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Impaired Mental Functions in Experimental Rats with Hyperthyroidism

Radjabova Feruza Kosim kizi [1], Jabbarova G. M. [2]

[1, 2] National University of Uzbekistan named after Mirzo Ulugbek, Department of Human and Animal Physiology

Abstract:

The relevance of the problem: The thyroid gland (glandula thyroidea) is an endocrine gland that synthesizes a number of hormones necessary to maintain homeostasis. The thyroid gland consists of two lobes and an isthmus. The lobes are adjacent to the trachea on the left and right, the isthmus is located on the anterior surface of the trachea. The upper border of the gland (lateral lobes) is the thyroid cartilage, the lower - 5-6 rings of the trachea. The gland tissue consists of follicles filled with colloid, which contains the iodine-containing hormones thyroxine (tetraiodothyronine) and triiodothyronine bound to the protein thyroglobulin. In the interfollicular space there are parafollicular cells that produce the hormone thyrocalcitonin. T3 is a more active hormone, but it is produced in small quantities and is quickly destroyed in the bloodstream. T4 is not broken down as quickly in the bloodstream and is produced in greater quantities than T3, so it is the main thyroid hormone. The action of hormones is very diverse. They affect all types of metabolism, the functioning of the heart, brain and lungs, growth, physical and mental development. It is known that hyperthyroidism is characterized by increased metabolic processes and elevated levels of free thyroid hormones in the blood serum. Symptoms of this pathology include palpitations, fatigue, weight loss, heat intolerance, anxiety and tremor. The diagnosis is based on both clinical manifestations and the results of laboratory evaluation of thyroid function. Correction largely depends on the course of the disease.

Keywords: hormones, L-thyroxine, “Maze” test, mental disorders, thyroid gland, hippocampal neurogenesis, catecholamine.

Purpose of the study: consisted of studying behavioral reactions and morphological parameters in rats with hyperthyroidism.

Methodology. The studies were carried out on white outbred mature male and female rats, weighing 100-120 g. All rats were kept under standard vivarium conditions at a temperature of 22-25°C. Experiments were performed in accordance with the principles and procedures outlined in the Guide for the Care and Use of Laboratory Animals. The model of hyperthyroidism was induced orally using the drug L-thyroxine at a dose of 50 mg/kg body weight in drinking water bowls daily for 30 days. The study of behavioral reactions in rats was carried out using the "Maze" test. The labyrinth is a complex structure consisting of many passages and dead ends. Animals are placed in this maze and must complete a certain task, such as finding the exit or completing all the passages within a certain time. Assessment of animal behavioral reactions is an integral part of many studies and makes it possible to detect disturbances in the functioning of the nervous system. Methods for assessing behavior in laboratory animals are as varied as the number of researchers using them. It is used to study the functioning of the nervous system, brain function, a number of psychological diseases, toxicology and the general effect of the administered drug on a living organism.

Initially, all animals were tamed to freely enter the "Labyrinth" and move around in it in order to avoid stress during the experiment. When holding rats in the "Labyrinth" for training purposes, they learned to find a way out. At first there were stops due to a new type of movement to another place for the first time, they passed on their own, but for a long time after adding food they began to monitor the food and quickly found a way out after 5 minutes without food they re-researched the finding of a way out was accelerated from the moment food was added .

For the first 7 days, the animals moved very slowly; after the drug was administered, they became active and quickly found a way out of the "Labyrinth".

For morphological analysis, serial sections of the thyroid gland were prepared, and the sections were visualized using the survey microscopy method.

Results and discussions: Triiodothyronine (T3) is one of the thyroid hormones, which is known to be a regulator of systemic action, controlling basal metabolism, nuclear and cytoplasmic protein synthesis, the permeability of cellular and subcellular membranes of phospholipid nature, as well as the functional state and structural features of ribosomes, mitochondria and plasma cells reticulum. The content of T3 in the blood is determined, on the one hand, by the rate of its secretion by the thyroid gland (controlled by the feedback law of the thyroid-stimulating hormone of the pituitary gland - TSH), on the other hand, by the rate of the thyroxine monoiodination reaction. Disturbances in the functional state of the thyroid gland and regulatory mechanisms in the hypothalamus-pituitary-thyroid link lead to the development of a number of independent nosological forms of diseases, and are also observed in some general somatic and oncological diseases. The main method for studying the pituitary-thyroid system of the body is to determine the concentration of protein-bound and free forms of thyroid hormones, as well as TSH in the blood using various saturation methods (radioimmunological, immunochemical, immunofluorescent, etc.). However, the study of thyroid hormones in the peripheral blood, determination of the TSH level, as well as a test with thyrotropin-releasing hormone reflect to a greater extent the processes of hormone synthesis in thyroid gland, the state of the regulatory systems hypothalamus - pituitary gland - thyroid gland and, to a much lesser extent, the processes of tissue metabolism of thyroid hormones, in particular T3, as the main carrier of the effects of thyroid hormones. Determination of the level of T3 in the body, based on the oral intake of a certain amount of T3 and the calculation of a certain integral indicator reflecting the amount of hormone entering the tissue over a certain time, made it possible to identify disturbances in the thyroid status of the body in patients with certain types of malignant neoplasms.

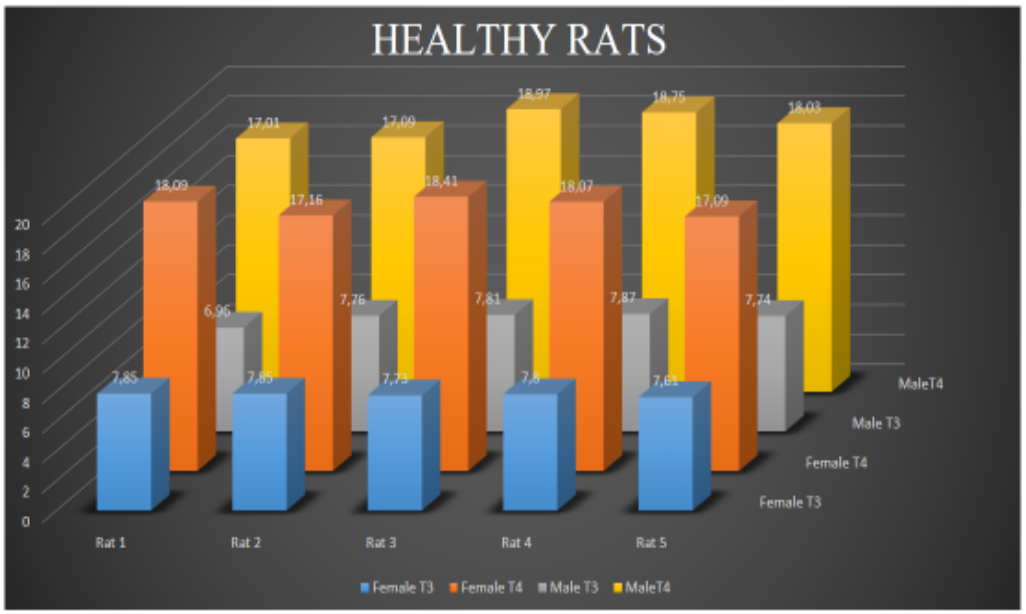
The purpose of this study was to develop a method for quantitative assessment of T3 metabolism at the tissue level with determination (in absolute units) of the body's need for T3 per unit time.

Animals experienced mental disorders due to hyperthyroidism (thyrotoxicosis). Thyroid dysfunction can significantly affect both the central and peripheral nervous systems. The thyroid

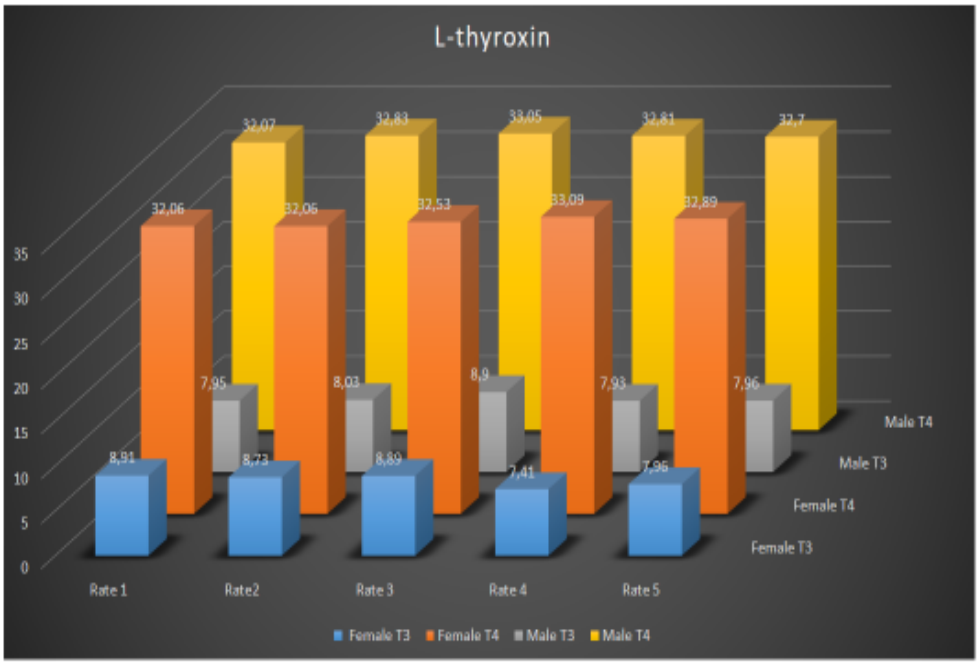
hormones thyroxine (T4) and triiodothyronine (T3) play critical roles in hippocampal neurogenesis, neuronal differentiation, and central nervous system function from early neurogenesis to brain maturation. With the development of hyperthyroidism, changes in serum levels of thyroid hormones T3 and T4 and a decrease in body weight were observed. Long-term hyperthyroidism also contributed to an increase in dopamine levels. During each day, food and water consumption was recorded, and the motor reactions of the rats were observed. In hyperthyroidism, damage to the nervous system is associated with the toxic effect of thyroid hormones, accelerated metabolism and increased sensitivity to catecholamines. Also, with the development of hyperthyroidism, glycogen and lipid reserves are depleted, the blood is oversaturated with tri- and tetraiodothyronine, which leads to weight loss and increased body temperature, accelerated metabolism, rapid hair growth, aging and hair loss. In addition, an excess of thyroid hormones in the blood, in particular an increase in the level of T4 and T3, as a consequence, an increase in the content of catecholamines in the myocardium, leads to an increase in heart rate. In our study, the administration of L-thyroxine led to the following changes: an increase in T3 levels by 1.1 times ($p<0.01$) and T4 levels by 1.7 times ($p<0.001$) (pic 1) compared to the intact control; decrease in TSH level by 2.6 times ($p<0.05$); the behavior of animals became aggressive, which was manifested in the formation of inter-male confrontations; visible changes in fur were noted; there was a decrease in body weight by 30% ($p<0.05$).

At week 8 of the experiment, blood was drawn to determine the level of total thyroxine (T4), triiodothyronine (T3).

In studies conducted in rats, a significant increase in the levels of serum T4 and T3 was determined, which was accompanied by effective syndromes and suppression of cognitive processes.



Pic1



Pic 2

Conclusion. Suppression of the functional characteristics of the thyroid gland is accompanied by psycho-emotional disorders, which develop depending on gender, etiogenesis and duration of the disease and, thereby, aggravate cognitive deficits in experimental animals.

L-Thyroxine at a dose of 50 mcg / kg, used for 30 days, causes hyperthyroidism, confirmed by the dynamics of thyroid hormone levels T3 and T4.

The administration of L-carnitine at a dose of 25 mg / kg per day for courses of 7 and 10 days normalizes dynamics of thyroid hormone levels T3 and T4, more effectively with 15-day use.

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