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FUNCTIONAL AND MORPHOLOGICAL CHARACTERISTICS OF THE ENDOCRINE SYSTEM IN THE PROGENY OF ADRENALECTOMIZED RATS

S. N. Antonova, M. I. Kandror,*
and A. Yu. Tsibulevskii

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Signs of premature maturation and activation of the pituitary-adrenocortical system were observed in the early postnatal period (70-90 h) in the progeny of rats adrenalectomized 1-3 and 7-9 days before parturition. The stronger response to stressor action than in the control (progeny of rats undergoing mock adrenalectomy and intact rats) was evidence of premature maturation of their suprahypophyseal regulatory mechanism also. Signs of functional exhaustion in the pituitary-adrenocortical system and also in the thyroid gland were found in sexually mature (6-10 months) rats obtained from adrenalectomized females.

KEY WORDS: adrenalectomy; progeny; adrenals; functional exhaustion.

Experimental investigations and clinical observations have demonstrated the effects of pathology of the maternal endocrine glands on the development and formation of the functions of the fetal glands [2, 4, 5, 8, 13]. In the postnatal period the consequences of these effects have been inadequately studied. Yet data on this problem could help to promote a better understanding of the mechanism of origin of some congenital endocrinopathies, and would be important for the choice of tactics in prevention and treatment.

In the investigation described below the effect of adrenalectomy on pregnant rats on the state of the pituitary-adrenocortical system of their progeny was studied.

EXPERIMENTAL METHOD

Altogether 420 animals of the first generation obtained from noninbred albino rats, either adrenalectomized 1-3 and 7-9 days before parturition, subjected (at the same time) to mock adrenalectomy, or intact, were investigated. The state of adrenocortical function was assessed in the newborn (70-90 h) and sexually

*Deceased.

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TABLE 1. Thickness of Adrenal Cortex and Concentration of Neutral Lipids in It in New-born Rats

Group of progeny	Thickness of cortical zone (M ± m)*			Concentration of neutral lipids †
	zona glomerulosa	zona fasciculata	zona reticularis	
From intact rats	10,0±0,7	41,1±1,8	51,2±1,3	4,0
From rats undergoing mock adrenalectomy 3 days before parturition P	12,1±0,7 >0,05	39,6±0,9 >0,05	51,6±0,2 >0,05	4,0
From rats adrenalectomized 3 days before parturition P	10,9±0,5 >0,05	45,9±1,8 >0,05	56,8±1,6 ≈0,05	5,1
From rats undergoing mock adrenalectomy 8 days before parturition P	9,1±0,6 >0,05	42,7±1,0 >0,05	51,8±1,1 >0,05	4,5
From rats adrenalectomized 8 days before parturition P	10,6±0,7 >0,05	47,4±0,5 <0,05	58,1±1,0 <0,05	6,1

* In ocular micrometer units.

† In points, based on results of semiquantitative analysis of histochemical reaction for neutral lipids.

TABLE 2. Corticosterone Concentration in Adrenals and Blood of Newborn Rats

Group of progeny	T Corticosterone concentration (M ± m)					
	in blood, µg/100 ml			in adrenals, µg/g		
	at rest	after stress	increase, %	at rest	after stress	increase, %
From intact rats P	6,8±0,5	7,9±0,5 >0,1	—	6,0±0,4	13,7±0,9 <0,001	128
From rats undergoing mock adrenalectomy 3 days before parturition P	7,4±0,4	7,9±0,5 >0,1	—	6,4±0,9	14,4±1,5 <0,001	125
From rats adrenalectomized 3 days before parturition P	9,4±0,6	10,4±0,3 >0,1	38	13,5±1,0	18,3±1,9 <0,05	36
From rats undergoing mock adrenalectomy 8 days before parturition P	7,8±0,5	9,1±0,5 >0,1	—	7,3±0,5	15,2±0,8 <0,001	108
From rats adrenalectomized 8 days before parturition P	8,5±0,6	11,5±0,7 <0,05	24	8,3±0,8	21,5±2,4 <0,001	159

TABLE 3. Relative Weight of Organs of Newborn Rats

Group of progeny	Relative weight, mg/g body weight								
	adrenals			thymus			spleen		
	n	M ± m	P	n	M ± m	P	n	M ± m	P
From intact rats	54	0,29±0,01		5	2,7±0,2		12	4,4±0,3	
From adrenalectomized mothers	18	0,37±0,01	<0,001	19	1,8±0,2	<0,002	18	2,5±0,2	<0,001

mature (6-10 months) rats at rest and after exposure to stress (bilateral mock adrenalectomy). The corticosterone concentration in the peripheral blood and adrenals [14], the ascorbic acid concentration in the adrenals [15], the concentration of neutral lipids in the adrenal cortex [9], the thickness of the cortex and its various layers, and the relative weights of the adrenals, thymus, and spleen were determined. In the adult progeny, the thyroglobulin concentration in the thyroid gland also was determined [7]. The results of the measurements were subjected to statistical analysis [3, 12].

EXPERIMENTAL RESULTS

The biochemical, morphological, and histochemical data point to increased functional activity of the pituitary-adrenocortical system in the early postnatal period in the progeny of the adrenalectomized mothers.

TABLE 4. Corticosterone Concentration in Adrenals of Sexually Mature Rats ($M \pm m$)

Group of progeny	Corticosterone concentration, $\mu\text{g/g}$			
	at rest	after stress	increase, in %	P
From intact rats				
males	9.1 ± 1.6	51.5 ± 7.0	466	<0.001
females	15.5 ± 2.8	61.1 ± 6.8	294	<0.001
From adrenalectomized mothers				
males	6.4 ± 0.8	35.1 ± 3.6	488	<0.001
females	31.8 ± 7.6	61.9 ± 7.4	94	<0.01

TABLE 5. Thyroglobulin Concentration in Thyroid Gland of Sexually Mature Rats

Group of progeny	Thyroglobulin titer		
	n	$M \pm m$	P
From intact rats	8	$1:128 \pm 17.6$	<0.001
From adrenalectomized mothers	29	1565 ± 7.1	

*Final dilution of extract from thyroid glands which was still precipitated by organ-specific reagent.

This is shown by hypertrophy and earlier differentiation of the layers of the adrenal cortex, an increase in the concentration of neutral lipids in the cortex (Table 1), and an increase in the concentrations of corticosterone in the blood and adrenals (Table 2), and also by an increase in the relative weight of the adrenals and a decrease in the relative weight of the thymus and spleen (Table 3). In the progeny of females adrenalectomized 1-3 days before parturition the hormone level in the adrenals was higher, but the concentration of neutral lipids in the cortex and its thickness were less than in the progeny of female rats adrenalectomized 7-9 days before parturition. After exposure to stress there was a more marked increase in the corticosterone level in the adrenals than in the control and the increase was greatest in the progeny from females adrenalectomized 7-9 days before parturition. Only this group of the progeny responded to stressor action by an increase in the blood level of the hormone (Table 2). The progeny of adrenalectomized mothers responded more frequently than that of intact rats to surgical trauma by a decrease in the ascorbic acid concentration (5 of 10 and 1 of 6 positive cases, respectively).

In the sexually mature progeny of rats adrenalectomized both 1-3 and 7-9 days before parturition, the relative weight of the adrenals and the blood corticosterone concentrations both initially and after stress were indistinguishable from the corresponding indices in control animals ($P > 0.1$). On microscopic investigation a tendency was observed for the concentration of neutral lipids in the adrenal cortex to fall and the character of their distribution was more uniform than in the control. It was therefore decided to study the concentration of corticosterone in the adrenals before and after exposure to stress (Table 4). The difference between the corticosterone concentration before stress in the progenies of the adrenalectomized and control rats was barely significant, although the hormone concentration in females of the experimental progeny was slightly increased, and in the males, on the other hand, there was tendency for it to decrease. The increase in the corticosterone concentration in the females of the experimental group after exposure to stress regularly remained behind the increase in the control females. Signs of functional exhaustion were found in other endocrine glands of the females of the experimental progeny.

Morphological examination of the thyroid gland revealed clear changes of a degenerative character: follicles of irregular shape, colloid stasis, excessive growth of connective tissue, marked infiltrations with leukocytes, and the appearance of ultimobranchial bodies. The differences observed in animals of different sexes were evidently connected with the unequal influence of maternal adrenalectomy on maturation of the male and female reproductive systems of the progeny. This was shown indirectly by the premature opening of the vagina in females from the progeny of the adrenalectomized rats; earlier descent of the testes was not observed in males from the progeny of the same rats.

It can be concluded from the results of this investigation that adrenalectomy on pregnant rats leads to premature maturation and activation of the pituitary-adrenocortical system of their progeny in the early post-natal period. Both synthesis of the hormone in the adrenal cortex and its liberation into the blood are activated, and these changes were particularly marked in the progeny of females adrenalectomized 7-9 days before parturition, i.e., definitely before the beginning of functioning of the embryonic pituitary-adrenocortical system [10, 11]. The fact that in this group of progeny an earlier response to stress was observed evidently signifies premature maturation of the suprahypophyseal regulatory mechanisms controlling the reactivity of that system. These observations support Gromov's concept of exhaustion of the endocrine system of the adult due to premature function of this system in the fetus [1, 5, 7].

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