MECHANISMS OF DISTURBANCE OF CATECHOLAMINE SYNTHESIS IN THE ADRENALS OF PHYSICALLY FATIGUED RATS

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The ability of the adrenals to synthesize catecholamines in the presence of various substrates was investigated in vitro. Experiments were carried out on rats under normal conditions and after swimming for 8 h. In the physically fatigued animals the conversion of noradrenalin, DOPA, and tyrosine, added in vitro, into catecholamines was inhibited, on the basis of which depression of the activity of phenylethanolamine-N-methyl-transferase, dopa decarboxylase and, possibly, tyrosine hydroxylase was postulated. After the end of swimming, and in the presence of L-tyrosine as substrate, noradrenalin synthesis was activated first (on the second day), and this was followed by gradual restoration (on the 7th day) of normal adrenalin synthesis. In rats trained for two months, in response to swimming for 8 h the degree of depression of catecholamine synthesis in the adrenals was much smaller than in untrained rats.

KEY WORDS: adrenals; catecholamines; enzymes of synthesis; physical fatigue.

During severe muscular fatigue the catecholamine content in the adrenals falls, the ability to form catecholamines after addition of their precursors in vitro is disturbed, and the synthetic ability of the adrenals in vitro in the presence of L-tyrosine is reduced [2-5].

In the investigation described below some mechanisms causing inhibition of catecholamine synthesis were studied. The duration of the disturbances and changes observed in trained rats, in which no decrease in the catecholamine concentration is found in the adrenals during prolonged physical exertion [1, 9], also were determined.

EXPERIMENTAL METHOD

Noninbred male albino rats weighing 250-350 g were used. In the experiments of series I the rats swam at a temperature of 32° C for 7-8 h, after which intact and swimming rats were decapitated, both adrenals were removed and cut into small pieces, and one of the adrenals was incubated for 1 h in Krebs–Ringer bicarbonate solution in the presence of the following substrates: nonadrenalin (3.2 μg per sample), dopamine (5 μg per sample), dopa (5 μg per sample), and tyrosine (1000 μg per sample). The second adrenal, incubation of which in the presence of the same substrates was immediately stopped by the addition of perchloric acid, was used as the control. The adrenalin and noradrenalin content was determined in the control and experimental samples, and synthesis of the catecholamines was estimated from the increase in their concentration in the experimental sample. In the experiments of series II the rats were decapitated 1, 2, or 7 days after the end of swimming. Intact rats were used as the control. The experiments of series III were carried out on rats trained for 2 months. The animals were trained by increasing the duration of swimming at a temperature of 32° C gradually each day, starting from 30 min. The last two weeks the rats swam for 2 h daily. On the day after the end of training some of the rats were decapitated without any further swimming, whereas the other rats were compelled to swim for 8 h and were then decapitated. The content of catecholamines in the adrenals was determined fluorometrically [7].

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TABLE 1. Catecholamine Synthesis in the Presence of Different Substrates in Adrenals of Intact Rats and Rats Swimming for 8 h

Group of rats	Substrate	Concentration of substrate	Adrenalin		Nonadrenalin	
			content (in μg/g)	synthesis (in nmoles/g/h)	content (in μg/g)	synthesis (in nmoles/g/h)
Intact	L-tyrosine (n=12)		378±23	+101±13,5	182±20	+78±27
	L-dopa (n=12)	200	372±8,6	+76±17,5	165±19	+45±50
	Dopamine (n=14)	200	350±15,3	+92±34	193±23	+47±18
	Noradrenalin (n=22)	128	356±22	+128±24	274±26	—114±44
Swimming	L-tyrosine (n=15)		238±28	0	174±9,2	0
	L-dopa (n=19)	200	283±17	0	190±27	0
	Dopamine (n=22)	200	290±15	0	181±30	+219±53
	Noradrenalin (n=29)	128	286±29	0	268±36	0

Legend: n — number of experiments.

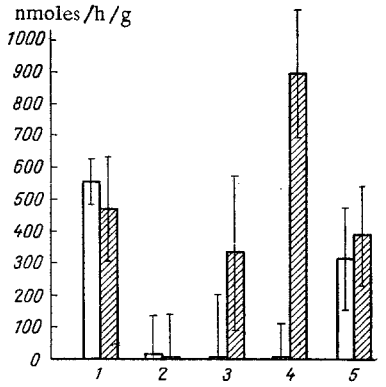

Fig. 1

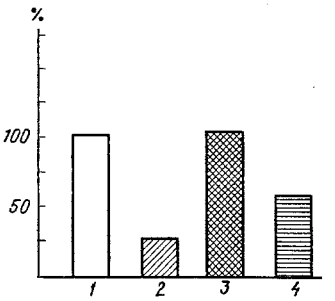

Fig. 2

Fig. 1. Synthesis of catecholamines (in nmoles/g/h) in adrenals of rats at various times after swimming. Unshaded columns show increase in adrenalin content in the presence of L-tyrosine; shaded columns give increase in noradrenalin content under same conditions. 1) intact rats (n=12); 2) swimming for 8 h (n=15); 3, 4, 5) 1, 2, and 7 days, respectively, after swimming (n = 19, 11, and 10).

Fig. 2. Adrenalin synthesis in adrenals of trained rats after swimming for 8 h. Ordinate, number of rats in which adrenalin synthesis was found in presence of L-tyrosine (in % of total number). 1) Intact rats (n=12); 2) untrained rats swimming for 8 h (n=12); 3) trained rats (n=9); 4) trained rats swimming for 8 h (n=12).

EXPERIMENTAL RESULTS AND DISCUSSION

In the presence of noradrenalin, intensive adrenalin formation and a decrease in the quantity of substrate were observed in the adrenals of the intact rats (Table 1). No increase in adrenalin or decrease in noradrenalin was found in the swimming rats. These results indicate that during prolonged swimming the activity of phenylethanolamine-N-methyltransferase, which converts noradrenalin into adrenalin, is inhibited.

In the presence of dopamine, increased adrenalin formation was found in the adrenals of the intact rats. Noradrenalin synthesis was increased only very slightly ($P > 0.05$). In the swimming rats noradrenalin formation was observed without any increase in adrenalin. The data given above, on inhibition of phenylethanolamine-N-methyltransferase activity in the rats during swimming, explain the accumulation of noradrenalin in the presence of dopamine in this case. The activity of dopamine-β-oxidase, which converts dopamine into noradrenalin, is evidently unchanged in rats by fatigue.

In the presence of dopa, a marked increase in the adrenalin content was observed in the adrenals of the intact rats, whereas noradrenalin formation was not statistically significant ($P > 0.05$). Neither synthe-

sis of adrenalin nor of noradrenalin could be observed in the swimming rats. These results indicate that the enzyme system decarboxylating dopa with the formation of dopamine is inhibited in rats during prolonged swimming. Similar inhibition was found in the presence of L-tyrosine, in agreement with data obtained in rats fatigued by running on a treadmill [6].

Determination of dopa in the adrenals in some of the experiments in the presence of L-tyrosine revealed no inhibition of its formation (13.2 ± 4.0 n moles/g/h in the control, 13.4 ± 4.5 n moles/g/h in the experiment). Both in the intact and the swimming rats the accumulation of dopa in the adrenals was extremely low and within the limits of experimental error.

The absence of changes in the dopa content in the presence of L-tyrosine cannot serve as evidence of normal tyrosine hydroxylase activity in the swimming rats, for a combination of inhibition of tyrosine hydroxylase with the reduced activity of dopa decarboxylase that was also found could produce similar results.

The data confirmed the decrease in the adrenalin content in the adrenals of swimming rats compared with intact animals described in the literature [1, 3, 8].

In agreement with the data described above, immediately after the end of an 8-h period of swimming, the synthesis of adrenalin and noradrenalin in the presence of L-tyrosine was sharply inhibited (Fig. 1). Adrenalin synthesis also was absent 24 h after the end of swimming, whereas small quantities of noradrenalin were formed. After 2 days there was a marked increase in noradrenalin synthesis, which was above the control level. Some restoration of adrenalin synthesis was observed 7 days after swimming, and noradrenalin synthesis was almost back to normal, although normal synthesis in general was not restored in the adrenals during this period. It is important to emphasize that normalization of adrenalin was preceded by increased synthesis of the precursor – noradrenalin.

In the experiments of series III (Fig. 2), under the influence of swimming for 8 h the inhibition of catecholamine biosynthesis in trained rats was much less marked than in untrained rats; this largely explains the absence of a decrease in the catecholamine content in the adrenals of trained rats during swimming [1, 9].

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