Role of Cardiopulmonary Receptors and Sino-Aortic Baroreceptors in General and Renal Circulatory Homeostasis

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ABSTRACT

Cardiopulmonary receptors stimulation preferentially inhibits renal sympathetic nerve activity. Renal vasodilation may result in addition to reflex control of releases of ADH and renin. Sino-aortic baroreceptors stimulation on the other hand causes vasoactions elsewhere, particularly in the skeletal muscles. In order to determine whether changes in cardiopulmonary inputs (by acute blood volume shifts of ±10% blood volume) have significant influence on the renal circulation under normal circumstances, experiments were carried out by using intact (A), vagotomized (B), sino-aortic denervation (SAD, C) and SAD and vagotomized (D) rabbits. This experimental design permitted determination of roles played by vagus nerves, and sino-aortic nerves in controlling renal circulation. General circulation was also characterized in these four groups of rabbits. Stepwise denervations (vagotomy, SAD, and SAD with vagotomy) resulted in progressive hypertension and decrease in cardiac output. Responses of renal blood flow during acute blood volume changes followed closely the changes in cardiac output, regardless of their neural status. That is to say that renal blood flow changes during blood volume shift essential the same as that of whole body responses. It is concluded that neither "low" nor "high" pressure receptors exert a rather minimal influence on renal blood flow under normal physiological conditions.

Key words: Neural control of renal circulation; General hemodynamics; Cardiopulmonary receptors; Sino-aortic baroreceptors; Hemorrhage; Blood volume expansion; Rabbits.

INTRODUCTION

Cardiovascular homeostasis is made possible by the central integration of a wide array of sensory information and by the proper transformation of this information into autonomic and humoral responses. Input from vascular baroreceptors, chemoreceptors, and input from somatic, visceral, and special sensory receptors provide neural centers with a complex profile of circulatory status. This information is processed in bulbar and suprabulbar centers and evokes adjustments counteracting cardiovascular perturbations.

Due mainly to relative easy access, a great deal of our knowledge on the circulatory control has been accumulated through experiments on the sensors located on the "high pressure" side of the circulatory system, namely the carotid sinus and aortic arch baroreceptors. On the contrary, controlled inputs to the sensors located on the "low pressure" side of the cardiovascular system are more difficult to apply, and hence their reflex role in normal homeostasis is still a matter of controversy. Nevertheless, available data now suggest that certain circulatory disorders, having body fluid volume abnormality, are linked to the reduced activity of cardiopulmonary receptors (Zucker and

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Gilmore, 1981; Thoren and Ricksten, 1981). By inference these receptors must normally regulate body fluid volume and indirectly the arterial blood pressure by reflex control of renal perfusion and its function.

Many investigators now agree that the so-called low pressure receptors have widespread distribution on the heart and capacitance vessels within the thorax, and their endings participate in the reflex control of 1) renal sympathetic nerve activity, 2) antidiuretic hormone secretion, 3) renin release, and 4) heart activity via cardiac sympathetic nerves. This knowledge has been summarized by Coleridge and Coleridge (1972), Shepherd (1973), Goetz, *et al.* (1975), Thames (1978), and more recently in a symposium proceeding edited by Hainsworth *et al.* (1979). All of these reflexes have direct or indirect effects on renal hemodynamics.

Available evidence indicates that thoracic capacitance vascular hypotension induces renal vasoconstriction, where hypertension induces just the opposite (Kahl, *et al.*, 1974; Goetz, *et al.*, 1975; Oberg, 1976). While these conclusions are generally correct, ambiguities nevertheless exist. First, most studies employed a severely distorted systemic circulatory status, such as cardiogenic and hemorrhagic shock, in affecting renal circulation. Direct and indirect hemodynamic effects and reflex influences are often difficult to separate. Secondly, results obtained from animal models that are devoid of arterial baroreceptors and vagal nerves do not answer the question of whether changes in cardiopulmonary input have significant influence on the kidney under normal conditions. Thirdly, prolonged systemic circulatory disturbances involve not only the nervous system but also humoral factors. Finally, changes in renal sympathetic nerve activity or changes in renal vascular conductance (or resistance) cannot be equated to a corresponding change in renal blood flow (RBF), since in most experiments the systemic arterial pressure was drastically altered by denervation. Typically, severe systemic hypertension existed following SA denervations and vagotomy. It is possible to show an increased renal sympathetic nerve activity in dogs with vagal cold block and functionless arterial baroreceptors (Mancia, *et al.*, 1973), but no change is seen in renal blood flow (Mancia, *et al.*, 1975). For these reasons, RBF was studied directly in the present study while employing rapid, short term perturbations and restorations (3 min. total) of cardiopulmonary receptors and systemic circulatory functions; and arterial baroreceptors were either left intact to freely sense arterial blood pressure changes, or denervated. In all experiments systemic circulatory condition was quantified so that its relation to renal blood flow could be determined.

METHOD AND MATERIALS

ANIMAL

Rabbits of mixed sexes served as the experimental animal. Body weight ranged from 2.4 to 4.2 kg with a mean weight of 3.1 ± 0.1 kg. A total of 24 animals was used in this study.

ANESTHESIA

The rabbits were anesthetized with an equal volume mixture of 25% urethane and 1% α-chloralose in normal saline. The rabbits received an initial dose of 5-6 ml/kg via a catheter in a peripheral ear vein, which was followed during the next 30 to 40 minutes by an additional 1 to 2 ml/kg. The combined dosages provided a satisfactory level of anesthesia for surgery and a stable experimental preparation. It proved unnecessary to give supplemental anesthesia throughout the entire experimental procedure. Care was taken to prevent body heat loss with a heat lamp and a heating pad.

HEMODYNAMIC MEASUREMENTS

Cardiac output (CO) was determined by a thermodilution technique. Fegler introduced this procedure first in 1954, and it has been widely used since in the rat (Lin, *et al.*, 1970A, 1970B; Baker and Lin, 1975; Hanwell, 1972), dog (Wessel, *et al.*, 1971), and in man (Vliers, *et al.*, 1973; Ganz and Swan, 1972; Stawicki, *et al.*, 1979). The reliability of this method in the rabbit was critically evaluated by Korner and Hilder (1974), White *et al.* (1974), Warren, *et al*, (1974), and most recently by Baker and Lin (1981). The thermistor probe (Fenwal GB3234 in PE 90 polyethylene tubing) was inserted via left femoral artery and was advanced to the thoracic aorta. The injection catheter (PE 90) was inserted into the right atrium via the jugular vein. A standardized volume (0.79 ml) of saline at room temperature was injected rapidly into the right atrium via a constant volume injector, and the temperature-time curve recorded onto a Beckman dynograph through a Yellowspring telethermometer (Fig. 1). A desktop computer program (Lin, 1979) facilitated exponential extrapolation of the primary thermodilution curve. Cardiac output was then determined from the following equation:

$$CO = V_i (T_b - T_i)\, 60K/A$$

where:

CO=cardiac output, ml/min

V_i=injection volume corrected for dead space, ml

T_b=blood temperature before injection, °C

T_i=injectate temperature, °C

A=area under the primary dilution curve, °C-sec.

$K = \frac{\text{(injectate spec. heat) (injectate spec. gravity)}}{\text{(Blood spec. heat) (Blood spec. gravity)}}$

$=1.037$

60=second-to-minute conversion

Renal blood flow (RBF) was determined by a local thermodilution technique. Fronek and Ganz (1960) first introduced this technique for estimating local blood flow, and it has since been used extensively by White, *et al.*, (1967, 1974) for determination of renal blood flow in the rabbit. This technique allows for frequent determinations and the use of a physiological indicator (saline), as well as the preservation of renal nerve activity which was often not the case in the application of electromagnetic flow cuff. The local thermodilution probe used in this study differed from others, and has been published recently (Baker and Lin, 1982). Briefly, local thermodilution probes were constructed using bead thermistors (Fenwal

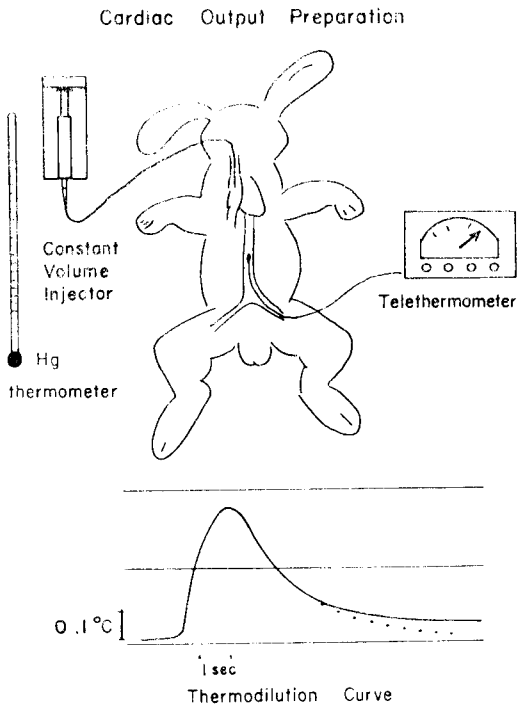

Fig. 1. Preparation for the determination of cardiac output by thermodilution. The injection catheter is located in the right atrium and thermistor probe in the abdominal aorta (Top). Output of the tele thermometer describes a cardiac output thermodilution curve which was recorded onto an analog recorder. Dots indicate the extrapolated exponential downslope.

GB3234). After soldering joints and thermistor leads in epoxy resin, the wires with the attached thermistor were pulled through a PE 90 polyethylene catheter so as to position the thermistor at one end of the catheter. The other end of the catheter was connected via a tight-fitting injection needle to a constant volume injector (see CO determination). The free end of the wires exited the catheter through a small side hole which was sealed with epoxy resin. The thermistor end of the catheter was plugged with epoxy (13 mm in length) and a small slit of one third of the circumference was made just beyond the plug at a 45° angle to the long axis of the probe. This slit enabled the injected fluid to travel against the direction of the blood flow and away from the thermistor initially, and thus assured good indicator-blood mixing.

After making a lateral abdominal incision exposing the left renal vein, a 19G needle was inserted through the kidney capsule and into the renal vein. The needle was removed and was quickly followed by the thermistor probe. Positioning the probe beyond the renal vein and into the inferior cava could be avoided by checking the effect of injecting cold saline into the femoral vein. Finally, before restoring the kidney to its normal anatomical location, the positon of the probe was secured by placing 1-2 drops of a tissue adhesive, methyl-2-cyano-acrylate (Eastman 910), on the kidney at the exit site of the probe. Renal blood flow was estimated by injecting 0.32 ml (gravimetrically calibrated) sodium chloride solution at room temperature through the thermistor probe into the renal vein, registering the temperature-time curve and calculating flow, in ml/min/kidney, by the equation:

$$RBF = V_i (T_b - T_i) 60K/A$$

All symbols used above can be found in CO determination section.

Blood pressure and heart rate. Arterial blood pressure (ABP) was measured from the right femoral artery with a Statham pressure transducer (P23Db) via a PE 90 polyethylene tubing. A Beckman dynograph provided recordings of pulsatile blood pressure traces as well as the electronically derived mean arterial blood pressure (MABP). The pulse pressure signal triggered a cardiotachometer, which displayed beat-to-beat heart rates (HR) on the dynograph. Renal vein pressure (RVP) was recorded by utilizing the injection port of the local thermodilution probe, between RBF determinations (see above).

Calculated variables. Stroke volume (SV, ml/beat) was calculated by dividing CO ((ml/min) by the HR (beat/min). Total peripheral resistance (TPR, mm Hg/(ml/min)) was calculated from the ratio of MABP and CO. Similarly, renal vascular resistance (RVR, mm Hg/(ml/min)) was obtained from the ratio of MABP minus RVP and RBF.

BLOOD VOLUME CHANGES

Blood volume (BV) was manipulated by rapid withdrawal (within 30 sec) via the femoral artery of 10% of the calculated BV (54 ml/kg) of the rabbit (Sjostrand, 1962), or by the rapid infusion of warmed (38°C) dextran (M. W. 73,000) achieved +10% BV as required. Otherwise, infusion of the previously withdrawn blood returned BV to control level. All syringes were heparinized.

DENERVATION

Aortic nerve denervation. The rabbit offers a unique anatomical advantage in the study of the various input components for reflex cardiovascular control. The aortic nerve of the rabbit is distinct and separate from the vagus nerves (Whitehouse and Grove, 1967). This arrangement enables the selective ablation of

aortic arch baroreceptors. This is not possible in the dog or cat requiring more difficult and elaborate procedures (Edis, *et al.*, 1970). Aortic nerves were located with the aide of a dissecting microscope and were sectioned near their origin by the anterior laryngeal nerve.

Carotid sinus nerve was sectioned by following the method of Alexander and Decuir (1966). Briefly, with the aid of the dissecting microscope, the carotid bifurcation was located and the common carotid artery was stripped free of other tissues. Similarly, both the internal and external carotid arteries also had all tissue teased away, for approximately 2 cm distance from the bifurcation.

The completeness of sino-aortic denervation (SAD) was tested by bilateral carotid occlusion. Abolition of hypertensive and tachycardiac responses followed a successful SAD. If SAD proved incomplete, the bifurcation was again cleaned and tested. If a small response persisted, the animal was not used.

Vagotomy. Fine sutures were placed around the right and left, and were sectioned after control experiments (see PROTOCOL, below).

PROTOCOL

Fig. 2 illustrates the protocol followed in this study. Blood volume (BV) changes (±10%) took approximately 30 seconds, and remained at each state for a total of 3 minutes. In case of starting with +10% BV first, the dextran solution was injected. Following period 5, the vagi were sectioned, and after the animal returned to steady state, the sequence of period 1 through 5 was repeated (Fig. 2).

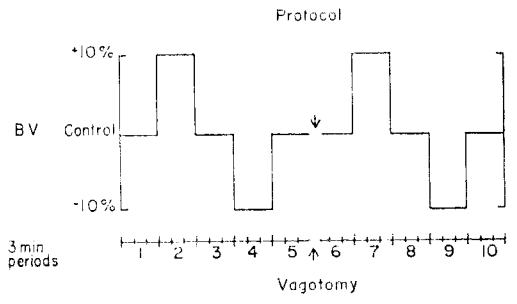

Fig. 2. Experimental protocol showing time sequence of blood volume shifts (±10%) pre- and post-vagotomy.

EXPERIMENTAL DESIGN AND STATISTICAL TREATMENTS

This study included 12 intact and 12 SAD rabbits. One half of each group having CO measured and in the other half RBF was determined. In both, intact and SAD groups, vagotomy was performed after the period 5 (PROTOCOL). Therefore, statistical significance of the differences between intact and SAD were made by grouped *t*-test, and that between pre- and post-vagotomy was determined by paired *t*-test. Since we used values from the intact group twice (intact vs. SAD, and intact vs. vagotomy), it required Bonferroni modified *t*-test. Simply stated, the critical *t* values at $p=0.025$ (0.05/2) for a given degree of freedom have to be exceeded in order to conclude a statistical significance at $p \leqq 0.05$ (Glantz, 1981; Wallenstein *et al.*, 1980). Results of BV shifts (±10%) were compared to each of its own control (normovolumia preceded each BV shift, Fig. 2). Thus, paired *t*-tests suffice. Again, we rejected null hypotheses when *p* values were equal to or less than 0.05.

RESULTS

CONTROL VALUES

Numerical values of normovolumic conditions are summarized in Table 1, and graphically in Fig. 3, where changes following BV shifts are also illustrated. MABP and HR values agree with published data (Edwards *et al.*, 1959; Korner, 1965; and Fox *et al.*, 1969). Resting CO measurements (202±18 ml/min/kg) is somewhat lower than the unanesthetized value

Table 1. Effect of nerve section in the normovolumic rabbits

VARIABLES	A	B	C	D	Group-*t* A-C	Pair-*t* A-B	Pair-*t* C-D
MABP, mm Hg	94±3	101±4	119±4	145±4	*	*	**
HR, beat/min	263±4	265±5	275±6	275±4			
CO, ml/min	606±54	570±54	531±48	399±30			*
SV, ml/beat	2.3±0.2	2.2±0.2	1.9±0.2	1.4±0.1	*		*
TPR, mm Hg/(ml/min)	0.16±0.02	0.18±0.02	0.22±0.02	0.36±0.03	*		**
RBF, ml/min/kidney	54±5	57±4	59±7	49±7			*
RVR, mm Hg/(ml/min)	1.74±0.11	1.77±0.14	2.02±0.04	2.96±0.36	*		*
RVR/TRP	11.22	9.83	9.02	8.15			
RBF/CO ×100, %	8.91	10.00	11.11	12.28			

A, Sinoaortic baroreceptor intact; B, Sino-aortic baroreceptor intact and vagotomy; C, Sino-aortic baroreceptor denervation (SAD); and D, SAD and vagotomy. There were 6 rabbits in each group with body weight averaging 3.1±0.1 kg. MABP. mean arterial blood pressure; HR, heart rate; CO, cardiac output; SV, stroke volume; TPR, total peripheral resistance; RBF, renal blood flow; RVR, renal vascular resistance. Values are mean±1 S. E.; * for $p<0.05$; and ** for $p<0.01$.

(252 ml/min/kg, Warren *et al.*, 1974), but are comparable with other reports (214 ml/min/kg, Korner, 1965; 175 ml/min/kg, Edwards *et al.*, 1959). RVR was 11 times TPR per kidney or 5.5 times TPR for both, and RBF constituted 17.82% of CO are also within normal ranges.

Sino-aortic denervation (SAD) eliminated the inhibitory inputs from the arterial baroreceptors to the CNS and hypertension resulted as expected. The absence of positive change in CO indicates peripheral vasoconstriction was the cause of the hypertension following SAD. Changes in RVR and RBF were not statistically significant, indicating RVR contributed little, if any, to the increased TPR. In fact, RVR/TPR decreased and RBF/CO increased, suggesting just the opposite (Table 1).

Vagotomy. After period 5, and returning the rabbit to a normovolumic state, bilateral vagotomy was performed in intact, as well as in SAD, rabbits (PROTOCOL, Fig. 2). Following vagotomy, MABP was elevated slightly in the intact (+7 mm Hg), but was severe in the SAD group (+26 mm Hg and +51 mm Hg, compared to intact group, Table 1). RBF and RVR were unchanged following vagotomy in intact rabbits, but increased following SAD and vagotomy. However, relative to the TPR, RVR decreases (RVR/TPR=11 in intact, but only 8 in the SAD vagotomized rabbits, Table 1). RBF also constituted a greater fraction of CO in SAD and vagotomized rabbits than in the intact (Table 1).

HYPERVOLUMIA and HYPOVOLUMIA

In this study, BV shifts (±10% BV) were accomplished by rapid withdrawal or infusion 30 sec and maintained for a total of 3 min. We subjected, 1) sino-aortic baroreceptor intact rabbits (intact), 2) intact rabbits following vagotomy, 3) sino-aortic baroreceptor denervated rabbits (SAD), and 4) SAD following vagotomy, to BV shifts.

Comparison Within Groups

Intact. Blood volume reduction caused significant increase, and BV expansion decreased MABP. Heart rate varied in the opposite directions of MABP changes. Stroke volume decreased with −10% BV, and increased with +10% BV. The combined changes in HR and

SV significantly reduced CO following BV reduction and enhanced CO with BV expansion. With BV shifts, reciprocal changes occurred in TPR, but not in RVR. RBF decreased with blood withdrawal and increased with infusion. RBF changes with unvaried RVR reflected transient effect of systemic circulation on RBF (Fig. 3).

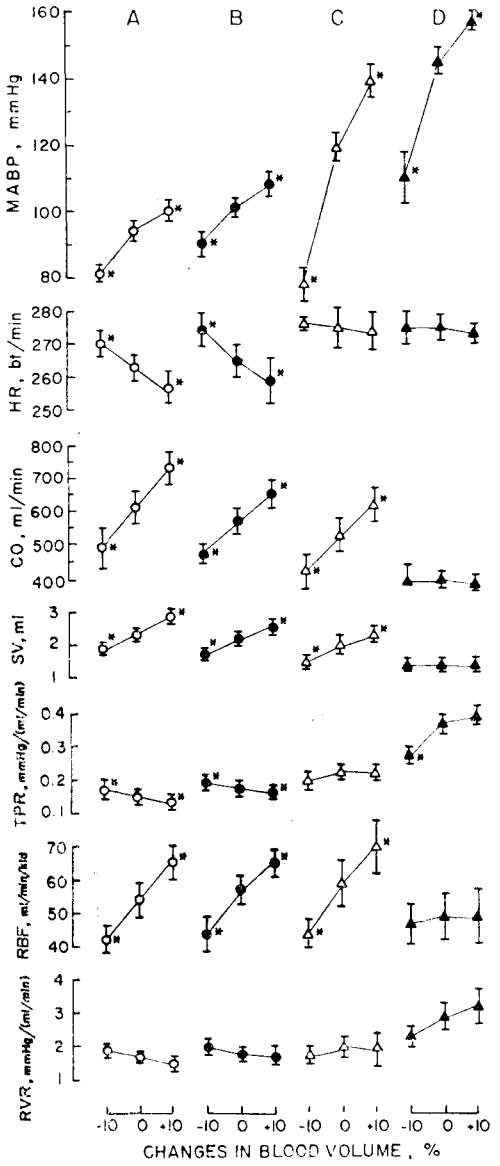

Fig. 3. General and renal hemodynamics resposes to ±10% blood volume changes in the sino-aortic baroreceptors intact (A), vagotomized (V), sino-aortic denervated (C), and sino-aortic denervated plus vagotomized (D) rabbits. Other abbreviations see Table 1. *, statistical differences at $p<0.05$ compared to normovolumic values.

Vagotomy. Alone did not alter the responses to BV shifts as described in intact rabbits (Fig. 3).

SAD exaggerated the hypertensive responses of BV expansion and hypotensive with BV reduction. BV shifts have no effect on HR, TPR, RBF, and RVR. BV expansion increased both SV and CO, and BV reduction had the opposite effects (Fig. 3).

SAD with vagotomy. BV shifts in this group influenced only the MABP (increase with +10% BV, and decreased with −10% BV). All other parameters remained unaffected by BV shifts.

Comparison Between Groups

RVR and TPR. The relationships between and CO, and between MABP and RBF are illustrated in Fig. 4. Progressive increases in RVR, as well as TPR, followed increasing steps of denervation, i.e., vagotomy, SAD, and SAD with vagotomy, as evidenced by the progressive-

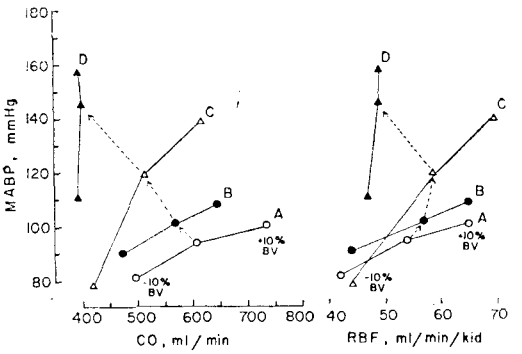

Fig. 4. Relationships between mean arterial blood pressure (MABP) and cardiac output (CO), and between MABP and renal blood flow (RBF) in various neural states and during acute blood volume shifts. A, sino-aortic intact rabbits; B, vagotomized rabbits; C, sino-aortic denervated rabbits; and D. sino-aortic denervated plus vagotomized rabbits.

ly steeper slopes of the MABP-blood flow relationships (changes from A to D, Fig. 4). Where individual values of RVR and TPR were elevated progressively following denervations, the RVR relative to TPR decreased progressively from 11.22 in the intact to 8.15 in the rabbits with SAD and vagotomy (Table 1, Fig. 5).

CO, RBF and MABF. Cardiac output decreased progressively as MABP rose, resulting from denervations. On the contrary, RBF varied less than 10% (+6% in intact with vagotomy, +9% in SAD, and −9% in SAD with vagotomy) from the intact values (Table 1, Fig. 4).

RBF and CO. RBF relative to CO increased from 8.91% in the intact animals to 12.28% in the rabbits with SAD and vagotomy (Table 1 and Fig. 5). This results indicate a relative renal vasodilation, rather than vasoconstriction, and neither sino-aortic baroreceptors nor cardiopulmonary receptors affect RVR significantly following short and moderate BV shifts. Changes in RBF reflect variations in systemic circulation prior to autoregulation and humoral factors coming into play.

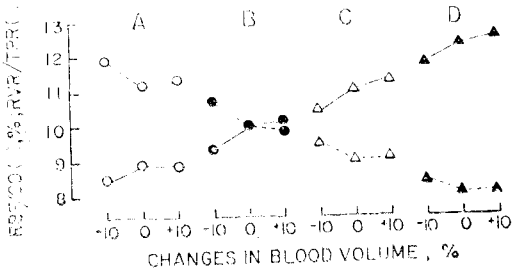

Fig. 5. Renal fraction of vascular resistance (RVR/TPR) and blood flow (RBF/CO, %) in sino-aortic baroreceptor intact (A), vagotomized (B), sino-aortic denervated (C), and sino-aortic denervated plus vagotomized (D) rabbits. Mean data calculated from values presented in Table 1.

Efficiency and sensitivity of ABP control. Ability to compensate for blood pressure changes lessened by progressive denervations. One way for expressing this ability is "Efficiency," which can be calculated according to Guyton *et al.* (1951) as:

$$\% \text{ Efficiency} = \left[1 - \frac{\Delta ABP \text{ (intact)}}{\Delta ABP \text{ (denervated)}}\right] \times 100$$

Opening of negative feedback loops decreased efficiency to compensate blood pressure changes resulting from hemorrhage or blood infusion. The intact rabbits showed a greater efficiency for restoring ABP in hemorrhage than in BV expansion (Table 2). Another way of expressing the ability to control ABP is the sensitivity of baroreceptor responses, i.e., $\Delta HR/\Delta APB$. The heart rate change per unit change in ABP decreased drastically as denervation progressed. Differences were not apparent between +10% BV and −10% BV (Table 2). These findings are presented here to show the preparations, used in this study, behaved as expected in regards to their blood pressure control by neural mechanisms.

Table 2. Efficiency and sensitivity of ABP control

Rabbit	−10% BV				+10% BV			
	ΔABP mm Hg	%E	ΔHR b/min	ΔHR/ΔABP b/min/mm Hg	ΔABP mm Hg	%E	ΔHR b/min	ΔHR/ΔABP b/min/mm Hg
Intact	−11	69	+7	−1.0	+ 6	50	−6	−1.0
Vagotomy	−11	69	+9	−0.82	+ 7	42	−6	−0.86
SAD	−41	−17	+1	−0.02	+20	−67	−1	−0.05
SAD+vagotomy	−35	0	0	0	+12	0	−2	−0.17

Mean data calculated from values presented in Table 1 and Fig. 3.

DISCUSSION

Overwhelming evidences exist favoring the participation of the cardiopulmonary (CP) sensory ending, whose afferents travel to the CNS via vagi and the spinal sympathetic nerves, in reflex control of antidiuretic hormone release (Goetz, *et al.*, 1975), renal sympathetic nerve activity (Karim, *et al.*, 1972; Mancia, *et al.*, 1973; Clement, *et al.*, 1972), renin release (Mancia, *et al.*, 1975; Thames, *et al.*, 1971), and heart activity (Karim, *et al.*, 1972; Linden, 1979). It is obvious that all these reflexes directly or indirectly affect renal circulation, as well as renal function, and eventually, also the general circulation. Therefore, in a long term and severe disturbance of general circulation, clear cut reflex control of RBF via the CP sensory endings cannot be made. This study presents evidence showing negligible reflex control of RBF by this mechanism. The results previously reported to the contrary, are attributable to indirect effects of factors other than reflex control of RBF via CP receptors agreeing with views held by Goetz, *et al.* (1975).

In most studies, stimuli to CP receptors were supplied by disturbances in systemic and/or pulmonary circulation. Thus, demonstration of changes in renal sympathetic nerve activity or changes in renal vascular resistance (or conductance) is not synonymous with alterations in RBF. For example, minimal change in RBF were observed during vagal cold block in anesthetized dogs, either with or without functioning arterial baroreceptors (Mancia, *et al.*, 1975), where this procedure was known to produce drastic effect of renal sympathetic nerve activity (Mancia, *et al.*, 1973). RBF reduction was negligible with increased RVR because MABP was also raised under such conditions. Undoubtedly, altered renal sympathetic nerve activity under such condition contribute significantly in restoring circulatory perturbation by means other than changes in RBF. Changes in RVR detected under various physiological conditions also cannot be automatically equated as change in RBF had occurred, unless MABP remains unchanged. For example, both TPR and RVR rose progressively, compared to the intact state following vagotomy, SAD, SAD and vagotomy. But RBF varied little because systemic ABP also rose under these conditions. It is no wonder that Goetz, *et al.* (1975) concluded, following extensive reviews, that "the available evidence suggests that atrial receptors exert a rather minimal influence on renal blood flow compared with the influences of other factors." The results presented here concur with this conclusion.

The evidence presented here indicates RBF was minimally affected by denervations of vagus nerve and arterial baroreceptors suggesting that these nerves play a negligible role in controlling RBF normally. These results agree with others in that increasing numbers of denervation elevated TPR and hypertension following stepwise elimination of inhibitory feedback loops. However, these results are in disagreement with others regarding the participation of renal vasculature in the widespread general vasoconstriction. The evidence that RVR/TPR fell and RBF/CO rose progressively with increasing denervations, and thus maintaining a RBF near the control level, further indicate unimportant roles played by vagus nerves and arterial baroreceptors in controlling RBF normally, as well as during moderate BV disturbances.

The significant pressure response with vagotomy and vagotomy following SAD implies that inputs from CP receptors exert continuous restraint on sympathetic adrenergic outflow (Mancia and Donald, 1975). Neither the source, nor the relative importance of these inhibitory inputs from CP receptors and arterial receptors have

been satisfactorily resolved. On the other hand, the moderate pressure response with vagotomy before SAD and very impressive responsive after SAD support the hypothesis of "mutually inhibitory addition" (Sagawa and Watanabe, 1965) and refute the hypothesis of simple addition. The results reported here suggest existence of convergent inhibitory synapses from vagal afferent nerves and sino-aortic nerves in the medulla. Inhibitory influence on the sympathetic adrenergic outflow is removed only when both are eliminated (SAD and vagotomy). Findings of several groups of investigators (Ott and Shepherd, 1973; Oberg and Whits, 1970) suggest inhibitory input from vagal afferent receptors is projected into the vasomotor center with outflows in the renal vascular bed. Input from aortic arch and carotid sinus baroreceptors on the other hand, have a preferential effect on neuronal pools with sympathetic outflow tracts to skeletal muscle and splanchnic vascular beds. The interplay between arterial baroreceptors and CP receptors on RBF remains to be elucidated (Mancia *et al.*, 1976). Where it is indisputable that receptors in the heart and the lungs contribute to the reflex control of renal sympathetic nerve activity, results of the present study indicate the changes of sympathetic nerve activity does not necessarily result in alteration in RBF.

The passiveness of the renal circulatory behavior presented in this study cannot be a result of neurologically non-responsive preparations. The diminishing control efficiency and baroreceptor sensitivity attributable to progressive denervations (Table 2) confirms previous reports, and are in keeping with the concept of negative feedback controls. The results presented in Table 2 indicate the magnitude of ABP changes in the intact rabbits resulting from-10% BV is only 30% (and 50% in+10% BV) of the changes occurred in the SAD and vagotomized rabbits. In other words, the baroreceptors prevented 70% of the decrease and 50% of the increased, and are thus 70% and 50% efficient, respectively. These values are similar in magnitudes as that reported by Guyton, *et al.* (1951) for the dog.

In summary, the evidence is presented showing TPR rose and RVR/TPR fell progressively following advancing denervations, indicating non-contribution of RVR to the rise of TPR and hypertension. Cardiac output was reduced but RBF/CO rose progressively following the same denervation procedures, suggesting a relative vasodilation in the kidneys. Responses of renal circulation to BV shifts resemble that of changes in cardiac output in the intact, vagotomized, SAD, and SAD with vagotomized rabbits, indicating negligible influence of these nerves on renal circulatory control, normally and during hemorrhage or infusion. Alterations of RVR were demonstrated with progressive denervations as well as during BV shifts, but concurrent changes in MABP maintained RBF within normovolumic ranges further indicating negligible reflex control of RBF during mild BV disturbances.

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心肺受器和竇弓壓力受器對體循環和腎循環恒定的功能

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摘 要

當心肺受器 (cardiopulmonary receptors) 受刺激時，首先抑制腎臟交感神經的活性，除了引起反射性的釋放抗利尿激素 (ADH) 和腎素 (renin) 外，還導致腎臟血管舒張反應。若刺激竇弓壓力受器 (sino-aortic baroreceptor)，則在其他各部位，對血管發生作用，特別是在骨骼肌上。

爲測出正常生理情況下，由於血容急速變化量 (±10%) 所引起心肺受器的反應對腎循環的影響，本實驗將動物（兎）分爲四組：(A) 對照組，(B) 切除迷走神經組，(C) 切除竇弓神經組，(D) 切除迷走竇弓神經組。記錄腎循環和體循環的反應，以決定迷走神經和竇弓神經控制腎循環的功能。

隨着逐步切除神經的情況（切除迷走神經，切除竇弓神經及切除迷走和竇弓神經），動物有漸進性高血壓和低心輸量的反應。當急速改變血容量時，引起腎血流速反應後，緊隨着就是心輸量變化，而這種情形，無論神經是否切除均會發生。換言之，血容量改變時，腎血流速的變化和整個個體的反應是相同的。因之，在正常生理狀況下，動物脈內低血壓受器或高血壓受器均不對腎血流速率發生效應。