

Conceptual Approaches to the Study of the Thyroid Gland at Different Levels of Its Integration into the Body

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The body is a complex self-regulating biological system. Its organizational structure can be simplified to three levels: organellocellular (basic), organic and systematically somatic. The activity of each element in the system occurs within the competence of the level which it belongs to. It causes different levels of hierarchical subordination in the body (see Table 1).

No.	Structural organization level	Hierarchy representative
I	Organelle-cellular	Cellular ultrastructures, cell
II	Organ-tissue	Specialized tissue, organ
III	System-somatic	Physiological/functional system, body

Table 1: Hierarchical levels of the biological system's structural organization

For a long stretch of time in the biomedical fields of knowledge the information has been accumulated about the phenomena and processes that occur in the body in the norm and in the pathology under the influence of various factors. The current stage of scientific knowledge development is characterized by the transformation of accumulated empirical information. Its tools are mathematical technologies permitting to perform in-depth analysis of the data obtained and to summarize the research results. Using a variety of mathematical approaches to the study of biological objects allows the researcher to study the connections between elements of biostructures located at the same hierarchical level, and to determine the connections between elements of biostructures at different levels.

The object of our research is the thyroid gland (TG) at different levels of the hierarchical organization: thyrocyte → TG as an organ → TG integrating into the body. The subject of the study is peculiarities of the TG morphofunctional status and the white male rats' body when consuming organic and inorganic iodine. Experiments with the use of laboratory animals were carried out in compliance with the Law of Ukraine "On Protection of Animals from Cruel Treatment" (No. 3447-IV of February 21, 2006), following the requirements of the Bioethics Committee of the Lviv Medical Institute (Protocol No. 22 of May 15,

2017), agreed with the provisions of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986). Studies are carried out using such components of mathematical analysis as mathematical statistics, principles of phase interval method and fuzzy logic, basics of clustering, correlation and regression analyzes.

Why is the TG studied? There are several explanations for this. First, thyroid pathology is one of the most common endocrine pathologies. Secondly, TG, due to peculiarities of its embryogenesis, anatomy and physiology, is very sensitive to a variety of influences, including environmental and social stress, which can be associated with a wide variety of thyroid pathology. It is this particular feature of the thyroid gland that permits to use its morphofunctional status as a sensitive indicator of environmental pollution. Finally, thirdly, the thyroid gland is connected to other endocrine glands and the brain via the hypothalamic-pituitary axis. This makes it to some extent a conductor of the symphony orchestra, called the body: activity of most organs and systems depends to a certain extent on the thyroid gland's functional activity. At the same time, information about the thyroid's bonds with other organs is reduced mainly to the finding of simultaneous changes in the thyroid gland's condition and the studied organ, which does not clearly explain the cause and effect interactions between them.

Our system-somatic thyroid research was aimed to study the effects of TG on the body and to identify organs that change depending on the thyroid status changes. When studying the thyroid gland's integration into the body, we proceeded from the fact that the mass of the organ/body is a general indicator of its condition. Then increasing or decreasing weight may indicate that there are certain changes in the body. Thus, the body weight growth in euthyroid rats, which was observed when consuming organic and inorganic iodine compounds, indicates the activation of metabolic processes. This can be confirmed by accelerated increase in the body weight after the first week of observation, which we qualify as the "anabolic jump phenomenon" and its short-term decrease after two weeks of consuming iodine-containing substances, which we have defined as "body weight inversion phenomenon" (5).

A sufficient amount of empirical evidence indicates a fairly common combination of the thyroid pathology with abnormalities in the morphological and functional status of the liver and adrenal glands. Having applied the method of correlation analysis, we established a reliable interdependence between the weights of the thyroid gland and adrenal glands, the thyroid gland and the liver, adrenal glands and the liver (12). Given that tyrosine is a substrate for the synthesis of both thyroid and steroid hormones, and the liver is the site of their metabolism, we

suggested to integrate these organs into a single functional module (12, 13). The body's activity at the system-somatic level of its hierarchical organization can be represented as the resultant interaction of different functional modules that are its components. This view is confirmed by the results of our studies (13), in which, using the method of regression analysis, it was revealed that when correcting the thyroid pathology by means of iodine-containing substances, body weight depends on the weights of the thyroid gland, adrenal glands and the liver (see Fig.1).

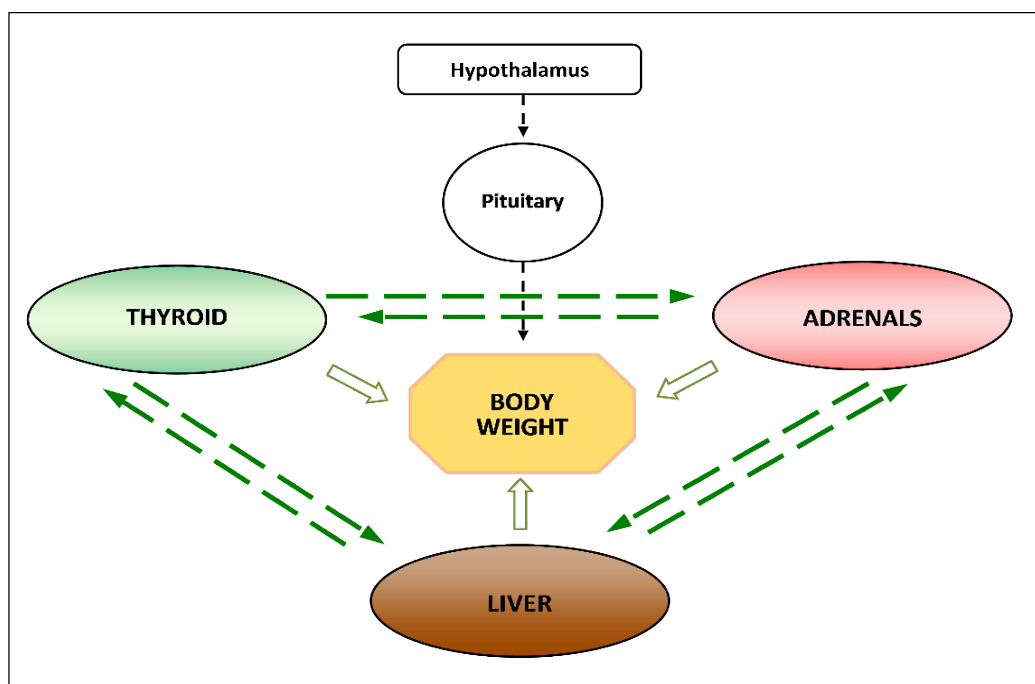


Figure 1: The scheme of functional connections between organs of the “thyroid gland – adrenal glands – liver” functional module (13)

In the study of TG at the organellocellular organization level, we proceed from the cybernetic conception of the cell as a self-regulating system, which in order to maintain homeostasis must constantly transform the internal and external influences that it is affected by (6). To deepen and optimize the study of the thyroid and other endocrine organs activity at the organellocellular level, we proposed the method of semi-quantitative analysis of electron diffraction patterns and the method for determining the hormone-producing cells profiles (1). Generally, their essence is as follows. Specific activity of the hormone-producing cell occurs in the following fields: 1) synthesis of the hormonal product; 2) secretion of the hormone produced; 3) the hormone entry into the intraorganic microcapillaries and its transport by the intraorganic microcapillary bed; 4) energy support of these processes. In this case, each of the activity fields, which we call “capacity profiles” (synthetic, secretory, transport, energy), will be implemented by a group of strictly specialized cellular organelles that form its cluster. Usually in electron microscopic studies, the organelles’ and their substructures’ status is described in words. Instead, when studying a particular cluster, we rank its constituent elements by size, shape, location, and other characteristics.

Then, using the principle of the phase interval, the condition/number of constituent elements in any activity field of the hormone-producing cell, we compare them to their condition/number in two controls, which are the norm and the pathology (untreated) (2, 11). This approach permits to represent qualitative and binary (non-numerical) cell data in their numerical equivalents, and to expose the obtained numerical information to various mathematical transformations. Further establishment of the presence, strength and direction of connections between ultrastructures permits to study in depth the intimate mechanisms of hormonopoiesis influenced by various factors. In particular, when analyzing thyroid electron diffraction patterns, we found that organic and inorganic iodine have certain differences in their influence on the follicular thyrocyte ultrastructures.

The results of the study on the features of the follicular thyrocyte activity synthetic and secretory fields when consuming organic and inorganic iodine against the background of subclinical hypothyroidism and subclinical hyperthyroidism were presented in (3, 4, 8-10). The results obtained interpretation was based on the classical

concept on the interdependence of structure and function. To study the interactions in the cluster of ultrastructures performing the same function (thyroid hormone synthesis or their secretion), we used the correlation analysis (3, 4, 8-11). The visual representation of the obtained results is carried out using graphical images – “intrasystemic correlation portraits” of different follicular thyrocyte activity fields (profiles) (9).

The study on peculiarities of the secretory cluster ultrastructures involvement into follicular thyrocyte activity with different TG functional states permitted to establish the following. In alimentary hypothyroidism, the intensity of hormone elimination is indicated by the microvilli of the apical plasma membrane - their length, number and density of location on the apical surface.

In potentiated subclinical hypothyroidism, the state and number of apical microvilli and lysosomes, which number and electron density degree are variable, serve as indicators of the hormone elimination intensity. In subclinical hyperthyroidism, the main organelles that implement hormone elimination are lysosomes and secretory granules, which intracellular localization, number and electron density degree vary over a wide range (10).

We propose to estimate the stages of morphofunctional changes in cells by means of change markers, dividing them accordingly by: 1) markers of primary changes; 2) markers of the majority of changes and 3) markers of final changes (see Table 2).

Marker type	Change process stage	Characteristics of the biological system state
Markers of primary changes	Initial	Excitation, functional tension: 1) impairment of primary functional equilibrium; 2) primary adaptation disorder
Markers of the majority of changes	Development	Functional changes, emergency state: 1) functional imbalance; 2) dysregulation of the system; 3) formation of system disorganization.
Markers of final changes	Completion	Organic changes: 1) final loss of primary properties; 2) acquiring new properties; a) formation of a new functional equilibrium, b) formation of adaptation to new existence conditions; 3) formation of a new system.

Table 2: Markers of changes in the biological system’s state

We found that when taking iodinated compounds against the background of impaired thyroid functional activity, the marker of initial

changes in the synthetic activity of follicular thyrocytes is the free ribosomes number growth in the cytoplasm. Meanwhile, an increase in the number of membrane bound ribosomes indicates stabilization of the hormonopoiesis intensity and is a marker of the vast majority of changes. The marker of the definitive positive changes in the synthetic process is normalization of the cytoplasmic electron density degree: if the influence of the factor causing the changes continues, the electron density of the cytoplasm will go beyond normal (8).

We are currently working on establishing the mathematical regularities of the of thyroid activity features at the organic level of its hierarchical organization. Indices of iodine content in the TG, hormonal activity of the intrafollicular colloid, the content of ascorbic acid in the adrenal glands and the liver tissues are subject to the analysis.

Thus, changes in the morphofunctional status of the TG influenced by the factors intended to correct its functional pathology, and features of the TG's relations with other organs, are of undoubted interest for researchers and practitioners. Based on the concept of the body integrity, our approach to the study of endocrine organs at different hierarchical levels of their organization permits to provably establish the interdependencies and interinfluences of different elements, belonging both to the same structural level (intrasystem analysis) and to different levels (intersystemic analysis) (7). We believe that studies using adequate mathematical technologies permit to comprehensively elucidate problems in any biological system (cell/organ/body) and to substantiate the conclusions drawn.

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