ENZYMES IN TRYPTOPHAN METABOLISM UNDER HYPOBARIC CONDITIONS

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The stress of exposure of animals to low atmospheric pressure is known to influence behaviour (Folk Jr., 1966). In view of the important role of 5-hydroxytryptamine (5-HT) in the regulation of mental state (Woolley and Shaw, 1954), the study of the enzymes metabolizing tryptophan under hypobaric conditions is of interest.

Apart from protein synthesis, tryptophan is metabolized by two pathways, one major and another minor involving tryptophan pyrrolase and tryptophan hydroxylase, respectively. The pyrrolase is the first enzyme in degradation of tryptophan and the hydroxylase is the rate-limiting enzyme (Lovenberg, Jequier and Sjoerdsma, 1967) in the formation of 5-HT. The concentrations of the brain 5-HT and the hepatic pyrrolase bear an inverse relationship (Green and Curzon, 1968) in the normal rats as well as during adaptive changes obtained on treatment with hydrocortisone (Knox and Mehler, 1951) or on secretion of adrenal cortex hormones stimulated under conditions of stress (Knox and Auerbach, 1955).

Since both the pyrrolase and the hydroxylase are oxygen dependent, the stress of exposure of animals to low atmospheric pressure and consequent hypoxia may be expected to decrease the rates of activities of the two enzymes in view of the limiting oxygen concentration. If such an effect should be compensated as part of regulatory mechanism during

acclimatization to prolonged exposures, it may be visualized that the concentration or the molecular capacity of the preformed enzymes would increase to assure the minimum supply of the products. The results presented here support this hypothesis.

Male albino rats from the stock colony, weighing 150-180 g., were exposed to an atmospheric pressure of 350 ± 5 mm Hg (corresponding to an altitude of about 20000 ft.) obtained by a balance of evacuation from one side and a leak on the other in a decompression chamber. Low pressure was obtained in the chamber in less than 3 min after the start of evacuation and was maintained for the specified period. At the end of the experimental period atmospheric pressure was restored, the animals were removed from the chamber and killed by stunning and decapitation. The livers were removed and homogenized in cold aq.KCl (1%, w/v; 3 ml/g. liver) and centrifuged at 20000 g for 45 min in Sorvall RC2 refrigerated centrifuge. The supernatant was used for determining the enzyme activities: tryptophan pyrrolase by the method of Knox and Auerbach (1955); tryptophan hydroxylase by the method of Freedland, Wadzinski and Waisman (1961) with the modification of adding 0.3 mg. of 6,7-dimethyl-5,6,7,8-tetrahydropterine cofactor and 0.56 mg. ferrous sulphate in 2.5 ml reaction mixture and 5-hydroxytryptophan decarboxylase by the method of Beiler and Martin (1954). The killings were always done at about 10 A.M. to avoid changes due to circadian rhythms (Rapport, Feigin, Burton and Beisel, 1966) of tryptophan pyrrolase. At a time, two control and two hypobaric exposed rats were tested.

The results in Table 1 show that the pyrrolase activity increased in the livers when the rats were exposed to 0.5 atmospheric pressure. The increases were 49% at 2 hours, 330% at 12 hours, 244% at 24 hours and 226% at 50 hours compared with the control animals. The hydroxylase activity was unchanged upto 12 hours but increased by about 50% at

24 hours and remained at this level on further exposure. There was no change in the activity of the decarboxylase. Further experiments are in progress to determine whether the increased activities are due to increased amount of the enzyme protein or increased activity of the

Table 1. Enzymes in Tryptophan Metabolism in Livers of Rats Exposed to Low Atmospheric Pressure

Enzyme	Time of exposure, hr.	Enzyme activity, μmoles/hr./g.liver	
		Control	Hypobaric
Tryptophan pyrrolase	2	2.92 ± 0.83	4.35 ± 0.77+
	12	2.17 ± 0.70	7.16 ± 1.80*
	24	2.35 ± 0.97	5.72 ± 1.60*
	50	2.60 ± 0.26	5.88 ± 0.39*
Tryptophan hydroxylase	2	0.64 ± 0.08	0.59 ± 0.06
	12	0.58 ± 0.17	0.61 ± 0.19
	24	0.67 ± 0.15	1.00 ± 0.14*
	50	0.64 ± 0.07	1.00 ± 0.03*
5-Hydroxytryptophan decarboxylase	2	2.92 ± 0.62	2.80 ± 0.40
	12	2.55 ± 0.16	2.33 ± 0.17
	24	2.38 ± 0.21	2.39 ± 0.20
	50	2.72 ± 0.14	2.84 ± 0.17

The values given are mean ± S.D. of 4-6 rats in each group
(significance : P values: * < 0.01; + < 0.05)

preformed enzyme and whether they are obtained by increased hydrocortisone or tryptophan known to induce the pyrrolase activity. These changes were not due to gross changes in the protein contents of the livers since these remained constant under the experimental conditions. The rapid

increase in the pyrrolase activity followed by slower increase in the hydroxylase activity suggest that adaptive changes are taking place at the enzyme level on exposure to hypobaric conditions.

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