THE EFFECT OF THE ADRENOCORTICOTROPIC HORMONE ON THE STATE OF THE SKIN RECEPTORS

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Hormones of the glucocorticoid type increase the resistance of the organism to the action of various pathogenic agents [1, 6, 7]. The mechanism of action of these hormones is considered to be the result of their effect on hyaluronidase activity and on the structure of the intercellular substance, on the intensity of intracellular metabolism, and so on. However, the reactivity of the organism is primarily dependent on the functional state of the nervous system, for it is this which reacts first to the action of any stimulus.

After exposure to very strong pathogenic agents, death takes place, as a rule, as the result of a disturbance of the function of vitally important centers. This makes it necessary to study the action of the adrenal cortical hormones, which affect the resistance of the organism and the functional state of the various divisions of the nervous system. Investigations conducted in our laboratory have shown that the increased excretion of glucocorticoids, caused by administration of ACTH, depresses the excitability and increases the resistance of the respiratory and vasomotor centers [2], and weakens and modifies the reflexes regulating the motor function of the stomach [4]. The changes produced in the nervous system by sensitization of the organism are not abolished by administration of ACTH.

In the present research we investigated the effect of hyperfunction of the adrenal cortex, produced by administration of ACTH, on the state of the skin receptors in the rabbit and frog.

TABLE 1. Effect of ACTH on the Reflex Time in the Frog by Türck's Method (in seconds)

Elements of variational series	Control	After injection of ACTH
N	10	11
V	0,5—2	0,5—3
M	1,2	1,9
σ	0,066	0,07
m	0,02	0,02
t	23,0	
P	0,001	

Note. In Tables 1-4 N denotes both the number of animals used and the number of tests.

EXPERIMENTAL METHOD

The hormone was injected subcutaneously into rabbits in two doses, one the day before the experiment and the other 3 h before the experiment, each of 5 units/kg body weight, and into frogs in one dose of 5 units to each animal, 3 h before the experiment. Male animals weighing about 20 g (16-22 g) were chosen for the experiment. In some experiments only 2 units of hormone was given to each frog.

The state of the receptors was judged from the character of the potentials developing in the peripheral end of the sensory cutaneous nerve after application of adequate stimuli to the receptors. The impulses were recorded on a type MPO-2 oscillograph (vibrator No. 1), with a balanced amplifier and symmetrical input.

The skin was stimulated by means of an automatic vibrator, giving rhythmic stimuli, Frey's hairs, and solutions of sulfuric acid of differing concentration. The excitability of the tested receptors was determined from the threshold of excitability and from the intensity of the reaction to weak stimuli, and their reaction to strong tactile or acid stimuli was noted. The rate of adaptation of the tactile receptors to constant pressure (5 g) was also determined. The beginning of adaptation, when slowing of the impulses began, and its end, when the impulses disappeared, were noted. When the automatic vibrator was used, the excitability and the rate of adaptation of the receptors could be judged in their more general features from the frequency of the impulses and the duration of the volleys.

TABLE 2. Effect of ACTH on the Character of the Volleys of Impulses in the Cutaneous Nerve of the Frog during Rhythmic Stimulation of the Skin

Elements of variational series	Duration of volley (in millisec)		Maximal frequency (in cps)	
	control	after injection of ACTH	control	after injection of ACTH
N	8	5	8	5
V	0,05—0,7	0,01—0,2	96—176	10—150
M	0,29	0,09	139	86
σ	0,21	0,08	27	6,8
m	0,08	0,03	10,4	2,9
t	2,2		5	
P	0,05		0,001	

TABLE 3. Effect of ACTH on the Character of the Volleys of Impulses in the Cutaneous Nerve of the Rabbit during Stimulation of the Skin with a Vibrator

Elements of variational series	Duration of volley in (millisec)		No. of impulses in vol.		Frequency (in cps)	
	control	after injection of ACTH	control	After injection of ACTH	control	after injection of ACTH
N	10	10	10	10	10	10
V	0,05—0,25	0,05—0,2	7—35	7—33	80—180	120—260
M	0,13	0,09	16	15	113	170
σ	0,058	0,042	8,1	7,4	32,5	41,1
m	0,019	0,014	2,7	2,4	10,8	13,7
t	2,1		0,3		3,3	
P	0,05		0,5		0,01	

TABLE 4. Effect of ACTH on the Threshold of Sensitivity of the Tactile Receptors of Frogs (in g)

Elements of variational series	Control	After injection of ACTH in doses of	
		5 units	2 units
N	14	10	4
V	0,01—0,02	0,02—0,1	0,01—0,02
M	0,0135	0,035	0,015
σ	0,0047	0,025	0,016
m	0,0013	0,008	0,01
t	2,6		
P	0,02		

EXPERIMENTAL RESULTS

After administration of 5 units ACTH to a frog, no visible changes were observed in its condition for a period of 3 h. The reflex time, determined by Türck's method, was slightly lengthened (Table 1).

In rabbits the injection of these doses of the hormone led to a slight lowering of the motor activity during the period of preparation of the animals for the experiment (tying down, dissection of the nerves, etc.).

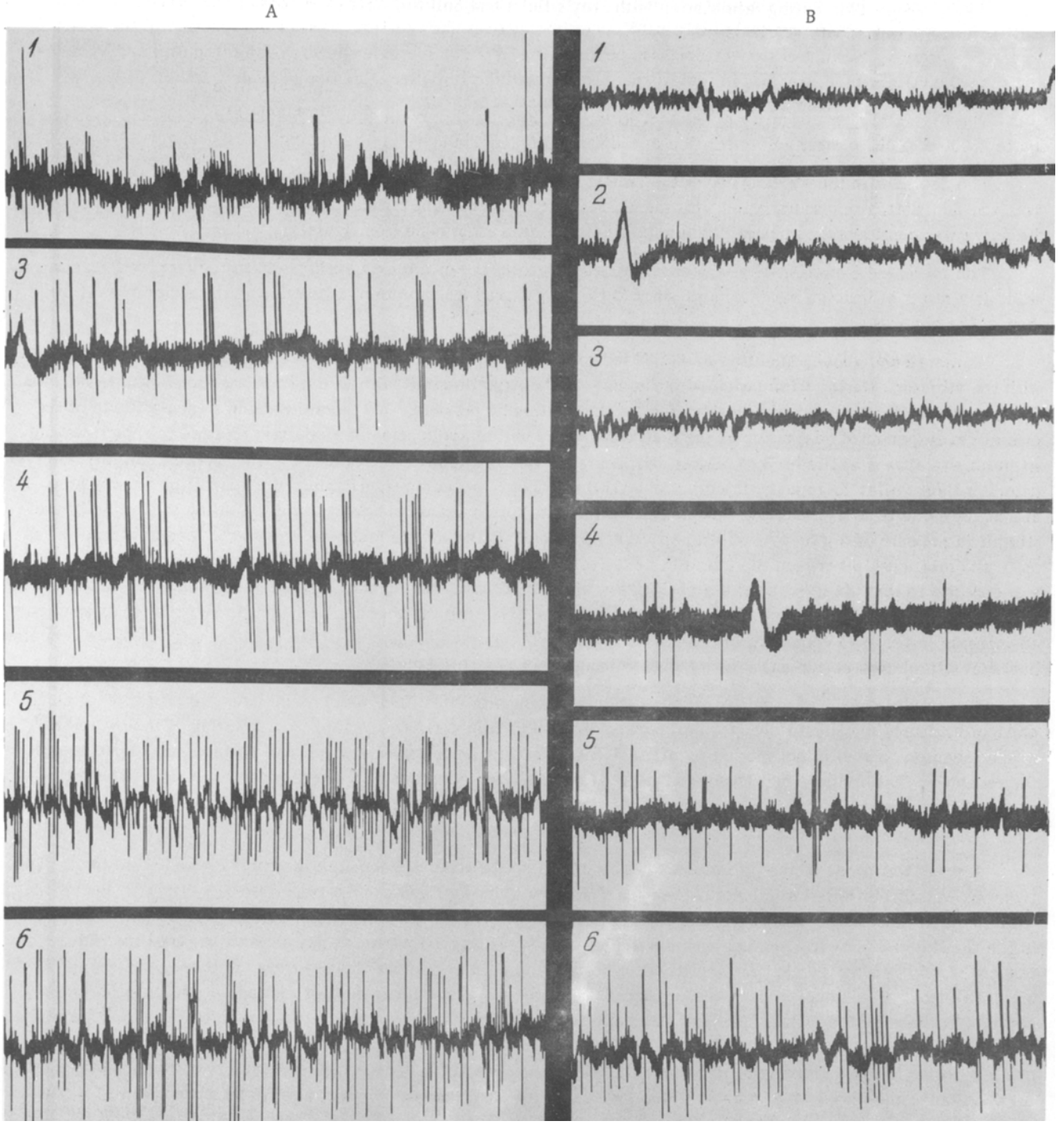
TABLE 5. Effect of ACTH on the Number of Impulses Passing from the Receptors of the Frog's Skin during Stimulation with Frey's Hairs and Sulfuric Acid (K – control, A – after injection of ACTH)

Elements of variational series	Number of impulses during stimulation								Adaptation time (in seconds)			
	0,01 *e*		0,02 *e*		0,05 *e*		5,0 *e*		beginning		end	
	K	A	K	A	K	A	K	A	K	A	K	A
N	15	10	15	10	3	9	15	10	14	10	14	10
V	0—22	Нет	2—66	0—60	38—52	0—34	14—92	22—220	0,4—21,5	0,2—3	2—23	1—6
M	7	0	36	11	46	17	52	90	4,6	1,2	9,5	3,1
σ	7,2	0	24,6	17,3	9	11,7	26,5	61	2,8	0,8	6,0	2
m	1,9	0	6,6	5,7	6,4	4,3	7,1	20,3	0,7	0,26	1,7	0,66
t	—		2,9		3,9		1,8		4,5		3,5	
P			0,01		0,01		0,05		0,001		0,01	

Continuation

No. of impulses during stimulation with sulfuric acid									
0,25%		0,5%		1%		2%		4%	
K	A	K	A	K	A	K	A	K	A
11	10	10	10	11	10	14	10	14	10
6—52	0—40	14—86	10—220	12—124	32—170	16—166	16—246	6—136	10—170
25	12	50	49	57	58	59	78	36	73
14,3	11,8	20,1	58,9	33,7	41,4	42,3	53,2	37,9	47
4,6	3,9	6,5	19,6	10,8	13,8	11,7	17,7	10,5	15,6
2,1		0,04		0,05		0,9		2	
0,05		0,5		0,5		0,2		0,05	

Note. N denotes the number of animals tested. In each animal the reaction of the receptors to stimulation by Frey's hairs and by acid was investigated.



Changes in the potentials arising in the peripheral end of the cutaneous sensory nerve of a rabbit in conditions of hyperfunction of the adrenal cortex. A) Experiment No. 15 (control); B) experiment No. 4 (after injection of ACTH); 1) pressure of 0.01 g; 2) pressure of 0.02 g; 3) action of 0.25% sulfuric acid; 4) action of 0.5% sulfuric acid; 5) action of 2% sulfuric acid; 6) action of 4% sulfuric acid. The photograph was taken at the beginning of the action of the corresponding stimulus. In the absence of stimulation impulses were never found in the nerve on testing.

During the action of the automatic vibrator rhythmic volleys of impulses developed. The duration of these volleys in frogs and rabbits was longer in control experiments than during stimulation of the function of the adrenal cortex. In frogs shortening of the volleys was accompanied by a considerable slowing of the impulses and by a decrease in their amplitude, whereas in rabbits the frequency of the impulses increased (Tables 2 and 3).

The threshold of excitability of the tactile receptors in the control frogs averaged 0.00135 ± 0.0013 g, changing to 0.035 ± 0.008 g after administration of 5 units of ACTH (Table 4).

The decrease in the excitability of the tactile receptors following administration of ACTH could also be seen from the fact that during stimulation with the hairs, exerting only slight pressure, the number of impulses arising in the nerve was considerably smaller in the animals receiving the hormone (see figure).

The increased excretion of glucocorticoids led to a lowering of the excitability also of the receptors reacting to acid, as a result of which a weak solution of acid (0.25%) caused a less intensive reaction in the experimental frogs than in the controls.

As mentioned above, injection of ACTH led to a shortening of the volleys arising during rhythmic stimulation with the vibrator. During stimulation with the hair in the experimental animals the impulses soon began to become fewer, and then disappeared completely, despite the continuing pressure. We therefore made a special study of the rate of development of adaptation of the tactile receptors during application of a constant pressure (a superthreshold stimulus was always applied – 5 g). After disappearance of the impulses the pressure was withdrawn, and this always caused a short volley to appear. Injection of ACTH was found to shorten significantly the adaptation time (Table 5), and at the same time to make the receptors more resistant to the action of strong stimuli. During the action of these stimuli (a pressure of 5 g or 2% and, in particular, 4% acid) on the tactile receptors and on the receptors reacting to acid, the relationship between the intensity of the reaction in the control experiments and after the injection of ACTH was opposite to that observed after the application of weak stimuli: the number of impulses in the afferent nerve was greater, not in the controls, but after administration of ACTH. It must be pointed out that in the control experiments an increase in the acid concentration from 2 to 4% caused a marked depression of the impulse activity of the receptors, but after stimulation of adrenal activity these changes were ill defined.

The results described in this paper show that administration of ACTH, which stimulates the excretion of glucocorticoids, causes significant changes in the state of the skin receptors, as revealed by a lowering of the excitability of the receptors, a significant shortening of the adaptation time at constant pressure, and an increased resistance of the receptors. It is evident that these changes in the functional properties of the receptors are associated with the effect of hormones on metabolic processes in nerve tissue and in the cells of non-free nerve endings.

SUMMARY

A study was made of the effect produced by ACTH on the state of cutaneous receptors of rabbit and frog. The hormone was administered to rabbits twice (in a dose of 5 units/kg) and to frogs once (5 units/animal). Receptors were stimulated by an automatic "toucher", and in frog – by Frey's hairs and sulfuric acid solutions. Impulses appearing in the skin nerve were recorded with the aid of a loop oscillograph. Prior to this, determination of the reflex time was done in frogs after Türck. Excitability of rabbits diminished and reflex time of frogs increased after the ACTH administration. The impulse discharge considerably decreased after stimulation with an automatic "toucher". With constant pressure by Frey's hairs receptor adaptation occurred very rapidly. The excitation threshold of tactile receptors and of receptors reacting to acid showed an essential rise, whereas the reaction of receptors to weak stimuli declined. Along with a reduction of receptor excitation there was a rise of receptor resistance to strong stimuli. In the latter instance the impulsation greatly decreased in control experiments, which did not occur after the ACTH administration.

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