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CONCEPT OF HYPOBIOTIC STATES OF ANIMALS OF COLD CLIMATE

ABSTRACT

Large animals that inhabit in regions with a cold climate tend to flow into hypobiotic states. These states are distinguished by reduced level of metabolism, that along with high thermal insulation of the body allow them to save energy resources and reduce feed intake in winter. In general, the dynamics (from summer to winter) of a number of physiological and biochemical indicators is largely similar to the dynamics of these indicators in hibernators. For the first time, it was found that the fraction 1-10 kD from the brain of a yakut horse, a yakut cow, a northern reindeer, an elk and a brown bear has hypometabolic, hypothermic, cardiotropic and central effects similar to those of similar fractions from the tissues of hibernators. The most promising sources for isolating and studying the structure of peptides responsible for the organization of hypobiotic states are the brain tissues of yakut horse and brown bear.Analyzing the influence low negative temperatures in annual vital function of hibernators and big mammals, authors come to **Conclusion** that extraordinary stability of animals it is not only developed ability of creating high heat insulation but against that background also of starting peptides regulation, which take part in decreasing of metabolism, and consequently of powers inquiry.

Keywords: hypobiosis, metabolism, temperature of body, motive activity, hibernators, brown bear, yakut horse, northern reindeer, elk, yakut cow, peptides.

Introduction

In the classification of hypometabolic states, proposed by N.N. Timofeev [1], the basis is the degree of inhibition of metabolism. To the «superficial»hypobiosisconcern the state of natural sleep and the winter sleep of the bears. Hypobiosis of the «average» depth is manifested by hibernators, falling into winter and summer hibernation with a pronounced decrease of metabolism and body temperature. In the «deep»hypobiosis, arbitrary movements and contractive thermogenesis are suppressed, but the basic vital functions are not violated. Such a state is reached in hibernators inhabiting the extracontinental climate. These are representatives of squirrel: the yakut long-tailed and arctic gophers, whose temperature in the abdominal cavity and the periphery of the body can drop below zero degrees, and the metabolic rate can drop in two orders of magnitude.

It seems that the last two directions of adaptation to low temperatures are a series of states physiologically similar to some extent. That is to say, they can be attributed to the states of reduced and limited ability to live.

Results and discussion

From the position of the hierarchical system approach it is distinguished the following main nodes that characterize the hypobiotic states: immobility is clearly manifested in hibernators (bats, chipmunks, gophers, groundhogs, bears).Transition to passive behaviorrequires special observations (raccoon dog, badger, yakut hare, voles etc.). An obligatory feature of the hypobiotic condition is a refusal of food or a decrease of the level of its consumption with varying degrees of utilization of endogenous reserves. The main component of hypobiosis is a decrease of the level of metabolism, and there is no strict dependence between metabolism and body temperature. Animals came out from these conditionsindependently.

At the tissue and cellular levelshypobiotic state is characterized by a reduction of the functional activity of the cardiovascular system, thyroid etc. Lipolytic activity of adipose tissue cells, the cells ability to maintain a high activity of ionic calcium pumps, and deeper, the preservation of mitochondrial membrane functions increase.

How often do these moments of hypobioticstates occur in non-gibernants? First of all, it is a marked reduction of motor activity in winter, which is noted in a number of species of deer, elk, bison, musk-ox, yakut horse, yakutcow and yak.

For the listed species, it is known examples of a decrease of metabolism in winter [9, 14, 15, 16, 17, 18, 19]. Thus, the yakut horse (mare) has a 40% lower level of metabolism in winter than in summer. In the yakut cow, metabolism declines by more than half - 55.8%,in she-deers of reindeer - from 26 to 59%, in yak (female) - 20% and in elk-cow with calf - 60%.

Moreover, in free-living species (musk-ox, deers, yakut horse, saiga antelope, roe deer, etc.) such metabolic alterations are combined with the phenomenon of winter hypophagy [8, 10, 11, 12, 20]. And with apparent saturation and changing gross consumption of food there is a starvation developing against the background of decrease of the protein content in plants from autumn to the end of winter.

An important sign of a tendency to fall into hypobioticstates could be the body temperature, but such data are not available. There are only measurements of the temperature of the peripheral parts of the body, more often it is rectal and subcutaneous temperature. Some decrease of that temperature in animals in winter indicates,first of all, the increase in the heat-insulating properties of the skin and deposits of subcutaneous fat.

Just as in the hibernators, deposition of fat in large animals occurs in autumn, and the deposition of protein and fat stores is divided in time. For example, in the yakut horse, the daily weight gain in August is 2-2.5, and in September is only 0.5 kg.

The tissues of northern animals contain high concentrations of polyunsaturated fatty acids and, according to this index, they are similar to those of hibernators. According to our data, in the blood plasma of yakut horse the content of polyunsaturated fatty acids in winter exceeds 50%. The yakut and kazakh horses that spend the winter under the open sky at a stern feed have the most fusible fat among domestic large mammals, comparable in this respect to wild large mammals.

The iodine number of fat in the yakut cow is significantly higher than in other breeds of cattle [18].

It is known that unsaturated fatty acids serve as the main substratum of free radical oxidation, whose products outside the norm can disrupt many processes and cell structures. The system of protection against endoperoxides is determined by various factors, including reduced glutathione (tripeptide containing sulfhydryl group - SH2). Reduced glutathione is a cofactor of enzymes destroying peroxide fatty acids.

It is established that the change of the glutathione content in the yakut horse has a pronounced seasonal character. Its high content is determined in winter and its low content is determined in summer. Along with this, it was shown that the highest antioxidant activity of lipids is high in winter, which is also due to the low level of products of lipid peroxidation.

The same is observed in hibernators.

In general, a number of agricultural animals of Yakutia are characterized by high indicators of the oxidation and reduction system of glutathione.

Both in hibernators and in large animals the albumin content, the main transporter of fatty acids and peptides (regulators of many functions in the body) increases in the blood in winter.

Seasonal changes in the activity of the thyroid gland are significant in a number of hibernators. The activity of the gland is minimal in hibernation. And the maximum activity is detected in spring after exiting it [27]. Analogy can be made with the northern reindeer, in the blood serum of which contains 30, 0 nmol / L of thyroxin and 0.3 nmol / L of triiodothyronine in winter, and in summer - 100.0 and 2.0, respectively.

Unidirectional represent shifts to winter in the structure of cell membranes in both the hibernator (gopher) and the yakut horse. This can be judged by the increase of erythrocyte resistance in the bloodstream.

It is also interesting that in such different species as the red-cheeked gopher (Novosibirsk region), the red vole and the yakut horse, the populations of mitochondria of hepatocytes become polymorphic in winter. The development of the lysosomal apparatus increases in these species in winter. All of it confirms the state of chronic starvation [30].

Thus, the animals of cold climate have the ability to fall into hypobiotic states characterized by a decrease of the metabolic level, which along with high thermal insulation of the body leads to a significant saving of energy reserves and allows surviving the winter with a lack of food and nutrients.

From a review of the seasonal dynamics of metabolic, tissue and subcellular reconstructions, although obtained in different species but, chiefly, in their natural habitat, it follows that many unique adaptations of animals living in a cold climate should be provided with reserve capacity of regulatory systems.

The abiotic factors, that vary abruptly, can lead to an intensification of a number of evolutionary ancient regulations, in particular peptide regulation. In other words, the amplification of the function occurs when the corresponding function is insufficient. And here we see the analogy between winter hibernation and adaptation of large animals to the cold. In support of this, an attempt was made to compare the biological activity of peptide fractions from the tissues of large animals and hibernators, believing that such an approach would facilitate the search of a link between the ability to fall in winter hibernation and the transition of non-hibernators to hypobiosis.

The search of regulators responsible for the organization of hibernation dates back to the 1930s. The first experiments on this direction were carried out by Kroll [citation]. The essence of these experiments was that from various tissues of hamsters, hedgehogs and bats that were in hibernation, he received extracts that were introduced to cats and dogs. These extracts caused dreamlike conditions in animals. In parallel, experiments were carried out with extracts from tissues of gophers and marmots. These extracts were introduced to white rats, after a short period of anxietythey have apathy and lethargy. Basic exchange decreased by 20 - 30%. In rabbits was noted a 28% decrease of blood pressureand a 20%decrease of the heart rate. In the 1950s, along with German researchers, work began in Canada and in the USA. In the USSR similar studies were initiated by S. Kolaeva in the Institute of Biophysics of the Academy of Sciences of USSR [33].

In the Institute of Biological Problems of the Cryolithozone, it began the work on the search and isolation of peptides responsible for the organization of hypometabolic states. They started with horses as the most accessible donors for obtaining active material. Later the circle of objects expanded [34, 35, 36, 37].

Even the first experiments on mice have shown that the material is quite active. Intraperitoneal injections of a peptide fraction weighing from 1 to 10 kD from the brain of horses seized in the winter at a dose of 1 mg / g caused a decrease of body temperature by 8-9 degrees, and a depression of metabolism by more than 60%.

Determination of the activity of the material obtained from summer and winter horses showed that in the first case its activity is weaker.

On isolated heart preparations (frog, cat), peptide fractions from the brain and small intestine of hibernatorgophers and from thebrain of yakut horse at a concentration of 2-10-4 g / l caused complete cessation of the heart. Comparison of the activity of fractions from these twospecies revealed that they have a similar cardiotropic effect and show activity in the same range of concentrations, namely from 2-10-6 to 9-10-5g / l. The introduction of fractions has a dose-dependent inhibition of heart rate and a decrease of the amplitude of mechanical activity [38].

The introduction of the fraction from the horse's brain inhibits the total protein synthesis in the liver and heart tissues of mice. After 30 minutes, the inclusion of amino acids in proteins decreases by 30-40%.

The investigation of the effect of different concentrations of the fraction on the rate of passive and active transport of Ca2+ to the vesicles of sarcolemma of cardiomyocytes has shown that the effect on calcium transport is the same as that of hibernator gophers, and in the same concentration range, from 10-7 to 3 x 10-5.

This same fraction also suppresses the conduction of the slow type of calcium channel of perforated cardiomyocytes of rats.

The successive separation of the fraction of 1 to 10 kD of the horse's brain led to the excretion of the octadecapeptide [39] having a pronounced hypothermic effect withintroduction to mice. When animals leave hypothermia, achieved with a lack of air, the introduction of the peptide inhibits the buildup of body temperature. In the experiment on isolated perforated cardiomyocytes, the octadecapeptide blocked calcium current at a concentration of 5 μM - by 35.5%, and in a concentration of 25 μM - by 59.1%.

From other species of animals, brown bear, northern reindeer, snow sheep, elk and yakut cow were examined for the content of hypometabolic factors. The peptide fraction was isolated in winter. It was found that the fraction from the elk's brain, introduced to the cold-adapted mice (the animals were kept at an air temperature of 5-10 °C) at a dose of 1 mg / g, lowered the metabolic rate from the initial one by 40%, and the northern reindeer'sfraction lowered the metabolic rate by 36%. Body temperature decreased by 2.6°. The same decrease in body temperature in mice was also caused by a fraction from the yakut cow. The introduction of a fraction from the snow sheep'sbrain reduced the temperature by 7.5°. A deeper effect was exerted by the fraction from the brain of the brown bear. The body temperature of mice was reduced by 9°, and the metabolism was reduced by 70% from the original level. Both intraperitoneal and intranasal introduction of the fraction prolonged mice the yield from the hypothermic state. And the time to get out of this state was 4 - 5 times higher than the time for heating the animals after introducing a fraction from the horse's brain.

Intraventricular introduction of the fractionin rats showed the following. They have a significant decrease of the number of behavioral reactions. Animals adopt a pose characteristic of sleep. They closed their eyes and fell into a dreamlike state. The electric activity of the brain, that was judged by an electroencephalogram (EEG), was also reconstructed. Initially, the EEG was characterized by a wide spectrum of frequencies in the delta, kappa alpha beta ranges. After the fraction introduction, the slow components (delta and kappa) were amplified and highfrequency components (alpha and beta) were suppressed. The fraction from the brain of gophers causes a reorganization of the behavior and the EEG that is similar in many respects to what was observed in experiments with a similar fraction of the bear's brain. In the experiments with the fraction from the bear's brain it was found that the proportion of paradoxical sleep persists. In gophers, as they dive into hibernation, episodes of paradoxical sleep become rare and disappear.

It was shown that some subfractionsreleased from the fraction 1-10 kD significantly inhibit the calcium current in perforated cardiomyocytes, some of them by 60%, the activity of fractions released from the tissues of hibernators is removed by naloxone (an opiate receptor blocker), while this is not observed in bears and in yakut horse, or this effect is masked.

Conclusions

Thus, large animals inhabiting regions with a cold climate tend to flow into hypobiotic states, which are distinguished by a reduced level of metabolism, that along with high thermal insulation of the body allows them to save energy resources and reduce feed intake in winter. In general, the dynamics (from summer to winter) of a number of physiological and biochemical indicators is largely similar to the dynamics of these indicators in hibernators. For the first time, it was found that the fraction 1-10 kD from the brain of yakut horse, yakut cow, northern reindeer, elk and brown bear has hypometabolic, hypothermic, cardiotropic and central effects similar to those of similar fractions from the tissues of hibernators. The most promising sources for isolating and studying the structure of peptides responsible for the organization of hypobiotic states are the brain tissues of the yakut horse and the brown bear.

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