A.V. Efremova

HUMORAL ASPECTS OF BROWN ADIPOSE TISSUE THERMOGENESIS AS A PHYSIOLOGICAL STRATEGY OF ADAPTATION TO COLD

DOI 10.25789/YMJ.2024.85.22
UDC 611.018.26: 612.592.1

The review is devoted to the study of humoral factors that directly affect the processes of non-contractile thermogenesis and the activity of brown adipose tissue. The review is based on research conducted in various research laboratories.

Keywords: thermogenesis, brown adipose tissue, adaptation, cold, insulin, glucagon.

Exposure to cold stimulates heat production through muscle tremors caused by contraction of skeletal muscles, as well as the influence of non-contractile thermogenesis. The concept of non-contractile thermogenesis was first proposed in Voight's research in 1878, the occurrence of non-contractile thermogenesis in the human body was accurately described by W. Cannon et al. [5] in 1927, who argued that the medulla oblongata of the adrenal glands plays a significant role in non-contractile thermogenesis. Currently, a number of studies have established that metabolic acclimatization to cold is characterized by an increase in non-contractile thermogenesis in the human body as a more effective way of obtaining heat than muscle contractions, and the main source of non-contractile thermogenesis is a unique brown adipose tissue (BAT), which is exclusively differentiated for thermogenesis and is the only known tissue whose main function is to produce heat. Enough works have been devoted to the biochemical and physiological mechanisms of the functioning of non-contractile thermogenesis and the role of BAT [3, 15, 40, 46].

Cold acclimatization enhances not only the metabolic activity of BAT, but also significantly proliferates this tissue. The degree of hyperplasia in the BAT is greater than in any other tissues or organs under various physiological stimuli. It is assumed that such features of BAT are under the control of numerous neuroendocrine factors. However, the mechanisms involved in this process have not been fully clarified. This review is devoted to the study of humoral factors that directly affect BAT, mainly on the basis of studies conducted in various research laboratories.

Humoral regulation of brown adipose tissue. Norepinephrine is the main regulator of the BAT function during acclimatization to cold. It is known that some hormones, such as adrenaline, glucocorticoids and thyroid hormones, are involved in the regulation of this tissue, enhancing its thermogenesis directly [40, 41]. Pancreatic hormone glucagon plays the role of an energy-supplying hormone, satisfying the increased need for energy and fuel during physical activity, fasting [17], pain syndrome, the influence of noise and fever [2]. What is of interest in studying the role of glucagon in the functioning of BAT during cold acclimatization.

Exposure to cold increases the level of glucagon in the blood plasma of rats at an early stage for 2 weeks at a temperature of 5 °C [21, 22], when the animals develop an almost maximum phase of non-shivering thermogenesis [15]. There is also a significant positive correlation between the concentration of glucagon and the level of free fatty acids in blood. It has been shown that the main substrate for non-shivering thermogenesis is fatty acids [28]. It was also found that the level of glucagon in blood plasma in men has significant seasonal fluctuations, so the level of glucagon is significantly higher in winter than in summer, and there is a positive correlation between the level of glucagon and the concentration of free fatty acids in blood plasma in general during the year [18]. These data suggest that glucagon may play a role in the development of cold acclimatization due to its lipolytic effect. However, the level of glucagon in blood plasma does not differ from the control value after prolonged cold acclimatization for 4 weeks, while it was noted that the glucagon-induced increase in oxygen consumption by the whole body, as well as intraperitoneal temperature and BAT temperature is greater in cold-acclimatized rats than in heat-acclimatized [20], and an increase in consumption oxygen and BAT temperature are positively correlated with BAT mass. A similar phenomenon is observed in the reaction to norepinephrine, as previously reported [15, 41]. Such an altered reaction of the body to biogenic factors such as norepinephrine and glucagon can provide a kind of adaptation effectiveness. This concept can be described as a "mechanism for saving on adaptation." Moreover, chronic administration of glucagon causes an increase in tolerance to cold and to non-shivering thermogenesis, possibly due to an increase in weight and an increase in the thermogenic ability of BAT [49]. Cold acclimatization increases the level of glucagon in BAT when the level of glucagon in plasma is the same as in rats in heat [12]. These data suggest that BAT is a target tissue for glucagon, and glucagon serves as one of the members of the humoral team, which is responsible for enhancing the processes of non-shivering thermogenesis in BAT during cold acclimatization. It is well known that an enhanced thermogenic reaction to norepinephrine, in addition to increased secretion of this sympathetic factor, is caused by cold acclimatization [15], and BAT is the dominant anatomical site of enhanced norepinephrine-induced non-contractile thermogenesis during cold acclimatization [10]. It is believed that such a contribution of BAT is mediated by an increase in mass (hyperplasia) [21], blood flow [10] and metabolic activity, estimated by the mitochondrial thermogenic ability of this tissue (an increase in the thermogenin protein UCP1) [45]. Thus, it can be concluded that in combination with norepinephrine and other hormonal factors, glucagon functions as

EFREMOVA Agrafena Vladimirovna – PhD in Biology, senior researcher at the the Yakut Scientific Center of Complex Medical Problems

a thermogenic hormone and participates in the regulation of non-contractile thermogenesis through the activation of BAT.

In vivo research. BAT in cold-adapted rats exhibits a greater thermogenic response to cold [9], norepinephrine [8, 24] and glucagon [8]. Increased non-contractile thermogenesis is associated with increased metabolism of free fatty acids and a decrease in respiratory metabolism [28]. The level of triglycerides decreases in the cells of the BAT of rats during acute exposure to cold and adaptation to cold [34]. It is assumed that the oxidation of fatty acids accounts for a large part of the thermogenesis of BAT during norepinephrine infusion [32]. It has been shown that the rate of fatty acid synthesis is more than ten times higher in rats with cold acclimatization compared with controls that were not exposed to cold [46]. These results indicate that fatty acids are the main energy substrates for BAT thermogenesis. In this context, it is interesting to note a lower venous drainage of free fatty acids from the BAT of cold-acclimated rats compared with the control group after infusion of norepinephrine [36] or glucagon [18, 21]. This may be due either to a decrease in lipolysis or to an increase in the utilization of free fatty acids in the BAT. When norepinephrine was administered to cold-acclimated rats and the control group, the concentration of glycerin did not have significant differences. Glycerol release is an indicator of the intensity of the lipolysis process, since glycerol is less utilized in adipocytes of white adipose tissue and BAT compared with free fatty acids [36]. Therefore, a low concentration of free fatty acids from the BAT adipocytes of rats acclimated to cold may be the result of increased utilization of free fatty acids under the influence of norepinephrine or glucagon. Since glucagon is known to stimulate the secretion of catecholamines, it is possible that an increase in the level of fatty acids in the blood and BAT is secondary to an increase in circulating norepinephrine levels. However, this is unlikely, since the response to glucagon does not change under the action of the propranolol Q blocker, which suppresses the lipolytic and calorigenic effects of catecholamines [19].

It is also suggested that the activation of BAT contributes to increased glucose consumption for thermogenesis, since this tissue has a high concentration of key glycolytic enzymes, hexokinase and 6-phosphofructokinase, and the activity of these enzymes doubles when adapting to cold [6]. In addition, it is believed that BAT can play an important role in glucose excretion after a carbohydrate load by controlling the concentration of glucose in the blood. It was found that the glycogen level in the BAT of cold-acclimated rats is lower [20], and glucagon infusion does not increase the glucose level in the venous drainage from the BAT, despite the increased glucose level in the systemic venous blood [24]. The data obtained show that glucose may be one of the exogenous substrates used by BAT, although its contribution to BAT thermogenesis may be relatively small [14, 32]. At the same time, glucose may be an important substrate for lipogenesis in BAT. It is known that the main fuel for thermogenesis in BAT are lipids synthesized de novo and stored in multilocular fat droplets in the cytoplasm of BAT adipocytes [14]. It has also been established that BCT has a high activity in lipogenesis, especially in animals acclimatized to cold. Thus, in the study Trayhurn P, 2018, it was shown that the total synthesis of fatty acids is three times higher than the total hepatic synthesis in rats with acclimatization to cold [46]. Another pancreatic hormone, insulin, is a powerful anabolic hormone, as well as an anti-lipolytic factor and stimulates lipid synthesis. Therefore, the action of insulin would be a necessary condition for maintaining a high thermogenic capacity of BAT. It has also been proven that glucose is the predominant substrate for the synthesis of fatty acids in BAT, and this process is stimulated by insulin [39]. In addition, it has been shown that tolerance to cold and to non-oxidative thermogenesis are markedly reduced in rats with streptozotocin diabetes mellitus [11], which may be due to some disorders in BAT caused by insulin deficiency, such as tissue atrophy, decreased ability to Q-oxidation of fatty acids and a decrease in the amount of mitochondrial uncoupling protein (UCP 1). A recent study [35] showed that insulin is involved in the regulation of the function of BAT in cold weather, directly demonstrating changes in the binding sites of insulin, as well as its content in BAT. The concentration of insulin in the BAT was increased both in rats exposed to acute exposure to cold, as well as in the group of rats exposed to prolonged exposure to cold, but it should be noted that insulin receptors were elevated in the first group of animals and were significantly lower in the second group. The exact mechanism of increasing the insulin content in adipose tissue remains unknown. However, there is an assumption that an increase in insulin in the tissue is associated with increased lipogenesis to meet the increased need for energy fuel in the cold. It has been shown that the internalized insulin receptor complex releases insulin and places it in cellular organelles such as lysosomes, Golgi apparatus [37] and nuclei [41, 42]. Moreover, several proofs indicate that intracellular insulin is associated with the proliferation and differentiation of BAT during adaptation to cold. Taken together, these data indicate that insulin may be closely related to the regulation of BAT function in many aspects.

The authors of the study showed that the systemic caloric effect of glucagon decreases with a deficiency of adrenocorticoids [7]. In thyroidectomized or adrenalectomized rats, glucagon infusion does not lead to an increase in the level of free fatty acids in the venous drainage from the BAT [19]. It is possible that the lipolytic and thermogenic effect of glucagon in BAT depends on the presence of thyroid and adrenocortical hormones.

Thus, in L. Jansky study, when norepinephrine is infused at a dose of 40 g intravenously / 100 g of body weight, it causes non-contractile thermogenesis in the body of rats [15]. Studies have shown that the administration of norepinephrine also increases the level of glucagon in both plasma and BAT adipocytes. The degree of increase of glucagon in plasma is higher, and the initial level of glucagon in BAT, as well as the level of glucagon induced by noradrenaline, is higher in cold-acclimatized rats than in the control group [25]. The results show that norepinephrine stimulates glucagon secretion, and cold acclimatization enhances this effect of norepinephrine, suggesting that the glucagon released by norepinephrine will interact with norepinephrine to enhance the process of non-contractile thermogenesis in BAT in the cold. However, exposure to cold stimulates glucagon secretion in adrenodemidulated and chemically sympathectomized rats to the same extent as in rats in control groups, which indicates that cold-induced glucagon release is at least partially independent of the sympathoadrenal system [13].

In vitro research. In vitro studies have been conducted in order to directly learn the regulatory mechanisms of the function of BAT. Isolated BAT cells, thin tissue sections or finely ground tissue blocks were used for in vitro studies. Norepinephrine and glucagon provide a comparable maximum response in the in vitro oxygen consumption by cells and tissue blocks of the BAT of rats [25, 26]. Thus, in vitro experiments revealed that the concentrations of glucagon and norepinephrine necessary for the effect were increased compared to concentrations in blood plasma. The thermogenic re-

sponse to glucagon in vitro is suppressed by thyroidectomy or adrenalectomy, as well as the lipolytic effect of animals acclimated to cold has increased metabolic activity, which is estimated by biochemical parameters associated with the mitochondrial thermogenic mechanism, such as the UCP1 protein [47].Therefore, it is expected that the BAT of cold-climatized animals will demonstrate an enhanced thermogenic response to norepinephrine or glucagon at the tissue or cellular level. Thus, in BCT adipocytes [33], BAT fragments [27] and BAT blocks [26] exposed to cold, a low reaction was detected, estimated by oxygen consumption and lipolysis processes stimulated by norepinephrine and glucagon, compared with the control. These in vitro results contradict the aforementioned in vivo data and biochemical results. An increase in the thermogenic response of BAT in cold-climatized animals may be caused by BAT hyperplasia [3], accompanied by an increase in the supply of energy substrates and oxygen due to increased blood flow through this tissue [10, 51]. Indeed, a positive correlation was noted between the mass of BAT and in vivo norepinephrine and glucagon-induced thermogenesis in BAT [8]. Another possible factor in the differences between in vivo and in vitro results is that the preparation of BAT cells or tissues has not yet been optimized. However, under the same in vitro incubation conditions, the tissue blocks of the BAT of guinea pigs acclimated to cold show an enhanced norepinephrine and glucagon-induced respiratory response, while rats acclimated to cold show a weakened one [26]. Oxygen consumption by brown adipocytes during norepinephrine stimulation was higher in guinea pigs acclimated to cold compared with controls [31, 38]. It has been shown that BAT is the main factor in enhancing non-contractile thermogenesis in guinea pigs exposed to cold. Therefore, it can be said that the in vitro BAT reaction well reflects the thermogenic function of tissues in vivo in guinea pigs, but not in rats. Such a discrepancy between the results in vivo and in vitro in rats suggests that in the BAT of cold-climatized rats there is a certain mechanism for protecting tissue with high thermogenic ability from excessive heat release and subsequent self-destruction during cold acclimatization. At the same time, the constant heat production of BAT in the cold is provided by an enhanced biochemical mechanism, such as activation or induction of the uncoupling protein UCP1 in tissue mitochondria [47]. An increase in the virothermogenesis of BAT in rats occurs mainly due to extensive hyperplasia [3, 4] and increased blood flow to the tissue [10, 51]. Prolonged infusion of norepinephrine [39] and glucagon [1, 49] in rats simulates cold acclimatization, increasing tolerance to cold due to stimulation of BAT. However, the BAT of rats with glucagon and norepinephrine infusion does not demonstrate an enhanced thermogenic response in vitro, as does the BAT of rats acclimatized to cold [3].

Conclusion. Activation of the sympathetic nervous system in BAT is mediated by central stimulation by humoral factors that have been proven to act directly on this tissue, such as insulin and glucagon. Therefore, it is appropriate to conclude that the function of BAT is regulated by numerous neuroendocrine factors through their peripheral and central action.

Brown adipose tissue, whose main function is to produce heat by dissipating energy, serves as a specific organ of adaptation to changes in ambient temperature. Numerous studies have proven that this unique tissue has cross-adaptability and is regulated by numerous neutroendocrine factors. But at the same time, there are still some gaps in the understanding of the mechanisms of regulation of this tissue. Therefore, further clarification of the processes and factors involved in the functioning of brown adipose tissue will contribute to our understanding of the adaptability of the body in cold conditions.

References

1. Billington CJ., Bartness TJ., Briggs J., Levine AS., Morley JE. Glucagon stimulation of brown adipose tissue growth and thermogenesis. Am J Physiol. 2019; 257:160-165, 2019.
2. Bloom SR., Daniel PM., Johnston DI., Ogawa O., Pratt OE: Release of glucagon, induced by stress. Q J Exp Physiol, 2019; 58: 99-108.
3. Bukowiesky L.J., Follea N., Valliere J., LeBlanc J. B-adrenergic receptors in brown adipose tissue. Characterisation and alteration during acclimation of rats to cold. Eur J Biochem. 2017; 92: P: 189-196.
4. Bukowiecki L, Collet AJ., Follea N, Cuay G. Brown adipose tissue hyperplasia: A fundamental mechanism of adaptation to cold and hyperphagia. Am J Physiol. , 202; 242: E353-359.
5. Cannon WB., Querido A., Britton SW., Bright EM: Studies on the conditions of activity in endocrine glands. XXI. The role of adrenal secretion in the chemical control of body temparature. Am J Physiol. 1927; 79: 466-507.
6. Cooney GJ., Newsholme EA. The maximum capacity of glycolysis in brown adipose tissue and its relationship to control of the blood glucose concentration. FEBS Lett. 2015; 148: 198-200.
7. Davidson IWF., Salter J.M., Best CH. The effect of glucagon on the metabolic rate of rats. Am J Chin Nut. 2019; 8: 540-546.
8. Doi K., Kuroshima A. Modified metabolic responsiveness to glycagon in cold-acclimated and heat-acclimated rats. Life Sci 30: 785 - 791, 2015.
9. Donhoffer Sz, Szelenyi Z: The role of brown adipose tissue in thermoregulatory heat production in the warm- and cold-adapted adult rat. Acta Physiol Sad Sci Hung. 2018 ; 32: 53-60.
10. Foster D.O., Freedman ML. Tissue distribution of cold-induced thermogenesis in conscious warm- or cold-acclimated rats reevaluated from changes in tissue blood flow. The dominant role of brown adipose tissue in the replacement of shivering by nonshivering thermogenesis. Can J Physiol Pharmacol. 2020; 57: 257-270.
11. Geleon A., Trayhurn P. Regylation of the level of uncoupling protein in brown adipose tissue by insulin. Am J Physiol. 2021; 258: 418-R424.
12. Habara Y., Kuroshima A. Changes in glucagon and insulin contents in brown adipose tissue after temperature acclimation in rats. Jpn J Physiol. 2017; 33: 661-665.
13. Habara Y., Ohno T., Yahata T., Kuroshima A. Effects of adrenal demedullation combined with chemical sympathectomy on cold-induced responses of endocrine pancreas in rats. Experientia. 2021; 39: 399-400.
14. Isler D.,Hill H.P., Meier MK. Glucose metabolism in isolated brown adipocyte under B-adrenergic stimulation. quantitive contribution of glucose to total thermogenesis, Biochem J. 2017; 245: 789-793.
15. Jansky L: Nonshivering thermogenesis and its thermoregulatory significance. Biol Rev. 1973; 48: 85-132.
16. Kikuchi K., Okano S., Nou T., Yahata T., Kuroshima A. Effects of chronic administration of noradrenaline and glucagon on in vitro brown adipose tissue thermogenesis. Jpn J Physiol. 2017; 45: 165-170.
17. Kuroshima A., Doi K., Ohno T: Role of glucagon in metabolic acclimation to cold and heat. Life Sci. 2020; 23: 1405-1410.
18. Kuroshima A., Ohno T., Doi K. In vivo lypolitic action of glucagon in brown adipose tissue of warm-acclimatised and cold-acclimatised rats. Experiential. 2017; 33: 240-242.
19. Kuroshima A., Doi K., Ohno T. Effects of adrenalectomy and thyroidectomy on in vivoaction of glucagon in brown adipose tissue. J Physiol Soc Jpn. 2018; 39, 405-408.
20. Kuroshima A, Ohno T. Gangliosides and energy substrates in brown adipose tissue of cold-acclimated rat. Jpn J Physiol. 2016; 38, 393.
21. Kuroshima A., Doi K: Is glucagon involved in cold acclimatisation? Experiential. 2020; 32: 473-475.
22. Kuroshima A., Doi K., Ohno T: Role of glucagon in metabolic acclimation to cold and heat. Life Sci. 2020; 23: 1405-1410.
23. Kuroshima A, Doi K., Ohno T. Seasonal variation of plasma glucagon concentrations in men. Jpn J Physiol. 2019; 29: 661-668.
24. Kuroshima A., Iron S. Physiological role of brown adipose tissue in cold acclimation with special reference to the participation of endocrine factors. Gunma Symp Endocrine. 2017; 8: 91-123.
25. Kuroshima A., Yahata T. Noradrenaline-induced changes in rat brown adipose tissue glycogen. Jpn J Physiol. 2015; 39: 311-315.
26. Kuroshima A., Yahata T., Ohno Y. Comparison of in vitro thermogenesis of brown adipose tissue in cold-acclimated rats and gun pigs. J Therm Biol. 2019: 109-114.
27. Kurahashi M., Kuroshima A. Characteristics of B-adrenergic receptors in brown adipocytes of temperature-acclimated rats. Biomed Res. 2017; 2: 126-133.
28. Lafrance L., Lagace G., Routhier D. Free fatty acid turnover and oxygen consumption. Effects of noradrenaline in non-fasted and nonanesthetized cold-adapt-

ed rats. Can J Physiol. 2018; 29: 661-668.
29. Lafrance L., Lagace G., Routhier D. Free fatty acid turnover and oxygen consumption> Effects of noradrenaline in nonfasted and nonanesthetized cold-adapted rats. Can J Physiol Pharmacol. 2020; 58, 707-804.
30. Lefebvre P: Glucagon and adipose tissue. Biochem Pharmacol. 2019; 24:1261-1266.
31. Lock R M., Rial E., Nicholls D.G. The acute regulation of mitochondrial protein conductance in cells and mitochondrial from the brown fat of cold- and warm- adapted guinea pigs. Eur J Biochem. 2019; 129: 381-387.
32. Ma SWY, Foster DO. Uptake of glucose and release of fatty acids and glycerol by rat brown adipose tissue in vivo. Can J Physiol Pharmacol. 2021; 64: 609-614.
33. Nedergaard J. Catecholamine sensivity in brown fat cells from cold-acclimated hamsters and rats. Am J Physiol. 2020; 242: 250-257.
34. Ogawa K., Ohno T., Kuroshima A. Effects of cold acclimation on cold-induced changes in lipid metabolism of rat brown adipose tissue. Jpn J Physiol. 2022; 42: 63-73.
35. Okano S., Kikuchi K., Kuroshima A. Alterations of insulin content and insulin binding to plasma membranes in rat brown adipose tissue during cold exposure and cold acclimation. Jpn J Physiol. 2021; 43: 51-65
36. Portet R., Laury MC., Bertin R., Hénault C., Hluzsko MT. Hormonal stimulation of substrat utilization in brown adipose tissue of cold acclimated rats. Proc. Soc. Exp Biol Med. 2018; 147: 807-812.
37. Posner BI. Khan M.N., Bergeron J.J.M. Endocytosis of peptide hormones and other ligands. Endocrinol Rev. 2020; 3: 280-298.
38. Rafael J., Fesser W., Nicholls D.G. Cold adaptation in guinea pig at level of isolated brown adipocytes. Am J Physiol. 2014; 250:228-235.
39. Ricquier D., Mory G., Hemon P. Effects of chronic treatments upon the brown adipose tissue of young rats. I Cold exposure and hyperthyroidism. Pfluger Arch, 2018; 362: 241-246.
40. Schonbaum E., Lomax P. Thermoregulation Physiology and biochemistry, Pergamon Press, New York. 2018.
41. Smith RE, Horwitz BA: Brown fat and thermogenesis. Physiol Rev. 2022; 49: 330-425.
42. Soler AP. Thompson K.A., Smith RM., Jarett L. Immunological demonstration of the accumulation of insulin, but not insulin receptors, in nuclei of insulin-treated cells. Proc Nail Asad Sci USA., 2019; 86: 6640-6644.
43. Skillat D., Bukowiesky L.J. Control of brown adipose tissue lypolisis and respiration by adenosine. Am J Physiol., 2022; 256: 555-559.
44. Svartengren J., Svoboda P., Drahota Z., Cannon B. The molecular basis for adrenergic desensitization in hamster brown adipose tissue: Uncoupling of adenylate cyclase activation. Comp Biochem Physiol., 2018; 78C: 159-170.
45. Trayhurn P., Nicholls DG. Brown adipose tissue, Edward Arnold, London, 2013.
46. Trayhurn P. Fatty acids synthesis in vivo in brown adipose tissue, liver and white adipose tissue of the cold-acclimated rat. FEBS Lett. 2018; 104: 13-16.
47. Trayhurn P. Brown adipose tissue and nutritional energetics - where we are now ? Proc Nutr Soc. 2021; 48: 165-175
48. Trayhurn P., Milner RE. A commentary on the interpretation of in vitro biochemical measures of brown adipose tissue thermogenesis. Can J Physiol Pharmacol 67: 811-819, 2022.
49. Yahata T., Ohno T., Kuroshima A: Improved cold tolerance in glucagon treated rat. Life Sci 28: 2603 - 2610, 2018.
50. Yahata T., Kuroshima A. Influence of endocrine and chemical factors on glucagon-induced thermogenesis in brown adipocytes. Jpn J Physiol 32: 303-307, 2020.
51. Yahata T., Habara Y., Kuroshima A. Effect of glucagon and noradrenalin on the blood flow through brown adipose tissue in temperature-acclimated rats. Jpn J Physiol. 250: P. 367-376, 2021.

S.K. Kononova

BIOETHICAL PRINCIPLES AND APPLIED BIOETHICS IN THE FIELD OF NEURODEGENERATIVE DISEASE RESEARCH IN YAKUTIA

DOI 10.25789/YMJ.2024.85.23

UDC 614.253:17.023

Applied bioethics is a field of knowledge, the subject of which is practical moral problems. The ethical principles that form the basis for applied bioethical research related to neurodegenerative disease in Yakutia are discussed. Applying the basic four ethical principles as starting points can lead to different answers regarding specific bioethical problems, in our case the moral problems of providing medical care to patients with neurodegenerative diseases.

Keywords: bioethics, applied ethics, neurodegenerative diseases, Republic of Sakha (Yakutia)

Introduction. Bioethics arose from the need to assess the positive and negative effects of new methods and technologies. Can bioethics prevent the unfair distribution of medical resources, treatments, and medicines among those in need? Bioethics acts as a kind of discussion platform, where scientists themselves, who have created breakthrough technologies, discuss the positive and negative consequences of inventions for both patients and society, and positive and negative criteria depend on knowledge, cultural level and prejudices of the era and society as a whole [8,9,11,46].

Perhaps it is bioethics that is the field of human knowledge where many areas of research have become entrenched and there are many directions for research: the philosophical study of the ethics of medicine, medical law, medical anthropology, medical genetics, medical sociology, health policy, health economics. Philosophers believe that bioethics is one of the branches of practical (or applied) ethics, which, in turn, is one of the branches of philosophy [5,12,45].

On the other hand, there is undoubtedly a problem that the philosopher Benatar (2006) calls the problem of "disciplinary slip", when a person moves from working in his own discipline, in which he is trained, to working in another, in which he is not trained. There are fewer obstacles for health care workers or scientists to engage in moral philosophy than there are for philosophers who would like to practice medicine. This does not prevent lawyers, doctors and scientists of various profiles from cooperating with philosophers on practical ethical issues or working independently to answer questions that are crucial for making ethical decisions [22,24,26,43].

According to Husseinov (2004), ethics is initially a practical science. In his opinion, ethics is a practical science, since it considers human actions and behavior from the point of view of their fundamental principles, and it is the point at which philosophy connects with practice, there-

KONONOVA Sardana Kononovna – Ph.D. in Biology, chief researcher of the Yakut Science Centre of Complex Medical Problems