THE INFLUENCE OF HORMONES OF THE POSTERIOR HYPOPHYSEAL LOBE ON THE STIMULATED THYROID GLAND

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 56, No. 9, pp. 107-111, September, 1963
Original article submitted November 12, 1962

Recently the possibility of hypothalamic influence on the thyroid gland has come to be quite important practically. Most authors ascribe this regulatory influence to the anterior hypothalamus [4-9]. Some investigators maintain that it is brought about by neuro-hypophyseal hormones of the hypothalamus (vasopressin-adiurentin and oxytocin) which stimulate hypophyseal thyrotropic function, and which are therefore transmitter substances humorally transmitting hypothalamic influence to the anterior hypophyseal lobe. However, elsewhere it has been pointed out that an excess of neurohypophyseal hormones produces the opposite effect namely a depression of thyroid function [2,3].

To investigate any possible influence of these hypothalamic products of the thyroid gland and to determine whether they act directly on the thyroid parenchyma or whether the effect is mediated by the thyrotropic hormone of the hypophysis, a parallel investigation had to be carried out; its object was to compare changes occurring in the thyroid gland and the intensity of thyrotropic hypophyseal function under conditions in which an excess of posterior hypophyseal lobe containing these neuro-hypophyseal hormones had been injected.

EXPERIMENTAL METHOD

The experiments were carried out on sexually mature rats weighing 150-200 g. For 20 days 28 of the rats received one unit each of pituitrin P subcutaneously; 28 animals were untreated and served as controls. Before the onset and at the end of the experiment measurements of the basal metabolic rate were made in Kalabukhov's apparatus [1]. At the end of each experiment an autopsy was performed on ten rats of each group to determine the histological structure of the thyroid gland, and to measure the amount of thyrotropic hormone in the hypophysis. The thyroids were weighed on a torsion scale and embedded in celloidin-paraffin. Sections were stained in azan. To determine the functional condition of the thyroids, the height of the thyroid epithelium was measured. In 18 rats of each series measurements were made of the absorption of I^{131} by the thyroid gland. The amount of the absorbed isotope was measured 2, 4, 6, 12, 24, and 48 hours after the subcutaneous injection of 1μ C of I^{131} without a carrier by means of a Geiger-Muller counter on a B-2 apparatus. The amount of I^{131} absorbed by the thyroid gland was calculated as a percentage of the injected substance.

To determine the amount of thyrotropic hormone in the rat hypophyses, they were treated with acetone and a homogenized suspension was injected into guinea pigs. The strength of the thyrotropic response of the guinea pig thyroid glands was deduced from the height of the cells of the thyroid epithelium.

All the results obtained were treated statistically to allow for the variation.

EXPERIMENTAL RESULTS

As a result of the injection of pituitrin P, thyroid function was reduced: in most cases the follicles were distended with a more or less firm colloid, the epithelial cells were low and cubical. The height of the thyroid epithelium was greatly reduced: in the control animals it was 8.627 ± 0.0742 μ, and in the experimental group it was only 6.256 ± 0.0609 μ, i.e., 63.5% of the control value (Fig. 1). At the same time there was a 13.7% reduction in the relative weight of the thyroids. The ability of the glands to take up I^{131} was also reduced (Fig. 2).

However, although the thyroid glands of the experimental group were in a depressed condition the amount of thyrotropic hormone in the hypophyses of animals receiving pituitrin P was not reduced but was the same as in the intact rats. The height of the thyroid epithelium of the guinea pig recipients which had received hypophyses of control rats was 10.973 ± 0.0989 μg, while in those which had received hypophyses from experimental rats weighed 11.256 ± 0.1001 μg (Fig. 3).

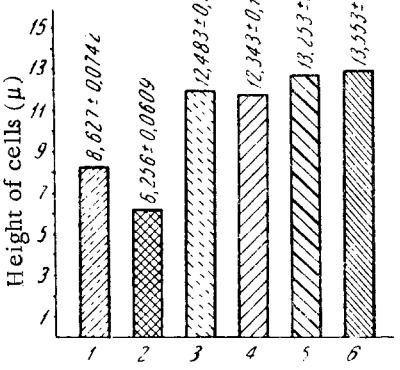

Fig. 1.

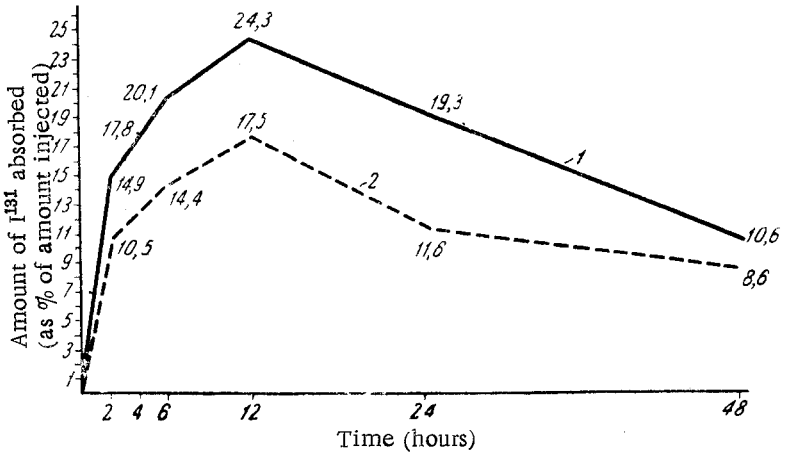

Fig. 2.

Fig. 1. Change in height of the thyroid epithelium in response to the injection of pituitrin P. 1) Intact rats; 2) injection of one unit per day of pituitrin P for 20 days; 3) daily injection of 10 mg per 100 g of 6-methylthiouracil for 20 days; 4) injection of pituitrin P and 6-methylthiouracil simultaneously for 20 days; 5) injection of pituitrin P given after treatment with 6-methylthiouracil; 6) injection of 6-methylthiouracil for 40 days.

Fig. 2. Absorption of I^{131} by the thyroids of rats treated for 20 days with pituitrin P. 1) Control; 2) experiment.

Thus posterior lobe pituitary hormones inhibit thyroid function. However, this inhibition occurs despite the normal amount of thyrotropic hormone in the hypophyses, i.e., it is not mediated by the anterior hypophyseal lobe.

We had to find out how pituitrin P would influence a thyroid gland previously stimulated by increased thyrotropic function of the anterior hypophyseal lobe.

The experiments were carried out on sexually mature male rats of the same weight. All the animals were divided into four groups of 28 animals. Those of the first group received 10 mg per 100 g weight of 6-methylthiouracil for 20 days. The second group received one unit of pituitrin P per day and the same amount of 6-methylthiouracil. Rats of the third group received the same amount of pituitrin P for 20 days during a period while the influence of 6-methylthiouracil developed; this was arranged by giving the methylthiouracil 20 days before the pituitrin P. Rats of the fourth group received the same amount of 6-methylthiouracil for 40 days.

As a result of a simultaneous injection of pituitrin P and 6-methylthiouracil for 20 days there was a considerable increase in the weight of the thyroid to 24.99 ± 1.801 mg per 100 g weight. Histologically it could be seen that the thyroid glands consisted of follicles containing no colloid; they had become converted into continuous cords of cells, or else contained only very small amounts of colloid. The cells of the thyroid epithelium were high, cylindrical, and swollen. The interfollicular islets were strongly developed, and the vessels were engorged. In the second group the height of the thyroid epithelium was 12.343 ± 0.1109 μ (see Fig. 1). However, 6-methylthiouracil alone gave exactly the same effect. Histologically the thyroid glands appeared precisely as we have already described. The relative weight of the gland and the height of the thyroid epithelium of rats of the first group were 25.02 ± 1.064 mg% and 12.483 ± 0.1159 μ. The absorption of I^{131} by the thyroids of the experimental rats did not differ from the value found in controls which received only 6-methylthiouracil. In both cases the ability of the thyroid to store iodine was greatly depressed, an effect which is characteristic of the action of 6-methylthiouracil (Fig. 4). In rats of both the first and second groups the basal metabolic rate was depressed on average by 17%.

Thus when 6-methylthiouracil and pituitrin P act together the latter exerts no influence on the thyroid itself.

However, a test of the hypophyses of rats for thyrotropic hormone shows that the amount in the hypophyses of rats which received pituitrin P and 6-methylthiouracil simultaneously was depressed considerably below the level found in animals receiving 6-methylthiouracil only. The height of the cells of the thyroid epithelium of the guinea pig recipients which received hypophyses of rats of the first group was 12.943 ± 0.0992 μ, whereas that of guinea pigs which had received hypophyses of rats of the second group was 10.276 ± 0.0958 μ, i.e., it did not exceed the value found in testing normal rat hypophyses (see Fig. 2). When pituitrin P was injected during the period when the action

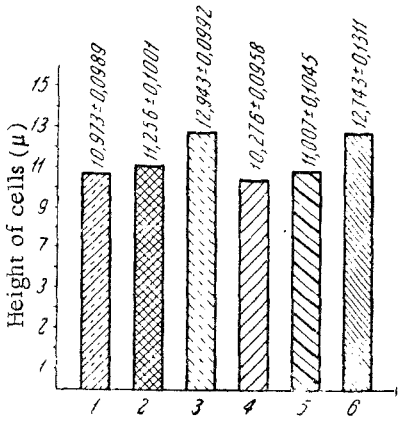

Fig. 3.

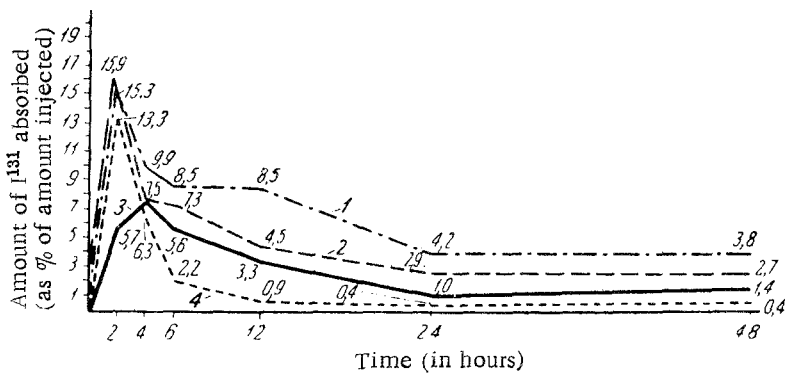

Fig. 4.

Fig. 3. Thyrotropic reaction of thyroids of guinea pig recipients. Indications as in Fig. 1.

Fig. 4. Absorption of I^{131} by thyroids of rats receiving pituitrin P and 6-methylthiouracil. 1) 6-methylthiouracil injected for 40 days; 2) injection of pituitrin P after 6-methylthiouracil treatment; 3) injection of 10 mg per 100 g weight of 6-methylthiouracil daily for 20 days; 4) injection of pituitrin and 6-methylthiouracil simultaneously for 20 days.

of 6-methylthiouracil was developing it exerted no influence on the thyroid gland itself. Histologically, in both cases the thyroid showed the typical response to 6-methylthiouracil. Neither the weight of the thyroid glands nor the height of the cells of the thyroid epithelium differed from the control values (group four). The same was true of the metabolic rate and of the uptake by the thyroid of I^{131} (see Fig. 4).

However, when pituitrin P is given during the action of 6-methylthiouracil, when the thyrotropic function of the hypophysis had previously been enhanced it was found that the amount of thyrotropic hormone in the hypophysis was reduced. This effect was well shown by a reduced height of the cells of the follicular epithelium in guinea pig recipients treated with injections of hypophyses of rats of the third group; this height was compared with that of the thyroid epithelium of guinea pigs which had received hypophyses of rats of the fourth group (see Fig. 2).

Thus when the thyroid gland is intact pituitrin P reduces its functional activity and the reduction occurs despite a normal amount of thyrotropic hormone in the anterior hypophyseal lobe; however, it exerts no influence on a thyroid affected by 6-methylthiouracil. However, in the latter case there is a reduction in the amount of thyrotropic hormone in the anterior hypophyseal lobe, an effect which may be due to an increased sensitivity of the thyroid to endogenous thyrotropic hormone associated with the injection of an excess of pituitrin P.

The results we have given on the one hand confirm the suggestions of Schindler [10] that vasopressin cannot be regarded as a chemical mediator which transmits hypothalamic influence homorally, and that this hypothalamic product does not act on the thyroid glands directly. In Schindler's experiments the injection of vasopressin caused an increased liberation of thyroxin and therefore produced an activation of the thyroid; however, the results of the experiments described above indicate on the contrary a reduction of thyroid function under the influence of an excess of pituitrin P. Nevertheless, the effect of pituitrin P is comparatively weak because it does not prevent the development of the typical response of the thyroid to the action of 6-methylthiouracil. At the same time in our experiments although pituitrin P did not change the normal intensity of hypophyseal thyrotropic function, it prevented the increase which would otherwise occur in response to the suppressive influence of 6-methylthiouracil on the the thyroid.

SUMMARY

When an excess of pituitrin P is given to male rats thyroid function is depressed although the hypophyseal thyrotropic hormone content remains normal. If 6-methylthiouracil and pituitrin P are given together the gland responds to the thiouracil in the normal way, although under these conditions there is no increase of hypophyseal thyrotropic function.

Therefore pituitrin P must act directly on the thyroid parenchyma without the involvement of the thyrotropic hormone of the adenohypophysis.

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