6. Bi P., Shan T., Liu W., Yue F., Yang X., Liang X.R., et al. Inhibition of Notch signaling promotes browning of white adipose tissue and ameliorates obesity. In: Nat Med. 2014, Nr. 20(8), p.911–918; Bjørndal B., Burri L., Staalesen V., Skorve J., Berge R.K. Different adipose depots: Their role in the development of metabolic syndrome and mitochondrial response to hypolipidemic agents. În: J. Obes. 2011, Nr. 2011.

7. Bouillaud F., Ricquier D., Thibault J., Weissenbach J. Molecular approach to thermogenesis in brown adipose tissue: cDNA cloning of the mitochondrial uncoupling protein. In: Proc. Natl. Acad. Sci. USA. 1985, Nr. 82, p.445–448.

8. Bouillaud F., Ricquier D., Thibault J., Weissenbach J. Molecular approach to thermogenesis in brown adipose tissue: cDNA cloning of the mitochondrial uncoupling protein. In: Proc. Natl. Acad. Sci. USA. 1985, Nr. 82, p.445–448.

9. Bjørndal B., Burri L., Staalesen V., Skorve J., Berge R.K. Different adipose depots: Their role in the development of metabolic syndrome and mitochondrial response to hypolipidemic agents. În: J. Obes. 2011, Nr. 2011; Cannon B., Nedergaard J. Brown adipose tissue: Function and physiological significance. În: Physiol. Rev. 2004, Nr. 84, p.277–359.

10. Bouillaud F., Ricquier D., Thibault J., Weissenbach J. Molecular approach to thermogenesis in brown adipose tissue: cDNA cloning of the mitochondrial uncoupling protein. In: Proc. Natl. Acad. Sci. USA. 1985, Nr. 82, p.445–448; Carpentier A.C., Blondin D.P., Virtanen K.A., Richard D., Haman F., Turcotte E.E. Brown Adipose Tissue Energy Metabolism in Humans. În: Front. Endocrinol (Lausanne). 2018, Nr. 9, p.447.

LIPID PROFILE AND LIPOTOXICITY IN PEOPLE WITH HYPOTALAMIC (MORBID) OBESITY

Boris Varsan[1], Anatolie Baciu[2], Vasile Fedash[2], Ion Mereuta[2]

[1] Diomid Gherman Institute of Neurology and Neurosurgery, Kishinev, Moldova;

[2] Institute of Physiology and Sanocreatology, Kishivev, Moldova
anatolikbacio@gmail.com

PROFILUL LIPIDIC ŞI LIPOTOXICITATEA LA PERSOANE CU OBEZITATE HIPOTALAMICĂ (MORBIDĂ)

Acumularea de grăsime viscerală determină un efect lipotoxic asupra hipotalamusului. Inflamaţia hipotalamică închide un cerc vicios, agravând perturbarea mecanismelor neuroendocrine de reglare a echilibrului me-

tabolic, inclusiv coordonarea consumului de energie (în timpul metabolis-mului de bază, activității fizice, termogenezei) și comportamentul alimen-tar adecvat. Grupul de studiu a inclus 62 de indivizi (femei) cu obezitate. Fiecare pacient a îndeplinit criteriile de diagnostic pentru sindromul hi-potalamic idiopatic – forma neuroendocrină cu obezitate. Studiul actual arată că obezitatea de origine hipotalamică este asociată cu o dislipidemie care progresează concomitent cu creșterea indicelui de masă corporală.

Introduction. Inflammation of the hypothalamus is one of the basic mechanisms of disorders of the normal physiological regulation of home-ostatic energy and plastic balance. Namely, discordances in this way lead to the genesis of metabolic syndrome, obesity and type 2 diabetes [1]. A diet with a high carbohydrate and lipid index is most likely the main beha-vioral and ecological factor, which makes a significant contribution to the development of inflammatory processes in the hypothalamus and the de-velopment of severe consequences for energy and plastic metabolism [2, 3, 4]. The bidirectional interdependence of brain function and metabolism is evidenced by the fact that discrete neural networks in the hypothalamus have the ability to detect fluctuations in the concentration of long-chain fatty acids in the bloodstream, sensitive to changes in carbohydrates, lipid and protein metabolism, thus ensuring regulation of nutritional behavior, food and water consumption [5, 6]. Defects of the neuronal response to negative feedback signals from obesity in the circulatory bed (leptin, in-sulin), leptin resistance and insulin resistance aggravate the inflammatory responses of cells, precisely because of excess visceral fat [7, 8, 9, 10]. A dangerous consequence of excess tissue lipids that are not suitable for their storage is lipotoxicity. Accumulation of visceral fat causes a lipotoxic effect on the hypothalamus, whose inflammation closes a vicious circle, aggravating the disturbance of neuroendocrine mechanisms to regulate metabolic balance, including coordination of energy consumption (during basic metabolism, physical activity, thermogenesis) and proper feeding behavior, as well as control of reproduction and growth [11, 12, 13]. With obesity, the hypothalamus becomes insensitive to leptin and insulin, whi-ch indicates a deterioration of the regulation of the energy balance by the hypothalamus. Accumulation of ectopic lipids in peripheral tissues, such as β cells of the pancreas, liver, heart, and skeletal muscle, continues to

increase the lipotoxic impact associated with insulin resistance, type 2 diabetes, hepatic steatosis, atherosclerosis, and heart failure [15].

The aim of the research consists of determining the dynamism of changes in lipid and atherogenic metabolism in obese people of hypothalamic origin. Objectives: to evaluate the type of adiposity and body mass, to estimate the plasma concentration of lipoproteins; to determine the atherogenic coefficient; perform a comparative analysis between the levels of plasma lipoprotein concentration and the atherogenic coefficient according to the severity of adiposity, to determine the evolution of dyslipidemia and atherogenicity in patients with hypothalamic obesity.

Material and method. The study group included 62 individuals (women) with obesity, the age limits varying between 18-53 years, with an average of 36.3 ± 3.4 years. Each patient met the diagnostic criteria for idiopathic hypothalamic syndrome – the neuroendocrine form with obesity. Adiposity in these patients is present from childhood or appeared until the age of 30 years and is associated with other neuroendocrine and thermoregulatory disorders, as well as with psychological, vegetative disorders due to the absence of organic brain or somatic lesions, which could develop obesity. Therefore, people with a history of organic brain or somatic lesions with signs of obesity and overweight were excluded from the study. Each patient included in the research list had abdominal obesity determined by the ratio between waist-to-hip ratio (WHR) and increased body weight, determined by body mass index (BMI). As is well known, abdominal obesity, characterized by increased adipose tissue surrounding the intra-abdominal organs, is also called visceral or central obesity (VO). The assessment of WHR and BMI values was performed according to the recommendations of WHO experts [WHO. Physical Status: The Use and Interpretation of Anthropometry: Report of a World Health Organization (WHO) Expert Committee. Geneva, Switzerland: World Health Organization; 1995]. The BMI value ≥ 30 kg / cm^2 determined the obesity, and the value of the WHR ratio ≥ 0.88 determined the visceral type of obesity. Of all the patients examined, with a pathological history, some people also had a diagnosis of type 2 diabetes (diabetes mellitus, T2D). These subjects were included and analyzed in a separate group. Thus, according to clinical data and the results of anthropometric measurements, patients were divided into two groups: patients with VO without T2D (n = 46), age limit: 18-46 years, mean age: 34 ± 3 years and patients with VO + T2D (n

= 16), age limit: 46-54 years, mean age: 48.3 ± 3.5 years. The duration of the disease from the establishment of the diagnosis is between 2-8 years, average: 4.7 ± 0.4 years. The control group included 15 normal-weight women, practically healthy; age limits: 20-47 years, average age: 34.2 ± 3.1 years. Plasma concentrations of triglycerides (TG) and total cholesterol (TC) were determined by the enzymatic method in the automatic analyzer (Analyzer A15, BioSystem S.A., Spain). High-density lipoprotein cholesterol (HDL-C) was dosed into the supernatant after serum precipitation of low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) with bivalent cations. LDL-C and VLDL-C values were calculated according to the Friedewald formula: LDL-C = TC - (TG / 5) - HDL-C (mg / dL). VLDL-C = TG / 5 (mg / dL). We can alternatively use units: mmol / L. The atherogenic coefficient (AC) was also established by calculation: AC = (TC - HDL-C) / HDL-C.

Results and Discussion. Dyslipidemia was determined at TG values > 1.8 (mmol / L) and / or TC > 6.2 (mmol / L), HDL-C < 1.0 (mmol / L). Blood was collected from each person on an empty stomach in the morning. The veracity of the statistical data obtained was estimated with the application of the t-Student criterion. As a criterion of statistically true significance, the level of significance lower than 0.05 ($P < 0.05$) was considered. The mean values of the WHR index in all patients were higher compared to the values in the control group. For those with VO without T2D, the mean WHR value was 1.28 ± 0.07; in patients with VO + T2D: 1.35 ± 0.08; and for the persons of the control group only: 0.74 ± 0.04. The average values of the WHR indices in patients with VO without T2D (*** – $P < 0.001$) and in those with VO + T2D (*** – $P < 0.001$) of the value average of the WHR index of the persons of the control group.

The BMI value in patients with VO without T2D was 38.8 ± 2.7; and in the case of VO + T2D: 45.8 ± 3.1; but in the persons of the control group only: 22.3 ± 1.3. It is obvious that a statistically authentic distinction was registered between the BMI values in patients with VO without T2D ($P < 0.001$), and in patients with VO + T2D ($P < 0.001$) compared to the subjects of the control group. These data demonstrate that the subjects in the study group and especially in the cases with VO + T2D had abdominal adiposity, ie visceral, against the background of significantly increased body weight compared to normal weight people. The values of the lipid profile indices in patients were modified and authentically differed from those of the con-

trol group. Hypertriglyceridemia and hypercholesterolemia characterized by elevated total cholesterol and decreased HDL-C with an increase in LDL-C, VLDL-C lipoprotein fractions of AC were revealed. Lipid profile values are altered in all patients depending on the severity of obesity. A statistically significant distinction was recorded between the values of the lipid profile indices and those of the subjects in the control group: TG in patients with VO Class II and VO Class III ($P < 0.001$); TC in patients with VO Class II ($P < 0.05$), VO Class III ($P < 0.01$); HDL-C in patients with VO Class I ($P < 0.05$); LDL-C in patients with VO Class I ($P < 0.05$) and VO Class III ($P < 0.001$); VLDL-C in all groups of patients with VO ($P < 0.001$) (Fig. 1.). Atherogenic coefficient (AC) in patients with VO Class I, Class II and Class III was significantly elevated ($P < 0.01$).
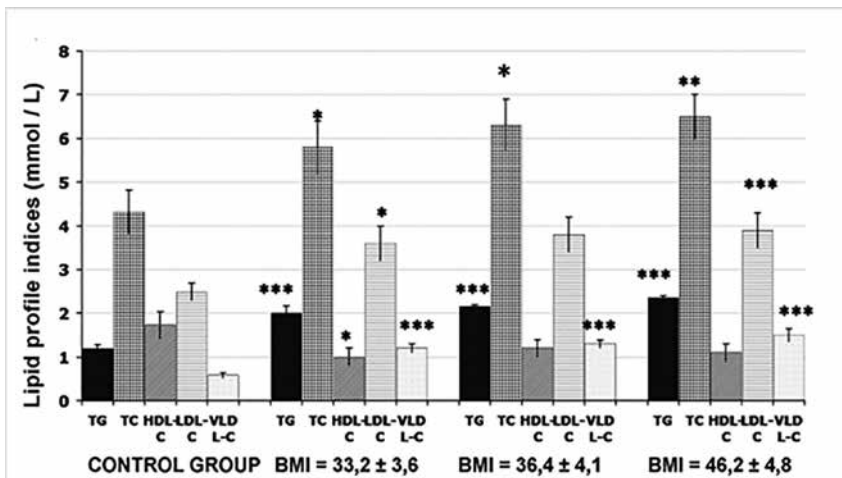

Fig.1. Lipid profile indices by severity of visceral obesity (VO)
Note: * - P < 0.050; ** - P < 0.010; ***- P < 0.001

Thus, obesity can be caused by pathology of the central nervous system and is accompanied by many associated diseases, which will subsequently decrease the hypothalamic production of neuropeptide Y. Adipose tissue is not only a deposit of energy that secretes fatty acids to provide fuel to the body, but also an endocrine organ producing high protein substances with important physiological functions. These factors determinate autocrine

and paracrine regulation mechanisms within adipose tissue and can substantially influence the functions of other organs, such as skeletal muscle, pancreas, and liver. The function of adipose tissue, as an endocrine organ, is important to understand the relationship and interrelationship between excess fat and pathological conditions, such as insulin resistance and type 2 diabetes, cardiovascular disease, obstructive sleep apnea and other types of nocturnal hypoventilation, type 2 diabetes, dyslipidemia, hypertension and thromboembolic disease.

Bibliographical references

1. Wadden TA, Berkowitz RI, Womble L.J. et al. Randomized trial of lifestyle modification and pharmacotherapy for obesity. In: N. Engl. J. Med. 2005, Vol. 353, p.2111-2120.
2. Wilnow T.E. Mechanism of hepatic chylomicron remnant clearance. In: Diab. Med. 1997, 14 (suppl. 3), p.75-80.
3. Maheus S.et al. Relationship between insulin- mediated glucose disposal and regulation of plasma and adipose tissue lipoprotein lipase. In: Diabetologia. 1997, Vol 40, p.850-858.
4. Strohl K.P., Strobel R.J. Obesity and pulmonary function. In: Bray G.A. Bouchrd C., James W.P.T. Handbook of obesity. New York, NY: Marceli Dekker, 1998, p.725-739.
5. Dedov I.I. et al. Obesity. MIA Moscow, 2006, p.451.
6. Gherasim L. et al. Medicina Interna. Vol 2. Boli cardiovasculare si metabolice. 2000, p.1323-1339.
7. Frayn K.N. Insulin resistance and lipid metabolism. In: Curr. Opin. Lipidol. 1993, Vol. 4, p.197-204.
8. Howard B.V. Insulin action in vivo: insulin and lipoprotein metabolism. International textbook of diabetes mellitus. 2d Ed. Wiley: Chester, 1997, p.531-539.
9. Reaven G.M. Insulin resistance, compensatory hyperinsulinemia and dyslipidemia in syndrome X. In: Aterosclerosis XI. Paris: Esevier, 1998, p.259-265.
10. Ferrannini E. et al. Insulin resistance and hypersecretion in obesity. In: J clin Invest. 1997, Vol. 100, p.1166-73.
11. Cicuttini F.M., Baker J.R., Spector T.D. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. In: J Rheumatol. 1996, Vol. 23, p.1221-1226.
12. Sugerman H.J., Windsor A.C.J., Bessos M.K., Wolfe L. Abdominal pressure, sagittal abdominal diameter and obesity co-morbidity. In: J. Int. Med. l997, Vol. 241, p.71-79.

13. Astrup A., Gotzche P.C., van de Werken K. et.al. Meta-analysis of resting me-
tabolic rate in formerly obese subjects. In: Am. J. Clin. Nutr. 1999, Vol. 69,
p.1117-1122.
14. Rader D.J. High-density lipoproteins as an emerging therapeutic target for
atherosclerosis. In: JAMA. 2003, Vol. 290, p.2322-2324.
15. Witztum J.I., Steinberg D. The oxidative modification hypothesis of atheros-
clerosis. Does in hold for humans? In: Trends Cardiovasc. Med. 2001, Vol. 11,
p.93-10.

ROLUL PLANTELOR MEDICINALE ONCOPROTECTOARE ÎN MODIFICAREA MICROBIOTEI INTESTINALE

Ana Leorda, dr. în șt.biol., conf. cercetător
Institutul de Fiziologie și Sanocreatologie, Chișinău, R. Moldova
leorda-ana64@mail.ru
Vlada Furdui, dr. în șt.biol., conf. cercetător
Institutul de Fiziologie și Sanocreatologie, Chișinău, R. Moldova
vlada.furdui@mail.ru
Dorina Tolstenco
Universitatea de Stat din Moldova
tolstencodorina@gmail.com

*THE ROLE OF ONCOPROTECTIVE MEDICINAL PLANTS
IN MODIFYING THE INTESTINAL MICROBIOTA*

*At the global level, humanity's interest in natural remedies of plant ori-
gin against many diseases of various etiologies is currently increasing.
A whole series of medicinal plants possess anticancer capabilities, but it
is necessary to elucidate those plants, which simultaneously demonstrate
prebiotic activity, a fact that will be the basis for the further development
of phytooncoprotective microbial preparations.*

Cancerul colorectal (CRC) reprezintă aproximativ 10% din noile cazuri
de cancer la nivel mondial.Rata sa de incidență este a treia dintre toate
tipurile de cancer la nivel mondial, iar rata mortalității este pe locul al
doilea dintre toate tipurile de cancer [1]. Creșterea constantă a morbidită-
ții oncologice și, în special, a cancerului colorectal afectează starea florei