EFFECT OF ADRENALIN ON ARTERIOVENOUS DIFFERENCE IN CONCENTRATION OF TOTAL AND INDIVIDUAL PHOSPHOLIPIDS IN WHOLE BLOOD

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Injection of adrenalin (0.5-1 mg) into the carotid artery of dogs caused, after an interval of 5-20 min, a substantial increase in the content of total and individual phospholipids (except lysolecithins) in the blood flowing from the brain.

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Our previous investigations revealed a large increase in the content of total phospholipids [5, 6] and of total, bound, and free cholesterol [6-8] in the blood flowing from the brain after electrical stimulation of the skin. The criticism was made that the action of adrenalin may have become implicated in a complex group of hormonal changes, developing under the influence of this stimulus [9]. The investigations of Esayan and co-workers [10] revealed a marked increase in the blood level of the catecholamines in unconditioned and conditioned defensive reflexes. Buniatian and co-workers [11] analyzed the hyperlgycemic effect produced by γ-aminobutyric acid injected intravenously and intraperitoneally in massive doses, and concluded that certain portions of the adrenal system were possibly involved in the sphere of its action.

Physiological states brought to light by the action of adrenalin, its stimulant action in small doses on the secretion of adrenalin-like substances in the body [12-15], and also the glycogenolytic and hyperglycemic effects observed in these circumstances play an essential role in the onset of the corresponding changes in the energy metabolism of the brain. This is important in the assessment of additional potential sources of energy for nerve tissue, important among which are phospholipids, taking part in the metabolism of the brain of animals under the conditions of glucose deprivation [16, 17].

For the reasons detailed above we decided to study the quantitative variations in the total and individual phospholipids of the blood flowing into and from the brain taking place under the influence of various doses of adrenalin.

EXPERIMENTAL METHOD

Experiments were carried out on dogs. The experimental procedures and the method of chromatographic fractionation of the phospholipids of whole blood were the same as in our previous investigations [18]. Adrenalin was injected into the carotid artery in doses of 0.5, 0.75, and 1 mg. Blood for the investigations was taken from the common carotid artery and external jugular vein before the experiment and 5 and 20 min after the corresponding manipulations.

EXPERIMENTAL RESULTS

At the beginning of the investigations we used small doses of adrenalin (0.1-0.3 mg per animal weighing 20 kg). Although under these conditions some of the characteristic external signs of excitation (mydriasis and a very small rise in the heart rate) developed, the study of the arteriovenous difference in the content of total and individual phospholipids revealed no appreciable changes. According to published reports [19], injection of adrenalin into the carotid artery in a dose of 10 μg/kg leads to the development of inhibition of central (brain) synapses. The equivalent dose for an animal weighing 20 kg is 0.2 mg, i.e., the dose which proved ineffective when studying the arteriovenous difference of phospholipids. For this reason we increased the dose of adrenalin to 0.5-1 mg.

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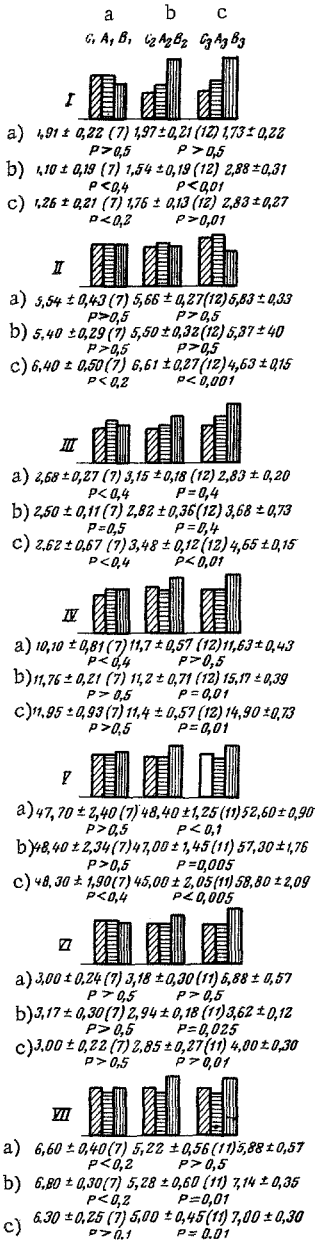

Fig. 1. Quantitative changes in phosphorus of individual phospholipids. I) Unidentified phospholipid; II) lysolecithins; III) monophosphoinositol phosphatides; IV) sphyngomyelins; V) lecithins; VI) serine phosphatides; VII) ethanolamine phosphatides of whole blood (arteriovenous difference; C) large subcutaneous vein of the leg, A) common carotid artery, B) external jugular vein) in μg/ml before experiment, and 5 and 20 min after injection of adrenalin.

In the concentration studied, adrenalin injected into the carotid artery evoked a number of signs of excitation, and against this background a marked increased was observed in the total phospholipid phosphorus concentration in the blood flowing from the brain. Studies of the chromatographic picture of individual phospholipids revealed characteristic aspects of the action of adrenalin on the arteriovenous difference in concentration of individual phospholipids in whole blood. As Fig. 1 shows, in contrast to all stimuli which we studied earlier (electrical stimulation of the skin, γ-aminobutyric acid), adrenalin raised the level of nearly all phospholipid fractions in the blood flowing from the blood flowing from the blood, i.e., of acid phospholipids (monophosphoinositol phosphatides, serine phosphatides, and an unidentified phospholipid of the first strain), and also all the neutral phospholipids (sphyngomyelins, lecithins, and ethanolamine phosphatides) except the lysolecithins, the content of which undergoes the opposite changes. This evidently takes place because of their absorption by the brain. The pattern described was seen most clearly 20 min after injection of adrenalin. As in the previous investigations the increase in the phospholipid phosphorus concentration in the blood flowing from the brain was chiefly attributable to neutral phospholipids, especially lecithin.

Changes in the arteriovenous difference in concentration of various substances connected with brain metabolism may take place on account of fluctuations in the velocity of the cerebral circulation. This was studied in a small series of investigations in which the tested doses of adrenalin were injected into the carotid artery. An initial and appreciable increase in the volume velocity of the cerebral circulation was observed, followed by a decrease and full restoration of the original picture within the first 5 min. We concluded from these findings that the quantitative changes observed in the total and individual phospholipids of whole blood, whether supplying the brain or flowing from it, were not due to these fluctuations in the cerebral circulation, but took place evidently as a result of corresponding changes in the metabolism of the nerve tissue. To confirm these hypotheses the quantitative changes in phospholipid phosphorus were determined at the same time in blood flowing from the leg muscles. The results of these investigations showed that the level of the individual phospholipids in whole blood taken from a large subcutaneous vein of the leg varied after injection of the tested doses of adrenalin within approximately the same limits as those observed in the arterial blood. It was thus clear that the increase in the arteriovenous difference in the phosphorus content of total and individual phospholipids in the blood flowing from the brain was specific, and probably dependent to some extent on changes in brain metabolism.

The action of larger doses of adrenalin (1.5-2 mg per animal) on the quantitative changes in the arteriovenous difference in the whole blood lipids was next studied. When these doses of adrenalin were injected into the carotid artery, marked excitation of the animal developed, usually followed in a few minutes by a sharp fall of general tone, drowsiness, and often a state of stupor. The study of the arteriovenous difference in concentration of total blood phospholipids against this background revealed opposite changes to those present at the beginning of these investigations, during the normal pattern of adrenalin excitation. In other words, a considerable decrease in the concentration of total phospholipids in the venous blood compared with the results of parallel tests on arterial blood and also

with initial tests on venous blood was found. The total phospholipid phosphorus concentration in the blood flowing from the brain 20 min after injection of adrenalin had fallen from 94 μg/ml (initial level) to 62 μg/ml, i.e., by approximately 34%. Our observations, coupled with data reported in the literature, give evidence to show that excitatory agents in large doses cause overstraining and exhaustion of the nervous system, as a result of which limiting inhibition develops, with changes opposite to the pattern of excitation [4, 10, 20]. This presumably explains the inhibition of the phospholipid metabolism of the brain studied by an isotope method and described by Dawson and Richter [21], during direct stimulation of the brain by electrodes applied to it. Using electrical stimulation of the skin, G. E. Vladimirov and co-workers [22] observed the opposite effect—a considerable increase in the rate of phospholipid metabolism (as phophorus) in the nerve tissue of albino rats at different time intervals. The results of several experiments demonstrate that, if given in different doses, the same stimulus may cause the development of diametrically opposite changes in nerve tissue metabolism. Our results are interesting in connection with assessment of the role of individual phospholipids in brain metabolism in different functional states, and they show the invalidity of earlier views on the functional indifference of the brain lipids and, in particular, of the phospholipids, to which the role purely of structural substances was ascribed.

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