Interaction between Cardiac Receptors and Sinoaortic Baroreceptors in the Control of Efferent Cardiac Sympathetic Nerve Activity during Myocardial Ischemia in Dogs

Robert B. Felder and Marc D. Thames

SUMMARY The purpose of this study was to determine the relative influence of arterial baroreceptors and of cardiac receptors with vagal afferents on efferent cardiac sympathetic nerve activity during coronary artery occlusion. Changes in heart rate (beats/min), arterial pressure (mm Hg), and integrated cardiac sympathetic nerve activity (CSNA, percent change from control; recorded from the cut central end of the left ventral ansa subclavia) were determined during transient (90-second) circumflex (Cx) and anterior descending (LAD) coronary artery occlusions. In dogs with carotid and aortic baroreceptors intact, increases (mean ± SE) in CSNA during Cx (7 ± 2%) and LAD (9 ± 5%) occlusions were similar despite a significantly greater fall in arterial pressure during Cx (-14 ± 3 mm Hg) than during LAD (-5 ± 2 mm Hg) coronary artery occlusion. Heart rate did not change during these occlusions. In three dogs, hypotension induced by inferior vena caval occlusion resulted in greater increases in CSNA than did comparable decreases in arterial pressure resulting from occlusion of LAD or Cx. In dogs with sinoaortic denervation, Cx coronary occlusion resulted in decreases in CSNA (-14 ± 4%), arterial pressure (-38 ± 6 mm Hg), and heart rate (-13 ± 5 beats/min), whereas LAD occlusion resulted in a small decrease in arterial pressure (-12 ± 5 mm Hg) and no change in CSNA or heart rate. Vagotomy abolished the decreases in CSNA and heart rate and attenuated the arterial pressure responses to Cx occlusion. We conclude that cardiac receptors with vagal afferents exert an inhibitory influence on cardiac sympathetic nerve activity during myocardial ischemia, particularly during inferoposterior ischemia, and that this influence limits the arterial baroreceptor-mediated increases in CSNA resulting from ischemia-induced hypotension.

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Twenty-nine dogs weighing 18-33 kg were anesthetized with sodium thiopental (30 mg/kg iv) and \( \alpha \)-chloralose (80 mg/kg, iv). Maintenance doses of \( \alpha \)-chloralose (10 mg/kg) were administered hourly. The dogs were intubated and mechanically ventilated and increases in efferent parasympathetic nerve activity and reflex increases in efferent sympathetic nerve activity (Kendrick et al., 1972; Ninomiya et al., 1971). Activation of cardiac receptors with vagal afferents during myocardial ischemia causes central inhibition of efferent sympathetic nerve activity and increases in efferent parasympathetic nerve activity (Öberg and Thoren, 1973; Thoren et al., 1976; Thames et al., 1978b; Thames and Abboud, 1979). Activation of cardiac receptors with sympathetic afferents may cause reflex increases in efferent sympathetic nerve activity (Malliani et al., 1969; Uchida and Murao, 1974). Thus, the net reflex response to coronary occlusion will depend importantly on the central integration of these inputs.

Finally, the changes in sympathetic outflow to the heart or to specific peripheral vascular beds will be determined by the relative influence of each of these receptor groups on the sympathetic outflow to each bed (Abboud et al., 1976; Little et al., 1975). The available evidence indicates that the arterial baroreceptors and cardiopulmonary receptors with vagal afferents exert inhibitory influences of similar magnitude on the vasomotor outflow to the kidney, whereas the arterial baroreceptors dominate the cardiopulmonary receptors in the control of sympathetic outflow to skeletal muscle (Thoren et al., 1976; Thames and Abboud, 1979). The relative influence of these receptor groups on the sympathetic outflow to the heart remains unknown. The present study was performed to determine the extent to which each of these receptor groups contributes to the reflex changes in preganglionic cardiac sympathetic nerve activity during transient anterior and inferoposterior myocardial ischemia.

The results indicate that the increases in sympathetic outflow to the heart observed during myocardial ischemia depend primarily on hypotension-induced decreases in arterial baroreceptor discharge, and that these increases are significantly limited by augmented activity of inhibitory cardiac receptors with vagal afferents. The inhibitory influence of cardiac receptors with vagal afferents is greater during inferior ischemia than during anterior ischemia. In the dog with sinoaortic and vagal nerves sectioned, we were unable to demonstrate that cardiac receptors with sympathetic afferents had an excitatory influence on efferent cardiac sympathetic nerve activity during brief coronary occlusion.

**Methods**

Twenty-nine dogs weighing 18-33 kg were anesthetized with sodium thiopental (30 mg/kg iv) and \( \alpha \)-chloralose (80 mg/kg, iv). Maintenance doses of \( \alpha \)-chloralose (10 mg/kg) were administered hourly. The dogs were intubated and mechanically ventilated with room air supplemented by oxygen. Arterial blood gases were measured, and PCO\(_2\) and pH were corrected when necessary by adjustments of the tidal volume or administration of sodium bicarbonate, respectively. Body temperature was maintained by external warming. Muscular movement was eliminated with decamethonium bromide (0.3 mg/kg, iv) during the recording of nerve activity. Estimated volume losses resulting from surgery were replaced by 6% dextran in normal saline (5 ml/kg, iv) prior to initiating the protocol.

**Experimental Preparations**

A midline cervical incision was used to expose the vagi and carotid arteries bilaterally, and a tie was placed loosely around each of the vagal nerves for subsequent vagotomy. In six dogs, bilateral vagotomy was performed immediately after isolation of the vagi. In 17 dogs, the carotid sinuses were denervated bilaterally by sectioning all vessels and nerves between the internal and external carotid arteries and by stripping these vessels of all visible nerves. The adequacy of carotid sinus denervation was assessed by observing the response of blood pressure, heart rate, and efferent cardiac sympathetic nerve traffic to bilateral carotid occlusion and release.

In six of the dogs with carotid sinuses denervated, the aortic baroreceptors also were denervated. The aortic depressor nerve was located as it coursed between the sympathetic and vagal trunks just caudal to the nodose ganglion. The nerve was identified by recording its typical pattern of neural discharge and then cut (Edis and Shepherd, 1971). The completeness of sinoaortic denervation was determined by measuring the changes in heart rate and efferent sympathetic nerve activity during stepwise decreases in systemic arterial pressure produced by inferior vena cava occlusion. Measurements were obtained at steady state 10-30 seconds after each decrement in arterial pressure.

A thoracotomy was performed in the 5th left intercostal space. The pericardium was opened and its free edges sutured to the chest wall to form a cradle for the heart. The left anterior descending (LAD) and circumflex (Cx) coronary arteries were exposed 1-2 cm from their origins through small longitudinal incisions in the overlying connective tissue, with care being taken to avoid damaging the nerves coursing along these vessels. A snare was placed loosely around each vessel for subsequent coronary occlusion. A snare was placed around the inferior vena cava just caudal to the right atrium for subsequent stepwise reductions in blood pressure induced by caval occlusion.

**Nerve Recordings**

A thoracotomy was performed in the 2nd left intercostal space. The left ventral ansa subclavia was used to record preganglionic cardiac sympathetic nerve activity (Wechsler et al., 1969). With
the aid of a dissecting microscope, the overlying parietal pleura was removed and the nerve was dissected free from surrounding connective tissue. The nerve sheath was removed and the ansa was cut near its junction with the caudal cervical ganglion. Movement of the nerve resulting from respiration was minimized by placing the nerve on a cup-shaped dissecting stage which retained a mineral oil pool to prevent dehydration of the nerve. Nerve activity was recorded from the whole ansa or, in most experiments, from bundles of fibers obtained from the whole nerve. Nerve traffic was recorded on Ag/AgCl or platinum-iridium electrodes connected to a Grass probe (HIP511E) and amplified by a Grass (P511) band pass amplifier. The high frequency cutoff was set at 1000–3000 Hz and the low frequency cutoff at 30 Hz. The amplifier output was audible over a loudspeaker and visible on a Tektronix (D13) dual-beam storage oscilloscope. The output was led also into a nerve traffic analyzer unit which counted spike potentials exceeding a selected voltage. Each action potential that exceeded the voltage setting of the window discriminator was rectified and integrated. The rising phase of each action potential triggered the rectified signal. Thus, the quantification of the activity was independent of the amplitude of individual spikes. The counter was digital in design, and the relationship between integrator output and spike frequency was linear up to a frequency of 10 kHz. A counter of similar design has been employed previously in the quantitation of multunit carotid sinus baroreceptor activity (Thames et al., 1978a). The integrated nerve activity and hemodynamic measurements were recorded continuously on a Gould (2400) strip-chart recorder, and a representative original record is shown in Figure 1.

**Hemodynamic Measurements**

Arterial blood pressure was measured with a catheter in the right femoral artery connected to a Statham (P23dB) transducer. Mean arterial pressure was obtained by electrical averaging. The heart rate was monitored by a cardiometer triggered by the QRS complex from the surface electrocardiogram.

**Protocols**

After completion of the surgical preparation, adequate time was allowed for stabilization of heart rate, arterial pressure, and efferent cardiac sympathetic nerve activity. Measurements of these variables were obtained over a 60- to 120-second control period. The left anterior descending or circumflex coronary artery was then occluded for 90 seconds during which continuous measurements of the above variables were made. Five minutes after release of occlusion, the other coronary artery was occluded for 90 seconds. Bilateral vagotomy then was performed, and 30 minutes later, the sequence of short-lasting coronary occlusions was repeated.

The dogs studied were divided into four groups according to the presence or absence of the carotid and aortic baroreceptors and of the vagal nerves. Group I consisted of 12 dogs with carotid and aortic baroreceptors intact during the first set of occlusions. Before the second set of occlusions, the aortic baroreceptor fibers were sectioned with the vagi. Group II consisted of five dogs with carotid sinuses denervated; the aortic depressor nerves were intact during the initial occlusions but were sectioned with the vagi before the second set of occlusions. Group III consisted of six dogs with sinoaortic denervation, in which the potential influence of arterial baroreceptors on changes in efferent cardiac sympathetic nerve activity during coronary occlusion was eliminated. Occlusions were performed in these dogs before and after vagotomy. Group IV consisted of six dogs in which the carotid sinus and aortic depressor nerves and the vagi had been sectioned initially. Three hours later, two sets of coronary occlusions (separated by 20 minutes) were performed. In three of these experiments, the ventral ansa was left intact, and sympathetic activity was recorded from the ventrolateral cardiac nerve, which contains predominantly efferent fibers (Armour and Randall, 1975). Group IV was studied to determine (1) the reproducibility of the sympathetic responses to coronary occlusions, (2) the effects of time after vagotomy on the responses to ischemia (Weaver, 1977), and (3) the effects of sectioning the afferent fibers in the ventral ansa (Seagard et al., 1978) on efferent sympathetic responses to ischemia.

**Data Analysis**

Changes in efferent cardiac sympathetic nerve activity, blood pressure, and heart rate produced by acute coronary occlusions were measured. Control values for these variables were determined during the 60- to 120-second interval preceding each coro-
TABLE 1  Control Mean Arterial Pressure and Heart Rate Prior to Occlusion in Groups I-IV before and after Vagotomy

<table>
<thead>
<tr>
<th>Group</th>
<th>Before vagotomy</th>
<th>After vagotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Circumflex MAP (mm Hg)</td>
<td>Circumflex HR (beats/min)</td>
</tr>
<tr>
<td>Group I</td>
<td>127 ± 5</td>
<td>124 ± 4</td>
</tr>
<tr>
<td>Group II</td>
<td>109 ± 9</td>
<td>112 ± 8</td>
</tr>
<tr>
<td>Group III</td>
<td>136 ± 14</td>
<td>132 ± 12</td>
</tr>
<tr>
<td>Group IV*</td>
<td>136 ± 13</td>
<td>118 ± 15</td>
</tr>
</tbody>
</table>

Group I = Sinoaortic baroreceptors present; Group II = carotid baroreceptors denervated; Group III = Sinoaortic baroreceptors denervated; Group IV = Sinoaortic and vagal nerves sectioned; MAP = mean arterial pressure, HR = heart rate

There were no significant differences in control heart rates or blood pressures within or among the groups.

* HR data obtained in three of six group IV animals.

Results

Comparisons within Groups

Table 1 shows the control arterial pressures and heart rates for all groups. There were no significant differences in arterial pressure and heart rate within each group prior to occlusion of the circumflex or anterior descending coronary artery either before or after vagotomy. Control values for nerve activity are not shown, since they were dependent upon the number of fibers from which recordings were obtained and the setting of the window discriminator level.

Group I—Sinoaortic Baroreceptors Intact (n = 12)

The mean changes in efferent cardiac sympathetic nerve activity, arterial pressure, and heart rate in this group are shown in Figure 2. Before vagotomy, circumflex occlusion resulted in a significantly greater fall in blood pressure (−14 ± 3 mm Hg) than did left anterior descending occlusion (−5 ± 2 mm Hg). However, the increase in nerve activity was not different during occlusion of the two vessels (Cx = 7 ± 2% LAD = 9 ± 5%). After vagotomy, the increases in nerve activity (Cx = 12 ± 2% LAD = 16 ± 2%) and decreases in arterial pressure (Cx = −4 ± 2 mm Hg LAD = −4 ± 1 mm Hg) were not different for circumflex and anterior descending occlusions. However, the arterial pressure responses to circumflex occlusion before and after vagotomy were statistically different.

In three dogs with vagal nerves and sinoaortic baroreceptors intact, we compared the increases in
TABLE 2. Change in Mean Arterial Pressure and Percent Change in Efferent Cardiac Sympathetic Nerve Activity Resulting from Inferior Vena Caval and Coronary Artery Occlusions

<table>
<thead>
<tr>
<th>Experiment</th>
<th>8/22</th>
<th>8/25</th>
<th>8/29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occlusion</td>
<td>ΔMAP</td>
<td>%ΔCSNA</td>
<td>ΔMAP</td>
</tr>
<tr>
<td>Cx</td>
<td>-30</td>
<td>+17</td>
<td>-25</td>
</tr>
<tr>
<td>IVC</td>
<td>-30</td>
<td>+93</td>
<td>-24</td>
</tr>
<tr>
<td>LAD</td>
<td>-11</td>
<td>+36</td>
<td>-38</td>
</tr>
<tr>
<td>LAD</td>
<td>-12</td>
<td>+56</td>
<td>-41</td>
</tr>
</tbody>
</table>

ΔMAP = change in mean arterial pressure (mm Hg); %ΔCSNA = percent change in cardiac sympathetic nerve activity; IVC = inferior vena cava.

Efferent cardiac sympathetic nerve activity during coronary occlusion and during comparable levels of hypotension produced by inferior vena caval occlusions (Table 2). The increases in nerve activity accompanying decreases in blood pressure induced by caval occlusion exceeded those observed during either circumflex or anterior descending occlusion. As described below, sinoaortic baroreceptor denervation eliminated the increases in nerve activity in response to caval occlusion.

Small and insignificant changes in heart rate occurred both during circumflex and during anterior descending occlusion in dogs with vagi intact. After vagotomy, increases in heart rate were noted during occlusion of either vessel (Cx = 4 ± 1 beats/min; LAD = 5 ± 2 beats/min). These heart rate responses did not differ significantly from those observed prior to vagotomy.

Group II—Carotid Sinus Denervation (n = 5)

In these dogs with the carotid sinuses denervated but aortic nerves intact, there was no change in blood pressure or nerve activity during bilateral carotid artery occlusion and release. The mean data for this group are shown in Figure 3. With the vagi intact, occlusion of the anterior descending and circumflex arteries resulted in small and insignificant increases in nerve activity, although there were moderate decreases in arterial pressure during occlusion of each vessel. After vagotomy and section of the aortic nerves, sympathetic nerve activity increased during circumflex occlusion (14 ± 5%) but was unchanged during anterior descending occlusion (−3 ± 2%). These changes in nerve activity during circumflex and anterior descending occlusion in vagotomized dogs were significantly different (P < 0.05) in spite of a comparable drop in blood pressure (Cx = −14 ± 3 mm Hg; LAD = −17 ± 2 mm Hg).

With the vagi intact, heart rate decreased during circumflex occlusion (−4 ± 3 beats/min) but not during anterior descending occlusion. After vagotomy, no changes in heart rate occurred during occlusion of either vessel. There were no significant differences in the heart rate responses to circumflex or anterior descending occlusions before or after vagotomy.

Group III—Sinoaortic Denervation (n = 6)

The completeness of sinoaortic baroreceptor denervation was tested after section of the aortic nerves and the carotid sinus nerves in five of the six dogs. A decrease in arterial pressure of −59 ± 9 mm Hg (induced by caval occlusion) resulted in an insignificant increase in cardiac sympathetic nerve activity (6 ± 4%), thus indicating minimal persistent baroreceptor influence. This finding suggests that, under the conditions of our experiments, the cardiopulmonary vagal afferents exert no significant tonic inhibitory influence on sympathetic outflow to the heart.

The changes in arterial pressure, nerve activity, and heart rate in response to coronary occlusion are shown in Figure 4. Before vagotomy, there was a significantly greater fall in blood pressure during circumflex (−38 ± 6 mm Hg) than during anterior

![Figure 3](http://circres.ahajournals.org/)

**Figure 3** Changes (mean ± SEM) in preganglionic cardiac sympathetic nerve activity (ΔCSNA, percent), mean arterial pressure (ΔMAP, mm Hg), and heart rate (ΔHR, beats/min) during circumflex (open bars) and during anterior descending (filled bars) occlusion before and after vagotomy in group II dogs (n = 5). The carotid sinus nerves were sectioned prior to all occlusions and the aortic depressor nerves were sectioned with the vagi. Significant differences (P < 0.05) between means for circumflex vs. anterior descending occlusion (*) are so indicated.
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FIGURE 4 Changes (mean ± SEM) in preganglionic cardiac sympathetic nerve activity (ΔCSNA, percent), mean arterial pressure (ΔMAP, mm Hg), and heart rate (ΔHR, beats/min) during circumflex (open bars) and during anterior descending (filled bars) coronary occlusion before and after vagotomy in group III dogs (n = 6). The carotid sinus and aortic baroreceptors were denervated prior to all occlusions. Significant differences (P < 0.05) between means for circumflex vs. anterior descending occlusion (*) and for pre- vs. postvagotomy (•) are so indicated.

descending (−12 ± 5 mm Hg) occlusion. A decrease in nerve activity was observed during circumflex occlusion (−14 ± 4%) but not during left anterior descending occlusion. After vagotomy, both occlusions resulted in insignificant changes in nerve activity and moderate decreases in blood pressure (Cx = −26 ± 6 mm Hg; LAD = −20 ± 4 mm Hg) which did not differ statistically. The changes in nerve activity during circumflex occlusion before and after vagotomy were significantly different, but those during anterior descending occlusion were not.

With the vagi intact, circumflex occlusion resulted in a significantly greater decrease in heart rate (−13 ± 5 beats/min) than did anterior descending occlusion (−2 ± 3 beats/min). After vagotomy, neither circumflex nor anterior descending occlusion resulted in significant changes in heart rate.

Figure 5 shows the changes in nerve activity, arterial pressure, and heart rate for each 12-second period of circumflex and anterior descending occlusion in dogs with sinoaortic denervation. An augmented inhibitory influence on cardiac sympathetic nerve activity is evident during the first 12 seconds of circumflex occlusion and increases to a steady state by 48 seconds of occlusion. Decreases in heart rate and arterial pressure tended to parallel the decrease in nerve activity, although the arterial pressure was still decreasing at the time the occlusion was discontinued. During anterior descending occlusion, changes in nerve activity were small and inconsistent, and the modest decreases in arterial pressure and heart rate stabilized early after occlusion.

Group IV—Sinoaortic and Vagal Denervation (n = 6)

In these six experiments, the carotid sinus nerves, aortic depressor nerves, and vagi were sectioned 3–4 hours prior to coronary occlusion. In three experiments, nerve activity was recorded from the ventrolateral cardiac nerve instead of the ventral ansa subclavia. The results were not influenced by the efferent nerve chosen for recording, and we therefore pooled the data for the six experiments for statistical analysis. There was no significant change in nerve activity during the first or second occlusion of either vessel (Table 3). There were no differences in the responses of nerve activity or arterial pressure to circumflex or anterior descending occlusion.

Comparisons among Groups

The differences among groups I, II, and III were analyzed to determine the relative influence of the aortic and carotid sinus baroreceptors on changes in cardiac sympathetic nerve activity, arterial blood pressure, and heart rate during brief coronary occlusion.

FIGURE 5 Time course of changes (mean ± SEM) in preganglionic cardiac sympathetic nerve activity (ΔCSNA), mean arterial pressure (ΔMAP), and heart rate (ΔHR) during the first 84 seconds of circumflex (○) and anterior descending (●) coronary occlusion in anesthetized dogs (n = 6) with carotid sinus and aortic nerves sectioned, but with vagal nerves intact. Data are shown for each consecutive 12-second period of occlusion.
Acute coronary occlusion alters the frequency of efferent neural discharge in the left ventral ansa subclavia, which carries a major portion of the sympathetic innervation of the heart (Randall, 1977). The present study indicates that cardiac sympathetic activity increases in response to coronary occlusion. These increases in cardiac sympathetic activity during myocardial ischemia are mediated by the arterial baroreceptors. The cardiac receptors with vagal afferents significantly limit these increases, especially during inferior ischemia. After sinoaortic and vagal denervation, we were unable to demonstrate that cardiac receptors with sympathetic afferents exerted an excitatory influence on efferent cardiac sympathetic responses to ischemia.

The relative influence of the sinoaortic baroreceptors in mediating changes in cardiac sympathetic nerve activity during coronary occlusion is apparent in comparisons of the responses of dogs with intact vagi but with different degrees of baroreceptor innervation. During circumflex occlusion, dogs with both carotid sinus and aortic baroreceptors intact (group I, Fig. 2) had increases in cardiac sympathetic nerve activity associated with moderate decreases in blood pressure. Those dogs with aortic but not carotid sinus baroreceptors intact (group II, Fig. 3) exhibited no change in nerve activity and moderate decreases in arterial blood pressure during circumflex occlusion. Dogs with sinoaortic denervation (group III, Fig. 4) had large decreases in nerve activity, in arterial blood pressure, and in heart rate during circumflex occlusion. A similar trend can be seen in the responses of these groups to anterior descending occlusion. These responses show that increases in efferent cardiac sympathetic nerve activity during ischemia are dependent upon the influence of both the carotid sinus and the aortic baroreceptors.

The inhibitory influence of cardiac receptors with vagal afferents can be assessed by comparing the effects of anterior and posterior ischemia on efferent cardiac sympathetic nerve activity, blood pressure, and heart rate. In sinoaortic denervated dogs with
vagi intact (Fig. 4). The inhibitory influence of the vagal afferents was unopposed and circumflex coronary occlusion caused a large decrease in blood pressure, heart rate, and sympathetic nerve activity, whereas anterior descending occlusion did not change sympathetic nerve activity and resulted in moderate decreases in arterial pressure and no change in heart rate. In dogs with aortic and carotid sinus baroreceptors intact (Fig. 2), although there was a greater fall in blood pressure during circumflex than during anterior descending occlusion, similar increases in cardiac sympathetic nerve activity during anterior descending and circumflex occlusion were observed. The absence of the expected greater increase in nerve activity concomitant with the greater decrease in blood pressure during circumflex occlusion in these experiments is evidence for an inhibitory influence of cardiac receptors activated by inferoposterior ischemia.

Activation of inhibitory receptors during anterior as well as posterior ischemia was evident from the larger increases in sympathetic nerve activity during hypotension induced by inferior vena caval occlusion than during a comparable fall in blood pressure during occlusion of either vessel (Table 2). Although not shown in the figures, further evidence of inhibitory receptor influence during anterior ischemia was observed in three dogs with arterial baroreceptors intact, in which frank decreases in cardiac sympathetic nerve activity, heart rate, and arterial pressure occurred during anterior descending occlusion. Vagotomy abolished these inhibitory responses to myocardial ischemia. These results suggest that cardiac receptors with vagal afferents are activated during anterior as well as inferoposterior myocardial ischemia, limiting the increases in efferent cardiac sympathetic nerve activity mediated by carotid and aortic baroreceptors. The inhibitory influence of these receptors is generally more prominent during inferoposterior than anterior ischemia, as shown in the present study and as previously reported (Thames et al., 1978b; Thames and Abboud, 1979).

The time course of the changes in cardiac sympathetic nerve activity during circumflex coronary occlusion in dogs with sinoaortic denervation (Fig. 5) suggests that the discharge of the inhibitory cardiac receptors becomes augmented during the first few seconds of occlusion and approaches a maximum during the first 90 seconds of occlusion. This interpretation is supported by the study of Thorén (1976) who found that the discharge frequency of ventricular receptors with nonmedullated vagal afferents increased during the first 10-45 seconds of coronary occlusion and reached a maximum after about 1 minute of occlusion.

The independent influence of cardiac receptors with sympathetic afferents on efferent cardiac sympathetic nerve activity during myocardial ischemia was assessed in groups II, III, and IV after arterial baroreceptor and vagal afferent pathways had been sectioned. In general, these dogs showed small increases in nerve activity during inferior ischemia and no change or a decrease in activity during anterior ischemia. The only increase in efferent cardiac sympathetic nerve activity, which might be attributed to the influence of cardiac receptors with sympathetic afferents, was observed during circumflex occlusion in group II (Fig. 3). However, we did not repeat the occlusions in this group after sectioning the dorsal roots to establish that the changes were mediated by cardiac sympathetic afferents.

It has been suggested that the effects of cardiac receptors with sympathetic afferents might best be seen when time is allowed after vagotomy for their influence to develop (Weaver, 1977). In groups II and III, we allowed an interval of 30 minutes after vagotomy prior to performing coronary occlusions. In group IV, a period of 3-4 hours was interposed between vagotomy and carotid sinus denervation and coronary occlusion. We found no evidence that this delay between vagotomy and coronary occlusion augmented the responses of efferent cardiac sympathetic nerve activity to transient ischemia. Although our results suggest that, after section of the sinoaortic and vagal nerves, cardiac receptors with sympathetic afferents have a minimal influence on efferent cardiac sympathetic nerve activity during ischemia, it is possible that, under these conditions, baseline sympathetic nerve activity was near the maximum. This might have prevented us from observing further increases when cardiac sympathetic afferents were activated during coronary occlusion. Thus, although our data do not allow us to exclude a role for the cardiac sympathetic afferents, under the conditions of our study, an influence of these afferents was not apparent.

Previous studies in which efferent cardiac sympathetic nerve activity has been recorded during acute coronary occlusion have reported conflicting results (Costantin, 1963; Gillis, 1971; Malliani et al., 1969). All of these studies were on cats. Costantin (1963) recorded sympathetic nerve activity from the left inferior cardiac nerve during transient occlusion of the anterior descending or left main coronary artery. He noted hypotension and decreases in nerve activity in three of five cats and no change in the other two. These responses were enhanced by carotid sinus nerve section and abolished by vagotomy. Our results are in agreement with those of Costantin and support the view that, during coronary occlusion, cardiac receptors with vagal afferents may have a physiologically significant influence in limiting cardiac sympathetic outflow induced by hypotension and baroreceptor withdrawal. In contrast, Malliani et al. (1969) recorded single unit and multifiber activity from the left T3 gray ramus during transient coronary occlusion with arterial baroreceptors intact. They reported that during coronary occlusion there was usually an increase in nerve activity and that this response was present after vagotomy and spinal cord section.
at Cl. They concluded that a cardiac sympatho-sympathetic reflex mediated at the spinal cord level was present and accounted for increases in nerve activity during coronary occlusion. Although this interpretation may be valid for vagotomized cord-sectioned cats, the presence of functioning carotid baroreceptors makes a similar interpretation for most of their experiments somewhat tenuous, as is evident from the results of the present study. Moreover, Gillis (1971) recorded sympathetic nerve activity from a nerve just central to the right stellate ganglion after permanent occlusion of the left main coronary artery. He noted increases in nerve activity, usually accompanied by hypotension and bradycardia, in 13 of 16 cats with sinoaortic and vagal afferents intact. Gillis indicated that the mechanism for the increases in sympathetic nerve activity was not determined by his studies, but suggested that arterial baroreceptors and cardiac receptors with sympathetic afferents may have contributed to this response. Animals subjected to combined vagotomy and spinal cord section showed no change in nerve activity during coronary occlusion. This study provides limited insight into the interactions between the sinoaortic baroreceptors and inhibitory cardiac receptors in the control of cardiac sympathetic nerve activity, since the efferent limbs of the reflex arc of both these receptor groups (sinoaortic and cardiac) were interrupted. However, these results differ importantly from the study of Malliani et al., since no changes in nerve activity were observed during coronary occlusion after vagotomy and spinal cord section. Thus, Gillis's data did not suggest the presence of a cardiac sympatho-sympathetic reflex mediated at the cord level.

In spite of the conflicting results from the studies summarized above, there is general agreement that the sympathetic nerves play an important role in the pathogenesis of ventricular dysrythmias associated with myocardial ischemia. Our results indicate that inhibitory cardiac receptors with vagal afferents may serve a protective role by limiting increases in cardiac sympathetic nerve activity during myocardial ischemia.

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