Distribution of autonomic nerves to the canine heart

MICHAEL P. KAYE, JOHN M. GEESBRENGTH, AND WALTER C. RANDALL
Departments of Surgery and Physiology, Loyola University Medical Center, Maywood 60153, and Research Service,
Hines Veterans Administration Hospital, Hines, Illinois 60141

KAYE, MICHAEL P., JOHN M. GEESBRENGTH, AND WALTER C. RANDALL. Distribution of autonomic nerves to the canine heart. Am. J. Physiol. 218(4): 1025-1029. 1970.—Ventricular contractile force and lead II ECG were recorded in 15 dogs under chloralose anesthesia prior to and following sectioning of the pulmonary artery, pulmonary veins, and venae cavae. All experiments were carried out on cardiopulmonary bypass. Both stellate ganglia and cervical vagosympathetic trunks were electrically stimulated before and after each surgical intervention. Sectioning of the vessels was randomized. The results indicate that major sympathetic inotropic fibers travel in the peripulmonary region or in the ventrolateral cervical cardiac nerve. Sympathetic chronotropic fibers approach the heart either in the peripulmonary tissues or the superior vena cava and pulmonary veins. Parasympathetic fibers enter the heart along the superior pulmonary veins and superior vena cava.

stellate ganglia stimulation; vagosympathetic stimulation; paracardiac nerve pathways; cardiac innervation; myocardial contractile force

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 atroventricular 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 the azygos 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.

represents a schematic illustration of the dog heart and depicts the sites of vessel transection as viewed from the animal’s right side.

In each animal, the right stellate ganglion, left stellate ganglion, and distal ends of the severed right and left cervical vagosympathetic trunks were stimulated in that order during the control state, following institution of total cardiopulmonary bypass and after each surgical intervention. A recovery phase of approximately 10 min was allowed between each intervention or stimulation.

RESULTS

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 Mizercs (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 the 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 in-
creased heart rate from 172 to 196 beats/min, left ventricu-
lar 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 in-
creased 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 par-
sympathetic excitation were subsequently abolished by
transection of the venae 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 venae 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 chron-
tropic 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 venae cavae.

Figure 6 summarizes the alterations in left ventricular
contractile force following interruption of the nerve path-
ways passing along the pulmonary artery and in the
VLCCN. When the pulmonary veins and venae 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 parasympathetic
nerves to the heart. This fact was demonstrated by a high
degree of consistency obtained in abolishing both chrono-
tropic and inotropic responses to stellate and vagal stimu-
lation 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
curve. 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 ap-
parent, however, that some chronotropic sympathetic
fibers must be distributed along the peripulmonary region
since an increase in rate may be seen with stellate stimula-
tion 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 ino-
tropic 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 cardiopulmo-
nary bypass was instituted, no clear cut explanation
for this enhanced positive inotropic response is available.
The data emphasize, however, that sympathetic pathways
affecting positive inotropic responses have not been sig-
nificantly 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 peri-
pulmonary 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 auto-
transplantation procedure were totally depleted from the
ventricles and the interventricular septum, and consid-
erably 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 neces-
sarily 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 iso-
lated 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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