

EFFECT OF PITUITRIN AND OXYTOCIN ON RESPIRATION OF THE ISOLATED THYROID

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The view that the thyroid function is dependent on the state of the central nervous system and, in particular, on the state of the hypothalamic nuclei is now universally held, although the intimate mechanisms of this relationship have not yet been finally elucidated.

With the discovery of the phenomena of neurosection in the supraoptic and paraventricular nuclei of the anterior hypothalamus [11, 17], the leading role in the regulation of the functions of the endocrine glands, and especially the thyroid, has come to be ascribed to the neurosecretory products of the hypothalamus. Investigations by various authors have shown that the hormones of the neurohypophysis cause depression of the functional activity of the thyroid [3, 5, 23, 7, 8, 18, 21, 22]. Meanwhile Reichlin [24], who injected pitressin into animals but deprived them of water, failed to observe the changes characteristically associated with these conditions in the functional activity of the thyroid.

Another factor not yet explained is whether the action of these neurosecretory substances (neurohypophyseal hormones) is mediated through the thyrotropic hormone of the anterior lobe of the hypophysis or whether it may act directly on the thyroid, "para-adenohypophyseally" as A. L. Polenov [6] describes it.

Apparent support for the first hypothesis is given by the findings of workers [14, 20, 25] who observed the accumulation of neurosecretory material in the nuclei of the anterior hypothalamus and migration of this material along the nerve fibers of these nuclei after partial thyroidectomy or as a result of the action of an antithyroid agent. Several workers [10, 12, 15] have noted an increase in the secretion of thyrotropic hormone by the anterior lobe of the hypophysis following administration of oxytocin.

In our previous investigations, however, injection of pituitrin P into rats caused depression of the functional activity of the thyroid with a normal content of thyrotropic hormone in the anterior lobe of the hypophysis. No change in the thyrotropic function of the anterior lobe of the hypophysis could be observed, likewise, following a combination of this preparation with 6-methylthiouracil, although the reaction of the thyroid to the antithyroid agent was perfectly cleared defined.

Kovacs and Vertes [19], in experiments in vitro, observed an increased absorption of I^{131} by thyroid slices after addition of preparations of the posterior lobe of the hypophysis (Piton, Glandutrin, oxytocin) to the incubation medium, whereas pitressin and Syntocinon had no such effect; the latter, however, apparently caused an increased secretion of thyrotropic hormone by the anterior lobe of the hypophysis.

It was necessary to establish whether the action of vasopressin and oxytocin on the thyroid is mediated by the thyrotropic hormone of the hypophysis or whether it is direct. We have investigated the effect of pituitrin P, pituitrin M, and oxytocin on the isolated thyroid. Since the functional activity of the thyroid is reflected quantitatively by the intensity of its respiration [1, 2] we determined the effect of oxytocin and pituitrin on the absorption of oxygen by thyroid tissue slices in a Warburg's apparatus.

EXPERIMENTAL METHOD

The respiration of the isolated thyroid glands of male rats weighing 150-250 g was investigated, for which purpose 50 mg samples of the gland were placed in one container of a Warburg's apparatus. The incubation medium

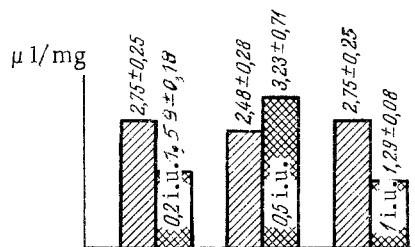


Fig. 1. Effect of pituitrin P on the respiration of the isolated thyroid. Lightly shaded columns – control; darker shaded columns – experiment.

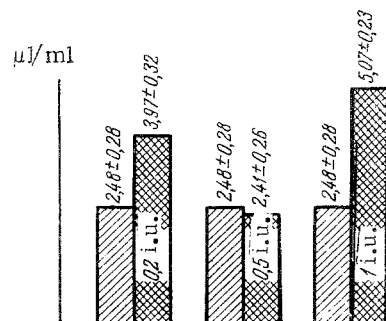


Fig. 2. Effect of pituitrin M on the respiration of the isolated thyroid. Legend as in Fig. 1.

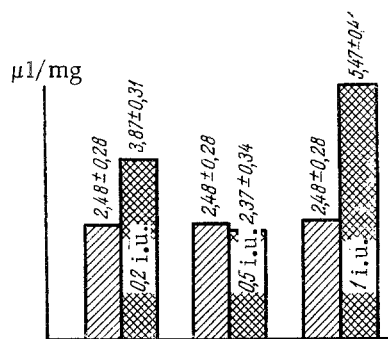


Fig. 3. Effect of oxytocin on the respiration of the isolated thyroid. Legend as in Fig. 1.

consisted of blood serum of the same animals, to which was added 0.2, 0.5, and 1 i.u. respectively of pituitrin P, pituitrin M, and a synthetic oxytocin preparation. The readings were taken in microliters of absorbed oxygen per milligram of fresh thyroid tissue. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

After the addition of 0.2 i.u. pituitrin P to the incubation medium the absorption of oxygen by the thyroid tissue fell. Whereas in the control series the oxygen consumption was 2.75 ± 0.25 μl/mg, after addition of pituitrin P this index fell to 1.59 ± 0.18 μl/mg (Fig. 1). Pituitrin P had a similar action on the thyroid tissue in a dose of 1 i.u. also. In this case the volume of absorbed oxygen also fell from 2.75 ± 0.25 μl/mg in the control series to

1.29 ± 0.08 μl/mg in the experimental. In a dose of 0.5 i.u., this preparation had no marked action on the respiration of the thyroid tissue. The increase observed in the volume of oxygen absorbed was not statistically significant (see Fig. 1).

Pituitrin M, in doses of 0.2 and 1 i.u., had a completely opposite action to that of pituitrin P on the respiration of the thyroid tissue. Addition of pituitrin M to the incubation medium in doses of 0.2 and 1 i.u. increased the oxygen absorption by the thyroid tissue to 3.97 ± 0.32 and 5.07 ± 0.23 μl/mg respectively, whereas in the controls the figure was 2.48 ± 0.28 μl/mg (Fig. 2). Addition of 0.5 i.u. pituitrin M had no action on the respiration of the isolated thyroid tissue.

The effect of oxytocin on the respiration of the thyroid parenchyma was completely identical with the action of pituitrin M (Fig. 3).

Hence pituitrin P, in doses of 0.2 and 1 i.u., caused a clear lowering of the absorption of oxygen by the tissue of the isolated thyroid gland. Conversely, pituitrin M and oxytocin, in the same doses, stimulated the respiration of the thyroid parenchyma. A dose of 0.5 i.u. of the preparation in all three cases gave no marked effect on the respiration of the isolated thyroid gland.

The experimental results disagree slightly with those obtained by Kovacs and Vertes, who, using a dose of 1 i.u. per 100 mg tissue (equal to our dose of 0.5 i.u. per 50 mg tissue), observed an increase in the uptake of I^{131} by thyroid tissue slices after the addition of oxytocin to the incubation medium. This apparent contradiction may be explained by the fact that pituitrin M (oxytocin) has a different action on the tissue respiration and growth of the thyroid parenchyma, on the one hand, and the uptake of radioactive iodine by the thyroid cells, on the other [3]. A similar phenomenon may also be observed in the dehydrated organism, when the output of neurosecretion from the hypothalamic nuclei into the blood stream is stimulated [4, 9]. Halmi [16] observed an increase in the ratio between

the concentrations of iodine in the thyroid gland and blood serum accompanying a decrease in the height of the cells of the thyroid epithelium. In similar experimental conditions we also found an increase in the absorption of I^{131} by the thyroid glands of rats although, according to the findings of D'Angelo [13], the blood concentration of thyrotropic hormone was lowered in these conditions.

The fact that in the investigations of Kovacs and Vertes pitressin had no effect on the thyroid was due, in all probability, to an unfortunate choice of dose of the drug, and also, possibly, to its different action on different aspects of thyroid function. The same explanation may probably serve to account for the absence of an effect of pitressin on the elimination of I^{131} by the thyroid noted by Reichlin.

The suggestion made by Kovacs and Vertes, that the secretion of thyrotropic hormone by the anterior lobe of the hypophysis is increased by the action of oxytocin, has not been proved for the experimental conditions cannot exclude another possible interpretation, namely that the sensitivity of the thyroid cells to thyrotropic hormone may change, as we have observed, during the combined action of pituitrin P and 6-methylthiouracil.

SUMMARY

A study was made of the effect of pituitrin P, pituitrin M and of oxytocin on the respiration of the isolated thyroid gland in the Warburg apparatus. Pituitrin P in doses of 0.2 and 1 i.u. depress respiration of thyroid parenchyma, whereas pituitrin M and oxytocin used in the same doses stimulate it. The dose of 0.5 i.u. is ineffective for all the three preparations.

Consequently, neurohypophyseal hormones may act on the thyroid parenchyma directly, avoiding the anterior lobe of hypophysis. The character of the action of these hormones largely depends on the dose. Neurohypophyseal hormones probably had a different effect on the respiration and growth of thyroid parenchyma on one hand, and on the iodine metabolism in the thyroid gland — on the other.

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