Central Effect of Intravenous Phenylephrine on Baroreflex Control of Renal Nerves

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SUMMARY Responses of renal sympathetic nerve activity were determined in eight chloralose-anesthetized rabbits during sustained (1-3 minutes) increases in arterial pressure induced by phenylephrine infusion, and as arterial pressure returned to control. In four of the eight experiments, aortic baroreceptor traffic was also recorded. When arterial pressure was raised from 81 ± 5 to 110 ± 7 mm Hg, renal nerve activity decreased from 30 ± 7 to 1 ± 1 imp/sec. Aortic nerve activity increased from 208 ± 35 to 346 ± 49 imp/sec. When pressure returned to control (81 ± 5 mm Hg), renal nerve activity remained inhibited (7 ± 2 imp/sec), even though aortic nerve activity had also returned to control (195 ± 33 imp/sec). Arterial pressure and traffic in the renal and aortic nerves returned to control over the succeeding 1 to 5 minutes. Transient increases in arterial pressure (lasting less than 1 minute) due to bolus injections of phenylephrine resulted in inhibition of renal nerve traffic followed by rapid recovery. In five rabbits with aortic and vagal nerves sectioned and both carotid sinuses isolated from the circulation, intravenous phenylephrine infusion augmented the gain of the isolated carotid baroreflex (particularly at low carotid sinus pressures). In nine experiments, injection of phenylephrine (0.01, 0.1, or 1.0 /xg) into the lateral ventricles did not change the basal renal nerve traffic but augmented the gain of the baroreflex control of the renal nerves. Our data indicate that peripherally infused phenylephrine can alter the arterial baroreflex control of the renal nerves by a central effect. The similar influence of infracerebroventricular phenylephrine on baroreflex control of the renal nerves is consistent with this view. (Hypertension 6: 906-914, 1984)

KEY WORDS • phenylephrine • rabbits • carotid baroreflex • vagi • infracerebroventricular • alpha adrenergic receptors

INCREASES in arterial pressure augment the discharge of arterial baroreceptors and result in baroreflex inhibition of sympathetic nerve activity.1 When pressure returns from an elevated level toward the control level, the arterial baroreceptor discharge decreases. In fact, because of hysteresis effects, one would expect less baroreceptor discharge at a given pressure when the pressure was falling than when it was rising.2 Thus, the expected reflex response would be that, as the pressure returned to control, sympathetic nerve activity at a given pressure would be higher when the pressure was falling than when it was rising. Put another way, hysteresis in the baroreceptors might be expected to translate into hysteresis in the baroreflex control of sympathetic outflow.

In preliminary studies, we found that when we raised arterial pressure transiently, the expected hysteresis effects were apparent in the responses of efferent renal sympathetic nerves. Surprisingly, when the pressure was raised by phenylephrine infusion for a sustained period (1 or more minutes), we noted that renal nerve activity failed to increase as anticipated during the drop of pressure toward control. This suggested to us the possibility that there are determinants of baroreflex control of sympathetic outflow during phenylephrine-induced increases in arterial pressure for which one cannot account based solely on baroreceptor input to the central nervous system. The major goal of this study was to determine if the sustained pressure elevation resulting from phenylephrine infusion modifies baroreflex control of sympathetic outflow to the kidney and to determine if this effect is mediated through an influence of phenylephrine on the baroreceptors, on
the central nervous system, or both. Our initial experiments suggested a central effect of infused phenylephrine on baroreflex control of the renal nerves. A second set of experiments supported this view. A final set of experiments demonstrated that intracerebroventricular injection of very small doses of phenylephrine mimicked the effects of systemic phenylephrine on baroreflex control of the renal nerves.

**Methods**

Adult New Zealand White rabbits weighing 2.5 to 3.5 kg were anesthetized initially with thiopental sodium, 30 mg/kg intravenously (i.v.), followed by alpha chloralose, 80 mg/kg i.v. Supplemental doses of chloralose, 10 mg/kg i.v. were given hourly. During the protocol, muscular activity was abolished with decamethonium bromide. After endotracheal intubation, the animals were ventilated artificially with room air supplemented with oxygen at a tidal volume of 10 ml/kg and at a frequency of 20 to 25 cycles/min. Arterial blood gases and pH were determined at intervals, and ventilatory rate was adjusted to keep pH between 7.45 and 7.55, PCO$_2$ between 25 and 40 mm Hg, and PO$_2$ in excess of 100 mm Hg. Body temperature was maintained by external warming.

**Preparations**

The left flank was opened to expose the left renal nerves. A branch of the nerves was separated from the surrounding connective tissue, cut distally, desheathed, and covered with mineral oil for subsequent recording of action potential from the central cut end of the nerve. In four experiments, the responses to phenylephrine-induced hypertension were determined after bilateral vagotomy. In these experiments, the vagi were identified by inspection in the midcervical region and then looped with silk threads for subsequent section. In four of eight experiments, the left aortic depressor nerve was identified near its junction with the superior laryngeal nerve and prepared for recording as outlined above. The nerve was left intact.

In five experiments, the aortic and vagal nerves were sectioned bilaterally, and both carotid sinuses were vascularly isolated from the circulation. A cannula connected to a pressor reservoir was positioned in each common carotid artery for control of pressure in the isolated sinuses. The reservoir was filled with a physiological salt solution equilibrated with 95% O$_2$, 5% CO$_2$, and buffered to pH 7.4.

In 19 experiments, phenylephrine or norepinephrine was injected intracerebroventricularly (i.c.v.). These injections were accomplished by placing the rabbit in a stereotaxic frame and by positioning a cannula in a lateral ventricle. The coordinates of the cannula in relation to the Bregma were 1.5 mm posterior, 3.3 mm lateral, and at a depth of 10 mm. The position of the cannula in the lateral ventricle was confirmed by the staining of all four ventricles following injection of 0.1 ml of methylene blue at the end of the experiment.

**Recording and Quantification of Nerve Traffic**

Recordings of renal nerve traffic were made from small branches of the left renal nerves or from bundles of fibers obtained from the nerves, and from the left aortic nerve. The nerves were placed on platinum irridium or on silver-silver chloride bipolar electrodes for subsequent recording of traffic. The techniques for amplification and quantification of renal nerve traffic have been presented previously in detail. In brief, the action potentials in the renal and aortic nerves were amplified by Grass band pass amplifiers (P51 U). The amplified signals were then fed into an oscilloscope so that the signals could be viewed, into an audio amplifier so that changes in nerve traffic could be detected via audible signal, and into a nerve traffic analyzer which discriminated each spike which exceeded a preselected level (just above the noise). Each spike that crossed the lower window discriminator level triggered a voltage step that was independent of spike amplitude. This counter was designed to quantitate traffic from two nerves simultaneously. These voltage steps then were integrated by the nerve traffic analyzer, which is digital in design and can integrate linearly at instantaneous spike frequencies up to 10 kHz. The raw renal and aortic electroneurograms along with the integrator outputs from the spike counter were displayed on an 1858 Visicorder (Honeywell, Denver, Colorado) or an electrostatic (ES 1000) recorder (Gould, Cleveland, Ohio).

**Protocols**

**Study 1**

The first experiments were conducted to determine if there is a difference between baroreflex-induced changes in renal traffic during transient in contrast to sustained phenylephrine-induced increases in arterial pressure. Pressure was raised transiently (for less than 1 minute) by bolus injection (n = 5) of phenylephrine (6-20 /l/kg). More sustained pressure elevations (n = 8) were achieved by phenylephrine infusion (10-20 /Ag/min). In the latter case, pressure was raised until renal nerve activity was abolished or nearly so, and the infusion was continued for 1 to 3 minutes. Then the phenylephrine infusion was discontinued, and renal nerve activity was recorded as pressure returned to or below control. Arterial pressure was monitored with a PE 50 catheter positioned via the femoral artery in the aorta and connected to a Century Technology pressure transducer.

**Study 2**

The second group of experiments was conducted to determine if the effect of sustained pressure elevation with phenylephrine resulted from an effect on the baroreceptors or in the central nervous system. In five experiments, the pressure in the vascularly isolated carotid sinuses was raised from 50 mm Hg to a higher pressure (105, 125, 145, 165, 185, or 205 mm Hg) for 20 seconds and returned to 50 mm Hg. This was repeated for each pressure indicated above. The pressure
was returned to 50 mm Hg before proceeding with the next pressure step to minimize rapid resetting of carotid baroreceptors. After determination of responses under control conditions, phenylephrine was infused intravenously for 2 minutes to raise pressure as in the protocol outlined above. The phenylephrine was then turned off, the pressure was allowed to return to control, and the carotid baroreflex stimulus-response relationship was determined again.

Study 3

The final group of experiments was conducted to determine if: 1) centrally administered phenylephrine could alter the gain of baroreflex control of renal nerve traffic; 2) this effect could also be induced by another alpha-adrenergic agonist; and 3) the effect could be blocked by central alpha-adrenergic blockade. In these experiments, arterial pressure was raised by abdominal aortic occlusion (for 30 seconds) and lowered by i.v. nitroglycerin infusion (15 fig). The vagi were cut in all experiments before starting the protocol. Basal values of arterial pressure and renal nerve traffic were obtained at least 20 minutes following the completion of the preparation. Responses of renal nerve traffic to changing arterial pressure were determined after i.c.v. saline (0.1 ml) and following i.c.v. phenylephrine (0.01, 0.1, or 1.0/Ag) or norepinephrine (0.01, 0.1, or 1.0/Ag). Aortic occlusions and nitroglycerin administration were performed in a similar fashion, after each injection of saline, phenylephrine, or norepinephrine. Each i.c.v. injection was separated from the previous injection by 15 minutes.

In four animals, saline (0.1 ml) was injected i.c.v. four times, and the baroreflex control of the renal nerve traffic was assessed after each injection of saline. These experiments served as controls for the effects of time and repeated i.c.v. injections on arterial baroreflex control of renal nerve traffic. After the fourth saline injection in these control animals, we injected i.c.v. the alpha-adrenergic receptor blocker phenolamine (5.0/Ag in O.1 ml in two animals and 50/Ag in O.1 ml in two animals), to determine if this would prevent the effect of i.c.v. phenylephrine (1.0/Ag in 0.1 ml) on baroreflex gain.

The i.c.v. nitroglycerin had no effect on basal arterial pressure or renal traffic. We did not test the effect of i.c.v. nitroglycerin on baroreflex gain.

Statistical Analysis

For Study 1, we determined the values for control, for maximum inhibition of renal activity, when mean arterial pressure initially had returned to control, and when renal nerve activity approached control. Each value was obtained from a 10-second recording period under steady-state conditions. The difference between control and interventions was determined by Bonferroni’s test for multiple comparisons.

For Study 2, the difference in responses to changes in isolated carotid sinus pressure during the last 10 seconds of each pressure step before and after phenylephrine infusion was determined by analysis of variance (ANOVA). Difference was considered to be significant for p < 0.05.

For Study 3, we compared the baroreflex gain (renal nerve traffic vs arterial pressure) after i.c.v. saline to the gain after i.c.v. phenylephrine, norepinephrine, or phentolamine followed by phenylephrine. Differences in responses were assessed by covariate ANOVA. Values of p < 0.05 were taken to be significant. Results are presented as means ± SE.

Results

In response to a sustained elevation in arterial pressure, renal nerve activity was inhibited, as expected (Figure 1). When the phenylephrine infusion was discontinued (Figure 1, second arrow), the pressure gradually returned toward control. Aortic nerve traffic fell toward control, yet renal nerve activity remained inhibited. Figure 2 summarizes the mean responses to 1 to 3 minutes of sustained elevation of arterial pressure followed by a gradual return to control. After maximal inhibition of renal nerve activity, the pressure continued to rise to 125 ± 3 mm Hg; it held at this level for 60 to 90 seconds and then returned to control. Renal nerve activity remained inhibited even when arterial pressure had returned to control. After an additional period of 1 to 5 minutes (mean 3.7 ± 1.5), renal nerve activity also recovered. In four of eight experiments, aortic nerve traffic was recorded simultaneously with renal nerve activity and, as expected, increased during phenylephrine infusion. When pressure returned to control, aortic nerve activity also returned to control, yet renal nerve activity remained inhibited.

In four of the eight experiments, the vagi were sectioned (aortic nerves intact) before the start of the protocol, and the results are summarized in Figure 2 as pooled data from all eight experiments. In two of the eight experiments, similar responses were observed before and following vagotomy. Thus, the effect of intravenous phenylephrine was not mediated by vagal afferent pathways.

In contrast to the effect of a sustained increase in arterial pressure, transient increases in pressure and inhibition of renal nerve activity were followed by rapid recovery of nerve activity as the pressure fell (Figure 3). In the recording shown in Figure 3, we see that the renal nerve activity had already returned to control at a time that the arterial pressure was above control. Similar results were obtained in five additional experiments (Figure 4). Aortic nerve traffic was recorded in four of these experiments. Following transient increases in arterial pressure, renal and aortic traffic recovered promptly.

Figure 5 contrasts the responses of renal nerve traffic and mean arterial pressure to changing isolated carotid sinus pressure before and after phenylephrine infusion. In these experiments, we determined the isolated carotid baroreflex stimulus vs response relationship, and then we infused phenylephrine to raise the mean arterial pressure above 100 mm Hg for 60 to 90 seconds. The infusion then was discontinued, pressure allowed
FIGURE 1. Continuous record of (top to bottom) integrated aortic nerve activity, aortic electro-neurogram, integrated renal nerve activity, arterial pressure, and renal electroneurogram. In the upper half of the figure, arterial pressure was raised with phenylephrine infused beginning with the first arrow and discontinued at the second arrow (lower half). This resulted in the expected increase in aortic and reflexive decrease in renal traffic. Mean arterial pressure was held at above 150 mm Hg for about 1 minute. Then, as shown in the lower trace, arterial pressure and aortic traffic returned toward control, without a return of renal nerve traffic. At the end of the record, mean arterial pressure was 90 mm Hg, and renal nerve traffic was less than 5 spikes/sec. At the same mean pressure near the beginning of the record (10-15 seconds after starting phenylephrine), renal nerve traffic was greater than 20 spikes/sec.

to return to control, and the stimulus-response relationship was determined again. Inhibition of renal nerve traffic by the isolated carotid sinus baroreflex was greater following phenylephrine infusion. The sensitivity (slope) of the baroreflex stimulus vs response relationship for renal nerve traffic was augmented after phenylephrine, but the plateau portion of the curve was not altered. The isolated carotid baroreflex control of the mean arterial pressure also tended to be augmented after phenylephrine infusion. However, responses of arterial pressure may be a less reliable index of baroreflex gain after phenylephrine infusion, for some residual effects of the drug on the peripheral circulation may persist. The mean values for basal mean arterial pressure and renal nerve traffic were 65 ± 5 and 75 ± 10 mm Hg and 78 ± 9 and 87 ± 15 imp/sec before and after phenylephrine infusion, respectively. These basal values were not significantly different. In three of five experiments, the stimulus-response relationship was determined again 15 minutes after discontinuation of phenylephrine and was found to be similar to the control relationship.
FIGURE 2. Mean data (n = 8) for responses to a prolonged infusion of phenylephrine of (top to bottom) mean arterial pressure, renal nerve traffic, and aortic nerve traffic. Data are shown for control (C), for initial maximal inhibition of renal nerve traffic (MI), for the initial recovery of mean arterial pressure following cessation of phenylephrine infusion (MAPR), and for recovery of renal nerve traffic (RNAR). Note that renal nerve traffic remained significantly depressed despite recovery of mean arterial pressure and aortic nerve traffic (MAPR).

FIGURE 4. Mean data (n = 5) for responses to a bolus injection of phenylephrine of (top to bottom) mean arterial pressure, renal nerve traffic, and aortic nerve traffic. Note that recovery of arterial pressure was accompanied by recovery of both renal and aortic traffic (MAPR). The format is the same as in Figure 2. Note the difference in the response to a bolus injection of phenylephrine and that to the infusion of phenylephrine in Figure 2.

FIGURE 3. Responses to a transient increase in arterial pressure of (top to bottom) integrated renal nerve activity, arterial pressure, and renal electroneurogram. Note that renal nerve traffic was totally inhibited after arterial pressure had risen 5 to 10 mm Hg. As pressure returned toward control, renal traffic reappeared at pressures well above those that had totally inhibited the traffic as the pressure rose.
The gain of the arterial baroreflex control of the renal sympathetic nerve traffic (Figure 6) was significantly increased after the i.c.v. injection of 0.1 or 1 fig of phenylephrine and tended to be increased \((p = 0.07)\) after 0.01 fig i.c.v. The gains of the reflex following the three different doses of phenylephrine were not different, although there was a tendency for the biggest effect to occur following the i.c.v. injection of the largest dose. These i.c.v. phenylephrine doses induced increases in the gain of the baroreflex in the absence of changes in basal arterial pressure or renal nerve traffic (Table 1). The i.c.v. norepinephrine did not alter basal renal nerve traffic or arterial pressure (Table 1), but significantly augmented the gain of the arterial baroreflex control of the renal nerve traffic (Figure 7) following injection of 0.1 \((n = 6)\) and 1.0 fig \((n = 6)\), but not of 0.01 fig \((n = 6)\).

Saline (0.1 ml) was injected i.c.v. four times in four rabbits, and baroreflex gain was assessed following each injection. The i.c.v. saline did not alter the basal arterial pressure, renal nerve traffic (Table 1), or baroreflex gain \((-3.7 \pm 1.9, -3.6 \pm 1.6, -3.0 \pm 1.1,\) and \(-3.3 \pm 0.8\%/\text{mm Hg} \text{ change in arterial pressure}). After the fourth saline injection and baroreflex testing, phentolamine (5-50 fig) was injected i.c.v. This did not alter the basal renal nerve traffic, or mean arterial pressure (Table 1), or baroreflex gain (Figure 8). The i.c.v. phenylephrine (1.0 fig) injected after phentolamine also failed to alter the baroreflex gain (Figure 8).

**Discussion**

Our findings suggest that there is an important and previously undescribed central nervous effect of infused phenylephrine on baroreflex control of renal nerve traffic. This influence was apparent after a sustained period of pressure elevation, but not after transient increases in pressure. We speculate that this

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![FIGURE 5. Relationship \((n = 5)\) between isolated carotid sinus pressure and renal nerve traffic (upper graph) and mean arterial pressure (lower graph). Stimulus response relations were determined under control conditions (o) and following infusion of phenylephrine and recovery to control pressure (*). Vagi and aortic nerves were sectioned in these experiments. Carotid baroreflex inhibition of renal nerve traffic was potentiated after treatment with phenylephrine.](image-url)

![FIGURE 6. Relationship \((n = 8)\) between changes in renal nerve activity (ordinate, &RNA, %) and changes in mean arterial pressure (abscissa, hMAP) during nitroglycerin-induced hypotension and aortic occlusion-induced hypertension after intracerebroventricular injections of saline (o) or phenylephrine (PE) 0.01 fig (o), 0.1 fig (L), and 1.0 fig (Q). The gain of the baroreflex increased from the initial value with saline \((-2.5 \pm 0.9 \%/\text{mm Hg})\) to PE 0.01 fig \((-3.3 \pm 0.61 \%/\text{mm Hg})\), PE 0.1 fig \((-4.0 \pm 0.8 \%/\text{mm Hg})\), and PE 1.0 fig \((-6.4 \pm 1.9 \%/\text{mm Hg})\) \(p = 0.07\) for PE 0.01 fig, and \(p < 0.05\) for 0.1 and 1.0 fig.](image-url)
difference was directly related to the quantity of phenylephrine that entered the brain. It was not mediated by vagal afferent pathways, since similar responses were observed in animals with the vagi sectioned or intact. It was not due to a central neural effect of phenylephrine that might be independent of the baroreflexes, since we found previously that vagotomy and denervation of the sinoaortic baroreceptors abolished changes in renal nerve activity during phenylephrine-induced increases in pressure in rabbits.

In addition, when we raised the arterial pressure with phenylephrine in the rabbits whose aortic and vagal nerves had been sectioned and whose carotid sinuses had been isolated from the circulation, there was no inhibition of renal nerve traffic. These observations also exclude any effects of phenylephrine on other peripheral sensory mechanisms as the basis of our findings.

The effect of phenylephrine on the baroreflex control of renal nerve traffic was not due to its effects on baroreceptors. We recorded aortic baroreceptor afferent traffic and detected no evidence of sensitization of these receptors by the infused phenylephrine (Figure 2).

The results of our experiments on rabbits with isolated carotid sinuses support the view that phenylephrine has a central effect on baroreflex control of the renal nerves. In these experiments, phenylephrine was excluded from the receptive regions so that the only remaining locations for its effect were the sympathetic ganglia, spinal cord, or brain.

How do the results of the isolated carotid sinus experiments (open loop) relate to the findings from our closed-loop studies? The isolated carotid sinus experiments indicated a marked sensitization of baroreflex control of renal nerve traffic by phenylephrine, particularly near the threshold end of the stimulus-response relationship. This accounted for the persistent inhibition observed in our closed loop experiments when pressure was returned to control after cessation of phenylephrine infusion. Thus, sensitization of the baroreflex by phenylephrine resulted in more prominent inhibition of renal nerve traffic at pressures that previously had resulted in only modest inhibition.

Although the closed- and open-loop baroreflex studies did not permit us to determine if the effects of prolonged phenylephrine infusion on the arterial baroreflex occurred in the brain, spinal cord, or sympathet-
ic ganglia, the results from the central injection of phenylephrine suggest that the brain was the likely site of the effect of systemic phenylephrine. We found that centrally injected phenylephrine augmented the gain of baroreflex control of renal nerve traffic. Similar findings were obtained with i.c.v. norepinephrine.

Finally, the effects of i.c.v. phenylephrine were prevented by central alpha-adrenergic blockade with phentolamine. There are important similarities between the effects of i.c.v. and systemically infused phenylephrine (open-loop isolated carotid sinus experiments). Both augmented the gain of the arterial baroreflex control of renal nerve traffic under circumstances in which neither basal arterial pressure nor renal nerve traffic was altered. These observations suggest that the phenylephrine, given i.c.v. or systemically, altered the baroreflex gain through a site(s) that has little tonic influence on arterial pressure or renal traffic even though it (they) significantly alters the baroreflex. Our experiments do not permit us to localize this effect to forebrain or hindbrain.

The findings we report here are consistent with the sympathoinhibitory effects reported previously for clonidine, a centrally acting $\alpha_2$ adrenergic receptor agonist that is thought to act, in part, by potentiating the arterial baroreflexes. Thus, our results are consistent with those that showed an augmented gain of the baroreflex control of the heart rate following clonidine administration. Unlike clonidine, central administration of phenylephrine does not change basal arterial pressure or sympathetic nerve activity. Thus, i.c.v. phenylephrine must act through stimulation of receptors other than just $\alpha_2$ receptors. Since both of the agonists (phenylephrine and norepinephrine) and the antagonist (phentolamine) that we used bind to both $\alpha_1$ and $\alpha_2$ adrenergic receptors, our experiments do not determine if one or both of these types of receptors account for the responses we observed. There has not, to our knowledge, been another study of the effect of central alpha-agonists (other than clonidine) on the baroreflex control of sympathetic outflow.

We did not report heart responses for any of our protocols, because the vagi was sectioned in most experiments. The heart rate either did not change or showed very small responses in these studies.

It is very unlikely that the effect of i.c.v. phenylephrine on baroreflex gain could be attributed to a leak of the drug into the systemic circulation. Doses of 0.01 or 0.1 $\mu$g injected systemically do not even alter arterial pressure or renal nerve traffic, and larger doses (1.0 $\mu$g) cause little or no changes in these variables.

It could be suggested that the effect on renal nerve traffic we observed following intravenous phenylephrine was due to stimulation of cardiac receptors with sympathetic afferents, since these receptors and their afferent pathways were intact in the experiments. This possibility seems unlikely to us. First, we have provided evidence in a preliminary report that there are no phenylephrine-induced changes in renal nerve traffic after vagotomy and sinoaortic denervation. Second, we have observed evidence for small, transient changes in sympathetic outflow to the hindlimb in rabbits with sinoaortic and vagal denervation during large phenylephrine-induced increases in arterial pressure (>40 mm Hg), greater than those induced in our experiments. Thus, if sympathetic afferents are activated during phenylephrine infusion, they appear to have, at most, small and transient reflex influences. In light of these observations, it is difficult to ascribe the effects we saw to activation of these sympathetic afferents. We cannot, however, completely exclude this possibility.

Our findings on the effects of prolonged phenylephrine infusion on baroreflex gain contrast strikingly with those reported by Richter and colleagues. They assessed the responses to sustained electrical stimulation of the carotid sinus nerves in anesthetized dogs. They found that high frequencies of stimulation caused an initial complete inhibition of sympathetic nerve traffic followed by a central escape from or adaptation to the inhibitory input from baroreceptor afferents. We have seen similar responses following electrical stimu-
lation of aortic nerves in rabbits (unpublished observation). The contrasting results of our closed-looped electrical stimulation experiments suggest an effect of phenylephrine on the baroreflex control of renal nerve traffic.

Our aortic nerve recordings point to a central effect of the infused phenylephrine, since we observed no sensitization of baroreceptors by phenylephrine. The isolated carotid sinus experiments strongly support the view that a central influence of phenylephrine on the baroreflex was increased under circumstances in which the phenylephrine was excluded from the receptive region. Finally, centrally administered phenylephrine mimicked the effect of systemic phenylephrine on the baroreflex control of renal nerve traffic.

Phenylephrine is used widely in the testing of baroreflex control of the sinus node. Our results indicate that studies on baroreflexes that employ phenylephrine should be limited to bolus administration or short-lasting infusions of this drug.

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