

COMPENSATORY HYPERTROPHY OF THE ADRENAL GLAND AFTER UNILATERAL ADRENALECTOMY IN JUVENILE RATS

V. F. Sidorova and E. N. Stepanova

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The definitive structure and function of the adrenal glands in rats are formed in the postnatal period [3, 5, 6, 10, 13]. This fact must certainly be reflected in the course and intensity of compensatory and repair processes in these glands. One of the most widely used methods of determining the compensatory powers of the adrenals is unilateral adrenalectomy, after which the residual gland hypertrophies [4]. This rule has been demonstrated for mature rats [8, 11, 12] and fetuses [9]. However, the special features of the response of the residual adrenal gland to unilateral adrenalectomy in the juvenile age period has hardly been studied [7]. The object of the present investigation was to study the response of the residual right adrenal gland of sexually immature rats of different ages to removal of the contralateral organ.

EXPERIMENTAL METHOD

Left-sided adrenalectomy was performed on noninbred young rats aged 1, 5, 10, 15, 20, and 30 days and the animals were killed 1, 3, 5, 7, 14, 21, and 30 days after the operation. Groups of rats identical in weight were chosen from the same litters for the control and these were killed at the same time as the corresponding experimental animals. At each time of the investigation 8-10 experimental and 8-10 control rats were used from each age group (altogether 800 rats). The body weight before the operation and before sacrifice, the weight of the removed adrenal and of the hypertrophied gland were determined in the experimental rats. In the control animals the body weight initially and before sacrifice and the weight of the left and right adrenals were determined. Two indices of hypertrophy [4] were calculated. The first (IH-1) was determined as the ratio of the weight of the hypertrophied adrenal to the weight of the right adrenal in the control (in per cent), the second (IH-2) as the ratio of the weight of the hypertrophied adrenal to the combined weights of the two control adrenals (in per cent). The adrenals were fixed in Carnoy's fluid and treated histologically. Paraffin sections 5 μ thick, taken from the central part of the gland, were stained with hematoxylin and eosin. The width of the zona glomerulosa and combined zona fasciculata and zona reticularis of the adrenal was measured with an ocular micrometer in a section with maximal area of the medulla (the structural center of the organ) at four opposite points in accordance with a scheme devised by ourselves (Fig. 1). The arithmetic mean width of each zone was calculated for the hypertrophied and both control adrenals. All numerical results were subjected to statistical analysis by the Fisher-Student method.

EXPERIMENTAL RESULTS

Regardless of age the body weight of all animals undergoing the operation was less than the body weight of the control rats at the overwhelming majority of times of investigation. The younger the animal at the time of operation, the greater the difference in weight (Table 1). The very slightly greater body weight of rats adrenalectomized at the age of 5, 10, and 15 days, observed at certain times of observation, was not statistically significant.

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TABLE 1. Changes in Body Weight of Experimental and Control Rats of Different Ages (in percent of initial weight) at Various Times after Unilateral Adrenalectomy

Age, days	Group of animals	Days after operation						
		1	3	5	7	14	21	30
1	E	105,3	118,0	176,9	205,2	317,6	829,7	739,1
	C	115,2	139,7	235,0	246,2	414,0	879,1	742,7
5	E	105,3	122,9	170,4	219,3	278,9	550,4	495,7
	C	109,0	138,0	185,6	192,0	235,8	567,3	556,2
10	E	107,0	120,9	136,5	153,7	177,3	236,4	329,9
	C	105,5	119,1	136,3	167,2	174,8	260,2	340,6
15	E	101,8	111,6	120,5	135,6	209,6	278,8	309,6
	C	105,6	114,1	121,0	147,3	199,6	303,3	320,9
20	E	103,5	128,6	139,0	137,7	160,8	204,9	221,5
	C	105,0	132,0	143,8	145,8	164,1	201,9	222,9
30	E	102,9	109,0	119,0	124,5	120,7	116,0	127,8
	C	104,0	111,1	120,2	124,4	120,7	123,4	135,0

Legend. E) Experiment, C) control.

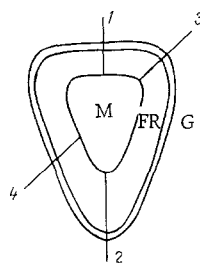


Fig. 1. Diagram of structure of rat adrenal and vectors for measurement of width of cortical zones. G) Zona glomerulosa, FR) z. fasciculata + z. reticularis, M) medulla. 1-4) Vectors of measurement.

The results of weighing the adrenals showed that the process of increase in weight of the residual (IH-1) in young rats begins on the first day after the operation, but differs in degree depending on the age of the rat at operation. For instance, in rats aged 1 day at operation the increase in weight of the right adrenal was only 1.4% of the weight of the right, control adrenal, in rats aged 5 to 20 days the increase was 10.8-14.8%, and in rats aged 30 days it was 31.8%. Such a sharp increase in weight of the residual organ can be explained as the response to stress, accompanied by postoperative hyperemia of the vascular network of the gland. Later during the observations no general pattern could be observed for the gain in weight of the organ, for this process followed a different course in each age group (Table 2). In rats aged 1 day, for instance, hypertrophy of the residual gland reached a maximum on the 5th day after the operation (133.6%). Later it decreased, and 1 month after the operation the weight of the residual adrenal was less than that of the control. In rats aged 5 days the increase in weight of the adrenal followed a fluctuating course, reaching a maximum on the 21st day, but also ceasing to rise on the 30th day. Hypertrophy of the adrenal in rats aged 10 days at operation was slight, and its peak, which occurred on the 1st day after the operation, was undoubtedly due to the reaction to stress. In rats aged 15 days the increase in weight of the organ was less than that in the control for 7 days, but by the 14th day a marked increase in weight of the adrenal was observed, followed again by a slow decline, which had still not ended 1 month after the operation. The residual adrenal in rats aged 20 days at operation was distinguished by a rather curious feature. Its weight decreased compared with the control during the first 14 days after the operation, but then began to increase rapidly, to reach a considerable value 1 month after the operation, 20% higher than the control. Rats aged 30 days were characterized by a small increase in weight of the residual adrenal, which ended 1 month after the operation.

Since when one part of any paired organ is removed it is necessary to know to what extent the residual part can make good the resulting deficiency, it was decided to compare the weight of the residual adrenal with

TABLE 2. Degree of Hypertrophy (in %) of Right Adrenal after Left-Sided Adrenalectomy in Rats of Different Ages at Various Times after Operation

Index of hypertrophy	Age, days	Days after operation						
		1	3	5	7	14	21	30
IH-1	1	101,4	97,5	133,6	128,0	100,0	112,6	91,3
	5	110,8	117,9	102,7	120,8	113,6	121,3	97,9
	10	114,8	103,5	109,6	110,9	96,9	93,6	97,0
	15	112,9	111,6	103,3	100,3	126,1	120,2	105,0
	20	113,9	117,9	112,4	108,9	89,2	104,7	120,0
	30	131,8	107,4	109,8	100,3	114,1	113,9	97,5
IH-2	1	46,5	43,3	66,2	54,5	47,6	54,1	44,4
	5	52,8	56,6	49,0	59,2	55,7	57,5	48,6
	10	55,0	51,1	54,1	53,2	46,8	44,9	47,0
	15	54,5	54,8	51,0	48,3	61,2	59,2	50,5
	20	56,4	52,4	52,7	54,3	42,8	50,3	58,7
	30	62,9	51,5	54,6	49,1	56,1	55,1	46,2

TABLE 3. Width of Zona Glomerulosa and Zona Fasciculata + Zona Reticularis in Hypertrophied Adrenal (in % of control) at Different Times after Operation

Zone of cortex	Age, days	Days after operation						
		1	3	5	7	14	21	30
Z. glomerulosa	1	88,8	98,1	98,7	108,4	112,8	104,8	126,5
	5	121,6	102,5	101,5	141,5	104,8	88,6	99,7
	10	108,4	107,1	110,1	105,1	125,6	116,6	97,6
	15	85,8	77,0	95,7	115,0	91,9	96,6	114,0
	20	85,8	98,1	109,2	105,9	111,3	97,0	105,9
	30	101,9	81,8	83,9	96,4	92,3	99,1	95,8
Z. fasciculata + Z. reticularis	1	111,5	103,0	109,0	105,6	106,6	112,5	107,5
	5	121,9	117,0	100,1	112,8	99,2	117,8	99,4
	10	111,6	96,5	84,4	104,9	104,4	110,0	112,3
	15	107,0	110,8	94,5	95,1	113,2	106,8	109,0
	20	94,9	103,3	105,2	94,5	106,3	110,9	121,1
	30	111,4	108,1	110,2	113,9	114,9	114,6	104,8

the combined weight of the two control glands (IH-2), considering that in rats at any stage of postnatal development the left adrenal as a rule is greater in size and weight than the right. It was found that in rats of the age groups studied restoration of the whole of the lost weight of the gland did not take place during the first month after the operation. The maximal index of hypertrophy (IH-2) was 66.2% (in rats aged 1 day, on the 5th day after the operation). IH-2 exceeded 50% 1 month after the operation only in rats aged 15 and 20 days, and in the rest it was below 50% (Table 2).

Measurement of the width of the zones of the cortex of the right adrenals (Table 3) showed that the thickness of the zona glomerulosa may be greater or less than the control depending on the time of investigation and the age of the animals at operation. For instance, in rats aged 1 day proliferation of the zona glomerulosa begins on the 7th day after the operation and reaches a maximum after 1 month (126.5% of the control). In rats aged 5 and 10 days initial widening of the zone was followed by narrowing, when the difference with the control was not significant. In rats aged 15 and 20 days the width of the zone was significantly greater than the control ($P < 0.05$) several times in the course of the investigation. So far as rats aged 1 month are concerned, at all times of the investigation the width of the zona glomerulosa in these animals did not reach the control level.

Most of the increase in volume of the adrenal cortex during hypertrophy was evidently accounted for by the combined zona fasciculata and zona reticularis. In fact, only in eight of the series investigated was the thickness of this combined zone somewhat less than the control, and in the remaining 34 series it was greater than the control. However, the increase in width was not always significant. Its maximal value was observed in rats aged 20 days 1 month after the operation (121.1% of the control, $P < 0.001$). The widening process began on the 1st day after the operation and followed a wavelike course (Table 3). A more standard response, expressed as predominant widening of the combined zona fasciculata and zona reticularis in the experimental rats compared with the controls was observed from 7 days after the operation for most age groups.

The degree of development of hypertrophy of the rat adrenal gland varies considerably depending both on the animals' age and the time elapsing after the operation. It is interesting to note that instability of development of compensatory hypertrophy also was observed in relation to ovaries of infantile golden hamsters [1] and the kidney in young rats [2]. A more penetrating analysis of the character of compensatory hypertrophy of the adrenal in the early postnatal period will be the subject of future research.

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SURFACE ACTIVITY OF PLASMA MEMBRANES

V. S. Gevod, V. I. Karamushka,
P. V. Pogrebnoi, T. G. Gruzina,
and V. K. Rybal'chenko

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Plasma membranes (PM) isolated from smooth-muscle tissues are vesicular formations [4, 6, 9]. They are characterized by activity of various enzymes connected with ATP hydrolysis and regulation of the ionic composition of the cytoplasm. However, direct experimental investigation of the functions of ion-transporting enzymes incorporated into the structure of PM is difficult. Attempts to insert such enzymes into flat lipid membranes have not yielded consistently reproducible results [5].

In the investigation described below surface activity of membrane preparations and their interaction with phospholipid monolayers, simulating the surface of the bilayer, were studied.

EXPERIMENTAL METHOD

PM were isolated from smooth-muscle tissue of the rabbit small intestine by differential centrifugation in a sucrose density gradient and were characterized electron-microscopically and biochemically as described previously [4]. The level of ATPase activity of PM was verified by a potentiometric method [1, 2]. The PM preparation was kept in medium containing 25% glycerol (by volume), 0.1 mM EDTA, 0.2 mM CaCl₂, and 5 mM imidazole, pH 7.2, at 0–4°C. ATPase activity persisted for about 1 month under these conditions.

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