Localized Neurogenic Vasoconstriction of the Basilar Artery

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Abstract:
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Ring segments from the caudal end of the basilar artery of the rabbit contract to electrical stimulation of their intramural nerve supply more than those from adjacent parts of the vertebral and the rostral three-fourths of the basilar arteries. The magnitude of developed neurogenic tension is approximately one-fourth that of the ear artery, a highly reactive muscular artery. The position of this reactive arterial segment suggests its role in the regulation of cerebral blood flow.

Additional Key Words cerebral circulation norepinephrine vertebral artery adrenergic plexus sympathetic innervation cerebrovascular tone

Recent histochemical and electron microscope studies have demonstrated the presence of adrenergic nerve terminals in the wall of cerebral blood vessels. The density and morphological characteristics of this innervation are similar to those of other arteries in the same animal. Despite these findings the functional importance of the autonomic innervation of the cerebral vessels has not been established experimentally. Until recently the consensus was that the cerebral vasculature is relatively unresponsive to nervous activity. Although this has been questioned recently by a number of investigators, in particular, D'Alecy and Feigl, the role of the innervation of the cerebral vasculature is somewhat of an enigma.

We have studied in vitro the neurogenic response of the basilar and the rostral ends of the vertebral arteries of the rabbit. A new method designed to utilize ring segments of small vessels was adopted.

Methods
The basilar, the rostral end of the vertebral arteries, and the proximal end of the ear artery were rapidly removed from exsanguinated adult white rabbits of either sex and placed in Krebs bicarbonate solution equilibrated with 95% O₂ and 5% CO₂ at room temperature. The composition of the Krebs was (in mM) Na⁺, 144.2; K⁺, 4.9; Ca²⁺, 1.3; Mg²⁺, 1.2; Cl⁻, 126.7; HCO₃⁻, 25.0; SO₄²⁻, 1.19; and glucose, 11.1; and contained 0.024 mM calcium disodium ethylene diamine tetra-acetate. All subsequent manipulation was carried out under a dissecting microscope in a shallow layer of the same solution in a Petri dish frequently bubbled with the gas mixture. Vessels were cleaned and 4-mm vessel ring segments were taken for study from five different positions (fig. 1) of the vertebral-basilar system and from the ear artery.

Vessels were cannulated with a stainless steel rod of hemispherical section about 1.5 cm long and 200 μ in diameter. A short piece of platinum wire, diameter 100 μ, was then inserted into the vessel adjacent to the flat surface of the stainless steel rod. This malleable wire was bent into a shape without stretching or distorting the vessel. Supported by the rod, the assembly was placed horizontally between two plastic hooks which were connected to a fixed Statham strain gauge (G10B ± 0.15 oz). The two dependent ends of the platinum wire were then secured in a plastic gate in such a way that no tension was exerted on the vessel. The plastic gate could be moved up and down by a micrometer control, and was used to control resting stretch, which was set at 0.25 gm. For further details see reference 8.

Field electrodes were placed parallel and on either side of the vessels for electrical stimulation of their intramural nerve supply. Trains of 200 biphasic square wave pulses from 1 to 50 Hz, 0.3 msec in duration, were delivered at supramaximal voltage. Contractile responses to this stimulation were completely blocked by tetrodotoxin (1 x 10⁻⁶gm/ml). Experiments were carried out at 38°C. The baths and strain gauges were mounted in such a way as to minimize vibration artifacts. Tension records were made on a Sargent Strip Chart Recorder or Beckman SII Dynagraph pen recorder.

An estimate of the layers of muscle cells in the walls of the basilar and ear arteries was made utilizing conventionally fixed paraffin embedded tissues, stained with hematoxylin and eosin, and Verhœff's and van Gieson stain. The number of layers of smooth muscle nuclei arrayed in the radial axis was estimated in at least...
two positions in each of three sequential 12 μ sections taken from each of three animals.

Results
The magnitude of the force developed by segments of the vertebral-basilar arterial system to transmural stimulation varied with the site of the segment studied. Ring segments from the caudal end of the basilar artery (fig. 1) developed greater force than those from other segments. At 25 Hz, the optimum frequency tested, these segments developed a mean peak force of 180 mg. This was approximately five to ten times greater than that recorded from other segments. No significant differences in the numbers of muscle cell layers in the media of the different vascular segments could be found (table 1). The general shape of the frequency-response curve was similar to that seen with other vascular preparations studied in vitro, the pulmonary artery of the rabbit 9 and the rat portal vein. 10 No response, however, was detected at 1 Hz.

In order to obtain some measurement of the reactivity of the caudal basilar segment in comparison to other muscular arteries, parallel studies were carried out on the rabbit ear artery. This vessel has the highest norepinephrine content of any rabbit artery measured 11 and for this reason is the most responsive to neural activity. At 25 Hz, the ear artery developed a mean peak force almost ten times that of the basilar artery segment.

Under the conditions of experimentation, since the ring segments are stretched between two parallel narrow transluminal wires, the opposite walls are parallel. The cross sectional area of muscle is proportional to the product of twice the thickness of the muscle layer and the length of the segment. Since segments of equal length were used, and assuming that wall thickness is proportional to the number of muscle cell layers in the wall, the ear artery should develop approximately twice the force of the caudal basilar segment, all other factors being equal. It can be seen that even after correction for wall thickness the ear artery develops approximately four times the tension of the caudal basilar artery segment (table 1).

Discussion
Although a number of investigators have shown that isolated preparations of cerebral blood vessels respond to vasoactive substances, 12-16 the contraction of these vessels to neurogenic transmitter in vitro has not been unequivocally demonstrated. Nielsen et al. 8 have shown that tyramine will induce a dose-related

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Number of muscle layers</th>
<th>Unstretched internal diameter (mm)</th>
<th>Tension developed at 25 Hz (mg)</th>
<th>Tension developed at 25 Hz/number of muscle layers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear</td>
<td>13.4 ± 0.57 (7)</td>
<td>0.50 ± 0.07 (5)</td>
<td>1,680 ± 336 (12)</td>
<td>126</td>
</tr>
<tr>
<td>Caudal basilar</td>
<td>6.0 ± 0.38 (7)</td>
<td>0.34 ± 0.5 (5)</td>
<td>178 ± 29 (7)</td>
<td>30</td>
</tr>
</tbody>
</table>

Mean ± SE (number of observations).
*For conditions, see text.
response in the isolated middle cerebral artery of the cat, and that this effect, in part at any rate, is dependent upon the release of adrenergic transmitter. However, the dimensions of this neurogenic component were not defined.

That these responses were due to activation of the neural ground plexus is proved by the observation that when supramaximal voltages were employed the response was eliminated by tetrodotoxin. This agent blocks the nerve-induced response in innervated smooth muscle preparations. Although the rate of rise of the frequency-response curve and the stimulation frequency giving the maximum contraction in the basilar artery are similar to other vascular preparations, no response was elicited at 1 Hz. Stimulation at this frequency has initiated responses in a number of rabbit vessels, including the pulmonary, ear and saphenous arteries (unpublished results, Bevan). In the rat portal vein, the mean response at 1 Hz was approximately 5% of the maximum. These findings are consistent with observations that the adrenergic innervation of the basilar artery in the rabbit is similar in position and density to that seen in many other arteries, but that the transmitter threshold is higher in cerebral vessels than in other regions.

The basis of the difference in reactivity to sympathetic neural influence of the caudal basilar and the ear artery, and between the caudal basilar and the vertebral and distal basilar, is not known. Our observations show that differences in the number of muscle cell layers in the vessel wall do not form the basis of these differences. Possible differences in the size and orientation of the cells, however, cannot be taken into account at the moment. It is known that the neural density in the ear artery is high and this may be the cause of the high reactivity of this vessel. However, quantitative comparisons of the plexus in the ear artery and the cerebral vessels is lacking.

Differences in the functional consequence of neural activity in the ear and the caudal basilar arteries may be less than differences in the developed force suggest. According to the Laplace law, the transmural pressure equals the circumferential tension divided by the vessel radius. If other factors are equal in both vessels, and if the radius and possibly the transmural pressure in the caudal basilar is smaller than in the ear artery, a smaller change in circumferential tension would be required to cause the same proportional change in resistance in the caudal basilar than in the ear vessel.

Since the rabbit brain receives its main arterial supply via the vertebral arteries, the reactive segment of the basilar artery is strategically placed to modify and regulate blood flow to the brain. Unfortunately insufficient information is obtained by in vitro techniques to permit an exact forecast of changes expected in vivo. At the moment the precise functional consequence of changes in sympathetic control of the caudal basilar artery segment is not known.

References

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