ROLE OF ADRENERGIC STRUCTURES IN FUNCTIONAL CONTROL OVER THE CEREBRAL CIRCULATION

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An investigation of the cerebral circulation by the thermoelectric method showed that stimulation of the cervical sympathetic nerve leads to considerable changes in the blood supply to the brain. The changes in blood flow are biphasic in character: An initial small increase is followed by a decrease below the original level. Pharmacological analysis with α and β adrenoblockers showed that the constrictor response of the cerebral vessels is due to excitation of α-adrenergic structures and the dilator response to excitation of β-adrenergic structures. A possible mechanism of these changes is postulated.

KEY WORDS: α- and β-adrenergic structures; α and β adrenoblockers.

When studying the role of the sympathetic nervous system in the regulation of the cerebral circulation most workers have noted that stimulation of the cervical sympathetic nerve (CSN) induces constriction of the cerebral vessels [3, 6, 7, 10]. However, some investigators found no appreciable effects [9, 12] or, on the contrary they actually found vasodilator responses of the cerebral vessels to stimulation of CSN [4, 8, 14]. Accordingly, opinions at present differ regarding the influence of CSN on the cerebral circulation.

The writer's earlier investigations [1] showed blocking the cervical sympathetic nerve changes the character of the response of the cerebral vessels to hypercapnia. Under these conditions the sympathetic nervous system clearly played a leading role in the regulation of the blood supply to the brain.

The object of the present investigation was to study the role of sympathetic influences and, in particular, the role of α- and β-adrenergic structures in the regulation of the cerebral circulation.

EXPERIMENTAL METHOD

Experiments on 47 cats weighing 2.5-3.5 kg were carried out under general anesthesia. The blood flow was recorded in symmetrical areas of the parietal cortex by means of thermoelectric probes suitable for qualitative analysis of the response of the blood flow to appropriate stimulation.

The CSN was stimulated unilaterally in its middle third. Maximal changes in blood flow in the parietal cortex occurred in response to electrical stimulation by square pulses (5-15 Hz, 1 msec, 5-10 V) and were unilateral in character.

Dihydroergotoxin (1 mg/kg) was used as the α adrenoblocker and propranolol (0.1 mg/kg) as the β adrenoblocker; both drugs were injected intravenously.

EXPERIMENTAL RESULTS

The very first experiments showed that the character of response of the blood flow in the parietal cortical vessels depended on the duration of CSN stimulation. Stimulation for 10 sec was accompanied by an increase in the blood flow in the parietal cortical blood vessels (Fig. 1a). On the cessation of stimulation the blood flow immediately began to decrease and fell below its initial level, to which it returned after

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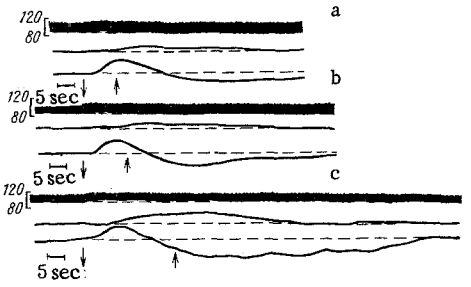

Fig. 1

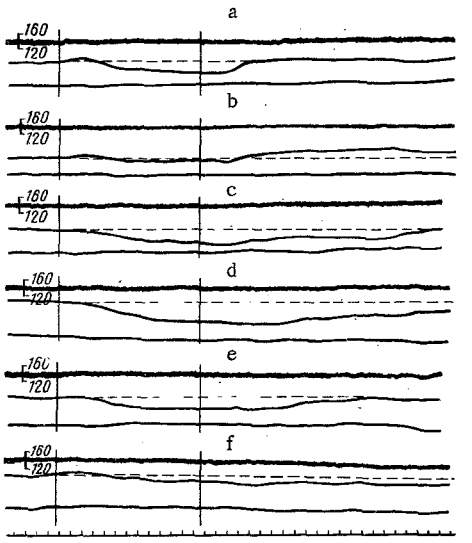

Fig. 2

Fig. 1. Effect of duration of stimulation on character of response of parietal cortical blood flow to stimulation of CSN: a) 10 sec, b) 15 sec, c) 30 sec. From top to bottom: arterial pressure, blood flow in symmetrical point of parietal region, blood flow in parietal region on side of CSN stimulation. Arrows mark beginning and end of stimulation. Time marker 5 sec.

Fig. 2. Change in character of response of cerebral blood flow in parietal region to CSN stimulation after blockade of adrenergic β receptors: a) character of changes in cerebral blood flow in response to CSN stimulation; b) 5 min after, c) 15 min after, d) 45 min after, e) 1 h after, and f) 2 h after injection of propranolol. From top to bottom: arterial pressure, parietal cortical blood flow on side of CSN stimulation, blood flow in symmetrical area of cortex. Vertical lines show beginning and end of stimulation. Time marker 5 sec.

1-2 min. Prolongation of CSN stimulation to 15 sec caused a decrease in the blood flow to be observed actually during stimulation (Fig. 1b). Accordingly, the duration of stimulation of the nerve was increased to 30 sec (Fig. 1c) and then to 1-2 min.

The experiments showed that the response of the parietal cortical vessels to prolonged stimulation (1-2 min) of CSN developed as follows. After a very short (10-15 sec) increase in the blood flow, it fell below the initial level. After the end of stimulation the blood flow returned to normal within 1-2 min.

The response of the parietal cortical vessels to prolonged CSN stimulation was thus biphasic in character: The first phase was a small increase in the blood flow, the second phase a decrease below the initial level followed by gradual recovery (Figs. 2a and 3a).

This biphasic character of the response of the parietal cortical vessels warrented an investigation of what factors gave rise to these effects during prolonged CSN stimulation. For this purpose the role and relative contribution of α- and β-adrenergic structures in this response were studied.

After intravenous injection of propranolol CSN was stimulated at an interval of 10-15 min (under the same conditions) and observations were made on the character of the responses of the cerebral vessels. As the blockade of the β-adrenergic structures developed the response of the cerebral vessels to CSN stimulation changed from biphasic to monophasic. The phase of increase disappeared 5-10 min after injection of the blocker, leaving only the phase of a decrease in the cerebral blood flow. The decrease in blood flow was more marked in this case than that after stimulation of CSN without the use of the blocker (Fig. 2b-e).

In the experiments with blockade of the α-adrenergic structures with dihydroergotoxin the response of the parietal cortical vessels to repetitive CSN stimulation also was changed. In this case conversion of the biphasic response of the blood flow into monophasic was of the opposite character. By contrast with the experiments with blockade of the adrenergic β receptors, in these cases only the phase of increase of blood flow remained (Fig. 2b-d).

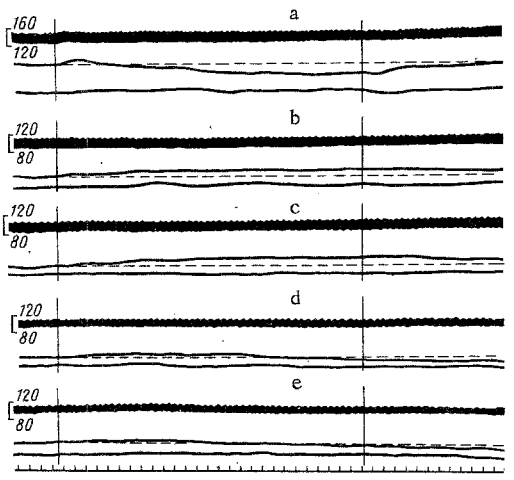

Fig. 3. Change in character of response of cerebral blood flow in parietal region to CSN stimulation after blockade of adrenergic α receptors. Legend as in Fig. 2.

Characteristically, 2-2.5 h after the injection of propranolol or dihydroergotoxin, the response of the parietal vessels to stimulation of CSN became similar to the original biphasic response (Fig. 2f, Fig. 3e). The experiments thus showed that adrenergic blockers can be used to subdivide the response of the parietal cortical vessels to electrical stimulation of CSN into its component parts: a phase of increase and a phase of decrease in the blood flow.

The results showing changes in the blood flow in the parietal region in response to stimulation of CSN against the background of blockade of one or another type of adrenergic structure are in harmony with the scheme proposed by Ahlquist [5]. According to this scheme, adrenergic α receptors, which react with catecholamines in smooth muscles, lead to vasoconstriction. In turn, adrenergic β receptors, when reacting with catecholamines acting upon them, lead to relaxation of the vessels and, correspondingly, to an increase in the blood flow.

The biphasic character of changes in the cerebral blood flow in response to electrical stimulation of CSN can evidently by explained by the cyclic nature of the action of biogenic amines through direct excitation of the corresponding adrenergic structures of the intracranial vessels. The beginning of CSN stimulation is accompanied by liberation of catecholamines, which also react with adrenergic β receptors (causing an increase in the blood flow), but prolonged stimulation and catecholamine accumulation cause activation of adrenergic α receptors, as a result of which the phase of increase in blood flow is replaced by a phase of decrease.

This hypothesis, in the writer's view, is supported by the results of pharmacological analysis of effects of catecholamines on the brain vessels. Gaevoi [2] and Oberdörster et al. [13], for instance, who investigated the character of responses of the cerebral vessels to various doses of adrenalin and noradrenalin, observed that the degree of vasoconstriction depends on the doses given. After administration of α adrenoblockers, noradrenalin did not alter the lumen of the vessels, whereas adrenalin not only did not constrict but, on the contrary, it actually dilated the vessels. After blockade of the adrenergic β receptors, the action of adrenalin and noradrenalin was more marked. These workers concluded from their observation that adrenalin in small doses reacts with adrenergic β receptors and in large doses with adrenergic α receptors. As regards noradrenalin, adrenergic β receptors are slightly sensitive whereas the α receptors are highly sensitive to it. It can accordingly be postulated that the authors cited above did not observe vasodilatation in response to adrenalin because the doses used were definitely greater than those capable of revealing the phase of interaction with adrenergic β receptors. The phase of decrease in blood flow exceeds the phase of increase in blood flow in all probability because all the catecholamines liberated during CSN stimulation are destined for the α receptors. Furthermore, some workers [11] have concluded that the vascular territory of the brain is in general a typical α region. Consequently, the vasoconstrictor responses of the vessels with a decrease in blood flow are more marked in character.

There is thus reason to suppose that the biphasic character of response of the cerebral vessels observed in these experiments to electrical stimulation of CSN can be explained by close interaction between α- and β-adrenergic structures.

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