Role of Angiotensin II in the Neural Control of Renal Function

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Abstract—The aim of the present study was to distinguish between the direct effects of the renal nerves on renal function and indirect effects via neurally mediated increased systemic angiotensin II. We applied low-level electrical stimulation (1 Hz) to the left renal nerves in pentobarbitone-anesthetized rabbits for 180 minutes and measured renal blood flow, sodium excretion, and urine flow rate from both the stimulated and the nonstimulated contralateral kidney in the presence and the absence of ACE inhibition (enalaprilat). Stimulation resulted in an angiotensin II–mediated rise in arterial pressure and decreases in renal blood flow, urine flow rate, and sodium excretion on the stimulated side. On the nonstimulated denervated side, we found no change in renal blood flow, but found a decrease in urine flow rate. With ACE inhibition, renal stimulation no longer caused an increase in arterial pressure, the antidiuretic responses of the stimulated kidney were attenuated, and, importantly, the decrease in urine flow rate on the nonstimulated kidney was completely abolished. We therefore propose that although a direct effect of the renal nerves on sodium excretion is clearly present, the antidiuresis and antinatriuresis observed during renal activation is further supported by a neurally mediated increase in systemic angiotensin II. (Hypertension. 2003;41:583-591.)

Key Words: sympathetic nerve activity ● renal blood flow ● rabbit ● antidiuresis ● antinatriuresis

An increasing number of studies suggest an important role for renal sympathetic nerve activity (RSNA) in the maintenance of renal function and arterial pressure. Renal denervation prevents the increase in arterial pressure with high dietary salt in rabbits with low baroreflex sensitivity,1 and in rats, renal denervation leads to a sustained reduction in arterial pressure when measured via telemetry.2 It has been suggested that the effect of RSNA on arterial pressure is, at least in part, mediated through the regulation of basal angiotensin II levels.3 Chronic intrarenal infusion of noradrenaline in dogs produces a sustained increase in arterial pressure, which can be abolished via blockade of angiotensin II.4 However, anatomical studies also indicate that the renal nerves innervate the tubules and vasculature, suggesting that the nerves may also mediate blood pressure through a direct action on sodium and water balance. Although several studies have described differences in the density of innervation to the tubules and vasculature,5,6 one difficulty is in identifying the direct effect of changes in activity on each of these sites. This difficulty arises because activation of RSNA at a level sufficient to alter renal blood flow (RBF) will also indirectly alter the secretion of renin and sodium excretion. Although it has been proposed that low levels of renal nerve activation are specific for the release of renin, and medium levels are specific for sodium excretion and renin release, with only high levels of activation affecting vasculature tone,7 it clearly needs to be considered that the resulting change in angiotensin II at low levels of nerve activation could itself affect urinary excretion.

In conscious dogs, carotid occlusion caused an increase in RSNA and produced a pronounced antinatriuresis that was not altered by ACE inhibition, suggesting that the renal nerves exert their action only via direct effects on the tubules.8 Conversely, a number of studies indicate that angiotensin II blockade markedly attenuates the antinatriuretic and antidiuretic responses of the kidneys seen with activation of the renin-angiotensin system.9,10 In addition, when the renin-angiotensin system was stimulated by low dietary sodium intake and RSNA was stimulated by low dietary sodium intake and RSNA increased, ACE inhibition completely eliminated the associated antinatriuretic and antidiuretic response.11 Thus, the extent to which changes in renal function in response to changes in RSNA are indirectly mediated by the renal angiotensin system remains controversial.

Although reflex activation of the renal nerves provides a means to assess how changes in the endogenous level of RSNA can affect renal function,12 a difficulty often arises in using stimuli that also directly alter arterial pressure and, thus, complicate the interpretation of results. A common alternative is electrical stimulation of the renal nerves. Typically, in this regard, previous studies report only the effect of brief periods of stimulation (<30 minutes).13–16 Although such short periods of stimulation may be long enough for direct effects on all aspects of renal function to be observed, one must consider that the effect of neurally mediated release of angiotensin II may take longer to be observed. When one considers that sympathetic nerve activity is a signal with a basal level of activity,17 it seems more reflective of the natural
condition to study the effect of longer-term low-level activation of the renal nerves.

The aim of the present study was to distinguish between the direct effects of the renal nerves and indirect effects via increased angiotensin II on the regulation of renal function. We applied low-level stimulation to the left renal nerves in anesthetized rabbits for 180 minutes and measured RBF, sodium excretion, and urine flow rate (UFR) from both the stimulated and the nonstimulated kidney with and without angiotensin converting enzyme inhibition.

Methods

Animal Preparation

All experiments were performed on New Zealand White rabbits of either sex, weighing between 2.2 and 3.4 kg, and were approved by the University of Auckland Animal Ethics Committee. Before the day of the experiment, rabbits were fed a diet of 100 g of standard rabbit chow (1% salt) each morning, with ad libitum access to water. Rabbits were not fed on the day of the experiment.

Anesthesia was induced by intravenous administration of pentobarbital (90 to 130 mg Nembutal, Virbac Laboratories New Zealand Ltd) into a marginal ear vein and was immediately followed by endotracheal intubation and artificial respiration. Anesthesia was maintained throughout the surgery and the experiment by pentobarbital infusion (20 to 60 mg/h).

The central ear artery was directly cannulated to monitor arterial pressure. Marginal veins in both ears were also cannulated. One marginal ear vein was used for the continuous infusion of both pentobarbital and Hartman’s solution, containing 20% Hemaccel (Hoechst Marion Roussel, Auckland New Zealand), at a rate of 15 mL·kg⁻¹·h⁻¹ to maintain fluid balance. The other marginal ear vein was used for the administration of ACE inhibitor (or saline in the control group). A heated pad was placed under the rabbit for the duration of the experiment to maintain body temperature at 37°C.

A retroperitoneal incision was made on both the left and the right side of the rabbit, and the kidneys were partially freed from surrounding tissue. The rabbit was then placed in an upright position and elevated on a small platform above the surgery table to aid collection of urine. Both ureters were catheterized (silastic tubing; ID, 0.64 mm; OD, 1.19 mm; Dow Corning Corporation) for collection of urine. Both ureters were catheterized (silastic tubing; ID, 0.64 mm; OD, 1.19 mm; Dow Corning Corporation) for collection of urine. The central ear artery catheter was connected to a pressure transducer (Cobe, Columbia), and the transit-time flow probes was connected to a flowmeter (T206, Transonic Systems). The acquired analogue signals were digitized and displayed continuously by a data acquisition program (Universal Acquisition, University of Auckland), which allowed continuous sampling at 500 Hz of arterial pressure (mm Hg) and RBF (mL/min). Heart rate (HR, bpm) was derived by the data acquisition program from the arterial pressure waveform. During each experiment, data were continuously displayed and saved at 500 Hz. Ureteral catheters were connected to the ureters with the renal arteries isolated and 10 V for 30 seconds. The left RBF response was measured and compared. The RBF response was found to be the same at that measured at the start of the experiment.

After surgical preparation, urine was collected until the flow rate had stabilized (~30 minutes) and then collected from each kidney in 5-minute collection periods throughout the remainder of the experiment. Baseline urine samples were collected for 30 minutes before the left renal nerves were stimulated at 1 Hz for 180 minutes, followed by a 120-minute recovery period.

In a separate group of animals (n=7) the above protocol was repeated in the presence of an ACE inhibitor (enalaprilat, Merck Research Laboratories). This was administered after the surgical preparation was complete, before the collection of urine. An initial bolus of 2 mg/kg was given, followed by a continuous intravenous infusion at a rate of 10 µg·kg⁻¹·h⁻¹. This dose of ACE inhibitor provides total blockade of the renin-angiotensin system in rabbits. A further group of animals (n=4) served as time controls in which data were collected for 5.5 hours with no stimulation or any other intervention performed. The preparation and protocol for these animals was identical, with the exception of the 3-hour period of electrical stimulation. The 4-Hz test pulses were applied at the beginning and end of the experiment, as was performed in all groups. We found the RBF response to be the same under both occasions. Furthermore, the RBF response to the test pulses was similar to that observed in animals that received 3 hours of electrical stimulation. In all animals, 2 arterial blood samples (0.3 mL each) were taken for the measurement of hematocrit. This was performed immediately before collection of baseline data and again at the end of the recovery period. At the conclusion of the experiment, each animal was killed with an intravenous overdose of pentobarbital (300 mg).

Data Analysis

Urine samples were collected for 5-minute periods throughout the experiment for the measurement of UFR and sodium excretion. Five-minute averages, corresponding to the 5-minute urine collection periods, were calculated for all other parameters (mean arterial pressure [MAP], HR, and RBF). All data were normalized by dividing values by the average baseline value from the 30 minutes before stimulation. This allowed for direct comparison of the responses to stimulation between groups when baselines differed.

Statistical Analysis

Data were analyzed using ANOVA, by groups (time control, stimulation in the intact condition, and stimulation in the presence of ACE inhibitor). The factors in this model were rabbit, time, and condition (baseline, stimulation, recovery) and the interaction time×condition. When an effect was significant, pair-wise comparisons were performed using the Bonferroni correction for multiple comparisons.

To compare between groups, a separate analysis was conducted for each parameter with the factors, group, with the error factor rabbit (group), condition, with the error term condition×rabbit (group) and the interaction group×condition with the error term group×condition×rabbit (group). When an effect was found to be significant, pair-wise comparisons were performed using the Bonferroni correction for multiple comparisons.
ferroni correction for multiple comparisons. All data are expressed as means, with error bars representing the SEM for that variable. Probability values <0.05 were considered significant.

**Results**

**Renal Responses to Nerve Stimulation in Animals With an Intact Renin-Angiotensin System**

Stimulation of the left renal nerves at 1 Hz for 3 hours resulted in a sustained increase in MAP, reaching a peak of 77±3 mm Hg within 35 minutes (baseline, 69±1 mm Hg) (Figure 1). When stimulation ended, MAP recovered back to baseline levels over the next 30 minutes. Baseline HR in these animals was 219±0.4 bpm and did not change with stimulation. Control hematocrit was 30±3%. This was unchanged at the end of the experiment (29±4%).

Left RBF abruptly decreased with the onset of stimulation, reaching an average of 31±1 mL/min (baseline, 40±1 mL/min). However, unlike arterial pressure, left RBF recovered during stimulation and, after 110 minutes, was not significantly different from baseline levels (Figure 1). Although left RBF tended to increase when stimulation was terminated, no significant change was seen. Baseline right RBF was 40±1 mL/min and did not change throughout the experiment (Figure 1). To take into account the effect of the change in arterial pressure on RBF, renal conductance was calculated for both the left and right kidneys, by dividing the respective RBFs by arterial pressure. Initially, stimulation significantly decreased left renal conductance (baseline, 0.58±0.01 mL·min⁻¹·mm Hg⁻¹), but this returned to baseline levels by approximately the same time as left RBF recovered (110 minutes after the onset of stimulation). Baseline right renal conductance was not significantly altered with stimulation (0.60±0.01 mL·min⁻¹·mm Hg⁻¹) (Figure 1).

Left UFR was significantly decreased during stimulation (0.38±0.01 versus 0.11±0.01 mL/min, *P*<0.001). However, unlike RBF, this remained significantly reduced throughout the whole stimulation and recovery period (recovery UFR, 0.17±0.01 mL/min). Although right RBF did not change during the stimulation period, right UFR was initially increased with stimulation, corresponding to the increase in arterial pressure; however, the average value throughout the stimulation period was significantly reduced (0.22±0.01 versus 0.64±0.04 mL/min baseline). Sodium excretion from the left kidney was significantly decreased during stimulation.
(38.6±0.7 versus 14.8±0.6 mmol/min) (Figure 1) but recovered back to levels not significantly different from baseline in the 2-hour recovery period (30.8±0.9 mmol/min). Overall, right sodium excretion was not altered during the stimulation period (54.6±4.4 versus 53.3±2.6 mmol/min). However, subsequent pair-wise comparisons (with appropriate post hoc statistical corrections) revealed that there was an initial significant increase in sodium excretion, which peaked after 40 minutes of stimulation (at about the same time that arterial pressure reached maximum levels) and then returned back to levels near the control level.

Effect of ACE Inhibition on the Renal Response to Nerve Stimulation
Baseline MAP was significantly lower in animals that received the ACE inhibitor (63±1 mm Hg ACE inhibited versus 69±1 controls). HR was unchanged. In contrast to the animals with an intact renin angiotensin system, animals that received the ACE inhibitor (n=7) showed no significant change in MAP during left renal nerve stimulation (Figure 2). Average baseline left RBF (43±1 mL/min) was significantly higher than in animals with an intact renin-angiotensin system. Although left RBF was initially decreased by a similar proportion with stimulation in both groups of animals, in the ACE-inhibited group, RBF recovered toward the baseline levels faster. To directly compare the response to stimulation in animals with and without ACE inhibition, all data were normalized by dividing values by the average baseline value from the 30 minutes before stimulation. This showed that in the presence of ACE inhibitor, the overall reduction in left RBF with stimulation was significantly smaller (P<0.001) (Figure 3). Because there was no change in MAP with stimulation in the ACE inhibitor group, renal conductance was calculated and compared between groups. Although baseline left renal conductance was significantly higher in the ACE inhibited group (0.68±0.01 mL/min/mm Hg⁻¹), the response to the stimulation of the renal nerve was significantly smaller than in the non-ACE-inhibited group (Figure 3). Right RBF was not altered during the stimulation period.

In ACE-inhibited animals, the reduction in left UFR to nerve stimulation was significantly attenuated (Figure 4). Although baseline UFR and the magnitude of the initial decrease in UFR were similar between groups, with ACE inhibition, UFR remained stable over time, whereas in the non–ACE-inhibited group it continued to decrease. Significantly, unlike the non–ACE-inhibited group, right UFR was unchanged during the stimulation period (Figure 4). Baseline left sodium excretion and the initial decrease with renal nerve stimulation were not significantly different between the non–ACE-inhibited and ACE-inhibited groups. However,
although the non–ACE-inhibited group did not show a recovery in sodium excretion throughout the stimulation period, the ACE-inhibited group experienced a significant return back toward control levels (Figure 5). Furthermore, sodium excretion from the right kidney was unaltered by stimulation in the ACE-inhibited group, whereas it was significantly decreased in the control non-ACE group (Figure 5).

**Time Control Animals**
All renal function parameters, MAP, and HR were stable throughout the 5.5-hour period of sampling.

**Discussion**
In the present study, we attempted to assess the relative importance of neurally mediated angiotensin II release versus the direct effects of sympathetic activity on renal function. Stimulation of the left renal nerves for an extended period of time (180 minutes) resulted in an angiotensin II–mediated increase in arterial pressure and a decrease in UFR from the nonstimulated kidney. With ACE inhibition, the antidiuretic responses of the nonstimulated kidney were completely abolished, and the responses of the stimulated kidney were attenuated. We therefore propose that the renal functional response to activation of the renal nerves is mediated by both the neurally mediated increases in angiotensin II and directly by the renal nerves.

Previously, it has been proposed that a 3-phase response of the kidney to the activation of the renal nerves exists, with low levels of renal nerve activation selectively causing renin release, medium levels causing changes in sodium excretion and renin release, and only high levels of activation affecting vasculature tone. However, this 3-phase hypothesis appears to be based on data collected under relatively short periods of electrical or reflex stimulation of the renal nerves, and may not reflect the normal situation of an ongoing level of sympathetic activity that is modulated up and down. Thus, these previous experiments appear not to have taken into account that changes in urinary excretion with stimulation may arise indirectly as a result of the neurally induced change in angiotensin. Our results indicate that although a direct effect of the renal nerves on sodium excretion is clearly present, the resulting increase in angiotensin II further supports the antidiuresis and antinatriuresis observed. Overall,
Arterial Pressure Changes

In the present study, the right kidney was denervated and functioned as a control for changes in circulating hormones (notably angiotensin II) and arterial pressure throughout the study. Although stimulation of the left renal nerves resulted in changes in left RBF and potentially in glomerular filtration rate (GFR), an effect that complicates interpretation of the changes in urine and sodium excretion in this kidney; in the right kidney, RBF and conductance were unaltered by the stimulation. Arterial pressure was increased during the stimulation and was associated initially with an increase in UFR on the right side; however, subsequently UFR was significantly reduced, despite arterial pressure remaining elevated. Importantly, these responses did not occur in the group that received the ACE inhibitor. Thus, we suggest that an increase in circulating levels of angiotensin II resulting from the low-level stimulation is sufficient to cause changes in excretory function on the contralateral denervated kidney.

Arterial Pressure Changes

A novel finding of the present study is that prolonged sympathetic activation can cause an angiotensin II–dependent increase in arterial pressure. This is an important observation for it supports the concept of chronic changes in sympathetic activity to the kidneys being involved in the long-term regulation of arterial pressure. We showed that low-frequency stimulation of the left renal nerves at 1 Hz resulted in a significant increase in arterial pressure that was abolished by ACE inhibition. Although some previous studies have indicated that arterial pressure is unchanged during renal nerve activation, it is likely that the shorter duration of the stimulation did not allow for the effect of increased angiotensin II to be observed. Our results show that in order to observe the effects of circulating angiotensin II, the length of the stimulation period is critical. There are other studies that support the finding of an angiotensin II–mediated rise in arterial pressure with sympathetic activation. In particular, an infusion of norepinephrine into the renal artery of uninephrectomized dogs for 7 days resulted in a progressive increase in arterial pressure, associated with a 2- to 3-fold increase in plasma renin activity. This increase in arterial pressure was abolished by clamping of angiotensin II levels via the ACE inhibitor captopril. Together these results suggest that the increase in arterial pressure with stimulation of the renal nerves is mediated by angiotensin II rather than by direct vasoconstrictor actions of the renal nerves.

It is unlikely that the rise in arterial pressure seen during stimulation was due to increased renal resistance for the following reasons: stimulation of the renal nerves initially caused a rapid reduction in RBF and decrease in conductance. This occurred in both ACE-inhibited and non-ACE groups at a similar initial magnitude. However, only in the non-ACE group did arterial pressure increase. Further, although conductance decreased in parallel with the change in RBF, the increase in MAP had a considerably slower onset. Finally, previously we have applied patterned stimulation to the renal nerves and recorded the RBF and MAP responses and found, using quite high frequencies of renal nerve stimulation (8 Hz, which reduced RBF by ~85%), that arterial pressure was unchanged.

Although it is well established that angiotensin II can rapidly alter renal function, it does not directly follow that the neurally mediated release and effect of angiotensin II occurs over a short time scale. Our results indicate that time for a neurally mediated increase in angiotensin II to affect renal function is such that short periods of stimulation (normally <20 minutes) are unlikely to reveal such effects. We have previously observed that although reflex activation of the renal nerves rapidly changes plasma renin activity, the renal functional effects of the response take longer to be apparent in a setting of altered MAP and RBF.

Even though arterial pressure was reduced with ACE inhibition, the magnitude of this decrease was actually quite small. Our previous studies using electrical stimulation of renal nerves and recording renal functional responses do not indicate changes in arterial pressure of such a magnitude alter the ability of the renal nerves to regulate renal function. Furthermore, although the baseline left conductance was higher in the ACE-inhibited group, the magnitude of the change during the stimulation was initially similar. Only with time was there a clear difference between the groups. Perhaps the best indication that the lack of responses in the ACE inhibition group were not due to the lower resting arterial pressure is the temporal nature of the responses. In particular, the initial response to the stimulation was similar in both animal groups and separated only with prolonged stimulation. If the lower resting MAP altered the ability of the nerves to change renal function, we would have expected this to be displayed as differences in the initial responses.

RBF Responses to Renal Nerve Stimulation

In the present study, left RBF decreased to ~30% of control within the first 5 minutes of stimulation, and then slowly recovered during the stimulation period and was not signifi-
cantly different to baseline after 110 minutes of stimulation. Previously, it has been shown that stimulation of the greater splanchnic nerve after adrenal medullectomy and servo control of renal arterial pressure, resulted in a large and rapid decrease in RBF on the stimulated side, but after 20 minutes of stimulation, RBF returned toward control.25 We observed that the initial decrease in RBF with stimulation was not altered by ACE inhibition. However, the time course of the RBF response was significantly altered, with RBF recovering toward baseline more rapidly in animals with ACE inhibition than without (35 versus 110 minutes until not significantly different from baseline). This suggests that angiotensin II is acting to sustain the vasoconstriction seen with renal nerve activation.

The finding that RBF recovered during nerve stimulation is interesting. Although we are unsure of the mechanism, we believe it is real and does not reflect a deterioration of the nerve as the response to subsequent 4-Hz stimulation was maintained. Furthermore, the effect on UFR and sodium excretion was sustained throughout the whole stimulation period.

Previously, it has been suggested that angiotensin II can act presynaptically to potentiate the release of norepinephrine from sympathetic nerve terminals and thus enhance the vasoconstrictor response to renal nerve activation.26,27 Specifically, the effect of angiotensin II on sodium excretion may occur predominantly via augmenting noradrenaline release from sympathetic nerve terminals, as renal denervation has been shown to reduce the effect of angiotensin II on proximal tubular chloride and water reabsorption by \( \approx 75\% \).28 However, our results do not agree with this proposal. In the present study, the right kidney was denervated and thus received no endogenous RSNA, yet still showed a significant reduction in UFR. This effect was absent in animals that received ACE inhibitor. These results indicate a direct effect of angiotensin II on excretory function.

**UFR and Sodium Excretion Responses to Renal Nerve Stimulation**

The role of angiotensin II in mediating changes in RBF, sodium excretion, and UFR independent of sympathetic activity has been a matter of debate. Low-level electrical stimulation has been shown to result in decreases in UFR and sodium excretion, but with ACE inhibition, this stimulation resulted in increases in UFR and GFR with no change in sodium excretion.9 The investigators concluded that an intact renin-angiotensin system was essential in order for activation of the renal nerves to cause antinatriuresis and antiureasis. We observed that blockade of the ACE inhibition significantly attenuated but did not abolish the antinatriuretic and antidiuretic response of the left kidney to left renal nerve stimulation (Figure 4). The magnitude of the initial decrease in sodium excretion was not altered by ACE inhibition, but the time course of this response was altered (Figure 5). Furthermore, on completion of the stimulation, a significant recovery was seen only in the animals treated with the ACE inhibitor. This attenuation with ACE inhibition confirms that angiotensin II plays a role in mediating the antinatriuretic and antidiuretic responses to renal nerve activation. Chronic infusion of norepinephrine into the renal artery of uninephrectomized dogs causing marked antinatriuresis has been shown to be attenuated \( \approx 50\% \) by clamping angiotensin II levels.4 Thus, it appears that the changes in urinary excretion seen with activation of the renal nerves is mediated by both the indirect effects of angiotensin II and the direct effects of the renal nerves.

One key aspect in the design of our study was the measurement of renal function from the contralateral denervated kidney, for this allowed us to distinguish between the direct effect of the nerves and the effect of circulating angiotensin II. Previously, 45 minutes of splanchnic nerve stimulation in the rat did not result in any change in urinary excretion on the nonstimulated side,21 whereas in the dog, prolonged stimulation (180 minutes) of the splanchnic nerve caused a 30% reduction in UFR and 40% reduction in sodium excretion from the nonstimulated kidney in the latter part of .25

Previously, Pelayo et al20 measured single nephron glomerular function during renal nerve stimulation (3 Hz) and observed that angiotensin inhibition significantly attenuated the decrease in GFR and vasoconstriction. Unfortunately, this study did not extend the stimulation for a longer period or lower stimulus intensity to determine if the changes in UFR or sodium excretion during ACE inhibition were affected independently from changes in GFR.

There are several findings of our study that indicate that changes in MAP are unlikely to account for the changes in UFR. First, the design of our study meant that urinary excretion was measured from both kidneys, yet only 1 kidney received nerve stimulation. Thus, although the right kidney showed an increase in UFR consistent with increased pressure, the left kidney, which naturally sees the same arterial pressure, actually showed a decrease in UFR. Furthermore, the temporal nature of the UFR responses also indicate that MAP was not the driving force behind the changes in UFR. As shown in Figure 1, MAP remained relatively constant between 25 to 150 minutes of stimulation; however, right UFR, although initially showing an increase, began to show a decrease (at \( \approx 50\) minutes) despite MAP remaining constantly elevated. The fluid infusion rate of 15 mL·kg\(^{-1}\)·h\(^{-1}\) has been extensively used in a range of our previous renal function studies. This rate is chosen specifically for its ability to maintain plasma osmolarity and hematocrit over an extended period of time in anesthetized rabbits.20,30

**Limitations**

It must be noted that in the present study, we did not measure GFR. However, we do not consider that measurement of GFR would have altered the interpretation of our results. Previously, we have observed GFR responds in parallel with changes in renal plasma flow during renal nerve activation.24 Furthermore, the renal responses of the right denervated kidney were completely abolished by ACE inhibition and did not involve changes in RBF. Carmines et al31 have shown that changes in filtration fraction are not necessarily indicative of selective alterations in vascular resistances and proposed that only with micropuncture and single nephron data can the filtered load on the tubules be precisely quantified. Such an approach would not have been possible with the present...
perspectives

We propose that the regulation of angiotensin II by the renal nerves contributes to the setting of arterial pressure. Furthermore, our study suggests that changes in urinary excretion resulting from activation of the renal nerves are mediated directly by the renal nerves and indirectly by neurally mediated increases in angiotensin II. The present study also indicates that angiotensin II contributes to the changes in RBF seen with activation of the renal nerves.

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References


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