A Cardiac Sympathovagal Reflex in the Cat

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ABSTRACT

The reflex changes in single cardiac vagal efferent fibers elicited by excitation of afferent cardiac sympathetic fibers were studied in cats anesthetized with chloralose and urethane. Efferent vagal and sympathetic units were dissected from the end of a cardiac nerve cut at its junction with the right atrium. In some cases, efferent vagal units were dissected from the cervical vagus. Excitation always evoked a clear reduction in the discharge of cardiac vagal units and a clear increase in the discharge of cardiac sympathetic fibers. The effects on cervical vagal efferents were variable. Hence, excitation of afferent cardiac sympathetic fibers could simultaneously elicit inhibition of the vagal outflow to the heart and excitation of the sympathetic outflow. By contrast, stimulation of the cut central end of the contralateral vagus produced the opposite effects. Convergence of afferent fibers in the vagi and the cardiac sympathetic nerves on the same cardiac vagal and cardiac sympathetic postganglionic neurons was demonstrated. Convergence from carotid sinus baroreceptors was also observed.

KEY WORDS: afferent cardiac sympathetic fibers, heart rate, myocardial contractility, pressor reflexes, vagal reflexes, myoelectrical activity in cardiac vagal or sympathetic units.

Methods

Cats were anesthetized with chloralose and urethane (60 mg/kg and 250 mg/kg, respectively, ip). Two cats anesthetized in this way were also decerebrated by transcollicular section, and three cats were decerebrated under transient ether anesthesia. All the cats were paralyzed with gallamine triethiodide and artificially ventilated so as to maintain arterial Po₂, Pco₂, and pH at about 90 mm Hg, 40 mm Hg, and 7.40, respectively. The guide lines of the American Physiological Society regarding anesthetized, curarized animals were followed. Methods of recording arterial blood pressure, electrocardiograms, and respiratory movements have been described previously (10). A ligature placed loosely around the descending thoracic aorta was tightened against a polyethylene tube to produce stenosis of this vessel.

Neural Activity in Cardiac Vagal or Sympathetic Units.—The chest was opened through a transverse incision that extended across the sternum into the fifth and the sixth intercostal spaces bilaterally. The right thoracic vagus was exposed at the thoracic inlet, and the azygos vein was removed to expose one of its cardiac branches (5). All other branches of the thoracic vagus were cut. This cardiac branch was then traced to its junction with the right atrium where it was cut and its central end reflected back from the heart.

Nerve filaments were dissected from this end and placed across platinum electrodes which were connected to Grass P511 a-c preamplifiers with a bandwidth of 10-10,000 Hz. The activity was recorded on tape (Hewlett-Packard 3907) and photographed from a Tektronix 505 oscilloscope, using a Grass C4 camera.

The impulse activity was limited to cardiac vagal units by excising the right stellate ganglion and all of its connections. Subsequent section of the right cervical vagus always abolished this neural activity. When necessary, the activity could be limited to cardiac sympathetic units by leaving the right stellate ganglion intact and cutting the right cervical vagus. The discharge ceased following right stellactomy.

In some experiments, the activity in the cut central end of slips of nerve dissected out of the right cervical vagus was registered.
Nerve Stimulation.—The cut central ends of the left inferior cardiac nerve, the left cervical vagus, and the left pericoronary nerve were stimulated (2). Pulses were generally 5–15 v, 0.5–3.0 msec, and 5–30 Hz.

Chemical Excitation of Afferent Cardiac Sympathetic Nerve Fibers.—The main left coronary artery was perfused with a constant flow pump (11). Veratridine, 1–8 µg, prepared as previously described (12), was injected into the inflow line in volumes of 0.2 ml or less. Similar volumes of saline were injected as a control. Veratridine in equivalent amounts was also injected into the right atrium and the root of the aorta.

Results

The neural activity of cardiac vagal efferent units was recorded in cats with systolic blood pressures ranging from 100 to 170 mm Hg. In general, the activity was spontaneous and irregular (Fig. 1a), and it had no correlation with respiration. However, a few units had a constant cardiac rhythm. The impulse activity of some fibers increased as blood pressure rose, and such fibers could be silent if the blood pressure was low enough. However, the activity of some units was not altered by changes in arterial blood pressure. More uniform responses were reported when the left vagus and one carotid sinus nerve were cut (5). We have not characterized in detail the units we recorded from, since such classifications have been made already (5, 13).

Effects of Stimulation of the Cut Central End of the Left Inferior Cardiac or the Left Cervical Vagus Nerve.—The neural discharge of 28 cardiac vagal efferent units was either completely abolished or greatly reduced during stimulation of the cut central end of the left inferior cardiac nerve (Fig. 1c). These results were obtained in 115 trials (100% success rate). The left cervical vagus had been cut previously in these cats. By contrast, stimulation of the cut central end of the left cervical vagus always clearly excited 18 units (33 trials, 100% success rate) (Fig. 1b). These effects were independent of changes in arterial blood pressure, which were minimal or absent. When present, the changes occurred after alteration of neural activity. Changes

![Figure 1](http://circ.ahajournals.org/)

**Effects of electrical stimulation on the neural discharge of a single efferent cardiac vagal fiber in a decerebrate, anesthetized cat.** a: Spontaneous activity. b: Electrical stimulation (5 v, 1.5 msec, 30 Hz) of the cut central end of the left cervical vagus. c: Electrical stimulation (10 v, 1.5 msec, 30 Hz) of the cut central end of the left inferior cardiac nerve. The tracings in each section are from top to bottom: respiration (positive-pressure inflation is an upward deflection), systemic arterial blood pressure, electrocardiogram, and neural activity.
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in heart rate were not observed, probably because the heart was largely denervated. The results were the same in cats with intact brains and in decerebrate cats, indicating that centers above the transcollicular section were not importantly involved in the response.

The effects of these two stimuli on cardiac sympathetic efferent units which were dissected out of the same cardiac nerve were examined. These units were spontaneously active and had an irregular rhythm which was not correlated with respiration. However, two fibers had a definite cardiac rhythm. The pattern of discharge was unaffected by cutting the right cervical vagus, and it was abolished by right stellpectomy. Stimulation of the cut central end of the left vagus produced a clear inhibition of the discharge in six units in each of 12 trials (Fig. 2a). This result should be compared with the striking excitation of cardiac vagal efferent units elicited by the same stimulus (Fig. 1b). Stimulation of the cut central end of the left inferior cardiac nerve provoked a marked excitation of impulse activity in the same cardiac sympathetic efferent fiber (Fig. 2b). Similar results were obtained in all 21 trials in six units. Again this excitatory response must be contrasted with the complete suppression of cardiac vagal efferent discharge by this stimulus (Fig. 1c).

**Effects of Chemical and Electrical Stimulation of Afferent Cardiac Sympathetic Nerve Fibers.**—Excitation of afferent nerve fibers in the cardiac sympathetic nerves can clearly inhibit cardiac vagal neurons. However, afferent fibers other than those arising from the heart are also excited by these stimuli. To restrict the stimuli to afferent cardiac sympathetic fibers, we either injected veratridine, which is known to excite afferent cardiac sympathetic fibers (14), into the coronary circulation or stimulated the cut central end of the left pericoronary nerve (2) in vagotomized cats. Injection of veratridine into the coronary arterial inflow tubing provoked a brief, but complete, suppression of the discharge of each of the four cardiac vagal efferent units tested (Fig. 2c). This brief inhibition was not fortuitous, since it did not occur during much longer control periods (2-5 minutes) than those shown in Figure 3. Neither injection of similar amounts of veratridine into the right atrium or the root of the aorta nor intracoronary injection of equivalent volumes of saline altered efferent vagal activity. Stimulation of the cut central end of the left pericoronary nerve produced a clear reduction in the activity of each of the three fibers tested.

**Effects of Afferent Cardiac Sympathetic Nerve Stimulation during Aortic Occlusion.**—Large increases in arterial blood pressure greatly increase the activity of carotid sinus baroreceptors. As a result, the discharge of cardiac vagal efferent units should also be greatly increased and the discharge of cardiac sympathetic efferent units greatly reduced. Thus, it would be of interest to determine whether the effects of afferent cardiac sympathetic

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**FIGURE 2**

Effects of electrical stimulation on the discharge of a single efferent cardiac sympathetic fiber in an intact, anesthetized cat. Tracings are as in Figure 1. a: Electrical stimulation (6 v, 1.5 msec, 30 Hz) of the cut central end of the left vagus. b: Electrical stimulation (10 v, 1.5 msec, 30 Hz) of the cut central end of the inferior cardiac nerve.
FIGURE 3
Effects of intracoronary injection of veratridine on the activity of a single efferent cardiac vagal fiber in an intact, anesthetised cat. At the arrow, 4 μg of veratridine was injected into the inflow tract of the coronary pump. The time necessary for the drug to reach the main coronary artery was estimated to be about 19 seconds. The neural discharge was briefly abolished 21 seconds after injection. Similar latencies for efferent sympathetic fibers have been reported (14). The continuous tracings (a–c) from top to bottom are: respiration, systemic arterial blood pressure, coronary arterial blood pressure, electrocardiogram, and neural activity.

nerve stimulation on these efferent pathways are still present during periods of increased arterial blood pressure. Figure 4a shows the response of a quiescent cardiac vagal efferent unit to stenosis of the thoracic aorta. When stenosis occurred, systemic arterial blood pressure rose to 275 mm Hg. The fiber was greatly excited and began to discharge in bursts having a cardiac rhythm. Afferent cardiac sympathetic fibers were then stimulated (solid line), and the discharge was clearly inhibited. When the stimulation was stopped but the stenosis maintained, the discharge resumed but not at its prestimulation level, possibly due to the duration of the aortic stenosis. When the aortic stenosis was released, neural activity ceased again. Similar results were obtained in all 30 trials on six units. Four of these units were spontaneously active at arterial blood pressures of 100 to 130 mm Hg. Cardiac sympathetic efferent units in this nerve were silenced by aortic occlusion (Fig. 4b, broken line). Despite this inhibition, stimulation of afferent cardiac sympathetic fibers excited these units (Fig. 4b, solid line). When the aortic occlusion was released, an increased discharge ensued, possibly due to the large fall in arterial blood pressure.

Effects of Stimulation of Afferent Cardiac Sympathetic Fibers on the Discharge of Cervical Vagal Efferent Units.—The reflex alterations in cardiac vagal efferent activity elicited by stimulation of afferent cardiac sympathetic nerve fibers were strikingly uniform. Therefore, the question arose as to whether other vagal efferent units sensitive to cardiovascular changes were similarly affected. For this reason, we examined the response of a less restricted population of vagal efferents. We selected nine fibers in the right cervical vagus which were excited by stenosis of the descending thoracic aorta. The control discharge of these units appeared to be similar to that observed in units dissected from the cardiac nerve. Stimulation of the cut central end of the left inferior cardiac nerve inhibited the discharge of two cervical vagal units, as was observed in the cardiac vagal units. However, the discharge of four cervical units was not affected, and in three cervical units it was clearly increased.
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Discussion

The activity of cardiac vagal efferent units was reflexly suppressed by electrical or chemical stimulation of afferent cardiac sympathetic nerve fibers. When the activity of these efferent units was enhanced by aortic occlusion, it could still be inhibited by such afferent stimulation. Since the afferent vagal and the afferent thoracic sympathetic fibers were cut, the enhanced activity was reflexly engendered at least in part by the carotid sinus baroreceptors (5); therefore, the baroreceptor and the afferent cardiac sympathetic fibers must converge on the same cardiac vagal neuron.

The uniformity of the responses of cardiac vagal efferents to afferent cardiac sympathetic nerve stimulation was striking. By contrast, the responses of cervical vagal efferents were highly variable. Since efferent units in the cervical vagus undoubtedly include noncardiac fibers, this variability is not really surprising. The uniform response does suggest, however, that the reflex effects on the cardiac vagal neurons are specific.

Efferent units in the cervical vagus which are reflexly excited by carotid sinus nerve stimulation have been described (15). These efferents were thought to be cardiac, but they were not excited by stimulation of the cut central end of the contralateral cervical vagus. However, we found that the cardiac vagal efferents were always reflexly excited by this stimulus. If the units we recorded from were representative of all cardiac vagal neurons, the
assumptions of the previous report (15) were probably not valid. In this regard, it is important to emphasize the advantage that seems likely to result from recording neural activity in vagal efferents that have been traced directly to the heart (5).

We previously presented evidence that nonvagal afferent thoracic fibers running in the cardiac sympathetic nerves inhibited cardiac vagal neurons (16). By restricting our stimuli to afferent cardiac sympathetic fibers only, we have now demonstrated the cardiocardiac nature of this reflex. This finding is important, because afferent cardiac sympathetic fibers are known to relay impulses concerning cardiac events, both continuously and intermittently (14). Therefore, this afferent pathway may exert a tonic influence on cardiac vagal neurons.

The latency of this reflex pathway has not been studied precisely; it is clearly less than 1 second (Figs. 1, 2, and 4), which is considerably less than the latency of several seconds required for the increase in heart rate elicited by excitation of afferent cardiac sympathetic fibers (4). We have attributed this relatively long delay to the time required for diffusion of the sympathetic transmitter to the sinoatrial node (4).

In the present experiments, we also showed that the same stimuli which reflexly inhibited cardiac vagal fibers excited cardiac sympathetic fibers. In earlier experiments there was less certainty concerning the destination of the fibers we studied (10, 14, 17), and it is noteworthy that the sympathetic units we studied electrophysiologically in these experiments were dissected from the cardiac nerve at its junction with the heart.

It is well known that reciprocal responses in cardiac vagal and sympathetic neurons are reflexly elicited from the sinoaortic baroreceptors. Stimulation of these receptors excites cardiac vagal neurons and inhibits cardiac sympathetic neurons. In the present experiments, a reciprocal effect was also strikingly demonstrated. However, in contradistinction to sinoaortic reflexes, the afferent cardiac sympathetic pathway reflexly inhibited cardiac vagal fibers and excited cardiac sympathetic fibers. These reciprocal responses should exert a synergistic excitatory effect on cardiac functions.

References

References
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