EFFECT OF TYROSINE ON CATECHOLAMINE BIOSYNTHESIS IN INTACT RATS

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The effect of administration of tyrosine in doses of 10-100 mg/kg on the concentration of catecholamines, their precursor (DOPA), and their metabolite (normetanephrine) in the blood and tissues of intact rats was investigated. Changes in the catecholamine concentration in the tissues studied 3 h after administration of 10 mg/kg tyrosine were not significant. Activation of catecholamine synthesis in the adrenals and hypothalamus was observed after doses of 25-100 mg/kg. After tyrosine in a dose of 100 mg/kg the changes in all the tissues investigated were more marked.

The stage of conversion of tyrosine into DOPA is the most important in the chain of catecholamine biosynthesis for it limits and controls the rate of catecholamine formation in the body [7]. After administration of C^{14}- or H^3-labeled tyrosine in low concentrations, the label can be found in all subsequent conversion products [5, 8, 10]. Investigations have shown that higher concentrations of tyrosine in animals exposed to the action of various stressors cause an increase in catecholamine synthesis [1, 4, 6, 9]. However, it is not known whether catecholamine synthesis depends on the dose of tyrosine injected, or which tissues of the body respond most intensively to its administration.

The object of the investigation described below was to study changes in the concentrations of adrenalin, noradrenalin, DOPA, and normetanephrine in the blood and certain organs (adrenals, heart, hypothalamic region) of intact rats after administration of various doses (from 10 to 100 mg/kg) of tyrosine.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 230-250 g. Four concentrations of tyrosine were made up in physiological saline. In order to dissolve the tyrosine in the physiological saline, 2 N NaOH was used and the pH was adjusted to 8.0-8.5. The animals received 3 ml of the suspension each by intraperitoneal injection. The rats were divided into five groups. The animals of group 1 (Control) received physiological saline, the pH of which was adjusted to 8.0-8.5, intraperitoneally; the animals of group 2 received 10 mg/kg tyrosine; group 3, 25 mg/kg; group 4, 50 mg/kg; and group 5, 100 mg/kg tyrosine by the same route. The animals were decapitated 3 h after treatment. The concentration of adrenalin, noradrenalin, DOPA, and normetanephrine in the tissues of the rats was determined by a fluorimetric method [2, 3].

Each series included 10 experiments, in each of which two experimental and two control rats were used.

EXPERIMENTAL RESULTS AND DISCUSSION

The statistical analysis of the experimental results is given in Table 1. After administration of tyrosine in a dose of 10 mg/kg significant changes were not found in the catecholamine concentration in the adrenals, heart, blood, or hypothalamus.

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TABLE 1. Concentrations of Adrenalin (A), Noradrenalin (NA), DOPA, and Normetanephrine (NM) in Rats after Administration of Tyrosine (M ± m)

Group	Adrenals (in μg/g tissue)			Blood (in μg/liter plasma)		
	A	NA	DOPA	A	NA	NM
1	438±45	225±33	21,13±1,405	5,83±0,72	7,72±0,72	3,05±0,35
2	508±67	383±101	29,1±4,55	7,07±0,87	10,3±1,37	4,12±1,15
3	613±64†	311±71	28,6±3,33†	9,7±1,3†	11,1±3,58	4,72±1,15
4	541±39*	315±36*	26,7±2,96*	10,1±2,2*	8,6±1,17	4,88±0,45†
5	721±68†	391±59†	3,37±4,37†	9,4±1,1†	7,58±1,33	4,91±0,78†

Group	Blood (in μg/g tissue)		
	A	NA	DOPA
1	0,0388±0,0030	0,149±0,027	0,033±0,0032
2	0,0489±0,0048	0,234±0,038	0,0415±0,00662
3	0,0624±0,0042†	0,233±0,040	0,0312±0,00455
4	0,0522±0,0045†	0,201±0,034	0,0372±0,00462
5	0,06±0,006†	0,228±0,034	0,0399±0,0054

Group	NM	Hypothalamus (in μg/g tissue)		
		A	NA	DOPA
1	0,0131±0,000755	0,227±0,028	0,86±0,09	0,163±0,018
2	0,0134±0,00272	0,191±0,054	1,03±0,17	0,290±0,067
3	0,0132±0,00098	0,269±0,040	1,00±0,09	0,202±0,061
4	0,0139±0,00144	0,302±0,051	1,21±0,17*	0,269±0,0805†
5	0,0161±0,00334	0,266±0,040	1,32±0,19†	0,274±0,0475†

*Changes statistically probable ($0.1 > P > 0.05$).

†Changes statistically significant ($P < 0.05$) compared with data for intact rats.

In the animals of group 3 (tyrosine 25 mg/kg) the adrenalin concentration in the adrenals was increased (by 40%); the adrenalin concentration in the blood was increased (by 65%), and the concentrations of noradrenalin and normetanephrine were unchanged; the adrenalin concentration in the heart was increased by 60%.

A statistically probable increase in the adrenalin, noradrenalin, and DOPA concentrations was observed in the adrenals of the animals of group 4 (tyrosine 50 mg/kg); the normetanephrine concentration in the blood was increased by 60%; the increase in the adrenalin concentration was statistically probable; the adrenalin concentration in the heart was increased by 35%; the DOPA concentration in the hypothalamus was increased by 65%, and a statistically probable increase in the noradrenalin concentration also was observed.

In the animals of group 5 (tyrosine 100 mg/kg) the adrenalin and DOPA concentrations in the adrenals were increased by 65 and 60%, respectively, and the noradrenalin concentration by 75%; the increase in the noradrenalin concentration in the heart was statistically probable; the noradrenalin and DOPA concentrations in the hypothalamus were increased by 55 and 70%, respectively.

Consequently, injection of tyrosine stimulated DOPA synthesis in the adrenals, and an increase in the DOPA concentration was observed after doses of 25-100 mg/kg. Later the DOPA was converted in the adrenals into noradrenalin and adrenalin, as shown by an increase in the noradrenalin concentration found after administration of tyrosine in doses of 50 and 100 mg/kg. The adrenalin concentration was increased with doses of 25-100 mg/kg.

The experimental results showing a simultaneous increase in the concentration of adrenalin in the adrenals, blood, and heart indicate stimulation of adrenalin synthesis in the adrenals. This led to an increase in its secretion into the blood and penetration into the heart. Accumulation of adrenalin in the blood

was not significant after tyrosine in a dose of 10 mg/kg but occurred in response to doses of 25-100 mg/kg. The accumulation of adrenalin in the heart tissue after injection of 10 mg/kg tyrosine was statistically probable, but with an increase in the dose of tyrosine the changes were more marked. In the hypothalamus no increase in the adrenalin concentration was observed after injection of tyrosine.

In the heart tissue, unlike the adrenals, no definite stimulation of noradrenalin synthesis was found after injection of tyrosine. No increase in the concentrations of DOPA, noradrenalin, or its principal metabolite by the O-methylation pathway (normetanephrine) was found. The increase in the normetanephrine concentration in the blood can only indicate and increase in the quantity of noradrenalin undergoing further conversion in the body but could not give evidence of its origin (from the adrenal or from the sympathetic nerve endings).

After injection of tyrosine, changes indicating stimulation of catecholamine synthesis were detected in the hypothalamus. The DOPA concentration was increased; the increase in the noradrenalin concentration was not significant after tyrosine in doses of 10 and 25 mg/kg, it was more marked after a dose of 50 mg/kg, and was definitely observed after a dose of 100 mg/kg.

Previous investigations showed that 60-150 min after intraperitoneal injection of DOPA in doses of 15 and 45 mg/kg more rapid activation of catecholamine synthesis took place in the heart, adrenals, and hypothalamus. Catecholamine synthesis in the heart took place most actively. After injection of tyrosine, no significant changes were found in the heart tissue. Meanwhile, the changes in the adrenalin concentration in the adrenals after injection of tyrosine were much more marked than after injection of DOPA.

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