Functional Studies of Right Cardiac Sympathetic Nerves and Ganglia in the Dog[1] (35663)

JOHN L. TOLLACK,[2] GUNTER GRUPP, AND WILLIAM C. FARR

Departments of Physiology and Medicine, Cardiac Laboratory, University of Cincinnati College of Medicine, Cincinnati, Ohio 45219

Many studies have provided detailed descriptions of the variations of sympathetic innervation of the dog heart (1–5), but only a few studies have been done to determine the locations of synaptic connections between pre and postganglionic fibers within this cardiac sympathetic system. Although most investigators have freely assumed that the stellate ganglia are the principal sites of ganglionic transmission in most animals, our previous studies indicate that the major site of synapse for sympathetic cardiac fibers in the dog occurs within the caudal cervical ganglia and not the stellates (6–8). On the other hand, Aiken and Reit (9) have shown a species difference; in the cat, these cardiac sympathetic synapses do predominate in the stellates.

The present experiments were designed to study under precise conditions the pathways taken by sympathetic nerves to the right side of the dog's heart in order to quantify and better define the functional distribution of pre and postganglionic chronotropic and inotropic fibers within the various pathways.

Methods. Open-chest experiments were done on 11 adult mongrel dogs of both sexes weighing 13–32 kg. The animals were anesthetized with sodium pentobarbital (30 mg/kg) given intravenously. Blood pressure was monitored from the descending aorta with a Statham pressure transducer, and heart rate was recorded by a tachograph. Contractile force was measured with a Walton strain gauge arch sutured to the anterior surface of the right ventricle. The myocardial fibers between the feet of the arch were stretched to such an extent that the maximum active tension was recorded during contraction.

In order to eliminate reflex effects on the heart, the cardiac nerves were decentralized in all experiments. Both vagosympathetic trunks were isolated and cut in the upper cervical region. The left stellate ganglion was removed, and the right stellate was decentralized by sectioning the right thoracic sympathetic trunk at T-5 and all communicating rami from C-6 to T-5.

The major nerve trunks located between the right stellate ganglion and the heart were carefully dissected free of surrounding connective tissue and stimulated using bipolar platinum electrodes. Rectangular pulses of supramaximal intensity (usually 20–30 V), having a duration of 1–2 msec and a frequency between 10–20 Hz, were applied to the isolated nerves. Both the nerve and electrodes were covered with mineral oil to reduce the spread of current to adjacent nerve structures.

Complete ganglionic blockade was induced by intravenous injection of hexamethonium chloride (20–30 mg/kg) and atropine sulfate (2–3 mg/kg). We and others (6, 10, 11) have shown that these doses are effective in completely blocking both nicotinic and muscarinic transmission in the cardiac ganglia of the dog but do not alter the effects of post-

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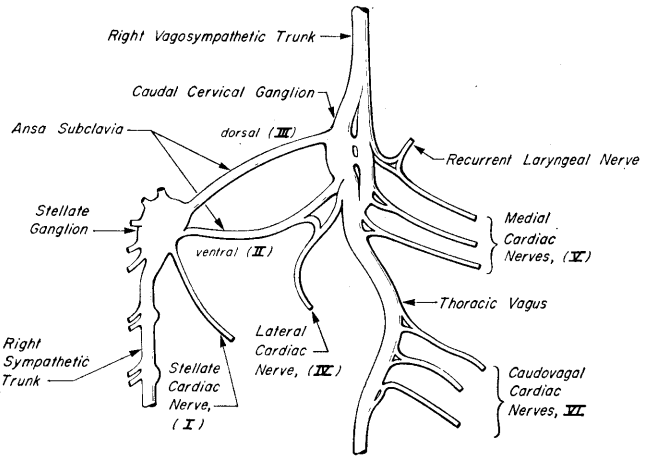

FIG. 1. Diagram of right cardiac nerve pathways in the dog. Although many anatomical variations exist, only those major nerve trunks of most frequent occurrence are illustrated. Roman numerals refer to the six primary nerve tracts discussed in the text and correspond to the six sites of nerve stimulation listed in Table I.

ganglionic sympathetic stimulation. Following ganglionic blockade, the individual nerves were restimulated using identical current parameters. Heart rate and contractile force responses to stimulation before and after ganglionic blockade were compared for the individual cardiac nerves. Differences in responses were tested statistically for significance using Student's paired t test.

Results. We observed many individual variations with respect to the peripheral pathways of right cardiac sympathetic nerves in the dog. A composite diagram illustrating those nerves which were found most frequently is shown in Fig. 1. A summary of the cardiac responses to supramaximal stimulation of these nerves before and after complete ganglionic blockade is presented in Table I.

We found direct branches from the right stellate ganglion to the heart in 5 of 11 dogs and designated these nerve trunks as "stellate cardiac nerves" (Fig. 1). Stimulation of these nerves before ganglionic blockade consistently produced large increases in heart rate but only slight increases in right ventricular contractile force (Table I; Site I). Ganglionic blockade had no effect ($p>.05$) on the rate or force responses to supramax-

TABLE I. Heart Rate and Right Ventricular Contractile Force Responses During Stimulation of Right Cardiac Nerves Before and After Complete Ganglionic Blockade.[a]

Site of nerve stimulation	No. of dogs	Heart rate (beats/min)				Contractile force (% change from prestimulation value)	
		Before blockade		After blockade		Before blockade	After blockade
		Basal	Response	Basal	Response	Response	Response
Site I	5	108 ± 5	+53 ± 7	91 ± 3	+56 ± 9[b]	+13 ± 6	+17 ± 5[b]
Site II	8	106 ± 3	+67 ± 4	93 ± 2	+31 ± 6[c]	+119 ± 8	+32 ± 4[c]
Site III	8	104 ± 4	+52 ± 6	93 ± 3	+10 ± 3[c]	+115 ±12	+7 ± 2[c]
Site IV	6	103 ± 5	+63 ± 9	96 ± 2	+58 ± 7[b]	+26 ± 7	+43 ±14[b]
Site V	8	109 ± 4	(Decrease)	93 ± 2	+29 ± 8	(Decrease)	+127 ±18
Site VI	8	108 ± 3	(Decrease)	93 ± 2	+43 ± 5	(Decrease)	+28 ± 7

[a] Values given are the mean ± SE.

[b] Responses are not significantly different from those before blockade ($p>.05$).

[c] Responses are significantly different from those before blockade ($p<.001$).

imal stimulation of these nerves.

In eight dogs, both the ventral and dorsal limbs of the right ansa subclavia were stimulated at their respective origins from the stellate ganglion (Fig. 1). Control stimulation of either limb produced large increases in both heart rate and contractile force (Table I; Sites II and III). Complete ganglionic blockade significantly reduced the cardiac responses to stimulation of the ventral limb (Site II) to less than 50% of control values ($p<.001$). The cardiac responses to stimulation of the dorsal limb (Site III) were also reduced by ganglionic blockade ($p<.001$), but to a far greater extent, and were completely abolished after blockade in three of eight dogs.

In six dogs, we found large nerve trunks exiting from the lateral aspect of the caudal cervical ganglion. These nerves often received small contributions from the ventral limb of the ansa and were designated as "lateral cardiac nerves" (Fig. 1). When stimulated before blockade, these nerves produced substantial increases in heart rate and relatively small increments in right ventricular contractile force (Table I; Site IV). Ganglionic blockade did not significantly alter the cardiac responses to stimulation of these nerves ($p>.05$).

In eight dogs, we stimulated cardiac nerves travelling in a medial direction from the caudal cervical ganglion, right recurrent laryngeal nerve, and cranial portion of the thoracic vagus. These nerve trunks were designated as "medial cardiac nerves" (Fig. 1) and correspond to the right innominate, recurrent cardiac and craniovagal nerves according to the terminology proposed by Mizeres (3, 4). In our study, these various nerve trunks were traced to the plexus of nerves just ventral to the bifurcation of the trachea. Control stimulation of these nerves elicited variable effects on rate and contractile force. While occasionally a pure sympathetic response could be observed, most often the responses consisted of decreases in both heart rate and right ventricular contractile force (Table I; Site V), indicating the presence of parasympathetic vagal fibers within these nerves. After ganglionic blockade, stimulation of these nerves consistently produced the greatest positive inotropic effects on right ventricular contractile force of any tract stimulated. The effect on heart rate was relatively moderate.

Caudovagal nerves, as previously described by Mizeres (3, 4) exit from the thoracic vagus in close proximity to the heart. We stimulated such nerves before and after ganglionic blockade in eight dogs. Before ganglionic blockade, stimulation invariably resulted in parasympathetic responses characterized by bradycardia and cardiac standstill under prolonged stimulation (Table I; Site VI). Following ganglionic blockade, stimulation produced substantial increases in heart rate but only slight changes in right ventricular contractile force.

Discussion. Most of our knowledge concerning the influence of sympathetic nerves on cardiac function has been obtained from electrical stimulation of the stellate ganglia, ansae subclaviae, caudal cervical ganglia, and individual nerves travelling to the cardiac plexuses of the dog. The assumption that the stellate ganglia are the principal sites of synapse between pre and postganglionic cardiac sympathetic neurons in this system was recently challenged (6–8). We observed in previous experiments (6) and in the present systematic study of right cardiac sympathetic pathways that the majority of fibers leaving the stellate ganglion are *preganglionic*. In fact, the only reliable *postganglionic* nerve emerging from the right stellate ganglion was an inconstant branch that did not join either limb of the ansa but coursed directly to the heart in 5 of 11 dogs (stellate cardiac nerves). It was interesting to ascertain whether more postganglionic chronotropic fibers could be demonstrated in the ventral limb of the ansa in dogs where stellate cardiac nerves do not exist. However, our data did not support this speculation.

The vast majority of right cardiac sympathetic nerves in the dog travel cranially from the stellate via the ansa subclavia and enter the caudal cervical ganglion. In terms of functional effects we found no difference between fibers coursing within the ventral and dorsal limbs of the right ansa; stimulation of both tracts elicited similarly large increases

in heart rate and right ventricular contractile force prior to ganglionic blockade. In terms of synapse we did find differences. The ventral limb contained varying numbers of both pre and postganglionic neurons, whereas the dorsal limb contained mostly preganglionic fibers.

Most nerve tracts originating distal to the caudal cervical ganglion are mixed nerves, containing both sympathetic and parasympathetic fibers. An exception to this general statement occurs when nerves exit directly from the lateral aspect of the caudal cervical ganglion; we found such nerves in 6 of 11 dogs (lateral cardiac nerves). These nerves are comprised of postganglionic sympathetic fibers which are primarily chronotropic in function. Other cardiac nerves originating from the right vagosympathetic trunk, recurrent laryngeal, and thoracic vagus carry both parasympathetic and postganglionic sympathetic nerves to the heart. In the present study we found that nerve tracts coursing to join the pretracheal plexus (medial cardiac nerves) constitute the major pathway for fibers influencing contractile force on the anterior surface of the right ventricle. On the other hand, nerves arising from the thoracic vagus closer to the heart (caudovagal fibers) contain many postganglionic sympathetic fibers which primarily influence heart rate.

In a recent paper, Wechsler *et al.* (12) have confirmed our conclusion that the caudal cervical ganglia contain the majority of cardiac sympathetic synapses in the dog. They, along with Brown (10), have suggested that synapses may occur as well at points distal to the caudal cervical ganglia. In fact, in 1939 Nonidez (2) demonstrated aggregations of ganglion cells at various sites above the arch of the aorta. Another interesting possibility in this regard, recently suggested by Smith (13), is that sympathetic preganglionics originating from the upper thoracic segments may traverse both stellate and caudal cervical ganglia, travel cranially to synapse within the superior cervical ganglion, and descend within the right vagosympathetic trunk to reach the heart. Aside from these minor variations, it is now well-established that most cardiac sympathetic synapses in the dog do occur in the region of the caudal cervical ganglion.

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