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EFFECT OF STRESS ON HORMONE LEVELS IN THE BLOOD SERUM OF RATS WITH ALIMENTARY OBESITY

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ABSTRACT

Nowadays obesity is considered a complex chronic disease that poses a serious threat to health due to its associated cardiovascular and metabolic complications. One of the key regulators that can trigger the development of pathological processes in obesity is adipose tissue hormones – adipokines, among which leptin, adiponectin, and visfatin should be highlighted. To assess the degree of influence of a stable emotional stress state on the secretory activity of adipose tissue in the blood serum of obese rats, changes in the level of adipose tissue hormones - leptin, adiponectin, and visfatin were analyzed. It has been shown that a decrease in serum leptin levels in conditions of chronic stress can cause eating disorders, and the level of the hormone visfatin depends not only on the amount of adipose tissue. The results of the study suggest that chronic stress on the background of obesity accelerates the development of insulin resistance.

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Introduction

Chronic stress, along with burdened heredity, a sedentary lifestyle, and an unbalanced diet, is one of the causes of obesity [1, 2]. It is well known that under stress, excessive release of the hormone cortisol occurs, which not only plays an important role in the adaptation of the human body but also contributes to an increase in appetite [3, 4]. Consequently, if the body experiences stressful effects for a long time, a vicious circle arises, leading over time to the development of obesity [5, 6].

Obesity is today considered a complex chronic disease that poses a serious threat to health due to its associated cardiovascular and metabolic complications [7, 8]. One of the key regulators that can trigger the development of pathological processes in obesity is adipose tissue hormones – adipokines, among which leptin, adiponectin, and visfatin should be distinguished [9, 10].

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The main physiological role of leptin in the body is to regulate energy metabolism and body weight [11]. Leptin is often called the satiety hormone [12]. It is believed that it acts in the hypothalamus as a blocker of the synthesis and release of neuropeptide Y, which causes hunger [13]. Adiponectin, unlike leptin, performs a protective function, increasing tissue sensitivity to insulin, and has cardioprotective effects [14].
The physiological role of the hormone visfatin is being actively studied, and there is evidence that indicates its involvement in the development of cardiovascular pathology and metabolic changes in obesity [15-17]. Given that this hormone acts like insulin, it can be assumed that in obesity it is involved in the pathogenesis of insulin resistance, diabetes mellitus, and its complications [18]. Adipokines play an important role in the development of early vascular and metabolic complications, but there is no clear evidence of this to date [19].
Thus, the work aimed to evaluate the effect of a stable emotional stress state on the level of adipose tissue hormones: leptin, adiponectin, and visfatin in the blood serum of rats on a model of alimentary obesity.

Materials and Methods

To simulate obesity, a fat component was added to the vivarium diet for 3 months: 3 g of pork fat daily with an initial body weight of 200 g of rats. Stable emotional stress was induced by immobilization, placing animals in special narrow pencil cases daily for 60 minutes for 10 days [20]. All animals were divided into 4 groups (10 animals each):

- group 1 (control): rats that were on a vivarium diet (state of physiological norm);
- group 2 (stress): intact animals subjected to chronic immobilization stress;
- group 3 (obesity + stress): obese animals subjected to chronic immobilization stress;
- group 4 (obesity): animals with alimentary obesity.

At the end of the experiment, rats of all groups were decapitated using a guillotine, and peripheral blood was taken [21]. To assess the degree of stress exposure, the serum level of corticosterone (an analog of cortisol in humans) was measured using the enzyme immunoassay on the BioTekELx80 ELISA analyzer (USA), and the mass of the adrenal glands was recorded.
Since the activation of the process of free radical oxidation in cells occurs during intensive or prolonged stress exposure to the body, the indicators of the system "lipid peroxidation - antioxidant protection" (LP–AOP) were determined [22]. The intensity of LP was judged by a change in the level of its main product – malonic dialdehyde (MDA), the content of which was determined by reaction with 2′-thiobarbituric acid [23]. The activity of superoxide dismutase (SOD), a key enzyme in antioxidant systems, was studied based on the degree of inhibition of the quercetin oxidation reaction [24]. The catalase activity (preventing the accumulation of hydrogen peroxide formed during the dismutation of the superoxide anion) was evaluated using a spectrophotometric method based on the ability of hydrogen peroxide to form a stable colored complex with molybdenum salts [25]. The extinction of the analyzed solutions was measured using an IFA-analyzer, BioTekELx80 (USA).
To confirm the correctness of the choice of a model of alimentary obesity, body weight was monitored throughout the experiment, and after decapitation, the animals were dissected and weighed for internal organs, and the percentage of visceral adipose tissue was estimated [26].
The levels of total cholesterol (TC), high and low-density lipoproteins (HDL, LDL), triacylglycerides (TG), glucose, amylase, and lipase enzymes were determined in blood serum using a BS-200 biochemical analyzer (China) using Randox reagents (Great Britain) and Diasens (Belarus) [27]. The content of total phospholipids in liver tissue was assessed using a method based on the detection of inorganic phosphorus formed during acid hydrolysis of phospholipids [28]. The levels of adipose tissue hormones (leptin, adiponectin, visfatin) were evaluated by enzyme immunoassay on a Chem Well analyzer (USA) using DRG test systems (Germany) [29].
The obtained data were statistically processed using the Statistica 12.0 software (USA). The normality of the distribution of indicators was checked using the Shapiro–Wilk test. The Student's t-test for independent samples or the nonparametric Mann–Whitney test were used for intergroup comparison. The results are presented in the form of an average value and a standard error of the average. The critical significance level (p) in testing statistical hypotheses in this study was assumed to be 0.05.

Results and Discussion

It was revealed that in rats of groups 2 and 3, the mass of the adrenal glands compared with the control was significantly increased (2.5 and 2 times, respectively). This fact can be explained as compensatory hypertrophy associated with the fact that the adrenal glands under chronic stress experienced significant functional stress [30]. In the same groups, the content of the main physiologically active hormone corticosterone, the main indicator of the rat body's response to a stress effect similar to cortisol in humans, significantly decreased in the blood serum of rats **(Table 1)**.
The data presented in **Table 1** indicate the fact of depletion of stress regulation mechanisms, which is also noted by other researchers [31, 32]. When analyzing the indicators of the LP–AOP system compared with those in the control group, an increase in the content of MDA ($p \leq 0.05$) in the blood serum of rats of all experimental groups was found. At the same time, a decrease in the activity of SOD and catalase was noted both in animals subjected to sustained emotional stress and in rats of the group 3 **(Table 1)**.

Table 1. Changes in the levels of corticosterone, malondialdehyde, superoxide dismutase, and catalase activity in the blood serum of obese rats under chronic stress

Experimental groups	Corticosterone, nmol/L	MDA, nmol/L	SOD, U/mL	Catalase, mcat/L
Group 1 (n = 10)	0.170 ± 0.04	10.580 ± 0.868	3.463 ± 0.236	8.303 ± 0.711
Group 2 (n = 10)	0.050 ± 0.03*	15.339 ± 0.397*	1.771 ± 0.092*	4.761 ± 0.237*
Group 3 (n = 10)	0.071 ± 0.03*	19.642 ± 0.396*	1.360 ± 0.080*	1.752 ± 0.177*
Group 4 (n = 10)	0.016 ± 0.03	14.287 ± 0.966*	3.309 ± 0.268	8.032 ± 0.819

* – significant differences from the control ($p < 0.05$)

A significant role in the occurrence of the observed changes could be played by developing metabolic acidosis, impaired oxygen transport, and a decrease in the production of major macroregion compounds [33]. At the same time, the decrease in the efficiency of the AOP system is most likely caused not only by a drop in the level of antioxidants or inhibition of anti-peroxide enzymes but also by blocking the processes of hydrogen supply under the action of, for example, metabolic poisons or other factors [34, 35].

In the group of experimentally obese rats, body weight monitoring showed an excess of this indicator by 18.8%, kidney weight increased by 26.0%, spleen by 33.0, and the amount of visceral fat by 80.0%. There was a significant ($p < 0.05$) decrease in the content of total phospholipids in liver tissue (by 47.0%) relative to the control. The TC level was 1,930 ± 0.174 mmol/L, which was 30.0% higher than their control values (1,468 ± 0.172 mmol/L). The obtained data can be explained by relative phospholipid deficiency due to impaired metabolic activity of the liver in obesity [36, 37].

Analysis of biochemical blood parameters showed that only in group 3 there was an increase in the levels of TC (0.98 ± 0.07 mmol/L in the control, 1.58 ± 0.07 mmol/L in the experimental group), LDL (0.1 ± 0.02 and 0.16 ± 0.02 mmol/L, respectively), and HDL (0.5 ± 0.055 and 0.8 ± 0.060 mmol/L, respectively) ($p \leq 0.05$). Most likely, this is due to the regulatory action of glucocorticoids, which are known to increase the production of lipids by hepatocytes by enhancing the expression of the fatty acid synthase gene [38]. In the same group, a significant increase in glucose levels was observed compared with the control: 3,6 ± 0.18 mmol/L and 4,9 ± 0,20 mmol/L.

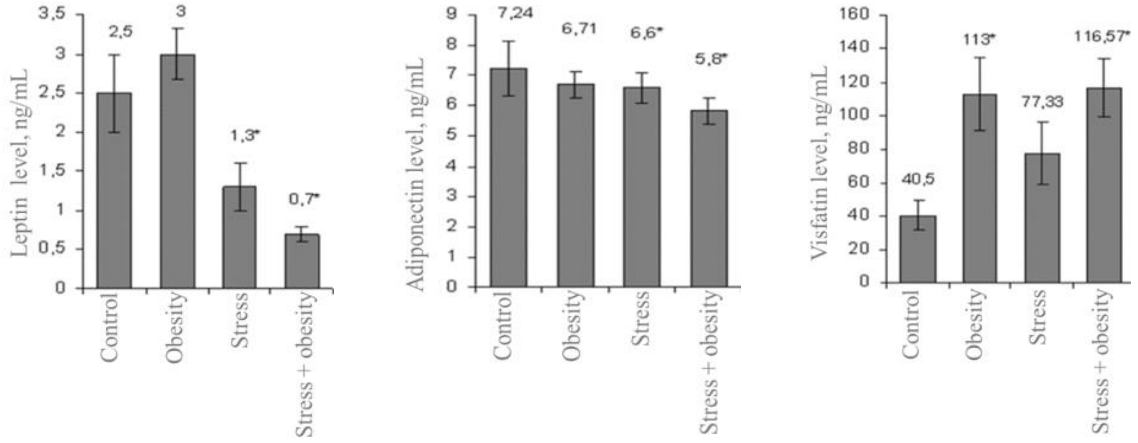
Data on the content of lipase and amylase enzymes are presented in **Table 2**. Under conditions of "pure" stress (group 2) and its combined effects with obesity, an increase in blood lipase and amylase levels ($p < 0.05$) was observed. This may indicate the onset of an inflammatory process in pancreatic tissue [39]. As is known, the development of pancreatitis is usually caused by the activation of pancreatic juice enzymes due to stress-induced regurgitation into the ducts of the contents of the duodenum, including bile [40, 41].

Table 2. Changes in the lipase and amylase activity in the blood serum under stable emotional stress of rats with alimentary obesity

Parameter	Group 1 (n = 10)	Group 2 (n = 10)	Group 3 (n = 10)	Group 4 (n = 10)
Amylase, U/L	973.8 ± 33.1	1470.6 ± 129.4*	1789.2 ± 148.5*	1076.5 ± 21.3
Lipase, U/L	23.8 ± 0.5	155.3 ± 14.2*	211.2 ± 59.2*	21.3 ± 2.6

* – $p < 0.05$

The study of the content of adipose tissue hormones showed that the level of leptin in blood serum significantly decreased in rats of groups 2 and 3, while in group 4 its amount was slightly increased ($p \geq 0.05$) **(Figure 1a)**. This fact in the latter case is explained by an increase in the volume of adipose tissue and an associated increase in the secretion of this hormone [42, 43]. In experimental individuals of all groups, there was a unidirectional tendency to decrease the amount of adiponectin in the blood **(Figure 1b)**. There was also a negative correlation with a weak link between adiponectin and glucose levels in group 3. Chronic stress in the presence of alimentary obesity may accelerate the development of insulin resistance since it is known that a decrease in the blood content of adiponectin is directly related to a decrease in insulin sensitivity [44]. This assumption requires concrete confirmation within the framework of a more complete and focused study.



a) b) c)

Figure 1. Changes in the hormone levels of leptin (*a*), adiponectin (*b*), and vistafatin (*c*) in the blood serum of rats with alimentary obesity under chronic emotional stress (n = 10 for each group). * – reliable differences from control ($p < 0.05$)

Interestingly, an increase in the level of visfatin in the blood was detected in rats from all experimental groups. It is especially clearly manifested in obesity and stress on the background of obesity ($p < 0.05$) **(Figure 1c)**. Most likely, this fact is due to an increase in the amount of adipose tissue [45]. In conditions of chronic asthma, the concentration of visfatin in the blood serum was also increased, which may be due to more complex biochemical reactions during its metabolism [46]. There was also a positive correlation between corticosterone and visfatin levels in group 3. Probably, under stress, there is an increase in the expression of the visfatin gene by glucocorticoids. This is a possible mechanism involved in the secretion of hormones by adipose tissue [47-50].

Conclusion

Thus, the analysis of the obtained results allows us to conclude that a decrease in the level of leptin in the blood under conditions of chronic stress may be a factor that disrupts eating behavior. At this stage of research concerning the content of adiponectin in the blood, it can be assumed that chronic stress on the background of obesity accelerates the development of insulin resistance in tissues and organs of the body. The level of the hormone visfatin depends not only on the amount of adipose tissue, its secretion is based on a more complex mechanism and may be associated with increased expression of the visfatin gene by glucocorticoids.

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References

1. Gonnella F, Konstantinidou F, Donato M, Gatta DMP, Peserico A, Barboni B, et al. The molecular link between obesity and the endometrial environment: A starting point for female infertility. Int J Mol Sci. 2024;25(13):6855. doi:10.3390/ijms25136855
2. Balditsyna E, Baklanov I, Baklanova O. Gender identity studies in the modern social theory: Research features. WinRS. 2019:43-51. doi:10.21064/winrs.2019.2.4
3. AlSahman L, AlBagieh H, AlSahman R. Is there a relationship between salivary cortisol and temporomandibular disorder: A systematic review. Diagnostics (Basel). 2024;14(13):1435. doi:10.3390/diagnostics14131435
4. Lin J, Li Y, Huang Z, Zhu Y, Li L, Yang H, et al. Rare correlation of somatic PRKACA mutations with pregnancy-associated aldosterone- and cortisol-producing adenomas: A case report and literature review. BMC Endocr Disord. 2024;24(1):116. doi:10.1186/s12902-024-01645-x
5. Sandoval-Bórquez A, Carrión P, Hernández MP, Pérez JA, Tapia-Castillo A, Vecchiola A, et al. Adipose tissue dysfunction and the role of adipocyte-derived extracellular vesicles in obesity and metabolic syndrome. J Endocr Soc. 2024;8(8):bvae126. doi:10.1210/jendso/bvae126

6. Oumeddour DZ, Al-Dalali S, Zhao L, Zhao L, Wang C. Recent advances on cyanidin-3-O-glucoside in preventing obesity-related metabolic disorders: A comprehensive review. Biochem Biophys Res Commun. 2024;729:150344. doi:10.1016/j.bbrc.2024.150344
7. Avogaro A. Diabetes and obesity: The role of stress in the development of cancer. Endocrine. 2024. doi:10.1007/s12020-024-03886-1
8. Alruwaili BF, Bayyumi DF, Alruwaili OS, Alsadun RS, Alanazi AS, Hadi A, et al. Prevalence and determinants of obesity and overweight among children and adolescents in the middle east and north African countries: An updated systematic review. Diabetes Metab Syndr Obes. 2024;17:2095-103. doi:10.2147/DMSO.S458003
9. Vitale E, Rizzo A, Santa K, Jirillo E. Associations between "Cancer Risk", "Inflammation" and "Metabolic Syndrome": A scoping review. Biology (Basel). 2024;13(5):352. doi:10.3390/biology13050352
10. Hao M, Lv Y, Liu S, Guo W. The new challenge of obesity - Obesity-associated nephropathy. Diabetes Metab Syndr Obes. 2024;17:1957-71. doi:10.2147/DMSO.S433649
11. Szumilas K, Wilk A, Szumilas P, Dziedziejko V, Pawlik A. Role of leptin and adiponectin in the pathogenesis of post-transplant diabetes mellitus. Prostaglandins Other Lipid Mediat. 2024:106876. doi:10.1016/j.prostaglandins.2024.106876
12. Harvey J. Novel leptin-based therapeutic strategies to limit synaptic dysfunction in Alzheimer's disease. Int J Mol Sci. 2024;25(13):7352. doi:10.3390/ijms25137352
13. Ferrario CR, Münzberg-Gruening H, Rinaman L, Betley JN, Borgland SL, Dus M, et al. Obesity- and diet-induced plasticity in systems that control eating and energy balance. Obesity (Silver Spring). 2024. doi:10.1002/oby.24060
14. Zhao YQ, Ren YF, Li BB, Wei C, Yu B. The mysterious association between adiponectin and endometriosis. Front Pharmacol. 2024;15:1396616. doi:10.3389/fphar.2024.1396616
15. Annie L, Pankaj PP, Kharwar RK, Singh A, Roy VK. Status of visfatin in female reproductive function under normal and pathological conditions: A mini review. Mol Biol Rep. 2024;51(1):631. doi:10.1007/s11033-024-09461-1
16. Velma GR, Krider IS, Alves ETM, Courey JM, Laham MS, Thatcher GRJ. Channeling nicotinamide Phosphoribosyltransferase (NAMPT) to address life and death. J Med Chem. 2024;67(8):5999-6026. doi:10.1021/acs.jmedchem.3c02112
17. Ozgencil F, Gunindi HB, Eren G. Dual-targeted NAMPT inhibitors as a progressive strategy for cancer therapy. Bioorg Chem. 2024;149:107509. doi:10.1016/j.bioorg.2024.107509
18. Gasparrini M, Giovannuzzi S, Nocentini A, Raffaelli N, Supuran CT. Inhibition of nicotinamide phosphoribosyltransferase (NAMPT) in cancer: A patent review. Expert Opin Ther Pat. 2024;34(7):565-82. doi:10.1080/13543776.2024.2367006
19. Kiełbowski K, Bakinowska E, Bratborska AW, Pawlik A. The role of adipokines in the pathogenesis of psoriasis - A focus on resistin, omentin-1 and vaspin. Expert Opin Ther Targets. 2024:1-14. doi:10.1080/14728222.2024.2375373
20. Lyashenko EN, Uzbekova LD, Polovinkina VV, Dorofeeva AK, Ibragimov SS, Tatamov AA, et al. Study of the embryonic toxicity of TiO2 and ZrO2 nanoparticles. Micromachines (Basel). 2023;14(2):363. doi:10.3390/mi14020363
21. Verevkina M, Goncharov V, Nesmeyanov E, Kamalova O, Baklanov I, Pokhilko A, et al. Application of the Se NPs-Chitosan molecular complex for the correction of selenium deficiency in rats model. Potravinarstvo Slovak J Food Sci. 2023;17:455-66. doi:10.5219/1871
22. Valgimigli L. Lipid Peroxidation and antioxidant protection. Biomolecules. 2023;13(9):1291. doi:10.3390/biom13091291
23. Zhou J, Li Z, Guo W, Wang Y, Liu R, Huang X, et al. Nano vitamin E improved the antioxidant capacity of broiler chickens. J Anim Sci. 2024;102:skae095. doi:10.1093/jas/skae095
24. Alhilal M, Erol HS, Yildirim S, Cakir A, Koc M, Alhilal S, et al. Medicinal evaluation and molecular docking study of osajin as an anti-inflammatory, antioxidant, and antiapoptotic agent against sepsis-associated acute kidney injury in rats. Ren Fail. 2024;46(2):2379008. doi:10.1080/0886022X.2024.2379008
25. Kadhim A, Ben Slima A, Alneamah G, Makni M. Assessment of histopathological alterations and oxidative stress in the liver and kidney of male rats following exposure to aluminum chloride. J Toxicol. 2024;2024:3997463. doi:10.1155/2024/3997463
26. Sadovoy VV, Selimov MA, Slichedrina TV, Nagdalian AA. Usage of biological active supplements in technology of prophilactic meat products. Res J Pharm Biol Chem Sci. 2016;7(5):1861-5.
27. Zimodro JM, Mucha M, Berthold HK, Gouni-Berthold I. Lipoprotein metabolism, dyslipidemia, and lipid-lowering therapy in women: A comprehensive review. Pharmaceuticals (Basel). 2024;17(7):913. doi:10.3390/ph17070913
28. Dirik H, Taşkıran AŞ, Joha Z. Ferroptosis inhibitor ferrostatin-1 attenuates morphine tolerance development in male rats by inhibiting dorsal root ganglion neuronal ferroptosis. Korean J Pain. 2024;37(3):233-46. doi:10.3344/kjp.24042
29. Sadovoy VV, Selimov M, Shchedrina T, Nagdalian AA. Nutritional supplement for control of diabetes. J Excip Food Chem. 2017;8352017:1843.
30. Herman JP, Tasker JG. Paraventricular hypothalamic mechanisms of chronic stress adaptation. Front Endocrinol (Lausanne). 2016;7:137. doi:10.3389/fendo.2016.00137
31. Bizerea-Moga TO, Pitulice L, Bizerea-Spiridon O, Moga TV. Exploring the Link between oxidative stress, selenium levels, and obesity in youth. Int J Mol Sci. 2024;25(13):7276. doi:10.3390/ijms25137276

32. Novinbahador T, Abroon S, Motlagh K, Abbasi K, Mehdizadeh A, Nejabati HR, et al. Surface markers on microparticles involved in obesity-derived diseases. Life Sci. 2024;352:122876. doi:10.1016/j.lfs.2024.122876
33. Hoffmanová I, Sánchez D. Metabolic acidosis and anaemia associated with dorzolamide in a patient with impaired renal function. Br J Clin Pharmacol. 2018;84(4):796-9. doi:10.1111/bcp.13499
34. Jomova K, Raptova R, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, et al. Reactive oxygen species, toxicity, oxidative stress, and antioxidants: Chronic diseases and aging. Arch Toxicol. 2023;97(10):2499-574. doi:10.1007/s00204-023-03562-9
35. Chaudhary P, Janmeda P, Docea AO, Yeskaliyeva B, Abdull Razis AF, Modu B, et al. Oxidative stress, free radicals and antioxidants: Potential crosstalk in the pathophysiology of human diseases. Front Chem. 2023;11:1158198. doi:10.3389/fchem.2023.1158198
36. Qureshi K, Abrams GA. Metabolic liver disease of obesity and role of adipose tissue in the pathogenesis of nonalcoholic fatty liver disease. World J Gastroenterol. 2007;13(26):3540-53. doi:10.3748/wjg.v13.i26.3540
37. Liu Y, Wu Y, Jiang M. The emerging roles of PHOSPHO1 and its regulated phospholipid homeostasis in metabolic disorders. Front Physiol. 2022;13:935195. doi:10.3389/fphys.2022.935195
38. Belyaev NG, Rzhepakovsky IV, Timchenko LD, Areshidze DA, Simonov AN, Nagdalian AA, et al. Effect of training on femur mineral density of rats. Biochem Cell Arch. 2019;19(2):3549-52.
39. Bastati N, Kristic A, Poetter-Lang S, Messner A, Herold A, Hodge JC, et al. Imaging of inflammatory disease of the pancreas. Br J Radiol. 2021;94(1123):20201214. doi:10.1259/bjr.20201214
40. Szatmary P, Grammatikopoulos T, Cai W, Huang W, Mukherjee R, Halloran C, et al. Acute pancreatitis: Diagnosis and treatment. Drugs. 2022;82(12):1251-76. doi:10.1007/s40265-022-01766-4
41. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg. 2019;14:27. doi:10.1186/s13017-019-0247-0
42. Vore AS, Marsland P, Barney TM, Varlinskaya EI, Landin JD, Healey KL, et al. Adolescent intermittent ethanol (AIE) produces lasting, sex-specific changes in rat body fat independent of changes in white blood cell composition. Front Physiol. 2024;15:1285376. doi:10.3389/fphys.2024.1285376
43. Ding Y, Lv S, Xie R, Ye W, Luo Y, Li Y. Association of weight-adjusted waist index and diabetic kidney disease in type 2 diabetes mellitus. Endocr Connect. 2024;13(4):e230491. doi:10.1530/EC-23-0491
44. Yue H, Zhang Q, Chang S, Zhao X, Wang M, Li W. Adiponectin protects against myocardial ischemia-reperfusion injury: A systematic review and meta-analysis of preclinical animal studies. Lipids Health Dis. 2024;23(1):51. doi:10.1186/s12944-024-02028-w
45. Arner P, Andersson DP, Arner E, Rydén M, Kerr AG. Subcutaneous adipose tissue expansion mechanisms are similar in early and late onset overweight/obesity. Int J Obes (Lond). 2022;46(6):1196-203. doi:10.1038/s41366-022-01102-6
46. Vishvanath L, Gupta RK. Contribution of adipogenesis to healthy adipose tissue expansion in obesity. J Clin Invest. 2019;129(10):4022-31. doi:10.1172/JCI129191
47. Szymanska K, Zaobidna E, Rytelewska E, Mlyczynska E, Kurowska P, Dobrzyn K, et al. Visfatin in the porcine pituitary gland: Expression and regulation of secretion during the oestrous cycle and early pregnancy. Sci Rep. 2023;13(1):18253. doi:10.1038/s41598-023-45255-4
48. Marroncini G, Naldi L, Martinelli S, Amedei A. Gut-liver-pancreas axis crosstalk in health and disease: From the role of microbial metabolites to innovative microbiota manipulating strategies. Biomedicines. 2024;12(7):1398. doi:10.3390/biomedicines12071398
49. Kusminski CM, Perez-Tilve D, Müller TD, DiMarchi RD, Tschöp MH, Scherer PE. Transforming obesity: The advancement of multi-receptor drugs. Cell. 2024;187(15):3829-53. doi:10.1016/j.cell.2024.06.003
50. Miao X, Alidadipour A, Saed V, Sayyadi F, Jadidi Y, Davoudi M, et al. Hepatokines: Unveiling the molecular and cellular mechanisms connecting hepatic tissue to insulin resistance and inflammation. Acta Diabetol. 2024. doi:10.1007/s00592-024-02335-9