EFFECT OF THE SYMPATHETIC NERVOUS SYSTEM ON HORMONE FORMATION IN THE THYROID

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Experimental and clinical observations show that thyrotropic hormone is not the only stimulator of the thyroid gland. The function of the thyroid can be regulated directly via its innervation and without the participation of the pituitary, i.e., by a parahypophyseal mechanism [3, 4, 11, 12]. The sympathetic division stimulates, while the parasympathetic depresses the thyroid gland [1, 17]. However, the problem of the role of the sympathetic and parasympathetic nervous system in the regulation of thyroid function has not been completely solved. Some investigators claim that the action of direct nervous impulses reaching the thyroid parenchyma is merely to produce vasomotor effects and they do not influence secretory processes [13-15].

Much information has recently been obtained showing that nervous impulses may have a direct influence on the hormone-producing activity of the thyroid gland [1-3, 4-16]. Factors acting on the sympathetic innervation of the thyroid produce changes in the functional activity of the gland [10-12, 17] which are reflected in the absorption of I^{131} [16], the liberation of hormones into the blood stream, the reaction of the thyroid parenchyma to thyrostatic substances [18], regeneration of the gland, and the sensitivity of the thyroid to thyrotropic hormone [6].

However, in the intact animal, during stimulation or blocking of the sympathetic innervation of the thyroid, no appreciable changes take place in either its function or its structure, and this is attributed to the action of thyrotropic hormone which, because it is a very powerful agent, masks the possible action of direct nervous impulses. If the production of thyrotropic hormone is eliminated or depressed and, consequently, its influence on the thyroid gland is abolished or weakened (as by the action of chlorpromazine) [5, 7, 9], the action exerted by sympathetic impulses on the thyroid began to be manifested even in the intact organism [7, 9]. However, these experiments demonstrated the influence of the sympathetic nervous system only on the ability of the thyroid to absorb iodine.

In the present investigation the effect of the sympathetic nervous system on synthesis of the thyroid hormones was studied.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 2.0-2.5 kg on which the operation of bilateral extirpation and chronic stimulation of the superior cervical sympathetic ganglia was carried out. Stimulation was achieved by wrapping the ganglia in a coil of thin silver wire. Ten days after the operation the rabbits received a subcutaneous injection of I^{131} in a dose of 5 μCi. The thyroid was removed 24 h later and treated by enzymic hydrolysis in phosphate buffer (pH 8.2-8.4). Chromatography of the hydrolysates was carried out on "Leningrad M" paper in a system butanol–ethanol–2N ammonia (5 : 1 : 2). X-ray film was then placed on the dried chromatogram and exposed for 10 days, after which the film was developed and tested with a densitometer. The iodine-containing compounds of the thyroid were estimated from the maxima of the curves and from the R_f values, taken from the book by Pitt-Rivers and Tata [19].

EXPERIMENTAL RESULTS

Analysis of the radiochromatograms (see table) of normal male rabbits by fractionation of the hormones showed that after distillation of the hydrolysates of the thyroid gland, iodinated amino acids were

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Table 1. Content of Iodinated Amino Acids in Thyroid Hydrolysates of Rabbits Undergoing Procedures Directed Toward the Superior Cervical Sympathetic Ganglia

Nature of procedure	DIT + MIT		I		T_4	
	$\bar{X}\pm S\bar{x}$	P	$\bar{X}\pm S\bar{x}$	P	$\bar{X}\pm S\bar{x}$	P
Control	70,02± 1,73	—	8,97± 0,62	—	14,73± 0,82	—
Sympathectomy	74,81± 1,22	<0,02	11,87± 0,66	0,002	13,5± 0,91	>0,01
Stimulation	74,4± 1,41	<0,05	8,3± 1,08	>0,1	18,05± 0,94	<0,01

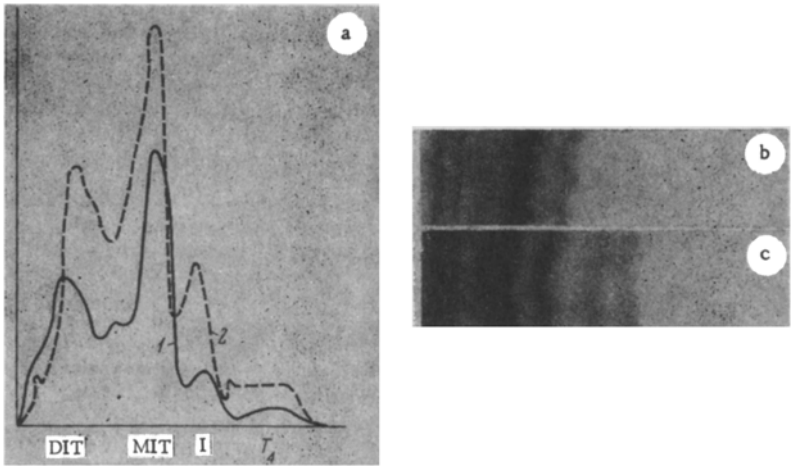

Fig. 1. Densitogram and chromatograms of hydrolysates of thyroid of a control (intact) rabbit and a rabbit undergoing prolonged stimulation of the superior cervical sympathetic ganglia. a) Densitogram (1, control; 2, stimulation of superior cervical sympathetic ganglia); b) chromatogram of thyroid hydrolysate of a normal rabbit; c) chromatogram of thyroid hydrolysate of a rabbit undergoing prolonged stimulation of the superior cervical sympathetic ganglia.

present in the following proportion: DIT + MIT* 70.02 ± 1.73%, I 8.97 ± 0.62%, and T_4 14.73 ± 0.82%.

After bilateral extirpation of the superior cervical ganglia, an increase in the size of the DIT and MIT bands was observed on the chromatograms and densitograms, for not only were they wider than in the control, but they produced more intense blackening of the photographic emulsion. The I band likewise was more intense. However, the T_4 band was almost the same as in the control. The results of the study of the iodinated amino acids in the hydrolysates of these glands showed that the mean content of the DIT + MIT fractions was increased by a statistically significant degree compared with the fractions of the iodine-containing components of normal animals (see table). The content of inorganic iodine in the sympathectomized rabbits also was increased. A difference was observed when the percentage absorption of I^{131} by the thyroid of normal rabbits (20 ± 1.3%) was compared with that in animals after removal of the superior cervical ganglia (14.6 ± 1.025%; $P < 0.002$). After removal of these ganglia, the thyrotropic function of the pituitary is considerably increased [8]. However, the excess of thyrotropic hormone must have stimulated the intrathyroid iodine metabolism and, in particular, must have intensified the formation of iodothyronines [20, 21]. The reaction taking place thus shows that a reduction in the flow of sympathetic impulses received

* For convenience the iodinated compounds of the thyroid are designated by abbreviations corresponding to the generally accepted symbols: thyroxin, T_4; diiodityrosine, DIT; monoiodityrosine, MIT; and inorganic iodine, I.

by the thyroid gland prevents the development of the effect of the thyrotropic hormone, in agreement with previous observations [6], showing that these nervous impulses increase the sensitivity of the thyroid gland to thyrotropic hormone.

This conclusion was confirmed by the results of the opposite experiment in which chronic stimulation of the superior cervical ganglia was carried out. In this case, the thyrotropic function of the pituitary was not increased, or was actually weakened compared with normal. Despite this fact, the chromatograms and densitogram (see figure) showed an increase in the size of the DIT, MIT, and T_4 bands, thus indicating a general increase in the intensity of intrathyroid hormone synthesis. The study of hydrolysates of the thyroid glands of these rabbits revealed a significant increase both in the inactive DIT + MIT fractions and in the true hormones of the T_4 fraction (see table). Some increase was also observed in the absorption of I^{131} by the thyroid to 23.7 ± 1.5% from the normal level of 20 ± 1.3% ($P = 0.05$).

The effect of the sympathetic impulses on hormone formation in the thyroid was thus visible even during the action of the thyrotropic hormone. The results described above show that the influence not only of the thyrotropic hormone, but also of sympathetic nervous impulses, is essential for the hormone-forming activity of the thyroid gland. The effect of the sympathetic impulses is exerted particularly in the final stage of intrathyroid hormonogenesis, for in their absence the combination of iodothyronines into iodothyronines is inhibited. The thyroid gland is thus regulated not only by thryotropic hormone, but also by the combined action of this hormone and efferent nervous impulses.

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