EFFECT OF ADRENALECTOMY ON INTENSITY OF PHOSPHOLIPID METABOLISM IN THE RAT BRAIN IN ANOXIA

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UDC 577.1:547.953:612.08.015:612.45

The velocity of incorporation of radioactive phosphate into individual phospholipid fractions (phosphatidic acids +polyglycerophosphatides, aminophospholipids, phosphoinositides, phosphatidylcholines, and sphyngomelins) of the cerebral hemispheres was investigated in adrenalectomized rats and rats undergoing the mock operation in anoxia. Metabolism of the investigated phospholipid fractions was depressed to a greater degree in the adrenalectomized animals than in those undergoing the mock operation, but practically equally for each fraction.

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A study of the effect of adrenalectomy on the intensity of metabolism of the total phospholipid (PL) fraction of the cerebral hemispheres of rats with normal and reduced oxygen concentrations in the inspired air showed that resistance to anoxia is decreased in adrenalectomized rats, and this is accompanied by a more marked decrease in the intensity of PL metabolism in the brain compared with animals of the control group. These differences in the response of normal and adrenalectomized animals to anoxia were absent if the latter animals received hydrocortisone, and it was therefore concluded that these changes were due to the absence or reduced content of adrenocortical hormones in the body. At a normal atmospheric pressure the intensity of metabolism of the total PL of the brain did not differ essentially in the animals of the control and experimental groups.

The object of the present investigation was to study the metabolic response of different PL fractions to anoxia and the effect of a sharp decrease in the corticosteroid content in the body on it.

EXPERIMENTAL METHOD

Experiments were carried out on adult male Wistar albino rats weighing 180-240 g. Bilateral total adrenalectomy was performed under ether anesthesia through a lumbar incision. After the operation the animals were kept on the ordinary laboratory diet with the addition of 1% sodium chloride solution. Three groups of rats were used in the experiments: group 1, undergoing a mock operation at normal atmospheric pressure; group 2, undergoing the mock operation at a reduced atmospheric pressure; group 3, adrenalectomized (on the 4th day after operation) and also under anoxic conditions.

Anoxia was produced in the rats in a pressure chamber at 220 mm Hg, the time taken to reach this "altitude" being 21 min from the start of the "ascent." Altogether the animals remained for 110 min in the pressure chamber.

To study the intensity of PL phosphate groups, the rats received a subcutaneous injection of radioactive phosphate ($Na_2HP^{32}O_4$) on a dose of 5 μCi/g body weight (animals of groups 2 and 3, immediately before transfer to the pressure chamber). The animals were decapitated 120 min after injection of the isotope, and the cerebral hemispheres were removed. Lipids were extracted by Folch's method with a 2:1 mixture of chloroform and methanol.

The PL were fractioned on silica gel columns by the method described by Dvorkin and co-workers [4]. The following PL fractions were obtained: phosphatidic acids +polyglycerophosphatides, aminophospholipids (consisting of a mixture of diacyl and plasmalogen forms of ethanolamine- and serinephosphatides, phosphoinositides, and a fraction of coline-containing PL. By means of gentle alkaline-hydrolysis by Dawson's

I. P. Pavlov Institute of Physiology, Academy of Sciences of the USSR, Leningrad. (Presented by Academician V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 68, No. 8, pp. 28-31, August, 1969. Original article submitted June 10, 1968.

TABLE 1. Relative Specific Radioactivity of Phosphorus of Individual PL Fractions from Cerebral Hemispheres of Animals Undergoing Mock Operation and of Adrenalectomized Rats in Anoxia

Group of animals	Index	Total PL	PL fractions						
			PA+PGP	APL			PI	PC	SPM
				total	diacyl	plasmalogen			
1	n	5	5	6	5	6	5	6	5
	M	1,98	5,67	0,68	0,96	0,53	9,65	1,21	0,38
	$\pm\sigma$	0,07	0,46	0,03	0,03	0,03	0,43	0,05	0,02
2-	n	5	6	6	6	6	5	6	5
	M	1,38	3,78	0,44	0,58	0,28	6,48	0,91	0,31
	$\pm\sigma$	0,02	0,23	0,02	0,03	0,01	0,35	0,04	0,02
	% Ascent of index for group 1	69,9	66,7	65,0	60,7	52,5	67,2	74,8	80,3
	P_1	<0,001	<0,01	<0,001	<0,001	<0,001	<0,001	<0,001	<0,05
3	n	7	6	7	7	7	5	5	4
	M	1,14	3,16	0,37	0,47	0,23	5,06	0,73	0,24
	$\pm\sigma$	0,04	0,09	0,02	0,03	0,02	0,32	0,04	0,01
	% Ascent of index for group 1	57,9	55,8	55,0	49,1	42,9	52,5	60,6	63,8
	% Ascent of index for group 2	83,0	83,7	85,1	81,3	81,2	78,1	80,7	78,3
	P_2	<0,001	<0,05	<0,05	<0,05	<0,05	<0,02	<0,02	<0,02

Note: P_1 represents criterion of significance of differences between relative specific radioactivity of PL for corresponding fractions from animals of groups 1 and 2; P_2, the same for animals of groups 2 and 3; individual PL fractions: PA+PGP) phosphatidic acids+polyglycerophosphatides, APL) aminophospholipids, PI) phosphoinositides, PC) phosphatylcholines, SPM) sphyngomyelins.

method [6] the fraction of aminophospholipids was separated into diacyl and plasmalogen forms, and the fraction of coline-containing PL into lecithins (phosphatidylcolines) and sphyngomyelins.

The content of lipid phosphorus and its radioactivity were determined in each fraction and the PL content of each fraction was calculated in μg P/g moist tissue. In all the PL fractions the relative specific radioactivity was calculated as the ratio between the specific radioactivity of PL phosphorus of each fraction and the specific radioactivity of the inorganic phosphate of the brain tissue. The relative specific radioactivity was used as criterion for assessing the intensity of metabolism of the phosphate groups of the individual PL fractions.

EXPERIMENTAL RESULTS

The content of total PL and their individual fractions in rats undergoing the mock operation, at a normal atmospheric pressure, corresponded to values obtained by other workers [1, 4] in experiments on intact animals. No differences were found in the content of the corresponding PL fractions in the brain tissue of animals of the three groups (Table 1). This is in good agreement with results obtained by other investigators [2, 3, 5] showing that the PL level in the brain is unchanged during exposure of the animal to various factors including anoxia. The relative specific radioactivity of all the investigated PL fractions was identical with the corresponding values for intact animals [1, 3].

The intensity of metabolism of all the studied PL fractions in the rats undergoing the mock operation and subjected to anoxia was reduced to the same degree as in intact animals [3]. The greatest decrease in metabolism in animals undergoing the mock operation was found in the fraction of plasmalogen aminophospholipids (by 47.5%), and the smallest in the fraction of sphyngomyelins (by 19.7%), while the metabolism of the other PL fractions was depressed about equally. By itself, therefore, the operation had no effect either on the content and metabolism of the individual PL fractions at a normal barometric pressure, or on the response of these fractions to anoxia.

With the same degree of anoxia, a decrease in the intensity of metabolism of all the investigated PL fractions also was observed in the adrenalectomized rats, but the changes in these animals were more marked than in those undergoing the mock operation. The degree of aggravation of depression of brain PL metabolism in the adrenalectomized rats compared with that in the animals undergoing the mock operation was practically the same for all PL fractions investigated (about 20%). The ratio between the degree of depression of metabolism of individual brain PL fractions in adrenalectomized rats was therefore the same as in animals undergoing the mock operation, i.e., metabolism of plasmalogen aminophospholipids was depressed to the greatest degree (by 57.1%), and that of sphyngomyelins by the least (by 36.2%). The decrease in metabolism of the other PL fractions was about 45% relative to the control.

This similarity between the response of individual brain PL fractions of adrenalectomized animals to general anoxia may perhaps indicate that under anoxic conditions some common link in the pathway of synthesis of individual members of the PL group is disturbed in these animals.

It may be concluded from the results of these investigations that it is only under extreme conditions, i.e., when all the adaptive forces of the body are under extreme distress (in anoxia, for example) that the influence of absence of corticosteroids on the metabolic reaction of the brain can be detected.

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