resembles changes in the hemodynamics following infusion of synthetic angiotensin-II into intact adult dogs [1].

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DEPENDENCE OF PHOSPHOLIPID METABOLISM IN VARIOUS PARTS OF THE RAT BRAIN ON THE DEGREE OF LOCAL CIRCULATORY DISTURBANCE (AFTER LIGATION OF THE CAROTID ARTERIES)

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After bilateral ligation of the common carotid arteries in rats the blood supply and phospholipid metabolism were reduced considerably in the cerebral hemispheres, to a lesser degree in the diencephalon and mesencephalon, but unchanged in the medulla and cerebellum. The dependence of the degree of depression of phospholipid metabolism on the degree of disturbance of the blood supply differed in the various parts of the brain. Restoration of the blood supply was not observed 5 h after ligation of the common carotid arteries.

KEY WORDS: cerebral ischemia; phospholipid metabolism.

Of all the cardiovascular diseases the cerebrovascular are among the commonest forms: Spasms of the cerebral vessels, and thrombosis and embolism of the brain are particularly serious. These diseases are associated with various degrees of cerebral ischemia, as a rule local; in turn, this leads to anoxia of the ischemic region of brain tissue. Elucidation of the mechanism of action of the ischemic form of cerebral anoxia on brain metabolism is an essential step to the fuller understanding of the pathogenesis of these diseases and, consequently, for their timely prevention and their rational, pathogenetically oriented treatment.

Different parts of the CNS are known to respond differently to anoxia and the duration of survival of nerve cells located at different levels of the CNS in an oxygen-free environment also differs [2, 4]. This difference is manifested in the general form as lowered resistance to anoxia of the phylogenetically younger nervous formations and the comparative resistance of the older portions of the CNS, and it is associated with definite functional, metabolic, and morphological differences between different levels of the CNS.

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TABLE 1. Uptake of Dye (in mg/g wet weight of tissue) and RSR of Phospholipids in Parts of the Rat Brain at Different Times after Ligation of Common Carotid Arteries

Part of brain	Statistical index	Control		90 min after ligation				300 min after ligation			
		amount of dye	RSR	amount of dye	percent of control	RSR	percent of control	amount of dye	percent of control	RSR	percent of control
Cerebral cortex	n	13	13	13		13		8		8	
	$\bar{X}$	0,35	1,16	0,10*	28,6	0,68*	58,6	0,08*	22,8	0,45* †	38,8
	$\pm S$	0,02	0,08	0,009		0,04		0,01		0,12	
Diencephalon	n	10	10	11		11		8		8	
	$\bar{X}$	0,45	0,98	0,25*	55,5	0,87*	88,7	0,26*	57,7	0,71*	72,4
	$\pm S$	0,03	0,10	0,02		0,07		0,04		0,10	
Mesencephalon	n	8	8	13		13		9		9	
	$\bar{X}$	0,41	0,95	0,32*	78,0	0,75*	78,9	0,29*	70,7	0,77*	81,0
	$\pm S$	0,03	0,06	0,02		0,03		0,03		0,09	
Cerebellum	n	13	13	14		14		10		10	
	$\bar{X}$	0,36	1,09	0,46	127,7	1,00	91,7	0,36	100,0	1,00	91,7
	$\pm S$	0,03	0,08	0,03		0,04		0,04		0,10	
Medulla	n	12	12	14		14		11		11	
	$\bar{X}$	0,45	0,82	0,48	106,6	0,80	97,6	0,42	93,3	0,69	84,1
	$\pm S$	0,03	0,03	0,03		0,05		0,04		0,05	
Spinal cord	n	13	13	13		13		12		12	
	$\bar{X}$	0,24	0,32	0,26	108,3	0,28	87,5	0,28	116,6	0,28	87,5
	$\pm S$	0,02	0,03	0,02		0,03		0,03		0,03	

Legend. *) Significance of differences from control; †) significance of differences between different times.

However, work in the writers' laboratory has shown that in general anoxia there are more similarities than differences in the changes in phospholipid metabolism in different parts of the CNS [3], despite an essential difference in the degree of disturbance of the functions of these various parts. This similarity can be explained on the grounds that the leading factor in the depression of phospholipid metabolism is hypothermia, accompanying the acute anoxia and affecting all parts of the brain equally. The writers have postulated that in one or other type of cerebral ischemia the picture may differ from that found in general anoxia, for even after bilateral ligation of the common carotid arteries in animals the blood supply to different parts of the brain is disturbed differently [1], and this could account for the differences in the degree of disturbance of metabolic processes in these parts of the brain.

The objects of the present investigation were as follows: to compare the degree of disturbance of the blood supply in different parts of the brain in rats at various times after one-stage ligation of both common carotid arteries; to compare the degree of depression of phospholipid metabolism in different parts of the brain under these conditions.

EXPERIMENTAL METHOD

The intensity of phospholipid metabolism of nerve tissue was determined by the rate of incorporation of radioactive phosphate. Adult male Wistar rats were given an intraperitoneal injection of radioactive $Na_2H^{32}PO_4$ in a dose of 5 μCi/g, 30 or 240 min after ligation of the common carotid arteries. The thorax was opened 5 min before decapitation, the descending part of the arch of the aorta was compressed, and 3 min later, 1 ml of a 1% solution of neutral red was injected from a syringe into the left ventricle in the course of 15 sec. The animals were decapitated 60 min after injection of the isotope and the brain and spinal cord were removed, carefully freed from blood vessels and meninges, and washed with physiological saline to remove blood, after which they were divided into appropriate parts. The ischemic brain was compared with the thoracic and lumbar portions of the spinal cord. Each part of the CNS was divided into two samples of equal weight: one for determination of the content and specific radioactivity (SR) of inorganic phosphate (IP), the other for determination of the content of neutral red in the brain substance, as an index of the intensity of the blood supply to that part of the brain. Phospholipids were extracted at room temperature by a mixture of chloroform and methanol (2:1) by Folch's method and the resulting extract was washed with 0.29 M NaCl to remove IP and other nonlipid, water-soluble phosphorus compounds. The phospholipid content (in mg phosphorus/g wet weight of tissue) and the relative SR (RSR), taken as a measure of the intensity of phospholipid metabolism and calculated as the ratio between SR of phospholipid phosphorus and SR of phosphorus of the tissue IP, were determined in each part of the brain. The neutral red was extracted from the weighed sample of brain tissue 3 times at room temperature with acidified 70° ethanol, in volumes of 5, 3, and 2 ml successively. After each extraction the samples were immediately centrifuged. The pooled supernatants were treated with 1.5 ml of cold ace-

tone to clear the opalescence and again centrifuged. The supernatant was poured into graduated tubes and evaporated in a water bath at 40°C. After cooling, the samples were examined with the FÉK-M photometer with a blue filter. The content of neutral red was expressed in $\mu g/g$ wet weight of tissue.

EXPERIMENTAL RESULTS AND DISCUSSION

The greatest degree of reduction of the blood supply after ligation of the common carotid arteries was observed in the cerebral hemispheres (Table 1). The decrease was less marked in the diencephalon and mesencephalon, but was also statistically significant compared with the control. In the cerebellum and medulla no changes were found in the content of dye after ligation of the common carotid arteries. Ligation of the common carotid arteries is known to act on the reflexogenic zones of the carotid sinus, causing a marked rise of blood pressure, and this in turn increases the blood flow throughout the arterial system of the brain. In the cerebellum and medulla the increase in the blood flow along the vertebral arteries, the main sources of blood supply to these parts, evidently compensates for the deficiency of the blood supply due to exclusion of the carotid arteries. No changes likewise were found in the blood supply to the spinal cord.

A similar picture was observed as regards the intensity of total phospholipid metabolism. As Table 1 shows, the rate of incorporation of ^{32}P into phospholipids was reduced most of all in the cerebral hemispheres, and it was reduced less in the diencephalon and mesencephalon, about equally in both. Meanwhile, no changes were found in RSR of phospholipids in the cerebellum and medulla and, naturally, in the spinal cord. In the cerebral hemispheres RSR of the phospholipids was reduced not only compared with the control, but also at different times: the difference between 30-90 min and 240-300 min was statistically significant.

It can be concluded from the analysis of these results that after ligation of the common carotid arteries in rats a marked decrease in the blood supply to the cerebral hemispheres is observed, with a smaller decrease in the diencephalon and mesencephalon. The decrease in the intensity of phospholipid metabolism also was more marked in the cerebral hemispheres than in the diencephalon and mesencephalon. In other parts of the brain and spinal cord no changes were found either in the blood supply or in phospholipid metabolism.

The absence of significant differences in the degree of disturbance of the blood supply in all parts of the brain 90 and 300 min after the operation is evidence that even 5 h after ligation of the common carotid arteries the blood supply is not restored.

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