Changes in muscle and renal vascular resistances when the traffic in aortic or vagal nerves was interrupted were compared during normocapnia and hypercapnia in rabbits. The rabbits were anesthetized with sodium pentobarbital, paralyzed, and artificially ventilated; the sinus nerves were cut. A hind limb and a kidney were perfused at constant flow with autologous blood. With the vagi cut or cooled, blocking the aortic nerves by cooling caused a 49% and a 28% increase in limb and kidney perfusion pressures, respectively, during normocapnia (end-tidal CO$_2$ 3–4%) and a 56% and a 69% increase during hypercapnia (end-tidal CO$_2$ 8–10%). With the aortic nerves cut or cooled, vagal cold block increased the limb and kidney perfusion pressures 10% and 15%, respectively, during normocapnia and 17% and 61%, respectively, during hypercapnia. These responses were attenuated, especially in the kidney, when one of these pairs of nerves was intact (aortic nerve or vagus) and the other pair was blocked. Thus, hypercapnia augmented the vasodepressor reflexes from the aortic arch and the cardiopulmonary area. The effects of this phenomenon were greater on the renal vascular bed than they were on the muscle vascular bed.

KEY WORDS  
carbon dioxide  
mechanoreceptors  
cardiopulmonary reflexes  
renal circulation  
muscle circulation

Stimulation of the pulmonary stretch receptors in the rabbit results in decreased sympathetic traffic to the kidney and muscle resistance vessels and vasodilatation. This reflex response is potentiated by hypercapnia, and the potentiation is greater in the renal vascular bed than it is in the muscle vascular bed (1). Since no systematic studies of the influence of CO$_2$ on the high-pressure baroreflexes are available, we analyzed the effect of hypercapnia on the aortic arch baroreflex and compared it with the effect on the reflexes subserved by vagal afferents.

Methods

The methods used in these experiments have been previously described in detail (2).

Albino rabbits (3.0–4.6 kg) were anesthetized with sodium pentobarbital (40 mg/kg, iv); anesthesia was maintained by additional hourly doses of about 6 mg/kg. In each rabbit the carotid sinuses were denervated, and in some rabbits the aortic nerves or the vagi were cut.

The vagi and the aortic depressor nerves were dissected free for about 3 cm caudal to the larynx.

Thermodes were applied to the nerves and perfused with iced saline to block nerve conduction. The block was reversed by perfusion with water at 30–40°C. The surface temperature of the thermodes was monitored by thermocouples, and cold block was assumed to be complete when a temperature of 2–5°C was attained. At the end of each experiment, cold block was again instituted, and the nerves were severed caudal to the thermodes. Since no further change in the measured hemodynamic variables occurred with nerve section, the cold block was assumed to be effective.

The rabbits were paralyzed with gallamine triethiodide and were ventilated artificially; the intratracheal pressure was measured with a strain-gauge transducer. The respiration was adjusted to 30 cycles/min and a tidal volume of 15 ml/kg. End-expiratory CO$_2$ was continuously measured with an infrared gas analyzer (Beckman Spinco). End-tidal CO$_2$ was changed by adjusting the partial pressure of CO$_2$ in the inspired gas. Several times in every experiment, arterial Po$_2$, pH, and Pco$_2$ were determined, and the arterial Pco$_2$ was compared with the end-tidal CO$_2$ concentration.

In these experiments, normocapnia corresponds to an end-tidal CO$_2$ of 3–4% (3) and hypercapnia corresponds to an end-tidal CO$_2$ of 8–10%.

Aortic blood pressure was measured by a catheter inserted into the right femoral artery and connected to a strain-gauge transducer.

To study changes in vascular resistance in the limbs, one hind limb was perfused at constant flow with autologous blood via a roller pump, and the perfusion pressure was measured. A tourniquet was used to exclude the paw circulation. To study changes in vascular resistance in the kidney, the left renal artery was cannulated and perfused at constant flow with autologous blood, and the perfusion pressure was measured.
Effect of Hypercapnia on Vascular Response to Nerve Block

In 11 rabbits, the effect of vagal block was studied with aortic nerves intact. The increase in renal perfusion pressure was about three times greater (Table 1). In 6 of these 11 rabbits the aortic nerves were blocked prior to the vagal block and in 13 other rabbits the aortic nerves were cut. In these 13 rabbits, aortic nerve block during normocapnia caused increases in renal perfusion pressure and limb perfusion pressure similar to those seen with the vagi intact, but the increase in renal perfusion pressure was greater than twice as great. Augmenting the end-tidal CO₂ prior to the block caused only small increases in aortic blood pressure and limb perfusion pressure, but the renal perfusion pressure increased by 23 mm Hg. With aortic nerve block, the increases in blood pressure and limb perfusion pressure were of similar magnitude to the increases during normocapnia but the renal response was three times greater (Fig. 1 and Table 1).

Vagal Nerve Block.—In 11 rabbits, the effect of vagal block was studied with aortic nerves intact. During normocapnia, the block caused a slight increase in aortic blood pressure and smaller, equal increases in limb and kidney perfusion pressures. Increasing the end-tidal CO₂ prior to the block caused only small increases in aortic blood pressure and in limb and kidney perfusion pressures; with vagal block, the increase in aortic blood pressure and in limb perfusion pressure was the same as it was during normocapnia, but the increase in kidney perfusion pressure was 5 times greater (Table 1). In 6 of these 11 rabbits the aortic nerves were blocked prior to the vagal block and in 13 other rabbits the aortic nerves were cut. In these 13 rabbits, aortic nerve block during normocapnia caused increases in blood pressure and limb perfusion pressure similar to those seen with the vagi intact, but the increase in renal perfusion pressure was more than twice as great.
Effect of hypercapnia (end-tidal CO₂ 8.0%) on circulatory changes caused by aortic nerve cold block in a rabbit with its sinus nerves and vagi cut. Top: Temperature of thermodes. Bottom: Aortic blood pressure, kidney (K) and hind-limb (HL) perfusion pressures, and right atrial pressure.

Vagal and Aortic Nerve Block.—In six rabbits the aortic baroreflex was studied during normocapnia and hypercapnia with the vagi intact and with the vagi blocked, and the vagal reflex was studied with the aortic nerves intact and blocked. A record from these experiments is shown in Figure 3. The results of these different procedures are summarized in Figure 4 and Tables 2 and 3. In these paired experiments the potentiation of aortic nerve block by exclusion of the vagi was determined. During normocapnia the increases in limb and kidney perfusion pressures were of equal magnitude, but during hypercapnia the increase in kidney pressure was more than three times that in the limb. The

Effect of hypercapnia on circulatory changes caused by vagal cold block in a rabbit with its sinus and aortic nerves cut. Top: Temperature of thermodes and intratracheal pressure. Bottom: Aortic blood pressure, kidney and limb perfusion pressures, and right atrial pressure.

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AORTIC AND VAGAL REFLEXES IN HYPERCAPNIA

Effect of vagal and subsequent aortic nerve block on aortic blood pressure and limb and kidney perfusion pressures in a rabbit with its carotid sinus nerves cut and ventilated at 30 cycles/min and tidal volume of 15 ml/kg. Top: Normocapnia (end-tidal CO₂ 3.5%), showing from top to bottom, temperature of thermodes, aortic blood pressure, and kidney and limb perfusion pressures. Throughout the experiment the vagi were on the thermodes. At the first pair of arrows the aortic nerves were also placed on the thermodes; at the second pair of arrows the aortic nerves were put on the neck musculature. Bottom: Same procedure during hypercapnia (end-tidal CO₂ 8.1%).

Discussion

Normocapnia.—During normocapnia, when vagal activity was absent, the aortic nerve block caused a greater increase in resistance in the hind limb than it did in the renal vascular bed; when aortic nerve activity was absent, vagal nerve block caused a small increase in limb resistance and only a slightly larger increase in renal resistance. Since the circulation of the paw was excluded, the changes in limb vascular resistance reflect changes in resistance in the muscles. These results are in accord with those of other studies. Kendrick et al. (6) observed that in cats a decrease in carotid sinus pressure causes a more marked increase in muscular resistance than it does in renal vascular resistance. Oberg and White (7) found, also in cats, that vagal nerve block causes renal vasoconstriction but has little effect on the muscle circulation and that clamping of the carotids causes little change in renal blood flow; however, because they did not measure blood gases or pH, we cannot make a direct comparison with the present findings. In the dog, Pelletier et al. (8) concluded that the vagal afferents have a smaller effect on muscle vessels than that exerted by the carotid sinus baroreceptors.

Hypercapnia.—During hypercapnia when vagal activity was absent, the aortic nerve block caused an increase in muscle resistance that was similar although slightly larger than that seen during normocapnia; the increase in renal resistance was three to four times greater and exceeded the increase in muscle resistance. When aortic nerve activity was absent, vagal nerve block caused a small increase in resistance in muscle, which was slightly larger than that seen during normocapnia. In contrast, the increase in renal resistance was very large and was five times greater than the increase seen during normocapnia. These studies of the effect of vagal block confirm our previous findings (2) that, in rabbits with denervated carotid and aortic chemoreceptors and baroreceptors, the increase in sympathetic outflow to the kidney caused by hypercapnia is much less when vagal afferents are intact. Folkow et al. (9) observed that clamping of the carotid artery in cats during
TABLE 3
Effect of Vagal Block with and without Aortic Nerve Block in Six Rabbits

<table>
<thead>
<tr>
<th>Aortic nerve</th>
<th>Site</th>
<th>Normocapnia</th>
<th>Hypercapnia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Δ Block</td>
<td>ΔΔ*</td>
</tr>
<tr>
<td>Intact</td>
<td>Aorta</td>
<td>102 ± 1</td>
<td>9 ± 3†</td>
</tr>
<tr>
<td></td>
<td>Limb</td>
<td>92 ± 5</td>
<td>5 ± 2</td>
</tr>
<tr>
<td></td>
<td>Kidney</td>
<td>86 ± 10</td>
<td>8 ± 2†</td>
</tr>
<tr>
<td>Blocked</td>
<td>Aorta</td>
<td>132 ± 5</td>
<td>14 ± 3†</td>
</tr>
<tr>
<td></td>
<td>Limb</td>
<td>127 ± 15</td>
<td>19 ± 7†</td>
</tr>
<tr>
<td></td>
<td>Kidney</td>
<td>105 ± 7</td>
<td>23 ± 12</td>
</tr>
</tbody>
</table>

All pressure values are means ± se.

*ΔΔ = potentiation of vagal block effect by prior block of aortic nerve.
†For difference, P < 0.05.
marked in the renal than in the muscle vessels? Our experiments do not provide the answer. Obvious considerations are the level of sympathetic traffic to both beds under control conditions, the response curve of both vascular beds to sympathetic stimulation (6, 12), and the sensitivity to CO₂ of the neuronal pools in the brain which control the sympathetic outflow to the peripheral vascular beds.

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Modifications of the Aortic and Vagal Depressor Reflexes by Hypercapnia in the Rabbit
NORBERT T. OTT and JOHN T. SHEPHERD

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