THE INFLUENCE OF THE CEREBRAL HEMISPHERES ON THE ADRENOCORTICOTROPIC ACTIVITY OF THE HYPOPHYSIS

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The present studies are based on the view, expressed by I. P. Pavlov, that all the functions of the organism are subject to regulating influences from higher divisions of the central nervous system. The work of B. V. Aleshin and his colleagues [1, 2] has shown that a mechanical influence exerted on the cerebral cortex alters the dependence of the thyroid gland and of sexual functions on the hypophysis.

Our earlier observations made it clear that the production of hormones in the adrenal cortex, and the transformation of these hormones, depend on impulses from the brain [8].

The purpose of the present investigation was to study the effect of a disruption of the normal state of the cerebral cortex on the adrenocorticortropic activity of the hypophysis. To answer this question, we examined the changes in the extent to which adrenocortical androgenic function is shifted in hypophysectomized rats given extracts of the hypophyses under investigation.

METHODS

The donors were male rabbits weighing 2-2.5 kg. The cerebral cortex was treated as follows: Silver plates were placed on the motor, olfactory, parietal, temporal, and occipital cortex along the midline, in such a way that one plate affected both cerebral hemispheres. The temporal lobe was subjected to a one-step operation in which two plates were placed upon the two halves of the cortex. In this way, a constant and prolonged disturbance of the normal condition of the brain was achieved.

Ten days after the operation these rabbits were sacrificed by injecting air into an ear vein; the content of adrenocorticotropic hormone (ACTH) in their hypophyses was then determined. The content of ACTH was determined and bio-assayed by the method of G. Sayers and M. Sayers [9], as modified by us [4], on hypophysectomized rats, 24 hours after hypophysectomy. For this purpose we determined the quantitative change in androgen content in the right adrenal $1\frac{1}{2}$ hours after injection of hypophyseal extract into the abdominal cavity.

The initial androgen content was determined from the left adrenal, which was removed before the extract was injected. The androgen content was determined by the method published by us previously [5], which makes use of the Zimmermann color reaction [10]. The androgen content was expressed in μg-%. Androgens were extracted from donor adrenals for biological testing in the same way as for the colorimetric determination of androgens. This extract was tested on the combs of day-old chicks by the method of Ya. M. Kabak [3].

In previous papers [6, 7] we discussed the effect of the superior cervical ganglia on the adrenocorticotropic function of the hypophysis. The effect of a disturbance of sympathetic activity on the adrenocorticotropic function of the hypophysis was established from the change in the androgen content in the adrenal cortex of hypophysectomized rats that received hypophyseal extract from donors whose superior cervical ganglia had either been removed or stimulated.

The reduction of the androgen content in the adrenal cortex of recipients after the injection of hypophyseal extract from sympathectomized donors, as compared with that observed after injection of hypophyseal extract from intact donors, was interpreted as indicating that the adrenocorticotropic activity of the hypophysis was elevated. On account of the low androgen concentration in the gland, it was assumed that androgen secretion exceeded androgen production in the adrenal cortex. On the other hand, the elevated androgen concentration in the adrenal cortex of recipients of hypophyseal extract from donors whose superior cervical ganglia had been stimulated was interpreted as due to a decrease in the adrenocorticotropic activity of the hypophysis.

But later experiments on rabbits, in which hormone production in the adrenal cortex and hormone secretion into the blood were studied simultaneously, showed that an elevation of the androgen content in this gland is accompanied by an increase in androgen secretion into the blood; when the androgen content in the adrenal cortex is reduced, the androgen level in the blood is also reduced. Thus we suggest that when hypophyseal adrenocorticotropic function is enhanced, not only the production of androgens in the adrenal cortex, but also the secretion of androgens into the blood, is increased.

TABLE 1. Androgen Content (in μg-%) in the Adrenal Cortex of Recipients Before and After Injection of Hypophyseal Extracts From a Normal Animal and From Animals Subjected to Mechanical Pressure on the Cerebral Cortex

No. of animal	Normal			Motor cortex			Olfactory cortex			Parietal cortex			Temporal cortex			Occipital cortex		
	left, before injection	right, after injection	difference from initial level	left, before injection	right, after injection	difference from initial level	left, before injection	right, after injection	difference from initial level	left, before injection	right, after injection	difference from initial level	left, before injection	right, after injection	difference from initial level	left, before injection	right, after injection	difference from initial level
1	150,8	244,4	+62,0	104,0	98,1	—5,7	80,2	69,6	—13,3	127,4	112,0	—12,2	134,7	203,0	+50,0	105,4	175,0	+66,0
2	150,0	212,5	+41,7	88,3	91,9	+4,0	90,9	71,2	—21,0	239,0	180,0	—24,7	103,0	196,0	+90,2	153,3	271,9	+77,4
3	159,9	278,7	+74,3	72,3	77,0	+6,5	85,0	82,0	—3,6	152,9	125,5	— 8,8	58,5	95,0	+60,6	164,9	232,2	+40,8
4	186,6	353,7	+89,0	82,5	78,0	—5,5	112,0	98,3	—12,3	198,0	173,0	—12,7	91,6	149,0	+62,6	139,2	201,6	+44,8
5	198,8	303,3	+52,6	112,6	104,2	—6,6	80,0	72,7	—10,0	213,0	184,3	—13,6	126,0	195,0	+54,7	212,1	286,0	+35,3
6	189,7	272,5	+49,0	98,7	86,7	—12,2	117,0	92,1	—21,3	187,2	158,0	—15,6	118,8	171,3	+44,1	97,8	167,4	+71,1
7	80,2	120,8	+50,0	135,2	151,3	+19,3	98,0	83,6	—14,7	174,1	149,6	—14,1	142,5	198,9	+39,5	222,0	299,7	+35,0
8	107,0	184,0	+72,0	123,6	213,2	—10,0	109,2	101,7	—6,9	108,7	91,0	—16,3	201,1	297,4	+47,9	148,0	215,1	+45,3
9	173,0	299,0	+74,2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Mean	155,0	252,0	+62,3	116,2	112,5	— 3,2	96,4	82,9	—12,8	175,3	146,8	—16,3	122,2	188,2	+54,0	155,3	231,1	+51,9

TABLE 2. Androgen Content in Adrenal Cortex of Donor Rabbits Before and After Mechanical Pressure on the Cerebral Cortex (in milligrams)

No. of animal	Weight of combs from intact chicks	Normal		Olfactory cortex		Parietal cortex		Temporal cortex		Occipital cortex	
		weight of combs after test of extract	difference from control (%)	weight of combs after test of extract	difference from control (%)	weight of combs after test of extract	difference from control (%)	weight of combs after test of extract	difference from control (%)	weight of combs after test of extract	difference from control (%)
1	12	18	+50,0	8	—55,6	8	—55,6	50	+211,1	45	+150,0
2	13	25	+92,3	14	—44,0	9	—64,0	57	+128,0	46	+84,0
3	10	15	+50,0	6	—59,7	11	—26,7	35	+133,3	34	+126,6
4	11	15	+36,4	11	—27,0	9	—40,0	37	+146,6	38	+153,3
5	13	18	+39,0	10	—45,6	8	—55,6	54	+200,0	39	+116,6
6	14	34	+143,0	19	—45,9	15	—55,9	126	+230,6	73	+114,7
7	13	24	+84,6	9	—59,4	10	—58,4	67	+180,0	50	+108,3
8	10	—	—	—	—	—	—	—	—	—	—
9	12	—	—	—	—	—	—	—	—	—	—
Mean	12,0	21,3	+77,5	11	—48,2	10	—51,1	60,7	+185,0	46,4	+121,0

RESULTS

Examination of hypophyses from intact donors. Adrenocorticotropic extract from the hypophyses of intact donors, when injected into recipients, produces a marked increase in androgen content in the adrenal cortex. Whereas the androgen content in the left adrenal averaged 155 μg-% before injection of the extract, that in the right adrenal after injection of the extract was 252 μg-%—i.e., the androgen content increased 62.3% in relation to the androgen content in the left adrenal. These values, which show the androgen content in the adrenals, were used as a control.

Subsequent observations on the content of ACTH in hypophyses of donors subjected to the application of silver plates on various lobes of the cerebral cortex showed that the disruption of the normal state of the cortex has different effects on the adrenocorticotropic function of the hypophysis, depending on the lobe involved (Table 1).

Application of plates to various regions of the cerebral cortex. Injection of adrenocorticotropic extract from the hypophyses of donors in which the plates were applied to the motor cortex did not cause an elevation of the androgen content in the adrenal cortex. Prior to the administration of extract, the androgen content in the left adrenal averaged 116.2 μg-%, and after injection the androgen content in the right adrenal was approximately the same (112.5μg-%), which is a difference of only 3.2% from the initial level. A comparison of these results shows that ACTH was practically absent from this extract. Thus, when the agent is applied to the motor cortex the result is a distinct reduction in the adrenocorticotropic activity of the hypophysis.

Similar results were obtained after injection of extracts from donors in which the plates were applied to the olfactory cortex. Thus, whereas the androgen content in the left adrenal before injection of the extract was 96.4 μg-%, on the average, after injection the androgen content in the right adrenal was still 82.8μg-%. Consequently, the androgen content in the right adrenal was reduced to 12.8% below the initial level.

The same result was observed following injection of hypophyseal extracts from donors in which the plates had been applied to the parietal cortex. Before the injection of extract, the androgen content in the left adrenal averaged 175.3 μg-%, and after injection the androgen content in the right adrenal remained at 146.8 μg-%, i.e., the androgen content was reduced 16.3% below the initial level.

The results of these three series of experiments demonstrate that adrenocorticotropic extract from hypophyses of donors subjected to the application of plates on the motor, olfactory, and parietal cortex not only does not cause the androgen content in the adrenal cortex of recipients to increase in relation to the controls, but even reduces the androgen level somewhat in relation to the initial level; this can be regarded as an indication that adrenocorticotropic activity has been reduced.

Hypophyseal extract from donors in which the plates were applied to the temporal and occipital lobes produced a noticeable increase in the androgen content in the adrenal

cortex of the recipients. The results of these studies showed that for the temporal-cortex group, whereas the androgen content in the left adrenal averaged 115.3 μg-% before injection, injection of hypophyseal extract from the donors of this group caused the androgen content of the right adrenal to increase to 231.1 μg-%, an increase of 51.9%. Thus, in this instance adrenocorticotropic activity did not undergo noticeable changes in comparison with the controls. The same result was obtained following injection of hypophyseal extract from donors of the occipital-cortex group. In the left adrenal prior to the injection of extract the androgen content was 122.2 μg-%, and in the right adrenal after injection it was 188.2 μg-%, i.e., the androgen content increased 54.9% in comparison with the initial level.

The values obtained in these two series of experiments show that the ACTH content does not change in relation to the control.

Investigation of androgens in adrenals of donors by means of comb growth in chicks. Tests of adrenal extract from intact donors resulted in a distinct increase in the weight of combs, which is evidence that the androgen content in these adrenals is elevated. The weight of combs from intact chicks averaged 12 mg, and in tests of androgenic extract from the adrenals of intact donors the weight of the combs increased to 21.3 mg, on the average—an increase of 77.5%. The weights of combs from chicks that were given adrenal extract from intact donors served as a control.

The results of the colorimetric determination showed that under the influence of ACTH contained in the hypophysis of intact donors, the androgen level in the adrenal cortex of recipients increased sharply: 62.3%, on the average. We found approximately the same increase in the weight of combs when we used extract from the adrenals of intact donors. On the other hand, extract from the adrenal cortex of donors in which plates were applied to the olfactory and parietal lobes caused no noticeable changes (11-10 mg, on the average) in the weight of combs. We may conclude that the adrenals of these donors contained practically no androgen (Table 2).

But adrenal extract from donors in which plates were applied to the temporal lobe increased comb weight to 46.4 mg, or 121%, in comparison with the control. Following application of plates to the occipital lobe, adrenal extract from the donors produced a still more pronounced increase in comb weight (60.7 mg). These results show that under these circumstances the androgen content in the adrenals is elevated in relation to the control (see Table 2).

Our observations on the changes in adrogen content in the adrenals of recipients and donors, presented in Tables 1 and 2, show that disruption of the normal state of different regions of the cerebral cortex has different effects on the processes of androgen formation in the adrenals.

SUMMARY

The author studied the effect of a disturbance in the normal state of the cerebral cortex on adrenocorticotropic activity of the hypophysis in rabbits. Shifts in the adrenocorticotropic activity of the hypophysis as a result of injury to the cerebral cortex were determined from changes in the androgen content in the adrenal cortex of hypophysectomized rats given extracts of these hypophyses. It was established that when silver plates are applied to the anterior part of the cortex of both hemispheres, the androgen content is diminished in the adrenal cortices of both donors and recipients; this may be regarded as an indication that the adrenocorticotropic activity of the hypophysis is reduced.

Conversely, the high androgen content in the adrenal cortex of hypophyseal extract donors and recipients following application of silver plates to the posterior cerebral cortex of donors (in comparison with the effect of hypophyseal extracts from intact animals) demonstrates that in this case the adrenocorticotropic activity of the hypophysis does not undergo substantial changes.

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