

NERVOUS CONTROL OF THE ADRENAL CORTEX

T. K. Dzharak'yan

S. M. Kirov Military Medical Order of Lenin Academy, Leningrad

(Presented by Active Member AMN SSSR A. B. Lebedinskii)

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Although there is some evidence of nervous control over the adrenal cortex, no direct influence of the central nervous system has yet been demonstrated.

Recently a number of reports have been made on the pathology of the adrenal cortex, particularly in radiation sickness, and they have suggested that a parahypophyseal influence is exerted on the gland [2,6].

In acute experiments on dogs, Yu. A. Pankov [5] showed that stimulation of the splanchnic nerve increased the rate of secretion of hormones from the adrenal cortex. In special experiments he demonstrated that the increase in the secretion was caused by a greater blood flow through the gland due to splanchnic stimulation.

It has been shown morphologically [3] that the adrenal cortex is rich in nerve ganglia and pathways, but shows no nerve endings. At the same time, V. I. Il'ina [3] has shown that denervation of the adrenals by section of the splanchnic nerves and removal of the semilunar ganglia causes dystrophic changes in the cortex; lipids (cholesterol) disappeared completely, and the secretory cells degenerated.

To follow up these results, we prepared to determine the effect of the nervous system on adrenal cortical function.

It is now accepted that the ascorbic acid content of the adrenals is an indication of the condition of the cortex. It is known also that immediately after giving an injection of ACTH, there is a marked reduction in the adrenal ascorbic acid content, and we have therefore studied how it is affected by denervation.

METHOD

The experiments were carried out on chinchilla rabbits weighing 2-2.5 kg.

The left adrenal was denervated in an aseptic abdominal operation performed under urethane anesthesia. The separate layers of the wound were closed by sutures, and healing took place uneventfully. After complete recovery and healing of the wound, but not until after the 15-18th day, the principal experiments were performed. The abdominal cavity was once more opened, and both adrenals removed and measurements of the ascorbic acid content made. They were weighed on a torsion balance and then triturated with sand and a 6% solution of metaphosphoric acid in twice distilled water (0.1 ml per 10 mg of tissue). The mixture was then centrifuged. One ml of the mixture was then titrated using 2,6-dichlorophenolindophenol as an indicator. An excess of indicator was added, and after 20 seconds of interaction the centrifuged fluid was extracted with isoamyl alcohol. A blank experiment was also made in which the same quantity of twice distilled water was used. The dyed extracts from the true and the blank experiment were estimated calorimetrically, and from the results the amount of ascorbic acid in the adrenals was calculated as mg percent.

RESULTS

The first control series of experiments was performed on eight healthy unoperated rabbits. These experiments were necessary to obtain information on the difference between the ascorbic acid contents of the right and left adrenals, because in the subsequent experiments the effect of the denervation was estimated in terms of the difference in vitamin C content of the innervated and denervated glands.

The results of these experiments are shown in Fig. 1.

It can be seen that the differences in ascorbic acid content between the left and right adrenals lie within the limits of $\pm 10\%$. The absolute amount of ascorbic acid varied in the different animals from 140 to 350 mg%, the

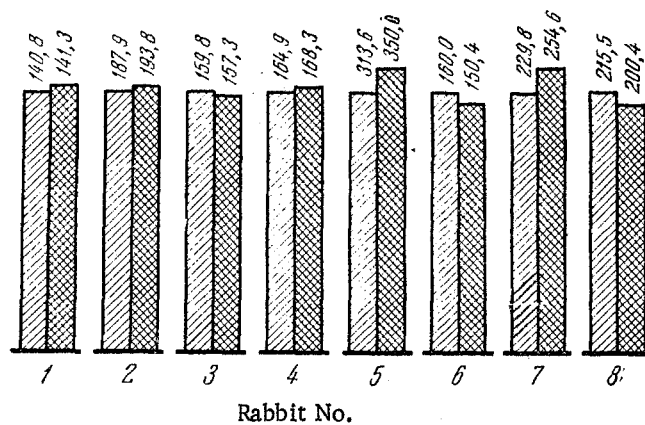


Fig. 1. Ascorbic acid content in the adrenals of the control rabbits. Columns shaded with oblique lines refer to the right adrenal (taken as 100); cross-hatched lines refer to the left adrenal (quantities expressed as a percentage of the content of the right gland); the figures above the columns indicate the amount of ascorbic acid in mg percent.

variation being probably due to individual characteristics and also to the fact that the experiments were carried out at different seasons. Other workers [1,4] have found similar values.

Section of the left splanchnic nerve did not introduce any difference in the ascorbic acid content of the left and right adrenals (Table 1).

TABLE 1. Ascorbic Acid Content of the Adrenals in Rabbits Before Partial Denervation of the Left Adrenal

Rabbit No.	Time after denervation, hr.	Ascorbic acid in the adrenal		
		right, mg%	left	
			mg %	as percentage of right adrenal content
Splanchnic nerve divided				
15	25	274.0	270.9	98
16	30	448.5	418.3	94
17	32	229.6	255.4	110
19	34	230.6	189.0	84
21	37	293.0	318.4	109
Splanchnic nerve divided, semilunar ganglion and the two upper ganglia of the abdominal sympathetic chain removed				
31	18	237.0	207.0	90
32	25	261.0	234.9	90
33	32	182.3	147.3	80
36	34	129.0	10.3	10

The observed variations did not differ from those in the control rabbits.

In two experiments prolonged electrical excitation was applied to the left splanchnic nerve; subsequent measurements revealed no difference in the adrenal ascorbic acid contents of the left and right sides.

Because the splanchnic innervation of the adrenals consists of cholinergic preganglionic fibers, in the next experiments we attempted to determine the effect on the adrenals of repeated intravenous acetylcholine injections.

The right adrenal was removed and its ascorbic acid content determined immediately, and then 5-6 injections

TABLE 2. The Effect of Repeated Acetylcholine Injections on the Adrenal Ascorbic Acid Content.

Rabbit No.	Ascorbic acid in the adrenal		
	right, mg %	left	
		mg %	as percentage of right adrenal content
18	304,0	268,0	89
20	210,0	201,0	96
22	276,7	163,0	61
23	172,0	162,2	96
24	148,8	140,3	95
25	201,6	205,2	102

of 0.4-0.6 mg acetylcholine were given at intervals of 10-15 minutes. The left adrenal was then removed, and its ascorbic acid content determined. The results of this experiment are shown in Table 2.

It can be seen from Table 2 that, as in the control experiment, the variations in the ascorbic acid content in the adrenals were within $\pm 10\%$, and only in one experiment was the left adrenal content 40% below the right.

The experiments therefore showed that as far as could be determined from the ascorbic acid content neither section of the splanchnic nerve nor its stimulation led to any change in the functional condition of the adrenal cortex.

Morphological studies [3] have shown that the adrenals are innervated by fibers entering from the semilunar ganglia. In the next set of experiments, therefore, in addition to sectioning the left splanchnic nerves, we removed the left semilunar ganglia, and also extirpated the two upper ganglia of the abdominal sympathetic chain. The experiments were performed from 18 to 36 days after the operation (see Table 1).

It can be seen from Table 1 that in all the animals the ascorbic acid content of the left adrenal fell below that of the right, though only in two animals did the difference exceed the variation found in the controls.

In our opinion, the uneven results of this set of experiments indicated an incomplete denervation of some of the adrenals, due to individual variability of the course of the nerve fibers.

In order to eliminate this cause of uncertainty, in the next set of experiments, in addition to removing the sympathetic ganglia already mentioned and sectioning the splanchnic nerves, any nerve fibers which could be seen running toward the adrenals along the blood vessels were also cut. This operation was performed with the help of a binocular loupe. In the operation, carbolic acid was applied to the vessels running toward the adrenal. In carrying out manipulations near the adrenal, great care was taken to avoid any damage to it.

The adrenal ascorbic acid content in these animals was determined 20 to 65 days after the operation (Fig. 2).

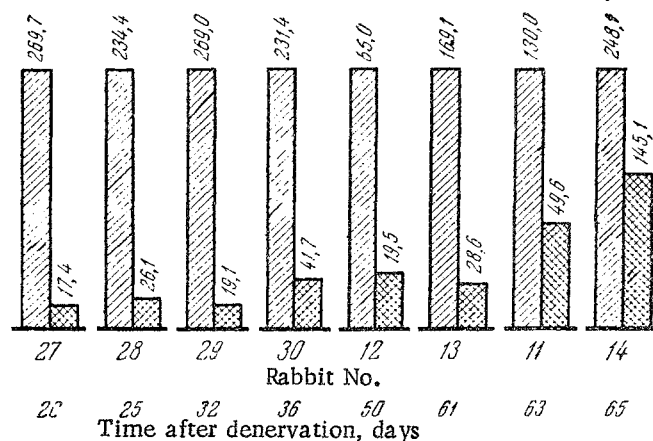


Fig. 2. Adrenal ascorbic acid content in rabbits after "complete" denervation of the left adrenal. Indications as in Fig. 1.

It can be seen from the figure that in all the animals there is a drop of 80% or more in the ascorbic acid content of the denervated gland, and the difference between the left and right glands is statistically significant (see Fig. 1). Typically, the greater differences occurred when the estimation was made early after the operation. At later times the difference was less marked and amounted only to 40-60%. Probably at these times there had been some recovery of the ascorbic acid content and some improvement in the functional condition.

Thus, the most extensive possible denervation of the adrenal gland leads to a marked change in the ascorbic acid, which must inevitably affect the production of the adrenal cortical hormone because of the important part played by vitamin C in the synthesis of corticoids.

In view of the results obtained by Yu. A. Pankova [5] quoted above, it might be thought that the changes in

the adrenal ascorbic acid content observed in our experiments were caused by changes in the blood supply to the denervated organ.

However, such a view is scarcely tenable because changes which we observed occurred between the 20th and 65th days after denervation, when the blood supply to the organ had probably been restored and when the adrenal tissues had become adapted to the new circulation.

In comparing our results with the morphological studies reported above, it seems more correct to attribute the observed changes to an arrest of central nervous trophic function.

SUMMARY

Rabbits were used to study the effect on function of denervating the adrenal gland. The amount of ascorbic acid in the gland served as an index. Twenty to sixty-five days after the splanchnic nerve had been divided, the semilunar ganglion and the two superior ganglia of the abdominal sympathetic chain excised, and the nerve fibers running to the adrenal gland along the blood vessels divided, the ascorbic acid content of the adrenal gland fell. The decrease was most marked between the 20th and 36th days. It is suggested that the CNS exerts a trophic effect on the adrenal cortex.

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