The Augmentor Action of the Sympathetic Cardiac Nerves

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An augmentor action of the cardiac sympathetic nerves is demonstrated to elicit profound elevations in systolic blood pressure. Diastolic pressure does not rise in an equivalent amount and significant increase in pulse pressure occurs. This persists for a considerable time after removal of the stimulation. During stimulation of the left cardiac sympathetic, an augmentor action is often not accompanied by acceleration. Stimulation of the right cardiac sympathetic evokes both effects. The elevation of blood pressure is chiefly produced by augmentation of ventricular beats, not by cardiac acceleration.

During investigations on the upper thoracic sympathetic outflows,1 electrical stimulation of the stellate ganglion and associated nerve pathways elicited profound elevations in blood pressure which were unexplained by conventional descriptions of the nervous control of the heart. Purely accelerator responses were rare, and pulse pressure changes of 80 to 100 mm. Hg frequently resulted.

The Cyon brothers2 were among the first to demonstrate acceleration and elevation of blood pressure during nerve stimulation. Hürthle3 showed that systole was abbreviated during the tachycardia induced by accelerator nerve stimulation. His observations were confirmed and amplified by Hunt4 who differentiated the action of these nerves on the periods of systole and diastole, both of which were significantly shortened. Wiggers and Katz5-7 arrived at essentially similar conclusions and demonstrated a specific action upon ventricular musculature. None of these reports emphasized systolic pressure alterations.

Kymographic tracings8-10 during stimulation of the accelerator nerves or the communicating rami of the upper thoracic spinal nerves generally show a rise in mean pressure, increased heart rate, and an apparent reduction in amplitude of pulse oscillation. Other workers,11-18 using more adequate recording equipment, observed that faradic stimulation influenced the heart in such a way that its "vigor of contraction appeared to increase greatly."

METHOD

Using either unipolar or bipolar stimulation tech-nics and an American Electronics model 104 square wave generator, controlled stimulating current pulses were delivered to both right and left thoracic sympathetic trunks. In this procedure, significant and consistent alterations in patterns of response were interpreted to indicate the entrance or exit of sympathetic nerve pathways mediating the recorded responses. Pulses having a duration of 10 msec., intensity of 0.5 to 5.0 volts, and frequencies varying from 0.5 to 20/sec. were employed. All stimulations were monitored by a DuMont cathode ray oscilloscope connected across the electrodes. Voltages reported are those read from the oscilloscope during stimulation. All experiments reported here were carried out in open chest dogs under Nembutal anesthesia. Blood pressure and heart rate were recorded optically from segment capsules or by a Sanborn electromanometer and Polyviso.

RESULTS

Analysis of records from optical tracings or from the electromanometer revealed significant and sometimes profound elevations in systolic pressure during stimulation of the stellate ganglion, frequently in the complete absence of acceleration and with minimal changes in diastolic pressure. Excitation of the right stellate generally induced greater acceleration, but augmentation was also present. Elevated pulse pressures were sustained for prolonged periods after cessation of stimulation. Comparative tracings are shown in figure 1.
top record was made at relatively slow speed and is characterized by systolic pressure elevations in excess of 50 mm Hg while diastolic pressure actually decreased. Stimulation was repeated on the left side and recorded at faster speed. The first evidence of change in pulse pressure appeared on the sixth cycle following initiation of stimulation, and this was followed by successive increments in pulse pressure to a maximum of 95 mm Hg. Heart rate remained unchanged. Stimulation of the right stellate ganglion elicited an augmentor response, again on the sixth cycle, with a progressive increase in pulse pressure. Acceleration was prominent and was accompanied by a moderate but sustained elevation in diastolic pressure. Similar recordings at still faster speeds revealed a much more rapid systolic upstroke coincident with the increased pressure. Table 1 summarizes observations in 6 animals which may be considered typical of approximately 50 animals studied. Augmentor responses were regularly elicited from stimulation of both sides, but were usually more profound on the left. Acceleration was generally more prominent on the right, and frequently absent or insignificant on the left.

Differentiation of fiber pathways mediating cardioacceleration from those mediating augmentation have not been reported, and indeed, it is not known whether separate pathways exist. Anatomical pathways of accelerator nerves pass through communicating rami of the T2 to T5 segmental nerves. In the present

<table>
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<th>Dog no.</th>
<th>Syst. mm. Hg</th>
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<th>Pulse Press.</th>
<th>Change in Heart rate</th>
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Table 1.—Blood Pressure Changes
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Via.

Selected records to illustrate varying blood pressure responses elicited by electric stimulation at each segmental level between T2 and T11. Three upper records at faster speeds than the lower three. Stimulating current for all stimulations, 2.1 volts, 10 msec., 20/sec.

studies, electrodes were placed successively at each interganglionic segment from the caudal pole of the stellate (T2 to T10 or T11), and controlled square wave pulses delivered. Figure 2 illustrates results of this procedure. Cardiovascular response was prompt and principally systolic when the trunk was stimulated at T2 with progressively lesser responses as the electrodes were moved caudalward. Little or no response was elicited at T0. Caudal to this level, pressor responses appeared, but were marked by an approximately equal rise in systolic and diastolic, much as expected during excitation of splanchnic constrictor pathways. Fifteen to 20 sec. later, a secondary rise in pressure occurred marked by a relatively greater change in systolic pressure. The long latency from beginning of stimulation to the secondary response, together with the secondary widening of pulse pressure can perhaps be explained by liberation of epinephrine or noradrenaline from the adrenal medulla. Thus the pressor responses elicited by stimulation at T2 to T5 were distinctly different from those produced by excitation of the caudal end of the thoracic trunk. In order to eliminate these splanchnic effects, the trunk was generally sectioned and dissected free immediately caudal to T5 or T6.

To eliminate the possibility of reflex vasoconstriction mediated by afferents ascending in the vagosympathetic trunk, the vagni were cut bilaterally just superior to the caudal cervical ganglion. Combined with section of the sympathetic trunk below the stellate, this operation served to isolate the major efferent sympathetic innervation of the heart. At the signals (top record, fig. 3), the left and then the
right vagi were sectioned. The heart did not accelerate appreciably following either operation, but a widened pulse amplitude did appear. The significance of this remains to be investigated. It is apparent from figure 3 that augmentor responses persisted in such neurally isolated cardiac preparations.

**DISCUSSION**

The early designation of the cardiosympathetics as accelerator nerves was evidently dependent upon two factors: (1) the use of stimulators with inadequate current parameters, and (2) the inability of recorders to follow faithfully rapid changes in pressure. The continued use of the term perpetuates the concept that acceleration is the most important (or only) function. The significance of an augmentor action seems to have been largely overlooked. The term augmentor was applied by Henderson and Barringer in 1913. In only a few of their animals was increased amplitude of stroke observed, and then only when the heart was beating with "considerably diminished vigor and arterial pressure was low." These authors state the augmentor effect never exceeded 30 per cent of the amplitude before stimulation and concluded therefore that it represented merely a modification of the acceleration.

The ending of sympathetic fibers on both nodal and muscle tissue of the atria and ventricles is well known. Whether specific accelerator pathways may be differentiated from augmentor is not yet known. At present, it seems probable that regardless of the pre- and postganglionic pathways traversed, the important determinant of motor response remains the specific site of termination on the heart. Elevation in systolic pressure with little or no alteration in heart rate or diastolic pressure implies an inotropic effect, probably mediated by liberation of norepinephrine. Sympathetic endings upon ventricular muscle might be
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expected to induce more powerful or augmented contractions. Fibers ending on or near nodal tissue might be expected to induce acceleration.

Augmented contractions would increase systolic ejection and the ventricle must then function with smaller residual volume until normal end systolic volume is restored. Such changes in contractile force have been demonstrated recently by Cotten.17 We would like to suggest the possible importance of these phenomena in the neural control of blood pressure and cardiac output during exercise, during activation of barostatic reflexes and in emotional or neurogenic hypertension.

One final point deserves emphasis. Independent of heart rate and venous return or atrial pressure, another important mechanism has been shown to be concerned in cardiac output. An immediate myocardial response to nerve stimulation without preliminary increase in presystolic fiber length best explains the prompt pulse pressure change. Apparent violation of the “all or none law” need not be troublesome because as Wiggers18 pointed out, the magnitude of response depends upon the physiological state of myocardial reactivity. Minute quantities of epinephrine produce increased systolic ejection with unchanging right atrial filling pressure or heart rate.19 This is in accord with Wiggers 20,21 observations, that adrenaline causes a more vigorous and more rapid ventricular contraction together with more complete relaxation in diastole. The data are compatible with the concept of Hamilton and Remington25 that changes in resistance to ejection and in myocardial stimulation are more important than change in diastolic size (filling pressure) in the regulation of stroke volume. It also provides the neural mechanism to account for cardiac adjustments observed26 in intact, unanesthetized dogs during exertion.

SUMMARY

Direct electrical stimulation of the left sympathetic nerves of the heart generally caused pronounced elevation of systolic arterial pressure without changes in heart rate. Stimulation of the right cardiac sympathetic nerves caused both acceleration and augmentation. Since cardioacceleration was frequently absent during stimulation it contributed relatively little to the elevated mean pressures. Pulse pressure remained elevated for prolonged periods following cessation of stimulation. The neural action may represent an important mechanism for the immediate alteration in stroke volume, independent of venous return or presystolic fiber length.

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