HEART FUNCTION AND ATPase AFTER 6-OHDA/Dowell


Myocardial Contractile Function and Myofibrillar Adenosine Triphosphatase Activity in Chemically Sympathectomized Rats

RUSSELL T. DOWELL, PH.D

SUMMARY The contractile properties and contractile protein enzymatic activity of skeletal muscle can be altered by neural influences. To determine whether similar influences apply to cardiac muscle, adult rats were chemically sympathectomized by intravenous injection of 6-hydroxydopamine (6-OHDA). After 2 weeks of treatment, rats were anesthetized and an index of myocardial contractile function which is accompanied by reduction in myofibrillar ATPase activity in chronically (2 weeks) sympathetically stimulated cardiac muscle was significantly different in 6-OHDA rats. Myofibrillar ATPase activity was 0.314 ± 0.014 μmol P i/mg per min in controls. Enzyme activity was significantly reduced to 0.230 ± 0.020 μmol P i/mg per min in 6-OHDA rats. The results demonstrate that a chronic reduction in sympathetically stimulated to the heart results in a decrease of an index of myocardial contractile function which is accompanied by reduced myofibrillar ATPase activity. Acute (16-18 hours) chemical sympathectomy depressed the contractile function index without altering ATPase activity. Bilateral adrenalectomy produced no further decrement in myofibrillar ATPase activity in chronically (2 weeks) sympathectomized rats. Therefore, it appears that the changes in contractile protein enzymatic properties are mediated by sympathetic neural influences and may involve the synthesis of new contractile protein activities with altered enzymatic properties.

Myocardial contractile function can occur with a variety of abnormal hormonal conditions, among which are adrenal insufficiency, hypoparathyroidism, hypothyroidism, and thyrotoxicosis. Contractile protein ATPase activity in the heart is concomitantly reduced under these circumstances. Conversely, both myocardial contractile function and contractile protein ATPase activity can be increased under hyperthyroid conditions.

The sympathetic nervous system exerts major regulatory

IN SKELETAL muscle, a direct relationship exists between muscle contractile properties and the ATPase activity of contractile proteins. Evidence is accumulating which suggests a similar relationship in cardiac muscle. Depressed

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influences on myocardial contractile function. Neural factors are known to modify skeletal muscle contractile function via alterations in contractile protein ATPase activity. The possibility that alterations in neural stimulation of the heart may alter contractile proteins, in a manner analogous to skeletal muscle, has not been explored. The present studies were undertaken to (1) examine the functional characteristics of hearts subjected to reduced levels of sympathetic stimulation, and (2) determine whether there were parallel alterations in contractile protein ATPase activity.

Methods

ANIMALS AND EXPERIMENTAL TREATMENT

Male Sprague-Dawley rats weighing 250–300 g were used in these experiments. Chemical sympathectomy was established by intravenous administration of 6-hydroxydopamine (6-OHDA). The drug was prepared immediately prior to injection (50 mg/kg) in physiologic saline containing ascorbic acid, 1 mg/ml, as recommended by de Champlain and Van Ameringen. In one group of rats the acute effects of 6-OHDA treatment were determined. Rats in this group received a single injection of 6-OHDA and were studied 16–18 hours later. In a separate group, drug injection was repeated at weekly intervals to achieve chronic chemical sympathectomy. These rats were studied at the end of the 2nd week of treatment, i.e., 7 days after the second 6-OHDA injection.

Since 6-OHDA treatment has been reported to elicit adrenal compensatory responses in rats, another group was studied to evaluate the extent of this compensation. Rats in this group were given 6-OHDA as described above. Two days after the initial drug injection, bilateral adrenalectomy was performed under ether anesthesia using a dorsal approach. Chronic sympathectomy then was established in adrenalectomized rats by weekly 6-OHDA injections. Adrenalectomized-sympathectomized rats were studied 2 weeks after the initial drug injection, i.e., 7 days after the second 6-OHDA injection. Adrenalectomized rats were provided with a 1% NaCl drinking solution ad libitum. Control rats were given sham injections of saline-ascorbic acid at the time intervals when 6-OHDA was administered.

HEMODYNAMIC MEASUREMENTS AND RESPONSES TO TYRAMINE INJECTION

At the appropriate time interval, rats were anesthetized with sodium pentobarbital (50 mg/kg, ip), weighed, and placed on positive-pressure ventilation (Harvard rodent respiratory) with room air via a tracheostomy. A jugular vein cannula was positioned to allow intravenous injections. A cannula was inserted at the bifurcation of the abdominal aorta to monitor systemic blood pressure. The heart was exposed by midline sternotomy, and left ventricular pressure was measured by puncturing the ventricle with a 22-gauge needle attached directly to a Statham P37 miniaturized pressure transducer. Heart rate was determined continuously with a cardiostimulator triggered by the left ventricular pressure pulse. The maximum rate of left ventricular pressure development (max dP/dt) was derived with an analog differentiator. This measurement was used as an index of myocardial contractility. The frequency response characteristics of the pressure measurement system and functional stability and responsiveness of the preparation have been described previously. All hemodynamic measurements were recorded simultaneously on a Beckman type R Dynograph.

After initial hemodynamic measurements had been completed, the responsiveness of the cardiovascular system to tyramine was evaluated. Tyramine was prepared fresh in physiologic saline containing Na-metabisulfite, 50 μg/ml. A volume of vehicle equivalent to the maximal volume of test drug was injected via the jugular vein cannula, and the cannula dead space was cleared by injecting an additional 0.3 ml of saline. The peak responses to vehicle injection were taken as control values. Tyramine (100 μg/kg) then was given in an identical manner and peak hemodynamic responses were recorded. After the preparation had returned to control levels (approximately 5 minutes), the responses to tyramine, 200 μg/kg, were determined. After recovery the heart was excised and placed into a beaker in crushed ice. When present, both adrenal glands were removed, pooled into a single sample, and weighed.

TISSUE AND MYOFIBRIL PREPARATION

Atria, great vessels, and the right ventricle were carefully removed from the excised heart. The remaining left ventricle plus interventricular septum was weighed and frozen. Subsequently, purified myofibrils were prepared from left ventricular tissue using minor modifications of the method described by Zak et al. Tissue was minced with scissors and homogenized in solution I [250 mM sucrose, 5 mM ethylene glycol bis-(β-aminoethyl ether)-N,N′-tetraacetic acid (EGTA), 5 mM MgCl2, 75 mM KCl, pH 6.8] with a ground glass homogenizer. Following centrifugation, the precipitate was washed with solution II (175 mM KCl, 5 mM EGTA, 5 mM MgCl2, 0.1% Triton X-100, pH 6.8) using a Dounce homogenizer to solubilize and remove contaminating membranes. The detergent was removed from the pellet by further washes with solution III [150 mM KCl, 5 mM ethylenediaminetetraacetic acid (EDTA), pH 7.0]. Purified myofibrils were resuspended in 50 mM tris(hydroxymethyl)aminomethane (Tris) buffer, pH 7.4, which contained 50 mM KCl. Protein concentration was measured by the biuret reaction and subsequently adjusted to 6 mg/ml with Tris-KCl buffer.

MYOFIBRILLAR ATPase ACTIVITY

Myofibrillar ATPase activity was measured in a reaction mixture containing 1 mM MgSO4, 0.1 mM CaCl2, 1 mM Na2ATP, 20 mM Tris, pH 7.4, and 1.2 mg of myofibrillar protein in a final volume of 4.0 ml. Sodium azide (2 mM final concentration) was routinely added to inhibit possible contaminating mitochondrial ATPase activity. The reaction was initiated by substrate (ATP) addition. After incubation for 2 min at 30°C, the reaction was stopped with 1 ml of 10% trichloroacetic acid. Precipitated protein was removed by centrifugation and the supernatant fluid was assayed for inorganic phosphate (P) by the method of Rockstein and Herron. Enzyme activity is expressed as micromoles of P, released per milligram of myofibrillar protein per minute.

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TABLE 1  Body Weight, Left Ventricle (LV) Weight, and Adrenal Weight of Rats in Acute and Chronic Experiments

<table>
<thead>
<tr>
<th>Group</th>
<th>Body wt (g)</th>
<th>LV wt (mg)</th>
<th>LV/body wt (mg/g)</th>
<th>Adrenal wt (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (8)</td>
<td>342 ± 17</td>
<td>675 ± 10</td>
<td>2.00 ± 0.09</td>
<td>42 ± 3</td>
</tr>
<tr>
<td>Chronic sympathectomized (7)</td>
<td>332 ± 13</td>
<td>623 ± 23</td>
<td>1.94 ± 0.06</td>
<td>44 ± 3</td>
</tr>
<tr>
<td>Adrenalectomized-sympathectomized (11)</td>
<td>292 ± 9*</td>
<td>607 ± 26*</td>
<td>2.09 ± 0.08</td>
<td>-</td>
</tr>
<tr>
<td>Acute sympathectomized (8)</td>
<td>249 ± 5*</td>
<td>569 ± 14*</td>
<td>2.29 ± 0.07*</td>
<td>43 ± 2</td>
</tr>
</tbody>
</table>

Values are means ± SE. The number of rats in each group is given in parentheses.
* P < 0.05 compared to control.

STATISTICAL METHODS

All experimental results were compared with appropriate control values by Student’s t-analysis. A P value of 0.05 or less was considered statistically significant.

Results

EFFECT OF EXPERIMENTAL TREATMENTS ON OVERALL GROWTH AND ORGAN WEIGHTS

The body weights and organ weights of rats at the time they were killed are shown in Table 1. Chronic chemical sympathectomy had no significant effect on either overall growth or left ventricular weight. Adrenalectomy combined with chronic sympathectomy resulted in significant reductions in body weight and left ventricular weight. Although statistically significant, the magnitude of weight loss in each case was relatively small (10-15%) and a normal left ventricle-body weight relationship was maintained in adrenalectomized-sympathectomized rats. Therefore, the above results indicate that the chronic experimental procedures used in the present study did not create disproportionate heart growth or atrophy.

In acutely sympathectomized rats the significantly lower body and left ventricular weights would be expected, because the additional 2-week growth period was not allowed. Nevertheless, a significant elevation in body weight and left ventricular weight ratio was present in these rats. Since only 16-18 hours had elapsed following drug treatment, it seems unlikely that significant amounts of myocardial tissue could have accumulated to account for the increased left ventricle-body weight ratio, especially in view of the absence of known stimuli for cardiac hypertrophy. A more likely explanation would be a transient body weight loss attributable to the acute effects of the drug.

It also should be noted that if either acute or chronic adrenal compensation occurred as the result of chemical sympathectomy, this compensation did not take the form of overt adrenal hypertrophy, because adrenal weights were nearly identical in all rats in which this measurement was made.

INITIAL HEMODYNAMIC MEASUREMENTS

Marked reductions in peak left ventricular pressure, mean arterial pressure and max dP/dt were observed in response to acute and chronic chemical sympathectomy as well as adrenalectomy plus sympathectomy (Table 2). In contrast, there was no evidence of significant alterations in heart rate (Table 2). When the capability for heart rate modulation via the parasympathetic nervous system is considered, the observed heart rates are not completely unexpected. On the other hand, mean arterial pressure and myocardial contractility are regulated primarily via the sympathetic nervous system, and reduced overall sympathetic stimulation would have profound effects on these parameters. The initial hemodynamic measurements provide evidence that significant reductions in overall cardiovascular sympathetic stimulation were achieved by the experimental treatments used in the present study. In addition, the marked reduction in the maximum rate of left ventricular pressure development which was observed in all experimentally treated rats suggests that the contractile state of the myocardium was significantly depressed because of the reduced sympathetic stimulation.

It is recognized that the maximum rate of left ventricular pressure development may be influenced by changes in heart rate, preload, and afterload. Although heart rate was not changed significantly by experimental treatments (Table 2) and myocardial preload (left ventricular end-diastolic pressure) remained constant (data not shown), significant alterations in afterload (mean arterial pressure) were present. For this reason a myocardial contractility index which is influenced to a lesser degree by changes in loading conditions, i.e., (max dP/dt)/(developed pressure at max dP/dt), was calculated from the initial hemodynamic mea-

TABLE 2  Initial Hemodynamic Measurements Obtained from Rats in Acute and Chronic Experiments

<table>
<thead>
<tr>
<th>Group</th>
<th>LVP (mm Hg)</th>
<th>MAP (mm Hg)</th>
<th>Heart rate (beats/min)</th>
<th>Max dP/dt (mm Hg/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (8)</td>
<td>133 ± 4</td>
<td>123 ± 5</td>
<td>419 ± 15</td>
<td>6710 ± 580</td>
</tr>
<tr>
<td>Chronic sympathectomized (7)</td>
<td>104 ± 6*</td>
<td>95 ± 6*</td>
<td>406 ± 11</td>
<td>4560 ± 420*</td>
</tr>
<tr>
<td>Adrenalectomized-sympathectomized (11)</td>
<td>79 ± 3*</td>
<td>68 ± 4*</td>
<td>439 ± 9</td>
<td>3480 ± 210*</td>
</tr>
<tr>
<td>Acute sympathectomized (8)</td>
<td>83 ± 6*</td>
<td>70 ± 7*</td>
<td>423 ± 14</td>
<td>3950 ± 610*</td>
</tr>
</tbody>
</table>

LVP = peak left ventricular pressure; MAP = mean arterial pressure.
Values are means ± SE. The number of rats in each group is given in parentheses.
* P < 0.05 compared to control.
measurements. Control values for \((\text{dP/dt})^{-1}\) were 163 ± 17 (mean ± SE) sec\(^{-1}\) in control rats. This contractility index was significantly reduced in all experimental groups studied. Therefore, it would appear that myocardial contractile function was, in fact, depressed by the experimental treatments and contractile function was accurately reflected by max \(\text{dP/dt}\) measurements.

**RESPONSIVENESS TO TYRAMINE**

The hemodynamic measurements of responses to tyramine injections are shown in Figure 1. The injection of drug vehicle volumes comparable to those used for tyramine injection served as a control for the drug responses. Control injections produced negligible hemodynamic effects when compared to initial hemodynamic measurements. In response to tyramine injections (100 /µg/kg and 200 /µg/kg), control rats exhibited appropriate and significant elevations in mean arterial pressure, heart rate, and max \(\text{dP/dt}\). Injection of tyramine, 200 /µg/kg, elicited near maximal \(\text{dP/dt}\) measurements and contractile function was accurately reflected by max \(\text{dP/dt}\) measurements.

In general, the heart rate responses to tyramine injections in the experimental groups paralleled the other hemodynamic responses. However, significant reductions in heart rate responsiveness to tyramine were observed only in acutely sympathectomized and sympathetically-denervated rats and only at the higher tyramine dosage. From these results, it would appear that adrenal medullary compensation or parasympathetic nervous system modulation, or both, are sufficient to maintain near-normal heart rate responsiveness in chronically sympathectomized rats.

**MYOFIBRILLAR ATPase ACTIVITY**

Since left ventricular myofibrils were prepared from rats that had been injected with tyramine, the possible effects of this drug treatment on myofibrillar enzyme activity required consideration. Four normal male rats weighing approximately 250 g were killed without hemodynamic evaluation, and left ventricular myofibrils were prepared from fresh tissue. There were no significant differences in either myofibrillar protein yield or ATPase activity when normal rats were compared to sham-injected controls. Therefore, small differences in age, functional evaluation, and storage of frozen tissue did not influence myofibrillar enzyme activity, and the enzyme results from normal and sham-injected rats were combined. The ability to detect differences in myofibrillar ATPase activity also was evaluated. Myofibrils were prepared from fast twitch rat skeletal muscle (tibialis anterior) obtained from the above four normal rats. The ATPase activity of tibialis anterior myofibrils was approximately twice \([0.750 ± 0.025 \text{ (mean ± SE)} \mu\text{mol P/\text{mg per min}}]\) that of left ventricular myofibrils. A direct, linear enzyme activity relationship was obtained when mixtures containing varying proportions of tibialis anterior and left ventricular myofibrils were assayed. Myofibrillar purity was confirmed by the sensitivity of myofibrillar ATPase to KCl. Enzyme activity was inhibited by more than 90% when left ventricular myofibrils were assayed in the presence of 200 mM KCl.

The myofibrillar results from control and experimental rats are shown in Table 3. There were no significant differences in myofibrillar protein yield in any of the groups studied. Chronic sympathectomy resulted in a significant reduction in ATPase activity. Possible adrenal medullary compensation had little influence on contractile protein enzymatic activity, since myofibrillar ATPase activity was reduced to comparable levels in adrenalectomized-sympa-
adrenergic nerve endings, 6-OHDA does not destroy adrenal medullary cells. Thus, adrenal compensation had occurred in response to chronic sympathectomy. The reduced enzymatic activity observed in chronically sympathectomized rats does not represent sulphydryl group modification within the protein molecules, since the preparation or assay of myofibrils in the presence of diithiothreitol (1 mM) did not influence enzyme activity. The presence of enzyme inhibitors was unlikely, because ATPase activity was additive in mixtures of myofibrils from control and chronically sympathectomized rats.

Discussion

Sympathetic neural control of the cardiovascular system encompasses both adrenergic nerve fibers and the adrenal medulla. In the present study, sympathectomy was produced by administering 6-OHDA, and the action of this compound on the several sympathetic nervous system components requires consideration. Treatment with 6-OHDA specifically destroys adrenergic nerve endings. Within 5 hours after a single 6-OHDA injection, endogenous myocardial norepinephrine levels are reduced by more than 90%; however, norepinephrine levels slowly recover with time to reach approximately 10–15% of normal levels after 8 days. Therefore, drug treatment must be repeated at weekly intervals if a chronic, low level of myocardial adrenergic nervous system components is to be maintained. In contrast to its action on adrenergic nerve endings, 6-OHDA does not destroy adrenal medullary cells. Thus, adrenal compensation after chemical sympathectomy is possible and indicated by elevated tyrosine hydroxylase activity in the adrenal medulla of 6-OHDA-treated rats.

In the present study, peripheral sympathectomy was clearly established by 6-OHDA treatment in view of the marked reductions in left ventricular and mean arterial pressures. In addition, an index of myocardial contractile function (max dP/dt) was depressed as the result of either acute or chronic sympathectomy. Nevertheless, adrenal medullary compensation represented a source of cardiovascular sympathetic stimulation that was potentially undetected by initial hemodynamic measurements. The extent of this potential compensation was evaluated by (1) determining the hemodynamic responses following release of endogenous catecholamines by tyramine, and (2) removing the source of sympathetic compensation via adrenalectomy. The tyramine results confirmed that adrenal medullary compensation had occurred in response to chronic sympathectomy. Chronically sympathectomized rats were able to increase mean arterial pressure, heart rate, and max dP/dt significantly in response to tyramine injection although the magnitude of these responses was attenuated. The sympathetic responsiveness appeared to originate from the adrenal medulla rather than regenerating nerve endings since (1) adrenalectomy abolished responsiveness to tyramine in chronically sympathectomized rats, and (2) responsiveness to tyramine was not present in acutely sympathectomized rats which were not allowed sufficient time to develop adrenal medullary compensation.

In chronically sympathectomized rats, depressed values for max dP/dt were accompanied by a reduction in contractile protein ATPase activity. Previous work by Rovetto et al. has shown reduced ATPase activity in myofibrils, actomyosin, and myosin from hearts of adrenalectomized cats. Reduced contractile protein ATPase activity correlates with the reduced cardiac performance associated with adrenal insufficiency. When cardiac function and myosin ATPase activity were determined in hypophysectomized rats, it was concluded that the absence of thyroid hormone reduces both myocardial contractile function and contractile protein enzymatic activity. The above studies suggest that a positive relationship exists between the enzymatic properties of myocardial contractile proteins and myocardial contractile function. The present studies provide evidence which supports and extends this conclusion. The index of myocardial contractile function was significantly depressed in chronically sympathectomized rats even though adrenal medullary compensation was evident. Max dP/dt was depressed further when the contribution of the adrenal medulla was eliminated; however, no further decrement in myofibrillar ATPase activity was observed. Since adrenal medullary cells are not destroyed by 6-OHDA and, in fact,
medullary catecholamine synthesis may be enhanced following 6-OHDA treatment, it seems likely that normal quantities of catecholamine will be released from the adrenal medulla in response to injections of tyramine which elicit near maximal responses. Nevertheless, the max dp/dt responsiveness of chronically sympathectomized rats was markedly attenuated. Taken together, the above results demonstrate that adrenal medullary catecholamines contribute to the modulation of myocardial contractile function; however, the intrinsic enzymatic properties of myocardial contractile proteins may define the upper limit of contractile function. With regard to the sympathetic nervous system, the enzymatic properties of myocardial contractile proteins would appear to be regulated by sympathetic nerve fibers rather than adrenal medullary catecholamines.

Direct neural control of contractile protein enzymatic properties has been clearly demonstrated for skeletal muscle. Following denervation, skeletal muscle myofibrillar ATPase activity is reduced. A more dramatic demonstration of neural control of contractile protein properties is provided by cross-innervation experiments. Fast twitch skeletal muscle is characterized by high levels of contractile protein ATPase activity, whereas slow twitch muscle shows lower ATPase activity. When fast twitch muscle is denervated and subsequently reinnervated with nerves from slow twitch muscle, the twitch properties and ATPase activity of the muscle assume the characteristics of slow twitch muscle. Conversely, slow twitch muscle assumes faster twitch properties and shows increased ATPase activity when reinnervated by nerves from fast twitch muscle. That there are altered ATPase activities of cross-innervated skeletal muscles suggests there is synthesis of contractile proteins with altered enzymatic properties. More specifically, different light chains of myosin may be synthesized, since this portion may have been synthesized. Since the half-life of heart muscle proteins is approximately 14–21 days, reduced sympathetic stimulation would not be expected to exert immediate effects on contractile protein ATPase activity if this effect required the synthesis of new proteins with altered enzymatic properties. The fact that acute chemical sympathectomy did not influence myofibrillar ATPase activity provides some evidence for this mechanism; however, the complete time course of the response remains to be determined, as does verification of the synthesis of structurally different contractile protein.

Although chronically reduced sympathetic stimulation to the heart clearly results in reduced myofibrillar ATPase activity, a direct neural effect is open to question because of the marked reductions in mean arterial pressure which accompanied chronic sympathetomy. Decreased mean arterial pressure would reduce myocardial afterload and, in turn, produce substantial reductions in cardiac work. Therefore, the possibility remains that decreased myocardial workload or an overall lower rate of work performance rather than any direct neural influence results in reduced myofibrillar ATPase activity. This possibility seems unlikely, because significant reductions in myofibrillar ATPase activity were observed in both dogs and rats in which left stellate ganglionectomy was performed to reduce sympathetic stimulation to the heart without altering myocardial afterload or rate of performing work (R.T. Dowell and H.L. Stone, unpublished observations).

The present studies demonstrate that a chronic reduction in sympathetic stimulation to the heart results in a depressed index of myocardial contractile function which is accompanied by reduced myofibrillar ATPase activity. It appears likely that the altered contractile protein enzymatic properties are caused directly by sympathetic neural influences and may involve the synthesis of new contractile protein(s) with altered enzymatic properties.

References

21. Thoenen H, Tramuze JR. Chemical sympathectomy by selective destruction of adrenergic nerve endings with 6-hydroxydopamine. Naunyn
The Effect of an Acute Increase in Renal Perfusion Pressure on Sodium Transport in the Rat Kidney

ROBERT T. KUNAU, JR., M.D., AND NORBERT H. LAMEIRE, M.D., PH.D.

SUMMARY We used micropuncture techniques to examine the intrarenal response to an acute elevation of the renal perfusion pressure. In one series of studies (epinephrine, group I) the renal perfusion pressure was acutely increased by intravenous epinephrine infusion; in another series, by bilateral carotid occlusion and vagotomy. A third series of studies (epinephrine, group II) was performed identically to the epinephrine, group I, studies except that the renal perfusion pressure was held constant during the epinephrine infusion. The results indicate that the increase in sodium excretion observed in these models cannot be attributed to enhanced sodium delivery from superficial cortical late distal tubule. Furthermore, we found that epinephrine infusion at a constant renal perfusion pressure (epinephrine, group I) did not affect fractional sodium excretion, although a small, but significant, decrease in the GFR and sodium delivery from the superficial cortical late distal tubule occurred. These data suggest that the natriuresis which follows an acute elevation of the renal perfusion pressure cannot be attributed to enhanced sodium delivery from superficial cortical late distal tubule but must result from (1) inhibition of sodium reabsorption in inner cortical nephrons or (2) an effect on sodium transport in the collecting system.

ACUTE ELEVATIONS in the renal perfusion pressure have been shown to result in parallel increases in the urinary excretion of sodium under a variety of circumstances.1-7 As this effect of perfusion pressure occurs in the absence of a detectable change in the filtered sodium load, it has been suggested that renal perfusion pressure can directly influence tubular sodium transport. Although micropuncture studies of the proximal convoluted tubule in the dog8 and rat4 have shown that an acute elevation in renal perfusion pressure can diminish fractional sodium reabsorption at this site, there is also strong, albeit indirect, evidence to indicate that sodium reabsorption in some segment(s) of the distal nephron also may be affected.8-4

Our present studies were performed to further characterize changes in sodium transport that occur in response to an acute elevation in renal perfusion pressure. In these micropuncture studies, sodium transport in the distal convoluted tubule of the rat nephron was examined prior to and after the perfusion pressure was increased acutely by epinephrine infusion and by bilateral carotid occlusion and vagotomy. The results indicate that the increase in sodium excretion observed in these models cannot be attributed to an increase in sodium delivery from the superficial distal convoluted tubule but must reflect an effect of perfusion pressure on sodium transport in deeper cortical nephrons or in the collecting system.
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R T Dowell

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