Cardiac Responses to Sympathetic Stimulation

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The cardiac responses to stimulation of sympathetic nerves to the heart were studied both in thoracotomized and in intact unanesthetized dogs. The changes in heart rate, left ventricular pressure, right and left ventricular dimensions and systemic arterial pressures were recorded. The powerful effects of sympathetic stimulation resemble cardiac responses to exercise more than those following administration of catecholamines. It is inferred that neural mechanisms may be more important for cardiac control during spontaneous activities than the circulating hormones.

Cardiac function is influenced both by neural reflexes and by circulating hormones. Since the autonomic nerves to the heart exert their influence by releasing neurotransmitters and since the circulating hormones are released by nerve stimulation, these two mechanisms are frequently treated as one. For example, it was formerly believed that under certain conditions, epinephrine was released both by sympathetic nerves in the heart and by the adrenal glands. More recently, impressive evidence1-5 has shown that norepinephrine (U.S.P. levarterenol) is the predominant transmitter substance released at sympathetic endings, and that only chromaffin tissues, most of which are concentrated in the adrenal glands, can release epinephrine. Today, levarterenol is regarded as having a local action at or near nerve terminals. This local action of levarterenol clearly cannot be duplicated by its intravenous administration. The functional effects of circulating levarterenol are very different from the effects of stimulating sympathetic nerves to the heart. For example, stimulating the sympathetic nerves to the heart generally produces tachycardia; intravenously administered levarterenol usually produces bradycardia. For these reasons, cardiac performance after stimulation of sympathetic nerves was studied in acute experiments and in intact, unanesthetized dogs.

Methods

Eighteen dogs, weighing between 8 and 12 Kg., were anesthetized with intravenous sodium pentobarbital (27 mg./Kg.) and placed on artificial respiration. An incision was made through the fifth left intercostal space. Variable resistance gages8 were sutured in the free walls of both right and left ventricles to record changes in their dimensions. The left ventricular dimensional gages were placed parallel to the mitral ring and midway between the ring and the apex; the gages on the right ventricle were placed just below the pulmonary conus and parallel to it. Effective left ventricular pressure was recorded from a differential transformer type of pressure gage,7 mounted near the apex of the heart with a short polyethylene tube extending into the ventricular chambers. The heart rate was recorded continuously by means of a condensor discharge system triggered at the same phase of each successive cardiac cycle. In 11 dogs, aortic pressure was also measured with either variable inductance or Statham strain-gage pressure transducers. The signals from the gages were amplified with Sanborn carrier wave amplifiers and recorded directly on a Polyviso.

In 12 acute experiments, the stellate ganglion, the aorta, subclavia, the caudal cervical ganglia6 and the cardiac nerves were carefully dissected bilaterally and stimulated electrically (20-50 V. and from 20-30 c.p.s.) for 12 to 15 seconds. In eight experiments the aorta was completely occluded just distal to the coronary arteries by means of a Potts' type arterial clamp for 20 to 30 seconds while sympathetic nerves were stimulated. This eliminated peripheral vascular responses and caused the ventricle to contract nearly isometrically.

* The nomenclature used here conforms to the description by N. J. Mizeres.
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Fig. 1. Changes in left ventricular circumference, effective left ventricular pressure, and right ventricular wall dimensions recorded during stimulation of left stellate ganglion, anterior root of the ansa subclavia and caudal cervical ganglion. Drawings are schematic representations of anatomical distribution of left sympathetic nerves to the heart in this dog. Stimulation of cardiac nerves (4, 5, 6) distal to caudal cervical ganglion (3) did not reproduce effects obtained by stimulating stellate ganglion, ansa subclavia or caudal cervical ganglion.

In the six chronic experiments, a stimulating electrode was placed around the anterior division of the ansa subclavia with its connections left intact. The chest wall was reconstructed, and the animals were allowed to recover. One to six days after the gages were installed, cardiac responses were recorded during electrical stimulation and during various spontaneous activities, including changes in position, startle, feeding and exercise.

RESULTS

Responses in anesthetized, open-chested dogs. Electrical stimulation of the intact left stellate ganglion caused reproducible changes of the type illustrated in figure 1. The changes in left ventricular circumference, left ventricular effective pressure, and right ventricular wall dimensions occurred, simultaneously, 2 to 4 seconds after stimulation was begun. The maximal response was attained in 7 to 10 seconds, and it continued at about that level during the remainder of the stimulation. The decrease in left ventricular dimensions amounted to about 40 per cent of the stroke amplitude. The effective systolic pressure in the left ventricle increased 60 to 120 mm. Hg, but the diastolic pressure often fluctuated in an unpredictable fashion. The decrease in right ventricular wall dimensions was about 30 per cent of the stroke change. The heart rate accelerated 1 to 3 seconds after the beginning of stimulation, and was persistently fast (over 210 beats/min.) during stimulation. After cessation of stimulation, the diastolic dimensions of both the right and left ventricles gradually increased and then returned to the control level after 90 to 120 seconds. The effective ventricular pressure re-
Fig. 2. Responses to stimulations of anterior root of ansa subclavia after successive transections of individual cardiac nerves distal to caudal cervical ganglion. Last remnants of response were completely abolished only after left vagus was severed. Drawing depicts schematically the anatomical distribution of left sympathetic cardiac nerves in this dog.

maintained at peak levels for 20 to 25 seconds and then slowly regained control levels 65 to 95 seconds later. The heart rate began to diminish when stimulation was discontinued and while the ventricular pressure still remained at peak levels.

Severing all the connections of the stellate ganglion except those to the ansa subclavia produced no change in the response to stimulation of this ganglion (fig. 1). Stimulation of the distal end of the severed thoracic chain caused no significant change in ventricular pressure, dimensions, or heart rate. The effect of stimulating the anterior root of the ansa subclavia closely resembled the response to stellate ganglion stimulation, but the responses were slightly smaller (fig. 1). Generally, stimulation of the posterior root of the ansa subclavia produced very slight responses, and stimulation of the nerves connecting the caudal cervical ganglion to the heart had very little effect. The changes produced by stimulating the caudal sympathetic ganglion could not be duplicated by stimulating any combination of the sympathetic nerves beyond this point. This suggested that other nerves conduct these impulses to the heart. To test this possibility, the anterior root of the ansa subclavia was stimulated after its connections were sectioned sequentially (fig. 2). The cardiac response was progressively diminished by this procedure, indicating that integrity of these nerves was essential to the original response.

The striking increase in left ventricular systolic pressure could result from greater cardiac output, increased peripheral resistance or both. There were no known neural connections between the point of sympathetic stimulation and
the principal sites of peripheral resistance (e.g., the splanchnic bed). To eliminate the possibility that the great increase in ventricular systolic pressure might have resulted from the release of neurohormones from the heart into the circulating blood, sympathetic stimulation was performed while the aorta was completely occluded just above the coronary arteries with a Potts' type clamp. After the aorta was abruptly occluded, ventricular pressure promptly increased about 50 mm. Hg and reached a plateau in about 10 seconds (fig. 3). The ventricular chambers were progressively distended, reaching a plateau in about the same time. The excursions during each cycle decreased 30 per cent from the right ventricular gage and 80 per cent from the left. These deflections probably resulted primarily from a change in shape rather than in volume. Blood could leave the left ventricle only through the coronary arteries or, possibly, through the mitral valves if they became incompetent because of massive ventricular distention.

Stimulation of the anterior branch of the ansa subclavia while the aorta was clamped greatly increased the ventricular pressure above
the levels attained after clamping of the aorta alone (fig. 3). The excursions during each stroke were greatly accentuated (fig. 3). About five seconds after stimulation was begun, the ventricular pressure reached a plateau and remained at that level throughout the stimulation period. Soon after the clamp was removed from the aorta, the ventricular pressure neared control values, as did the ventricular dimensions. The aortic pressure records displayed very large pulse pressures.

Responses in unanesthetized, intact dogs. Figure 4 shows the typical response to electrical stimulation of the anterior branch of the ansa subclavia several days after operation. The response in the unanesthetized dogs was only slightly smaller than that in the thoracotomized animals. The responses to certain types of spontaneous activity (e.g., exercise, eating) resembled those produced by electrical stimulation of the sympathetic cardiac nerves.

DISCUSSION

Electrical stimulation of sympathetic nerves to the heart produced consistent effects on effective ventricular pressure, heart rate, aortic pressure, and heart dimensions in 18 dogs. The systolic pressures in the left ventricle and aorta were greatly elevated. Systemic hypertension is usually attributed to increased peripheral resistance or increased cardiac output; increased rate of ventricular ejection and arterial distensibility may also have roles. However, stimulation of the stellate ganglion elevated systolic pressure in thoracotomized dogs after all known connections to the peripheral vasculature had been severed. Sympathetic stimulation could cause a rise in systolic arterial pressure because of increased cardiac output and more rapid ventricular ejection. Peripheral vasoconstriction might result from a release of neurohormones from the heart into the circulating blood. Arterial distensibility might be reduced by circulating catecholamines or from the neural stimulation.

The reduction in the systolic and diastolic dimensions of both ventricles during and immediately after electrical stimulation could result from an increase in heart rate, an increase in the contractility of the cardiac muscle fibers or a combination of the two (fig. 1). The tachycardia and changes in ventricular dimensions occurred when either the right or the left stellate ganglion were stimulated, denoting a very wide distribution of nerve fibers. In spite of the elevated systolic pressure, the tachycardia persisted. It is worthwhile to note here that a similar pressure rise from epinephrine injection produces bradycardia.

The effects of stimulating the stellate ganglion, ansa subclavia and caudal cervical ganglion were never duplicated by stimulating cardiac nerves beyond this point, either individually or in any combination. The explanation for this observation is not clear. Perhaps the high threshold of the post ganglionic fibers was involved, at least in part. Also, there may have been sympathetic nerves passing to the heart which were not stimulated; perhaps some sympathetic fibers to the heart travel along the vagus nerve, or along some presently unknown route.

When the heart was made to contract nearly isometrically by clamping of the aorta (fig. 3), the ventricular pressure increased abruptly, but a further and much greater increase was obtained with additional electrical stimulation of cardiac nerves. This increase in the ventricular pressure can only be explained by a change in contractility of the muscle fibers. These powerful sympathetic effects (fig. 3) very strongly suggest that neural controls play an important role in the regulation of cardiac function.

SUMMARY

Direct electrical stimulation of sympathetic cardiac nerves produced consistent changes in cardiac function including tachycardia, more complete systolic ejection and systemic hypertension. The changes occurring in ventricular dimensions during direct sympathetic stimulation are believed to result from changes in heart rate as well as from an increase in the contractility of the heart muscle. Clamping of the aorta increased left ventricular pressure by about 90 per cent. Sympathetic stimulation while the aorta was clamped
increased left ventricular pressure by an additional 120 per cent (over 300 mm. Hg). The greatly increased tension exerted when the ventricle was contracting almost isometrically unquestionably represents a change in the contractile characteristics of the heart muscle fibers. These powerful sympathetic effects suggest that the neural factors may be far more important than circulating hormones to the control of the heart.

Spontaneous activity (e.g., feeding or exercise) produce effects which resemble the responses to direct electrical stimulation of sympathetic nerves to the heart.

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