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Short Communication

Reversibility of Adaptation, Phenomena of Physiological and Pathological Maladaptation

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Abstract

The possibility of a reverse development of the process of long-term adaptation is expressed in the gradual disappearance of adaptation to physical exertion, hypoxia, and chemical factors after the cessation of these factors. It has been shown that at this time there is a rather rapid disappearance of the systemic structural trace that forms the basis of each of these adaptation options (a decrease in skeletal muscle mass, the number of mitochondria in them, a decrease in lung and heart muscle mass after cessation of physical exertion, a decrease in the mass of the right ventricle of the heart and the gradual disappearance of polycythemia after the body leaves hypoxia, a decrease in activity of the microsomal oxidation system and liver mass after discontinuation of the administration of poisons).

Keywords: adaptation; physiological maladaptation; pathological maladaptation

Introduction

The possibility of a reverse development of the process of long-term adaptation is expressed in the gradual disappearance of adaptation to physical exertion, hypoxia, and chemical factors after the cessation of these factors. It has been shown that at this time there is a rather rapid disappearance of the systemic structural trace that forms the basis of each of these adaptation options (a decrease in skeletal muscle mass, the number of mitochondria in them, a decrease in lung and heart muscle mass after cessation of physical exertion, a decrease in the mass of the right ventricle of the heart and the gradual disappearance of polycythemia after the body leaves hypoxia, a decrease in activity of the microsomal oxidation system and liver mass after discontinuation of the administration of poisons). The mechanism of this phenomenon is that immediately after a sharp decrease in the load on any of the organs forming the functional system responsible for adaptation, there is a sharp drop in RNA synthesis and a decrease in the number of polysomes. As a result, protein synthesis in the organ decreases and begins to lag behind its decay — the mass of organ structures decreases**.** Thus, in experiments after a 45-day pressure chamber adaptation at an "altitude" of 7000 m, rats showed a 42% increase in the weight of the ventricles of the heart, and protein synthesis in the heart by the inclusion of labeled amino acids was increased by 20%. 3 days after the cessation of hypoxic effects, the weight of the ventricles remained increased by 40%, and the intensity of protein synthesis decreased to the control level. On the 7th and 15th days of readaptation, the weight of the ventricles was increased by 35 and 10%, respectively, and protein synthesis in the heart during these periods was reduced by 40 and 30%, respectively, compared with the control. On the 30th day of readaptation, ventricular weight and protein synthesis in the heart were at the control level [1]. In another laboratory study, the mass of the right ventricle of the heart and the RNA content in the myocardium of this ventricle were determined at various times after the termination of 20-day pressure chamber adaptation of rats at an "altitude" of 6000 m. After the end of the course of exposure, hypertrophy of the right ventricle and an increase in its RNA content were observed. By the 10th day of deadaptation, 54% of hypertrophy and 57% of adaptive RNA growth had been lost. After 20 days, 81% of hypertrophy was lost, and the RNA content returned to normal levels. 40 days after the cessation of hypoxic effects, the mass of the right ventricle and the RNA content in it did not differ from the control [2]. Approximately the same rate of reverse development of the systemic structural trace of adaptation has been demonstrated in studies of other laboratories. Thus, in experiments, hypertrophy of the left ventricle of the heart was caused by narrowing of the ascending aorta in rats. 28 days after surgery, the mass of the left ventricle and its RNA content were increased by about 50%. After that, cardiac hyperfunction was abruptly stopped by removing the ring that narrows the aorta. The mass of the ventricle and the RNA content in it decreased steeply in the next three days, then they decreased more slowly and after 20 days did not differ from the control. This kind of reversibility has been proven at the present time and after the long-term existence of

compensatory devices in humans. Thus, the large hypertrophy of the left ventricle of the human heart caused by aortic valve disease undergoes a complete reverse development within the next year after a successful surgical operation that eliminated the defect by transplanting new valves. At the same time, the mass of the ventricle decreased by about 90 g and the disorders of contractile function observed with severe hypertrophy were eliminated [3]. These facts indicate that a decrease in the synthesis of nucleic acids and proteins plays an important role in the reverse development of the adaptive structural trace. The question of the possible role in this process of mechanisms responsible for the destruction of cellular structures, such as lysosomal enzymes or lipid peroxidation products, is currently the subject of research. In relation to the heart, it has been shown that the reverse development of hypertrophy caused by narrowing of the aorta is not accompanied by activation of lysosomal enzymes, and the reverse development of hypertrophy caused by the administration of thyroxine is accompanied by such activation. For another adaptive structural trace, namely, an increase in the power of the microsomal oxidation system that occurs when a poison is introduced into the body, it has been shown that membrane lipid peroxidation plays a role in its reverse development. Thus, the increase in the power of the microsomal oxidation system and the content of cytochrome P-450 in the liver caused by the administration of 20-methyl-holontren undergoes a reverse development after the cessation of the administration of this carcinogen. In the process of reverse development, i.e. During the breakdown of excess cytochrome P-450 and the disassembly of the sarcoplasmic reticulum membranes that have become redundant, activation of lipid peroxidation of the membranes and the action of lipid hydroperoxides on these structures play an important role [2]. Thus, a decrease in the intensity of protein synthesis and, possibly, the activation of structural degradation mechanisms rather quickly lead to the reverse development of the adaptive trace.

There is also evidence that, in addition to the factors just mentioned, the genetically determined instability of proteins formed during adaptation to proteolytic enzymes can play an important role in eliminating the adaptive structural trace. Thus, during stress or under the influence of externally administered glucocorticoids, the liver activates the synthesis of gluconeogenesis enzymes, which ensure the transformation of the body's structural resources into energy resources necessary in an extreme situation. After the extreme situation has passed, such a transformation becomes at least unnecessary and, moreover, prevents the restoration of lost structures and the development of reparative processes. Accordingly, when studying one of the enzymes of tyrosine transferase (TAT) neoglucogenesis, it turned out that in the first 5 hours after the introduction of hydrocortisone, its activity increases 10-fold, and in the next 10-15 hours it manages to decrease again to a normal level. TAT is represented in the liver by so-called A-isozymes, which move towards the anode during electrophoresis, and K-isozymes, which shift towards the cathode under the same conditions. These isozymes are encoded in various cistrons of the liver cell genome. Under the influence of glucocorticoids, cistrons encoding exclusively A-isozymes are activated, respectively, an adaptive increase in A-isozyme biosynthesis becomes the basis for an overall increase in TAT activity under stress. This isozyme is disproportionately less resistant to the action of proteolytic enzymes than isozyme K; it is rapidly destroyed, and that is why the activity of TAT decreases rapidly, returning to its initial level in a timely manner. A completely similar situation has been proven for adaptive insulin-induced activation of hexokinase biosynthesis and other enzymes. Thus, it seems that we are talking about a general pattern, which consists in the fact that an organism genetically determines not only the possibility of structural changes forming the basis of adaptation, but also the timely reverse development of these changes. There are at least three types of molecular mechanisms responsible for the reverse development of the systemic structural trace, namely: decreased synthesis of RNA and proteins, activation of specialized mechanisms of structural breakdown, and genetically determined instability of structures formed during adaptation to natural degradation mechanisms. The existence of various mechanisms that duplicate each other to varying degrees, "erasing" the systemic structural trace and ensuring the reverse development of adaptation, indicates the great biological significance of this process. Indeed, the reverse development of adaptation, or deadaptation, is an expression of the body's remarkable ability to eliminate unused structures. This is a necessary prerequisite for the use of released structural resources in other body systems and, thus, a prerequisite for transitions from one adaptation to another under the influence of the environment [4].Considering readaptation as a physiological process, and its high rate as a prerequisite for the formation of new long-term adaptive reactions in the body, it should be borne in mind that the organism of higher animals is evolutionarily determined to live in a relatively permanent environment, to which it gradually adapts. This is probably why the rate of de-adaptation is only relatively high compared to the initial state, but at the same time it is less than the rate of adaptation development. This important circumstance is the basis for the accumulation of adaptive changes under periodic, sometimes not too frequent environmental influences, the traces of each of which do not disappear completely and, combining with each other, form the basis of a gradually developing adaptation [5]. It is important to emphasize here that the process of disappearance of the adaptive structural trace at its final stage is slower than at the beginning; often in a latent form, adaptive traces persist in the body for a very long time. This phenomenon is most clearly expressed for higher long-term adaptive reactions based on brain memory; in this area, the "revival" of long-unused skills, "forgotten" foreign languages, etc. is well known. The higher stability of adaptive structural traces fixed in the brain compared to traces of simpler adaptive reactions is manifested, in particular, in the fact that during the process of readaptation, after complete cessation of physical exertion, the body's aerobic capacity and associated endurance gradually disappear, and special skills — the ability to perform a certain exercise — persist for quite a long time. and they can often be demonstrated by an already well-trained person. The process of disappearance of the structural trace of adaptation and adaptation itself with a return to the conditional norm corresponding to the given type and period of ontogenesis, in essence, cannot be designated otherwise than physiological readaptation. This readaptation should be distinguished from the situation caused by special conditions of hypokinesia and weightlessness, in which the process begins in a normal organism and leads to an unusual decrease in the mass and power of key cell structures, a decrease in the efficiency of entire functional systems against the norm. Such a deadaptation is an obvious prerequisite for many diseases and, apparently, can be designated as pathological deadaptation[6]. Pathological maladaptation develops on the basis of the same molecular mechanisms as physiological maladaptation, but its quantitative result significantly reduces the functional capabilities of organs and systems. This is especially convincingly demonstrated in relation to the lack of adaptation to physical exertion resulting from prolonged hypokinesia. In accordance with the developed idea of the crucial role of the relationship between function and the genetic apparatus in the mechanism of adaptation and readaptation, the essence of phenomena in hypokinesia is that reducing the load on the functional system responsible for the body's motor reactions, and in particular on the heart and skeletal muscles, reduces the function of the cells forming this system. In response, the activity of various transcriptons of the genetic apparatus of cells decreases by no means to the same extent. The activity of transcriptons encoding short-lived proteins decreases to the greatest extent, and as a result,

selective atrophy of short-lived membrane structures of cells responsible for the reception of mediators and hormones, ion transport and energy supply develops. Since these structures make up only a small part of the cell mass, but are a necessary part of the cell's vital activity, hypokinesia at a certain stage of its development may be characterized by a relatively small decrease in mass and a sharp drop in the functional capabilities of the heart and skeletal muscles. In other words, during de-adaptation, the following should be observed: a relatively small atrophy of cardiac and skeletal muscles; a sharp decrease in the mass of sarcolemmal, sarcoplasmic, and to a lesser extent mitochondrial membranes in muscle cells; a significant decrease in muscle functionality[7]. This suggests that an adaptive increase in the capacity of organs and systems can indeed be provided by a genetically determined increase in the mass of predominantly short—lived cellular structures, while the decrease in the capacity of organs and systems during pathological readaptation is based on the opposite situation - selective atrophy of short-lived cell membrane structures. It must be borne in mind that the prerequisite for the disease may be not only a deep, obviously pathological maladaptation. There may be situations when the process of physiological readaptation acquires a certain role in the development of pathological conditions. One of the situations of this kind is observed when an organism, adapted to a certain factor or set of factors throughout its life, changes its living conditions at a late stage of ontogenesis and loses the systemic structural trace that forms the basis of adaptation. When trying to return to the previous living conditions, i.e. To implement the adaptation, it turns out to be necessary to restore the previous systemic structural trace by activating the synthesis of nucleic acids and proteins. However, under aging conditions, the activity of the genetic apparatus of differentiated cells and, consequently, the renewal of structures are reduced — the body cannot build all the necessary structures, and the "structural cost" of adaptation turns out to be too high. This kind of situation underlies many cases of chronic altitude sickness, which develops in elderly mountaineers of the Peruvian Andes when they return to an altitude of 4,000 m after a stay on the plain. This disease is manifested by a decrease in external respiration — hypoventilation and compensatory mobilization of hematopoiesis and blood circulation. When studying the mechanism of hypoventilation, it turned out that patients with chronic altitude sickness have a reduced degree of hyperventilation that occurs in response to the introduction of carbon dioxide, i.e., the sensitivity of the respiratory center to CO2 is reduced. Based on this, it can be assumed that the wear of the neurons of the respiratory center is the main mechanism of chronic altitude sickness. When adapting to hypoxia, the respiratory center performs moderate but continuous hyperfunction and is the target of hypoxemia. Both of these factors can activate the genetic apparatus of neurons through energy deficiency and cause activation of the synthesis of nucleic acids and proteins there. This increase in synthesis is apparently not infinite, since repeated activation of the genetic apparatus of a wide variety of differentiated cells, including neurons, may result in the exhaustion of their ability to synthesize RNA and proteins, i.e. depletion [8]. Such local deterioration of differentiated cells, which carry out prolonged hyperfunction, forms the basis of a number of diseases. One can imagine that this deterioration is most likely when the activation of the genetic apparatus necessary for the restoration of the structural basis of adaptation is repeated many times and occurs under aging conditions. Thus, it is in old age that the loss of long-term adaptation, which may be necessary in the future, poses the greatest risk. Maintaining the structural foundations of the necessary adaptation in the future by relatively small periodic loads on a responsible functional system is a disproportionately more economical process option than repeated cycles of readaptation - readaptation, since each such cycle has a fairly high structural cost. In summary, it should be emphasized that the process of deadaptation is an expression of the reversibility of any long-term adaptation, is a necessary prerequisite for the formation of new adaptive reactions of the body and changes in the entire phenotype in accordance with the requirements of the environment. This process is ensured by reducing the systemic structural trace of adaptation by reducing the synthesis of nucleic acids and proteins based on the mechanism of the relationship between the function and the genetic apparatus of cells forming the functional system responsible for adaptation, as well as due to the above-discussed molecular mechanisms of accelerated degradation of structures. In this case, the short-lived membrane structures of the cell are atrophied first and to the greatest extent, the increased capacity of which is the essence of adaptation and adaptive increase in functionality. With physiological readaptation, this process ensures that the body returns from adaptation to a certain conditional norm, and with further progression it leads to selective atrophy of key cell structures, profound functional impairment, and can be designated as pathological readaptation. Thus, deadaptation, as well as adaptation, has only relative biological expediency.

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