Integrated Carotid Chemoreceptor and Pulmonary Inflation Reflex Control of Peripheral Vasoactivity in Conscious Dogs

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SUMMARY The interaction of carotid chemoreceptor and pulmonary inflation reflex control of vascular responses in the mesenteric, renal, and iliac beds was examined in conscious dogs by comparing responses to chemoreceptor stimulation (intracarotid injection of nicotine or cyanide) during spontaneous and controlled respiration. A biphasic response was evoked which was characterized by an initial bradycardia, an increase in mean arterial pressure, and a marked increase in resistance in the iliac (102 ± 17% [mean ± se]) as compared with the mesenteric (16 ± 3%) and renal (9 ± 2%) beds. After the chemoreceptor-induced increases in ventilation, there was a later phase characterized by tachycardia, a decrease in mean arterial pressure, and a striking decrease in resistance in the iliac (−51 ± 2%) as compared with the mesenteric (−4 ± 4%) and renal (−11 ± 3%) beds. Alpha-blockade with phentolamine nearly abolished the early vasoconstriction and later vasodilation. When the chemoreceptor induced increase in respiration was prevented, or after bilateral vagotomy, there was significantly more (P < 0.01) vasoconstriction in all three beds and no later vasodilation. After mechanical hyperinflation of the lungs, a striking decrease in resistance was observed in the iliac (−56 ± 3%) as compared with the mesenteric (−17 ± 5%) and renal (−6 ± 5%) beds; these responses were not observed after alpha blockade or after vagotomy. Responses to carotid chemoreceptor stimulation were not observed after carotid sinus nerve section. Thus, carotid chemoreceptor stimulation in conscious dogs with spontaneous respiration results in a biphasic vascular response. Pulmonary inflation reflexes attenuate the initial vasoconstrictor response to carotid chemoreceptor stimulation and are responsible for the later period of vasodilation.

STIMULATION of the carotid chemoreceptor reflex evokes bradycardia1–5 and increases arterial pressure and regional vascular resistance 6–9 accompanied by an increase in respiratory drive. The latter induces reflex effects through stimulation of pulmonary or thoracic stretch receptors10–20 which modulate the direct effects of chemoreceptor reflex activation and must be considered as part of the integrated response in the intact conscious animal. Although the integrated response has been shown to differ in terms of the effects of these reflexes on the coronary circulation in conscious and anesthetized dogs,20 the extent to which these important reflexes interact in the control of regional vascular resistances in the intact, conscious animal remains speculative.

The primary goal of this study was to examine the peripheral vascular responses to carotid chemoreceptor stimulation in the conscious dog. To separate direct chemoreceptor effects from those modulated by pulmonary inflation reflexes, the influences of the latter were eliminated by examining responses to intracarotid nicotine or cyanide with controlled ventilation on the one hand, and with spontaneous ventilation but after vagal afferents had been sectioned, on the other. In addition, to simulate the effects of the chemoreceptor-induced hyper-ventilation, the responses to mechanically induced pulmonary hyperinflation also were examined. To examine afferent mechanisms, responses were examined before and after carotid sinus nerve section and vagotomy. To examine efferent mechanisms, responses were examined before and after administration of alpha and beta adrenergic, cholinergic, and histaminergic blocking agents.

Methods

Fourteen mongrel dogs (20–32 kg) were studied in the conscious state. Through a midline laparotomy, using pentobarbital sodium (30 mg/kg, iv) anesthesia, Doppler ultrasonic or electromagnetic flow transducers (Zepeda Instruments) were placed around superior mesenteric (10 dogs), left renal (12 dogs), and left iliac (14 dogs) arteries. Heparin-filled Tygon catheters were chronically implanted in the aorta to measure arterial pressure (14 dogs), and in one of the main carotid arteries with the tip just proximal to the carotid sinus, ensuring that the carotid arteries remained patent. Hydraulic cuff occluders also were implanted bilaterally on the carotid arteries (5 dogs) and distal to all implanted electromagnetic flow transducers on the peripheral arteries.

Arterial pressure was measured with the previously implanted heparin-filled Tygon catheter and a Statham
Regional blood flow was measured with either an ultrasonic Doppler flowmeter system or an electromagnetic flowmeter system (Benton Instruments). The ultrasonic Doppler flowmeter system, which has been described in detail previously, has a reliable zero reference and, in these experiments, zero blood flow was determined repeatedly and was confirmed by calibration when the animal was killed. The relationship between flow velocity, measured by the Doppler flowmeter, and volume flow is linear as long as the cross-sectional area of the blood vessel within the transducer remains constant. This linear relationship was confirmed by means of timed collections of blood flow. At autopsy, it was observed that the vessels were firmly adherent to the flow transducers through a fibrous scar, which minimized changes in the cross-sectional area of the blood vessel within the flow transducers. The electromagnetic flowmeter system also was used for peripheral flow measurements, in particular in the iliac and mesenteric arteries, since reverse flow may occur in those beds. When the electromagnetic flowmeter was used, zero flow was determined by inflating a previously implanted hydraulic occlusive cuff.

The experiments were conducted 2–4 weeks postoperatively when the dogs had recovered from surgery and were again vigorous and healthy. Records of regional blood flows, arterial pressure, heart rate, and respiratory movement, monitored by a pneumograph, were obtained continuously while the unsedated dogs were resting quietly in the control state as well as during all interventions.

Chemoreceptor stimulation was accomplished by injection of nicotine (0.2 μg/kg) or sodium cyanide (2.0 μg/kg) into the intracarotid catheter. Dogs were also studied in the conscious state after (1) beta receptor blockade with propranolol (1.0 mg/kg), (2) cholinergic blockade with atropine (0.1 mg/kg), (3) histaminergic blockade with tripeleminamine (2 mg/kg), and (4) alpha receptor blockade with phentolamine (1 mg/kg). Blockade was induced with single agents, as well as in the sequence described. The adequacy of beta receptor blockade was tested with atropine (0.1 mg/kg), (3) histaminergic blockade with tripelennamine (2 mg/kg) and (4) alpha receptor blockade with phentolamine (1 mg/kg). Blockade was induced with single agents, as well as in the sequence described. The adequacy of beta receptor blockade was tested with atropine (0.1 mg/kg), (3) histaminergic blockade with tripelennamine (2 mg/kg), and (4) alpha receptor blockade with phentolamine (1 mg/kg). Blockade was induced with single agents, as well as in the sequence described.
Effects of Chemoreceptor Stimulation

Intact Conscious Dogs with Spontaneous Respiration

Systemic Effects

The early phase was characterized by a 17 ± 4% reduction in heart rate (control = 85 ± 4 beats/min); an increase in mean arterial pressure of 10 ± 2% (control = 98 ± 4 mm Hg), and an increase in depth and rate of respiration. The late phase was characterized by a 26 ± 6% increase in heart rate and a decrease in mean arterial pressure of 9 ± 3% below the control level. All these changes were significant, P < 0.01. During the ventilatory response, arterial blood gases did not change significantly from control levels for oxygen tension (PO₂) of 85 ± 3 mm Hg, carbon dioxide tension (PCO₂) of 30 ± 1.0 mm Hg, and pH of 7.40 ± 0.02.

Regional Flows and Resistances (Table I)

Mesenteric bed (N = 10): During the early phase, flow fell by 6 ± 2% (P < 0.05, control = 262 ± 22 ml/min) and resistance increased by 16 ± 3%. During the late phase, flow still was decreased by 6 ± 2% (P < 0.05) but resistance no longer was different from control.

FIGURE 1  Effects of carotid chemoreceptor stimulation with nicotine in a conscious dog on mean arterial pressure, phasic and mean renal, mesenteric, and iliac blood flows, and respiration as monitored with a pneumatic cuff. During spontaneous respiration (left panel), chemoreceptor stimulation elicited an initial bradycardia and reduction in iliac flow with an increase in depth and rate and respiration. Following the respiratory changes, there was tachycardia and a striking increase in iliac flow. There were only minor changes in flow in the renal and mesenteric beds. During controlled respiration (right panel), chemoreceptor stimulation elicited a greater increase in mean arterial pressure, bradycardia, and marked reductions in flow in all beds, but the tachycardia and later increase in iliac flow were not observed.
Renal bed \((n = 12)\): During both phases, flow did not change significantly. However, during the early phase, resistance increased by 9 ± 2% and in the late phase fell in 11 of 12 dogs; the average for all dogs was a decrease of 11 ± 3%.

Iliac bed \((n = 14)\): During the early phase, flow decreased by 39 ± 4% (control = 130 ± 10 ml/min) while resistance rose by 102 ± 17%. During the late phase, flow increased by 90 ± 8% and resistance decreased by 51 ± 2%. These changes were significant \((P < 0.01)\).

Both the early vasoconstriction and late vasodilation occurring in the iliac bed in response to carotid chemoreceptor stimulation with nicotine or cyanide were significantly greater \((P < 0.01)\) than the changes occurring in the mesenteric and renal beds. Moreover, the early vasoconstriction in the mesenteric bed was greater than that observed in the renal bed \((P < 0.01)\).

**Intact Conscious Dogs with Controlled Respiration \((n = 11)\)**

**Systemic Effects**

During the early phase there was a decrease in heart rate of 27 ± 4% \((control = 89 ± 9 beats/min)\) and an increase in mean arterial pressure of 49 ± 8% \((control = 108 ± 4 \text{ mm Hg})\). However, in contrast to the dogs with spontaneous respiration, there was no late tachycardia and arterial pressure remained elevated by 24 ± 7%. All these responses were significant \((P < 0.01)\) and were different \((P < 0.01)\) than those observed with spontaneous respiration.

**Regional Flows and Resistances (Table I)**

**Mesenteric bed \((n = 8)\):** During the early phase, flow decreased by 46 ± 8% \((P < 0.01)\), control = 163 ± 25 ml/min) and resistance increased 187 ± 33%. During the late phase, resistance remained elevated by 57 ± 11%. In contrast to dogs with spontaneous respiration, the initial vasoconstriction was significantly more intense and resistance remained elevated during the late phase.

**Renal bed \((n = 8)\):** During the early phase, flow did not decrease significantly but resistance increased by 46 ± 15%, a significantly more intense vasoconstrictor response than observed in dogs with spontaneous respiration. During the late phase, resistance did not decrease, in contrast to what was observed in animals with spontaneous respiration.

**Iliac bed \((n = 11)\):** During the early phase, flow decreased by 60 ± 5% \((P < 0.01)\), control = 140 ± 21 ml/min) and resistance increased by 334 ± 47%. During the late phase, flow returned to the control value and resistance remained elevated by 56 ± 17%. These changes were significantly different from those observed during spontaneous respiration.

Thus, in contrast to dogs with spontaneous respiration, when the influence of the pulmonary inflation reflexes was eliminated, carotid body chemoreceptor stimulation induced an intense early vasoconstriction in all three beds and the late phase, involving a decrease in vascular resistance, was not observed. Moreover, the most striking vasoconstriction with chemoreceptor stimulation was observed in the iliac bed, and the least potent vasoconstriction was observed in the renal bed.

**Bilateral Cervical Vagotomy \((n = 7)\)**

**Systemic Effects**

Following carotid chemoreceptor stimulation, heart rate remained constant at 162 ± 7 beats/min during the early and late phases of the response. During the early

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**Table 1. Effects of Carotid Chemoreceptor Stimulation on Regional Resistances**

<table>
<thead>
<tr>
<th></th>
<th>Mesenteric</th>
<th></th>
<th>Renal</th>
<th></th>
<th>Iliac</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (\text{mm Hg/ml per min})</td>
<td>Early %</td>
<td>Late %</td>
<td>Early %</td>
<td>Late %</td>
<td>Early %</td>
</tr>
<tr>
<td><strong>Spontaneous respiration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No block</td>
<td>0.45</td>
<td>±0.06</td>
<td>±3.4</td>
<td>0.67</td>
<td>±0.06</td>
<td>±2.3</td>
</tr>
<tr>
<td>SEM</td>
<td>±0.06</td>
<td>±4.0</td>
<td>±4.0</td>
<td>±0.08</td>
<td>±3.9</td>
<td>±3.5</td>
</tr>
<tr>
<td>B block</td>
<td>0.48</td>
<td>±0.06</td>
<td>±4.9</td>
<td>0.67</td>
<td>12.0*</td>
<td>±16.8*</td>
</tr>
<tr>
<td>SEM</td>
<td>±0.08</td>
<td>±4.3</td>
<td>±3.9</td>
<td>±0.11</td>
<td>±17.7</td>
<td>±3.4</td>
</tr>
<tr>
<td>B and C block</td>
<td>0.53</td>
<td>±0.07</td>
<td>±6.1</td>
<td>±0.13</td>
<td>±6.3</td>
<td>±4.4</td>
</tr>
<tr>
<td>SEM</td>
<td>±0.06</td>
<td>±4.9</td>
<td>±6.3</td>
<td>±0.10</td>
<td>±9.8</td>
<td>±5.5</td>
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<tr>
<td>B, C and H block</td>
<td>0.90</td>
<td>±0.10</td>
<td>±6.5</td>
<td>1.09</td>
<td>6.3</td>
<td>−9.3</td>
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<tr>
<td>SEM</td>
<td>±0.13</td>
<td>±5.6</td>
<td>±5.5</td>
<td>1.99</td>
<td>63.2*</td>
<td>−52.3*</td>
</tr>
<tr>
<td>B, C, H, and A block</td>
<td>0.55</td>
<td>±0.08</td>
<td>±6.1</td>
<td>±0.07</td>
<td>±1.3</td>
<td>±0.10</td>
</tr>
<tr>
<td>SEM</td>
<td>±0.13</td>
<td>±5.4</td>
<td>±5.5</td>
<td>±0.15</td>
<td>±3.2</td>
<td>±3.6</td>
</tr>
</tbody>
</table>

|                  | Control \(\text{mm Hg/ml per min}\) | Early \%| Late \%  | Early \%| Late \%  | Early \%|
| **Controlled respiration** |            |         |          |          |          |         |
| No block         | 0.82       | ±0.14  | ±3.3     | 0.79    | ±0.10   | ±14.9   |
| SEM              | ±0.10      | ±11.1  | ±8.1     | ±0.10   | ±47.4   | ±16.7   |

\(B = \text{beta; C = cholinergic; H = histaminergic; A = alpha.}\)

* Response significantly different from control \((P < 0.05)\).

† Response significantly different from control \((P < 0.01)\).

§ Response significantly different from spontaneous respiration, unblocked state \((P < 0.05)\).

\(|\text{REFLEX CONTROL OF REGIONAL BEDS/Rutherford and Vatner}\)
phase, mean arterial pressure increased 35 ± 7% \( (P < 0.01, \text{control} = 117 \pm 12 \text{ mm Hg}) \), and during the late phase, which closely followed an increase in ventilation, remained elevated by 27 ± 8% \( (P < 0.05) \). These responses were significantly greater \( (P < 0.01) \) than prior to vagotomy.

**Regional Flows and Resistances**

- **Mesenteric bed \( (n = 5) \):** During the early phase, flow fell, but not significantly \( (\text{control} = 261 \pm 23 \text{ ml/min}) \), and resistance rose by 184 ± 80\% \( (P < 0.05, \text{control} = 0.44 \pm 0.06 \text{ mm Hg/ml per min}) \). During the late phase, flow and resistance were not significantly different from control. The early increases in resistance were significantly greater \( (P < 0.05) \) than in intact dogs with spontaneous respiration.

- **Renal bed \( (n = 6) \):** Flow did not change significantly during the early or late phase. However, during the early phase, resistance rose by 66 ± 26% and in the late phase remained elevated by 32 ± 8% \( (P < 0.05, \text{control} = 0.83 \pm 0.20 \text{ mm Hg/ml per min}) \). These increases in resistance were significantly greater \( (P < 0.01) \) than in intact dogs with spontaneous respiration.

- **Iliac bed \( (n = 7) \):** During the early phase, flow fell by 48 ± 5% \( (P < 0.01, \text{control} = 93 \pm 11 \text{ ml/min}) \) and resistance increased by 205 ± 55%. During the late phase, flow and resistance were not significantly different from control, but the early increases in resistance were significantly greater than in intact dogs with spontaneous respiration (Fig. 2).

**Carotid Sinus Nerve Section \( (n = 3) \)**

After carotid sinus nerve section, intracarotid nicotine and cyanide did not change ventilation, heart rate, mean arterial pressure or regional resistances indicating that in the intact dog these agents were acting solely as peripheral carotid chemoreceptor stimulants rather than exerting a direct effect on peripheral vessels or on central nervous system receptors.

**Efferent Blockades, Conscious Dogs, Spontaneous Respiration (Table 1)**

- **Beta Receptor Blockade \( (n = 12) \)**

  Beta receptor blockade with propranolol did not affect responses of heart rate, regional flows, and regional resistances to carotid chemoreceptor stimulation.

- **Beta Receptor and Cholinergic Blockade \( (n = 11) \)**

  The control heart rate was 149 ± 8 beats/min, and following carotid body chemoreceptor stimulation there was no early decrease or later increase in rate. Changes in regional flows and resistances after carotid chemoreceptor stimulation were not significantly different from the unblocked state.

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**RESPONSE OF ILIAC BED TO CAROTID CHEMORECEPTOR STIMULATION**

![Figure 2](http://circres.ahajournals.org/)

**Figure 2** Effects of carotid chemoreceptor stimulation are compared on iliac resistance in intact conscious dogs with spontaneous respiration (open bars), after bilateral vagotomy with spontaneous ventilation (cross-hatched bars), and in intact dogs with controlled respiration (solid bars). The early response is shown on the left and the late response on the right. Significant responses are denoted by the symbols, while control values (in mm Hg/ml per min) prior to stimulation are shown at the base of the bars. With spontaneous respiration there was an initial increase in iliac resistance and later, following the increase in depth and rate of respiration evoked by chemoreceptor stimulation, there was a marked decrease in resistance. When the effects of pulmonary inflation reflexes were eliminated either by controlling respiration or by sectioning vagal afferents, there was not only a significantly greater early increase in iliac resistance, but also the later phase of iliac vasodilation was abolished.
Resistance substantially (−40 ± 4%), but this decrease was mechanical hyperinflation of the lungs still decreased iliac (P < 0.01, control = 98 ± 5 mm Hg) and heart rate increased 15 ± 4% (P < 0.01, control = 80 ± 8 beats/min). During succinylcholine infusion, carotid occlusion increased mean arterial pressure by 29 ± 3% (P < 0.01) and heart rate by 14 ± 4% (P < 0.05) from similar control values. These changes were not significantly different.

**Discussion**

Carotid chemoreceptor stimulation induces direct chemoreceptor reflex effects, which include an increase in the depth and rate of respiration. This in turn evokes secondary reflex effects from pulmonary inflation reflexes. Accordingly, both of these reflexes may have played a role in response to carotid body chemoreceptor stimulation in the conscious dog, since a biphasic response of regional resistances and heart rate was observed. The early phase was characterized by bradycardia and peripheral vasoconstriction, and the late phase occurred immediately after the chemoreceptor reflex mediated ventilatory changes and was characterized by tachycardia and peripheral vasodilation. It appeared that the early phase was due primarily to the chemoreceptor reflex, and that late phase may have been due to pulmonary inflation reflexes.

If this hypothesis were correct, then the late phase of tachycardia and vasodilation should be eliminated by either preventing the changes in respiration or sectioning pulmonary inflation afferents, which travel primarily in the vagus. Indeed these interventions both intensified the early chemoreceptor-mediated peripheral vasoconstriction and abolished the late period of vasodilation (Fig. 2). Carotid chemoreceptor stimulation in dogs with ventilation controlled during succinylcholine infusion failed to elicit an increase in ventilation, whereas carotid chemoreceptor stimulation after vagotomy in dogs with spontaneous respiration still elicited an increase in ventilation, but no longer elicited peripheral dilation, since the primary afferent limb of the pulmonary inflation reflex had been eliminated. Finally, if this reflex could be attributed to stimulation of pulmonary or thoracic stretch receptors, then simple hyperinflation of the lungs should evoke peripheral vasodilation. Indeed this is what was observed (Fig. 3).

In the conscious dog with spontaneous respiration, chemoreceptor reflex-mediated peripheral vasoconstriction was most intense in the limb. Prior studies on this topic have been controversial. Bernthal and Schwindt found similar amounts of constriction occurring in the intestine and limb, but did not examine the renal bed.
Little and Öberg found less renal constriction than in the intestinal and limb beds. The opposite response, i.e., most intense renal vasoconstriction, was reported by Parker et al. Daly and Scott observed constriction in muscle and skin but not in intestine, but the renal bed was not examined.

In this study, when ventilation was controlled the early chemoreceptor-induced increases in resistance were more

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Effects of Mechanical Hyperinflation on Iliac Resistance</th>
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<tr>
<td></td>
<td>Control (mm Hg/ml per min)</td>
</tr>
<tr>
<td>No block</td>
<td>1.80 ± 0.29</td>
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<tr>
<td>Beta (B) block</td>
<td>1.90 ± 0.29</td>
</tr>
<tr>
<td>B and cholinergic (C) block</td>
<td>1.10 ± 0.13</td>
</tr>
<tr>
<td>B, C, and histaminergic (H) block</td>
<td>1.48 ± 0.37</td>
</tr>
<tr>
<td>B, C, H, and alpha block</td>
<td>0.96 ± 0.15</td>
</tr>
<tr>
<td>Vagotomy</td>
<td>1.19 ± 0.19</td>
</tr>
</tbody>
</table>

* Response significantly different from control (P < 0.01).
† Response significantly different from unblocked state (P < 0.01).
intense, but still showed a differential pattern of response with the most striking constriction in the iliac bed and the least constriction in the kidney. Sustained vasoconstriction occurred in the limb and gut, but not in the kidney, further suggesting that the renal bed was less sensitive to chemoreceptor stimulation than the other two beds. However, it could be that local autoregulatory mechanisms were most powerful in the kidney and whereby more effectively opposed the neural vasoconstrictor action.

It was conceivable that succinylcholine infusion could have altered autonomic tone and been responsible for the greater peripheral vasoconstriction observed with chemoreceptor stimulation. To test this hypothesis, another stimulus to neurally mediated sympathetic vasoconstriction, i.e., bilateral carotid occlusion, was examined. Bilateral carotid occlusion elicited similar increases in arterial pressure in the presence and absence of succinylcholine, in contrast to chemoreceptor stimulation which induced significantly greater pressor responses in the presence of succinylcholine. Accordingly, the augmented pressor effect was attributed to the absence of ventilatory reflexes, rather than to an effect of the drug, succinylcholine.

It is likely that the vasoconstriction and bradycardia observed after injection of nicotine or cyanide into the carotid artery was due to activation of the chemoreceptor reflex. Jacobs et al. have demonstrated convincingly that these drugs stimulate carotid body chemoreceptor rather than carotid sinus baroreceptor afferents. Moreover, if carotid baroreceptor afferents had been stimulated, then reflex dilation rather than constriction would have occurred, and ventilation would not have increased strikingly. It was demonstrated that the drugs did not stimulate receptors in the central nervous system, by observing no systemic effects upon reinjection of intracarotid nicotine or cyanide after section of the ipsilateral carotid sinus nerve.

Both the late period of vasodilation following carotid chemoreceptor stimulation and the vasodilation following mechanical hyperinflation of the lungs were characterized by a differential pattern of response, with the most intense vasodilation occurring in the limb. Daly and Robinson also observed that the reflex vasodilation arising from lung inflation in the dog was most intense in the limb. While most other studies did not examine the effects of this reflex on the various peripheral beds, studies in this field have demonstrated intense reflex limb dilation in response to lung inflation. It is important to mention that mechanical hyperinflation of the lungs decreases venous return, cardiac output, and, consequently, arterial pressure. The fall in arterial pressure should have elicited baroreceptor-mediated iliac vasoconstriction, which may have led to some underestimation of the potency of the lung inflation reflex.

The efferent mechanism for the initial chemoreceptor reflex-induced bradycardia and later pulmonary inflation reflex-induced tachycardia involved activation and withdrawal of vagal tone, respectively, as observed by others. Moreover, initial iliac vasoconstriction and later vasodilation were due primarily to alpha adrenergic mechanisms; this also is consistent with results of prior studies by Daly et al. A small component of the reflex vasodilation following mechanical hyperinflation may have been due to cholinergic activation, since the response was slightly, but significantly, attenuated by atropine. However, the major fraction of the vasodilation was blocked by phentolamine, indicating it was due to release of alpha adrenergic sympathetic tone. It is important to point out that the reflex limb vasodilation did not appear to be mediated by histamine. Moreover, the later period of vasodilation was different from the vasodilation in the paw observed by Calvelo et al. since, in that study, dilation was not affected by alpha adrenergic receptor blockade.

In conclusion, carotid chemoreceptor stimulation in conscious dogs with spontaneous respiration results in a biphasic vascular response. Initially there is bradycardia and more marked alpha adrenergic vasoconstriction in the iliac as compared with the mesenteric and renal beds. Later following the carotid chemoreceptor-evoked increase in ventilation, there is tachycardia and marked withdrawal of alpha adrenergic constrictor tone in the iliac, as compared with the mesenteric and renal beds. Thus, in the conscious animal, pulmonary inflation reflexes are sufficiently powerful to attenuate the initial vasoconstrictor response to carotid chemoreceptor stimulation and to reverse the constriction to a later period of intense vasodilation.

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References

11. Daly M de B, Hazzledine JL: The effects of artificially induced hyperventilation on the primary cardiac reflex response to stimulation of the carotid bodies in the dog. J Physiol (Lond) 168: 672-688, 1963
18. Paintal AS: Vagal sensory receptors and their reflex effects. Physiol Rev 53: 159-227, 1973
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