MORPHOFUNCTIONAL CHANGES IN THE THYROID GLAND IN DIFFERENT VARIANTS OF CHRONIC EXPERIMENTAL STRESS

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At the present time, the simulation of the general adaptation syndrome (GAS), a triphasic nonspecific reaction of the organism to an injurious agent, is quite widely used in experimental investigations. Painful electrodermal effects accompanying immobilization of the experimental animal [2, 21], or without immobilization [1, 22, 23, 29, 30], as well as prolonged stimulation of negative emotiogenic zones of the brain [5, 8, 16, 20], in particular the ventromedial nucleus of the hypothalamus (VMN), whose leading role in the mediation of the influences of emotional excitations on the internal organs is generally known [7, 20], are not infrequently used to reproduce the GAS.

The mechanisms of involvement of the hypothalamus-hypophysis-thyroid complex in the pathogenesis of the stress syndrome have not been unambiguously interpreted up until the present time [1-3, 9, 11-13]. There is, in these terms, a certain interest in comparing various methodological approaches to the reproduction of the GAS.

The aim of the present investigation was a comparative study of the structural-functional parameters of the thyroid gland (TG) occurring with various methods of formation of the GAS.

MATERIALS AND METHODS

The study was carried out in 20 mongrel rabbits, weighing 2–2.5 kg, divided into four groups. Chronic stress was induced in the animals of the 1st group by means of a 30-day stimulation of the VMN by means of an ESL-2 electrostimulator based on the appropriate stereotaxic coordinates [6]. The animals of two other groups were subjected over the course of 15 days to painful electrodermal effects; in particular, the duration of the daily sessions in the rabbits of the 3rd group increased gradually; the 4th group of animal served as the control.

The animals were sacrificed using ether fumes; the TG was fixed in Bouin’s fluid, and embedded in paraffin following the generally accepted procedure. Serial sections, 5–6 µm in thickness, were stained with hematoxylin and eosin, and subjected to stereometric analysis; the volumetric density of the structural components, the sclerosis coefficient, and the organ’s vascularization index were determined in the process. The volume of the nuclei of the follicular cells was approximated by the ellipsoid of revolution. The level of triiodothyronine (T3), thyroxine (T4), thyrotropin (TTH), and cortisone was determined by the method of radioimmunoassay, using domestic and foreign kits of the Amersham (Great Britain) and Mallinckrodt Diagnostica (FRG) companies. All of the numerical data were analyzed statistically using Student’s test of the significance of differences of the arithmetic means.

RESULTS AND DISCUSSION

Fundamental significance is ascribed in the dynamics of the formation of the GAS to the phasic secretion into the circulatory bed of the glucocorticoid hormones. An increased level of the latter in the blood serum in many ways assures the resistance of the organism to an injurious agent (the GAS stage of resistance). At the same time, exhaustion of the adrenocortical function corresponds to the dysadaptation of the organism as a whole. The dynamics observed in the experiment of the level of cortisone in the blood (see Fig. 1a), the most active endogenous glucocorticoid [4], attests to the resistance of the animals of the 2nd group to the stressor factor and to the gradual exhaustion of compensatory-adaptive mechanisms when the stressor load is intensified in the 3rd group. This conclusion makes it possible to compare two different models of the stress reaction of the organism and to follow the histophysiological changes in the TG in relation to the dynamics of the GAS.
Fig. 1. Content of hormones in the blood of control and experimental rabbits (X ± S\textsubscript{E}) Along the ordinate: concentration of hormones; a) Cortisone (in nmole/liter); b) T4 (in nmole/liter); c) T3 (in nmole/liter); d) TTH (in µg/liter); along the abscissa: groups of animals. Asterisk, significance of differences (p < 0.001) as compared with the control.

An increase in the content of T4 in the blood is observed under the conditions of emotional-painful stress (2nd and 3rd groups); this increase is pronounced in the presence of exhaustion of the adaptive reactions in the 3rd group (see Fig. 1b). The stereotaxically determined effect on the hypothalamus (1st group) does not induce substantial changes in the content of T4 in the blood (see Fig. 1b). At the same time, the T3 level in all experimental groups (1st-3rd) significantly exceeds the analogous parameter of the control group: by factors of 3.6, 2.0, and 1.8, respectively (see Fig. 1c). Thus, the formation of the GAS governs the activation, which is adaptive in character, of the processes of secretion of thyroid hormones (TH) into the circulatory bed with subsequent exhaustion of adaptive potentials.

These changes in the content of hormones in the blood are observed against the background of the absence of thyrotropic effects vis-à-vis the adenohypophysis when electrodermal stimulations are applied (2nd and 3rd groups of the experiment), and against the background of intensification of stimulation of the thyroid parenchyma by means of TTH (see Fig. 1d) in the presence of an effect on the hypothalamus (1st group). It is of interest to compare the more than three-fold increase in the level of TTH during stimulation of the VMN with the highest concentration of thyroliberin in this nucleus as compared with other divisions of the brain [19].

The simultaneous increase in the level of TTH and T3 in the 1st group (see Fig. 1c and d) points to the capacity of high concentrations of the tropic hormone to channel hormonogenesis in the TG in the direction of the synthesis of T3. It is known that the physiological activity of T3 exceeds the analogous parameter of T4 by factor of 4-5 [4, 18]. Therefore, this energy- and substrate-sparing transformation of the hormonopoietic processes can completely explain the somewhat unexpected decrease in the height of the thyroid epithelium in the animals of the 1st group (see Table 1). Under physiological conditions only about 20% of T3 is secreted directly by the TG, while the remaining 80% is a product of monodeiodination of T4 in the peripheral tissues [4, 18]. However, information regarding the compensatory inactivation of peripheral 5-deiodinase in the presence of an increase in the level of TTH in the blood [24] should be adduced in favor of an initially thyroid origin of the prevalent portion of T3 in the serum of the animals of the 1st group. Moreover, there are data in the literature regarding the reshaping of hormonogenesis in the TG toward the synthesis of T3 in the presence of the effect of high concentrations of TTH [17]. The stability of the T4 content in the serum of the rabbits of the 1st group (see Fig. 1b) may be associated with the inhibition of its secretion on the basis of the ultrashort-loop feedback principle.

The TTH concentration statistically close to the control in the animals of the 2nd and 3rd groups (see Fig. 1d) excludes the possibility of the variability of the specific transhypophyseal influence on the TG. Consequently, the significant increase in TH content (see Fig. 1b and c) during the electrodermal effects on the rabbits is the result of the thyroid parenchyma-stimulating effect of other regulatory mechanisms. Among these, in the first place, should be noted the hypertonus of the sympathicoadrenal system that is characteristic for the GAS [14, 27, 28], as well as the activating influence of steroid compounds on the processes of synthesis and incretion of TH [13].

The results of the morphometric analysis of the TG attest to an increase in a relative volume of the stromal elements of the organ (see Table 1) in the presence of an emotional load, both of central (1st group) and of peripheral