

## STUDY OF THE SINGLE AND CHRONIC EFFECT OF HYPOXIA ON THE FUNCTIONAL ACTIVITY OF THE REPRODUCTIVE GLANDS IN EXPERIMENTAL ANIMALS UNREACHED SEXUAL MATURITY

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**ABSTRACT.** In order to study changes in the hormonal activity of the sex glands under the influence of hypoxia on the body in prenatal and postnatal ontogenesis, the question of studying the dynamics of sex hormones in the blood during hypoxia in immature animals was studied. The facts we have discovered about how the activity of the gonads in immature animals' changes under chronic exposure to mild and severe forms of hypoxia give reason to conclude that if mild hypoxia and its chronic effects partially weaken the activity of the gonads, then their secretory activity is affected by severe hypoxia, especially it causes more abrupt changes under the influence of the chronic form. Since the secretion of sex hormones is under the control of the hypothalamic-pituitary system, it can be assumed that with severe hypoxia, the activity of this system may undergo negative changes, and, of course, this situation cannot but affect the functions of the sex glands (gonads). It can be assumed that severe hypoxia affects the synthesis of sex hormones and inhibits these processes to some extent.

**Keywords:** sex hormones, hypoxia, prenatal and postnatal ontogenesis, hypothalamic-pituitary system.

### I. Introduction

It is well known that in animal organisms, sexual difference (sexual differentiation or sexual dimorphism) is one of the most important biological, basic hereditary (genetic) traits acquired in the process of evolution. A special place among other forms of animal behavior is occupied by sexual behavior, thanks to which it is possible to preserve the existence of the species, increase the number of male and female individuals, as well as the future generation (reproduction). This form of behavior is considered one of the necessary conditions for life.

It has long been known that the regulation of the processes of sexual differentiation and sexual behavior in higher animals is carried out with the help of special genetic mechanisms, a number of hormonal substances, and certain structures of the central nervous system. A special role in these processes is played by sex chromosomes, specific pituitary tropic hormones (follicle-stimulating, luteinizing), sex hormones and some neurosecretory products of the hypothalamus. From the conducted fundamental research, it became clear that differentiated and developing male and female gonads acquire the ability to synthesize the corresponding hormones from a certain period due to the genetic information embedded in the genetic apparatus of the embryo during intrauterine embryogenesis, and the sex hormones produced by them become reproductive organs in the embryo, have a strong stimulating effect on the formation, as well as on the sexual specialization of special neural networks of the brain, including the hypothalamus [1,2,3].

The course of these processes was studied in more detail in mice and rats, representatives of mammals. As you know, the estrus period in these animals lasts about 20-21 days. Some researchers found, that in rats on the 13-14th day of insemination (embryonic stage), the male gonads and their interstitial cells begin to synthesize the sex hormone testosterone, and on the 17-18th day (embryonic stage) the amount of this hormone in the blood reaches a maximum. During fetal development, the release of a large amount of testosterone into the blood in the form of the hormone androgen is characterized as a critical stage in the life of the fetus. It is assumed that at this stage the genetic sex of the future organism is completely determined

[4,5,6]. They show this as strong evidence that the amount of testosterone in the blood gradually decreases in the last days before the birth of the body and within 10 days after birth. According to other researchers, the definition of a male or female organism in prenatal ontogenesis is determined not by the hormone testosterone itself, but by the estrogen hormone estradiol formed from it [7, 8]. It is shown that both male and female gonads are formed morphologically and physiologically during intrauterine and early postnatal development.

Sex hormones are physiologically active substances of a steroid nature. Sex steroids circulate in the blood in free and bound form, physiological effects are largely associated with the action of free hormones. Most of the amount of testosterone and estradiol (up to 70%) is associated with  $\beta$ -globulins, less - with albumin, but only 1% freely circulates in the blood [9]. These hormones can effectively influence the synthesis of neurotransmitters in the brain [10,11]. Their production and blood levels in certain gonads are regulated by hypothalamic-neuroendocrine and pituitary-tropic hormonal mechanisms, as are the hormones corticosterone, cortisol, and thyroxine. The secretory capabilities of the sex glands are more often regulated by libin-releasing factors of the hypothalamus, gonadotropic hormones of the anterior pituitary gland - follicle-stimulating hormone and luteinizing hormone [12].

The issue of studying changes in the hormonal activity of the gonads under the influence of hypoxia on the body in prenatal and postnatal ontogenesis has not been sufficiently elucidated in the literature materials available to us in recent years. Empirical studies in this area are sporadic, but a consensus has not yet been formed. In our presented work, we studied the issue of studying the dynamics of sex hormones in the blood during hypoxia in immature animals.

## II. Methods

The object of the study were male and female rats 2 months of age. The animals used were grouped by sex. Each group was divided into control and experimental subgroups according to the applied models of hypoxia. In animals of the control and experimental groups, venous blood was taken (from the femoral vein of the hind limbs) and sex hormones - testosterone and estradiol - were determined in plasma by enzyme immunoassay. The amount of hormones studied at the beginning was determined in the norm. After 5, 10 and 15 days after the use of relatively mild (moderate) and severe hypoxia chronically (for 5 days, 20 minutes each day), the studied hormones were determined again. As models of hypoxia, respiration in an environment of 85% nitrogen ( $N_2$ ) + 15% oxygen ( $O_2$ ) (mild hypoxia) and respiration in an environment of 95%  $N_2$  + 5%  $O_2$  (severe hypoxia) were used.

## II. Results and Descutions

The results of our research are shown in Figures 1 and 2. In the studied 2-month-old male rats, normal levels of testosterone hormone in these periods are determined on average within the range of 22-25 ng/dl. This level indicates a significant activity of the functions of the gonads (semen) in males at the age of 2 months. At this time, the amount of the sex hormone estradiol in the blood of 2-month-old female rats normally ranges from 34-37 ng/dl. Comparing these quantitative indicators, it is known that the secretory activity of the gonads in 2-month-old female rats is higher than in males of the same age (Figure 1, 2).

This pattern, which normally manifests itself in the spectrum of sex hormones in 2-month-old rat pups, does not change so dramatically after exposure to mild chronic hypoxia. It is more or less noticeable that a weak but prolonged hypoxic load still affects the activity of the gonads, and this effect is of a kind of negative nature.

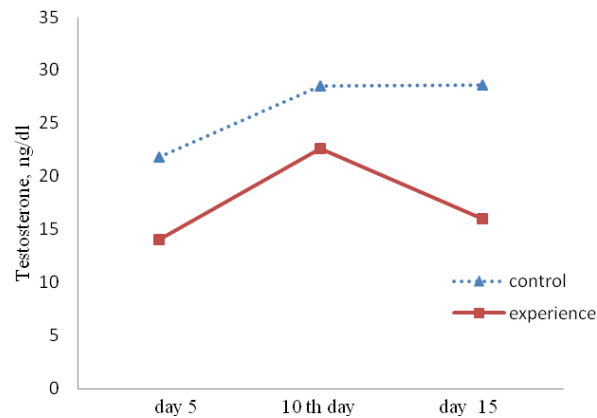


Figure 1. Changes in blood testosterone levels in 2-month-old male rats under conditions of normal and severe chronic hypoxia.

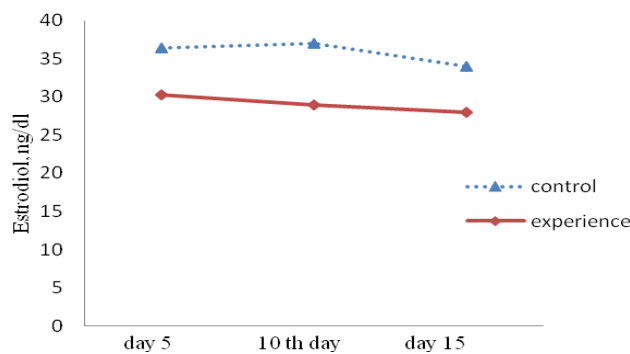


Figure 2. Curves of changes in the amount of estradiol in the blood of 2-month-old female rats under conditions of normal and severe chronic hypoxia

Thus, the amount of testosterone in the blood is less than normal on all days of the experiment, and on the last days of the experiment (10th and 15th days) even a statistically significant ( $p < 0.05$ ) decrease in its amount is recorded). At the same time, the amount of the prescribed hormone in the blood decreases to 25.6 and 22.0 ng/dl, respectively (norm: 28.5 and 28.6 ng / dl, respectively). Relatively mild chronic hypoxia in the blood of 2-month-old female rats causes only a slight decrease in the amount of estradiol, which ranges from 33-35 ng / dl. Given this fact, it can be assumed that 2-month-old female rats are more tolerant to hypoxic effects than male rats of the same age, and they have a significantly higher ability to adapt to mild hypoxia.

This picture, which normally appears in the spectrum of sex hormones in 2-month-old rats, does not change so sharply after exposure to mild chronic hypoxia. It is more or less noticeable that a weak but long-term hypoxic load still affects the activity of the gonads, and this influence has a kind of negative character. Thus, the amount of testosterone in the blood is less than the norm on all days of the experiment, and in the last days of the experiment (the

10th and 15th days), even a statistically significant ( $p < 0.05$ ) decrease in its amount is registered. At the same time, the amount of the prescribed hormone in the blood decreases to 25.6 and 22.0 ng/dl, respectively (norm: 28.5 and 28.6ng/dL, respectively). Relatively mild chronic hypoxia in the blood of 2-month-old female rats causes only a slight decrease in the amount of estradiol, which fluctuates between 33-35 ng/dL. Considering this fact, it can be assumed that 2-month-old female rats are more tolerant to hypoxic effects than male rats of the same age, and they have a significantly higher ability to adapt to mild hypoxia.

In continuation of this study, sex hormones were determined in the blood of 2-month-old male and female rats after severe chronic hypoxia. From the results obtained in this series of experiments, it is clear that severe chronic hypoxia can seriously disrupt the hormonal activity of the gonads of 2-month-old rats. In our

experiments, it was established that the levels of testosterone and estradiol hormones in the blood of animals of both sexes are statistically significantly ( $p < 0.05$ ;  $p < 0.01$ ) reduced over a long period of time under the influence of severe chronic hypoxia. These reduction limits for testosterone were recorded between 14-22 ng/dl, for estradiol between 28-30 ng/dl, depending on the duration of the determination. Referring to these indicators, it can be said that male 2-month-old rats are more sensitive to the effects of severe hypoxia than females, as a result of which their sexual hormonal reactions are more pronounced.

Thus, the facts discovered by us about how the activity of the gonads in immature animals changes during chronic exposure to mild and severe forms of hypoxia give us the reason to conclude that if mild hypoxia and its chronic effects partially weaken the activity of the gonads, then their secretory activity is affected severe hypoxia, especially it causes more drastic changes under the influence of the chronic form. Since the secretion of sex hormones is under the control of the hypothalamic-pituitary system, it can be assumed that with severe hypoxia, the activity of this system may undergo negative changes, and, of course, such a situation cannot but affect the functions of the gonads (gonads). It can be assumed that pronounced hypoxia affects the synthesis of sex hormones and to some extent inhibits these processes. It is difficult to say at what stage of their biosynthesis such an effect occurs. Here it is necessary to say a few words about the biosynthesis processes of androgens and estrogens in the animal body. Androgenic steroids are known to be produced in the Leydig cells of the testes, the ovaries, the placenta, and the reticular layer of the cortex of the adrenal glands. Exogenous steroids are predominantly synthesized in the cells of the inner lining of the ovarian follicles and partly in the granular cells covering the inner spaces of the follicles. Synthesis of estrogens also occurs in the corpus luteum, male gonads, and in some pathologies in the reticular layer of the adrenal cortex. Cholesterol is considered the precursor of both types of sex hormones. Androgen biosynthesis in the testicles and ovaries is regulated by luteinizing hormone (LH), a pituitary tropic hormone. The biosynthesis of estrogens is also carried out according to the above scheme, in addition, androgens themselves can act as a source of estrogen formation. The production of these types of sex hormones is regulated by follicle stimulating hormone (FSH), a pituitary tropic hormone. Apparently, the processes of synthesis and secretion of androgens and estrogens are associated with extensive and very complex chemical reactions and transformations. The question of which of these phenomena undergoes major changes during hypoxia is a difficult problem for experimental studies.

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