EFFECT OF THE SYMPATHETIC NERVOUS SYSTEM ON CHANGE IN RESISTANCE OF THE BLOOD–BRAIN BARRIER IN ARTERIAL HYPERTENSION

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In recent years a new trend has evolved in the study of the effect of the sympathetic nervous system (SNS) on resistance of the blood–brain barrier (BBB) in arterial hypertension [5]. Electrical stimulation of the superior cervical ganglion (SCG) during arterial hypertension has been shown to protect the BBB against rupture [6, 9, 10]. The present writer showed that natural activation of SNS can also preserve the integrity of the BBB and the vascular bed of the brain [1]. The results of this investigation suggested that the adaptive-trophic function of the SNS is realized through regulation of the blood pressure in capacitive vessels. This hypothesis has also been proved in the literature [2, 7, 8]. This regulation, in the present writer's opinion, is effected through a change in the passive and active damping properties of the walls of the resistive vessels, which respond differently to changes in vascular tone [3, 4].

The aim of the present investigation was to study the effect of a change in rigidity of the walls of the brain vessels to regulation of permeability of the BBB in arterial hypertension. A change in rigidity was produced by removal of SCG, by reflex activation of SNS combined with self-regulating responses of the cerebral vessels, and by intravenous injection of angiotensin (AT) or noradrenalin (NA).

EXPERIMENTAL METHOD

Experiments were carried out on cats of both sexes weighing from 2.7 to 4.0 kg under chloralose anesthesia (40 mg/kg) with the addition of pentobarbital (6 mg/kg). The right SCG was removed from 12 animals and a mock operation performed on another four. The arterial pressure (BP) was measured by means of a strain gauge transducer in the right brachial artery. Changes in the systemic BP were induced by means of an apparatus for creating hemodynamic shock (AHDS; Fig. 1). The AHDS consisted of two air reservoirs (1 and 2) into which air was pumped up to an assigned level by the compressor 5, thus creating a pressure controlled by the manometers 7. Reservoir 3 of the apparatus was half filled with blood-substitute fluid, kept at constant temperature (38 ± 0.5°C) by means of the apparatus 4. The reservoir 3 was connected by the catheter 8 to the animal's abdominal aorta. The pressures assigned in reservoirs 1 and 2 could be transmitted separately by means of the cocks 6 to reservoir 3. If the assigned pressure was lower then the animal's systemic BP, blood from the abdominal aorta entered the reservoir 3 and the animal's systemic BP was kept at the low level. If the assigned pressure was higher than the systemic BP, the blood substitute fluid from reservoir 3 entered the animal's abdominal aorta and the systemic BP was maintained at a high level. The AHDS was connected to the animal's abdominal aorta. Not less than 1 h after removal of the SCG and 10-15 min before a sharp rise in BP, a 3% solution of Evans' blue in 10% albumin solution was injected intravenously into the animal as a marker of disturbance of the permeability of BBB. Before a sharp rise in BP, to trigger reflex activation of the SNS and to obtain the greatest difference for the change in rigidity of the vascular walls between the circulatory systems of the desympathized and intact cerebral hemispheres, BP was first lowered (in the experiments of series I to 50-60 mm Hg and in series II to 70-80 mm Hg). In both series BP was kept low for 25-40 sec, after which it was raised sharply to 230-240 mm Hg and kept at that level for not less than 4 min by means of the AHDS and intravenous injection of AT or NA in doses of 30 and 40 μg/kg/min, respectively. In series I AT (NA) began to be in-

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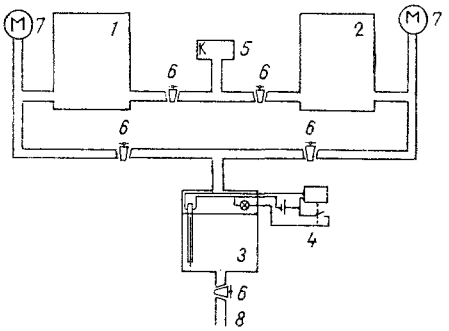

Fig. 1. Scheme of the AHDS.

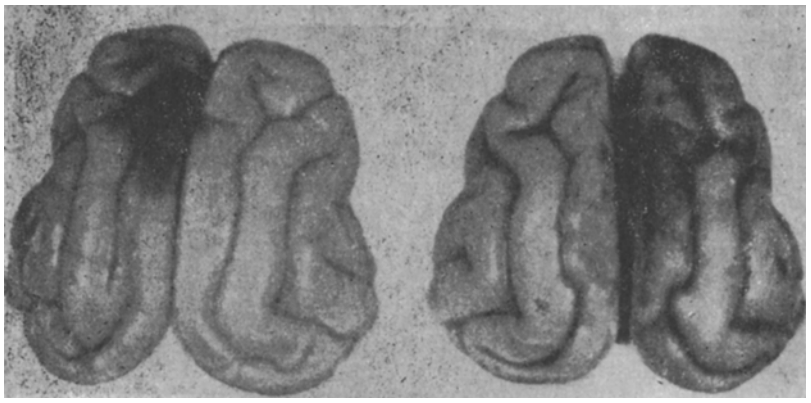

Fig. 2. Disturbance of BBB in cat cerebral hemispheres. Staining of intact (a) and desympathized (b) cerebral hemispheres by extravasation of Evans' blue.

jected immediately after the rise of BP, in series II after the fall of BP. At the end of the experiment the animal was killed by intravenous injection of saturated KCl solution. Disturbance of the permeability of the BBB was estimated visually by the intensity of staining of the cerebral hemispheres due to extravasation of Evans' blue.

EXPERIMENTAL RESULTS

In the experiments of series I the brain of five of the six animals was stained by extravasation of Evans' blue; in all five animals the right, desympathized hemisphere was stained more strongly (Fig. 2b). No staining was observed in one animal. Staining of the iris of the eyes was observed in all six animals, more intensively in the right eye. In one of the two control animals of this series, in which the iris of the two eyes was stained equally, no staining of the cerebral hemispheres was observed, whereas in the other there was no difference in the intensity of staining of the irises and cerebral hemispheres.

By contrast, in the experiments of series II more intensive staining of the left, intact hemisphere was observed in four of the six animals (Fig. 2a). In the other two animals staining of the hemispheres was not observed. Unlike the animals of series I, more intensive staining of the iris of the left eye than of the right was observed. In two control animals of this series staining of the right and left hemispheres and of the iris of the right and left eyes did not differ in intensity.

When BP fell to the lower limits of the self-regulating capacity of the cerebral circulation (50-60 mm Hg) dilatation of the cerebral vessels took place. This phenomenon was evidently based on a decrease in rigidity of the vascular walls, i.e., an increase in their passive damping properties and an associated impairment of their vasoconstrictor properties (a reduction in their active damping properties). In the half of the brain with intact sympathetic innervation activation of SNS during hemorrhagic hypotension was to some extent counteracted by the processes mentioned above, preventing a decrease in rigidity of the vascular walls and preserving the ability of the vessels to contract actively (damping of the intravascular pressure). As the result of this, during the subsequent sharp rise in systemic BP the per-

meability of the BBB was disturbed in the desympathized cerebral hemisphere on account of inadequate damping of the intravascular pressure along the path to the exchange vessels, whereas BBB of the intact hemisphere remained relatively well preserved (Fig. 2b).

Lowering BP in the experiments of series II to 70-80 mm Hg led to a more moderate self-regulatory decrease in rigidity of the walls of the cerebral vessels, which was evidently restored to normal in the desympathized hemisphere after injection of AT or NA, whereas in the intact hemisphere it was considerably increased, reducing the passive damping properties of vessels of the intact hemisphere to a minimum. As a result of this, by the laws of wave interference and damping [3, 4], the intravascular blood pressure in the circulatory system of the intact hemisphere increased considerably and could not be extinguished on the way to the exchange vessels on account of the active damping component. The increase in intravascular pressure in the capillaries led to distrubance of the tight junction between the endothelial cells and breakdown of the BBB of the intact hemisphere despite the relative integrity of BBB of the desympathized hemisphere (Fig. 2a). It can be tentatively suggested that fine control of BBB permeability under normal conditions is also achieved through regulation of the intravascular pressure, which does not disturb the tight junction between the endothelial cells, as in the present case, but alters the area of the diffusion surface of the capillary wall on account of moderate stretching by intravascular pressure.

It must be pointed out that, for reasons of an evolutionary nature that are quite clear, the cerebral circulation responds to physiological vasoconstrictor stimuli by a smaller narrowing of its lumen, and it is therefore quite possible that the passive component of damping plays a more important role in the regulation of BBB permability than in regulation of the permeability of other tissue–blood barriers. The above arguments are also valid, evidently, for explanation of the staining of the irises.

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