Adrenalin Inhibits the Thyrostimulating Effect of Vasopressin in Rats

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It is an acknowledged fact that in mammals the thyroid gland is mainly stimulated by the thyrotropic hormone of the pituitary (TSH). However, the results of numerous observations are in contradiction with this thesis. Thus, for certain pathologies a permanently elevated TSH level does not affect thyroid function [1]. A nonconformity between the TSH level and the thyroid hormone content in the blood has also been detected under the influence of long-term or repeated thyroliberin injection [4,15]. The data concerning thyroid reaction under conditions of transitory, nonspecific stress, for example, ether anesthesia, rigid immobilization, and pain stress are of great importance [7,11,12].

These effects are accompanied by a rise of the adrenalin level in the blood as well as of nonapeptide hormones, *i.e.*, vasopressin and oxytocin (VP and OT); however, the thyroid remains inactive or its function is even inhibited.

At the same time, a transitory cooling may activate thyroid function in hypophysectomized rats deprived of thyrotropocytes of the anterior lobe of the hypophysis to the same extent as in intact animals [6]. The injection of both exogenous VP and OT does not affect the thyroid in hypophysectomized rats. However, the injection of neurohormones in combination with stress factors does result in thyroid stimulation [5].

Experiments *in vitro* have demonstrated that nonapeptide neurohormones, when added to incubation medium, cause thyrocyte stimulation [2].

This contradiction in the data on thyroid reaction under stress conditions both in animals with intact pituitary and in hypophysectomized rats, as well as experiments on the isolated thyroid fragments, prompted us to study the reaction of the thyroid under the influence of such essential components of the neurohormonal reaction to stress factors as VP and adrenalin.

MATERIAL AND METHODS

Experiments were carried out on Wistar rats weighting 150-200 g in the fall-winter season. Both hypophysectomized and intact animals were used in the experiments. Hypophysectomy was carried out using transphenoidal method 7 days prior to the experiment.

Both intact and hypophysectomized rats were injected intraperitoneally with one of the neurohormones or with their combination. Minimum doses of VP, OT, or adrenalin were chosen to provide a neurohormone level in the blood similar to that in stressed animals. Four groups of animals were studied: 1) OT injection in a dose of 15, 150, or 1500

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ng/100 g body weight; 2) VP injection in a dose of 5, 50, or 500 ng/100 g body weight; 3) adrenalin injection in a dose of 0.4 pmole/100 g body weight; 4) VP injection in a dose of 50 ng/100 g in combination with adrenalin injection in a dose of 0.4 pmole/100 g body weight.

Intact animals served as controls in all test groups.

The animals were decapitated 20 min after neurohormone injection, and blood samples were taken for a radioimmunological determination of the hormone content. Triiodothyronine (T_3) and thyroxine (T_4) were determined in the samples by the use of standard kits (Institute of Bioorganic Chemistry of the Belorussian Academy of Sciences) and TSH (Mallincrodt Diagnostics, Germany).

The thyroid was fixed with Bouin's fluid. Paraffin sections were stained with azo after Heidenhain. Thyroid functional activity was evaluated morphometrically by the changes of thyrocyte height. The results were processed statistically using the nonparametric Wilcoxson-Mann-Whitney test.

RESULTS

Oxytocin in any dose used does not affect the functional state of the thyroid in either intact animals or hypophysectomized rats, except for a T_4 increase in hypophysectomized rats (up to 134%, $p<0.05$). Similarly, the injection of OT has no effect on the level of TSH. Vasopressin in any dose used has no effect on the TSH level in the blood in intact rats, but results in an increase of thyrocyte height as well as an increase of the content of sorptive vacuoles in the colloid and a pronounced hyperemia of the gland. At the same time, the T_3 content increases in the blood plasma. Thyroid activation is not dose-dependent (Fig. 1).

In hypophysectomized rats the thyroid reaction to VP differs somewhat from that described above. Thus, the minimum VP dose affecting the thyroid in intact animals has no influence on the gland in hypophysectomized rats, which is in accordance with published data [5]. This seems to be due not so much to the decreased thyroid activity after the operation as to the considerably lower VP level in the blood of such animals as compared to the control animals. However, in these animals VP in a dose of 50 ng/100 g body weight leads to an increase of thyrocyte height, an intensified thyroid hyperemia, and an increase of the T_3 and T_4 concentration in the blood (see Fig. 1). The same thyrocyte reaction to VP injection has been previously reported for hypophysectomized sterlet [10].

VP in a dose of 500 ng/100 g body weight causes an increase of thyrocyte height and the development of all the other morphological symptoms of boosted thyroid activity in both nonoperated and hypophysectomized rats; at the same time, the T_3 concentration decreases reliably, while the T_4 concentration remains on the baseline level.

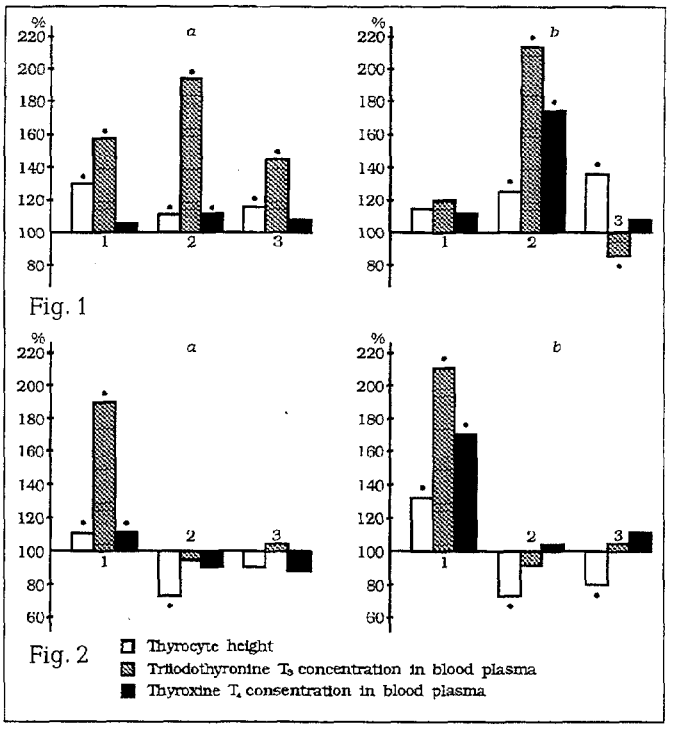

Fig. 1. Effect of vasopressin in various doses on thyroid gland 1) 5.0 ng/100 g; 2) 50.0 ng/100 g; 500 ng/100 g body weight. $p<0.05$ as compared to values prior to neurohormone injection (100%). a) intact animals; b) hypophysectomized animals.

Fig. 2. State of thyroid after neurohormone injection: 1) VP in a dose of 50.0 ng/100 g; 2) adrenalin in a dose of 0.4 pmole/100 g; 3) combination of VP (50.0 ng/100 g and adrenalin (0.4 pmole/100 g body weight).

The changes of the T_3 concentration cannot be the result of a reduction of its release into the blood during the 20 min experiment, since its half-life is 24 h [17]. Consequently, the only logical explanation is acceleration of the T_3 metabolism in the peripheral tissues induced by VP injection in large doses followed by an increase of its concentration in the blood (see Fig. 1).

The injection of adrenalin in a dose increasing its concentration in the blood up to the "stress" level (0.4 pmole/100 g) lowers thyroid functional activity, as shown in the reliable decrease of thyrocyte height, although no discernible changes are detected in the thyroid hormone concentration in the blood. The thyroid reaction to adrenalin is the same in both the nonoperated and hypophysectomized rats (see Fig. 2).

Adrenalin injection in combination with VP in a dose of 50 ng/100 g, which is known to affect the thyroid both in intact and in hypophysectomized rats, suppresses the stimulating effect of VP on the thyroid.

In nonoperated animals injected with adrenalin in combination with VP all indexes remain on the control level, while in hypophysectomized rats the thyrocyte height decreases reliably, just as with the injection of adrenalin alone. Thus, under stress conditions in nonoperated rats the simultaneous rise of both the adrenalin and VP level in the blood is responsible for thyroid inactivity, although the injection of adrenalin alone in sufficient dose leads to thyroid stimulation.

The results obtained seem to be in contradiction with the data on thyroid stimulation in hypophysectomized rats by VP in combination with immobilization stress [5]. However, it should be taken into account that noradrenalin, secreted primarily in the adrenal medulla in hypophysectomized rats [16], seems to be the main component of the catecholamine neurohormones released into the blood under stress; additionally, VP alone has been shown to stimulate the formation of noradrenalin in the adrenal medulla in rats [14]. A corresponding stimulation of the chromaffin tissue of the "adrenal glands" in frogs has been found *in vivo* and *in vitro* [8].

Noradrenalin in combination with VP, as shown in *in vitro* experiments [3], has the opposite effect on the thyroid cells as compared with the effect of adrenalin. This is probably responsible for the differences in the thyroid reaction to immobilization stress in nonoperated and hypophysectomized animals. It is interesting to note that under the simultaneous influence of both catecholamines and TSH on the isolated thyroid the reaction to adrenalin is opposite to that to noradrenalin injection [13].

The results obtained validate Polenov's idea about the dual control of the functions of the peripheral endocrine glands by monoamine (catecholamine) and peptide (nonapeptide) neurohormones [9].

Thus, the results of our investigation confirmed that thyroid function is determined not only by the TSH level, for, even in the absence of changes in this level, it may be stimulated by vasopressin. However, under conditions of simultaneous increasing in both the vasopressin and adrenalin concentrations in the blood (as in the case of stress situations), the effect of adrenalin is shown to be predominant, inhibiting the thyrostimulating action of vasopressin.

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