EFFECT OF CATECHOLAMINES ON GLUCOSE-6-PHOSPHATE DEHYDROGENASE, TRANSKETOLASE, AND GLUCOSE-6-PHOSPHATASE ACTIVITY IN THE RAT LIVER

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Single intramuscular injections of adrenalin and noradrenalin (30 and 150 μg/100 g body weight respectively) were given separately or in combination to rats. After injection of the hormones, activity of glucose-6-phosphate dehydrogenase (G6PD) transketolase, and glucose-6-phosphatase was determined in liver homogenates. A parallel increase was observed in the specific activity of these enzymes during the first 15 min (most marked after administration of noradrenalin), but after 30 min, G6PD activity was reduced (injection of adrenalin, noradrenalin, and a mixture of the hormones), and normal activity of the enzymes was restored after 2 h.

Data on the effect of catecholamines on the activity of transketolase – the limiting enzyme of the nonoxidative branch of the pentose-phosphate cycle in the liver [2, 3] of adrenalectomized rats – were described previously [1].

The object of the present investigation was to study the activity of this enzyme in the liver of intact rats 5, 15, 30, and 120 min after separate and combined administration of adrenalin and noradrenalin. Parallel determinations were made of the activity of glucose-6-phosphate dehydrogenase (G6PD), the limiting enzyme of the oxidative branch of the pentose-phosphate cycle [12], and of glucose-6-phosphatase (G6Pase), the key enzyme of gluconeogenesis which competes with it at the substrate level [13]. Injection of adrenalin is known to increase G6Pase activity [7] and CO_2 formation from glucose labeled at the first carbon atom [4]. There is no information in the literature on the effect of noradrenalin or a mixture of the hormones on the activity of these enzymes.

EXPERIMENTAL METHOD

Experiments were carried out on 72 nulliparous female rats weighing 180-220 g. In series I (four experimental groups) the effect of adrenalin, noradrenalin, and a mixture of both on activity of G6PD, transketolase, and G6Pase was investigated 5 min after intramuscular injection of the hormones. Rats of group 1 received an injection of 0.1 ml physiological saline (control), group 2 received a 0.1% solution of adrenalin hydrochloride (0.03 ml/100 g body weight), group 3 received a 0.2% solution of noradrenalin tartrate (0.15 ml/100 g body weight), and the rats of group 4 received both hormones simultaneously in the same doses. The experiments of series II-IV differed in that samples were taken from the animals 15, 30, and 120 min after the injection respectively. In all series the hormones were injected between 6 and 7 A.M.

The samples were taken and prepared for analysis as described previously [1]. Transketolase activity was determined by the method of Bruns et al. [5] and expressed in μmoles sedoheptulose-7-phosphate (S7P)/mg protein/h. G6Pase activity was estimated from the increase in content of inorganic phosphorus during incubation for 15 min at 37°C. The composition of the incubation medium was: 0.2 M tris-maleate buffer, pH 6.5; 0.4 M glucose-6-phosphate (G6P, disodium salt); 0.1 ml liver extract diluted so that during

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TABLE 1. Activity of G6PD, Transketolase, and G6Pase and Protein Content in Rat Liver Homogenates at Various Times after Injection of Catecholamines (M±m)

Hormone injected	Activity of enzymes			Protein content (in mg/g fresh liver tissue)
	G6PD (in μmoles $NADP \cdot H_2$/mg protein/h)	transketolase (in μmoles S7P/mg/protein/h)	G6Pase (in μg P/mg protein/h)	
	After 5 min			
Control	0,43±0,032	0,19±0,016	176,8±12,8	108,5±2,55
Adrenalin	0,57±0,07[1]	0,22±0,015	162,8±11,6	108,1±9,78
Noradrenalin	0,44±0,04	0,27±0,012[1]	379,6±11,2[1]	108,5±2,87
Mixture of hormones	0,65±0,07[1]	0,27±0,007[1]	123,2±8,4[1]	110,9±1,89
	After 15 min			
Control	0,29±0,037	0,22±0,007	202,0±24,4	122,9±1,7
Adrenalin	0,47±0,036[1]	0,24±0,007	362,8±19,2[1]	112,0±5,75
Noradrenalin	0,46±0,057[1]	0,26±0,025	495,2±32,0[1]	101,5±7,78[1]
Mixture of hormones	0,45±0,055[1]	0,34±0,056[1]	441,6±46,0[1]	88,2±8,4[1]
	After 30 min			
Control	0,39±0,028	0,21±0,019	264,0±29,2	89,0±5,50
Adrenalin	0,27±0,029[1]	0,22±0,013	244,8±24,0	109,7±9,75
Noradrenalin	0,23±0,093[1]	0,34±0,020[1]	449,2±27,2[1]	81,3±1,53
Mixture of hormones	0,28±0,028[1]	0,40±0,033[1]	417,6±22,8[1]	77,3±4,39
	After 120 min			
Control	0,26±0,028	0,16±0,024	146,4±29,2	116,5±5,95
Adrenalin	0,40±0,045	0,18±0,013	193,2±20,8	119,8±8,05
Noradrenalin	0,32±0,023	0,18±0,018	206,8±20,8	134,5±2,12[1]
Mixture of hormones	0,37±0,037	0,16±0,007	360,4±29,6[1]	147,5±4,65[1]

Note. Six animals were used in each group.

incubation of the samples for 15 min not more than 50% of the initial concentration of G6P was converted. The total volume of the mixture was 1.5 ml. The reaction was stopped and the phosphorus concentration determined with the aid of molybdenovanadate reagent in perchloric acid [9]. Enzyme activity was expressed in micrograms phosphorus/mg protein per hour. G6PD activity was determined by the method of Kornberg and Horecker [8] and expressed in μmoles NADP reduced by the enzyme/mg protein per hour. Protein was determined by Rider's method [11].

EXPERIMENTAL RESULTS AND DISCUSSION

The results in Table 1 show that 5 min after injection of adrenalin the G6PD activity was significantly increased while the activities of transketolase and G6Pase were unchanged. After injection of noradrenalin no change was observed in G6PD activity, transketolase activity was increased slightly, while G6Pase activity was doubled. After injection of a mixture of the hormones G6PD and transketolase, activities rose while G6Pase activity fell slightly.

Tests carried out 15 min after injection of adrenalin showed an increase of 60% in G6PD activity and of 80% in G6Pase activity while transketolase activity was unchanged; similar results were observed after injection of noradrenalin. After injection of a mixture of the hormones, the G6PD, transketolase, and G6Pase activities were increased by 55, 54, and 118%, respectively.

Tests carried out 30 min after injection of adrenalin showed a decrease of 40% in the G6PD activity while the transketolase and G6Pase activities were indistinguishable from the control. A decrease in G6PD activity was also observed after injection of noradrenalin (by 40%) and a mixture of the hormones (by 28%), while the transketolase and G6Pase activities were increased by 62 and 170% respectively, after injection of noradrenalin and by 190 and 158% respectively, after injection of the mixture of hormones.

In tests carried out 2 h after the injections the difference between the activities of the enzymes in the control and experimental groups were no longer significant, except in the case of G6Pase activity: after injection of the mixture of hormones it was increased by 147%.

In response to separate and combined administration of adrenalin and noradrenalin, changes were thus observed in the activities of G6PD, transketolase, and G6Pase throughout the period of observation (from 5 min to 2 h). The character and degree of the changes differed for each enzyme studied.

The increase in G6Pase activity in response to injection of adrenalin and noradrenalin is linked with activation of adenylate cyclase by these enzymes and an increase in the concentration of cyclic AMP [10]. The latter activates phosphorylase [7] and enzymes of gluconeogenesis [6]. The fact that there are considerable differences between the character and intensity of the changes in activity of the test enzymes after separate and combined injections of the catecholamines suggests that the two hormones act by different mechanisms.

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