EFFECT OF THYROXIN ON ACCUMULATION OF RADIOACTIVE IODINE IN THE THYROID GLANDS OF HEMITHYROIDECTOMIZED RATS OF DIFFERENT AGES

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In experiments on hemithyroidectomized male rats aged from 2 to 20 months administration of thyroxin in a dose of 1 μg/100 g body weight led to a significantly greater inhibition of accumulation of radioactive iodine in the residual lobe of the thyroid gland on the 5th day of the experiment in rats aged 16-20 months than in animals aged 2-2.5 months. The results confirm the earlier conclusion that the hypothalamic-hypophyseal threshold for homeostatic inhibition by thyroxin falls with age.

KEY WORDS: *Thyroid gland; thyroxin; aging; hypothalamic-hypophyseal threshold for inhibition.*

It was shown previously that during aging of male rats from 2 to 16 months the inhibitory action of thyroxin on compensatory hypertrophy of the thyroid gland (TG) increases in intensity [2]. The results were regarded as evidence of a decrease (and not an increase, as is observed in energy, adaptive, and reproductive homeostats [5, 6]) in the threshold of sensitivity of the hypothalamic–hypophyseal–thyroid system (HHTS) with age to homeostatic inhibition.

To continue the analysis of relations existing within the system regulating activity of HHTS, in the investigation described below the effect of thyroxin on accumulation of ^{131}I was studied in the residual lobe of TG remaining after hemithyroidectomy in rats of different ages. Enlargement of the lobe of TG remaining after unilateral thyroidectomy, a change in the biosynthesis of thyroid hormones in it, and the inhibition of these processes by thyroxin are known to take place through the participation of hypothalamic-hypophyseal mechanisms [1, 7, 11].

EXPERIMENTAL METHODS

Experiments were carried out on 288 male rats aged 2-2.5, 4-5, 8-10, and 16-20 months. Under superficial ether anesthesia the right lobe of TG was removed from the rats and weighed. Animals receiving thyroxin (from Reanal, Hungary) were given it by intraperitoneal injection 1-1.5 h after the operation and for the next 3 days. Thyroxin was given the last time at 1 p.m. on the 4th day of the experiment. Some of the animals undergoing the operation ("compensatory hypertrophy" group) were given an injection of physiological saline instead of thyroxin at the above-mentioned times. At 10 a.m. on the 4th day of the experiment, each of the thyroidectomized and control rats was given in intraperitoneal injection of 1 μCi ^{131}I without carrier. The rats were decapitated 24 h later (on the 5th day of the experiment) and the residual lobe of TG (or the whole TG of the control animals) was weighed. The duration of the experiment was restricted to 5 days because of data in the literature indicating the adequate intensity of compensatory hypertrophy of TG at this period and of the accumulation of radioactive iodine in it [4]. Radiometry of TG was carried out for 10 sec on a scintillation counter. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

As Table 1 shows, injection of thyroxin in a dose of 2 μg/100 g body weight into the rats daily led to inhibition of the accumulation of ^{131}I in TG of the rats of the different age

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TABLE 1. Effect of Thyroxin on Accumulation of ^{131}I by Thyroid Gland of Rats of Different Ages (M±m)

Group of animals	Accumulation of ^{131}I by thyroid gland of rats of different ages			
	2-2½ months	4-5 months	8-10 months	16-20 months
Control (intact rats)	100 (5/25)	100 (4/21)	100 (4/21)	100 (3/19)
Compensatory hypertrophy	75,7±7,5 (5/32)	101,2±2,7 (3/14)	68,3±11,3 (3/17)	56,4±13,3 (2/14)
Thyroxin:				
2 μg/100 g body weight/day	20,7±9,0 (3/20)	33,3±14,0 (2/11)	26,1±10,9 (3/16)	25,0±14,4 (1/9)
1 μg/100 g body weight/day	60,3±10,5 (3/18)	47,7±12,9 (3/15)	30,0±11,7 (2/13)	21,9±8,6 (3/23)

Note. 1) Results expressed as radioactivity of TG of thyroidectomized rats (receiving physiological saline of thyroxin) as a percentage of radioactivity of TG on control rats of corresponding age, taken as 100%.
2) Number of experiments indicated in parentheses in numerator, number of animals used in experiment in denominator.

groups of approximately the same level. Meanwhile, after injection of a smaller dose of thyroxin (1 μg/100 g body weight) a distinct difference was observed between the rats of different ages: Accumulation of ^{131}I in TG of the rats aged 16-20 months was inhibited more than in the rats aged 2-2.5 months ($P < 0.05$). Similar results were obtained when the data were calculated not as percentages, but as the number of counts of radioactivity per milligram weight of TG.

These experiments thus showed the same regular pattern as those based on gravimetric data [2]: The inhibitory action of thyroxin increases as the animals grow older. The fact must be noted that in the rats aged 8-20 months undergoing hemithyroidectomy, but not receiving thyroxin, the relative level of radioactivity in TG was lower than in the younger animals (Table 1); this could evidently explain the greater effect of thyroxin in older rats. In the writers' opinion, this fact does not, however, invalidate the basic conclusion of this investigation, for under the conditions of the model used the decrease in accumulation of ^{131}I in TG with age in the course of compensatory hypertrophy could be the result of elimination of radioactive iodine from TG under the influence of increased production of thyrotropic hormone [1].

It can be concluded from these results that with age the hypothalamic-hypophyseal threshold for inhibition by thyroxin falls, with a consequent reduction in TG activity during aging and in certain pathological states [3, 10, 12]. Since the use of exogenous thyroid hormones as a "compensatory measure" in certain situations could lead to even greater inhibition of the function of the endogenous TG [8, 9], a promising method of acting upon HHTS could perhaps be through the use of substances aimed at normalizing the hypothalamic-hypophyseal threshold for homeostatic inhibition [5, 6].

Considering that the thyroxin preparation used can be metabolized into tri-iodothyronine, which may be the basic hormone of TG, the final conclusion regarding age changes in the threshold for homeostatic inhibition in HHTS can be drawn only after experiments with triiodithyronine, and also with somostatin, a modulator of HHTS activity.

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