflow varies more in hypertensive than in normotensive subjects. In view of the findings shown in figure 7 it seems likely that there is a causal relationship between the degree of directional dependence and the variability of the threshold. Therefore, the reason for hypertensive subjects having a higher variability of the threshold may be the greater directional dependence. Could this finding be of importance for the pathogenesis of the hypertension? Probably not. In animal experiments it has repeatedly been shown that for a given blood pressure, baroreceptor firing is stronger when pressure is increasing than when it is decreasing.34-37 Although central mechanisms cannot be excluded,29 it seems likely that this baroreceptor hysteresis, is an important reason for the directional dependence of the MSA found in the present study. In animals with experimental hypertension, the working range of the baroreceptors becomes reset and their sensitivity to blood pressure changes becomes reduced.31,33,35 In addition, Angell-James50 found that the baroreceptor hysteresis to rising and falling pressures was more pronounced in

Discussion

The hypertensive patients in the present study do not comprise a homogeneous group with regard to the type and severity of hypertension. In the majority, the clinical diagnosis was essential hypertension but two patients were thought to have borderline and two renal hypertension. An additional three subjects had abnormal renal arteriograms but the changes were not considered as clinically significant. Despite this inhomogeneity the material has been treated as one group, the aim being to investigate whether hypertension as such is associated with an abnormal sympathetic outflow, rather than separating between different types of hypertension. The results do not, however, give any hint of differences between subjects with hypertension of different etiologies.

Static Blood Pressure Level

Although the material is too small for a definite conclusion, the present study does not provide evidence for an increased "level" of MSA in hypertension. It is true that there was a weak tendency for higher "levels" of MSA at higher blood pressures but this was probably due to the hypertensive subjects being older than the normotensive controls. Thus, to the extent that the strength of the MSA is reflected in the plasma level of noradrenaline, the present results agree with those of Lake et al.11 who found no significant difference in plasma noradrenaline levels between age-matched normo- and hypertensive subjects at rest. In this context it should be remembered, however, that the sympathetic outflow is controlled regionally14 and therefore the present results must not be generalized to other vascular beds.
hypertensive than in control animals. If the hysteresis is increased also in hypertensive man it would provide a possible explanation for the increased directional dependence in hypertensive subjects found in the present study. In view of these considerations, there seems to be no need to suspect that any of the observed differences in MSA between normo- and hypertensive subjects are of primary importance for the pathogenesis of the hypertension. On the contrary, the differences can be explained by such changes of arterial baroreceptor function that are known to occur secondary to the blood pressure elevation.

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References


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