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ROLE OF THE CHOLINERGIC NERVOUS MECHANISM IN REGULATION OF AN ADEQUATE BLOOD SUPPLY TO THE RABBIT CEREBRAL CORTEX

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The principal vascular effector regulating an adequate blood supply to the cerebral cortex is the system of small pial arteries (caliber under 100 μ), including its active parts or sphincters, at places where the small pial arteries branch from larger ones, and terminal segments of the pial arterial network, namely the precortical arteries [1, 5, 6, 12]. The mechanism of regulation of an adequate blood supply to the cortex may involve both direct action on smooth muscles of the vessels, which are effectors of humoral agents formed in brain tissue, and neurogenic vasomotor influences on them, or the combined action of both these mechanisms.

The aim of this investigation was to study the role of cholinergic control in regulation of an adequate blood supply to the cerebral cortex.

EXPERIMENTAL METHOD

Experiments were carried out on 12 rabbits of both sexes weighing 2-3 kg. The animals were anesthetized by intravenous injection of urethane (1 g/kg) and additionally immobilized with the muscle relaxant suxamethonium (10 mg/kg, intravenously). The lungs were ventilated by an artificial respiration apparatus and the depth and frequency of respiration were maintained at the same level as before injection of suxamethonium. After tracheotomy the skull was widely trephined for intravital microfilming of the pial arteries. The pial arteries were photographed under a magnification of 80. The negatives thus obtained were

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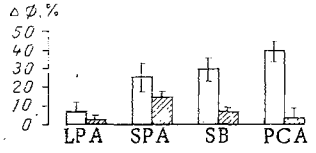

Fig. 1

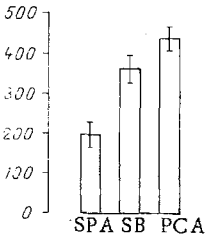

Fig. 2

Fig. 1. Dilatation of different parts of pial arterial system (in % of original) before (unshaded columns) and after (shaded columns) blocking of cholinergic transmission by atropine under conditions of enhanced brain neuronal activity due to application of 0.5% strychnine. LPA) Large pial arteries (over 100 μ); SPA) small pial arteries (under 100 μ); SB) sphincters of branches; PCA) precortical arteries. Data shown as arithmetic mean values and their errors.

Fig. 2. Density of cholinergic fibers in region of different parts of pial arterial network (arithmetic mean values and their errors). Legend as to Fig. 1. Data from [7].

projected on a large screen and the relevant regions of the pial arterial network were measured frame by frame (the final magnification of the object was 500). The results are presented below in the form of arithmetic means and their errors. The significance of differences was determined by Student's test. The adequate blood supply to the brain tissue was disturbed by application of 0.5% strychnine solution to the brain surface, stimulating its activity. Since strychnine does not dilate the pial arteries through its direct action on their walls [4], it might be suggested that the vasodilatation thus arising depended on cortical influences on the vessels. Cholinergic transmission to the walls of the pial arteries was blocked by microapplication of a 70 μM solution of atropine in artificial CSF of the following composition: 156 mM Na^+, 3 mM K^+, 1.5 mM Ca^2, 151 mM Cl^-, 11 mM HCO_3^-, which itself did not affect the vascular smooth muscles, to their walls. A glass micropipet, with a tip 5-8 μ in diameter, was used for microapplication. By means of a rigid polyethylene tube the micropipet was connected to a microsyringe with a capacity of 25 μl. The micropipet was introduced into the subarachnoid space surrounding the pial arteries by means of a micromanipulator under microscopic control. The results of the physiological experiments agreed with data on acetylcholinesterase activity in different segments of the pial arteries determined histochemically in rabbits [7, 9].

EXPERIMENTAL RESULTS

Serial microfilming at the beginning of the experiments showed that the diameter of the vessels studied under control conditions was unchanged as a rule. Only infrequent (two or three times per hour) changes, negligible in magnitude, in the diameter of the small pial arteries, sphincters, ramifications, and precortical arteries were observed.

After local application of strychnine to the brain surface the characteristic response of the pial arteries and their active segments (sphincters of branches and precortical arteries) was dilatation; the degree of dilatation of the different segments, moreover, differed (Fig. 1). Dilatation was strongest in the precortical arteries, less strong in sphincters of branches, and weaker still in the small pial arteries (caliber under 100 μ). Dilatation of pial arteries over 100 μ in caliber was very weak.

After cholinergic nervous transmission had been blocked by atropine (Fig. 1) functional dilatation of the vascular effectors regulating the adequate blood supply to brain tissue (small pial arteries, sphincters of branches, and precortical arteries) was much weaker than before the blockade; the differences, moreover, were statistically significant ($0.05 < P < 0.1$ for small pial arteries, $0.001 < P < 0.01$ for sphincters of branches, and $P < 0.001$ for

precortical arteries). However, the reduction in the degree of dilatation under these conditions took place in the opposite order, i.e., the degree of dilatation of the small pial arteries was greater than that of the sphincters of the branches, and in the latter, it was greater than in precortical arteries (although in this last case the differences were not statistically significant).

These data show that regulation of an adequate blood supply to brain tissue can take place at the level of the territory of one radial artery. Less frequently sphincters of branches in whose territory of distribution several precortical arteries, giving rise to radial arteries, may often be found, are involved in this regulation. The function of the small pial arteries, in whose territory several sphincters and a correspondingly larger number of precortical arteries may be found, is even less conspicuous. No significant difference could be found between the degree of dilatation of the large pial arteries before and after blocking of cholinergic transmission. This also indicates that these vessels do not play an active part in this type of regulation of the cerebral blood flow.

The differences found correlate with the density of the cholinergic innervation in the region of different segments of the pial arteries participating in the blood supply to the cerebral cortex. Although the diameter of the small afferent pial arteries is always greater than the diameter of the sphincters of the branches and precortical arteries, the density of cholinergic fibers in the region of these latter was much greater (Fig. 2). It can be postulated that the cholinergic innervation of the large branches of the pial arteries is destined for other types of regulation of the cerebral blood flow.

It can be concluded that functional dilation of the small pial arteries and their active regions (sphincters of branches and precortical arteries) in connection with regulation of an adequate blood supply to the cerebral cortex is largely determined by a cholinergic nervous mechanism. Regulation of the blood flow can take place in extremely small regions of the cortex, i.e., at the level of territories of distribution of a single radial artery, which in rabbits measures 0.2 mm^2 of the cortical surface [13]. The great importance of the morphologically demonstrable abundant innervation of the walls of the pial arteries, whose physiological role was once considered to be negligible, must be emphasized. The present experiments are in agreement with the gradually accumulating physiological [2, 3, 10], and pharmacological [8, 11] evidence of the neurogenic and, in particular, cholinergic control of an adequate blood supply to the brain tissue.

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