α-ADRENERGIC STRUCTURES OF THE INTRACRANIAL VESSELS AND THEIR ROLE IN REGULATION OF THE CEREBRAL CIRCULATION

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Radioiosotopic, electromagnetic, and resistographic investigations showed that division and stimulation of the cervical sympathetic nerves leads to considerable changes in the cerebral blood supply. The absence of fluctuations in the pH of the CSF during electrical stimulation of the sympathetic nerves suggests that spasm of the intracranial arteries is unconnected with changes in metabolism but is brought about by direct excitation of adrenergic structures of the intracranial vessels by mediator. Pharmacological analysis with the aid of α- and β-adrenoblocking drugs showed that the constrictor response of the cerebral vessels is due to excitation of α-adrenergic structures.

KEY WORDS: cerebral circulation; nervous control of the cerebral circulation; α-adrenergic structures.

The writers showed previously that activation of the sympathico-adrenal system by injection of potassium chloride into the lateral ventricles and by electrical stimulation of the afferent fibers of somatic nerves is accompanied by a marked constrictor response of the cerebral vessels [4]. Other evidence in support of the role of the sympathetic innervation in the control over cerebrovascular tone is given by observations showing that catecholamines and stimulation of sympathetic nerves lead to constriction of the lumen of the intracranial arteries [1, 2] and a decrease in the intracranial blood flow [6, 7, 10, 12, 13, 15].

However, it has been argued that sympathetic influences are not of decisive importance in the regulation of intracranial vascular tone [8, 11]. In particular, the possibility of any direct effect of noradrenalin on the brain vessels has been denied, and according to one report the sensitivity of the pial arteries to noradrenalin depends on the pH of the CSF [16].

The object of the present investigation was to study the role of adrenergic structures of α- and β-types in the mechanism of the constrictor responses of the intracranial vessels. This line of investigation is important to reveal the functional importance of the sympathetic innervation in the control over the cerebral circulation and in the development of cerebrovascular disorders.

EXPERIMENTAL

Experiments were carried out on 52 cats weighing 3-4 kg anesthetized with urethane (0.5 g/kg) and chloralose (50 mg/kg) and artificially ventilated.

The cerebral blood flow was determined with the aid of radioactive xenon-133 [5] and an electromagnetic blood flow meter. The pick-up of the flow meter, 2 mm in diameter, was placed on the common carotid artery of the cats, but the extracranial branches of the artery along the course of the blood flow and before it entered into the brain were ligated. Meanwhile, the EEG in the parietal region, the ECG in lead II, and the blood pressure in the femoral artery were recorded.

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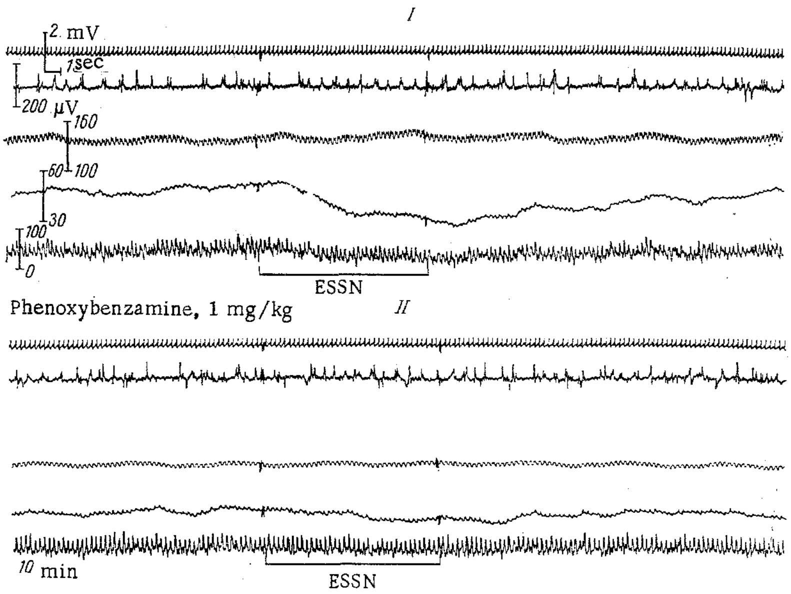

Fig. 1. Effect of phenoxybenzamine (1 mg/kg, intravenously) on responses of the intracranial blood flow to electrical stimulation of the cervical sympathetic nerve in a cat: I) control response; II) 10 min after injection of phenoxybenzamine. From top to bottom: ECG in lead II, parietal EEG, arterial pressure (in mm Hg), mean phasic blood flow in right carotid artery (in ml/min), and marker of stimulation (ESSN).

In order to differentiate the vascular component of the effect of the drugs on the cerebral hemodynamics, in another series of experiments the carotid and vertebral arteries were perfused bilaterally and separately [3].

To study the effect of drugs on nervous regulation of the cerebral circulation, their effect on responses of the intracranial blood flow and the tone of the intracranial vessels to stimulation of the cervical sympathetic nerves was investigated. The sympathetic nerves were stimulated with square pulses (3-10 Hz, 1 msec, 3-10 V). The pH, pCO_2, pO_2, and percentage of oxyhemoglobin were determined in samples of arterial blood by means of the ABC-1 instrument (radiometer). In a separate series of experiments the hydrogen ion concentration and oxygen tension were recorded in the CSF.

Tests were carried out with the α-adrenoblockers phenoxybenzamine (0.5-1.0 mg/kg) and dihydroergotoxin (1 mg/kg), the β-adrenolytic propranolol (0.5-1.0 mg/kg), and noradrenalin (2-10 μg). The drugs were injected into the femoral vein and, in some experiments, into the carotid and vertebral arteries.

RESULTS AND DISCUSSION

The investigation began with the study of the effect of division and stimulation of the cervical sympathetic nerves on the blood supply to the brain. Experiments with division of the sympathetic nerves showed that this operation led to a marked increase in the intracranial blood flow (on the average by 30%), due to a decrease in cerebrovascular tone. The sympathetic nerve was then stimulated electrically in the neck. Stimulation of the cervical sympathetic nerve was accompanied by a marked decrease in the volume velocity of the cerebral blood flow. Under these circumstances the intracranial circulation was reduced by $51 \pm 3.1\%$, indicating a high degree of participation of the vasomotor (neurogenic) component in the regulation of cerebrovascular tone and, consequently, of the blood supply to the brain tissue (Fig. 1). In experiments using the resistographic method, bilateral stimulation of the cervical sympathetic trunks at the level of the stellate ganglia was accompanied by a marked constrictor response of both arterial systems of the brain. The mean increase in tone in the vessels of the carotid system was $37 \pm 3.1\%$ and in those of the vertebral arterial system $27 \pm 1.6\%$ (Fig. 2).

Determination of the parameters of the acid–base balance and the oxygen tension in arterial blood samples before and during electrical stimulation of the cervical sympathetic nerves revealed no significant differences in the pH, pO_2, pCO_2, and percentage of oxyhemoglobin. Similar results were obtained in experiments to determine the hydrogen ion concentration and oxygen tension in the CSF (Table 1). It must be pointed

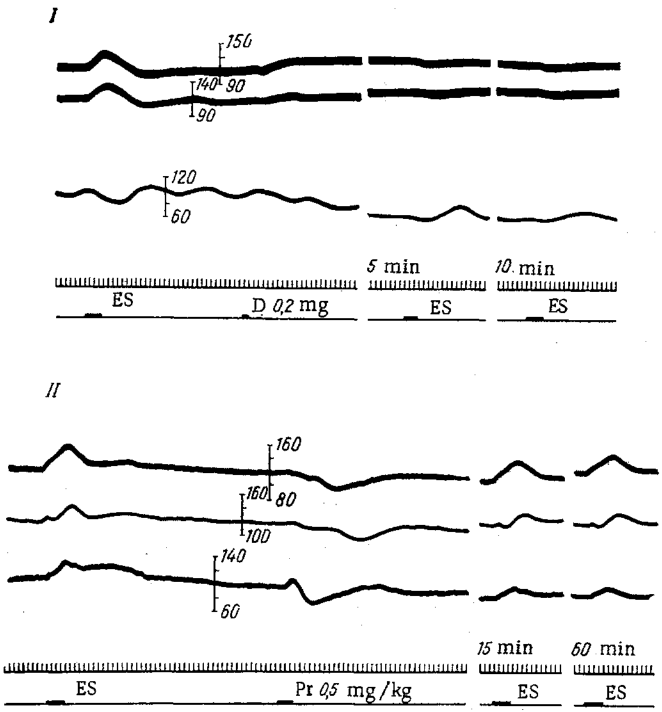

Fig. 2. Effect of dihydroergotoxin (0.2 mg by intracarotid injection) (I) and propranolol (0.5 mg/kg, intravenously) (II) on constrictor responses of intracranial vessels to bilateral electrical stimulation of the cervical sympathetic trunks in cats. From top to bottom: perfusion pressure in maxillary arteries, resistogram of vertebral arteries, arterial pressure, time marker 5 sec; marker of stimulation (ES) and injection of drugs.

TABLE 1. Effect of Electrical Stimulation of Cervical Sympathetic Nerves on Parameters of Acid–Base Balance and Oxygen Tension in Arterial Blood and CSF

	Arterial blood				CSF	
	pH	pO_2 (in mm Hg)	pCO_2 (in mm Hg)	HbO_2 (in%)	pH	pO_2 (in mm Hg)
Control	7,25±0,029	103±3,6	41±4,3	87±1	7,36±0,028	79±8,6
Stimulation	7,25±0,028	99±3,5	47±5	87±1,2	7,35±0,022	75±12

out, however, that during stimulation of the sympathetic nerves some tendency for pCO_2 to rise in the arterial blood and for pO_2 to fall in the CSF was observed. These tendencies were evidently due to constriction of the cerebral vessels and to a diminution in the blood supply to the brain.

The results indicate that the sympathetic nervous system plays an important role in the regulation of the cerebral circulation. The absence of fluctuations in the pH of the CSF during electrical stimulation of the cervical sympathetic nerves demonstrates that spasm of the intracranial arteries is not connected with changes in metabolism but is brought about through direct excitation of adrenergic structures of the intracranial vessels by the mediator. In order to discover which type of adrenergic structure participates in the development of these constrictor responses, the effect of pharmacological agents selectively inhibiting α- and β-adrenergic structures on these responses was studied. The experiments showed that phenoxybenzamine (1 mg/kg) considerably inhibits the responses of the cerebral blood flow to stimulation of adrenergic nerves (Fig. 1). The other α-adrenoblocking agent, dihydroergotoxin, had the same action. One of the experiments in which a technique of resistography and intracarotid injection of dihydroergotoxin (0.2 mg) was used is illustrated in Fig. 2. Meanwhile, the β-adrenoblocking agent propranolol did not weaken responses of the intracranial vessels to stimulation of the cervical sympathetic nerves (Fig. 2).

This analysis thus showed that the constrictor response of the cerebral vessels is caused by excitation of α-adrenergic structures. Special experiments with noradrenalin confirmed this conclusion. When injected into the arterial systems of the brain, noradrenalin considerably reduced the volume velocity of the intracranial blood flow.

The results described above provide conclusive evidence of the importance of α-adrenergic structures of the intracranial vessels in the regulation of the cerebral circulation and in the development of intracranial angiospasms.

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