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Moderate Hypoxia And Systemic Hormonal Reactions In Early Postnatal Ontogenesis In Different Experimental Animals (Overview)

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Abstract. In the article presents and discusses some experimental data about of abilities of a number of functionally interconnected endocrine glands in rats and rabbits under hypoxia of moderate load.

Key words. moderate hypoxia, endocrine glands, systemic hormonal reactions, postnatal ontogenesis,

Along with the central nervous system (CNS) and under certain conditions (for example, in the initial stages of postnatal ontogenesis, etc.), more prolonged and large-scale, than the central nervous system, the neuroendocrine-endocrine system plays an important role in the integration, regulation and coordination of a number of intracellular metabolic processes, physiological functions, adaptive and behavioral reactions of the animal organism under at those or other extreme or stressful conditions[1, 2, 4, 7].

The impact of various stressors (chemical, physical, etc.) as a rule, causes a burst of secretory activity of a number central and peripheral links of the endocrine system, and this can have particular significance for the survival of the animal organism[5,9, 14, 16]).

It is characteristic that those endocrine glands that are more actively involved in the development of stress reactions and adaptation, their hormone-forming (and probably also hormone-secreting) functions are under the control of higher central regulators, among which, first of all,concerns hypothalamus and its neurosecretory neuron complexes[16,18, 23]. It has been established, that located in the paraventricular nuclei (PVN) of the hypothalamus, neurosecretory cellular formations have broad nerve connections shuc as both sensory and integrative centers of the brain,and as in particular with the main endocrine organ-the pituitary. It is also known that PVN neurons produce several types of hormone-like releasing factors (releasing factors) of peptide nature (liberins and statins) that have specific functions, effects, they exert a pituitary and through it to certain peripheral endocrine glands regulating (stimulating or inhibiting) action[17, 19, 24, 25]. Thus, can assume that, from early ontogeny in the animal body are formed the hormonal function system such as hypothalamic-pituitary-adrenocortical, hypothalamic-pituitary-thyroid and hypothalamic-pituitary-gonadal.

There are strong judgments about the fact that in the body the key hormonal axis of the stress reaction is the hypothalamic-pituitary-adrenocortical system (H-PACS), and the hypothalamic corticotropin-releasing factor (CRF) is the first stress mediator, the trigger for the release of pituitary adrenocorticotropic hormone (ACTH). And he also controls the hormonal function of the adrenocortical gland (adrenal cortex) by the mechanism of negative feedback[18, 20, 21]. Corticosteroid hormones such as glucocorticoids (corticosterone, cortisol) are excreted into the bloodstream of cyst of the adrenal glands have, as known, a wide spectrum of physiological action. It is directed mainly, for maintenance and regulation of catabolic processes in organs and tissues, essentially on the mobilization of compensatory-adaptive forces of the body under stresses[2, 7]. Proceeding from the central idea of the theory of G.Sellet about stress, various strong external factors (stressors) can cause sustainable tension in the human and animals organisms , some and the same general shifts (or symptoms), among which especially noticeable and nonspecific is hypertrophy of the adrenal cortex, activation of its secretory function and intensive release of glucocorticoid hormones into the blood. The modern notion about of these hormones is based on convincing experimental and clinical data, according to which both corticosterone and cortisol (hydrocortisone) acts mainly in the role of as "stress hormones and adaptation".

To some extent, the same role can plays both thyroid hormones (thyroid gland), and especially thyroxine (T_4). It is well known that,hypothalamic thyrotropin-releasing factor (TRF), as well as CRF,has a direct specific effect on the pituitary gland and regulates the formation in it of a thyroid-stimulating hormone (TSH), in turn it stimulating the thyroid gland[28]. Its thyroxine, like glucocorticoids, has a wide-profile regulating action, in particular, it actively participates in the regulation of bioenergetic metabolism[3].

At present, for many researchers in the experimental physiology, as well as clinically obvious that in a complex study of hypoxic conditions in the organism still are remains many unclear and poorly studied questions. It is known that hypoxia (lack of oxygen in the organisme) can often accompany vital activity of organisme and have to it a negative, lethal, action. This factor in famous degree is both simultaneously strong stressor and a pathogenic factor of a wide range of influence. Therefore, of particular interest is to researches hormonal reactions in the developing organism, and especially in the early periods in postnatal development. Again like to stress that in this aspect not conducted so many experimental and clinical studies.

Judging by the literature (a few experimental works), to hypoxia very strongly reacts hormonal links of adaptive orientation. Very interesting experimental data are presented by Y.N.Orestenko with authors (1986), who studied hypothalamic effects of influence of hypoxia to the organisme. It was shown that, under conditions of chronic experiments on rats line Wistar subjected to hypoxia detected cyclic enhancement of the functional activity of the neurosecretion of the paraventricular nucleus of the hypothalamus with parallel oppositely directed manifestations from the side of the dorsal hippocampus.

Hypoxic adaptation of the organism was accompanied by a consistent development of activation of different structures of the hypothalamus.

The most interesting, in our opinion, may be a result of those studies which we have the opportunity to present changes in neurosecretory and hormone-forming functions as central, and as peripheral links of an integral neuroendocrine-endocrine functional system under hypoxia. Such studies proved to be more effective and valuable due to the use in the domain of definition of concentrations of neurosecrets and hormones in the tissue media and blood such highly sensitive methods as radioimmunoassay (RIA),immunoenzymatic analysis (IEA), and various variants of immunoassay (fluorescent immunoassay, luminescent analysis), as well as other modern methods such as enhanced luminescence, electrochemical, and biosensory. In addition, it was created a number of more advanced and high-precision instruments and the corresponding reactive sets (whales) for measurement in bio-liquids of various hormones by nature. About these techniques detailed information is given in the works of G.Lindstedt, A. Jacobson (2000), V.A. Dalkhov, I.Kh. Rakova, V.E Rybakov (2006) and other authors. As noted N.V.Goncharov (2001), development and implementation in practice high-sensitivity radioimmunoassay technologies and various immuno-enzymatic methods for the analysis of hormones in tissue liquid and in blood plasma became one of the defining achievements of modern biology and medicine and have opened new opportunities for modern endocrinology. By the way, in the last ten years, some work on hormonal analysis in hypoxia was performed on the basis of above listed methods of radio-, and immunoenzyme analysis.

Stay of the animal organism under stress and in the conditions of moderate or more severe hypoxia, as believe many researchers primarily, quite pronounced is develop interconnected systemic(nervous, hormonal and immune) of adaptive responses[1, 2, 3], and apparently, they prevail over other possible shifts in various links of general metabolism and organ-cellular functions. As already noted, in the development of such reactions, some functionally interacting endocrine systems plays an extremely important role. One of the main "starting" centers and mechanisms of adaptation is the hypothalamus and production in it neurosecretes, activated is sufficiently express in the initial phases of development of hypoxic conditions. In this case, acceleration of the processes of development of those hypothalamic releasing factors (HRF and TRP), which by axons of secretory neurons enter directly into the neurohypophysis and stimulate secretion in the adenohypophysis ACTH and TSH (TSG), key tropic hormones that trigger subsequent hormonal reactions of adaptive orientation.

In this connection, special attention should be paid to experimental work to the study of the state of CRF in an animal organism (or corticoliberin) synthesizing structures of the hypothalamus and the content of the CRF itself under hypoxic effects. So, for example, according to the data of Y.M. Kolesnik, Y.K.Oristenko and A.B. Abramov (1993), in the onset of hypoxic exposure in rats significant is detected activation of synthesis and accumulation of CRF in neurosecretory neurons in the region CRF of hypothalamus, which can entail manifestations activity of synthesis ACTH in the adenygipophysis and and

the subsequent stimulation of the production of glucocorticoid hormones in the adrenal cortex. It is important to note that, in the neurosecretory areas of the hypothalamus and in the level of pituitary, function molecular receptor modulating adrenocorticotropin action [34] and receptors of glucocorticoid hormone participating in the mechanisms regulation of hypothalamic neurosecretion and pituitary ACTH-function. In addition, to the processes of activation and inhibition of neurosecretion of the hypothalamus and tropic pituitary function has a direct relationship monominergicheskie and GABA-ergic mechanisms [26, 33], determining of character of responses hormonal responses under stress, including in the states of hypoxia.

In a number of experimental studies, is indicated that depending on in what period of ontogeny occurs hypoxia, response hormonal reactions may acquire ambiguous character. According to the research of R.Herman, L.Longo, R.Megrvern (1994), in rats prenatal hypoxia led to a decrease concentrations of corticosterone in the blood, and testosterone in postnatal ontogenesis and this affects to their field behavior.

I would like also to stops on our experiments carried out on immature animals (rats and rabbits), who were subjected to a single-entry moderate hypoxia in 1- and 2 months and in different sexual maturation. According to some generalized data [17], rats reach sexual maturation at 9-16 weeks, and rabbits - at 5-11 weeks of age. In some experiments was used more adults (3 months) rats and rabbits. In this studies, we traced their early hormonal reactions of the pituitary gland, adrenal cortex, thyroid gland and sexual glands, for a one-time effect of a moderate form of experimental hypoxia. As a hormone in the plasma of blood was determined was determined content of ACTH and TTH(or TBG) of the pituitary gland, corticosterone and cortisone of the adrenal cortex, thyroxine (T_4) of the thyroid gland, testosterone and estradiol of the sex glands.

To determine them, we used individual sensitive methods of immunoassay, sets of reagents ADVIASentaurCP and automatic immunoassayers IMMULITE -2000 XPIи COBASe 411. All analyzes were performed in a highly biochemical laboratory at the State Medical University (Baku), on a contractual basis on scientific cooperation. Our experimental results are more detail illuminated in a number of previously published papers[12, 13, 31, 32].

The studies were carried out as can be seen from the above, guided by the system methodology and system approaches which in the last decades in the began to occupy experimental physiology an important place to solving more fundamental problems both theoretical and practical character. We thought that, they are very important in experimental endocrinology on the issues of hypoxia, which is one of the major tasks, standing in the precomplex medical and biological research at the present time. Specifically, our experiments on hypoxia mainly concerned only those hormonal links that were formed in the filo-and ontogenesis as functionally interrelated and system-forming, and more integrated in reactions to the effects of strong factors of the external and internal environment, which includes hypoxia. This is

primarily the pituitary-adrenocortical and pituitary-thyroid systems. Modes of experimental hypoxia and the timing of the experiments were chosen in such a way, that the reactions of these systems could be traced in dynamics over short periods with minimal intervals.

Thus, it was revealed that concentration of the hormone ACTHof the pituitary gland in plasma of blood of the rats aged 1 month. varied within the range of 78-83 pg / ml,in the rats 2 months. age, within the limits of 140-160 pg / ml, in rabbits of the same age - within the range of 60-65 and 96-104 pg / ml, respectivelyIn case of application regime of moderate hypoxia (breathing in a pressure chamber with a mixture of gases 15% O_2 and 85% N_2, for 20 minutes) on the first day of the experiment the concentration of ACTH increases sharply (on average, up to 120 pg / ml), and then the reaction acquires a fading character. In the rats of the 2 months. age she is more or less weak, and level of ACTH is nearly normalized on the 5th day of the experiment. In rabbits 1 month. age, a significant increase in ACTH after moderate hypoxia was recorded on day 3 of the experiment (up to 98 pg / ml). Such a reaction was preserved for the next term, but in 2 months. shift ACTH in the direction of increase is less pronounced, but maintains the same dynamics.

A parallel measurement in the blood of rats and rabbits of both ages concentrations of adrenocortical hormones of corticosterone and cortisol, the synthesis and secretion of which is controlled by the production of ACTH the pituitary, showed that under moderate hypoxia in the early period occurs accelerated release into the blood a significant amount of corticosterone and cortisol. This adrenocortical reaction to some extent adequate to that, which can be observed in side of ACTH - a pituitary gland function, very often develops under stresses. For example, rats 2 months. age. in 1 day of moderate hypoxia the level of cortisol and corticosterone in the blood (background, 2,5 and 5,0 mg / dl, respectively) increases to 4,9 and 7,6 mg / dl, in rabbits of the same age, the level of these hormones (background, 6,0 and 3,8 mg / dl, respectively) reaches up to 8,0 and 5,4 mg / dl. Later in both types of laboratory animals the concentrations and cortisol, and corticosterone are reduced to control values, especially on day 3 of the experiment. The results of the study of the ТТГ-function of the pituitary gland in rats in norm and after moderate hypoxia showed the following picture: concentration of TTH in the blood of rats in 1 and 2 months. (background indicators of 2,4 and 3,5 IU/ml, respectively)begins to rise slowly after hypoxia, and on the third day of the experiment reaches to the maximum -4,5 and 5,2 IU/ml, corresponding to these age groups. And at the same time, a sharp increase in the concentration of TTH in the blood of rabbits in 1 month. age (background-2,8 IU/ml) was noted in the 1st and 5th day of experiment to 4.1 and 4,3 IU/ml and in the blood of rabbits in 2 months. age (background – 4.8 ME/ml) on 3 day of experiment to 5,5 IU/ml. In these terms are observed increases of reactions from the side of thyroid (thyroid) gland. The level of thyroxine (T4) in the blood was of an oscillatory nature with peaks of sharp growth during an increase in the TTH- function of the pituitary gland.

Increasing concentrations of T_4 was observed on 3 -th day after hypoxia to 3,6 / mg / dl (background, 1,8 mg / dl), at rat 3 months - on day 5-th of the experiment - up to 6,4 mg / dl (background, 3,4 mg / dl). A significant shift towards growth of T4 occurred in rabbit kiddy and rabbits of the same age only on the 3rd day of the experiment, in the future,was observed recession of reaction. The experiments we performed on male and female rats in 2 months. age and in whose blood determine concentrations of testosterone and estradiol are norm and after moderate hypoxia within a half-month with intervals of 5 days, showed that quantitative changes in these hormones to the side of enhancing the are observed only in remote terms of the experiment (on the 10th and 15th days of the experiment). Testosterone in males increased from 21,8 -28,5 ng / ml (normal) to 33,5 ng / ml, while estradiol in females increased from 13,0 - 17,2 ng / ml (normal), up to 36,0 ng / ml. Apparently, such late reactions to hypoxia from the side of the gonadal glands,may be associated with late excitation of sexual centers location in the central nervous system and hypothalamus and which determine the level of sexual behavior and the activity of FSH and LH-functions of the pituitary gland[30]. In previous works, we pointed out that in changes of the metabolism and functions of organism under hypoxic conditions, as a rule, are manifested early (primary) and late (secondary) reactions up to systemic and behavioral. Such reactions are especially characteristic at the level of the central nervous system [11] and such develop, according to some literary and our data, in the endocrine system.

In this way, in the experimental animals in early postnatal ontogenesis even moderate hypoxia causes expresse hormonal reactions systemic character. In particular, pituitary-adrenocortical (adrenal cortex) functional hormonal system, very active reacts to this hypoxic load. The pituitary thyroid (thyroid) functional hormonal system is connected to the response to hypoxia, later and less pronounced. In the reactions of both functional endocrine systems during moderate hypoxia clearly manifested species, ages and sexual differences. We believe that, some posthypoxic reactions in the certain extent remind hormonal reactions (especially, on an example HPACS) developing under stress.

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