CHOLINERGIC MECHANISM OF CORONARY VASODILATATION

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During electrical stimulation of preoptic area of the hypothalamus, dilatation of blood vessels of the skeletal muscles is accompanied by active dilatation of the coronary vessels. The response of the coronary vessels is blocked by atropine.

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Numerous investigations, mainly by Swedish physiologists [1, 2, 4, 10, 12, 13], have shown that stimulation of the motor cortex, the corpus callosum and hypothalamus causes vasodilatation in the skeletal muscles and vasoconstriction in several internal organs (kidneys, intestine). This reaction is seen particularly clearly during stimulation of the preoptic area of the anterior hypothalamus (the "protective center" of emotional responses). Muscular vasodilatation is blocked by atropine. It is, therefore, due to excitation of the cholinergic fibers of sympathetic nerves.

It is not yet clear whether the cholinergic mechanism of vasodilatation also applies to the coronary vessels. Unlike the vessels of skeletal muscles, the myocardial vessels are under direct adrenergic control [3]. In recent years by direct stimulation, cholinergic vascular fibers have been discovered in the cardiac sympathetic nerves [9], although the reactions of the coronary vessels to stimulation of the centers of cholinergic sympathetic innervation have not been studied.

In this paper, we describe data showing that during stimulation of the hypothalamus cholinergic dilator responses may be observed in the same experiments both in the blood vessels of skeletal muscles and in the heart.

EXPERIMENTAL METHOD

Acute experiments were performed on cats anesthetized with chloralose (50 mg/kg). The bipolar stimulating electrode was introduced into the preoptic area of the anterior hypothalamus on the left side, 1.5 mm below the anterior cerebral commisure (stereotaxic coordinates: A = 14.5, L = 1.5, H = 1.5). Stimulation was by square pulses (voltage 6 V, frequency 40 cps, pulse duration 1.5 msec, duration of stimulation 1 min). The volume velocity of the blood flow was recorded by a thermoelectric method in one branch of the left descending coronary artery (exposed heart, artificial respiration), and in the femoral vein. The venous outflow reflects the blood supply to the hind limb sufficiently completely [1, 4]. Changes in the thermoelectric current were recorded visually on the scale of a mirror galvanometer; or, after amplification by a F-117 photoelectric amplifier, they were recorded on a type N-700 loop oscillograph. The blood pressure was measured in the carotid artery by a mercury manometer and recorded on a kymograph or oscillograph, in the latter case, the resistance of a column of salt solution in the mercury manometer being measured by platinum electrodes soldered into the manometer. Before the experiment began the vagus nerves were divided bilaterally in the neck (to exclude compensatory baroreceptor reflexes on the heart).

EXPERIMENTAL RESULTS AND DISCUSSION

In all 14 experiments (53 tests) stimulation of the preoptic area lowered the arterial pressure on the average by 30.9±1.7 mm. The depressor reaction began 5-10 sec after stopping the stimulation. The arterial pressure returned to its original level 2-9 min after the end of stimulation. An increase in venous outflow from the hind-limb muscles was constantly observed against the background of the depressor reaction. The venous outflow remained high for 30-180 sec after stimulation (Fig. 1, A).

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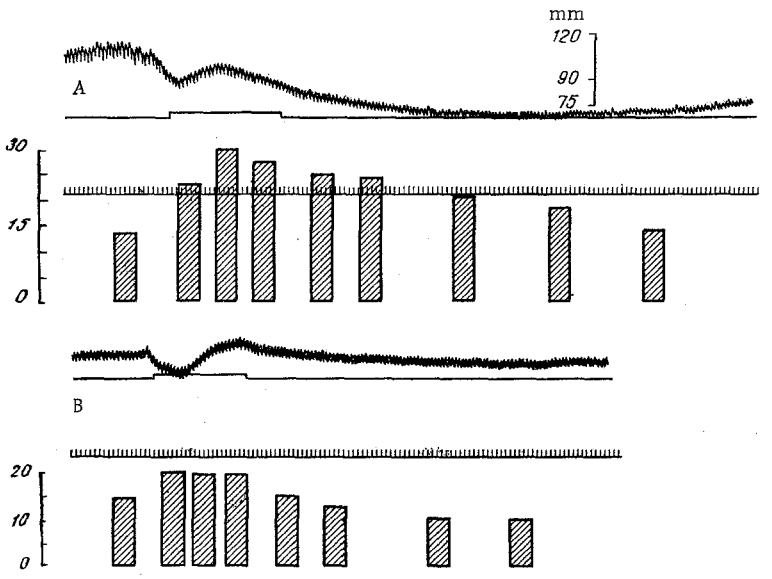

Fig. 1. Changes in blood pressure and in muscular and coronary blood flow during stimulation of preoptic area of hypothalamus in a cat. A) Reaction of muscular vessels; B) coronary. Experiment on February 7, 1966. From top to bottom: blood pressure, stimulation marker, time marker (3 sec), volume velocity of blood flow expressed in mm of galvanometer scale.

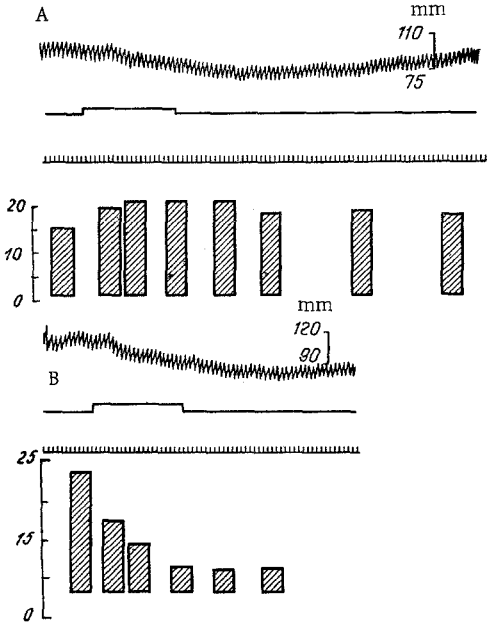

Fig. 2

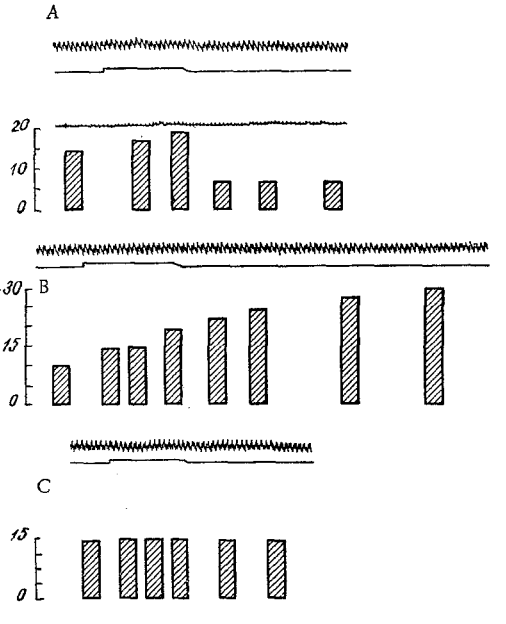

Fig. 3

Fig. 2. Reaction of coronary blood flow to stimulation of preoptic area of hypothalamus (A) and distortion of reaction after injection of atropine (B). Legend as in Fig. 1. Experiment on December 12, 1965.

Fig. 3. Changes in muscular and coronary blood flow during stimulation of preoptic area of hypothalamus in a cat with denervated adrenal (second adrenal removed). A reaction of coronary vessels; B) muscular; C) abolition of reaction of muscular vessels by atropine. Legend as in Fig. 1. Experiment on January 14, 1966. Arterial pressure on all kymograms at level of 75 mm.

In 12 of the 14 experiments an increase in the coronary blood flow was observed against the background of the depressor reaction. This reaction was usually found only during stimulation, starting 10-15 sec after its beginning; after stimulation the blood flow fell still further (Fig. 1B), and then rose again to its initial level when the arterial pressure restored. In two experiments, with a particularly marked fall of arterial pressure (by 40 and 70 mm), a decrease in the coronary blood flow was observed during stimulation.

The pulse rate during stimulation was the same as initially (159±3.2/min).

Intravenous injection of atropine (0.5 mg/kg) abolished (after 15-20 min) the increase in venous outflow from the limb and in the coronary blood flow during stimulation (Fig. 2B). Acetylcholine (20 μg/kg, intravenously) reproduced the change in coronary blood flow observed during hypothalamic stimulation.

Stimulation of the "protective center" of the hypothalamus leads to liberation of adrenalin by the adrenals [8, 11, etc.]. To exclude this factor, four experiments were performed on animals after preliminary (3-4 days beforehand) denervation of one adrenal and removal of the other. In three experiments of this series the arterial pressure was stabilized at a low level and remained unchanged during stimulation, while the increase in the coronary blood flow and venous outflow from the limb persisted (Fig. 3). In one experiment the changes were essentially indistinguishable from those in the main series.

Hence, during stimulation of the center of cholinergic muscular vasodilatation in the diencephalon, an accompanying dilatation of the coronary vessels takes place. The active character of this coronary dilatation is shown by independence of the changes in the coronary blood flow of fluctuations of blood pressure (an increase in blood flow during the depressor reaction or in the absence of changes in pressure). The cholinergic nature of the reaction of the coronary vessels is demonstrated by its blocking by atropine and reproduction by acetylcholine. Cholinergic influences on the coronary vessels were mediated through the sympathetic cardiac nerve, for the vagus nerves had been divided.

In general, the character of the changes in blood pressure during stimulation of the hypothalamic center of cholinergic sympathetic vasodilatation depends on the balance between muscular vasodilatation and the accompanying vasoconstriction in the abdominal viscera [3, 4]. Meanwhile strengthening of the cardiac contractions is observed [12]. The dilatation of the muscular and coronary vessels which we recorded should, therefore, be regarded as part of a generalized excitation of the sympathoadrenal system mediated through cholinergic channels. The absence of changes in pulse rate suggests that in our experiments no stimulation of the cardio-inhibitory center of the diencephalon took place, during excitation of which general vasodilatation, weakening of the cardiac contractions, and bradycardia resulting from inhibition of sympathetic tone are observed [5-7].

It may be postulated that the vessels of the skeletal and heart muscle are indistinguishable, in principle, as regards the neural mechanism of their dilatation during stimulation of the diencephalon, although the coronary vasodilatation is evidently less marked.

Uvnäs [13] showed that muscular vasodilatation is not accompanied by an increase in oxygen absorption. This type of vasodilatation is, of course, favorable to the heart because, while ensuring a rapid inflow of blood, it is not accompanied by any increase in metabolism of the myocardium.

The biological significance of cholinergic coronary dilatation in the intact organisms is not perfectly clear. It is perhaps exhibited only in specific conditions when adrenergic influences on the heart are removed. However, the possibility is not ruled out that this mechanism is one of a series of adaptive neurogenic reactions of the heart to physical loading.

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