EFFECT OF ADRENERGIC DRUGS ON VENOUS DRAINAGE FROM THE RAT BRAIN

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Experiments on rats showed that if the arterial pressure was stabilized isoprenaline considerably increased the cerebral blood flow. Blocking the β-adrenergic receptors of the cerebral vessels (by propranolol or netalid) was followed by a lasting decrease in the cerebral blood flow. Against this background the vasodilator action of isoprenaline was not exhibited. Noradrenalin had a weak effect on the cerebral blood flow, and after blocking of the α-adrenergic systems of the vessels by dihydroergotamine, it had no action whatever. Evidently β-adrenergic receptors are predominant in the blood vessels of the rat brain.

According to Ahlquist [9], the vascular effects of adrenergic mediators are due to their interaction with the α- and β-adrenergic systems of the vascular wall. The question of the localization and function of α- and β-adrenergic receptors in the various regions of the vascular system and, in particular, in the brain, has not yet been adequately studied.

Most workers [4, 6, 10, 13] recognize the presence of α- and β-adrenergic structures in the cerebral vessels. It was accordingly decided to investigate the role of these structures in changes in the cerebral blood flow in rats, using various adrenomimetic and adrenolytic drugs.

EXPERIMENTAL METHOD

Experiments were carried out on albino rats of both sexes weighing 200-300 g, anesthetized with urethane (1 g/kg intraperitoneally). The tone of the cerebral vessels was estimated from the change in the cerebral blood flow (in ml/100 g brain tissue/min) determined by the writers' modification of Alyukhin's method [1]. In the first place, the design of the clamp provided for occluding the cranial veins of the rat was simplified. A standard lid-retractor, to the blades of which two segments made from a rubber stopper were attached, was used as the clamp. These segments acted as plugs which closed the lumen of the cranial vessels while the blood flow was being measured. Second, the design of the cannula connecting the venous sinus with the measuring pipet was simplified. The cannula was made from an injection needle 1.3 mm in diameter. The shaft of the needle was moulded at the posterior end, and bent while hot to an angle of 90°. The end of the needle for insertion into the sinus was beveled at an angle of 60-70°. The cannula was connected with the measuring pipet by means of a rubber tube which was compressed by a light clamp when no measurements were being taken.

In most experiments, to exclude the effect of possible changes in the systemic arterial pressure on the cerebral circulation, the systemic pressure was stabilized by means of a hemobarostat [3], filled with the blood of a donor rat (3-5 ml). Throughout the experiment the arterial pressure was recorded in the abdominal aorta through a polyethylene catheter connected to a mercury manometer.

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TABLE 1. Effect of Adrenergic Drugs on Cerebral Blood Flow in Rats

Drug given	Dose of drug (in μg/kg)	No. of animals	Rate of cerebral blood flow			
			initial background	1 min	5 min	30 min
Physiological saline		5	100	102,0	103,1	95,9
Isoprenaline	5	5	100	169,5*	191,7 *	126,4
Noradrenalin	5	7	100	123,2	107,0	93,7
Propanolol	100	7	100	76,8 *	64,8 *	76,6 *
Netalid	50	5	100	80,2	63,0 *	83,7
Dihydroergot-amine	200	10	100	67,8 *	81,0	113,3
	100	10	100	90,0	83,5	92,0

*Difference from original background statistically significant ($P < 0.05$).

TABLE 2. Effect of Adrenomimetics Given Against the Background of the Action of Adrenolytics on the Cerebral Blood Flow in Rats

Drug given	Dose of drug (in μg/kg)	No. of animals	Rate of cerebral blood flow				
			init. backgr.	1 min after injec. of adreno-lytics	after injection of adrenomimetics		
					1 min	5 min	30 min
Propanolol + Isoprenaline	50 + 5	5	100	74,3 *	135,0 *	125,0 *	95,0
Propanolol + Isoprenaline	100 + 5	5	100	68,9 *	74,8	72,8	73,0
Dihydroergotamine + Noradrenalin	100 + 5	6	100	77,8 *	76,3	73,2 *	89,5

*Difference statistically significant ($P < 0.05$): for adrenolytics, relative to initial background, for adrenomimetics, compared with level of blood flow after administration of adrenolytics.

The adrenergic drugs used for analysis were injected in a small volume of physiological saline (0.2-0.3 ml) directly into the internal carotid artery in the following doses (in μg/kg body weight): noradrenalin 5, isoprenaline 5, propranolol 50 and 100, netalid* 200, dihydroergotamine 100.

EXPERIMENTAL RESULTS AND DISCUSSION

The mean original background level of the cerebral blood flow of the rats in these experiments was 66.3 ± 4.58 ml/100 g brain tissue/min, in agreement with data in the literature [1]. In the animals of the control group, intracarotid injection of physiological saline (0.1 ml/100 g) caused no significant change in the cerebral blood flow during 30 min of observation (Table 1).

Intracarotid injection of 5 μg/kg of the β-adrenomimetic isoprenaline, while the arterial pressure was stabilized, caused a marked increase in the volume velocity of the cerebral blood flow compared with its initial level throughout the period of observation. The effect reached a maximum at the 5th minute (91.7%).

Blocking the β-adrenergic receptors of the cerebral vessels by intra-arterial injection of netalid (200 μg/kg) and, in particular, of propranolol (50 and 100 μg/kg) was accompanied by a persistent decrease of the blood flow in the brain (Table 1). Against the background of the decrease in the cerebral blood flow induced by propranolol (100 μg/kg), isoprenaline did not exhibit its vasodilator action (Table 2). After

*The Soviet equivalent, inetol, synthesized at the Khar'kov Research Institute of Endocrinology, was used.

partial blocking of the β-receptors (50 μg/kg propranolol) the effect of isoprenaline remained, although it was weaker than in the intact animals (Table 1).

In experiments with intracarotid injection of the α-adrenomimetic noradrenalin (5 μg/kg), the cerebral blood flow was increased after 1 min, but for the next 30 min it was not significantly different from its initial value. This transient increase in the blood flow was seen mainly when the systemic arterial pressure was not stabilized, and it coincided with the time of its maximal elevation. In marked degrees of hypertension, there is passive dilatation of the cerebral vessels [2, 14]. In the experiments with stabilized pressure, the change in the cerebral blood flow must evidently be attributed to definite inertia of the hemobarostat used, so that it was unable to compensate in time for the rapidly developing pressor response. Support for this interpretation is given by the results of the experiment using the α-adrenolytic dihydroergotamine. As the results given in Table 1 show, injection of 100 μg/kg of this drug had no significant effect on the cerebral blood flow of the experimental animals. Meanwhile, against the background of the developing block of the α-adrenergic systems of the peripheral blood vessels, injection of noradrenalin caused no changes in the systemic arterial pressure or in the volume velocity of the cerebral blood flow (Table 2).

Some conclusions regarding the comparative role of the α- and β-adrenergic structures in regulation of cerebral vascular tone can be drawn from analysis of these results. Judging from the change in the total cerebral blood flow under the influence of adrenergic agents, most of the adrenergic receptors in the blood vessels of the rat brain are evidently of the β-type. It is evidently through their intervention that endogenous physiologically active substances possessing β-adrenomimetic properties participate in the formation of the "tonic dilatation" of the cerebral vessels [11, 12].

If these results are compared with those obtained by other workers [2, 4, 7] in experiments on rabbits, cats, and dogs, the existence of marked specific differences in the numerical relationships between the α- and β-adrenergic systems in the cerebral vessels of animals of different species. The evolutionary aspect of this problem is evidently of great interest on its own account, in connection with the hypothesis of the dominant role of an increased blood concentration of noradrenalin and serotonin in the genesis of spasm of the cerebral vessels in man [5, 8].

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