EFFECT OF ADRENALECTOMY ON TYROSINE RETENTION BY LIVER AND ON ITS BLOOD LEVEL IN DOGS AND RATS

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Interest in the subject of induced synthesis of the adaptive enzymes is due largely to the fact that they are found not only in microorganisms but also in mammals. Their induction in mammals is very complex, and, in relation to many enzymes, is under dual control: substrate and hormonal [7]. This dual control has been demonstrated precisely for the enzyme system catalyzing the first stage of decomposition of the amino acid tyrosine [1, 9, 10].

It is not yet clear, however, whether hormonal control of the activity of these enzymes is constant, or whether it is required only if the concentration of the corresponding substrate in the blood or tissues rises. In order to elucidate this problem, we investigated the tyrosine concentration in the blood serum of rats and dogs after bilateral adrenalectomy.

EXPERIMENTAL METHOD

The blood tyrosine was determined by the method of Udenfriend and Cooper [11]. Adrenalectomy was performed on rats under ether anesthesia through a dorsal incision in one stage. After the operation the drinking water was replaced by 1% sodium chloride solution. As a rule the animals withstood the operation well. In some rats a sham adrenalectomy was performed, in which all steps of the operation were carried out but the adrenals were left in situ. Blood for determination of tyrosine was collected from the cervical vessels of decapitated rats, sacrificed between 1 and 21 days after the operation. The results were analyzed statistically, and groups compared by the criterion t, calculated by the alternative variation method. The difference between the groups was regarded as significant if $t \geq 3$. Blood from 203 rats was tested, of which 103 were healthy, 25 had undergone the sham operation, and 75 had undergone true adrenalectomy.

EXPERIMENTAL RESULTS

The results in Table 1 show that the blood tyrosine concentration was unchanged after both sham and true adrenalectomy, at least until the 3rd day after the sham operation, when it rose by a statistically significant amount over the normal level. However, the difference between the results on the third day after the true and sham operations was not significant.

The liver plays an important part in tyrosine metabolism [5, 8], and in particular it retains tyrosine intensively: the concentration of tyrosine in the blood in the hepatic vein is always less than in the portal and arterial blood [3].

In order to study the effect of the adrenal cortical hormones on the intensity of retention of tyrosine by the liver, we carried out experiments on 6 adrenalectomized and angiostomized dogs.

The adrenals were removed and angiostomy cannulas introduced into the portal and hepatic veins in two stages: 1) removal of the left adrenal and introduction of cannulas into the portal and hepatic veins by I. A. Pigalev's method [2]; 2) removal of the right adrenal 18-60 days after the first operation.

The first operation was withstood well. After removal of the second adrenal, two dogs died from acute adrenal failure; 4 dogs survived while receiving a daily injection of DOCA in a dose of 5-15 mg (in some cases periodic injections of 50 mg of cortisone were given). After the hormone injections were discontinued signs of increasing adrenal failure developed, with characteristic changes in the serum potassium and sodium levels (Table 2).

The tyrosine concentration in blood from the various vessels was determined after removal of the left adrenal and angiostomy (1st period), after removal of the right adrenal and compensatory administration of hormones (2nd

TABLE 1. Tyrosine Concentration (in mg%) in the Blood of Rats after Sham and True Adrenalectomy (Normal 2.08 ± 0.08)

Time after operation (in days)	Sham adrenalectomy		True adrenalectomy		Criterion t for comparison between true and sham adrenalectomy
	M±m	criterion t when compared w/normal	M±m	criterion t when compared w/normal	
1st	1,92±0,14	1,0	2,57±0,35	1,3	1,8
2nd	2,23±0,07	1,4	2,47±0,31	1,2	0,8
3rd	2,60±0,14	3,3	2,46±0,27	1,4	0,5
4th	—	—	2,16±0,18	0,4	—
5th	2,28±0,10	1,5	2,10±0,11	0,2	1,2
6th	—	—	2,29±0,30	0,7	—
7th	2,01±0,18	0,4	2,56±0,16	2,7	2,3
8th	—	—	2,65±0,28	1,9	—
9th	—	—	2,34±0,09	2,2	—
10th	1,97±0,08	1,0	2,07±0,26	0,4	0,4
21st	—	—	2,47±0,13	2,6	

TABLE 2. Changes in the Serum Potassium and Sodium Levels (in mg%) in a Dog after Bilateral Adrenalectomy and Discontinuing Administration of DOCA

Time after discontinuing DOCA injections (days)	Potassium	Sodium	Ratio K/Na
3rd	20	467	0,043
5th	25	280	0,089
8th	50	240	0,208

TABLE 3. Serum Tyrosine Concentration (in mg%) in Blood Vessels of Dogs

Procedure	Criterion for comparison between portal and hepatic veins	Femoral artery		Portal vein		Hepatic vein	
		M±m	t*	M±m	t*	M±m	t*
Angiostomy (normal)	4,1	2,35±0,09	—	2,62±0,13	—	1,93±0,11	—
Removal of left adrenal and angiostomy (1st period)	7,9	2,14±0,07	1,9	2,38±0,06	1,7	1,75±0,05	1,5
Removal of right adrenal and replacement hormone therapy (2nd period)	5,6	2,24±0,06	0,9	2,58±0,8	0,3	1,99±0,07	0,5
Discontinuation of hormone therapy (3rd period)	4,6	2,21±0,04	1,4	2,64±0,13	0,01	1,91±0,09	0,1

*By comparison with normal.

period), and after discontinuing hormone therapy (3rd period). During all the periods blood was taken between 2 and 7 times from each dog, usually 3 or 4 times. The blood tyrosine concentration was also determined in 3 dogs subjected to angiostomy only. The results, analyzed statistically, are given in Table 3. The difference between the blood tyrosine concentrations in the portal and hepatic veins was significant in all periods. However, adrenalectomy and discontinuing administration of hormones to cause adrenal failure did not change the blood tyrosine levels in the femoral artery or the portal and hepatic veins. Comparison of the blood tyrosine levels in the same vessels at different periods showed that the differences were not significant (the criterion $\underline{t}$ varied between 0.01 and 1.9). No statistically significant increase or decrease in the retention of tyrosine by the liver could be found in any of the adrenalectomized dogs ($P > 0.1$).

Bilateral adrenalectomy in rats and dogs, leading to marked adrenal failure, thus had no effect on the tyrosine concentration in pooled rats' blood or in the blood from individual vessels in dogs.

The retention of tyrosine by the liver also remained unchanged. It seems that in " resting" conditions the tyrosine metabolism is largely autonomous and not under the control of the adrenal hormones, but determined by enzyme-substrate relationships. The "correcting" influence of the adrenal cortical hormones is probably exerted in extraordinary circumstances (tyrosine intake, irradiation, and so on), and is aimed at restoring the disturbed equilibrium. The following fact tends to support this view. Whole-body irradiation of rats leads to a significant increase in the oxidation of tyrosine in the liver [3], whereas irradiation of adrenalectomized rats does not have this effect [4]. Evidently the corticosteroid regulation of the activity of enzyme systems catalyzing the decomposition of tyrosine during stress reactions does not take place by a change in the substrate level, but is under the direct control of the adrenal cortex. Similar results have been obtained in relation to the system catalyzing the decomposition of tryptophan [6].

SUMMARY

A study was made of the effect produced by adrenalectomy on retention of thyrosin by the liver and on its blood level in dogs and rats. A two-stage operation of adrenal gland excision was performed in dogs in conjunction with placing the angiostomic cannulae on the portal and hepatic veins; this has made it possible to obtain blood from the mentioned vessels in conditions of adrenal insufficiency.

As established, bilateral adrenalectomy in dogs and rats had no effect on thyrosin content in the blood and on the intensity of its retention by the liver. Evidently, in conditions of "rest" thyrosin metabolism is sufficiently autonomous and does not depend on adrenal hormones. "Correcting" effect of adrenal cortical hormones is probably manifested only in extraordinary cases.

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