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Effects of carbonic anhydrase inhibitors upon cerebral cortex oxygen availability and resistance to hypoxia

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Acetazolamide has been used in the treatment of respiratory insufficiency and appears to aid accommodation to altitude in man. This drug is able to increase cerebral blood flow without influencing the cerebral metabolic rate of oxygen. This effect seems to be due to raised pCO_2 of brain tissue (Gotoh, Meyer & Tomita, 1966).

The influence of carbonic anhydrase inhibitors (acetazolamide, methazolamide, dichlorphenamide) upon cerebral tissue pO_2 has been studied in unanaesthetized rabbits with chronically implanted oxygen electrodes. Intravenous administration of these drugs (5–25 mg/kg) rapidly induced a significant and long-lasting rise of cerebral pO_2. Meanwhile, the pO_2 response to CO_2 inhalation was not reduced.

Resistance to atmospheric decompression in mice was increased by carbonic anhydrase inhibitors, but these drugs displayed no protection against asphyxial hypoxia in rats.

These results are in accordance with the reported clinical data.

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Long-lasting effects of the opening of the blood brain barrier on the modifications induced by intracarotid injection of noradrenaline

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There are three problems concerning the haemodynamic effects of noradrenaline: (1) Does noradrenaline cross the blood brain barrier, when injected into the carotid artery? (2) What are the effects of such an injection on cerebral blood flow, whether the blood brain barrier is opened or not? (3) Which haemodynamic effects might be considered to be of central origin?

The following observations were made on dogs: (1) Vertebral blood flow was decreased after the intracarotid injection of noradrenaline. Thus, the vertebral artery is responsive to noradrenaline. After the blood–brain barrier had been opened (urea 36%, 10 ml), the decrease of the vertebral blood flow was more marked and so was related to the effects of noradrenaline itself on the vertebral artery and/or its underlying system. (2) Cardiac output increased immediately after the injection of noradrenaline subsequent to the first injection of urea. Thus, there must be central cardiostimulating structures responsive to noradrenaline. (3) Mean arterial blood pressure, total peripheral resistance and heart rate decreased, and femoral blood flow increased only after the injection of noradrenaline given after a second injection of urea.

Hence, the bradycardia and the increase of cardiac output, which are both centrally mediated, are therefore related to two different mechanisms, since noradrenaline increased cardiac output immediately after the first injection of urea, but induced bradycardia only after the second injection of urea. Thus, the effects of noradrenaline can be modulated by modifications of the permeability of the blood brain barrier.