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Competition between Sympathetic Vasoconstriction and Metabolic Vasodilation in the Canine Coronary Circulation

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SUMMARY The role of a-receptor constriction of coronary vessels in response to cardiac sympathetic activation was evaluated in closed-chest, chloralose-anesthetized dogs. Cardiac sympathetic activation was produced (1) directly by intracoronary norepinephrine infusion at several different rates and (2) reflexly by carotid sinus hypotension. The resulting changes in coronary blood flow and myocardial oxygen consumption were recorded before and after a-receptor blockade with dibozane (3.0 mg/kg, iv) or phenoxybenzamine (0.5 mg/kg, intracoronary). The changes in coronary blood flow were normalized to changes in myocardial metabolism by division of the oxygen delivery (coronary blood flow times arterial oxygen content) by the change in myocardial oxygen consumption per 100 g of myocardium. Before a-receptor blockade, either intracoronary norepinephrine infusion or reflex sympathetic activation from the carotid sinus resulted in an increase of only 0.85 ml/100 g min"1 in oxygen delivery for each increase of 1 ml/100 g min"1 in cardiac oxygen consumption. Under these circumstances, myocardial oxygen extraction increased and coronary venous oxygen content fell. After a-receptor blockade, either intracoronary norepinephrine infusion or a carotid sinus reflex resulted in an increase of 1.23 ml/100 g min"1 in oxygen delivery for each increase of 1 ml/100 g min"1 in cardiac oxygen consumption. Myocardial oxygen extraction and coronary venous oxygen content changed only slightly after a-receptor blockade. The greater coronary vasodilation and lesser change in cardiac oxygen extraction after a-receptor blockade were significantly different (P < 0.001) from the values before blockade. It is concluded that the coronary a-receptor constriction mechanism competes with metabolic vasodilation during sympathetic activation even when there are large increases in myocardial metabolism. The net effect of the a-receptor constrictor influence is to restrict the metabolically related flow increase by about 30%, thus increasing oxygen extraction and decreasing coronary venous oxygen content.

IT HAS LONG been known that stimulation of the sympathetic innervation of the heart results in tachycardia and augmented contractility, accompanied by increased myocardial oxygen consumption, increased coronary blood flow, and decreased coronary sinus oxygen content.14-16 Coronary sinus oxygen content decreases because coronary blood flow responses do not quite match alterations in myocardial oxygen metabolism. The imbalance may reflect the normal operation of the local metabolic control of coronary flow, or it may be due to a limiting effect of sympathetic coronary vasoconstriction on the extent of local metabolic vasodilation. The cardiac vessels have autonomic innervation, and the direct result of sympathetic activation is coronary vasoconstriction.6-8, 10-15 Sympathetic vasoconstriction is mediated through a-receptors.11, 12, 14, 16

A previous study in this laboratory demonstrated that sympathetic a-receptor coronary vasoconstriction is capable of competing with local metabolic control and lowering coronary sinus oxygen tension after adrenergic B-receptor blockade.17 In that study the positive inotropic and chron-
otropic effects of sympathetic stimulation were blunted by propranolol, so that there was little increase in myocardial oxygen consumption, and coronary α-receptor vasoconstriction was unmasked. Because of the β-receptor blockade, the previous study did not show whether the effects of sympathetic coronary vasoconstriction would be overwhelmed in the presence of the large increase in cardiac oxygen metabolism that normally results from sympathetic activation.

The objective of the present study was to determine whether sympathetic coronary α-receptor vasoconstriction is capable of modulating coronary blood flow and thus oxygen delivery to the heart in the absence of β-receptor blockade. A comparison of coronary blood flow normalized against myocardial oxygen consumption before and after α-receptor blockade indicated that a direct coronary vasoconstrictor effect significantly limits oxygen delivery to myocardium during sympathetic activation.

Methods

General Preparation

Twelve male closed-chest dogs weighing 21–30 kg were studied. Each dog was anesthetized with an initial injection of α-chloralose (100 mg/kg, iv) approximately 1 hour after sedation with morphine sulfate (2.5 mg/kg, sc) and a continuous infusion of additional α-chloralose (10 mg/kg per hour, iv) during the experiment. Each dog was atropinized (0.5 mg/kg, iv) following completion of surgery and cannula placement. Ventilation was with room air enriched with a mixture of 40% oxygen in nitrogen gas supplied from a positive-pressure pump (Harvard 601) operating with a 5-cm H₂O end-expiratory back pressure. Oxygen enrichment was adjusted by means of a variable demand valve so that arterial blood oxygen tension was kept between 125 and 150 mm Hg throughout the experiment. End-expiratory carbon dioxide was monitored continuously with an infrared absorption meter (Beckman LB-2) and held between 4.5% and 5% by adjustment of respiration rate and tidal volume. Blood coagulation in the extracorporeal circuits was prevented by infusion of sodium heparin (750 U/kg plus 250 U/kg per hour, iv), and the metabolic acidosis associated with chloralose anesthesia was counteracted by a continuous infusion of 150 mEq sodium bicarbonate (5 ml/kg per hour, iv). Rectal temperature was held at 37°C with a heating pad and temperature controller. (Yellow Springs 73A).

A schematic diagram of the experimental preparation appears in Figure 1. A Y cannula arrangement (not illustrated) was used to accept blood from the central left common carotid artery and direct it to both the cranial left and right common carotid arteries. This arrangement ensured perfusion of both carotid sinuses under control conditions and enabled simultaneous experimental reduction of both carotid sinus pressures.

Perfusion of Left Coronary Artery

Blood was supplied to the left coronary artery at constant pressure through the special cannula shown in Figure 1, a modification of the transducer described by Smith et al. The cannula was advanced through the right carotid artery into the ascending aorta, and a balloon near its tip was inflated. The cannula tip was then inserted into the left coronary artery ostium until the balloon sealed the lip of the ostium. Left coronary artery pressure at the cannula tip was measured through a small, stainless steel internal auxiliary tube. Blood was obtained from the left femoral artery and passed through a servo-controlled roller pump (modified Sarnes 3500), an extracorporeal electromagnetic flow transducer (Zepeda SWF-3RD), and an infusion site before entering the coronary cannula. The roller pump was connected in a servo loop to pump automatically at the rate necessary to maintain 90 mm Hg pressure at the tip of the cannula in the left coronary ostium.
experiment by adjustment of the servo-controlled perfusion pump to maintain mean left coronary artery pressure 25 mm Hg above mean aortic pressure and injection of approximately 1.5 ml of an intense blue dye (crystal violet in 1 N ammonia) into the perfusion cannula. Any leakage from the left coronary artery into the ascending aorta caused dye streaks in the aorta that were easily detected post-mortem. All dogs in which leakage occurred were excluded from the study. The dye also served to mark the area of the myocardium perfused during the experiment; this area was separated from the rest of the myocardium and weighed at the end of each experiment and was found to have an average weight of 81.3 ± 3.7% (st) of the total myocardial weight in the 12 dogs studied.

Oxygen Measurements

A Sones catheter (USCI no. 007538) was advanced into the coronary sinus via the right jugular vein and right atrium under fluoroscopy. Measurements of the exact placement of the catheter tip post-mortem ranged from 31 to 44 mm into the coronary sinus in the 12 dogs studied. Blood was withdrawn continuously from the coronary sinus catheter at a rate of 12 ml/min with a roller pump (Cole-Parmer 4420). This combination of withdrawal rate and cannula tip placement was chosen to prevent contamination of the coronary sinus sample with blood from the right atrium. Coronary sinus blood passed a spectrophotometric oximeter cuvette (Waters 0-500), the withdrawal pump, a sampling site, and an oxygen tension cuvette before returning to the left jugular vein. Provision was made for either coronary sinus blood or arterial blood to be drawn through the oxygen-measuring and -sampling circuit.

Blood samples were taken for generating the oximeter calibration curve and establishing the current hemoglobin concentration. Each sample was analyzed for oxygen content (Lexington Instruments Lex-O2-Con) and for hemoglobin content by the cyanmethemoglobin method. The oxygen-carrying capacity of each blood sample was calculated by multiplying the measured hemoglobin content by 1.34 ml O2/g Hb.

Experimental Protocol

The responses to a series of intracoronary norepinephrine infusions and carotid artery occlusions were recorded before and after α-receptor blockade with either dibozane or phenoxybenzamine. Each experimental maneuver lasted from 1 to 3 minutes and was terminated when left coronary artery flow and coronary sinus oxygen saturation reached steady values.

In the dibozane experiments (four dogs), intracoronary norepinephrine (10 μg/ml saline) was administered with a syringe pump at infusion rates of 1.0, 1.5, 2.0, 3.1, 4.1, and 6.2 μg/min. Alpha-receptor blockade was effected by the intravenous infusion of dibozane (3 mg/kg, iv).

In the phenoxybenzamine experiments (eight dogs), both vagus nerves were cut in the neck. Intracoronary norepinephrine was administered at infusion rates of 1.7, 3.4, and 6.8 μg/min, and the reflex effects of two levels of carotid sinus hypotension were recorded. Alpha-receptor blockade was effected by a slow intracoronary infusion (0.74 ml/min) of phenoxybenzamine (0.5 mg/ml saline) in an attempt to maximize coronary blockade and minimize peripheral blockade. The total dose of phenoxybenzamine was 0.5 mg/kg.

Data Analysis

Data were analyzed from two time points associated with each norepinephrine infusion or carotid occlusion response. Control values were read from the period immediately before each experimental maneuver. Final response values were read during the steady period near the end of each norepinephrine infusion or carotid occlusion. Changes in myocardial oxygen delivery (flow) were plotted against changes in myocardial oxygen consumption. For quantitative analysis it was useful to characterize individual responses by a single dimensionless measure, the response slope, defined as the change in oxygen delivery divided by the change in oxygen consumption. This procedure has the effect of normalizing coronary flow responses against metabolic changes, so that discrepancies between oxygen supply and demand of the myocardium are readily apparent.

All reported standard error values are measures of variability between dogs and were derived from data sets containing one value from each dog studied. When multiple determinations for the value of a particular variable were made within a single experiment, the average of these represented that dog in the overall data analysis. The statistical significance of differences observed for a variable before and after α-receptor blockade was evaluated with a two-tailed, paired t-test (df = n - 1, for n animals).

Results

The responses to intracoronary norepinephrine infusion before and after α-receptor blockade are shown in Figure 2. Norepinephrine infusion increased left coronary artery flow and decreased coronary sinus hemoglobin-oxygen saturation. Note that the norepinephrine infusion before α-receptor blockade produced a lesser rise in coronary flow and a greater fall in coronary sinus oxygen saturation than the norepinephrine infusion following α-receptor blockade. The slight flow overshoot at the offset of infusion before α-blockade was observed in all 12 dogs studied. Flow overshoot was not observed following α-receptor blockade. In these experiments, changes in coronary artery flow indicate changes in coronary artery vascular conductance, since coronary perfusion pressure was held at 90 mm Hg by the servo system regardless of changes in aortic pressure.

The reflex responses to carotid artery occlusion before and after α-receptor blockade are shown in Figure 3. Carotid artery occlusion increased coronary flow, decreased coronary sinus oxygen saturation, and increased aortic pressure both before and after α-receptor blockade. As with norepinephrine infusion, the carotid occlusion before α-receptor blockade produced a lesser increase in flow and a greater decrease in coronary sinus oxygen saturation than did the carotid occlusion following α-receptor blockade.
INTRACORONARY NOREPINEPHRINE CONTROL AFTER PHENOXYBENZAMINE

CORONARY FLOW (mL/min)

200-

100-

0

SINUS OXYGEN SATURATION (%)

NE INFUSION

30 sec

NE INFUSION

HEART RATE (beats/min)

200-

100-

0

Figure 2 Myocardial responses to intracoronary norepinephrine infusion before and after α-receptor blockade with phenoxybenzamine (0.5 mg/kg, intracoronary). Norepinephrine infusion (NE) caused a lesser increase in coronary blood flow and a greater decrease in coronary sinus hemoglobin oxygen saturation before α-receptor blockade than after blockade. Changes in coronary flow are due to changes in coronary vascular conductance, since coronary perfusion pressure was servo controlled at 90 mm Hg. Atropine, administered at the onset of the experiment, was responsible for the high heart rate. The norepinephrine infusion rate was 6.8 μg/min in each case, and 148 g of myocardium were perfused. Figures 2-4 present data from the same dog.

Figure 4 illustrates, for a single experiment, how α-receptor blockade affected the relationship between changes in coronary flow (expressed as arterial oxygen delivery) and changes in myocardial oxygen consumption induced by intracoronary norepinephrine infusion and carotid artery occlusion. An arrow in Figure 4 represents the response to a single norepinephrine infusion or carotid occlusion. The tail of each arrow indicates the control values of oxygen delivery and oxygen consumption before norepinephrine infusion or carotid occlusion, whereas the head indicates the steady values during the experimental maneuver. Norepinephrine infusion and carotid occlusion increased oxygen consumption and oxygen delivery in all instances. However, the differences between the slopes of the arrows before and after α-receptor blockade indicate an altered relationship between oxygen consumption and delivery. Coronary blood flow (oxygen delivery) increased less in relation to oxygen consumption before α-receptor blockade than after blockade. Before α-receptor blockade, increased oxygen consumption was accompanied by increased oxygen extraction; however, following blockade, oxygen extraction remained nearly constant (at about 70%) even during substantial increases in oxygen consumption. As a consequence of increased extraction,
coronary sinus oxygen levels fell to low values when oxygen consumption was increased before α-receptor blockade.

Figure 5 shows the change in oxygen delivery accompanying the change in oxygen consumption for all the trials with norepinephrine infusion and carotid occlusion in this study. Each point represents one norepinephrine infusion or carotid occlusion, and closed and open symbols represent trials before and after α-receptor blockade, respectively. The magnitude of the change in oxygen consumption was purposely modulated in this study by variation of the rate of norepinephrine infusion or the degree of lowering carotid sinus pressure. The changes in oxygen consumption shown in Figure 5 represent increases over the control oxygen consumption (Table 1), ranging from a few percent to more than 100%. For a particular set of experimental conditions, the response slope was quite independent of the magnitude of the change in oxygen consumption. It is evident from Figure 5 that the change in oxygen delivery associated with a given change in oxygen consumption (the response slope) was consistently less before α-receptor blockade than after blockade. For the same norepinephrine-induced change in oxygen consumption, the oxygen delivery increased 39% more after dibozane (P < 0.001) and 46% more after phenoxybenzamine (P < 0.001). For equal carotid sinus reflex-induced changes in myocardial oxygen consumption, oxygen delivery increased 51% more after coronary α-receptor blockade with phenoxybenzamine (P < 0.001). No statistically significant differences in response slope were detected between norepinephrine infusions before dibozane, norepinephrine infusions before phenoxybenzamine, or carotid occlusions before phenoxybenzamine. Neither were there statistically significant differences between the response slopes for norepinephrine infusions after dibozane, norepinephrine infusions after phenoxybenzamine, or carotid occlusions after phenoxybenzamine.

Systolic blood pressure and heart rate are factors that influence the systolic compression of myocardial vessels and, thus, coronary blood flow. Since changes in heart rate and systolic blood pressure were not identical before and after α-receptor blockade, we evaluated the possible roles of these factors by plotting them against changes in myocardial oxygen consumption (the normalizing variable used in this study) produced by intracoronary norepinephrine infusion or carotid occlusion before and after α-

#### Table 1: Effect of α-Receptor Blockade on Control Values

<table>
<thead>
<tr>
<th></th>
<th>Intracoronary phenoxybenzamine blockade (n = 8)</th>
<th>Intravenous dibozane blockade (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Left coronary flow</td>
<td>87.7 ± 10.4</td>
<td>80.9 ± 9.5</td>
</tr>
<tr>
<td>(ml/100 g/min⁻¹)</td>
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<tr>
<td>Oxygen delivery</td>
<td>18.4 ± 1.9</td>
<td>17.2 ± 1.9</td>
</tr>
<tr>
<td>(ml/100 g/min⁻¹)</td>
<td></td>
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</tr>
<tr>
<td>Oxygen consumption</td>
<td>13.7 ± 1.1</td>
<td>12.6 ± 1.3</td>
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<tr>
<td>(ml/100 g/min⁻¹)</td>
<td></td>
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</tr>
<tr>
<td>Oxygen extraction (%)</td>
<td>75.9 ± 3.6</td>
<td>73.9 ± 2.8</td>
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<tr>
<td>Coronary sinus Po₂ (mm Hg)</td>
<td>17.2 ± 1.1</td>
<td>18.1 ± 1.0</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>196 ± 7</td>
<td>188 ± 13</td>
</tr>
<tr>
<td>Mean aortic pressure (mm Hg)</td>
<td>120 ± 3</td>
<td>108 ± 4</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SEM.
Heart rate and aortic pressure responses before and after alpha-blockade

Figure 6 Changes in heart rate (upper panel) and systolic aortic blood pressure (lower panel) in relation to changes in myocardial oxygen consumption produced by intracoronary norepinephrine infusion and carotid occlusion before (solid symbols) and after (open symbols) alpha-receptor blockade. Alpha-receptor blockade had no consistent or statistically detectable effect on the magnitude of the change in heart rate or systolic blood pressure that accompanied a given change in myocardial oxygen consumption. (In contrast, note the extremely consistent effect of alpha-receptor blockade on the relationship between oxygen delivery and oxygen consumption shown in Figure 5.)

Figure 7 Summary of the effect of alpha-receptor blockade on myocardial responses to intracoronary norepinephrine infusion and carotid occlusion for all dogs of this study. Crossed brackets at left indicate mean ± SE. (n = 12) of the control values of oxygen consumption, oxygen delivery, and oxygen extraction before (solid) and after (broken) alpha-receptor blockade. These control values were not significantly altered by alpha-receptor blockade. The shaded areas show the direction of change (mean response slope ± 1 SE, n = 12) produced by norepinephrine infusion or carotid occlusion. Before alpha-receptor blockade, a sympathetic coronary alpha-constrictor influence limited, by about 30%, the increase in oxygen delivery accompanying an increase in oxygen consumption; thus, oxygen extraction increased rapidly with augmented oxygen consumption.

Discussion

The data indicate that coronary vessels are simultaneously subjected to an alpha-receptor constrictor influence and a metabolic vasodilator influence during either intracorono-
nary norepinephrine infusion or a carotid sinus reflex. Net vasodilation results, but it is not of sufficient magnitude to increase coronary blood flow in proportion to increased myocardial metabolism. A functionally significant competition between local metabolic and sympathetic control of the coronary circulation is indicated, since changes in coronary flow did not keep pace with changes in myocardial oxygen consumption before α-receptor blockade. The α-receptor constrictor influence causes myocardial oxygen extraction to increase and coronary venous blood oxygen content to fall by limiting the increase in oxygen delivery associated with a given increase in myocardial oxygen consumption.

The results may be conveniently discussed in relation to the major factors that determine coronary blood flow: (1) coronary perfusion pressure, (2) systolic myocardial extravascular compression of coronary vessels, (3) local metabolic control, and (4) neural control.

**Perfusion Pressure**

Coronary artery pressure was held constant at 90 mm Hg with a servo-controlled pump before and after α-receptor blockade. Therefore, it is unlikely that the observed effects of α-receptor blockade were the result of an altered coronary perfusion pressure.

**Systolic Compression**

With each cardiac contraction, the myocardium compresses the coronary vessels and impedes flow. The impediment to flow offered by compressive forces in the heart is related to systolic blood pressure and heart rate. The possibility that a greater influence from systolic compressive forces before α-receptor blockade than after blockade might account for the results of this study was evaluated by an examination of systolic blood pressure and heart rate responses. As seen in Figure 6, there is much scatter and overlap between the changes in heart rate or systolic pressure before and after α-receptor blockade. The disorder in Figure 6 should be contrasted with the distinct separation of oxygen delivery data before and after α-receptor blockade shown in Figure 5. It is unlikely that the consistent effect of α-receptor blockade on oxygen delivery shown in Figure 5 is a secondary result of the factors related to systolic myocardial compression shown in Figure 6.

**Metabolic Control**

Coronary blood flow is strongly linked to myocardial metabolism through local metabolic control of the coronary vessels. The importance of direct coronary α constriction during sympathetic activation was evaluated in this study from its influence on the relationship between coronary flow and myocardial metabolism. The data obtained after α-receptor blockade and presented in Figures 5 and 7 illustrate the intrinsic local metabolic control of the coronary circulation without an α-receptor vasoconstrictor influence. The consistency with which increases in oxygen consumption were linearly matched by increased oxygen delivery (augmented flow) after α-receptor blockade is noteworthy and can be appreciated from the slight scatter of the open points in Figure 5 and the small standard errors for α-receptor-blocked conditions in Figures 5 and 7.

The most likely interpretation of these results is that direct α-receptor vasoconstriction of coronary vessels counteracted roughly 30% of the dilation expected from local metabolic mechanisms. This estimate of the relative potency of the α-receptor constrictor mechanism rests on the assumption that the strength of the metabolic vasodilator influence on coronary vessels is related to the rate of myocardial oxygen consumption. An implication of this assumption is that a hypothetical line in Figure 7 would represent a line of equal local metabolic vasodilator influence upon coronary arteries.

Another possibility is that the strength of the metabolic vasodilator influence depends somehow upon the balance between oxygen consumption and oxygen delivery. Thus the strength of the local vasodilator influence might be more closely related to oxygen extraction than to oxygen consumption. The implication would be that a hypothetical line in the lower panel of Figure 7 would represent a line of equal local metabolic vasodilator influence upon coronary vessels. From the average response slope values presented in Figure 7, it may be calculated that oxygen delivery increased 0.6 ml/100 g min⁻¹ for each 1% increase in oxygen extraction before α-receptor blockade, whereas it increased 3.0 ml/100 g min⁻¹ for the same increase in oxygen extraction after α-receptor blockade. By this alternative analysis, the α-receptor constrictor mechanism prevented 80% of the dilation expected of the local metabolic vasodilator system.

The differences observed before and after α-receptor blockade are not likely to have been due to a difference in metabolic status before and after the blockade. The control oxygen consumption and oxygen extraction values were not significantly different before and after α-receptor blockade for all 12 dogs, as shown in Figure 7.

The relative importance of neural vs. metabolic control of the coronary circulation might be biased in this type of experiment by overperfusion of the coronary circulation. That is, if coronary blood flow were artificially high or myocardial oxygen consumption unusually low, metabolic control would be blunted and autonomic effects enhanced. This was not the case, as shown in Table 1. Control coronary blood flow was about 80 ml/100 g min⁻¹ for myocardial oxygen consumptions of about 12 ml/100 g min⁻¹, which resulted in oxygen extractions of over 70% and coronary venous oxygen tensions of about 17 mm Hg.

**Neural Control**

Parasympathetic effects were prevented by atropine and vagotomy in these experiments. Coronary vessels do exhibit primary β-receptor vasodilation, but it is unlikely that this mechanism played a role in these experiments. Intra coronary isoproterenol infusion produces primary β-receptor coronary vasodilation but norepinephrine does not, and sympathetic stimulation results in a feeble β-receptor vasodilation, which can only be observed after α-receptor blockade. In any case, activation of coro-
nary $\beta$-receptors would have been a factor both before and after $\alpha$-receptor blockade.

Sympathetic $\alpha$-receptor coronary vasoconstriction is well recognized and has been demonstrated in numerous laboratories. $^{6,8,14-16}$ When $\beta$-receptor blockade is used to blunt changes in myocardial metabolism, sympathetic activation produces coronary vasoconstriction and decreased coronary venous oxygen levels. $^{6,8,17-19}$ The coronary vasoconstriction and depressed venous oxygen tension due to sympathetic nerve stimulation observed in a $\beta$-receptor blocked preparation are prevented by $\alpha$-receptor blockade. $^{20}$ In the absence of $\beta$-receptor blockade, electrical stimulation of the stellate ganglion has been reported to produce a lesser coronary vasodilatation than that resulting when coronary sinus oxygen levels are reduced to similar levels by systemic hypoxia. $^{7}$

The present results with intracoronary norepinephrine infusion are very similar to those obtained by Imai et al., $^{28}$ with catecholamine infusions in an isolated, supported heart-lung preparation. Oxygen extraction and coronary venous oxygen tension were not reported by Imai et al., but myocardial oxygen consumption was low (3 ml/100 g min$^{-1}$) in their preparation.

Reflex sympathetic $\alpha$-receptor coronary vasoconstriction in response to carotid sinus hypotension has been reported previously in $\beta$-receptor-blocked preparations. $^{29,30}$ Electrical stimulation of the carotid sinus nerve, which mimics increased carotid sinus pressure, produces inhibition of coronary sympathetic constrictor tone. $^{31,32}$ In the present experiments a restriction of flow and oxygen delivery was observed before $\alpha$-receptor blockade but not afterwards; the most probable interpretation of these results is that an $\alpha$-receptor vasoconstrictor mechanism limits coronary blood flow during reflex sympathetic activation from the carotid sinus baroreceptors.

In conclusion, this study indicates that a coronary $\alpha$-receptor constrictor mechanism is important even when competing with the metabolic vasodilator influence of large increases in myocardial metabolism produced by intracoronary norepinephrine or carotid sinus reflex sympathetic activation. The net effect of the $\alpha$-receptor constrictor influence is to restrict the metabolically related increase in coronary flow by about 30%, thus increasing oxygen extraction and decreasing coronary venous oxygen content.

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