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

JOHN D. RUTHERFORD AND STEPHEN F. VATNER

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 (−3 ± 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 4−9 accompanied by an increase in respiratory drive. The latter induces reflex effects through stimulation of pulmonary or thoracic stretch receptors10−26 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,26 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 hyperventilation, 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. 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 tripelemamine (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 isoproterenol (1 μg/kg, iv), that of cholinergic blockade with acetylcholine (40 μg/kg, iv), that of histaminergic blockade with histamine (0.5 μg/kg, iv), and that of alpha receptor blockade with norepinephrine (1 μg/kg, iv).

To examine the effects of chemoreceptor stimulation in the absence of changes in ventilation and secondary reflex effects of pulmonary inflation, 11 dogs were studied during succinylcholine infusion (2 mg/kg per min) with ventilation controlled. Since these dogs were not anesthetized, care was taken not to perform any intervention or experiment that was not tolerated by the conscious dogs in the absence of succinylcholine, as has been done previously in conscious rabbits and dogs. It is important to mention that this agent is used frequently in veterinary practice in conscious primates, horses, goats, deer, and swine. Tachycardia, a prominent feature of the canine response to discomfort, was not observed in the present study. The dogs were intubated after the larynx had been sprayed with a topical anesthetic (Cetacaine; Cetylite Industries). Ventilation was controlled by a respirator as is done routinely in conscious patients. Intracarotid administration of nicotine or cyanide was repeated before and after autonomic blockades in the dogs with their ventilation controlled during succinylcholine infusion; these interventions all were tolerated well and evoked no evident discomfort in the conscious dogs when their breathing was spontaneous.

The increase in depth of respiration that occurred following intracarotid injection of nicotine or cyanide in the conscious dog with spontaneous respiration was simulated in eight dogs whose respiration was controlled during succinylcholine infusion. This was done by briefly increasing the rate of the Harvard respirator and obstructing the expiratory valve to produce pulmonary hyperinflation similar in volume to that observed in dogs with spontaneous respiration. The effects of intracarotid administration of nicotine and cyanide as well as mechanical pulmonary hyperinflation were examined 12–24 hours after carotid sinus nerve section in three dogs and 6–24 hours after bilateral vagotomy in five dogs. Both of these latter procedures were performed under general anesthesia with a short acting barbiturate, sodium thiopental (10 mg/kg, iv).

To determine whether succinylcholine infusion affected all reflex effects due to an action of the drug on the autonomic nervous system, in five dogs the effects of 60-second bilateral carotid occlusion were compared in the presence and absence of succinylcholine infusion.

During the experiments involving chemoreceptor stimulation and hyperinflation, arterial samples from the aortic catheter were collected in a heparinized glass syringe, and arterial blood gases were measured with a Radiometer acid-base analyzer (PHM 71 Mk 2) and blood microsystem (BMS 3 Mk 2) (Radiometer).

The data were recorded on a multichannel tape recorder and played back on a direct-writing oscillograph. Electronic resistance-capacitance filters with 2-second time constants were used to derive mean arterial blood pressure and mean regional blood flows. Mean regional vascular resistances were calculated as the quotients of mean arterial pressure and regional blood flows. The results were compared by the group t- or paired t-test. Average values ± SEM are reported throughout.

Results

Intracarotid administration of nicotine or cyanide in the intact conscious dog elicited a biphasic cardiovascular response (Fig. 1). The first phase (termed the early phase) was characterized by bradycardia, an increase in regional resistances, and an increase in depth and rate of respiration. The second phase (termed the late phase) closely followed the respiratory changes and was characterized by tachycardia and a decrease in regional resistances. The peak of the early phase occurred 6.5 ± 0.4 seconds after injection of nicotine or cyanide, and the peak of the late phase occurred 12.3 ± 0.9 seconds later. All changes discussed in the Results are statistically significant. If the precise confidence level is noted in the figures or tables, it is not repeated in the Results. Responses of all dogs were in the same direction unless specifically noted otherwise.
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 (\( P_{O_2} \)) of 85 ± 3 mm Hg, carbon dioxide tension (\( P_{CO_2} \)) 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% \( (P < 0.05, \text{control} = 262 \pm 22 \text{ ml/min}) \) 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.
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 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
phase, mean arterial pressure increased 35 ± 7% (P < 0.01, control = 117 ± 12 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 (control = 261 ± 23 ml/min), and resistance rose by 184 ± 80% (P < 0.05, control = 0.44 ± 0.06 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, control = 0.83 ± 0.20 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, control = 93 ± 11 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.
Changes in regional flows and resistances following carotid body chemoreceptor stimulation were not significantly different from those observed in the unblocked state, although the control values were significantly higher in each of the beds \( (p < 0.01) \) than in the unblocked state.

**Beta Receptor, Cholinergic, Histaminergic Blockade \( (n = 7) \)**

In marked contrast to the experiments conducted in the absence of \( \alpha \)-receptor blockade, the early and late responses of the iliac bed to carotid body chemoreceptor stimulation were significantly reduced and indeed almost abolished by the addition of alpha receptor blockade. In three dogs studied on a separate day, alpha blockade alone induced a similar abolition of the early constrictor and late dilator response to carotid chemoreceptor stimulation.

**Effects of Mechanical Hyperinflation**

**Intact Conscious Dogs \( (n = 8) \)**

**Systemic Effects**

Heart rate increased by 20 ± 5% \( (\text{control} = 73 ± 9 \text{ beats/min}) \) and mean arterial pressure decreased by 9 ± 3% \( (\text{control} = 113 ± 6 \text{ mm Hg}) \). These changes were significant \( (p < 0.01) \). During mechanical hyperinflation, arterial blood gases did not change significantly from control values for oxygen tension \( (\text{PO}_2) \) of 100 ± 3 mm Hg, carbon dioxide tension \( (\text{PCO}_2) \) of 26 ± 3 mm Hg, and pH of 7.42 ± 0.02.

**Regional Flows and Resistances**

Following mechanical hyperinflation of the lungs, there were no significant changes in renal flow or resistance \( (\text{control} = 1.77 ± 0.12 \text{ mm Hg/ml per min}) \). Mesenteric flow remained unchanged but resistance decreased by 17 ± 5% \( (p < 0.05, \text{control} = 0.72 ± 0.13 \text{ mm Hg/ml per min}) \). In the iliac bed, however, flow increased 118 ± 25% \( (p < 0.01, \text{control} = 74 ± 11 \text{ ml/min}) \) and resistance decreased by 56 ± 3% \( (p < 0.01) \) (Fig. 3).

Thus, mechanical pulmonary hyperinflation results in a substantial decrease in iliac resistance which is significantly greater than the change in resistance in the mesenteric or renal beds \( (p < 0.01) \).

**Bilateral Cervical Vagotomy \( (n = 5) \)**

Following bilateral cervical vagotomy, there was no iliac vasodilation during mechanical hyperinflation of the lungs (Table 2).

**Efferent Blockades \( (n = 6) \) (Table 2)**

Following \( \beta \)-adrenergic blockade, increases in iliac flow and decreases in iliac resistance were observed with mechanical hyperinflation. Cholinergic blockade reduced iliac resistance \( (p < 0.05) \). After cholinergic blockade, mechanical hyperinflation of the lungs still decreased iliac resistance substantially \( (−40 ± 4\%) \), but this decrease was slightly less \( (p < 0.01) \) than in animals without autonomic blockades. Addition of histaminergic blockade did not modify the response further. However, after addition of alpha adrenergic receptor blockade, hyperinflation no longer induced iliac vasodilation.

**The Effects of Carotid Occlusion in the Conscious Dog \( (n = 5) \)**

During a 60-second bilateral carotid occlusion in conscious dogs with spontaneous respiration, mean arterial pressure increased by 30 ± 5% \( (p < 0.01, \text{control} = 98 ± 5 \text{ mm Hg}) \) and heart rate increased 15 ± 4% \( (p < 0.01, \text{control} = 80 ± 8 \text{ beats/min}) \). 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,\(^a\) which include an increase in the depth and rate of respiration. This in turn evokes secondary reflex effects from pulmonary inflation reflexes.\(^a\) 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.\(^a\)

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.\(^b\) 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 succinylcholine infusion 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 Schwind\(^c\) found similar amounts of constriction occurring in the intestine and limb, but did not examine the renal bed.

---

\(^a\) Refers to previous studies on this topic.

\(^b\) Refers to specific interventions tested in the study.

\(^c\) Refers to another study by the same authors.
Little and Öberg\(^2\) 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.\(^5\) 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 2**  
**Effects of Mechanical Hyperinflation on Iliac Resistance**

<table>
<thead>
<tr>
<th></th>
<th>Control (mm Hg/ml per min)</th>
<th>% Change from control</th>
</tr>
</thead>
<tbody>
<tr>
<td>No block</td>
<td>1.80 ± 0.29</td>
<td>-56 ± 3.3*</td>
</tr>
<tr>
<td>Beta (B) block</td>
<td>1.90 ± 0.29</td>
<td>-49.9 ± 9.0*</td>
</tr>
<tr>
<td>B and cholinergic (C) block</td>
<td>1.10 ± 0.13</td>
<td>-40.0 ± 4.1*†</td>
</tr>
<tr>
<td>B, C, and histaminergic (H) block</td>
<td>1.48 ± 0.37</td>
<td>-41.9 ± 4.7*</td>
</tr>
<tr>
<td>B, C, H, and alpha block</td>
<td>0.96 ± 0.15</td>
<td>-6.7 ± 4.0†</td>
</tr>
<tr>
<td>Vagotomy</td>
<td>1.19 ± 0.19</td>
<td>-10.1 ± 6.8†</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 thereby 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 most 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.

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.

Acknowledgments

The technical assistance of P. Quinn and W. Thomas Menders and the help in preparation of the manuscript by E. Tenenholtz and C. Conran are appreciated, as well as the generous supplies of phentolamine from Ciba Pharmaceutical Co. and propranolol from Ayerst Labs.

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: 873-899, 1963
18. Paintal AS: Vagal sensory receptors and their reflex effects. Physiol Rev 53: 159-227, 1973
Integrated carotid chemoreceptor and pulmonary inflation reflex control of peripheral vasoactivity in conscious dogs.
J D Rutherford and S F Vatner

Circ Res. 1978;43:200-208
doi: 10.1161/01.RES.43.2.200

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/43/2/200.citation