Inhibition of the Aortic Depressor Reflex by Continuous Carotid Sinus Nerve Stimulation[1] (37428)

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One of the most important control mechanisms in the regulation of the circulation is the sino-aortic depressor reflex. Increasing pressure in the baroreceptive areas, or electrical stimulation of the afferent fibers emanating from these areas, results in a decrease in heart rate, systemic blood pressure and peripheral vascular resistance (1). Although it has generally been assumed that both carotid and aortic baroreceptors influence the cardiovascular regulatory centers in a similar fashion, a preliminary observation by Beck and Brody (2) demonstrated that electrical stimulation of the central ends of the cut vagi in the dog resulted in reflex vasodilatation, which unlike that resulting from sinus nerve stimulation, could not be sustained.

In the present investigation, the effect on reflex vasodilatation of selective carotid sinus and aortic baroreceptor stimulation was evaluated to determine if any interactions could be demonstrated between the baroreceptor afferents. This report presents evidence for a previously undescribed inhibitory influence of the carotid sinus reflex on the depressor reflex.

Materials and Methods. Two methods of inducing the baroreceptor reflex were studied. In 6 mongrel dogs anesthetized with pentobarbital (30 mg/kg), paralyzed (decamethonium, 0.25 mg/kg) and ventilated artificially, the carotid sinus nerves were exposed and sectioned. The aortic depressor fibers were located in the vagosympathetic trunk approximately 30 mm below the carotid bifurcations and identified by the production of hypotension upon electrical stimulation. The vagi were sectioned and the central ends of the two aortic depressor nerves and the two carotid sinus nerves were placed upon fixed stainless steel stimulating electrodes and bathed in mineral oil. In 6 other animals, the baroreceptors were excited by increasing pressure in the carotid sinuses and/or the aortic arch. The carotid bifurcations were completely isolated according to the nonflow-through technique of Moissejeff (3). Cannulae from a Sigmamotor pump were placed in each common carotid artery below the bifurcation. Removal of a clamp on the perfusion tubing distal to the operating pump subjected the carotid baroreceptors to a pulsatile pressure with a mean of 200 mm Hg, and a 40 mm Hg pulse. The frequency of the pulses was 100 per minute. Pressure was adjusted by changing the resistance of an outflow tube on the distal side of the pump between the pump and cannulated arteries. To excite the aortic baroreceptors, intraaortic pressure was increased by inflation of a balloon resting in the aorta at the point of origin of the left subclavian artery.

Changes in peripheral vascular resistance were measured in the right hind limb of each animal perfused at a constant rate by a Sigmamotor pump interposed between the sectioned iliac artery (4).

Results and Discussion. Electrical stimulation of carotid and aortic baroreceptor afferents results in an immediate transient vasodilatation followed by a sustained vasodilatation of lesser magnitude. The tracing in Fig. 1 illustrates the vasodilator reflex in the limb and the fall in systemic blood pressure in response to electrical stimulation of carotid sinus and aortic depressor nerves (ADN). It is evident from the tracing that

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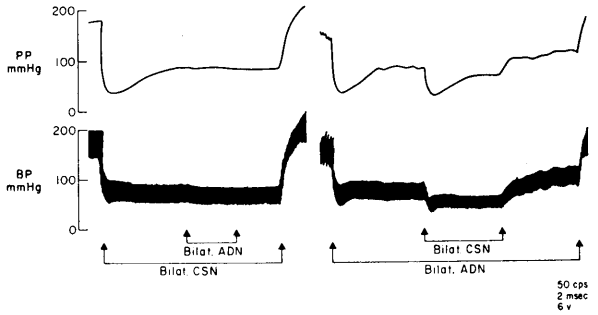

FIG. 1. The effects of continuous bilateral (bilat) carotid sinus nerve stimulation (CSN) and subsequent bilateral aortic depressor nerve (ADN) stimulation on limb perfusion pressure (PP) and systemic blood pressure (BP) in the anesthetized dog and vice versa. Time base: bilateral ADN stimulation on the left performed for 1 min, 15 sec as shown by the interval between the arrows.

carotid sinus and aortic depressor nerve stimulation both result in transient vasodilator responses of nearly equal magnitude. The effects of continuous carotid sinus nerve stimulation on the response to subsequent aortic depressor nerve stimulation, and vice versa, are also illustrated. The major finding was that the response to aortic depressor stimulation was blocked during continuous carotid sinus stimulation. This blockade occurred even though considerable potential to dilate further was present. On the right side of the figure, it can be seen that the ability of ADN stimulation to lower perfusion was the same as that of carotid sinus stimulation, *i.e.*, perfusion pressure fell to approximately 40 mm Hg in both cases. However, during continuous carotid nerve stimulation, no response to ADN stimulation was seen even though perfusion pressure could have been reduced by approximately 50 mm Hg. However, the converse of this situation was found not to be true. Continuous stimulation of aortic depressor fibers failed to block the response to subsequent carotid sinus nerve stimulation. This is further evidence that the block is specific and not the result of loss of vasodilator capacity.

The effects of exciting carotid and aortic baroreceptors by increased sinus or aortic pressure on the perfusion pressure and systemic blood pressure responses were similar to those produced by electrical stimulation of sinus and aortic nerves. It should be noted, however, that in distinction to electrical stimulation, continuous carotid sinus pressure activation did not block the responses to subsequent aortic baroreceptor excitation.

A schematic diagram summarizing the changes in limb perfusion pressure produced by the two methods of eliciting the baroreceptor reflex is presented in Fig. 2. The numerical and statistical summaries of the

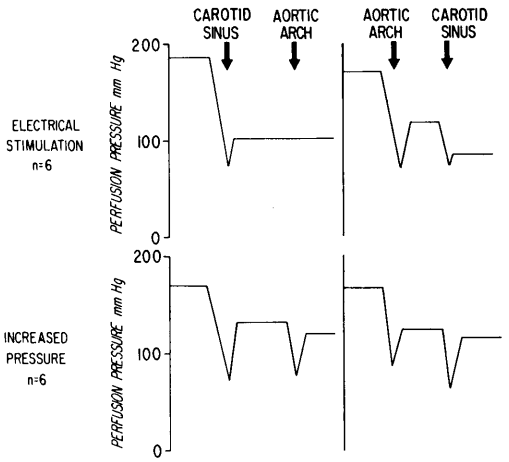

FIG. 2. Average changes in limb perfusion produced by electrical and pressure activation of the baroreceptor reflex. Note the well-maintained vasodilator response to carotid sinus nerve stimulation (upper left). This response was significantly greater ($p < 0.05$) than the maintained response to any of the other interventions. Also note the absence of the aortic reflex during carotid sinus nerve stimulation. There was no statistically significant difference between the peak dilator responses elicited by either electrical or pressure activation of the sino-aortic reflex. Statistical analyses were performed using either grouped or paired comparison t tests (5).

TABLE I. Interactions Between Baroreceptor Afferents Excited Electrically or by Increased Pressure.[a]

	Magnitude of transient reflex dilatation			Magnitude of transient reflex dilatation		
	Sinus	Sinus during arch activation	Diff ± SE	Arch	Arch during sinus activation	Diff ± SE
Electrical stimulation ($n = 6$)	—0.59	0.38	0.21 ± .06[b]	0.58	0	0.58 ± .06[c]
Increased pressure ($n = 6$)	—0.56	—0.45	0.11 ± .05	—0.46	—0.40	0.06 ± .04

[a] Values are ratios of the change in perfusion pressure due to treatment, divided by the perfusion pressure prior to the response. Comparisons were made with paired-comparison t test.
[b] Indicates a significant difference, $p < 0.05$.
[c] Indicates a significant difference, $p < 0.001$.

vasodilator responses produced by baroreceptor activation and interactions between baroreceptors are found in Tables I and II. The maximum transient vasodilatation in the hind limb was the same whether the reflex was elicited by aortic or carotid baroreceptors (Table I). There was also no difference in the transient reflex response produced by electrical or pressure activation. Additionally, as shown in Fig. 2 and Table I, there was no statistically significant difference in the level of the sustained vasodilator response produced by aortic depressor nerve stimulation or by pressure activation of carotid sinus or aortic arch baroreceptors. However, the sustained response produced by electrical stimulation of carotid sinus nerves was significantly greater ($p < 0.05$) than the sustained response produced by any of the other interventions (Table II).

The ability of carotid sinus nerve stimulation, but not increased carotid sinus pressure, to block the response to aortic depressor nerve stimulation is also summarized in Fig. 2 and Table I. The mean level of sustained perfusion pressure during continuous sinus stimulation was 103 mm Hg and the mean maximum level of the transient dilatation produced by aortic nerve stimulation in the absence of continuous sinus nerve stimulation was 75 mm Hg. The potential existed, therefore, for a dilatation of at least 28 mm Hg, yet none occurred.

The effects noted on limb vascular resist-

TABLE II. Magnitudes of Sustained Dilatations Produced in the Hind Limb by Bilateral Electrical Stimulation of the Carotid Sinus and Aortic Depressor Nerves and by Pressure on the Carotid Sinus and Aortic Arch Regions.[a]

	Sustained dilatation		
	Sinus	Arch	Diff ± SE
Electrical stimulation ($n = 6$)	—0.46	—0.22	0.24 ± .04[b]
Increased pressure ($n = 6$)	—0.24	—0.21	0.03 ± .04
Difference ± SE	0.22 ± .05[c]	0.01 ± .06	

[a] Values are ratios of the change in perfusion pressure due to treatment, divided by the perfusion pressure prior to the response. Horizontal comparisons were made with paired-comparison t test, while vertical comparisons are group t tests. The greater the negative value the greater was the dilatation.
[b] Indicates a significant difference, $p < 0.01$.
[c] Indicates a significant difference, $p < 0.001$.

ance were also seen on arterial pressure. Continuous CSN blocked the fall in arterial pressure produced by ADN stimulation but not vice versa (Fig. 1).

The blockade of the response to aortic nerve stimulation in the face of continuous sinus nerve stimulation is intriguing. In all experiments, even though the magnitude of the transient dilatation produced by aortic depressor nerve stimulation was greater than the sustained dilatations resulting from continuous sinus nerve stimulation, the response to aortic nerve stimulation was blocked. This would seem to indicate that the mechanism for the blockade involves more than a simple lack of sufficient neurogenic tone which could be removed by the aortic depressor reflex. At present, however, the precise mechanism of the blockade remains obscure although it is interesting to note that Gabriel and Seller (6) have reported electrophysiologic evidence demonstrating that evoked potentials in the medullary vasomotor area produced by electrical stimulation of one baroreceptor afferent could be reduced by 50% during concomitant stimulation of the contralateral baroreceptor afferent nerve.

A brief discussion of the possible participation of chemoreceptor fibers in the observed interactions between carotid sinus and aortic depressor nerves is warranted. Since the chemoreceptor afferents originating in the carotid and aortic bodies are carried with the baroreceptor afferents, electrical stimulation of the carotid sinus and aortic depressor nerves should theoretically excite chemoreceptor afferents as well as baroreceptor afferents. When the potent chemoreceptor stimulant, potassium cyanide, was administered iv (1 mg/kg) to some animals prior to raising sinus or aortic pressure, the systemic effects of chemoreceptor activation were clearly present (increased blood pressure and respiratory rate) yet no blockade of either the sinus response by the aortic arch baroreceptors or blockade of the arch response by carotid sinus baroreceptors could be detected. In similar experiments, potassium cyanide introduced into the isolated carotid sinus was without effect in producing a blockade of the aortic arch baroreceptor response. Thus even intense chemoreceptor activation fails to block reflex vasodilatation evoked by increased aortic arch pressure.

It is tempting to speculate that the interactions observed between electrical stimulation of carotid sinus and aortic depressor nerves might result from the excitation of fibers from an unidentified peripheral receptor, whose afferent fibers are contained in the carotid sinus but not aortic depressor nerves. The proposed receptor could be capable of sustaining a large reflex vasodilatation and also of blocking the aortic depressor reflex. It is probable that the receptor is not of the ordinary "stretch" type since the selective carotid sinus baroreceptor stimulus of increased pressure failed to result in a sustained reflex vasodilatation of comparable magnitude to that resulting from electrical stimulation of the carotid sinus nerves. Furthermore, no blockade of the response to aortic baroreceptor stimulation was observed during continuous elevation of sinus pressure. The function of the postulated receptor in overall cardiovascular regulation remains to be defined.

Summary. The aortic depressor reflex cannot be elicited in anesthetized dogs during continuous carotid sinus nerve stimulation. It is postulated that the blockade of the aortic reflex is due to excitation of unidentified afferent fibers contained in the carotid sinus nerve, which probably do not arise from chemoreceptors and which are apparently not of the classical baroreceptor type since the selective stimulus of increased sinus pressure failed to block the aortic reflex.

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