Insignificant Bilateral Convergence of Preganglionic Vagal Fibers on Postganglionic Neurons to the Canine Heart

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We determined the extent of convergence of preganglionic fibers from the right and left vagus nerves on postganglionic neurons that supply the sinoatrial node in chloralose-anesthetized dogs. We administered hemicholinium-3 and stimulated the right vagus nerve at a high frequency to deplete acetylcholine from the postganglionic parasympathetic neurons supplied by that nerve. We compared the effects of this “depletion regimen” with the responses in two control groups: a stimulation control group, which was subjected to high-frequency right vagus stimulation only, and a drug control group, which received a hemicholinium-3 infusion only. The effects of right vagus stimulation did not differ from those of left vagus stimulation in either of the control groups. In the animals subjected to the depletion regimen, the responses to right vagus stimulation were almost abolished. However, the left vagus nerve retained its ability to prolong cardiac cycle length in these animals. Thus, our experiments indicate that left vagus preganglionic fibers do not converge with right vagus preganglionic fibers on a substantial pool of postganglionic neurons that innervate the canine sinoatrial node. (Circulation Research 1990;67:556-563)

Convergence of several synaptic axons on individual postsynaptic neurons is an important integrating mechanism in the nervous system. Anatomic and functional studies have shown that preganglionic parasympathetic fibers converge on postganglionic neurons in the hearts of nonmammalian species. Roper and Ko1 estimated that about one third of the cardiac ganglion cells in the frog heart receive bilateral innervation from preganglionic vagus nerve fibers. Similarly, by measuring acetylcholine (ACh) overflow in the isolated, innervated chicken heart, Lindmar et al2 have provided convincing evidence for bilateral vagal innervation of cardiac postganglionic neurons. These investigators depleted ACh by combining prolonged unilateral vagus stimulation with the infusion of hemicholinium-3 (HC-3), a drug that inhibits ACh synthesis in parasympathetic nerve terminals.3,4 Thereafter, the ACh overflow from the chicken heart evoked by contralateral vagus nerve stimulation was reduced by about 75%, a result that signifies substantial convergence of right and left vagal fibers on common postganglionic neurons.

Evidence for convergence of preganglionic parasympathetic fibers onto postganglionic neurons in the mammalian heart, however, is indirect and controversial.5,6 In an effort to settle this controversy, we designed experiments to test for convergence of preganglionic nerve fibers from the right vagus (RV) and left vagus (LV) nerves on common postganglionic neurons in the dog heart. Our protocol was based on the experimental design used by Lindmar et al2 to test for convergence in the chicken heart.

Figure 1 presents the expected responses to vagus stimulation in the presence (panels A–D) or absence (panels E–H) of convergence of parasympathetic fibers to the sinoatrial node. In this figure, postganglionic neurons a, b, and c are supplied by preganglionic fibers from the LV nerve, RV nerve, or both. This model assumes that stimulation of a fiber from either cervical vagus nerve would ordinarily activate all the postganglionic neurons it supplies. Thus, in Figure 1A, stimulation of the LV would fire postganglionic neurons a and b, and stimulation of the RV would fire neurons b and c.

We postulated that if a significant number of preganglionic LV and RV fibers converged on postganglionic neurons to the sinoatrial node, and if we depleted ACh from all postganglionic neurons (b and c) supplied by preganglionic RV fibers (by a combi-

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Received August 21, 1989; accepted April 10, 1990.
natin of HC-3 and prolonged RV stimulation), then the subsequent response to LV stimulation would be significantly diminished. Under such conditions, LV stimulation would fire only fiber a (Figure 1B), rather than fibers a and b. Conversely, if preganglionic LV and RV fibers did not converge on common postganglionic neurons (Figure 1E), then the response to LV stimulation would not be affected by depletion of ACh from postganglionic neurons innervated by the RV (Figure 1F).

Figure 1 demonstrates other potential patterns of ACh depletion that might have resulted from our protocol in either the presence (panels C and D) or the absence (panels G and H) of convergence. For example, if ACh were depleted from convergent preganglionic RV fibers before the postganglionic neurons could be depleted (Figure 1C), LV test responses (firing of postganglionic neurons a and b) would not differ from the control responses. In contrast, if ACh were depleted from preganglionic and postganglionic fibers simultaneously (Figure 1D), the responses to LV stimulation would be less than the control response; only fiber a would be activated. In the absence of convergence, neither preganglionic depletion (Figure 1G) nor combined preganglionic and postganglionic depletion (Figure 1H) of ACh from RV neurons would affect the response to LV stimulation.

The examples cited above demonstrate that, if preganglionic RV and LV fibers do not converge on common postganglionic neurons, the site of ACh depletion (panels F, G, and H) from RV fibers would not affect the response to LV stimulation. If RV and LV fibers do converge, and if our regimen depletes the postganglionic fibers innervated by the RV first or if it depletes preganglionic and postganglionic fibers simultaneously, then the responses to test LV stimulation would be attenuated. If, however, our regimen depletes preganglionic RV fibers first, before postganglionic fibers can be depleted, then our experimental design would not constitute a valid test for convergence; the response to LV stimulation would not be attenuated.

Therefore, we carried out one series of experiments in anesthetized dogs to deplete ACh from RV fibers by a combination of HC-3 administration and intense, sustained RV stimulation, and then tested the response to a standard LV stimulus. We conducted a second series of experiments to determine whether the ACh depletion of RV fibers occurred primarily at the preganglionic or at the postganglionic level.

Materials and Methods

General Preparation

We carried out experiments on 21 mongrel dogs of either sex. Their weights ranged from 17 to 33 kg. Each animal was premedicated with morphine sul-

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**Figure 1.** Possible effects of a depletion regimen, consisting of hemicholinium-3 (HC-3) infusion and intense right vagus (RV) stimulation, on the responses to test stimulations of the left vagus (LV) and RV nerves. Panels A-D: Expected responses when preganglionic fibers from LV and RV converge on a substantial pool of postganglionic neurons. Panels E-H: Expected responses when there is no appreciable convergence. Postganglionic fibers are labeled a, b, and c. Filled circles represent nerve terminals filled with neurotransmitter; open circles are nerve terminals that have been functionally depleted of neurotransmitter.
fate (2 mg/kg i.m.) and was anesthetized with α-chloralose (75 mg/kg i.v.). We monitored femoral arterial pressure and cannulated one femoral vein for administration of fluid and drugs. We blocked the β-adrenergic receptors with an initial intravenous injection of propranolol (1 mg/kg), and we gave supplemental doses of 0.5 mg/kg every 2 hours.

We cannulated the trachea, instituted positive pressure ventilation, and opened the chest transversely. We inserted a bipolar catheter into the right atrial appendage to record the atrial electrogram. The electrogram served as input to a parallel logic analog computer (EAI 580, Electronics Associates), which computed the duration of each cardiac cycle. We recorded the atrial electrogram, cardiac cycle length (CCL), and arterial blood pressure on a Gould recorder (ES 1000, Gould Instruments, Cleveland).

We tightly ligated the vagosympathetic trunks at the midcervical level to interrupt conduction and inserted stimulating electrodes (insulated to within 1 mm of the tip) into the cardiac segments of each vagus nerve. This electrode placement produces stable responses for several hours. Each stimulating electrode was connected to an electronic stimulator with an isolation unit (model SD9, Grass Instrument Co., Quincy, Mass.).

**Experimental Design**

The experimental design to test for convergence included the following three groups: 1) a “depletion” group, which received both HC-3 and tonic RV stimulation; 2) a “drug control” group, which received HC-3 only, and 3) a “stimulation control” group, which received RV stimulation only. We randomly assigned each animal to one of the three groups; each group consisted of five animals.

At the beginning of each experiment, we determined the CCL responses to three “test” stimulations to each vagus nerve. All stimulation voltages were supramaximal (6–10 V), and the pulse duration was 1 msec. For our test stimuli, we stimulated the nerves at a frequency that increased CCL by more than 500 msec; the same test stimulus characteristics were maintained throughout the experiment. Each test stimulation train was about 15 seconds in duration, and at least 60 seconds was allowed to elapse between stimulations.

After the control data were obtained, animals in the depletion and drug control groups received a 10-ml bolus injection of HC-3 (0.55 mg/kg i.v.), followed by a continuous infusion of the drug (22 μg/kg/min) for the 2-hour duration of each experiment. We infused an equivalent volume of saline into the animals of the stimulation control group. Each animal received a total of 570 ml infusate during the 2-hour experiment.

In the depletion and stimulation control groups, we delivered sustained, high-frequency, supramaximal vagus stimulation to the RV nerve. We began this “intense” RV stimulation 5 minutes after the beginning of the drug or saline infusion, and we continued stimulation for 120 minutes. We temporarily discontinued the intense stimulation at predetermined times (2.5, 30, 45, 60, 75, 90, 105, and 120 minutes) after the onset of drug or saline infusion to determine the chronotropic responses to test stimulations of the RV and LV nerves. The responses to these test stimulations were used as an index of neurotransmitter depletion from the parasympathetic nerves that supply the sinoatrial node. We did not apply the regimen of sustained, high-frequency, supramaximal RV nerve stimulation in the drug control group.

The responses of the three groups were assessed by an analysis of variance. The experiments contained three factors: V, the specific nerve trunk that was stimulated; T, the time at which the test stimulations were delivered; and G, the experimental group. There were two levels (LV and RV nerves) of factor V, nine levels (0, 2.5, 30, 45, 60, 75, 90, 105, and 120 minutes) of factor T, and three levels (drug control, stimulation control, and depletion groups) of factor G. F tests were used for all planned comparisons of mean values.

**Results**

**Depletion Regimen**

A typical response to the depletion regimen is illustrated in Figure 2. In this experiment, the basic cycle length was 480 msec. A control test stimulus (6 Hz) to the RV nerve before HC-3 infusion increased CCL to 1,340 msec, a 179% increase. Similarly, a control test stimulus (13 Hz) to the LV nerve increased CCL to 1,200 msec, a 150% increase. After 120 minutes of HC-3 infusion and intense RV stimulation, test stimulation (6 Hz) of the RV increased

![Figure 2. Changes in cardiac cycle length produced by test stimulations of the right (8 V, 6 Hz, 1 msec) and left (8 V, 13 Hz, 1 msec) vagus nerves in a representative experiment under control conditions and after 120 min of hemicholinium-3 infusion combined with intense stimulation of the right vagus nerve. Right and left vagal stimulation frequencies were adjusted to 6 and 13 Hz, respectively, to elicit approximately equal chronotropic responses.](http://circres.ahajournals.org/)

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**Note:** The diagram provided in Figure 2 illustrates the changes in cardiac cycle length produced by test stimulations of the right and left vagus nerves in a representative experiment under control conditions and after 120 minutes of hemicholinium-3 infusion combined with intense stimulation of the right vagus nerve. The stimulations were adjusted to 6 and 13 Hz, respectively, to elicit approximately equal chronotropic responses. This demonstrates the differential effects of vagal stimulation on cardiac cycle length, with the right vagus nerve showing a greater response at lower frequencies compared to the left vagus nerve. The data highlight the importance of specific vagal nerve stimulation protocols in assessing cardiac responses.
CCL to 530 msec from a basic cycle length of 500 msec, only a 6% increase. Test stimulation (13 Hz) of the LV, on the other hand, increased CCL to 1,100 msec, a 120% increase. Thus, the combination of HC-3 infusion and prolonged RV stimulation markedly attenuated the response to RV stimulation, but only slightly diminished the response to LV stimulation.

Figure 3 shows the time courses of the responses to test stimulations of the RV and LV nerves in the three groups of animals. In the depletion group (Figure 3A), RV stimulations prolonged CCL by 867±87 (SEM) msec before we started the depletion regimen (t=0). The RV responses decreased substantially within 2.5 minutes after beginning the depletion regimen, and they were almost abolished after 120 minutes (52±13 msec). In contrast, the responses to LV stimulation decreased from a control value of 645±49 to 437±64 msec at 2.5 minutes after the beginning of the depletion regimen. The responses then remained stable at about this level for the remainder of the 2-hour period (456±61 msec at 120 minutes). During the period of sustained, intense, RV stimulation, the responses to the test stimulations of the RV nerve were much more attenuated (p<0.0001) than were those to LV stimulation.

To determine the separate effects of the two components of our depletion protocol, we measured the effects of HC-3 infusion alone in the drug control group and of intense RV stimulation alone in the stimulation control group. HC-3 infusion alone decreased the chronotropic responses to test stimulations of the LV and RV nerves (Figure 3B). The response to the test stimulation of the RV nerve decreased from 876±90 msec (t=0) to 406±46 msec 2.5 minutes after the beginning of HC-3 infusion. The response then stabilized at 546±43 msec after 120 minutes of drug infusion. The initial response (t=0) to test stimulation of the LV was 641±74 msec. The response then decreased to 380±34 msec (t=2.5 minutes) and stabilized at 514±57 msec (t=120 minutes). Intense RV stimulation by itself did not significantly affect the chronotropic responses to test stimulation of either vagus nerve (Figure 3C).

Figure 4 compares the chronotropic responses to the test stimulations of the RV and LV nerves before and at the end of the experimental periods in these three groups of animals. The data were evaluated by an analysis of variance; the factors were group, vagus nerve, and time.

Although the initial chronotropic responses (t=0) to test stimulation of the RV nerve (Figure 4A) were similar in the three groups (shaded bars), the final

![Figure 3](https://example.com/figure3.png)

**Figure 3.** Mean changes (±SEM) in cardiac cycle length (ΔCCL) elicited by test stimulations of the right and left vagus nerves in a "depletion group" of animals that received the combination of hemicholinium-3 infusion and intense right vagus stimulation (panel A), in a "drug control group" that received only hemicholinium-3 infusion (panel B), and in a "stimulation control group" that received only right vagus stimulation (panel C). There were five animals in each group.

![Figure 4](https://example.com/figure4.png)

**Figure 4.** Changes (±SEM) in cardiac cycle length elicited by test stimulations of the right (panel A) and left (panel B) vagus nerves before (t=0) and after 120 minutes of combined hemicholinium-3 infusion and tonic right vagus stimulation (depletion group), of hemicholinium-3 infusion alone (drug control group), or of intense right vagus nerve stimulation alone (stimulation control group). Groups are the same as those presented in Figure 3.
responses (t=120 minutes) differed markedly ($p=0.0001$). In addition, the interaction between treatment group and time was pronounced ($p<0.00001$); that is, the difference between the responses to nerve stimulation at $t=0$ and $t=120$ depended on the group to which the animal belonged. The most pronounced difference prevailed in the depletion group. The mean response at 120 minutes in this group diminished to 6% of the mean initial response.

The chronotropic responses to the test stimulations of the LV nerve did not change appreciably over the 120-minute observation period in the stimulation control group (Figure 4B). However, in the depletion group, the mean response at 120 minutes was 71% of the control response. Similarly, in the drug control group, the mean response at 120 minutes was 80% of the control response. The changes in the depletion group over the 120-minute observation period were not significantly different ($p=0.5$) from those in the drug control group.

**Site of Acetylcholine Depletion**

Figures 3 and 4 show that the depletion regimen virtually abolished the chronotropic response to RV stimulation, but its effect on the response to LV stimulation was not significantly greater than the effect of HC-3 alone in the drug control group. These results suggest negligible convergence of fibers from the RV and LV nerves on common postganglionic neurons, as illustrated by panels E and F in Figure 1. In this figure, the depletion regimen (panel F) abolishes the response to RV stimulation, but does not appreciably affect the response to LV stimulation.

However, if our depletion regimen had actually depleted the ACh from preganglionic neurons well before it could have depleted the ACh from the postganglionic neurons, our experimental design would not have been able to distinguish between the presence or absence of convergence. Consider, for example, that left and right preganglionic fibers did converge on a substantial pool of postganglionic neurons, as illustrated in Figures 1A–1D. Consider also that our depletion regimen had depleted the ACh from the preganglionic neurons of the RV before the postganglionic neurons innervated by those preganglionic neurons could have been depleted. Panels C and G in Figure 1 show that the responses to RV and LV stimulations would not depend on the presence (panel C) or absence (panel G) of substantial convergence. Therefore, we conducted an additional series of experiments to verify that the postganglionic parasympathetic neurons were indeed the neurons from which ACh was depleted by our depletion regimen.

We devised methods to stimulate postganglionic vagus nerve fibers in the walls of the right atrium and to measure the effect on atrial contraction. We inserted a small balloon into the right atrial appendage and anchored the balloon near the tip of the auricle. We introduced 1–2 ml saline into the balloon and assessed atrial contraction by measuring the pressure changes in the balloon.

Stimuli to the intramural nerve fibers were generated by an electronic stimulator (Grass SD9) connected to two electrodes attached to the base of the right auricle. One electrode was attached near the junction of the auricle with the superior vena cava, and the other near the junction of the auricle with the inferior vena cava.

The stimulator, controlled by an analog computer, generated brief bursts of electrical pulses (10–15 V, 1-msec duration, 4–5 pulses per burst, 4-msec interval between pulses). The stimulus bursts were used to pace the atrium at a frequency that was just greater than the control heart rate. All pulses in the burst except the first were delivered during the atrial refractory period. The bursts of pulses served not only to pace the heart, but also to stimulate the intramural nerve fibers. We gave propranolol (1 mg/kg i.v.) to block any $\beta$-adrenergic effects caused by stimulation of intramural sympathetic fibers.

We conducted preliminary experiments in two animals to verify that our technique for stimulating intramural nerve fibers did activate postganglionic parasympathetic neurons. The results of one of these experiments are shown in Figure 5. In this animal, treated with propranolol, cervical vagus nerve stimulation inhibited the atrial contraction by 84%, and intramural nerve stimulation inhibited the atrial contraction by 46%. After we gave hexamethonium, a ganglionic blocking drug, the effect of cervical vagus nerve stimulation on atrial contraction was abolished, whereas intramural nerve stimulation retained its ability to inhibit atrial pressure (44% inhibition). The effects of this protocol in the second animal were similar to those shown in Figure 5. In one other animal that was given propranolol but not hexamethonium, atropine (0.1 mg/kg i.v.) abolished the atrial contractile responses to cervical vagus stimulation and to intramural nerve stimulation. We conclude that the effects of our procedure for stimulating the intramural nerve fibers in the right atrium are mediated almost exclusively by postganglionic parasympathetic fibers.

We conducted three additional experiments to determine whether the postganglionic parasympathetic fibers were the critical sites at which neurotransmitter was depleted by our regimen. We implemented our depletion regimen, except that we stimulated intensely both cervical vagus nerves instead of just the right nerve. We compared the chronotropic and atrial contractile responses to test stimulations of the cervical vagus nerves and of the intramural auricular nerve fibers before ($t=0$) and during the 120-minute depletion regimen (Figure 6). The atrial contractile response to test stimulation of the intramural nerve fibers was used to assess the extent of neurotransmitter depletion from the postganglionic parasympathetic nerve fibers. In contrast, the chronotropic response to test stimulation of both cervical vagus nerves was used to assess the extent of
depletion from the combined system of preganglionic and postganglionic parasympathetic nerve fibers.

Under control conditions (t=0), intramural nerve stimulation diminished the atrial contraction by 33%; in Figure 6, this represents the control response (100%). The magnitude of this response declined progressively throughout the depletion regimen (p<0.0001). At the end of 120 minutes, the contractile response was diminished to 18±9% (SD) of control.

Similarly, the chronotropic responses to test stimulation of the cervical vagus nerves were diminished by the depletion protocol (p<0.0001). Under control conditions (t=0), bilateral vagus stimulation decreased heart rate to 101 beats per minute from a prestimulation value of 142 beats per minute; this constitutes the control response (100%). At the end of 120 minutes of the depletion protocol, the chronotropic response to the same test stimulation was only 22±6% as great. The time course of the chronotropic responses to cervical vagus stimulation was not significantly different (p=0.6) from that of the atrial inotropic responses to stimulation (Figure 6).

**Discussion**

We measured the chronotropic response to vagus nerve stimulation to test for convergence of preganglionic parasympathetic neurons from the RV and LV nerves on postganglionic neurons that innervate the sinoatrial node of the canine heart. Our results (Figures 3A and 4A) show that administration of HC-3, combined with sustained, intense stimulation of the RV nerve, markedly diminished the ability of the RV nerve to prolong CCL. However, this same regimen had a much less pronounced effect on the chronotropic response to LV stimulation (Figures 3A

**Figure 5.** Effect of vagus nerve stimulation (10 V, 1.5 Hz, 1 msec) and intrinsic nerve stimulation (15 V, 3 pulses/burst, 4 msec interpulse interval) before (panels A and B) and after (panels C and D) hexamethonium administration (5 mg/kg i.v.). The atrium was paced to produce a cardiac cycle length of 360 msec. After drug infusion, vagus stimulation had no effect at the control frequency of 1.5 Hz, and minimal effect at 12 Hz. Intrinsic nerve stimulation retained its inhibitory effect.
and 4B). This effect on the LV responses was no greater than the effect produced by a 2-hour infusion of HC-3 alone (Figures 3B and 4B), a procedure that does not functionally deplete ACh. We define “functional depletion” to mean a reduction in the releasable pool of ACh that is pronounced enough to interfere with neurotransmission.

The results displayed in Figures 3 and 4 suggest, therefore, that our depletion regimen did not functionally deplete ACh from any substantial pool of postganglionic neurons on which preganglionic fibers from the RV and LV nerves converged. For this conclusion to be valid, however, we must demonstrate that our depletion regimen did functionally deplete ACh from postganglionic parasympathetic fibers. Whether this depletion had occurred either before (Figure 1, panels B and F) or at the same time as (Figure 1, panels D and H) it had depleted ACh from preganglionic fibers would not be relevant. Either condition would permit the responses to RV and LV stimulation to distinguish between the presence or absence of significant convergence. However, if our depletion regimen had functionally depleted ACh from preganglionic fibers first, which would have prevented functional depletion from postganglionic fibers, our test stimulations could not have distinguished between the presence or absence of appreciable convergence (Figure 1, panels C and G).

Our experiments (Figure 6) did indeed show that the depletion regimen severely impaired neurotransmission from postganglionic parasympathetic nerve fibers. In these experiments, combined HC-3 infusion and bilateral vagus nerve stimulation markedly attenuated the atrial inotropic responses to test stimulation of the parasympathetic nerve fibers in the right atrial wall. We know that these intramural nerve fibers were postganglionic, because in two control animals not subjected to the depletion regimen, when we injected hexamethonium to block ganglionic transmission, the atrial inotropic response to cervical vagus stimulation was abrogated, but the response to intramural nerve fiber stimulation was unaffected.

In the animals subjected to the depletion regimen, the time course of the responses to combined preganglionic and postganglionic nerve fiber stimulation (cervical vagus stimulation) was parallel to that of the responses to postganglionic intramural nerve fiber stimulation (Figure 6). Thus, we conclude that the attenuated responses to vagus test stimulation in animals exposed to the depletion regimen was a result of ACh depletion predominantly from postganglionic neurons or proportionately from preganglionic and postganglionic neurons.

HC-3 has two major actions: it inhibits ACh synthesis by suppressing choline transport into the nerve endings,3,4,9 and it inhibits the response of the effector cell to ACh.4,9-11 Administration of HC-3, combined with intense stimulation of the vagus nerves, depletes the neuronal content of ACh and thereby diminishes the release of ACh from the nerve terminals. HC-3 also has an effect on cardiac and smooth muscle cells that mimics muscarinic blockade; it selectively antagonizes the action of ACh.11 We will refer to this effect as a “postjunctional” effect, because it occurs on the effector cell side of the neuroeffectector junction.

The reduction in the response to vagus nerve stimulation (Figure 3) that occurred immediately after the beginning of the HC-3 infusion (t=2.5 minutes) is most likely a postjunctional inhibitory influence on the cardiac effector cell membrane. This diminished response was equally evident in the depletion and drug control groups (Figure 3, panels A and B). This postjunctional effect complicates the interpretation of our experiments, because the neuronal depletion of ACh and the muscarinic blockade of the effector cells both have similar functional effects, namely, attenuation of the chronotropic response to nerve stimulation.

Inclusion of the drug control group (Figure 3B) permitted us to evaluate the contribution of the postjunctional influence of HC-3 infusion to the overall effects of the depletion regimen on the test responses to vagus stimulation. Figure 3B demonstrates that the postjunctional effect is evident within 2.5 minutes, and it persists at a fairly constant level for the duration of the infusion. The responses to LV stimulation at the end of the full depletion regimen were not significantly different from the responses to HC-3 infusion alone (Figure 4B). Hence, we conclude that the diminished responses at 120 minutes in the depletion and drug control groups are ascribable to the postjunctional influence of HC-3 on the effector cells. Thus, the depletion regimen must have produced negligible depletion of neurotransmitter in the postganglionic fibers supplied by the LV nerve.

Fee et al.2 have identified a pulmonary vein fat pad containing vagal synapses that regulate sinoatrial node function. The entire input to the sinoatrial node region from both vagus nerves may course through this fat pad. These investigators also identified a similar epicardial fat pad that contains parasympathetic synapses that regulate atrioventricular conduction. The presence of synapses for RV and LV fibers in such restricted areas suggests that preganglionic RV and LV fibers that affect specific cardiac functions may converge on common postganglionic nerve fibers in the canine heart. Hence, the detailed knowledge about the synaptic vagal connections may have important implications about the discrete neural regulation of specific cardiac functions.

The presence of convergence of preganglionic fibers from the RV and LV nerves on postganglionic parasympathetic neurons is well-established in hearts of certain nonmammalian species.1,2 However, evidence for such convergence in mammals has been indirect and controversial.5,6 Hondegem et al.5 observed that, at low stimulation frequencies, the changes in heart rate elicited by RV and LV stimulation were algebraically additive. However, at stimulation frequencies greater than 3 Hz, the decrease in heart rate evoked by combined LV and RV
stimulation was substantially less than the sum of the individual responses. Parker et al. reported that the prolongation of CCL caused by any combination of left and right nerve stimulation was always less than the sum of the prolongations evoked by separate stimulations, even when they used low stimulation frequencies. They reasoned that if left and right preganglionic fibers converged on a substantial pool of common postganglionic neurons, bilateral stimulation would be expected to lead at times to neural facilitation rather than occlusion, especially when low stimulation frequencies are used. They never observed such facilitation, however, but only occlusion. Therefore, they concluded that their experimental results were probably not ascribable to the occlusion caused by bilateral convergence on common postganglionic neurons. Our data agree with their conclusion; our results indicate that the extent of bilateral convergence of preganglionic cardiac vagal fibers on common postganglionic neurons is negligible.

Acknowledgment

The authors are grateful to Frank Walters for his skilled technical assistance.

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Key Words: acetylcholine • autonomic ganglia • heart rate • hemicholinium-3 • parasympathetic nervous system
Insignificant bilateral convergence of preganglionic vagal fibers on postganglionic neurons to the canine heart.

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*Circ Res.* 1990;67:556-563
doi: 10.1161/01.RES.67.3.556

*Circulation Research* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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