DOI: https://doi.org/10.17816/RCF562841
Research Article

Reduction of compulsive overeating in rats caused by maternal deprivation in early ontogenesis with the use of a new ghrelin receptor antagonist agrelax

Andrei A. Lebedev [1], Sarng S. Purveev [1, 2], Natalia D. Nadbitova [1], Aleksey V. Lizunov [1], Eugenii R. Bychkov [1], Valeriya V. Lukashkova [1], Natalia R. Evdokimova [1], Maria A. Netesa [1], Viktor A. Lebedev [1], Petr D. Shabanov [1]

[1] Institute of Experimental Medicine, Saint Petersburg, Russia;
[2] Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russia

ABSTRACT

BACKGROUND: Factors that may trigger episodes of binge eating include mental and physical stress, dietary restrictions of high-calorie foods. In a rodent model it has been shown that intermittent consumption of high-calorie foods causes binge eating regardless of body weight gain.

AIM: To investigate the effect of a novel ghrelin receptor antagonist Agrelax on binge eating in in adult rats after maternal deprivation in early ontogeny.

MATERIALS AND METHODS: Animals were weaned for 180 min from day 2 to day 12 after birth; males 90–100 days of age were used in the experiments. In the development of binge eating, animals received a high-carbohydrate diet (Nutella paste — based chocolate mixture) for 1 h every day or every third day for 1.5 months. Fifteen minutes before feeding, the chocolate paste was placed within 5 cm of reach with visual contact. Agrelax, a novel ghrelin receptor antagonist, was administered intranasally 1μg/1μl, 20μl for 7 days.

RESULTS: Maternal deprivation induced bindge eating of high-calorie foods in adult rats. When chocolate was given 3 times a week, its consumption increased ($p < 0.001$) in the maternal deprivation group relative to the control group. After a course of administration of agrelax, chocolate consumption did not differ significantly from that in the control group. The daily consumption of standard food did not differ relative to the control group both before and after the course of agrelax administration. When chocolate was given daily, the maternal deprivation rats did not develop food addiction. At the same time agrelax did not induce a change in chocolate consumption relative to the control group.

CONCLUSIONS: The findings suggest new ways to synthesize pharmacological agents of peptide nature based on ghrelin and its antagonists for correction of food addiction caused by psychogenic stresses in ontogenesis.

Keywords: bindge eating; maternal deprivation; agrelax; ghrelin.

To cite this article:
Lebedev AA, Purveev SS, Nadbitova ND, Lizunov AV, Bychkov ER, Lukashkova VV, Evdokimova NR, Netesa MA, Lebedev VA, Shabanov PD. Reduction of compulsive overeating in rats caused by maternal deprivation in early ontogenesis with the use of a new ghrelin receptor antagonist agrelax. *Reviews on Clinical Pharmacology and Drug Therapy.* 2023;21(3):255–262. DOI: https://doi.org/10.17816/RCF562841

Received: 14.07.2023 **Accepted:** 21.07.2023 **Published:** 29.09.2023

УДК 616.092
DOI: https://doi.org/10.17816/RCF562841
Научная статья

Снижение компульсивного переедания у крыс, вызванного материнской депривацией в раннем отногенезе, с применением нового антагониста рецепторов грелина агрелакс

А.А. Лебедев [1], С.С. Пюрвеев [1, 2], Н.Д. Надбитова [1], А.В. Лизунов [1], Е.Р. Бычков [1], В.В. Лукашкова [1], Н.Р. Евдокимова [1], М.А. Нетеса [1], В.А. Лебедев [1], П.Д. Шабанов [1]

[1] Институт экспериментальной медицины, Санкт-Петербург Россия;

[2] Санкт-Петербургский государственный педиатрический медицинский университет, Санкт-Петербург, Россия

АННОТАЦИЯ

Актуальность. Факторы, которые могут вызывать эпизоды компульсивного (приступообразного) переедания, включают психические и физические стрессы, ограничения в питании высококалорийной пищи. В модели компульсивного переедания на грызунах показано, что прерывистое потребление продуктов высококалорийной пищи вызывает компульсивное переедание независимо от увеличения массы тела.

Цель — исследование действия нового антагониста рецепторов грелина агрелакса на компульсивное переедание у половозрелых крыс, вызванное материнской депривацией в раннем онтогенезе.

Материалы и методы. Животных со 2-го по 12-й день после рождения на 180 мин отлучали от матери, в опытах использовали самцов в возрасте 90–100 дней. При выработке компульсивного переедания животные получали в течение 1 ч диету с высоким содержанием углеводов (смесь на основе шоколадной пасты «Nutella») каждый день или каждый третий день в течение 1,5 мес. За 15 мин до кормления шоколадную пасту помещали в 5 см досягаемости при визуальном контакте. Агрелакс, новый антагонист рецепторов грелина, вводили интраназально в дозе 1 мкг / 1 мкл, 20 мкл в течение 7 дней.

Результаты. Материнская депривация вызывала компульсивное переедание высококалорийной пищи у половозрелых крыс. При выдаче шоколада 3 раза в неделю в группе с материнской депривацией его потребление увеличивалось ($p < 0{,}001$) относительно контрольной группы. После курса введения агрелакса потребление шоколада достоверно не отличалось от показателя в контрольной группе. Суточное потребление стандартного корма не отличалось относительно контрольной группы как до курса введения агрелакса, так и после. При выдаче шоколада ежедневно у крыс с материнской депривацией пищевая зависимость не вырабатывалась. При этом агрелакс не вызывал изменения потребления шоколада относительно контрольной группы.

Заключение. Полученные данные предполагают новые пути синтеза фармакологических средств пептидной природы на основе грелина и его антагонистов для коррекции пищевой зависимости, вызванной психогенными стрессами в онтогенезе.

Ключевые слова: компульсивное переедание; материнская депривация; агрелакс; грелин.

Как цитировать:
Лебедев А.А., Пюрвеев С.С., Надбитова Н.Д., Лизунов А.В., Бычков Е.Р., Лукашкова В.В., Евдокимова Н.Р., Нетеса М.А., Лебедев В.А., Шабанов П.Д. Снижение компульсивного переедания у крыс, вызванного материнской депривацией в раннем отногенезе, с применением нового антагониста рецепторов грелина агрелакс // Обзоры по клинической фармакологии и лекарственной терапии. 2023. Т. 21. № 3. С. 255–262. DOI: https://doi.org/10.17816/RCF562841

Рукопись получена: 14.07.2023 **Рукопись одобрена:** 21.07.2023 **Опубликована:** 29.09.2023

ЭКО•ВЕКТОР

INTRODUCTION

Compulsive (binge) overeating disorder is characterized by the intermittent and excessive consumption of palatable food in short periods. Unlike bulimia or anorexia nervosa, this behavior is not accompanied by compensatory behaviors [1]. Factors triggering episodes of compulsive overeating include mental and physical stress and dietary restrictions on high-calorie foods.

Intermittent consumption of high-calorie foods was shown in a rodent model to cause binge overeating, irrespective of weight gain or obesity [2]. Several rodent models of binge overeating were investigated. Intermittent exposure to a fat source was used in a restricted access model to induce episodes of overeating [2]. The experiment indicated the involvement of several neurotransmitter systems in binge overeating, particularly opioids, serotonin, dopamine, and hormones [3].

Ghrelin, an orexigenic peptide identified and described in the late 20th century, comprises 28 amino acids. Ghrelin is predominantly synthesized in the lateral region of the arcuate complex of hypothalamic nuclei by endocrinocytes of the cardiac mucosa of the cardiac part of the stomach and enters the bloodstream [4]. Ghrelin isoforms include acylated ghrelin (acetyl-ghrelin), nonacylated (desacyl-ghrelin), and obestatin, as well as two molecular forms of the ghrelin receptor (GHSR1A and GHSR1B). GHSR1A is the only one with biological activity [4]. Ghrelin receptors are localized in the digestive tract, adrenal glands, thyroid gland, heart muscle, and brain (hypothalamus, pituitary, hippocampus, amygdala, trunk nuclei, and neocortex) [4]. Ghrelin regulates eating behavior, psychostimulant and alcohol dependency [5], and stressor reactions [6]. Patients with compulsive overeating had decreased levels of peripheral ghrelin before eating, possibly related to the disorder's neurochemical mechanisms [7].

There is currently a lack of research papers addressing the involvement of the ghrelin system in food addiction. The mechanisms of ghrelin receptors' impact on reinforcement and emotional behavior systems under various environmental influences are unclear. Agrelax, a peptide antagonist of ghrelin developed by the Institute of Experimental Medicine, is active against GHSR1A ghrelin receptors [8].

The study aimed to investigate the effect of a new antagonist of ghrelin receptors agrelax on compulsive overeating induced by maternal deprivation in early ontogenesis in adult rats.

MATERIALS AND METHODS

The experiments were conducted on 32 male and five female Wistar rats weighing 200–250 g from the Rappolovo Laboratory Animal Nursery (Leningrad region). The animals were kept in vivarium conditions in standard plastic cages with free access to water and food from 8:00 to 20:00 at 22°C ± 2°C under inverted light conditions. During the experiment, the principles of humane laboratory rat treatment were observed in accordance with the Rules of Laboratory Practice in the Russian Federation (Order of the Ministry of Health of the Russian Federation, 2003, No. 267).

After they arrived from the nursery, the animals were quarantined for 2 weeks in the appropriate block of the vivarium. Female Wistar rats were kept in plastic cages (40 × 50 × 20 cm) of five individuals, each with access to water and food *ad libitum*. One male was placed in each cage. The next day, females' vaginal swabs were obtained to identify spermatozoa, and the onset of pregnancy was recorded using light microscopy, which was considered Day 0. Animals were housed in separate cages after pregnancy onset. The pregnancy lasted 20 ± 2 days.

The animals were divided into groups. Group 1 included nonstressed animals who had access to the chocolate diet daily. Group 1md included animals after maternal deprivation accessing the chocolate diet daily. Group 2 consisted of nonstressed animals that accessed the chocolate diet thrice weekly. Group 2md had animals after maternal deprivation accessing the chocolate diet thrice weekly.

A model of maternal weaning

From Days 2 to 12 of the postnatal period, rats were placed in individual plastic cups for 180 min every day for 10 days. Visual contact with the mother was excluded. Rats were grown in standard cages with five individuals in each cage after maternal deprivation and milk feeding. The experiment used males aged 90–100 days and weighed 200–250 g.

Method of compulsive overeating of high-calorie food

Animals in the experimental groups were given 1-h access to a high-carbohydrate diet (Nutella chocolate paste-based mix) every day (group 1md) or every third day (group 2md). The control animals consumed only standard pelleted rat food. The high-calorie food consisted of a paste made from Nutella chocolate paste (Ferrero, Alba, Turin, and Italy), ground rat pellet food (4RF18; Mucedola; Settimo Milanese), and water in the following

DOI: https://doi.org/10.17816/RCF562841

ratio: 52% chocolate paste, 33% food pellets, and 15% water. The diet had a calorie value of 3.63 kcal/g. Standard pelleted rat food was placed inside a metal mesh container suspended from the front wall of the cage; it was taken from the cage to estimate food intake by weighing it. The Nutella paste mixture was poured into a cup; the handle of the cup was put into the metal wall of the cage. The chocolate paste feeder was positioned within 5 cm of the animals and in full visual contact 15 min before feeding. The cup with the chocolate paste was placed inside a container with a metal mesh suspended from the cage's front wall. The animal was able to see and smell the paste. During this 15-min period, the rat performed repetitive movements of the forelegs, head, and trunk to access the paste but failed to reach it. This manipulation increased serum corticosterone levels [9]. The cup was placed in the cage after 15 min to make the paste available to the rats. Before the overeating period, the standard rodent food in each cage was weighed to estimate the following day's 24-h food intake. The rats were situated in separate cages 15 days after the start of the chocolate diet experiment and fed the chocolate diet for another 30 days. The amount of standard food eaten and the amount of chocolate paste eaten per 1 h of access were recorded. The weight of the animals was measured once a week on a certain day.

In Week 6 of the experiment, rats were administered a peptide analog of the ghrelin antagonist agrelax intranasally at a dose of 1 μg/1 μL, 20 μL for 7 days, which was synthesized in the S.V. Anichkov Department of Neuropharmacology at the Institute of Experimental Medicine using a genetically engineered method [8].

The Graph Pad Prizm v.6 software was used for statistical processing of quantitative data. The statistical significance of differences between groups was determined using a one-factor analysis of variance. Only two groups were compared using the Student's *t* test for independent samples.

RESULTS AND DISCUSSION

When the effect of maternal deprivation on daily chocolate intake was examined, it was shown that the average daily chocolate consumption over 10 days of testing decreased ($p < 0.05$) in group 1md compared with the control (intact) group 1. Similarly, it reduced ($p < 0.05$) when aggrelax was introduced compared with the control (intact) group 1. When the effect of maternal deprivation on standard feed intake was investigated, the average daily intake in group 1md was found to be unchanged relative to the control (intact) group 1 and did not differ from the control (intact) group 1 after the introduction of aggrelax (Fig. 1).

When the effect of maternal deprivation on chocolate consumption was studied three times a week, it was found that the average daily chocolate intake over the 10 days of testing was increased ($p < 0.001$) in group 2md relative to the control (intact) group 2 and remained unchanged relative to the control (intact) group 2 after consumption of the standard feed. The average daily intake of chocolate in group 2md after administration of aggrelax three times per week for 10 days did not differ relative to the control (intact) group 2 and did not differ from the control (intact) group 2 after consumption of standard feed (Fig. 2).

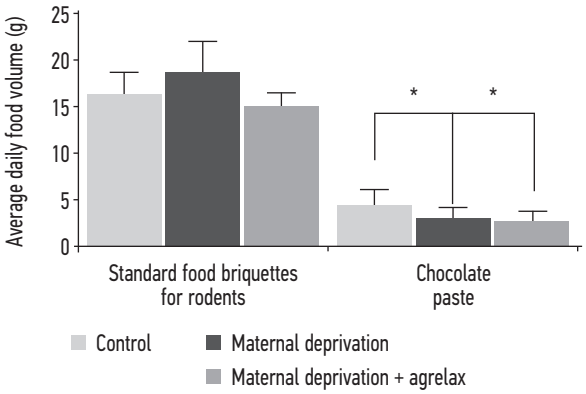

Fig. 1. The effect of maternal deprivation on the consumption of standard feed and chocolate during daily chocolate delivery. *$p < 0.05$ relative to the control (intact) group of animals

Рис. 1. Влияние материнской депривации (МД) на потребление стандартного корма и шоколада при ежедневной выдаче шоколада. *$p < 0,05$ относительно контрольной (интактной) группы животных

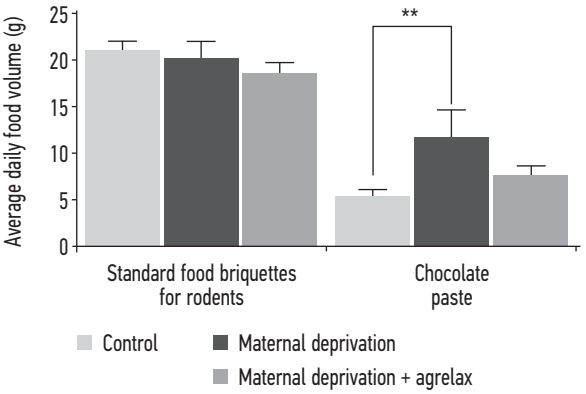

Fig. 2. The effect of maternal deprivation on the consumption of standard feed and chocolate paste when giving out chocolate 3 times a week. The average daily intake is shown. **$p < 0.001$ relative to the control (intact) group of animals

Рис. 2. Влияние материнской депривации (МД) на потребление стандартного корма и шоколадной пасты при выдаче шоколада 3 раза в неделю. Показано среднее суточное потребление. **$p < 0,001$ относительно контрольной (интактной) группы животных

The term "food addiction" refers to compulsive eating behavior associated with a lack of control over food [1, 2]. Eating behavior can be regulated by both homeostatic (related to energy need/storage) and hedonic (dopaminergic brain reward system) pathways, which control energy intake and body weight [10].

The present study produced compulsive overeating using the high-calorie food overeating method. Chronic maternal deprivation stress was shown to cause increased signs of compulsive overeating of high-calorie foods. In a restricted access model of compulsive overeating, episodes of overeating are generated by intermittent exposure to a carbohydrate and fat source [2]. Our findings of reduced high-calorie food intake in rats after maternal deprivation with a daily food ration support using an intermittent food regimen in developing compulsive overeating. In the control group of rats who received chocolate paste daily, elements of compulsive overeating behavior and withdrawal from the chocolate diet were found. This can be explained by the inclusion in the experiment of elements of waiting for food for 15 min during visual contact with food, which is consistent with literature data [9].

The chronic stress of maternal deprivation in animals is a model of human maternal neglect. Data from an experimental model of weaning from the mother in early ontogenesis show that stress significantly impacts the formation of compulsive overeating [9]. Early mental stress has a long-term impact on development and socialization in children and adolescents, increasing the risk of developing eating disorders and compulsive overeating. Adolescence is characterized by hormonal changes and an imbalance of excitation and inhibition processes, highlighting the vital role of neurochemical intracerebral processes in the formation of compulsive overeating [9].

Experimental modeling of several clinical manifestations allows direct investigation of neurochemical mechanisms underlying compulsive overeating. The experiment demonstrated the involvement of neuroendocrine processes and several neurotransmitter systems, particularly in its occurrence. In addition, opioid, dopamine, and serotonin systems are involved in forming positive emotions in compulsive overeating [3]. In addition to these primary mediators, the ghrelin system is involved in the mechanisms of compulsive overeating, as demonstrated in the present study.

Ghrelin acts primarily in the hypothalamus and stimulates eating behavior to regulate energy homeostasis [11]. Previously, we found that chronic stress of isolation rearing activated eating behavior and weight gain in rats [12]. Ghrelin signaling in brain regions outside the hypothalamus is important because of its impact on learning and memory, reward and motivation, and anxiety and depression. Corticoliberin-producing (CRH) neurons of the hypothalamic paraventricular nucleus are potential targets of ghrelin activity during stress. Ghrelin administration has been demonstrated to activate these neurons [13]. The target of ghrelin action under stress appears to be the extended amygdala system, which includes the bed nucleus of the terminal striatum, the central nucleus of the amygdala, the nerveless substance, and the shell of the contiguous nucleus, being an extrahypothalamic CRH system [13]. The extended amygdala structures receive inputs from dopaminergic neurons in the ventral tegmental area and are the main functional system for realizing the emotional–motivational effects of various narcogens. Blocking CRH in the central nucleus of the amygdala, the bed nucleus of the terminal striatum, and the contiguous nucleus eliminates or significantly reduces the activating effects of addictive drugs [14].

CONCLUSIONS

In conclusion, the study found that chronic maternal deprivation stress causes increased signs of compulsive overeating of high-calorie foods. Intranasal administration of agrelax, a novel ghrelin receptor antagonist, reduces food addiction manifestations in rats after maternal deprivation with intermittent consumption of high-calorie foods. This approach suggests new methods for synthesizing and using peptide-based pharmacological agents based on ghrelin and its antagonists for treating food addiction caused by psychogenic stresses in early ontogenesis. When daily chocolate consumption was examined, the average daily consumption, pre- and postinduction of agrelax, was lower ($p < 0.005$) in the maternal deprivation group than in the control group, indicating no food addiction was evident. Therefore, the development of compulsive overeating in rats with maternal deprivation depends on intermittent consumption of high-calorie tasty foods.

ADDITIONAL INFORMATION

Authors' contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study. The contribution of each author: A.A. Lebedev, S.S. Pyurveev, N.D. Nadbitova, A.V. Lizunov, E.R. Bychkov, V.V. Lukashkova, N.R. Evdokimova, M.A. Netesa, V.A. Lebedev — writing an article, data analysis; P.D. Shabanov — editing an article, developing a general concept.

Competing interests. The authors declare that they have no competing interests.

Funding source. The work was carried out within the framework of the state task of the Ministry of Education and Science of Russia FGWG-2022-0004 for 2022–2025 "Search of molecular targets for pharmacological action in addictive and neuroendocrine disorders and the creation of new pharmacologically active substances acting on CNS receptors".

REFERENCES

1. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. 5th edition*. Arlington, VA: American Psychiatric Publishing, 2013. DOI: 10.1176/appi.books.9780890425596

2. Boggiano MM, Artiga AI, Pritchett CE, et al. High intake of palatable food predicts binge-eating independent of susceptibility to obesity: An animal model of lean vs obese binge-eating and obesity with and without binge-eating. *Int J Obes*. 2007;31(9):1357–1367. DOI: 10.1038/sj.ijo.0803614

3. Nathan P, Bullmore E. From taste hedonics to motivational drive: central μ-opioid receptors and binge-eating behavior. *Int J Neuropsychopharmacol*. 2009;12(7):995–1008. DOI: 10.1017/s146114570900039x

4. Gnanapavan S, Kola B, Bustin SA, et al The tissue distribution of the mRNA of ghrelin and subtypes of its receptor, GHS-R, in humans. *J Clin Endocrinol Metab*. 2002;87(6):2988–2991. DOI: 10.1210/jcem.87.6.8739

5. Lebedev AA, Karpova IV, Bychkov ER, Shabanov PD. The ghrelin antagonist [D-LYS3]-GHRP-6 decreases signs of risk behavior in a model of gambling addiction in rats by altering dopamine and serotonin metabolism. *Neurosci Behav Physiol*. 2022;52(3):415–421. DOI: 10.19163/MedChemRussia2021-2021-259

6. Patterson ZR, Ducharme R, Anisman H, Abizaid A. Altered metabolic and neurochemical responses to chronic unpredictable stressors in ghrelin receptor-deficient mice. *Eur J Neurosci*. 2010;32(4):632–639. DOI: 10.1111/j.1460-9568.2010.07310.x

7. Geliebter A, Marci EG, Sami AH. Plasma ghrelin concentrations are lower in binge-eating disorder. *J Nutr*. 2005;135(5):1326–1330. DOI: 10.1093/jn/135.5.1326

8. Lebedev AA, Lukashkova VV, Pshenichnaya AG, et al. A new ghrelin receptor antagonist agrelax participates in the control of emotional-explorative behavior and anxiety in rats. *Psychopharmacology and biological narcology*. 2023;14(1):69–79. (In Russ.) DOI: 10.17816/phbn321624

9. Piccoli L, Micioni Di Bonaventura MV, Cifani C, et al. Role of orexin-1 receptor mechanisms on compulsive food consumption in a model of binge eating in female rats. *Neuropsychopharmacology*. 2012;37(9):1999–2011. DOI: 10.1038/npp.2012.48

10. Rossi MA, Stuber GD. Overlapping brain circuits for homeostatic and hedonic feeding. *Cell Metab*. 2018;27(1):42–56. DOI: 10.1016/j.cmet.2017.09.021

11. Alvarez-Crespo M, Skibicka KP, Farkas I, et al The amygdala as a neurobiological target for ghrelin in rats: neuroanatomical, electrophysiological and behavioral evidence. *PloS one*. 2012;7(10):e46321. DOI: 10.1371/journal.pone.0046321

12. Vetlugin EA, Bychkov ER, Abrosimov ME, et al. Anxiolytic and antidepressant effects of melanin-concentrating hormone 1 receptor antagonist SNAP 94847. *Pediatrician (St. Petersburg)*. 2022;13(1):25–34. DOI: 10.17816/PED13125-34

13. Cabral A, Suescun O, Zigman JM, Perello M. Ghrelin indirectly activates hypophysiotropic CRF neurons in rodents. *PloS one*. 2012;7(2): e31462. DOI: 10.1371/journal.pone.0031462

14. Roik RO, Lebedev AA, Shabanov PD. The value of extended amygdala structures in emotive effects of narcogenic with diverse chemical structure. *Research Results in Pharmacology*. 2019;5(3):11–19. DOI: 10.3897/npharmacology.5.38389

СПИСОК ЛИТЕРАТУРЫ

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th edition. Arlington, VA: American Psychiatric Publishing, 2013. DOI: 10.1176/appi.books.9780890425596

2. Boggiano M.M., Artiga A.I., Pritchett C.E., et al. High intake of palatable food predicts binge-eating independent of susceptibility to obesity: An animal model of lean vs obese binge-eating and obesity with and without binge-eating // Int J Obes. 2007. Vol. 31, No. 9. P. 1357–1367. DOI: 10.1038/sj.ijo.0803614

3. Nathan P., Bullmore E. From taste hedonics to motivational drive: central μ-opioid receptors and binge-eating behavior // Int J Neuropsychopharmacol. 2009. Vol. 12, No. 7. P. 995–1008. DOI: 10.1017/s146114570900039x

4. Gnanapavan S., Kola B., Bustin S.A., et al The tissue distribution of the mRNA of ghrelin and subtypes of its receptor, GHS-R, in humans // J Clin Endocrinol Metab. 2002. Vol. 87, No. 6. P. 2988–2991. DOI: 10.1210/jcem.87.6.8739

5. Lebedev A.A., Karpova I.V., Bychkov E.R., Shabanov P.D. The ghrelin antagonist [D-LYS3]-GHRP-6 decreases signs of risk behavior in a model of gambling addiction in rats by altering dopamine and serotonin metabolism // Neurosci Behav Physiol. 2022. Vol. 52, No. 3. P. 415–421. DOI: 10.19163/MedChemRussia2021-2021-259

6. Patterson Z.R., Ducharme R., Anisman H., Abizaid A. Altered metabolic and neurochemical responses to chronic unpredictable stressors in ghrelin receptor-deficient mice // Eur J Neurosci. 2010. Vol. 32, No. 4. P. 632–639. DOI: 10.1111/j.1460-9568.2010.07310.x

7. Geliebter A., Marci E.G., Sami A.H. Plasma ghrelin concentrations are lower in binge-eating disorder // J Nutr. 2005. Vol. 135, No. 5. P. 1326–1330. DOI: 10.1093/jn/135.5.1326

8. Лебедев А.А., Лукашкова В.В., Пшеничная А.Г., и др. Новый антагонист рецепторов грелина агрелакс участвует в контроле эмоционально-исследовательского поведения и уровня тревожности у крыс // Психофармакология и биологическая наркология. 2023. Т. 14, № 1. С. 69–79. DOI: 10.17816/phbn321624

9. Piccoli L., Micioni Di Bonaventura M.V., Cifani C., et al. Role of orexin-1 receptor mechanisms on compulsive food consumption in a model of binge eating in female rats // Neuropsychopharmacology. 2012. Vol. 37, No. 9. P. 1999–2011. DOI: 10.1038/npp.2012.48

10. Rossi M.A., Stuber G.D. Overlapping brain circuits for homeostatic and hedonic feeding // Cell Metab. 2018. Vol. 27, No. 1. P. 42–56. DOI: 10.1016/j.cmet.2017.09.021

11. Alvarez-Crespo M., Skibicka K.P., Farkas I., et al The amygdala as a neurobiological target for ghrelin in rats: neuroanatomical, electrophysiological and behavioral evidence // PloS one. 2012. Vol. 7, No. 10. ID e46321. DOI: 10.1371/journal.pone.0046321

12. Ветлугин Э.А., Бычков Е.Р., Абросимов М.Е., и др. Анксиолитическое и антидепрессивное действие SNAP 94847, антагониста рецептора 1-го типа меланин-концентрирующего гормона // Педиатр. 2022. Т. 13, № 1. С. 25–34. DOI: 10.17816/PED13125-34

13. Cabral A., Suescun O., Zigman J.M., Perello M. Ghrelin indirectly activates hypophysiotropic CRF neurons in rodents // PloS one. 2012. Vol. 7, No. 2. ID e31462. DOI: 10.1371/journal.pone.0031462

14. Roik R.O., Lebedev A.A., Shabanov P.D. The value of extended amygdala structures in emotive effects of narcogenic with diverse chemical structure // Research Results in Pharmacology. 2019. Vol. 5, No. 3. P. 11–19. DOI: 10.3897/npharmacology.5.38389

AUTHORS' INFO

***Andrei A. Lebedev,** Dr. Biol. Sci. (Pharmacology), professor, head of the Laboratory of General Pharmacology, Department of Neuropharmacology; address: 12 Akademika Pavlova st., Saint Petersburg, 197022, Russia;
ORCID: 0000-0003-0297-0425; eLibrary SPIN: 4998-5204;
e-mail: aalebedev-iem@rambler.ru

Sarng S. Pyurveev, junior research associate, Department of Neuropharmacology; assistant professor;
ORCID: 0000-0002-4467-2269; eLibrary SPIN: 5915-9767;
e-mail: dr.purveev@gmail.com

Natalia D. Nadbitova, Cans. Sci. (Med.), research associate, Department of Neuropharmacology;
e-mail: natali_805@mail.ru

Aleksey V. Lizunov, Cand. Sci. (Biol.), research associate, Department of Neuropharmacology;
e-mail: izya12005@yandex.ru

Eugenii R. Bychkov, Cand. Med. Sci. (Pathophysiology), head of the Laboratory, Department of Neuropharmacology;
ORCID: 0000-0002-8911-6805; eLibrary SPIN: 9408-0799;
e-mail: bychkov@mail.ru

Valeriya V. Lukashkova, postgraduare student, Department of Neuropharmacology.

Natalia R. Evdokimova, Cand. Sci. (Biol.), research associate, Department of Neuropharmacology;
e-mail: aalebedev-iem@rambler.ru

ОБ АВТОРАХ

***Андрей Андреевич Лебедев,** д-р биол. наук, профессор, заведующий лабораторией общей фармакологии, отдел нейрофармакологии им. С.В. Аничкова; адрес: Россия, 197376, Санкт-Петербург, ул. Академика Павлова, д. 12;
ORCID: 0000-0003-0297-0425; eLibrary SPIN: 4998-5204;
e-mail: aalebedev-iem@rambler.ru

Сарнг Саналович Пюрвеев, науч. сотр. отдела нейрофармакологии им. С.В. Аничкова;
ORCID: 0000-0002-4467-2269; eLibrary SPIN: 5915-9767;
e-mail: dr.purveev@gmail.com

Наталья Дмитриевна Надбитова, канд. мед. наук, научн. сотр. отдела нейрофармакологии им. С.В. Аничкова;
e-mail: natali_805@mail.ru

Алексей Владимирович Лизунов, канд. биол. наук, научн. сотр. отдела нейрофармакологии им. С.В. Аничкова;
e-mail: izya12005@yandex.ru

Евгений Рудольфович Бычков, канд. мед. наук, заведующий лабораторией отдела нейрофармакологии им. С.В. Аничкова; ORCID: 0000-0002-8911-6805;
eLibrary SPIN: 9408-0799; e-mail: bychkov@mail.ru

Валерия Владимировна Лукашкова, аспирант отдела нейрофармакологии им. С.В. Аничкова.

Наталья Ремовна Евдокимова, канд. биол. наук, научн. сотр. отдела нейрофармакологии им. С.В. Аничкова;
e-mail: aalebedev-iem@rambler.ru

* Corresponding author / Автор, ответственный за переписку

AUTHORS' INFO

Maria A. Netesa, postgraduate student, Department of Neuropharmacology; e-mail: saintula@gmail.com

Viktor A. Lebedev, Cand. Sci. (Biol.), research associate, Department of Neuropharmacology;
ORCID: 0000-0002-1525-8106; eLibrary SPIN: 1878-8392;
e-mail: vitya-lebedev-57@mail.ru

Petr D. Shabanov, Dr. Med. Sci. (Pharmacology), professor and head of the Department, Department of Neuropharmacology;
ORCID: 0000-0003-1464-1127; e-Library SPIN: 8974-7477;
e-mail: pdshabanov@mail.ru

ОБ АВТОРАХ

Мария Алексеевна Нетеса, аспирант отдела нейрофармакологии им. С.В. Аничкова; e-mail: saintula@gmail.com

Виктор Андреевич Лебедев, канд. биол. наук, научн. сотрудник отдела нейрофармакологии им. С.В. Аничкова;
ORCID: 0000-0002-1525-8106; eLibrary SPIN: 1878-8392;
e-mail: vitya-lebedev-57@mail.ru

Петр Дмитриевич Шабанов, д-р мед. наук, профессор, заведующий отделом нейрофармакологии им. С.В. Аничкова;
ORCID: 0000-0003-1464-1127; e-Library SPIN: 8974-7477;
e-mail: pdshabanov@mail.ru