TITLE: EVIDENCE AGAINST CENTRAL CHEMORECEPTOR CONTROL OF CEREBRAL BLOOD FLOW WITH HYPOXIA.

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Introduction: Hypoxia increases cerebral blood flow (CBF). However the precise mechanism by which this occurs is unclear. We hypothesized that a central chemosensitive area in the medulla could regulate CBF during hypoxia[1]. We reasoned that if an O_2 sensitive area were located on the surface of the ventrolateral medulla, surrounding this sensor with cerebrospinal fluid with a high PO_2 would attenuate the CBF response to systemic hypoxia.

Methods: Six sodium pentobarbital anesthetized (30 mg/kg, iv), mechanically ventilated adult mongrel dogs were studied. A catheter was placed in the left femoral artery and advanced into the left ventricle for injection of radiolabelled microspheres. The other femoral artery was cannulated and a catheter was advanced into the descending aorta for obtaining the arterial reference blood sample during the microsphere injection. The omocervical artery was cannulated and used for continuous monitoring of systemic arterial blood pressure and for arterial blood samples. For cerebral venous sampling, a catheter was inserted into the sagittal sinus. Two 16G angio catheters were inserted into the cisterna magna for a cisterna-cisterna perfusion system. The cisterna magna was perfused with fluorocarbon (FC) having a PO_2 of 153 ± 1 (FC153) or 645 ± 19 mmHg (FC645) (X ± SE) and the animals were made hypoxic by inhalation of a reduced O_2 mixture in nitrogen at constant ventilation for 10 to 20 minutes. Measurements were taken before, during and after hypoxia, and the order of administration of FC153 or FC645 was randomized in each experiment. The mean value before and after hypoxia measurements were used as control values for hypoxia. Regional cerebral blood flow was measured using radiolabelled microspheres (15 ± 1.5 μm). FC-43 emulsion (The Green Cross Co.) was used for this experiment. Just before the experiment 400 ml of FC-43 was mixed with 100 ml of stock solution (Na^+ 612 mEq/L, Cl^- 524, HCO_3^- 100, Urea 24, K^+ 12, Ca^{2-} 5.2, Mg^2 3.2) to make the final solution the same as mock CSF. The solution was then separated into two flasks and one was bubbled with 95% O_2 and 5% CO_2 premixed gas and the other with 95% air and 5% premixed gas for more than 30 minutes in the water bath of 38°C. FC solution was perfused with a Harvard pump at the rate of 3.8 ml/min.

Results: In all animals, arterial PCO_2 and pH were maintained within physiological ranges. With FC153, a decrease in CaO_2 (arterial O_2 content) form control (19.4 ± 0.9) to 6.5 ± 0.5 vol% increased CBF from 35 ± 4 to 111 ± 13 ml/min/100g and medullary blood flow from 33 ± 4 to 178 ± 31 ml/min/100g. When the cisternal perfusion solution was changed to FC 645, and CaO_2 was reduced from 18.2 ± 1.0 to 6.4 ± 0.5 vol%, CBF and medullary blood flow increased from 36 ± 4 to 107 ± 10 and 33 ± 3 to 164 ± 23 ml/min/100g, respectively (figs. 1 & 2). Other regional brain areas showed similar changes (fig. 2).

Conclusion: These data do not support the idea that a central chemosensitive area on the surface of the medullar controls CBF during hypoxia. Either the putative chemosensitive region is too deep in the brainstem to be affected by a change in PO_2 at the surface, or the local hypoxic response in the cerebrum compensates for the blocade of the postulated centrally-mediated response.

References:

1. Traystman RJ, Gurtner GH, Nichols DG, Jones Jr MD, Koehler RC, McPherson RW, and Rogers MC: Central chemoreceptor regulation of cerebral blood flow, Neural Regulation of Brain Circulation. Edited by Owman CH, Hardebo JE. North Holland, Elsevier Science Pubs., 1986, pp.169-178

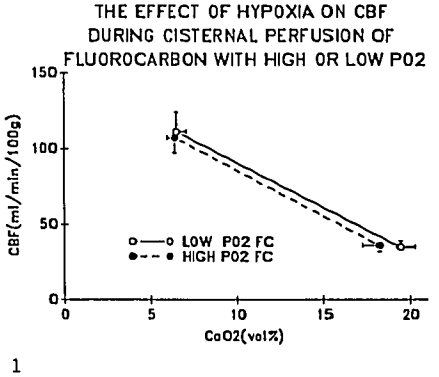

fig. 1

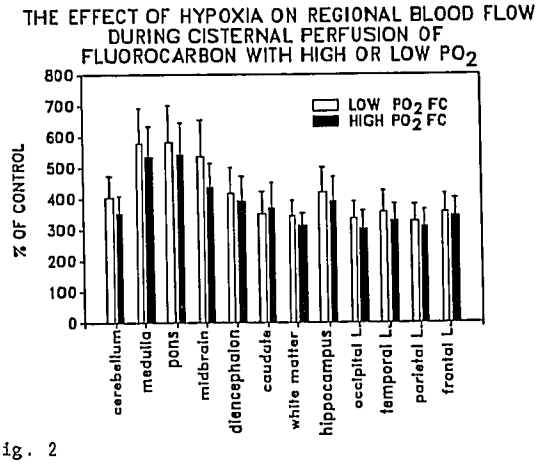

Fig. 2