Carotid Sinus Baroreceptor Reflex Effects upon Myocardial Contractility

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At the present time, the reflex effects of stimulation of the carotid sinus baroreceptors on atrial and ventricular dynamics are the subject of controversy. Several investigators have suggested that stimulation of the carotid sinus baroreceptors has a reflex negative inotropic effect directly upon cardiac performance. The work of Sarnoff and co-workers has adduced substantial evidence for this concept. Salisbury et al., however, after comparing the effects of occluding the aorta, brachiocephalic artery, and common carotid artery, denied the existence of this reflex effect. They suggested that the changes in cardiac performance observed by previous investigators might have been the indirect result of reflex changes in venous return, arterial impedance, and heart rate; or that they might have been due to the existence of excessively high heart rates, or to concomitant cerebral ischemia.

The purpose of the present study was to examine this problem under more rigorously controlled conditions. Experiments were done on an innervated, metabolically supported, but hydraulically isolated, auxotonic left heart preparation. Sixteen experiments were performed in an innervated, metabolically supported, but hydraulically isolated, auxotonic left heart preparation. The experimental dogs weighed 15.0 ± 2.7 kg (mean ± sp), and the donor dogs, 22.4 ± 4.2 kg. All animals were anesthetized with morphine sulfate, 2 mg/kg iv, followed 45 minutes later by a warmed infusion of urethane, 600 mg/kg iv, and chloralose, 80 mg/kg. A bilateral, high cervical vagotomy was performed, and both carotid sinus nerves were dissected free. A right-sided, isolated carotid sinus preparation was made in five animals. Intermittent, positive-pressure breathing was instituted through a tracheal cannula, and a bilateral thoracotomy was performed in the fourth intercostal space. Heparin, 3.4 mg/kg iv, was administered to prevent blood coagulation and supplementary doses were repeated every 30 minutes. A large-bore cannula was inserted in the brachiocephalic artery (fig. 1, BC), and the cephalic portion of the experimental animal was perfused with arterial blood from the donor animal by means of a Sigmamotor pump. The superior vena cava (SVC) was cannulated, and the cephalic venous blood was returned to an external jugular vein of the donor. A large-bore cannula, connected to a reservoir (RES) filled with arterial blood, was inserted into the left atrial appendage. A large-bore cannula was also inserted into the descending thoracic aorta (AO) and was advanced upstream until its tip was just distal to the origin of the left subclavian artery (LS). From this cannula, the left ventricular output was diverted to the reservoir through an artificial external circuit, containing an adjustable resistance (R, a screw clamp) and a heat exchanger (H). The resistance was preset to establish arterial pressure at a normal level, and then was kept constant during the subsequent experiments and observations. The inferior vena cava and the hilus of the right lung were ligated. The coronary venous blood was returned to an external jugular vein (EJV) of the donor animal from a cannula inserted in the left pulmonary
artery (PA). Oxygenated blood was returned from the donor animal to the left atrial reservoir through a sidearm of the arterial line of the cephalic perfusion system. The blood level in the reservoir was kept constant by means of an overflow system (OF). The temperatures of the blood in the left atrial reservoir and brachio-ccephalic artery were kept constant at 37°C. The sinoatrial node was crushed, and the right atrial appendage was stimulated at a constant rate by an electronic stimulator. In nine experiments, the heart rate was lower than 150 beats/min (137 ± 19), and in seven experiments, it was between 150 and 176 beats/min (159 ± 7.5).

Phasic or mean pressures were recorded by means of strain gauges (SG) from the left atrium, aortic arch at the origin of left subclavian artery, cephalic perfusion system, and isolated carotid sinus. In all experiments, phasic flow was recorded with an electromagnetic flowmeter (FM) in the artificial external left ventricular circuit close to the origin of the left subclavian artery, and mean brachiocephalic arterial inflow was measured in ten experiments. The methods of recording phasic pressure, phasic flow, power, external work, and ventricular output (total left ventricular output minus coronary flow) were identical to those described previously. In the present study, cardiac output and work were not computed on a beat-by-beat basis, but over a constant time interval, usually five seconds. These values were called "accumulated" volume and work, and are proportional to stroke work and stroke volume at constant heart rates. As pointed out previously, during steady state observations, stroke work and stroke volume computed at the level of the left subclavian artery are virtually identical to values obtained at the root of the aorta. The phasic flow and power curves are not identical, however, to tracings obtained at the root of the aorta because of the compliant aortic segment between the flowmeter probe and the aortic valves; the directional changes are probably similar, however. Coronary blood flow was measured under steady state conditions by collecting the outflow from the cannulated pulmonary artery in a graduated cylinder during timed intervals.

ISOVOLUMETRIC PREPARATION

In one vagotomized and six nonvagotomized mongrel dogs, weighing 16.6 ± 2.2 kg and anesthetized as above, a right-sided, isolated carotid sinus preparation was made. The cephalic portion of the animal was perfused as described above, but with blood equilibrated with 95% O₂ and 5% CO₂ in a rotating disc oxygenator (fig. 2).

Diagram of the isovolumetric preparation. SC, subclavian artery; T, temperature probe; RCC, right common carotid artery; LCC, left common carotid artery; CCC, cannula in the right common carotid artery; LAC, cannula in the lingual artery. Other symbols as in figure 1.
The aorta (AO) was ligated just distally to the left subclavian artery (SC). The coronary vascular bed was perfused with arterial blood from the oxygenator by a Sigmamotor pump through a cannula in the left subclavian artery. Coronary inflow was kept constant during the observations since the pump had a constant output. This was verified in three experiments in which coronary inflow was recorded by an extracorporeal probe of a square-wave electromagnetic flowmeter. Coronary perfusion pressure was always kept higher than peak left ventricular systolic pressure. The coronary venous blood was returned to the oxygenator by a cannula inserted through the azygos vein into the right atrium and right ventricle. The inferior vena cava and hili of both lungs were ligated. Through a small incision made in the left ventricular apex, a latex balloon attached to the tip of a rigid cannula was inserted into the left ventricular cavity and fixed to the apical myocardium by a purse-string suture. A cannula with multiple side holes near the tip was also inserted through the same incision to prevent any accumulation of blood in the left ventricle. For the same reason, the left atrium was drained through a cannula inserted by way of a pulmonary lobular vein. The balloon was filled with 0 to 20 ml saline, which was always less than the unstretched volume of the balloon. At the end of each experiment, the left ventricular cavity was opened, the position of the balloon was verified, and the outflow tract was carefully inspected for aortic regurgitation. Heart rate was kept constant at 164.2 ± 23.6 beats/min by electrical stimulation of the right atrial appendage and/or right ventricle.

Results

EFFECTS OF SUPRAMAXIMAL STIMULATION OF CAROTID SINUS NERVES ON AUXOTONIC PREPARATION

The right side of figure 3 shows the effects of supramaximal stimulation of the left carotid sinus nerve in a representative experiment. An immediate decrease in systolic and diastolic aortic pressure occurred, reaching a maximum decrement of 28 and 12 mm Hg, respectively, 25 seconds after start of the stimulation. Accumulated volume decreased 35.4 ml/5 sec, and accumulated work, 4.83 mm Hg-liters/5 sec. Peak aortic flow and power displayed the same directional changes. Mean left atrial pressure rose immediately and reached a maximal increase of 1 mm Hg. Coronary blood flow decreased from 39 ml/min during the control period to 31 ml/min at the point of the maximum cardiac response. Systolic brachiocephalic pressure decreased 28 mm Hg and diastolic pressure 26 mm Hg. Despite continued stimulation, the magnitude of the described hemodynamic changes started to diminish 30 to 40 seconds after the onset of stimulation. Complete recovery (not shown on fig. 3) was observed after the stimulation stopped. Supramaximal stimulation of the right carotid sinus nerve for 28 seconds revealed similar effects (fig. 3, left side). An initial response to mechanical traction on the nerve may be observed just prior to electrical stimulation.

Both carotid sinus nerves were stimulated supramaximally in 11 experiments in a similar fashion. Analysis of these data showed that there existed a significant difference (P < 0.02) between the means of the control values of systolic aortic pressure, mean left atrial pressure, accumulated work and volume and their values during electrical stimulation.

EFFECTS OF CHANGES IN MEAN BRACHIOCEPHALIC PRESSURE ON AUXOTONIC PREPARATION

In another experiment, illustrated in figure 4, the mean brachiocephalic pressure was reduced over a 12-second period from 180 mm Hg to 76 mm Hg. Seven seconds after the cephalic perfusion pressure started to decrease, a gradual increase in systolic and diastolic aortic pressures occurred and reached maximal increments of 21 mm Hg and 6 mm Hg, respectively. Accumulated volume increased 21.5 ml/5 sec, accumulated work, 3.45 mm Hg-liters/5 sec, and coronary blood flow rose from 44 to 88 ml/min. Mean left atrial pressure fell 1.2 mm Hg, and the left ventricular ejection period, as measured on the aortic pressure tracing, shortened from 0.075 sec to 0.064 sec.

Figure 5 presents the pooled data of 12 experiments in which mean brachiocephalic...
perfusion pressure was varied in a stepwise fashion over a wide range. For purposes of comparison, the reference range of perfusion pressure was arbitrarily taken as 60 to 90 mm Hg. An elevation of mean perfusion pressure above the reference level caused a statistically significant decrease in systolic aortic pressure, accumulated work, and accumulated volume ($P < 0.05$), and an increase in mean left atrial pressure ($P < 0.004$). The opposite effects occurred when mean perfusion pressure was lowered below the reference range. The latter changes were statistically significant ($P < 0.04$), except for aortic

![Graph and Table]

**Figure 3**
Effects of supramaximal electrical stimulation of the right carotid sinus nerve (left half of record) and left carotid sinus nerve (right half of record) upon the auxotonic left ventricular preparation in a representative experiment. Upward arrows signify the onset of stimulation; downward arrows, the termination. Stimulus frequency, 60 cycles/sec; intensity, 30 v; form, rectified sine wave. Heart rate constant at 90 beats/min.
systolic pressure, accumulated work, and accumulated volume in the pressure range 30 to 60 mm Hg. This lack of statistical significance was probably due to aberrant values in two experiments.

Figure 6 shows the response to variations in brachiocephalic arterial perfusion pressure after bilateral section of the carotid sinus nerves in the same experiment illustrated in figure 4. To the right of the center of figure 6, reduction of the mean brachiocephalic arterial pressure from 170 to 94 mm Hg caused only small changes in left ventricular performance in comparison to the effects of a similar change in perfusion pressure in the same animal with both sinus nerves intact.
(fig. 4). However, lowering mean brachiocephalic arterial pressure from 164 to 20 mm Hg (fig. 6, left side) for a period of 48 seconds caused a gradual increase in systolic aortic pressure (12 mm Hg), accumulated volume (7 ml/5 sec), and accumulated work (0.92 mm Hg-liter/5 sec). Mean left atrial pressure decreased 0.4 mm Hg. In seven experiments, after section of both carotid sinus nerves, there were no statistically significant differences ($P > 0.1$) between reference values of aortic and atrial pressure, accumulated work, and accumulated volume and their values in the pressure ranges 90 to 130 mm Hg and > 130 mm Hg. However, in the pressure range 0 to 30 mm Hg, highly significant ($P < 0.025$) changes in these 4 parameters were observed which were directionally similar to

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**FIGURE 5**

Effects of changes in mean brachiocephalic arterial pressure on the auxotonic left ventricle in 12 experiments in which the carotid sinus nerves were intact. Values of systolic aortic pressure, mean left atrial pressure, accumulated work, and accumulated volume in the pressure range 60 to 90 mm Hg are arbitrarily taken as reference values. Changes in each of these parameters in the arbitrarily selected pressure ranges (0 to 30; 30 to 60; 90 to 130; > 130 mm Hg) are expressed as percentage changes from the reference values. Dots represent changes in individual experiments; horizontal lines represent mean ± standard error, and $P$ represents the level of statistical significance.
those observed before section of the sinus nerves. In this pressure range, brachiocephalic flow was negligible. In the pressure range of 30 to 60 mm Hg, the changes after section of the carotid sinus nerves were definitely smaller than before section, but only a few observations were made.

**EFFECTS OF PRESSURE CHANGES IN AN ISOLATED CAROTID SINUS PREPARATION ON AUXOTONIC PREPARATION**

The effects on left ventricular performance of stepwise variations of nonpulsatile pressure in an isolated carotid sinus preparation are shown in the left half of figure 7. A pressure rise from 0 to 80 mm Hg had only a slight effect on left ventricular performance; a further elevation to 120 mm Hg had a moderate effect, and a final increase to 160 mm Hg had a pronounced effect. At the highest pressure level, systolic and diastolic pressures decreased 18 and 13 mm Hg, respectively, accumulated work, 2.5 mm Hg-liters/sec, accumulated volume, 12.8 ml/5 sec, and coronary blood flow fell from 65 to 56 ml/min. Mean

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**Figure 6**

Effects of changes in mean brachiocephalic arterial pressure on the auxotonic left ventricle after both carotid sinus nerves had been sectioned in the same experiment depicted in figure 4. Heart rate constant at 150 beats/min.
left atrial pressure rose 1.6 mm Hg. Reduction of the carotid sinus pressure to 96 mm Hg was followed by an almost complete return of all these indices of ventricular performance to their values at 0 mm Hg intrasinusal pressure. As shown on the right side of figure 7, elevation of the nonpulsatile pressure in the same experiment from 200 to 300 mm Hg had no effect. Upon subsequent reduction to 0 mm Hg, changes in cardiac per-

![Figure 7](image)

**Figure 7**

Effects of changes in nonpulsatile pressure in an isolated right carotid sinus upon the aorto-tonic left ventricle in a typical experiment. Mean brachiocephalic arterial pressure 100 mm Hg. Heart rate constant at 145 beats/min.

_Circulation Research, Vol. XV, October 1964_
Effects of changes in nonpulsatile pressure in an isolated right carotid sinus preparation upon the auxotonic left ventricle in four experiments. Values of systolic aortic pressure, mean left atrial pressure, accumulated work, and accumulated volume at 0 mm Hg intrasinusal pressure considered as reference values. Changes in each index of cardiac performance expressed as percentages of the reference values. Each point represents the average change in a given pressure range (30 mm Hg steps) for several observations in an individual experiment.

Coronary blood flow was correlated with aortic pressure and accumulated volume, but it correlated best with accumulated work. In three isolated carotid sinus experiments, there was a statistically significant, positive, linear correlation between changes in work and
coronary flow ($r = 0.92, P \leq 0.04$). In a fourth experiment, $r$ was equal to 0.88, but showed only borderline ($P = 0.06$) statistical significance.

**EFFECTS OF PRESSURE CHANGES IN ISOLATED CAROTID SINUS ON ISOVOLUMETRIC PREPARATION**

In a representative experiment (fig. 9, left side), elevation of the nonpulsatile pressure in the carotid sinus from 0 or 100 mm Hg to 200 mm Hg was followed by an immediate decrease (12 mm Hg) of the peak systolic pressure. Peak systolic pressures at nonpulsatile intrasinusal pressures of 0 and 100 mm Hg were practically equal. At constant flow, coronary perfusion pressure dropped 2.6 mm Hg when the intrasinusal pressure was raised to 200 mm Hg. High-speed tracings in another experiment, (fig. 9, right side) show that a rise of carotid sinus pressure from 100 to 200 mm Hg decreased not only the peak but also the slope of the left ventricular pressure curve, and increased the duration of left ventricular systole while end diastolic pressure remained constant.

In four of seven experiments, a rise of carotid sinus pressure from 0 to 100 mm Hg to 200 mm Hg caused a decrease in peak systolic left ventricular pressure of 12.5 to 17.5%. A decrease of about 5% was observed in the three other experiments. In three of the four most reactive preparations, no detectable changes in end diastolic pressure occurred. The four other experiments showed very small random variations in end diastolic pressure which appeared to be unrelated to the pressure level in the carotid sinus. The coronary perfusion pressure remained constant in one experiment. In five experiments, decreases of 1.2 to 2.6 mm Hg, and in one experiment, a reduction of 9 mm Hg in coronary perfusion pressure were observed when the carotid sinus pressure was elevated to 200 mm Hg.

**Discussion**

The present study demonstrates clearly that
electrical stimulation of the carotid sinus nerves and mechanical stimulation of the carotid sinus baroreceptors depresses the performance of a hydraulically isolated, auxotonic or isovolumetric left heart preparation. This depression is characterized in the auxotonic preparation by a decrease of aortic pressure, ventricular output, and external work, and by a rise in mean left atrial pressure. In the isovolumetric preparation, less peak tension is generated and it is developed at a slower rate.

Prolonged anesthesia, extensive surgery, and dissection in the upper mediastinum, with possible disruption of some nerve fibers, probably interfered with cardiac responses. Greater effects might have been observed if a bilateral carotid sinus preparation had been used.\(^1\) However, application of pulsatile instead of nonpulsatile pressure to the isolated carotid sinus should probably not have increased the maximal responses.\(^1\) Moreover, in the auxotonic preparation, the changes in left atrial inflow and left ventricular output were limited, since variations in mean left atrial pressure were only about 5 to 10% of the total hydrostatic pressure head.

It has been shown amply that stimulation of the carotid sinus baroreceptors causes reflex changes in heart rate, arteriolar resistance, venous return, and rate of secretion of the adrenal medulla.\(^1\) All these variables are known to affect cardiac performance. In the present study, heart rate was kept constant by electrical pacing in all experiments. The coronary blood flow in the auxotonic preparation was always less than 10% of the total left ventricular output. Consequently, any primary reflex changes in the resistive and elastic properties of the coronary vascular bed had little influence on total arterial impedance. The resistive and elastic properties of the remnant of the aorta and of the artificial external circuit were certainly not appreciably influenced by carotid sinus baroreceptor reflexes. This strongly suggests that only minor reflex changes in total arterial impedance occurred and could not be responsible for the observed changes in ventricular performance.

For the same reason, homeometric autoregulation, which may occur as an adaptation to changes in peripheral resistance,\(^1\) was of little significance in the auxotonic preparation. The coronary vascular bed was perfused independently from the cephalic portion of the animal in the isovolumetric preparation, so that reflex changes in the cephalic arterial resistance did not affect coronary perfusion pressure or inflow.

In the auxotonic preparation, the venous return to the left atrium was dependent upon the diameter and length of the inflow cannula, the viscosity of the blood, and the hydrostatic pressure head (pressure difference between the blood levels in the left atrial reservoir and mean left atrial pressure). Since the blood level in the atrial reservoir was kept constant, changes in venous return to the left atrium depended only upon variations in mean left atrial pressure and were not influenced by reflex changes in venomotor tone. It is clear that in the isovolumetric preparations, reflex changes in venomotor tone were of no significance.

Changes of the adrenal medullary secretion in the experimental animals did not occur, since only the head and the heart of the animals were perfused. In the donor animals (auxotonic preparation), attempts were made to prevent large variations of the systemic arterial pressure. Nevertheless, in some experiments the systemic blood pressure tended to decrease when the brachiocephalic arterial pressure in the experimental animal was elevated for a long period of time. Release of catecholamines may have occurred under such circumstances. However, elevation of brachiocephalic arterial pressure caused a depression of ventricular performance when the sinus nerves were intact. After section of these nerves, only negligible effects were observed when brachiocephalic arterial pressure was varied over values in excess of 60 mm Hg. From this we conclude that changes in the level of the catecholamines in the arterial blood of the donor animals were of little significance in the auxotonic preparation.

Since reflex changes in heart rate, arterial
impedance, venomotor tone, and the level of circulating catecholamines could have affected cardiac performance only to a negligible extent, the observed changes in atrial and ventricular dynamics must be attributed almost exclusively to reflex effects upon the myocardium itself, the coronary vascular bed, or both. This reflex must have been mediated by the sympathetic nervous system, since left ventricular performance is not affected directly by vagal stimulation,17 and since both vagi were cut in the auxotonic preparation. In the isovolumetric preparation, coronary inflow and hence myocardial oxygen supply were kept constant. Reflex changes in the coronary vascular bed could alter coronary perfusion pressure itself and thus possibly affect left ventricular contractility and distensibility.18 However, the observed changes in coronary perfusion pressure were very small, so that lessened development of tension in the isovolumetric left ventricle during carotid sinus baroreceptor stimulation must be attributed to a reflex negative inotropic effect directly upon the ventricular myocardium. Our data show that in three out of seven experiments, static distensibility M of the isovolumetric left ventricle did not change at all during carotid sinus baroreceptor stimulation. It is unlikely that in the four other experiments changes in static distensibility of the left ventricle occurred, although this possibility could not be completely excluded because of small random variations in ventricular end diastolic pressure. Our data correspond with the observations made by many others on the static extensibility of the isometric papillary muscle,21,22 and the static distensibility of the isovolumetric ventricle during catecholamine administration or sympathetic stimulation.

In the auxotonic preparation, reflex changes in the coronary vascular bed were probably not responsible for the observed changes in cardiac performance. As pointed out above, coronary perfusion pressure, an important determinant of cardiac function,18,19 could not change appreciably as a direct result of reflex coronary vasoconstriction or vasodilatation. The reduction in coronary flow during carotid sinus baroreceptor stimulation was not necessarily a cause of the depression in cardiac performance because a decrease in ventricular contractility occurred in the isovolumetric preparation despite the fact that coronary inflow was kept constant. Consequently, the observed changes in atrial and ventricular dynamics must be attributed mainly to reflexes acting directly upon the myocardium.

These reflexes could conceivably cause a depression of left atrial transport function, a reduction in left ventricular distensibility, or a decrease in left ventricular contractility. The decrease of the height of the left atrial “a” wave found in five experiments during carotid sinus baroreceptor stimulation (fig. 7) must be attributed to a reflex negative inotropic effect directly on the left atrial myocardium. This lowered “a” wave cannot be explained by an altered ventricular distensibility, since the magnitude of the “a” wave and of mean left atrial pressure varied in opposite directions. Our observations in the isovolumetric left heart preparation demonstrated clearly that carotid sinus baroreceptor stimulation provokes a reflex depression of ventricular contractility; it is very likely, therefore, that this effect also was present in the auxotonic preparation. Left ventricular volume, or some index of it (circumference or segment length), was not measured in our experiments. Conflicting results have been reported on the effects of spontaneous variations in sympathetic tone,28 catecholamine infusion,28,29 and electrical stimulation of cardiac sympathetic nerves30 on ventricular distensibility during auxotonic contraction. Observations under isometric or isovolumetric conditions do not necessarily apply to an auxotonic left ventricle. For these reasons, we cannot exclude the possibility of a reflex decrease in ventricular distensibility in the auxotonic preparation during carotid sinus baroreceptor stimulation.

During electrical stimulation of the carotid sinus nerves in the auxotonic preparation, both baroreceptor and chemoreceptor fibers must have been stimulated.14 It is very likely
that the baroreceptor fibers were mainly responsible for the observed reflex changes in left atrial and ventricular contractility. Downing et al. 31 presented evidence that hypoxic stimulation of the carotid body has a slight reflex negative inotropic effect upon cardiac performance. Conversely, Kahler et al. 32 postulated the existence of a reflex positive inotropic effect. Careful examination of the latter data, however, suggested strongly that their conclusions were erroneous, 33 since the marked hypotension which occurred during anoxia in those animals with denervated carotid sinuses probably impaired ventricular performance. Therefore, it is likely that part of the reflex depression of atrial and ventricular contractility in the present study during sinus nerve stimulation was due to activation of the chemoreceptor fibers. However, since the reflex effects on cardiac contractility caused by anoxic stimulation of the chemoreceptors are only slight, 31 it is suggested that the pronounced cardiac responses observed in our experiments during electrical stimulation of the carotid sinus nerves (fig. 3) were due mainly to baroreceptor fiber activation.

Electroneurographic studies of the carotid sinus nerves in the cat 34 and rabbit 35 have demonstrated that hypotension or ischemia of the carotid sinus region causes stimulation of the carotid body. On the other hand, nonpulsatile pressure in the isolated carotid sinus of the dog 36 must be elevated above 60 mm Hg before stimulation of the baroreceptors occurs. Chemoreceptor stimulation probably has a reflex negative inotropic effect on the heart, 31 and consequently, it might be expected that a rise of nonpulsatile pressure in the isolated carotid sinus preparation from 0 to 60 mm Hg should enhance cardiac performance. This was never observed and suggests that chemoreceptor stimulation associated with very low intrasinusal pressures was of little significance in our experiments.

Koch 12t) observed no reflex effects upon systemic blood pressure or heart rate in the dog when nonpulsatile pressure in the carotid sinus was varied over ranges below 60 or above 210 mm Hg. He observed maximal effects in the pressure range from 90 to 130 mm Hg. In the present experiments, similar observations were made for left ventricular performance. The configuration of the curves in figure 8 representing the reflex effects on the auxotonic left ventricle of stepwise increases in nonpulsatile, intrasinusal pressure are similar to Koch's curves for blood pressure and heart rate.

Reduction of pulsatile brachiocephalic arterial perfusion pressure to below 30 mm Hg probably causes stimulation of the carotid body 34, 35 and a complete cessation of baroreceptor stimulation. 31 The observation that, in this pressure range, similar reflex effects were observed before and after section of both carotid sinus nerves (figs. 4 and 6) suggests that ischemia of the central nervous system was the most important factor. 36 After bilateral section of the carotid sinus nerves, reduction of brachiocephalic arterial pressure to between 30 and 60 mm Hg enhanced ventricular performance slightly, probably owing to mild ischemia of the central nervous system. It is likely that this ischemia of the central nervous system also acted synergistically with the carotid sinus baroreceptors at the lower perfusion pressures in the carotid artery in the study of Sarnoff and his collaborators. 9 In the left segment of figure 4 in their report, when perfusion pressure in the carotid artery was suddenly diminished to less than 50 mm Hg, aortic pressure and flow increased suddenly and then continued to rise at a more gradual rate during the 2.5 minutes at this low perfusion pressure. The delayed progressive increase of pressure and flow can probably be ascribed largely to ischemia of the central nervous system, whereas the initial changes are related to pressoreceptor reflexes. The elevation of the brachiocephalic arterial pressure from 60 to 200 or 250 mm Hg in the present study did not affect ventricular performance appreciably after denervation of the carotid sinuses. This suggests that intracranial baroreceptors 37 were of little importance in our study.

Our data confirm the principal conclusions of Sarnoff and his collaborators, 9 namely that
the carotid sinus baroreceptors exert a reflex inotropic effect upon the myocardium. On the other hand, our results contradict those of Salisbury et al.7 In their studies, however, any reflex changes in myocardial contractility were probably difficult to detect. First of all, their experiments were done under pentobarbital anesthesia, which depresses the carotid sinus baroreceptor reflexes.8 Occlusion of the common carotid artery is not the most effective procedure for varying the intensity of baroreceptor stimulation.9 Furthermore, by intentionally keeping right atrial inflow constant in order to eliminate reflex changes in venous return, and by allowing only small to moderate rises in left ventricular peak systolic pressure, only limited changes in ventricular external work could have occurred. Under these conditions, refined, sensitive methods for computing left ventricular external work, power, and rate of change of ventricular pressure might have shown definite changes in cardiac performance. In a recent study from this laboratory in the auxotonic preparation was similar to that of Salisbury et al. in that the effects of aortic and brachiocephalic artery constriction were measured during comparable alterations of peripheral resistance. Venous return was not restricted in these experiments. Under these conditions the left ventricle performed considerably more work from a lower mean left atrial pressure during brachiocephalic artery occlusion than during aortic occlusion. Certain observations reported by Salisbury and his collaborators do indicate that, during common carotid artery occlusion, cardiac sympathetic tone probably did increase. Indeed, the observed changes in the individual components of the left atrial pressure tracing and in the speed of left ventricular relaxation during certain experimental procedures with heart rates above 140 beats/min might very well have been due to differences in sympathetic tone.

Summary

The reflex effects of stimulation of the carotid sinus baroreceptors on left atrial and ventricular performance have been studied in an auxotonic and an isovolumetric left heart preparation, which was innervated, though completely isolated hydraulically. Reflex changes of heart rate, arterial impedance, venous return, and level of circulating catecholamines were prevented from influencing cardiac performance. In the auxotonic preparation, stimulation of the carotid sinus baroreceptors decreased aortic pressure, cardiac output, and external left ventricular work. Simultaneously, mean left atrial pressure rose definitely. In the isovolumetric preparation, a decrease of the left ventricular peak systolic pressure was observed. These changes in atrial and ventricular dynamics were attributed primarily to a reflex negative inotropic effect directly upon the atrial and ventricular myocardium, mediated by the sympathetic nervous system. No definite changes in distensibility of the isovolumetric left ventricle were observed, although this could not be excluded in the auxotonic preparation. Primary changes in the coronary vascular bed were not considered to be responsible for the observed changes in atrial and ventricular dynamics.

References

6. Sarsoff, S. J., Gilmore, J. P., Brockman, S. K., Mitchell, J. H., and Linden, R. J.: Regulation of ventricular contractile force by the cardio-
MYOCARDIAL CONTRACTILITY

...tid sinus. Its effect on atrial and ventricular dynamics. Circulation Res. 8: 1123, 1960.


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Circ Res. 1964;15:327-342
doi: 10.1161/01.RES.15.4.327

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4371

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
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