

EFFECT OF THYROIDECTOMY ON FUNCTION OF THE HYPOTHALAMO-HYPOPHYSEO-ADRENAL SYSTEM

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UDC 612.433+612.45+612.826.4]-06:612.445

The content of ascorbic acid in the adrenals and of ACTH in the pituitary and the corticotropin-releasing activity of the hypothalamus (CRF activity) were studied at various times after thyroidectomy in experiments on 63 albino rats. The CRF activity was increased and the content of ACTH and ascorbic acid was halved 1 and 5 days after the operation. By the 14th day the CRF activity was reduced, the ACTH content was increased to the normal values, and the ascorbic acid level was largely restored. Thyroidectomy led to a disturbance of all the chief components of the hypothalamo-hypophyseo-adrenal system, including CRF production.

Investigations have shown [2, 3, 5, 8, 11, 12] that reciprocal relationships exist between the secretion of pituitary thyrotropic hormone (TTH) and ACTH. Accordingly, hypothyroid states leading to an increase in TTH secretion should inhibit ACTH production and cause a corresponding decrease in the functional activity of the hypophyseo-adrenal system. This effect would be facilitated by a decrease in the utilization of corticosteroids by the tissues in the presence of a thyroid hormone deficiency [9, 13]. On the other hand, by the feedback principle, reduced production of corticosteroids should activate production of the corticotropin releasing factor of the hypothalamus (CRF) and the subsequent synthesis and secretion of ACTH. In hypothyroidism complex dynamic relationships may thus arise between individual components of the hypothalamo-hypophyseo-adrenal (HHA) system. Their detailed study must include not only determination of the activity of the hypophyseo-adrenal complex, but also the CRF activity of the hypothalamus.

The object of the present investigation was to study the state of adrenal function, the ACTH content in the pituitary, and the CRF activity of hypothalamic extracts of rats with experimental hypothyroidism caused by thyroidectomy.

EXPERIMENTAL METHOD

Experiments were carried out on 63 adult male rats. The rats of group 1 were left intact (control). Thyroidectomy was performed on the animals of group 2. The rats of group 3 underwent a mock thyroidectomy (control of the stressor action of the anesthetic and the operation itself). All the animals were decapitated, and the left adrenal and pituitary glands and the hypothalamus were removed (in group 2, 24 h and 5 and 14 days after thyroidectomy). The state of adrenal function was estimated from the content of ascorbic acid in the glands determined by the method of Roe and Kuether [10]. The ACTH content in the pituitary was measured in 56 recipient rats by the method of Birmingham et al. [7] in Skebel'skaya's modification [4]. The CRF activity of the hypothalamus was determined by the method of Arimura et al. [6]. The essence of this method is the preparation of hypothalamic extracts and the subsequent testing of their activity on recipient rats after preliminary suppression of function of their HHA system by means of a special "cocktail" (chlorpromazine, morphine, and nembutal). The level of CRF activity of the hypothalamus was judged from the difference between the ascorbic acid content in the left (before injection) and right (1 h after intravenous injection of the extract) adrenals of 47 recipient rats.

Department of Pathological Physiology, A. M. Gor'kii Donetsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR, N. A. Yudaev.) Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 73, No. 4, pp. 19-21, April, 1972. Original article submitted July 1, 1971.

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TABLE 1. Content of Ascorbic Acid in Adrenal and ACTH in Pituitary Gland and CRF Activity of Hypothalamic Extracts at Various Times After Thyroidectomy

Group of animals	No. of animals	Ascorbic acid (in mg %)		ACTH (in i.u./100 μ g acetone-treated pituitary tissue)		Corticotropin releasing activity of hypothalamic extracts (in mg % ascorbic acid)	
		$M \pm m$	P	$M \pm m$	P	$M \pm m$	P
1	18	422 \pm 5,25		7,08 \pm 0,34		144 \pm 2,59	
2.	15	228 \pm 2,21	<0,001	3,8 \pm 0,29	<0,001	171 \pm 0,90	<0,01
after 24h	11	289 \pm 5,7	<0,001	3,8 \pm 0,09	<0,001	151 \pm 2,31	>0,005
" 5 days							
after 14 days	13	311 \pm 4,81	<0,001	7,5 \pm 0,32	>0,5	134 \pm 0,98	<0,01
3 (after 24 h)	6	406 \pm 15,2	>0,5	8,0 \pm 0,57	>0,5	145 \pm 3,6	>0,5

EXPERIMENTAL RESULTS

It follows from Table 1 that the ascorbic acid content in the adrenals, the ACTH content in the pituitary, and the CRF activity of the hypothalamus of the intact rats were within normal limits [1, 4]. A significant increase in CRF activity was observed 24 h after thyroidectomy. Since it was accompanied by a marked decrease (by half) in the ACTH content in the pituitary and ascorbic acid content in the adrenal, it is probable that the acutely arising deficiency of thyroid hormones led to activation of the HHA system. The stressor effect of the operation trauma and the anesthetic was ruled out because the mock thyroidectomy did not give rise to similar changes. This pattern of activation of the HHA-system still remained 5 days after thyroidectomy.

The situation was rather different 14 days after thyroidectomy: with a significant decrease in CRF activity the ACTH content in the pituitary was increased to normal values and the ascorbic acid content in the adrenal was largely restored. During a more prolonged state of hypothyroidism, production of corticotropin releasing factor by the hypothalamus was evidently slightly reduced, so that the degree of activation of the hypophyseo-adrenal complex was correspondingly lowered.

The function of the HHA system thus undergoes phasic changes in the course of hypothyroidism.

These results suggest that changes in the HHA system cannot be explained by a simple scheme of reciprocal relationships between the pituitary tropic hormones (TTH \rightleftharpoons ACTH), but that other components of regulation are also involved and, in particular, an increase in the CRF activity of the hypothalamus.

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