Interrelationship Between the Thyroid Gland and Sympathetic Function

Many manifestations of the thyroid hormones are very similar to those of the sympathetic activity. Several hypotheses have been reported to explain the possible relations existing between the thyroid function and catecholamines, such as: synthesis modifications[1], decrease of catabolism[2], modifications of the enzymatic system involved[3], variations in turnover[4], and storage of sympathetic amines[5,6], changes in the sensitivity of receptors[7], activation of adenylcyclase[8], and phosphorylase[9].

In a previous paper[5], we found that the urinary excretion of catecholamines increased and the 3-methoxy-4-hydroxy mandelic acid decreased in the experimental hyperthyroidism, whereas no significant modifications were induced in hypothyroidism. Supposing that the parameters studied reflect the events taking place in the different tissues, investigations were performed on the contents and the concentrations of catecholamines and glycogen in 2 organs having different activities but being sensitive to the thyroid and sympathetic function, such as the submaxillary gland[10] and the heart[11] of rats in whom experimental hyper- and hypothyroidism was induced.

Materials and methods. Wistar male rats were used. Catecholamines were determined in the submaxillary gland and heart of animals divided into 3 groups: a) control animals; b) animals injected with 30 μg sodium triiodothyronine (T_3) i. p. daily for 1 week; c) 40-day-old rats injected with 1 mCi ^{131}I i. p. 6 weeks before the experiments. The modifications of glycogen in those organs were determined in 4 groups of animals: a) controls; b) injected with 30 μ*M* isoproterenol i. p. $^1/_2$ h before the experiments; c) injected with ^{131}I; d) administered with ^{131}I plus 30 μ*M* isoproterenol i. p. $^1/_2$ h before the experiments. Rats were guillotined between 9 and 12 h in order to avoid circadian modifications[12], the organs being quickly removed and placed in cooling mixture, weighed and subjected to the methods described below.

Catecholamines were extracted following VON EULER and LISHAJKO[13]. Fluorometric evaluation was performed by COHEN and GOLDENBERG'S method[14]. Results are given in μg/organ ± S.E.M. (contents) and μg/g of fresh tissue ± S.E.M. (concentration), for norepinephrine (NE) and epinephrine (E) respectively. Glycogen was determined according to the method of ROE and DAYLEY[15], results being given in μg/100g g of tissue ± S.E.M. Glycemia was carried out using the SOMOGYI-NELSON method, results being given in mg/100ml ± S.E.M. All the results were subjected to Student's *t*-test. Experimental hyper- and hypothyroidism was evaluated by using the following parameters: body-weight curve, heart rate through electrocardiographic tracing on a polygraph, and the determination of glycemia in venous blood. In order to compare the modifications in the weight of the organ under study, the organ-weight/animal-weight relationship was established.

Results. For animals treated with T_3, controls and ^{131}I respectively, the organ-weigth/body-weight relationship in the submaxillary gland was: 1.43, 1.00 and 0.60 $\times 10^{-3}$; in heart it was: 4.55, 3.63 and 2.53×10^{-3}; heart rate was: 520 ± 7, 380 ± 10 and 236 ± 8 beats per min;

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Table I. Effects of T_3 and ^{131}I on the content and on the concentration of NE and E of the submaxillary gland and the heart

Submaxillary gland Experiment		Catecholamines/organ		Catecholamines/g of tissue	
		NE (μg ± SEM)	E (μg ± SEM)	NE (μg/g ± SEM)	E (μg/g ± SEM)
T_3	(11)	0.16 ± 0.02	0.025 ± 0.002	0.73 ± 0.17	0.07 ± 0.01[a]
CONTROL	(14)	0.17 ± 0.02	0.026 ± 0.002	0.82 ± 0.12	0.19 ± 0.02
^{131}I	(10)	0.14 ± 0.01	0.048 ± 0.002[a]	1.33 ± 0.15[a]	0.48 ± 0.03[a]
Heart Experiment		**Catecholamines/organ**		**Catecholamines/g of tissue**	
		NE (μg ± SEM)	E (μg ± SEM)	NE (μg/g ± SEM)	E (μg/g ± SEM)
T_3	(8)	0.40 ± 0.02[a]	0.078 ± 0.012	0.67 ± 0.06	0.06 ± 0.01
CONTROL	(9)	0.28 ± 0.02	0.087 ± 0.011	0.40 ± 0.05	0.12 ± 0.01
^{131}I	(8)	0.29 ± 0.03	0.110 ± 0.015	0.33 ± 0.05[b]	0.21 ± 0.03[a]

T_3; triiodothyronine; NE; norepinephrine; E; epinephrine; SEM; standard error of the mean; ( ); number of cases.
[a] $P < 0.001$. [b] $P < 0.005$.

glycemia was: 135 ± 8, 98 ± 2 and 85 ± 4 mg/100ml. Hyperthyroid animals lost 24% of their body-weight during the treatment, whereas those injected with ^{131}I put on 34%.

T_3 caused an increase of the contents and concentration of NE in the heart and a decrease of E concentration in the 2 organs studied. In ^{131}I-treated animals, there was an increase of NE concentration and of E contents and concentration in the submaxillary glands, whereas E concentration increased in myocardium (Table I).

^{131}I did not alter the glycogen of the organs studied. Administration of isoproterenol to control rats significantly decreased glycogen both in the submaxillary gland and the heart 30 min after being injected, which effect was not observed in hypothyriod animals subjected to the same treatment (Table II).

Table II. Effects of isoproterenol and ^{131}I on the concentration of glycogen of the submaxillary gland and the heart

Experiment Glycogen		Submaxillary gland (μg/100 g ± SEM)	Heart (μg/100 g ± SEM)
Control	(8)	46.1 ± 1.8	88.3 ± 3.2
Isoproterenol	(8)	14.5 ± 1.1 [a]	28.5 ± 0.7 [a]
^{131}I	(8)	41.9 ± 3.6	104.6 ± 3.9
^{131}I + Isoproterenol	(8)	30.5 ± 4.2	98.4 ± 3.7

(), number of cases; SEM, standard error of the mean. [a], $P < 0.001$.

Discussion. T_3 caused in the rat's submaxillary glands a hyperactivity characterized by a maximum increase of secretory responses[16] and hypertrophy noticeable not only on account of the increase in weight but also owing to the histological modifications observed[17]. In the heart, there was an increase in weight. The fact that the amount and concentration of the heart NE is increased would indicate a decrease of its turn-over and release. The decrease of E concentration in both organs is partly to be attributed to the hypertrophy observed and to a higher release coinciding with the metabolic and hemodynamic effects of hyperthyroidism.

In ^{131}I-treted animals there was a decrease in the activity of both submaxillary gland and heart, with a loss of weight. The increase of NE concentration in the submaxillary gland may be attributed to the modifications in the weight of the gland because the amount keeps constant. On the other hand, there was a marked increase (concentration and content) of E which might indicate that its release or catabolism have decreased. The increase of E concentration in myocardium – probably owing to a lower release or catabolism – are in agreement with the metabolic and cardiocirculatory events of hypothyroidism.

Glycogen in the submaxillary gland and heart, which was not modified in ^{131}I-treated animals inspite of the variations in the concentration of endogenous catecholamines, was altered by an exogenous one, isoproterenol, in the organs of control animals, but this effect was not noticed in ^{131}I-treated animals. This suggests that thyroid hormones could modify the sensitivity of adrenergic receptors.

In short, it might be said that the heterogeneity of opinions regarding the thyroid and sympathetic function might derive from the different behavior of the several tissues having their own metabolism, so that NE and E turn-over would be affected according to the predominance of their metabolic or hemodynamic functions. It is possible that the action of thyroid hormones on catecholamines operates at different levels: modification of storages, increase in the sensitivity of receptors and inhibition of their catabolism.

Resumen. Se estudió en ratas Wistar macho, el efecto de la triiodotironina y el ^{131}I sobre el contenido y concentración noradrenalina y adrenalina, en glándula submaxilar y corazón. Se estudió también, el efecto del isoproterenol sobre el glucógeno de ambos órganos en animales controles e hipotiroideos experimentales. Se observó un comportamiento diferente en los depósitos de noradrenalina y adrenalina en los órganos estudiados. La triiodotironina produjo una disminución en la liberación o catabolismo de las catecolaminas y el ^{131}I parece causar el efecto opuesto y una disminución de la sensibilidad de los recptores adrenérgicos.

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[18] We wish to thank the Consejo Nacional de Investigaciones Cientícas y Técnicas de la República Argentina, for providing a grant and to express out gratitude to Laboratories Glaxo (Bs. As.) for providing thyroid hormones.

Triiodothyronine and Thyroxine: Induction of Mitosis in Adult Frogs[1]

Triiodothyronine (T_3) and thyroxine (T_4) are able to induce metamorphosis in larval amphibia[2]. In so doing, these hormones, as part of their overall effect, instigate mitotic activity in a number of tissues[3–6]. KALTENBACH and HOBBS[6] indicated that the action of thyroxine upon tadpole ocular tissue, such as retina, cornea and lens, might be direct. When cholesterol pellets containing thyroxine were introduced into the orbit, mitosis was stimulated in the tissues mentioned. While there are also reports showing the iodinated phenols can trigger proliferation in adult mammalian tissues[7–9], it has not been considered likely that these materials effect the same phenomenon

[1] This work was supported by USPHS Grant No. EY 00281-09 from the National Eye Institute, and Fight for Sight Grant-in-Aid No. G-496.
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