

THE RELATIONSHIP OF COGNITIVE FUNCTIONS AND GLUCOSE IN EXPERIMENTAL HYPOTHYROIDISM

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Abstract. *Thyroid hormones are one of the important factors for brain development and normal functioning. In thyroid dysfunction, regardless of age, defects in the body's cognitive functions have been found. This study examines the relationship between impaired cognitive function associated with the presence of thyroid dysfunction and its changes in glucose homeostasis. For this purpose, laboratory rats with a weight of 180-220 g were diagnosed with hypothyroidism, their ability to find their way in a special maze was studied, and the function of the brain was evaluated. It was found that the average time to find the way in the maze of healthy rats taken for the experiment was 3.2 ± 0.56 minutes, while the rats in the hypothyroid group could find the way in 5.3 ± 0.63 minutes ($P=0.05$). In hypothyroidism, general metabolism slows down. At the same time, energy supply to the brain, i.e. glucose consumption decreases and its amount in the blood increases. As a result, retardation of mental and physical development, loss of memory and attention, disorientation in time and space, and other mental defects can be observed.*

Key words. *Hypothyroidism, cognitive functions, glucose.*

Introduction

Currently, hypothyroidism is considered as one of the urgent problems of modern medical sciences, especially endocrinology. Thyroid gland diseases rank second among endocrine pathologies.

The thyroid gland is one of the most important glands in the body's endocrine system that synthesizes hormones that control the main metabolism [13]. Thyrotropin-releasing hormone (TRH) secreted from the anterior lobe of the pituitary gland regulates the activity of the thyroid gland, and in turn, the secretion of thyrotropin-releasing hormone from the hypothalamus is controlled [7]. The thyroid gland secretes the thyroid hormones triiodothyronine (T3) and thyroxine (T4). These hormones control several important physiological processes of the body. For example, thyroid hormones are very important in the body for processes such as energy exchange, formation and development of the central

nervous system, tissue differentiation, cell division [15], and thermoregulation to be normal [12]. T3 and T4 determine the morphological and functional development of the brain and the body as a whole during fetal development and neonatal period. At a later age, thyroid hormones increase the activity of metabolic processes, and in physiological concentrations they have a clear anabolic effect, stimulate lipogenesis and oxidation of fatty acids, gluconeogenesis and glycogenolysis, and increase the absorption of glucose by fat and muscle tissue. Thyroid hormones have a positive inotropic and chronotropic effect on the heart, increase the minute volume of blood circulation, expand skin arterioles, increase synthesis of bone tissue and ensure growth [17]. Because thyroid hormone affects growth, development, and many cellular functions, thyroid hormone deficiency has far-reaching effects on the body. Thyroid hormone deficiency can cause various symptoms such as cold intolerance, fatigue, constipation, bradycardia, low mood, and weight gain [2].

Hypothyroidism is a clinical syndrome resulting from a long-term, permanent lack of thyroid hormones in the body or a decrease in their biological effect at the tissue level. Hypothyroidism can have many causes. There are primary, secondary and tertiary hypothyroidism. In the primary form, the process that leads to the development of hypothyroidism is localized directly in the thyroid gland. If the decrease in the function of the thyroid gland occurs due to the lack or absence of the effect of thyrotropin hormone or thyrotropin-releasing hormone, then secondary or tertiary hypothyroidism occurs in the body. In addition, peripheral hypothyroidism, which is associated with resistance or low sensitivity of cell and tissue receptors to thyroid hormones, is also distinguished. With a lack of thyroid hormones, which occurs in various forms of hypothyroidism, serious changes develop in all organs and systems without exception. The main reason for their damage is a sharp decrease in the production of a number of cell enzymes, which leads to a decrease in metabolic processes and a significant decrease in the demand for oxygen, a slowdown in oxidation-reduction reactions and, as a result, a decrease in metabolic indicators. A universal symptom that manifests itself in severe hypothyroidism is mucinous swelling (myxedema), which is most often expressed in connective tissue structures. Disturbance of glycosaminoglycan metabolism - protein degradation products with increased hydrophilicity (derivatives of protein, glucuronic and

chondroitin acids) lead to accumulation in mucous membranes, skin and subcutaneous tissues, muscles [16].

Prenatal and postnatal thyroid hormones are important for the development and maturation of the mammalian brain. Serious anatomical and physiological abnormalities in brain functions are observed in hypothyroidism and hyperthyroidism of the thyroid gland [5,8]. Dysfunction of the mother's thyroid gland, in turn, can be due to various reasons, iodine deficiency is important. For many years, iodine deficiency was considered a problem limited to certain geographical areas of the planet. Scientists have found out that among the patients of this region, alarming consequences of cognitive functions are observed, and they have a low IQ level. Attention deficit and hyperactivity disorders have been observed in children born to mothers with hypothyroidism. For a long time, the main factor responsible for changes in the neurological development of the fetus was defined as maternal hypothyroidism (in the early stages of pregnancy, low free thyroxine (fT4) and an increase in the concentration of thyroid-stimulating hormone (TSH) in plasma. Thus, in a pregnant woman neurodevelopmental defect in the fetus were thought to be unlikely when the thyroid gland was found to have normal function. However, epidemiologic and experimental studies over the past two decades have shown that fetal neurodevelopment is not only hypothyroid when the mother is hypothyroid, but also „hypothroxinemic” in the early stages of pregnancy [5].

Materials and methods

Male rats with an average weight of 180-220 g were used for the experiment. In the first part of the experiment, the rats were divided into groups. Group 1 intact (n=6), group 2 hypothyroid group (n=6). All rats were fed a standard diet. Mercazolil drug was dissolved in 1 ml of water at a dose of 1.2 mg/100 g to induce a hypothyroidism model and was injected orally into the stomach through a special probe for 21 days. This drug has an antithyroid effect and blocks the peroxidase enzyme that ensures iodination of thyronine amino acid as triiodo- and tetraiodothyronine. As a result, there is a decrease in the synthesis of thyroid hormones [17]. After 21 days, in order to check the cognitive functions of healthy and hypothyroid rats, a special maze with a size of 45x90x10 cm was conducted. *Contur plus* glucometer was used to determine the amount of glucose in the blood.

Results and discussions

Preliminary morphophysiological studies during the experiment showed that hypothyroidism developed in white rats of the experimental groups as a result of the use of the thyrostatic mercazolil drug for 21 days. Physiological examination of experimental animals revealed clinical manifestations of hypothyroidism - graying of fur, loss of appetite, increased mass and decreased motor activity (Table 1).

Table 1. Clinical manifestations of hypothyroidism

Groups	Healthy	Hypothyroidism
Signs		
Drowsiness	-	+
Swelling	-	+
Yellowing of the skin	-	+
Cold intolerance	-	+
Mass gain	-	+
Decreased appetite	-	+

The analysis of the movement activity of the rats showed that the rats in all the experimental groups moved more slowly than the control group during the observation period of their behavior in the maze (Table 2).

Table 2. The weight, movement activity and glucose level in the rats with hypothyroidism

№	Groups	n	Healthy	Hypothyroidism	P value
	Indicators				
1	Weight (g)	6	205,2±8,6	215,2±5,2	0,2
2	Time to find your way through the maze (minut)	6	3,2±0,56	5,3±0,63	0,05
3	Glucose (mmol/l)	6	5,1±0,41	6,3±0,6	0,1

A decrease in thyroid function has been found to have a detrimental effect on cognitive functions, regardless of age. The reason for this is that in hypothyroidism, the energy supply of the brain, that is, the consumption of glucose, decreases. As a result, there is a decrease in neurotransmission, processes necessary for memory and other higher brain functions. Low glucose absorption in the brain is usually accompanied by a decrease in mental and motor activity [1]. Thyroid

hormones regulate glucose homeostasis by interacting with the entire central nervous system and its surrounding target organs. Glucose metabolism has been extensively studied in individuals with thyroid dysfunction. Thyroid hormones affect many aspects of glucose metabolism in terms of insulin sensitivity, activity and metabolism, and glucose uptake and absorption. Conversely, in hypothyroid patients, insulin fails to stimulate glucose uptake by muscle and adipose tissue [3,11]. Several epidemiological studies have shown that untreated thyroid dysfunction may increase the risk of type 2 diabetes. Similarly, among adolescents with thyroid dysfunction, the risk for type 2 diabetes increases before the age of 30, or vice versa. A significantly increased risk of thyroid cancer has been observed in patients with diabetes [4].

Significant neurocognitive deficits in hypothyroidism, decreased memory, attention and perception, executive functions, retardation of intellectual development, disorientation in time and space, and other mental defects may occur as a result of decreased glucose absorption and increased blood glucose [6,10]. During the experiment, the concentration of glucose in the blood of rats in healthy and hypothyroid groups was determined using a Contur plus glucometer. According to it, it was found that the amount of glucose in the blood of hypothyroid rats was 1.2 times higher than that of healthy rats ($P=0.1$). As a result of testing the ability of experimental animals to find their way in a maze, it was found that the cognitive functions of hypothyroid rats were impaired. This condition may be the result of reduced absorption of glucose into the brain tissues as a result of decreased metabolism in hypothyroidism. Glucose is an important metabolic fuel for the brain. A sudden decrease in brain glucose leads to impairment of cognitive and reflex functions, loss of consciousness, seizures, permanent and irreversible brain damage, and may even lead to death if not corrected quickly [9].

The cognitive effects of glucose supplementation may vary among people. Some information about this contradicts each other. Some studies show that normal consumption of glucose normalizes the cognitive functions of the brain. According to some literature, the human body has the ability to produce enough glucose, and brain functions do not depend on the amount of glucose received from the external environment [14].

As a result of slowing down of metabolism in hypothyroidism, it leads to the accumulation of derivatives of macromolecules in the mucous membranes, skin and subcutaneous tissues, and the formation of swelling. As a result, an increase in mass is observed. During the

experiment, the mass of healthy and hypothyroid rats was compared, and it was found that the mass of hypothyroid rats increased by 1.04 times the mass of healthy rats. ($P=0,2$).

Conclusion

This study was carried out in order to determine the changes in the cognitive functions of the brain in thyroid dysfunction and its dependence on glucose. According to the obtained results, it was found that the time of finding the way in the maze of rats in hypothyroidism is slowed down and the concentration of glucose in the blood is increased. We can consider this condition as a disorder of brain function as a result of low absorption of glucose, which is the main nutrient of the brain. Currently, in the continuation of the research, it is planned to use various biologically active compounds isolated from plants in order to correct these parameters. Taking into account the antioxidant, anti-inflammatory, antithrombotic, antidiabetic effects of biologically active compounds, positive results are expected from future experiments.

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