Comparison of 1-Hour and 24-Hour Blood Pressure Recordings in Central or Peripheral Baroreceptor–Denervated Rats

R. Allan Buchholz, John W. Hubbard, and Marc A. Nathan

SUMMARY We compared the mean arterial pressure and heart rate activity of conscious, unrestrained rats during 1-hour and 24-hour continuous recording sessions, 3 to 4 weeks after either sinoaortic denervation, placement of electrolytic lesions in the nucleus tractus solitarii, or sham operations. Sinoaortic denervation and nucleus tractus solitarii lesions both eliminated the reflex bradycardia to a phenylephrine-induced pressor response. No difference was found in the average level and lability of the mean arterial pressure between 1-hour and 24-hour recordings for any group. No elevation in the average mean arterial pressure of rats with nucleus tractus solitarii lesions was observed, although a mild hypertension was noted in half the sinoaortic-denervated rats, while the other half were normotensive. Group differences were not found for heart rate or heart rate variability; however, 24-hour recordings yielded significantly higher values than 1-hour recordings for all groups. Both medullary lesions and sinoaortic denervation significantly increased the lability of the mean arterial pressure, but the magnitude of the increase was significantly greater in the rats with lesions. The lability of the mean arterial pressure in sinoaortic-denervated rats depended largely on movement-related depressor responses that produced a negative skew in the frequency distribution of their mean arterial pressure. Rats with nucleus tractus solitarii lesions exhibited both pressor and depressor responses that resulted in pressure distributions that had a slight positive skew similar to that displayed by control rats. It is concluded that short-term continuous recordings of mean arterial pressure and heart rate accurately estimate the altered cardiovascular activity of baroreceptor-denervated rats. The differences in the cardiovascular responses of central and peripheral baroreceptor–denervated rats are believed to be due to the more extensive destruction by nucleus tractus solitarii lesions of central neurons and pathways involved in cardiovascular regulation.

(KEY WORDS • baroreceptor reflexes • sinoaortic denervation • nucleus tractus solitarii • lesions • arterial pressure • lability)

The cardiovascular response to sinoaortic denervation (SAD) has been studied in rats, cats, rabbits, and dogs. Many of these investigations reported sustained hypertension following peripheral disruption of the arterial baroreceptor reflexes. However, recent reports have challenged these findings, suggesting that the observed hypertension was dependent on the methods of measurement, the duration of measurement, and the environment in which the arterial pressure was recorded. The one consistent finding shared by all of these studies was a marked increase in the moment-to-moment variability of the mean arterial pressure (MAP) after SAD.

Central disruption of the arterial baroreceptor reflexes by placement of lesions in the nucleus tractus solitarii (NTS), the primary site of baroreceptor afferent termination, has been reported to produce a chronic elevation of MAP, with or without an increase in arterial pressure variability, in cats and dogs. However, none of these studies used long-term continuous arterial pressure recordings. In addition, the average level of the MAP after NTS lesions in cats was found to depend somewhat on the environment in which recordings were made. In contrast, the
Materials and Methods

Long-Evans male rats (Charles River, Wilmington, MA, USA) weighing 300 to 400 g were used as subjects. The rats were housed individually in standard laboratory cages, with ad libitum access to food and water. The experimental groups consisted of rats with electrolytic lesions placed in the NTS (n = 10) or SAD (n = 12). The control group consisted of NTS sham-operated (n = 6) or SAD sham-operated (n = 6) rats. All rats were maintained on a 12-hour light, 12-hour dark cycle. Data collection began 3 to 4 weeks after placement of the lesions and 2 days before cardiovascular monitoring was scheduled to occur. With the rats under halothane (2–3% in 100% oxygen) anesthesia, Teflon-tipped Tygon cannulas,23 filled with heparin (50 U/ml) in normal saline, were inserted into the abdominal aorta and inferior vena cava through the left femoral artery and vein, respectively. The free ends of the cannulas were passed subcutaneously and exteriorized at the top of the skull. Each cannula was threaded through a stainless steel tube, and the tubes were vertically oriented and cemented to the skull with dental acrylic. Upon completion of the operation all rats were treated with a single injection of penicillin G benzathine (Bicillin), 60,000 U. Each rat was then placed in a 30 x 30 x 30-cm Plexiglas cage with a grid floor for the duration of the experiment. The arterial cannula, protected by a lightweight metal spring, was attached to a hydraulic swivel (Instech, Horsham, PA, USA), thereby allowing the rat complete freedom of movement throughout the cage. Patency of the arterial cannula between periods of data collection was maintained by administration of heparinized saline (0.17 ml/hr) with an infusion pump. The venous cannula was flushed daily with 0.1 ml of heparinized saline and sealed with a stainless steel plug except during drug injections. Ad libitum access to food and water was available throughout the experiment.

Cardiovascular Monitoring

Arterial pressure and HR were recorded in the conscious, freely moving rat by connecting the arterial cannula through the fluid swivel to a pressure trans-
Results

Effect of Nucleus Tractus Solitarii Lesions and on Sinoaortic Denervation on Baroreceptor Reflex Sensitivity

A bolus injection of phenylephrine that increased SAP by 30 to 40 mm Hg caused little or no reflex bradycardia in rats with SAD or NTS lesions. The mean slopes of the BRS curves for the NTS lesion (-0.109 ± 0.027 msec/mm Hg) and SAD (0.010 ± 0.028 msec/mm Hg) groups did not differ from each other, and both were significantly less than the slope of the control group (0.688 ± 0.092 msec/mm Hg). No correlation existed between baseline HR and BRS in control rats.

Effect of Nucleus Tractus Solitarii Lesions and Sinoaortic Denervation on Arterial Pressure and Heart Rate

There was little variation in the values of the average (mean) level and lability (SD) of the MAP for each hour of a 24-hour recording session (Figure 1). The largest deviation of an hourly MAP from the 24-hour average for any group was only 3 to 4 mm Hg. Not surprisingly then, the average level and lability of the MAP for each group were comparable whether computed from 1-hour (360 data points) or 24-hour (8460 data points) arterial pressure recordings, as summarized in Table 1. The MAP of the control group tended to be lower during the late morning and early afternoon hours than at night. However, no significant diurnal rhythm was apparent for either the SD or average level of the MAP for any group.

The average MAPs of SAD rats, computed from the 1-hour and 24-hour recording sessions, were slightly but significantly higher than the average 1-hour and 24-hour MAPs of the NTS lesion and control rats (see Table 1). The MAP was elevated in the SAD group because half the rats had an average MAP that was higher than the highest value seen in the other two groups (Figure 2). This resulted in a significantly greater variance in the distributions of the means of the individual 1-hour (not shown) and 24-hour recordings of the MAP of SAD rats as compared with the other groups. There was no difference in the lability of the MAP or resting HR between the SAD rats that had an elevated MAP and those that did not.

The lability of the MAP was significantly greater in the SAD and NTS lesion groups, as compared with the control group (see Figure 1 and Table 1). However, the average lability of the MAP of the NTS lesion group during either 1-hour or 24-hour recording periods was significantly greater than that of the SAD group. In addition, there was a notable difference in the characteristics of the lability of the MAP between the groups.
FIGURE 1. Hourly averages (means) and the standard deviation of the mean arterial pressure (lability) computed from 24-hour continuous pressure recordings in rats with sinoaortic denervation (SAD) or nucleus tractus solitarii (NTS) lesions and control (CON) rats. Values represent mean ± SEM.

(Figure 3). Fluctuations in MAP as large as 160 to 180 mm Hg were observed in some rats with NTS lesions. These changes consisted of both pressor and depressor responses and often were unassociated with movement or the occurrence of any overt environmental stimuli. The range of change in the arterial pressure of SAD rats was more restricted than that of the NTS lesion group, with changes in MAP only occasionally exceeding 60 to 80 mm Hg. Moreover, depressor responses seemed to occur much more frequently than pressor responses. The depressor responses often were associated with postural adjustment or ambulation. In contrast to the SAD or NTS lesion rats, the MAP of control rats was relatively stable.

Frequency histograms of 1-hour (not shown) and 24-hour arterial pressure recordings from control rats typically showed narrow ranges and prominent peaks (Figure 4). The frequency histograms of SAD and NTS lesion rats demonstrated a much wider dispersion of pressures. Since an apparent flattening and skewing of the MAP frequency distributions of SAD and NTS lesion rats was observed, tests of skewness ($G_1$) and kurtosis ($G_2$), as described by McNemar and Snedecor, were applied to each 1-hour and 24-hour MAP frequency distribution for all rats. Skewness or kurtosis, or both, is present if the value of $G_1$ or $G_2$ deviates significantly from zero. Evaluation of the 24-hour recordings revealed a significant negative skewing.

### Table 1. Comparison of the Mean and Standard Deviation (an Index of Lability) of the Mean Arterial Pressure with the Median and Average Absolute Deviation (an Index of Lability) of the Mean Arterial Pressure in the Three Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean MAP (mm Hg)</th>
<th>SD MAP (mm Hg)</th>
<th>Median MAP (mm Hg)</th>
<th>AAD MAP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 hour</td>
<td>24 hours</td>
<td>1 hour</td>
<td>24 hours</td>
</tr>
<tr>
<td>Control (n=12)</td>
<td>115±2</td>
<td>117±2</td>
<td>6.2±0.5</td>
<td>7.9±0.4</td>
</tr>
<tr>
<td>SAD (n=12)</td>
<td>125±3*</td>
<td>124±3*</td>
<td>22.5±1.9*</td>
<td>22.0±1.7*</td>
</tr>
<tr>
<td>NTS lesion (n=10)</td>
<td>115±4</td>
<td>114±3</td>
<td>28.5±2.2†</td>
<td>28.9±2.1†</td>
</tr>
</tbody>
</table>

Values are means ± SEM. MAP = mean arterial pressure; SD MAP = standard deviation of the MAP; AAD MAP = average absolute deviation of the MAP; SAD = sinoaortic denervation; NTS = nucleus tractus solitarii.

*p < 0.05 compared with control and NTS lesion groups.

†p < 0.05 compared with control group.
FIGURE 2. Distribution of the means of the individual 24-hour recordings of mean arterial pressure of control (CON; n = 12) rats and rats with sinoaortic denervation (SAD; n = 12) or nucleus tractus solitarii (NTS) lesions (n = 10). One-hour recordings (not shown) yielded similar distributions. The variance of the distribution of the means of the rats with SAD was significantly greater than that of the other groups. Circles with bars indicate group mean ± SEM. Star indicates significant group differences (p < 0.05).

(n = 12; mean $G_i = -0.4203 \pm 0.0599$) of the MAP distributions of SAD rats. In contrast, a significant positive skewing of the MAP distributions of NTS lesion (n = 10; mean $G_i = 0.2292 \pm 0.0469$) rats was observed. Although not readily apparent on visual examination, the MAP frequency distributions of the control rats also exhibited a significant positive skew (n = 12; mean $G_i = 0.4405 \pm 0.0581$). Moreover, the negative skew of the 24-hour MAP frequency distributions of SAD rats was significantly different from the positive skew of the MAP distributions of the control and NTS lesion rats. However, no difference in the skewness of the MAP frequency distributions was observed between control and NTS lesion rats. Tests of kurtosis confirmed the visually prominent peaking of the 24-hour MAP distributions of control rats (n = 12; mean $G_2 = 1.3632 \pm 0.722$) and the noticeable flattening of the MAP distributions of SAD (n = 12; mean $G_2 = -0.1133 \pm 0.120$) and NTS lesion (n = 10; mean $G_2 = -0.2574 \pm 0.2130$) rats. Statistical analysis indicated that the MAP distributions of the SAD and NTS lesion rats were significantly flattened in comparison to the peaked distributions of the control rats. The skewness and kurtosis of the MAP distributions from the 1-hour recordings were not different from those calculated from the 24-hour recordings.

The negatively skewed MAP frequency distributions of SAD rats reflected the increased frequency of occurrence of depressor responses in SAD rats. This type of frequency distribution was observed in all SAD rats regardless of their average MAP or the duration of the recording period. In contrast, both control and NTS lesion rats exhibited a somewhat greater ratio of pressor to depressor events that produced a slight positive skewing of their MAP frequency histograms (see Figure 4).

Because the frequency distributions of MAP for all groups exhibited significant skewing that could influence the mean value of each distribution, we felt it necessary also to evaluate the median of each frequency distribution, since this measure is not influenced by extreme scores or deviations in symmetry. Table 1 shows the average median value and the average absolute deviation (AAD), an index of lability, of the MAP for the 1-hour and 24-hour recordings for each group. The AAD from the median is analogous to the SD from the mean as an index of dispersion.35 Despite the significant skewing of the MAP frequency distributions, little difference was found between the average mean and median values of the MAP for any of the groups.

FIGURE 3. Continuous arterial pressure and heart rate recordings from representative control (CON; n = 12) rats and rats with nucleus tractus solitarii (NTS) lesions (n = 10) or sinoaortic denervation (SAD; n = 12). Note that the increased variability of the rats with NTS lesions was characterized by both depressor and pressor responses, while the rats with SAD exhibited primarily depressor responses.
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Figure 4. Frequency histogram distributions calculated from 24-hour recordings of mean arterial pressure in rats from the control (n = 12), sinoaortic denervation (SAD; n = 12), and nucleus tractus solitarii (NTS) lesion (n = 10) groups. Only the data of three rats from each group were selected for display for purposes of clarity and because their mean level and lability of mean arterial pressure were representative of their group averages. The average and the standard deviation (SD, an index of lability) of the mean arterial pressure are shown above each plot.

Nonparametric analysis of the median and AAD of the MAP revealed the same relationships between 1-hour and 24-hour recordings and between groups as were found by parametric analysis of the mean and SD of the MAP (see Table 1).

No significant differences in the mean HR or HR variability were found between the three groups for either 1-hour or 24-hour recordings (Figure 5, Table 2). However, the HR and HR variability for all groups were higher at night when the rats were more active (see Figure 5). Thus, the mean HR and HR variability for all groups were significantly higher during the 24-hour as compared with the 1-hour recordings. No consistent deviation in the symmetry of the HR frequency distributions was noted for any of the groups, and nonparametric analyses of these data were not performed. Table 2 shows the average median and AAD of the HR for each group, which generally reflected the same pattern of responses presented by the mean and SD of the HR. No correlation was found between the MAP and HR for any group.

Localization of Lesions

Figure 6 depicts the site of maximum damage caused by electrolytic lesions of the NTS. The average size of the lesions is shown along with the boundary of the single largest lesion found in any rat. The lesions destroyed the solitary tract and much of the medial NTS. Minor and more variable damage was done to the lateral NTS and dorsal motor nucleus of the vagus in some rats. The site of maximum damage of the lesions was located 8 ± 32 μm rostral to the obex, with an average rostral-caudal extent of 515 ± 36 μm. The average diameter of the lesions was 373 ± 34 μm.

Discussion

The results of the present study indicate that SAD and lesions of the NTS effectively disrupted normal baroreceptor reflex function. This effect was demonstrated in both groups by the lack of reflex bradycardia to a drug-induced pressor response and the destabilization of the arterial pressure, the hallmark of baroreceptor deafferentation. Evaluation of short-term and long-term measurements of cardiovascular activity indicated that 1-hour continuous recordings assessed the changes in arterial pressure regulation associated with central or peripheral baroreceptor denervation as adequately as 24-hour continuous recordings. Both measurement periods revealed a small but significant elevation of the average MAP only in SAD rats. The average MAP of the NTS lesion rats did not differ from that of control animals, thus confirming our earlier findings.23 There was a significant increase in the lability of the MAP for both SAD and NTS lesion rats. However, NTS lesion rats showed significantly greater arterial pressure variability than SAD rats. Furthermore, the characteristics of the MAP frequency distributions of NTS lesion, SAD, and control rats were markedly different. The MAP frequency histograms of SAD rats exhibited a pronounced negative skew, while those of control and NTS lesion rats had a positive skew. The observed changes in arterial pressure regulation after central or peripheral baroreceptor denervation were not associated with any change in HR or HR variability.

To our knowledge, the only investigation that directly compared the long-term effects of NTS lesions and SAD on mean arterial pressure was performed on dogs; both procedures were found to produce sustained hypertension.12 These results disagree with our current findings on the chronic effects of NTS lesions and SAD in rats and with the more recent studies on the effects of the SAD procedure in dogs6 and rats.13 The reason for this disparity may be that in the former study the average MAPs of SAD and NTS lesion dogs were determined by recording a single value of the arterial pressure only during periods in which pressure remained stable for at least 10 minutes. Since the hall-
FIGURE 5. Hourly averages (means) and the standard deviation (lability) of the heart rate computed from 24-hour continuous pressure recordings in rats with sinoaortic denervation (SAD) or nucleus tractus solitarii (NTS) lesions and control (CON) rats. Values represent mean ± SEM.

TABLE 2. Comparison of the Mean and Standard Deviation (an Index of Lability) of the Heart Rate with the Median and Average Absolute Deviation (an Index of Lability) of the Heart Rate in the Three Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean HR (beats/min)</th>
<th>SD HR (beats/min)</th>
<th>Median HR (beats/min)</th>
<th>AAD HR (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 hour</td>
<td>24 hours</td>
<td>1 hour</td>
<td>24 hours</td>
</tr>
<tr>
<td>Control (n=12)</td>
<td>363 ± 10</td>
<td>378 ± 8*</td>
<td>36.4 ± 3.5</td>
<td>44.6 ± 2.9*</td>
</tr>
<tr>
<td>SAD (n=12)</td>
<td>383 ± 9</td>
<td>397 ± 7*</td>
<td>28.9 ± 3.2</td>
<td>34.7 ± 2.7*</td>
</tr>
<tr>
<td>NTS lesion (n=10)</td>
<td>372 ± 7</td>
<td>378 ± 8*</td>
<td>31.5 ± 2.5</td>
<td>36.4 ± 1.7*</td>
</tr>
</tbody>
</table>

Values are means ± SEM. HR = heart rate; SD HR = standard deviation of the HR; AAD HR = average absolute deviation of the HR. See Table 1 for key to other abbreviations.

*The combined group averages of the 24-hour sessions were significantly greater than those from the 1-hour sessions, as indicated by a significant sessions effect with analysis of variance, p < 0.05.

Figure 6. Line drawing of coronal section of the caudal medulla at the level of the obex showing the site of maximum damage caused by electrolytic lesions of the nucleus tractus solitarii. The average size of the lesion (cross-hatched area) is shown, surrounded by the boundary (broken line) of the single largest lesion found in any rat. AP = area postrema; Io = inferior olive; Na = nucleus ambiguus; NTS = nucleus tractus solitarii; NTSV = nucleus tractus spinalis trigemini; nX = dorsal motor nucleus of the vagus nerve; nXi = nucleus of the hypoglossal nerve; Ts = tractus solitarius; TV = tractus spinalis trigemini.

Mark of baroreceptor denervation appears to be a marked instability of the arterial pressure, it is debatable whether single measurements made only during brief periods of pressure stability provide an accurate estimate of the actual time-averaged MAP. Furthermore, such a measurement procedure precludes the evaluation and comparison of the variability of the arterial pressure produced by central and peripheral interruption of the baroreceptor reflexes.

Cowley et al. proposed that long-term continuous recordings are necessary to determine accurately the average level and lability of the arterial pressure in baroreceptor-denervated animals. They suggested that in previous studies the hypertension observed after SAD was due to intrusive measurement procedures or brief recording periods, or both. Support for their hypothesis was provided by the findings that little or no elevation in MAP was found in dogs or rats after SAD when 24-hour continuous recordings of arterial pressure were made in an environment of low ambient pressure.
stimulation. However, no systematic comparisons were made between 24-hour recordings and measurement periods of shorter duration to determine if the long-term sessions were needed to characterize properly the altered hemodynamics of baroreceptor-denervated animals. We have demonstrated that 24-hour continuous recordings are not essential to assess accurately the average level and lability of the MAP in control, SAD, or NTS lesion rats. Continuous 1-hour recordings of arterial pressure provided a satisfactory estimate of the lability and actual long-term average of MAP. In fact, selection of any 1-hour average of the MAP or the SD of the MAP from the 24-hour recordings for any given group (see Figure 1) yielded a value that was highly similar to the 24-hour average computed for that group. Moreover, the significant skewing of the MAP distribution of all groups appeared to have little impact on the average level of the MAP. Comparable results were obtained from 1-hour and 24-hour recordings regardless of whether the mean or median value of each MAP frequency distribution was used (see Table 1). Thus, our results agree with those of Fink et al.,31 who found that brief daily recordings of intra-arterial pressure produced an average MAP that was the same as that calculated from continuous 24-hour recordings. However, their measurement procedure precluded assessment of the variability of the MAP during short-term recording sessions.

Although measurement periods of relatively short duration appear to be adequate for the determination of the average level and lability of the MAP, they may not accurately reflect the long-term average HR and HR variability in the rat. As shown in Table 2, the mean levels of HR and HR variability, regardless of group, were significantly higher when calculated from the 24-hour recordings as compared with the 1-hour recordings. The 1-hour cardiovascular recordings in the present study were always made during the late morning and early afternoon hours, which generally corresponded with the time of least activity and lowest HRs (see Figure 5). Since HR is strongly influenced by somatomotor activity,25 recording sessions that include periods of high activity (night) as well as low activity would be expected to yield higher values for the average HR and HR variability.

Several studies have reported a significant increase in arterial pressure after SAD in the rat.11,13,33 However, Norman et al.13 showed that chronic SAD rats were not hypertensive when 24-hour measurements of arterial pressure were made in an environment of low ambient stimulation. Data from another study also suggested that sustained hypertension was not present after chronic SAD in rats, since no structural changes in the heart or vasculature were detected.34 A recent report did find significant ventricular hypertrophy after SAD, but only in male rats.33 In the current investigation, we found a small but significant increase in the average MAP of the SAD group 3 to 4 weeks after denervation. The MAP of the SAD group was higher in comparison to the control and NTS lesion groups even when 24-hour recordings were made under the same environmental conditions. Other studies have shown that after peripheral disruption of the baroreceptor reflexes, some animals exhibit an elevated MAP while others remain normotensive.6,14,35 We found that the MAP of the SAD group was increased because half the rats had an average MAP higher than the highest value exhibited by either NTS lesion or control rats (see Figure 2). Thus, the controversy over whether hypertension is observed after chronic SAD may, to some extent, depend on the relative balance between the number of animals that exhibit an elevated arterial pressure and those that do not.

The reason for the elevated arterial pressure in some rats after SAD is unknown. One possibility may be that the level of the MAP after SAD may depend on the preSAD blood pressure and baroreceptor reflex function. We did not determine preSAD arterial pressure and baroreceptor reflex function because of the technical difficulty in maintaining patent cannulas in rats for the extended periods required for both predenervation and postdenervation measurements. However, the BRS of SAD rats that were normotensive was not significantly different from that of SAD rats that exhibited an elevated MAP. Alternatively, we evaluated only the cardiometer component of the baroreceptor reflexes. Thus, it is possible that sufficient reflex control of vasomotor tone remained in some SAD rats such that normotensive arterial pressures were maintained. This may have occurred because aberrantly coursing arterial baroreceptor afferents were carried in the vagi of some rats. However, other investigators have suggested that increased MAP lability is indicative of disrupted baroreceptor reflex function.5,7 Therefore, the possibility that selective cardiometer baroreceptor denervation occurred seems unlikely since the increase in the lability of the MAP was reasonably uniform for all SAD rats.

The slightly elevated arterial pressures seen in some of the SAD rats could be due to inadvertent destruction of cardiopulmonary afferents carried in the vagus. Typically, SAD animals are quite hypertensive initially,15-17 but eventually arterial pressure falls to nearly normal levels.15,18 It has been hypothesized that the reduction of arterial pressure after the initial hypertensive stage in SAD animals may be due to tonic inhibition of sympathetic activity by cardiopulmonary afferents.18,19 Kezdi et al.38 have shown increased C-fiber activity from cardiopulmonary receptors after SAD in dogs and suggest this may be sufficient to return pressure to normal or near normal levels. However, Walgenbach and Donald39 found that, although cardiopulmonary reflexes do exert tonic vasomotor inhibition, this is insufficient to maintain pressure near normal levels in the absence of the arterial baroreceptor reflexes. Furthermore, if damage to the cardiopulmonary reflexes accounted for the mild hypertension in some rats after SAD, then the arterial pressure of all rats with NTS lesions should be similarly elevated, since vagal afferents project densely to the area of the NTS that is consistently destroyed by the lesion.18 However, as we have demonstrated here and in a pre-
vious study, rats in which NTS lesions were placed several weeks earlier have normotensive pressures. Therefore, some mechanism other than disruption of cardiopulmonary reflexes must be responsible for the differential elevation of arterial pressure after SAD.

Arterial pressure was more variable after lesions of the NTS than after SAD. It is possible that the presence of intact cardiopulmonary reflexes in the SAD preparation may continue to partially buffer moment-to-moment changes in arterial pressure. As mentioned before, the dense projections of the cardiopulmonary afferent fibers to the NTS should have been destroyed by placement of the lesions. Thus, the greater lability of the MAP in NTS lesion rats could be due to the combined disruption of the baroreceptor and cardiopulmonary reflexes. However, the findings of two studies fail to support this argument. First, Thoren suggests that the slowly reacting cardiopulmonary receptors seem to be relatively insensitive to the moment-to-moment changes in blood pressure seen after baroreceptor denervation. Second, Walgenbach and Donald recently showed that cardiopulmonary deafferentation did not affect the lability of the arterial pressure in dogs, in either the presence or absence of functioning arterial baroreceptor reflexes. Therefore, it is doubtful that concomitant destruction of the baroreceptor and cardiopulmonary reflexes contributed markedly to the differences in the lability of arterial pressure of the SAD and NTS groups. A more likely explanation may be attributed to the destruction by the lesions of second-order neurons in the NTS and fibers of passage from other areas of the brain involved in cardiovascular regulation.

We do not know the exact mechanism (or mechanisms) responsible for the difference in the shape of the MAP frequency distributions of SAD and NTS lesion rats. However, we noted that depressor responses were frequently associated with changes in body position or locomotion in SAD rats, an observation made in several other studies. In contrast, the direction of change in the MAP of NTS lesion rats was not necessarily related to such behavior. Sinoaortic-denervated rats have been shown to exhibit augmented vasodepressor responses to centrally applied catecholamines. Since SAD does not affect the integrity of neurons on which baroreceptor afferents terminate, an enhanced vasodepressor response to central catecholamines could be a consequence of both a loss of baroreceptor reflex feedback and an increased catecholamine sensitivity of medullary neurons involved in cardiovascular regulation. Although the role of central catecholamines in movement-related cardiovascular adjustments is unknown, the increased frequency and magnitude of depressor events in SAD rats may be dependent on the disruption of normal somatomotor-baroreceptor reflex integration. Alexander et al. recently proposed a link between cortico-somatomotor integration and baroreceptor reflex function by demonstrating a reduction in tyrosine hydroxylase activity and dopamine content in the caudate and substantia nigra of SAD rats. Furthermore, group III and IV muscle afferents involved in cardiopulmonary adjustments to exercise have been shown to project directly to the medial NTS at the level that baroreceptor afferents also terminate. Because NTS lesions destroy the primary terminations and many of the second-order neurons mediating baroreceptor input, the ability of other structures to influence or be influenced by the activity of these cells is lost. Thus, the more extensive destruction by the lesions of pathways involved in sympathetic modulation are probably responsible for the difference in the characteristics of arterial pressure lability after central versus peripheral baroreceptor denervation.

In summary, we have demonstrated that short-term continuous recordings of arterial pressure and HR can provide an accurate estimate of the changes in cardiovascular regulation of either centrally or peripherally baroreceptor-denervated rats. We found that only SAD produced a significant increase in the average MAP. However, the magnitude of the elevation of arterial pressure may be somewhat fortuitous. In the present study, only a mild hypertension was noted in the SAD group because half of the rats had elevated arterial pressures, whereas the other half were normotensive. Other studies reporting more severe hypertension may have contained a greater proportion of animals with elevated arterial pressures. We also showed that both central and peripheral disruption of the baroreceptor reflexes produced a significant increase in the lability of the MAP. However, arterial pressure was significantly more variable after NTS lesions than after SAD. The lability of arterial pressure of SAD rats depended largely on brief, movement-related depressor responses that resulted in a negative skewing of their MAP frequency distributions. Rats with NTS lesions exhibited a greater incidence of pressor responses, yielding a slight positive skew in their MAP frequency distribution similar to that of control rats. Although the differences in the average level and lability of the MAP of SAD and NTS lesion rats may depend on the actions of the cardiopulmonary reflexes, a more probable explanation may be ascribed to the additional destruction by the lesions of central neurons and pathways participating in cardiovascular regulation.

Acknowledgments

We thank Tony Wen and LuAnn Laubach for their excellent technical assistance during the conduct of this study and Joann Faulconnier, Anna Aaron, and Hilda Gutierrez for the preparation of this manuscript.

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Hypertension. 1986;8:1154-1163
doi: 10.1161/01.HYP.8.12.1154

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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