Peripheral Vascular Effects of Histamine Administered into the Cerebral Ventricles of Anaesthetized Cats

The effects produced by histamine after intraventricular administration are different from those after systemic (e.g. subcutaneous or intravenous) administration. In conscious cats, intraventricular histamine produces a peculiar pattern of behavioral changes[1]. In anaesthetized cats, a blood pressure rise is produced[2,3]. Little is known about the factors involved in producing this pressor effect of histamine. The present paper describes some observations on the effect of intraventricular histamine on the vascular resistance in two different regions.

Methods. Cats weighing 2.0 to 4.6 kg were anaesthetized with ether-chloralose (70–80 mg/kg). Blood pressure was recorded in a femoral artery. Histamine was injected into the lateral ventricle through an intraventricular cannula[3,4]. The histamine (50 or 100 μg) was dissolved in 0.2 ml Tyrode solution, and was washed in by another 0.2 ml Tyrode solution. In a few exceptional experiments the injections were followed by a profound lowering of the blood pressure, and a concomitant decrease in peripheral vascular resistance. These effects could be reproduced by intravenous injections of histamine. In these experiments, post mortem dissection of the brain showed that the cannula did not communicate freely with the lumen of the ventricle. It was concluded that on injection a rapid absorption of histamine into the blood stream had occurred. These experiments were discarded.

In some experiments histamine, instead of being injected, as described above, was perfused through the ventricular system, from the lateral ventricle to the cisterna magna[5]. Some of these experiments had to be discarded because of intracranial bleeding when the animal was heparinized.

The arrangements for the recording of blood flow were similar to those described by ABRAHAMS, HILTON, and ZBROZYNA[6]. Blood from the hind leg, or forepaw, was collected from the femoral, or cubital, vein, and was passed through PVC tubing to a photo-electric drop recorder connected to an ordinate recorder. The blood was collected in a reservoir from which it was continuously returned by a digital pump to a suitable vein. At the start of the experiment, the reservoir was filled with dextran solution (Rheomacrodex 10%, Pharmacia).

Immediately before the cannulation of the veins, 50 mg (5000 units) of heparin were injected intravenously. The dose was repeated at intervals of 30 to 60 min. In some experiments bilateral adrenalectomy was performed through a midline abdominal incision.

Results. Except for the instances referred to above when histamine penetrated into the blood stream, the circulatory responses to histamine observed after ventricular perfusion and intraventricular injection were similar.

In Figure 1 simultaneous elevation of the arterial blood pressure and decrease in blood flow show that the intraventricular histamine caused an increase in the vascular resistance in the forepaw. Although such an increased resistance was regularly observed in the forepaw following intraventricular histamine, the elevation of the blood pressure was sometimes smaller than that shown in Figure 1. In Figure 2 the rise in pressure was inconspicuous, but the decrease in flow clearly showed an increased resistance. Also the opposite case occurred, i.e little decrease in flow, but large elevation of arterial blood pressure, again permitting the conclusion that there was, in fact, an increased resistance to flow in the forepaw (Figure 3).

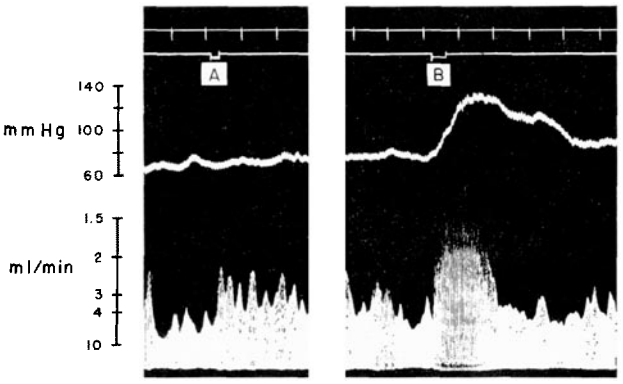

Fig. 1. The effect of intraventricular injection of histamine on arterial blood pressure and venous outflow from forepaw. Cat, 2.6 kg, chloralose anaesthesia. Records from above: time marker (min), signal, arterial blood pressure, venous outflow. A: control injection (Tyrode solution). B: histamine injection (100 μg).

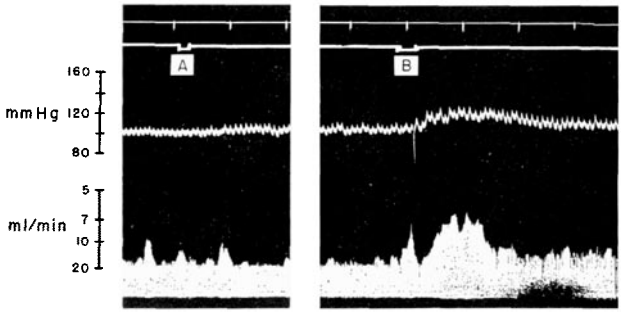

Fig. 2. The effect of intraventricular injection of histamine on arterial blood pressure and venous outflow from forepaw. Cat, 3.5 kg, chloralose anaesthesia. Records as in Figure 1. A: control injection (Tyrode solution). B: histamine injection (50 μg).

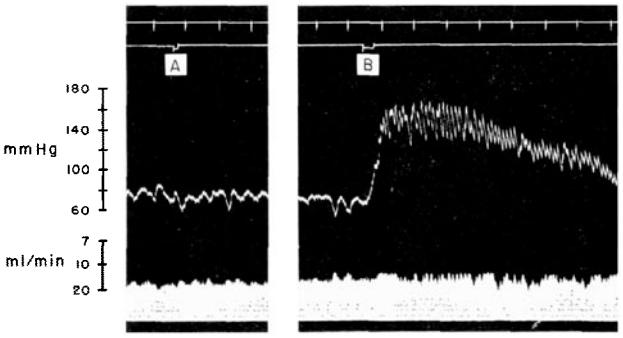

Fig. 3. The effect of intraventricular injection of histamine on arterial blood pressure and venous outflow from forepaw. Cat, 4.6 kg, chloralose anaesthesia. Records as in Figure 1. A: control injection (Tyrode solution). B: histamine injection (100 μg).

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In the hind leg, the vascular resistance was either unchanged, or increased, after intraventricular histamine. Figure 4 shows an experiment where histamine produced a moderate increase in resistance. Decrease in resistance was not observed.

In three experiments on blood flow from the forepaw, acute bilateral adrenalectomy was performed prior to the intraventricular administration of histamine. Adrenalectomy did not prevent the pressor response nor the increase in vascular resistance.

Discussion. If the vascular changes in the forepaw are regarded as representative of the skin, the present experiments show that one part of the response to intraventricular histamine is vasoconstriction in the skin. The observations on hind legs indicate that such vasoconstriction is less pronounced, or absent, in skeletal muscle. The role of the adrenals in producing these responses was not investigated in detail, but the responses were not entirely dependent on the presence of the adrenals. This would suggest that there is a nervous pathway, independent of the adrenals, by which intraventricular histamine produces peripheral vasoconstriction. This interpretation is in agreement with the observation by TRENDELENBURG[8] that spinal section prevented the blood pressure rise after intraventricular histamine. Obviously peripheral vasoconstriction is one factor responsible for the pressor effect of intraventricular histamine. Whether there are others in addition (e.g. increased cardiac output) is not known.

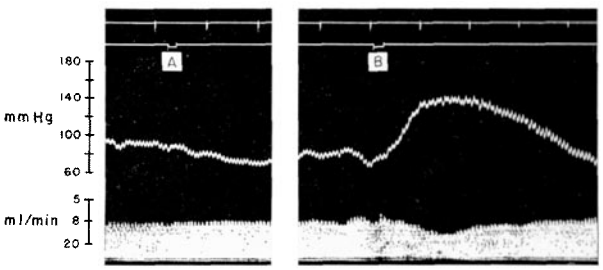

Fig. 4. The effect of intraventricular injection of histamine on arterial blood pressure and venous outflow from a skinned hind leg. Cat, 4.1 kg, chloralose anaesthesia. Records as in Figure 1. A: control injection (Tyrode solution). B: histamine injection (100 μg).

Although it seems clear that histamine in these experiments exerted a direct effect on the brain, this does not necessarily mean that histamine has direct effects on neurons. It could for instance be an action directly on brain blood vessels, as has been claimed for other vasoactive drugs[7]. That the action of intraventricular histamine is a 'true' drug effect is indicated by the observation that the chemically similar substance, methylhistamine (1-methyl-4(β-aminoethyl)-imidazole), is far less active[8], and also by the inhibition of the pressor response by mepyramine[8].

The effects of histamine on the brain may be of physiological significance in view of the fact that histamine is normally present in the brain[8], where it is concentrated in those regions of the brain stem which are most likely to be reached by histamine administered into the ventricular system[9-11].

Zusammenfassung. An narkotisierten Katzen wurden der arterielle Blutdruck und der venöse Ausfluss aus der Vorderpfote oder aus dem Hinterbein registriert. Injektionen von Histamin in die Hirnventrikel bewirkten Erhöhung des Blutdruckes und Vasokonstriktion in der Vorderpfote. Im Hinterbein war die Vasokonstriktion weniger ausgesprochen. Auch nach Entfernung der Nebennieren war der Pressoreffekt vorhanden, woraus folgt, dass die periphere Vasokonstriktion für den durch intraventrikuläres Histamin hervorgerufenen Pressoreffekt verantwortlich ist.

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[11] This work was supported by the Swedish Medical Research Council (Project No. W 349). Rheomacrodex was kindly supplied by Pharmacia, Uppsala (Sweden).

Effect of Internal Radiophosphorus Irradiation on the Ovary of *Puntius sophore* Hamilton

Histological, histochemical and cytochemical studies on the fish gametes have been carried out extensively by various workers, but literature dealing with the effect of radiation on fish gametes is rather scanty. Effect of X-ray irradiation on fish gametes and developing embryo has been studied by some workers[1-3]. Availability of radioisotopes from atomic piles has made it possible to study the effect of internal β- and γ-rays on various tissues. Internal exposure is usually more significant since radioactive substances may enter into the metabolism of the organism and become preferentially deposited in particular organs rather than being uniformly distributed throughout the body. In the present study, an attempt has been made to study the effect of internal P^{32} radiation on the ovary of *Puntius sophore* Hamilton.

By the courtesy of the Fisheries Department of the Government of Rajasthan, *Puntius sophore* were collected from the local tanks and they were acclimatized to the

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