Distribution of autonomic nerves to the canine heart

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Studies of autonomic pathways to the heart have been reported by many investigators, but there is relatively little description of the paracardiac location of these fibers. Many experimental and clinical procedures involve disruption and dissection of the paracardiac tissues, yet little consideration has been given to the effects of these procedures on cardiac innervation.

Cooper et al. (2) recently offered histological evidence from feline hearts of the peripulmonary course of sympathetic fibers with dense parasympathetic plexuses located on the posterior surface of the heart at the junction of the interatrial septum and the atrioventricular groove. Chemical analysis of the myocardium following modified cardiac autotransplantation reveals total depletion of ventricular and reduction of atrial catecholamines. These data suggest the atria and ventricles receive some of their sympathetic innervation via topographically separate fiber pathways (1).

Utilizing techniques of segmental denervation, sympathetic projections onto the epicardial surface of the heart were recently reported (3, 6). From these studies, an idealized pattern of nerve projections from both left and right stellate ganglia was constructed.

In order to delineate the pathways of these fibers as well as parasympathetic fibers in the immediate paracardiac regions, experiments were performed in which the pulmonary artery, venae cavae, and pulmonary veins were systematically severed. Data obtained in response to autonomic nerve stimulation following the vascular transections permit a description of the primary pathways followed by the canine cardiac nerves just prior to their entrance into the cardiac tissues.

Methods

Mongrel dogs weighing 12-18 kg were premedicated with 2 mg/kg phencyclidine HCl and anesthetized with chloralose (80 mg/kg). Positive-pressure respiration was instituted by endotracheal intubation and both vagosympathetic trunks were isolated in the neck. The chest was opened by bilateral thoracotomy and sternal transection, and both stellate ganglia were isolated and decentralized.

Following heparin administration, the superior vena cava was cannulated through theazygos vein and the inferior vena cava through a cannula inserted into the femoral vein. Arterial return was through the femoral artery. Oxygenation was accomplished by use of either a 2-LF miniprime bubble oxygenator (Travenol Laboratories) or a 13-inch Kay-Cross disc oxygenator primed with lactated Ringer solution. Flow rates ranged from 80 to 100 ml/kg-min and were held constant throughout the procedure once adequate perfusion had been established. After beginning extracorporeal circulation, total bypass was instituted by snaring both venae cavae. Positive-pressure respiration was discontinued following institution of total cardiopulmonary bypass.

Standard ECG limb lead II was recorded in all experiments. A Walton Brodie strain-gauge arch was sutured to the anterolateral surface of the left ventricle in all animals and to both right and left ventricles in many experiments. All recordings were made on a Grass model 7 polygraph. Stimulation of vagus nerves and stellate ganglia was by bipolar electrodes from a Grass model 5 stimulator with stimulation parameters of 10 cycles/set, 5 msec, and 5 v. Voltage was maintained constant as monitored on a cathode-ray oscilloscope throughout each period of stimulation.

Fifteen experiments serve as the basis for this report. In all animals, the pulmonary artery, pulmonary veins, and venae cavae were severed in the following manner: the pulmonary artery just distal to the pulmonic valve, the pulmonary veins intrapericardially as close as possible to their entrance into the pericardium, the superior vena cava at the junction with the azygos vein, and the inferior vena cava just before it entered the pericardium. The order in which the vessels were severed was randomized. Figure 1
FIG. 1. Schematic illustration of dog heart which depicts sites of vessel transection as viewed from dog's right side. RV = right ventricle, PA = pulmonary artery, A = aorta, RA = right atrium, LA = left atrium, SVC and IVC = superior and inferior vena cava. Dashed lines indicate sites of vessel transection. See text.

FIG. 2. Response of strain-gauge arches on right and left ventricles (RV, LV) to stimulation of stellate ganglion and cervical vagosympathetic trunks. Onset of stimulation indicated by event marker between tracings of strain-gauge arches.

Figure 2 illustrates an experiment in which the pulmonary artery was the first vessel to be transected, followed successively by the ventrolateral cervical cardiac nerve (VLCCN), as designated by Mizeres (4), venae cavae, and pulmonary veins. Recordings from strain-gauge arches on the right and left ventricles are shown. During control stimulation of the right stellate ganglion while on bypass, heart rate increased from 144 to 240 beats/min, while right ventricular contractile force increased 60% and left ventricular contractile force increased 14%. During left stellate stimulation heart rate increased from 132 to 210 beats/min, right ventricular contractile force increased 156%, and left ventricular contractile force increased 57%.

During both right and left vagal stimulation in the control period a marked cardiac slowing and progressively decreasing amplitude of contractile force was noted.

Following transection of the pulmonary artery, contractile force was markedly decreased on both ventricles. Stimulation of the right stellate ganglion resulted in an increase of heart rate from 126 to 216 beats/min without change in contractile force of either ventricle. Stimulation of the left stellate ganglion, on the other hand, increased heart rate from 132 to 204 beats/min with augmentation of 67% in left ventricular contractile force. No increase in right ventricular contractile force occurred and this was true in all experiments in which the pulmonary artery was sectioned while the VLCCN remained intact. The response to vagal stimulation remained almost identical to that observed in the control stimulation.

Following transection of the VLCCN where it crossed the left pulmonary veins, right and left stellate ganglia stimulation resulted in increases of heart rate from 132 to 210 and from 144 to 204 beats/min, respectively. Responses to vagal stimulation were again almost identical to those illustrated in the control periods. Transection of the venae cavae in this animal produced little further alteration in response to either stellate or vagal stimulation.

FIG. 3. Response of strain-gauge arches on right (RV) and left (LV) ventricles to stellate and vagal stimulation. ECG = lead II. Fast tracings taken during stimulation have been deleted as indicated by break in continuity of records.
Recordings following transection of the pulmonary veins, leaving the heart attached only to the aorta, were uninfluenced by nervous excitation. The heart rate at this time was 138 beats/min and no change in rate or contractile force was induced by either stellate or vagal stimulation which had previously elicited marked chronotropic alterations.

Figure 3 illustrates an experiment in which the pulmonary veins were severed as the first procedure. The inferior pulmonary veins were frequently sectioned prior to severing the superior pulmonary veins, but response to vagal stimulation remained unchanged from control and, hence, these experiments are not separately illustrated. In Fig. 3, the VLCCN was carefully separated from the pulmonary veins and left atrium and was severed only as the final procedure.

During the control period, while on bypass, right stellate stimulation increased heart rate from 144 to 210 beats/min. Right ventricular contractile force increased 167% while left ventricular contractile force increased 141%. Left stellate stimulation increased heart rate from 132 to 162 beats/min and contractile force of right and left ventricles 69 and 40%, respectively. Supramaximal stimulation of both right and left vagi induced marked bradycardia. The ECG regularly revealed A-V block during strong vagal stimulation.

Following transection of the pulmonary veins positive inotropic responses to stellate stimulation remained essentially unchanged from control. Heart rate increased from 150 to 216, and from 126 to 150 beats/min with right and left stellate stimulation, respectively. The negative chronotropic effect of right vagal stimulation was distinctly decreased, whereas that of left vagal stimulation was nearly abolished, heart rate slowing only from 144 to 126 beats/min.

Figure 3 next shows responses following transection of the venae cavae. Inotropic responses to stellate stimulation were again essentially unchanged. Heart rate increased from 120 to 150 beats/min during both right and left stellate stimulation and the electrocardiogram confirmed the presence of sinus rhythm. However, no change in heart rate occurred during either right or left vagal stimulation. Transection of the pulmonary artery and VLCCN (not shown) ultimately deleted both the positive inotropic and chronotropic responses to sympathetic stimulation.

Figure 4 illustrates an experiment in which the pulmonary artery and VLCCN were transected as the initial procedure. Control stimulation of the right stellate ganglion resulted in characteristic increases in rate and force of contraction (rate: 114-268 beats/min; contractile force increase: right ventricle 85%, left ventricle 36%). Left stellate stimulation increased rate from 126 to 168 beats/min; right ventricular contractile force 208%, and left ventricular contractile force 62%. Right vagal stimulation caused marked bradycardia and depression of contractile force in both ventricles. Pronounced postvagal tachycardia appeared promptly after cessation of stimulation. The left vagus produced bradycardia with depression of left
ventricular contractile force, but without significant post-stimulation tachycardia.

After transection of the pulmonary artery, contractile force again was markedly attenuated, even during the prestimulation control period. Right stellate stimulation increased heart rate from 168 to 228 beats/min with no change in contractile force. Left stellate stimulation increased heart rate from 172 to 196 beats/min, left ventricular contractile force 44%, and right ventricular contractile force 37%. Responses to right and left vagal stimulation were unchanged from control. After cutting the VLCCN, tachycardia still characterized right stellate stimulation (162 to 338 beats/min) but augmentation in contractile force was absent. During left stellate stimulation, rate increased from 168 to 180 beats/min, but again there was no increase in contractile force. With right and left vagal stimulation, characteristic bradycardia and diminution of contractile force were noted. These responses to parasympathetic excitation were subsequently abolished by transection of the veina cavae and pulmonary veins (not shown, Fig. 4).

Figures 5 and 6 summarize the alterations in response to autonomic nerve stimulation in all of the animals studied. The percent change in heart rate elicited by electrical stimulation of the stellate ganglia and the vagosympathetic trunks in the control period, when the pulmonary artery and VLCCN were cut first, and when the pulmonary veins and veina cavae were cut first, is illustrated in Fig. 5. The positive chronotropic influence of the right stellate ganglion was not significantly decreased by transection of the pulmonary artery and VLCCN. However, this chronotropic influence was decreased when all dorsal connections to the heart were severed. Neither of these procedures significantly altered changes in heart rate induced by left stellate stimulation, but it was noted that in most instances pacemaker activity was shifted to a site other than the sinus node with left stellate stimulation.

Transection of the pulmonary artery and ventrolateral cervical cardiac nerve resulted in little or no alteration in negative chronotropism accompanying vagal stimulation, whereas such influences were consistently obliterated by section of the pulmonary veins and veina cavae.

Figure 6 summarizes the alterations in left ventricular contractile force following interruption of the nerve pathways passing along the pulmonary artery and in the VLCCN. When the pulmonary veins and veina cavae were sectioned as the first procedures, there was a greater increase in left ventricular contractile force to both right and left stellate ganglia stimulation. This is in marked contrast to the effects of transection of pulmonary artery and VLCCN. Following these procedures all inotropic response to stellate stimulation was abolished.

DISCUSSION

Surprisingly little variability appeared in anatomical pathways followed by the sympathetic and parasym pathetic nerves to the heart. This fact was demonstrated by a high degree of consistency obtained in abolishing both chronotropic and inotropic responses to stellate and vagal stimulation by selective sectioning of cardiac and paracardiac tissues. Fibers which effect positive inotropic influences on the ventricles travel primarily through peripulmonary tissues and through the ventrolateral cervical cardiac nerve. In most animals, both ventricles receive inotropic fibers which travel along the main pulmonary artery, and the left ventricle receives fibers as well from the VLCCN. The results of the present experiments confirm the important inotropic innervation of the left ventricle by the VLCCN (3).

Sympathetic fibers which exert positive chronotropic influences travel to the sinus node along the great veins as they approach the cranial aspect of the atria. It is apparent, however, that some chronotropic sympathetic fibers must be distributed along the peripulmonary region since an increase in rate may be seen with stellate stimulation after all venous connections to the heart have been severed. Remaining fibers from the left stellate ganglion influenced primarily the A-V node, while right stellate stimulation most frequently resulted in an increase in sinus rate.

A large preponderance (if not all) parasympathetic fibers enter the atria along the superior vena cava and the superior pulmonary veins. No evidence for negative inotropic or chronotropic activity during vagal stimulation was noted after all venous connections to the heart were severed. An enhanced positive inotropic response to stellate stimulation was noted when the venous trunks were severed as the first procedure. Since the cervical vagosympathetic trunks were transected in all animals before cardiopulmonary bypass was instituted, no clear cut explanation for this enhanced positive inotropic response is available. The data emphasize, however, that sympathetic pathways effecting positive inotropic responses have not been significantly interfered with by section of the venous trunks.

The data support the studies of Cooper (2) (cats) which suggested a concentration of sympathetic fibers in the peripulmonary area. They also offer functional confirmation of data derived from myocardial catecholamine analyses following transection of the aorta, pulmonary artery, and left atrium. Catecholamines following this modified autotransplantation procedure were totally depleted from the ventricles and the interventricular septum, and considerably reduced in both atria (1). In view of these data, experiments involving sympathetic innervation of the heart should be carefully evaluated if dissection in the peripulmonary region has been carried out. Further, recognizing that these data are not necessarily applicable to man, consideration should be given to avoiding unnecessary dissection between the aorta and pulmonary artery. Such disruption of peripulmonary tissue could cause alteration of myocardial contractility in isolated segments of the heart or even in an entire ventricle. Conversely, if such data can be proved to be applicable in man, denervation procedures beneficial in some cardiac diseases may be developed.

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