Comparison of Vascular Reactivity in Spinal Cord and Brain

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SUMMARY The local tissue PO₂ in the brain cortex and in the spinal cord of rats was examined with ultramicroelectrodes. In the spinal cord the PO₂ was highest in white matter, intermediate in dorsal horn gray matter, and lowest in the ventral horn gray matter. In the gray matter of the cord, as well as in the brain, the PO₂ at a fixed locus was found normally to oscillate. CO₂ responses were more brisk in the cord than in the brain while the responses to hypoxia were similar. Therefore, it appears that the physiological regulation of blood flow in the spinal cord is qualitatively similar to that of the brain.

Introduction

THE PROBLEMS of tissue oxygen supply within the central nervous system have until now mainly been investigated in the brain. The extent to which the spinal cord oxygen supply is regulated similarly to the brain has only a limited experimental basis. Field et al. found that the blood flow of the thoracic and lumbosacral spinal cord of anesthetized rabbits was markedly independent of arterial blood pressure, based on heat clearance measurements. They found that blood flow increased during hypoxia but no evidence of a vasodilator effect by CO₂. Otomo et al. observed directly the exposed pial vessels of dogs and concluded that the spinal cord blood flow was passively responsive to systemic arterial pressure. Capon showed a moderate vasodilator effect of CO₂ in the spinal cord and thought it was less prominent than in the brain. With the heat clearance method Palleske and Herrmann investigated the blood flow of lumbar spinal cord of miniature pigs. They found the responsiveness to blood pressure, arterial PO₂, and PCO₂ was similar in the spinal cord and in the brain. Similar results were obtained by Wüllenweber in man, by Flohr et al. in cats, and by Tschantzer in dogs.

In this report we wish to present some physiological observations concerning the oxygen supply of the cerebral cortex and the spinal cord of rats based on measurements with ultramicro-oxygen electrodes.

Methods

Oxygen Electrodes

Gold ultramicro-oxygen electrodes were produced according to the method of Erdmann et al. and are illustrated in figure 1. A glass-coated gold wire (gold diameter 1 to 5 μ, glass coating 5 to 10 μ) was cut into pieces of 1 to 2 cm in length. These pieces were obliquely ground after casting them in acrylic. The acrylic was then dissolved in acetone. Using fine forceps and a dissecting microscope the glass coating was clipped from the unground end of the gold core and attached to copper conducting wire with conductive coating. The system was then inserted into a glass capillary pipette and fixed with two-component glue. By electrolysis a recessed chamber of about 5 μ in depth was made in the electrode tip serving to limit the diffusion area and stirring sensitivity of the electrode. The outside of the glass shaft of the electrode to within a few microns of the gold wire tip was painted with silver lacquer and this was connected to a conducting wire which served as the reference electrode. Finally the electrode tip was covered with a water-carrying highly adhesive oxygen-pervious membrane (Rhoplex). Calibration of the electrode was performed in 0.2 M KC1 at 37°C, using 100% nitrogen and 5% oxygen. The electrodes were polarized at -800 mV, the current flow amplified as in figure 2, and the output monitored on a DC recorder.

Anesthesia and Preparation of the Animal

The surgical procedures were performed under pentobarbital anesthesia with an initial dose of 40 mg per kilogram of body weight intraperitoneally, paralysis with pancuronium bromide, and artificial ventilation via a tracheostomy. After exposure of the calvarium, a hole (2 mm in diameter) was drilled in the parietal bone and the dura removed. An oxygen electrode was inserted into the cortex and held rigidly in place throughout the experiment at a depth of 100 to 200 μ. At the thirteenth thoracic vertebra, a laminectomy was performed. After careful removal of the dura the lumbar enlargement of the spinal cord was exposed and another oxygen electrode inserted at 0.7 mm lateral to the dorsal spinal artery. The animal's head was fixed in a headholder and the vertebral column in another holder. The animals were ventilated with a mixture of 21% O₂ and 79% nitrous oxide. They were carried throughout the experiment on nitrous oxide-oxygen anesthesia. Femoral artery and vein catheters were placed for monitoring blood pressure and for drug infusion.

Monitoring

These experiments numbered 15 in toto. All of the animals were female albino Wistar rats weighing 250 to 300 gm. Tracheal CO₂ was monitored continuously with an infrared analyzer and manipulated during the course of the experiment by adding known concentrations of carbon dioxide to the inspired gases. Arterial PO₂, pH, and Pco₂ were determined at the beginning of the experiment and the respirator stroke volume altered to maintain a PO₂ greater than 90 mm Hg and a Pco₂ between 36 and 38 mm Hg. Thereafter the animal was maintained in a steady state. Mean arterial pressure was monitored with a Statham strain gauge connected to the femoral artery catheter. Rectal temperature was...
monitored with a thermistor probe and maintained at 37° ± 1° with a heat lamp.

Results

Po2 Profile

When the oxygen microelectrode was moved forward into the spinal cord, the oxygen partial pressure along the course of the electrode tract was registered. Such a registration is called the Po2 profile. This has characteristic features in different tissues depending on the capillary density of the tissue, and the diffusion coefficient for oxygen in the tissue. The insertion of the electrode into the spinal cord involves penetration through tissue areas with histologically different characteristics and different physiological functions. In histological sections we verified the course of the micro-electrode. When the electrode was inserted as in these experiments 0.7 mm lateral to the dorsal median sulcus of the lumbar enlargement, it passed through a thin layer of white matter, and at a depth of 200 to 300μ it entered the dorsal horn gray matter. As the electrode was moved forward, it passed at a depth of 1,000 to 1,200μ into the ventral horn and at a depth of 2,000 to 2,200μ it entered the ventral white matter. According to the morphological structures, the registered Po2 values had characteristic changes of mean tissue Po2, as seen in figure 3. In the dorsal white matter the tissue Po2 ranged between 20 and 40 mm Hg. The peaks and valleys of the profiles were relatively broad. In the dorsal horn, the tissue Po2 varied between 10 and 20 mm Hg and the peaks and valleys were significantly closer and more distinct. Great tissue Po2 changes in relatively short distances were noted. The tissue Po2 values in the ventral horn were still lower than in the dorsal horn. Here the tissue Po2 was as low as 3 mm Hg in the broad valleys and not higher than 20 mm Hg at the peaks. In the ventral white matter again high tissue Po2 values were registered with relatively broad peaks up to 30 mm Hg.

Po2 Waves

Continuous registration of tissue Po2 at a fixed location in the spinal cord and the brain cortex usually revealed oscillation of the tissue Po2. The oxygen cycle frequency was counted as one-half the number of crossings of the mean Po2 during successive one-minute periods (fig. 4). The oscillations of the brain cortex Po2 were not very regular, varying from two to eight per minute. In the spinal cord the oscillations were quite regular with a frequency of 7 to 16 per minute. At a constant Pco2 and blood pressure, cycle frequency in either tissue would vary randomly ±30%. In general we noted in the spinal cord larger amplitudes of Po2 waves than in the cerebral cortex. In both tissues the amplitudes became smaller at lower tissue Po2.

Po2 Profile of the Spinal Cord

The highest Po2 values are in the white matter. The gray matter of the dorsal horn shows higher values than the ventral horn.
Hypercapnia and Its Effect on Tissue $P_{O_2}$

Simultaneous $P_{O_2}$ registration of the brain cortex and the spinal cord was performed while the animal was subjected to hypercapnia. As illustrated in figure 5, an immediate effect of hypercapnia could be seen on the tissue $P_{O_2}$ of the brain cortex and the spinal cord. In response to a step change in inspired CO$_2$, the tissue $P_{O_2}$ increased to a new steady state value within a few seconds. When the CO$_2$ was discontinued there followed, with a brief delay, a rapid return to the initial value. The regulation of tissue $P_{O_2}$ in the brain cortex occurred mostly with a longer time interval than in the spinal cord. In the spinal cord as well as in the brain cortex the restoration of the initial $P_{O_2}$ value usually occurred following an undershoot-overshoot reaction, although this was somewhat less distinct in the spinal cord than in the cerebral cortex. The spinal cord demonstrated a shorter-lasting and indistinct undershoot and nearly no overshoot prior to returning to the pre-CO$_2$ steady state level of $P_{O_2}$. Immediately or shortly after this change the $P_{O_2}$ oscillations resumed, initially with a small amplitude and irregularity, gradually returning to normal. The undershoot-overshoot reaction in the brain cortex was more distinct. It occurred with a much longer time constant. The $P_{O_2}$ waves of the brain cortex had a broad amplitude and a slow frequency until the initial $P_{O_2}$ level was resumed.

Hypoxia and Re-oxygenation

Hypoxia was made by turning off the respirator for a brief interval. $P_{O_2}$ levels in the spinal cord and brain of 0 mm Hg were always associated with a flat EEG. As shown in figure 6, shortly after discontinuing ventilation, the tissue $P_{O_2}$ of both the spinal cord and brain dropped to zero and after resumption of ventilation there was immediate recovery with overshoot in both tissues followed by return to the initial value. The recovery process was essentially the same in both tissues.

Discussion

$P_{O_2}$ Distribution in the Spinal Cord

Some aspects of $P_{O_2}$ in the spinal cord suggest that the profiles of the $P_{O_2}$ distribution can be correlated with capillary density. The broad peaks and broad valleys which are seen in the white matter correlate with a low capillary density of 200 mm of total capillary length per cubic millimeter of tissue. Sharp peaks and narrow valleys in the gray matter correlate with the capillary density varying from 900 to 1,200 mm total capillary length per cubic millimeter of tissue. The mean tissue values, however, do not fit with the capillary density of the tissue. Although the capillary density of white matter is significantly less than that of gray matter, the mean tissue $P_{O_2}$ values are much higher in the white matter. This may be explainable by a significantly higher oxygen consumption rate in the gray matter. Furthermore, it should be noted that mean $P_{O_2}$ values in the dorsal horn gray matter are higher than those of the ventral horn gray matter.

It has been shown by van Harreveld that there is a different sensitivity to anoxia of the neurons of the dorsal and ventral horn, those of the ventral horn being more sen-
sitive particularly in the medial region. This differential susceptibility may correlate with the findings in this study that the resting levels of PO2 in the ventral horn are lower, perhaps reflecting a higher rate of oxygen consumption there. It is known, for example, that a reduction in the tissue PO2 of only a few millimeters of mercury is sufficient to stop the spontaneous electrical activity of the motor neurons of the ventral horn.15

PO2 Waves

It has been observed that the local PO2 of the brain and other organs oscillates with a frequency of three to ten per minute.12,13 As the underlying mechanism of this, local oscillations in flow with constant oxygen consumption are presumed. Measurements of local microflow with the local hydrogen generation method by Stosseck has provided evidence that the flow does oscillate.14 Halsey and McFarland15 discussed a feedback control system in which a change in tissue PCO2 causes a change of the precapillary arteriolar radius influencing local resistance to flow and hence changes in clearance of metabolically generated CO2. In this system a finite time delay interval is present between the clearance of metabolic CO2 from the tissue and the response by the precapillary arteriole. Such a delay in a feedback control system would inevitably produce oscillations.

In our experiments we noted different PO2 wave behavior in the spinal cord and in the brain cortex. Whereas the oscillation frequency in the brain cortex was two to eight cycles per minute with varying amplitudes, the spinal cord showed a more regular and rhythmical frequency of 7 to 16 cycles per minute. The different mechanisms maintaining an optimal blood flow were best seen after termination of hypercapnia. The brain cortex showed a slow recovery with vigorous overshoot-undershoot reactions with progressively decreasing amplitude over some minutes before returning to the initial PO2 mean level and oxygen wave frequency. In the spinal cord, PO2 behavior was somewhat different with a quicker return to the initial level. It would appear that the spinal cord blood flow regulation is somewhat more sensitive to CO2 than is that in the brain cortex.

Hypercapnia and Hypoxia

Administration and termination of hypercapnia caused qualitatively similar increases and decreases in tissue PO2 in the spinal cord and cerebral cortex. The responses also were similar when hypoxia was induced by interrupting ventilation. When ventilation was resumed, there was a rapid recovery in both tissues with a persisting slow overshoot phase continuing for one to two minutes with no significant difference between the two tissues.

References

Comparison of vascular reactivity in spinal cord and brain.
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