Вестник Пермского университета. Серия Биология. 2022. Вып. 4. С. 340–346.
Bulletin of Perm University. Biology. 2022. Iss. 4. P. 340–346.

НЕЙРОБИОЛОГИЯ

Научная статья
УДК 57.024
doi: 10.17072/1994-9952-2022-4-340-346

Влияние галоперидола на формирование поведенческих паттернов у взрослых крыс

Мария Константиновна Гузенко[1], **Эдуард Арменакович Коркотян**[2,3✉]
[1, 2] Пермский государственный национальный исследовательский университет, Пермь, Россия
[3✉] Институт им. Вейцмана, Реховот, Израиль, Eduard.korkotian@weizmann.ac.il, https://orcid.org/0000-0001-5515-3387

Аннотация. Представлено применение нового подхода к анализу поведения лабораторных крыс, основанного на цветовом кодировании видеоряда. Были выявлены особенности поведения у крыс, инъецированных галоперидолом. У экспериментальной группы двигательная активность на периферии оказалась достоверно ниже контрольной. Более того, прослеживалась тенденция к существенному снижению двигательной активности во второй половине тестового периода. У контрольной и экспериментальной групп наблюдалась выраженная разница в таких паттернах, как продвижение вперед, повороты вправо, влево и развороты назад. Среди статических критериев, достоверная разница в пользу контроля наблюдалась в пропорции следующих типов поведения: обнюхивание воздуха, стенок, пола, обследование лунок арены, стойки на задних лапах с опорой и без. Применение разработанного нами метода совмещения в одном кадре трех временных точек: настоящего, ближайшего и более отдаленного будущего, впервые позволило установить ряд важных закономерностей. Так, у группы, получившей галоперидол, гораздо сильнее, чем в контроле, оказалась выражена предсказательность будущего двигательного паттерна на основе текущего положения головы и/или туловища животного. Кроме того, для животных, инъецированных галоперидолом, была свойственна выраженная стереотипность моторной активности с доминированием однонаправленного движения. Метод совмещения кадров способен обеспечить объективность и высокую надежность при наиболее сложном виде поведенческого анализа, выявлении динамических паттернов. В дальнейшем эти сведения потребуются для получения оптимального массива и приемлемого разнообразия данных для применения к ним методов машинного обучения и автоматизации процесса распознавания паттернов.

Ключевые слова: галоперидол, тест «открытое поле», паттерны поведения, временное цветовое кодирование, двигательная активность, экстрапирамидные расстройства

Для цитирования: Гузенко М. К., Коркотян Э. А. Влияние галоперидола на формирование поведенческих паттернов у взрослых крыс // Вестник Пермского университета. Сер. Биология. 2022. Вып. 4. С. 340–346. [На англ.]. http://dx.doi.org/10.17072/1994-9952-2022-4-340-346.

Благодарности: выражаем благодарность Санкт-Петербургскому государственному химико-фармацевтическому университету и лично доктору медицинских наук, профессору, заведующему кафедрой фармакологии и клинической фармакологии СПХФУ Оковитому Сергею Владимировичу за предоставленные экспериментальные материалы.

NEUROBIOLOGY

Original article

The effect of haloperidol on the formation of behavioral patterns in adult rats

Maria K. Guzenko[1], **Eduard Korkotian**[2,3✉]
[1, 2] Perm State University, Perm, Russia
[3✉] The Weizmann Institute of Science, Rehovot, Israel, eduard.korkotian@weizmann.ac.il, https://orcid.org/0000-0001-5515-3387

Abstract. The application of a new approach to the analysis of the behavior of laboratory rats based on the color coding of the video frame sequence is presented. Behavioral features were identified in rats injected with haloperidol. In the experimental group, motor activity on the periphery of arena was significantly lower than in the control group. Moreover, there was a tendency to a significant decrease in physical activity in the second half of the test period. In the control and experimental groups, there was a pronounced difference in such patterns as moving forward, turning right, left and turning back. Among the static criteria, a significant difference in favor of the control was observed in the proportion of the following types of behavior: sniffing the air, walls or floor, examination of the arena holes, rearings with and without support. The application of the self-developed method, combining three time points in one frame: the present, the nearest and the more distant future, allowed us to establish a number of important rules. Thus, in the group that received haloperidol, the prediction of the future motor pattern based on the current position of the head and/or body of the animal turned out to be much stronger than in the control group. In addition, for animals injected with haloperidol, a pronounced stereotype of motor activity was characteristic. The combined frames were able to provide objectivity and high reliability in the most complex behavioral analysis, the dynamic patterns. In the future, this information will be required to obtain an optimal array and an acceptable variety of data for applying machine learning methods and automating the process of pattern recognition.

Keywords: haloperidol, open field test, behavioral patterns, temporal color coding, motor activity, extrapyramidal disorders

For citacion: Guzenko M. K., Korkotian E. The effect of haloperidol on the formation of behavioral patterns in adult rats. *Bulletin of the Perm University. Biology*. Iss. 4 (2022): pp. 340-346. http://dx.doi.org/10.17072/1994-9952-2022-4-340-346.

Acknowledgments: we express our gratitude to the St. Petersburg State Chemical-Pharmaceutical University (SPCPU) and personally to the Doctor of Medical Sciences, Professor, Head of the Department of Pharmacology and Clinical Pharmacology of the SPCPU Okovitoy Sergey Vladimirovich for the provided experimental materials.

Introduction

Traditionally, experiments conducted on laboratory animals for various scientific purposes retain a high level of importance and relevance. First, the data obtained in such studies are needed in the pharmaceutical industry [Sysoev et al., 2022], since the life and health of human patients depend on the results, evaluating the effectiveness and safety of drugs.

Schizophrenia is a serious and still insufficiently understood mental disorder that affects about 1% of the general population [Harris et al., 2013]. Despite the fact that the true causes and mechanism of development of this disorder have not been well established, there are quite effective medical approaches of the treatment that can supress many of the schizophrenic symptoms. However, a complete cure of such patients is not yet possible, although in some cases a long-term remission can be achieved. The most common medicine that has been successfully used for a long time to treat the symptoms of the schizophrenia spectrum is the antipsychotic drug haloperidol. Nevertheless, a number of features and side effects [Irving et al., 2006] characterizes the action of the drug. In experimental practice, when evaluating the pharmacological effect, it is customary to rely on the degree of suppression of disorders at the behavioral level [Drozdov et al., 2011].

Behavior is an objective indicator of the functioning of the nervous system and the effects of pharmacological drugs on the body. Understanding the activity of the brain as a whole is based not only on the study of molecular, genetic, physiological and other aspects, but also on behavioral features that clearly reflect the key function of the brain – control of movements and motor activity in general.

One of the main difficulties in interpreting the results of behavioral tests is the subjectivity of the assessment of certain isolated criteria by different researchers [Tecott, Nestler, 2004]. Often it results in an oversimplification and one-pointedness of the range of selected analysis methods. In our study, we made an attempt to get as close as possible to the automated method of recording and processing animal behavior patterns, using the video sequence color coding method [Molodij, 2020]. Thus, the purpose of our study is to reveal the effects of haloperidol on the formation of behavioral patterns in laboratory rats in the open field test using novel self-developed color-coding method.

Materials & Methods

Animals. The study was carried out in accordance with the principles of the Basel Declaration and the Order of the Ministry of Health of the Russian Federation dated April 1, 2016 No. 199n “On Approval of the Rules for Good Laboratory Practice”, as well as the recommendations of the Russian Ministry of Health. The rats were kept under standard vivarium conditions on a 12-hour day/night cycle and with free access to water and food. The experiments were carried out on 20 outbred male rats weighing 250-300 g.

Animal sampling and description of experiments. The animals were divided into 2 groups of 10 rats in each. Experimental animals were injected with a solution of haloperidol intraperitoneally at a concentration of 0.3 mg/kg, with an injection volume of 0.5 ml. As a control, physiological saline was administered, also in a volume of 0.5 ml. The drug exposure time was 20 minutes [Sysoev et al., 2022]. Next, the rats were placed in the “open field” setup, which was a round black experimental arena, 97 cm in diameter, divided into 19 sectors of equal area, and equipped with holes in the floor. Video recording was carried out using a Canon 5D camera, at the rate of 30 frames per second, for 3 minutes, at 320 lux illumination. The camera was controlled remotely using the EOS Utility software. The images of arena were displayed on the experimenter's monitor.

Visualization and data analysis. The following behavioral patterns were recorded: moving forward, turning the head/body to the right, to the left, turning back, standing on the hind legs with and without support against the wall, examining holes, sniffing the space, grooming, and freezing.

Most of the video recordings were viewed in their original form. At that time, the main patterns were identified, described and counted. Further, using the Python programming language in the Google Colab environment, the records were processed using the OpenCV library. Color-coding of video recordings made it possible to display the present (t=0), the near future (t=0.33 s) and the more distant future (t=1.66 s) in different colors and combine all three in one frame. Thus, each frame was the result of the augmentation procedure.

Statistical analysis. Statistical processing of the results was carried out using the Student's t-test or the Mann-Whitney U-test using the Past and Excel computer programs. The normality of data distribution in the samples was determined using the Shapiro-Wilk test. For the actual presentation of the obtained data, such indicators of descriptive statistics as the arithmetic mean ± standard error of the mean (SEM) were used. Differences between groups were recognized as statistically significant if the probability of the calculated difference between the samples was $p < 0.05$. If the significance limit was exceeded, the differences were considered non-significant (N.S.). In addition, when studying the dependence of the expression of motor activity in experimental rats on the time factor, one-way analysis of variance (ANOVA) was used, followed by a pairwise post hoc comparison based on the Tukey's test. Differences were defined as significant at $p < 0.05$.

Results and Discussion

The open field test makes it possible to analyze motor activity, exploratory behavior, and anxiety in rats and mice [Carola et al., 2002]. The analysis of motor patterns of behavior is one of the main reasons for conducting this test. Therefore, from the total volume of the revealed patterns, we first studied the motor ones. Among the variety of dynamic patterns, to assess the overall motor activity in the center and on the periphery of the arena, we took into account the following simple ones: forward movement, turns to the right, left and 180°, as well as the direction of the head forward, right or left. Injection of the antipsychotic drug haloperidol resulted in significant differences in the motor activity of the animals compared to the control, and mainly at the periphery of the arena. In the group that received haloperidol, motor activity in the periphery was significantly lower and amounted to 19.3±1.18 cases of any dynamic patterns compared to 42.2±4.24 in the control; $p < 0.001$ (Fig. 1). It is interesting to note that there were no significant differences in motor activity in the center of the field between the groups, since the representatives of both groups spent a relatively small part of the time in the central sectors of the arena compared to the time spent near the walls of the field.

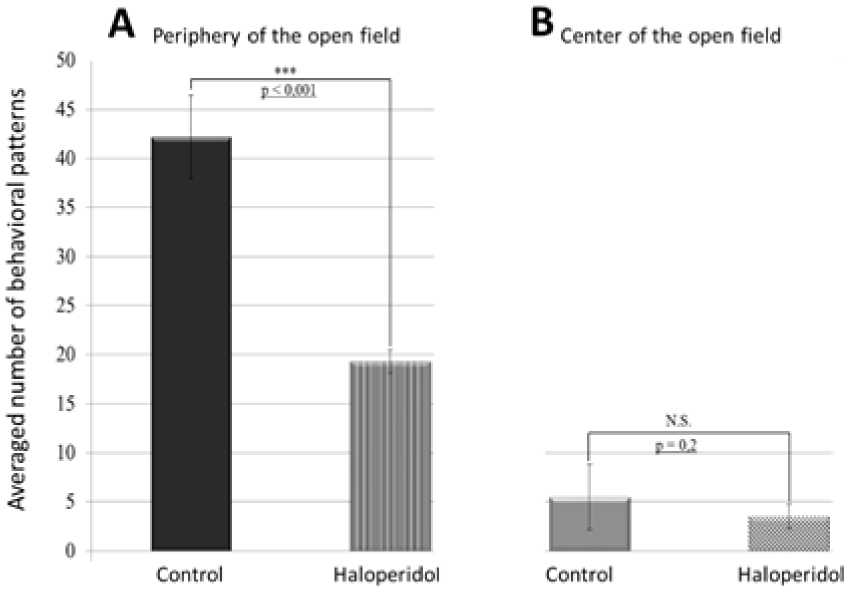

Fig. 1. The average number of overall dynamic behavioral patterns on the periphery (A) and in the center (B) of the «open field» arena of the «Control» (left columns) and "Haloperidol" (right columns)

In general, many researchers determine the restless behavior or anxiety of animals by the proportion of time spent in the open space of the arena compared to hiding in the shelter [Wahlsten, 2011]. However, as a rule, the very fact of a shorter stay in the center is explained by natural causes, since rodents tend to avoid large, open, and brightly lit spaces [Prut and Belzung, 2003].

We calculated the average sum of patterns for consecutive 30-second segments of a total 3-minute-long recording. Thus, the total registration time was reduced to six discrete time points. During the first minute of registration, the activity in both groups was the same. Later, in animals injected with haloperidol, a gradual decrease in activity began, and by the last minute of the recording, their activity fell to minimal values.

This tendency to decrease in activity may indicate insufficiency in the action of the dopaminergic system of the brain, antagonized by haloperidol. It is well known that dopamine plays a key role in the modulation of motor functions. The lack of its synthesis, overproduction, as well as blocking of dopamine receptors, leads to the development of pathological forms of some forms of behavior, manifested in violations of locomotion. Thus, dopamine deficiency leads to hypokinesia, as in Parkinson's disease [Zvezdochkina et al., 2004].

Based on the dispersion analysis of recorded time points, it was found that the dynamics of changes in the activity of two groups differ significantly at three time points: 4, 5, and 6, which corresponded to the last 1.5 minutes of recording. It follows that animals treated with haloperidol cease to reveal curiosity and normal activity much earlier than control animals. The calculated probabilities of differences for the mentioned time points were: $p < 0.0006$, $p < 0.0002$, and $p < 0.0001$ for the points 4, 5 and 6, respectively.

It has been previously found that treatment with haloperidol, as well as with similar antipsychotics, pronounces extrapyramidal disorders [Strange, 2008]. Side effects of a dynamic nature that affect motor activity are associated with symptoms such as tremor, bradykinesia, muscle rigidity, etc. Indeed, while observing the video files, we have identified a number of cases that confirm mentioned phenotypes. For example, most treated rats often stood still or freeze for various periods, while convulsively shaking their heads or, as it were, “nodding”. In general, their movements were slowed down, with repeated cases of uneven gait and atypical paw placement or "sliding" on their side to the left or right against a background of general unsteadiness.

Figure 2 shows a pairwise comparison of the main motor patterns in two groups of rats. Analysis using the Student's t-test showed that the p-values of the differences in the number of head turns to the right and left were statistically insignificant (in all cases $p > 0.05$).

The average number of movements in the control group was as follows: forward 12.2±2.4, 180º turns 3.3±0.4, right and left 11.8±1.9 and 11.6±2.2, respectively. For the group treated with haloperidol, these parameters were: forward 3.6±1.0, backward 1.8±0.5, right and left 3.2±0.6 and 3.6±0.6, respectively. Statistical analysis demonstrated that the numbers of shifts forward and turns to the sides and back in the treated group were significantly smaller compared to the control: $p<0.004$, $p<0.001$, $p<0.002$ and $p<0.028$, respectively.

In addition to the mentioned motor patterns, the following indicators were also calculated: sniffing the walls, floor, air, grooming, rearing with and without support on the wall, etc. Applying the Mann-Whitney test, we found that the differences between the control group and the haloperidol-treated group were significant for most indicators: air sniffing 4.7±0.65 vs. 12.1±2.9 ($p < 0.05$), wall sniffing 2.9±0.8 vs. $p < 0.001$), floor sniffing 0.4±0.2 vs. 2.2±0.5 ($p < 0.02$), rearing with support 1.2±0.5 vs 4.4±1.0 ($p < 0.4$) and without support 0.2±0.1 vs 1.6±0.6 ($p < 0.02$). The cases of grooming among groups did not differ statistically ($p > 0.05$). The "freezing" pattern was recorded only in the group injected with haloperidol solution.

Such indicators of behavioral activity, which are mentioned above, as a rule, indicate the degree of orienting-exploratory activity, anxiety, and the emotional component as such. Thus, a study conducted by Zvezdochkina et al. [2004] revealed a pronounced decrease in orienting-exploratory behavior in laboratory rats after injection of haloperidol in the open field test, as well as a decrease in the number of grooming acts, which has considered indicating an increase in anxiety and the development of inhibitory processes in the CNS. However, such an indicator as grooming cannot be defined as an unambiguous factor of anxiety, since it can also mean a comfortable and calm state in which the animal is. Based on this, the variability of this parameter should not be considered as a marker of the effect of haloperidol, or any other pharmaceutical preparation of a similar family. It is also undeniable how important the role of the emotional component in motor functions is, since it has been found that it is the mesocorticolimbic pathway that modulates the responses that are associated with fear and anxiety [De Souza Caetano et al., 2013].

A study by Drozdov et al. [2011] also confirms a decrease in locomotor activity in rats after haloperidol administration. It appears that our results are not random, but reflect an objective trend. The dose factor of the administered drug, as we assume, is also of great importance. Studies have not found a minimum dose that would cause the effect of reducing motor functions. Nevertheless, the inhibition of motor activity in rats in the study by Amtage and Shmidt [2003] was registered already following the introduction of 0.1 mg/kg of haloperidol. This does not exclude the onset of catalepsy. As a rule, it is initiated at doses higher than previously described, however, at a dose of 0.1 mg/kg, the development of catalepsy is not excluded.

Using color-coding corresponding to three time points, we tried to predict the future position of rats based on the position of the head, tail, or torso. To do this, we have chosen four patterns that will happen in future: shift forward, 180º turn, right and left turns. The collected quantitative data were divided among these four groups. It has been suggested that the turn of the tail in one direction or another serves as a sign by which one can determine the likelihood of certain patterns in the near future. It also drew attention to the fact that animals often turn their tail and/or head in the direction of future movement. For analysis, three parts of body were selected in the present: the position of the head, tail and torso. Each of the factors was related to the future in the following way: can the position of each part of the body serve as a predictive guide for future movement to the right, left, forward or backward?

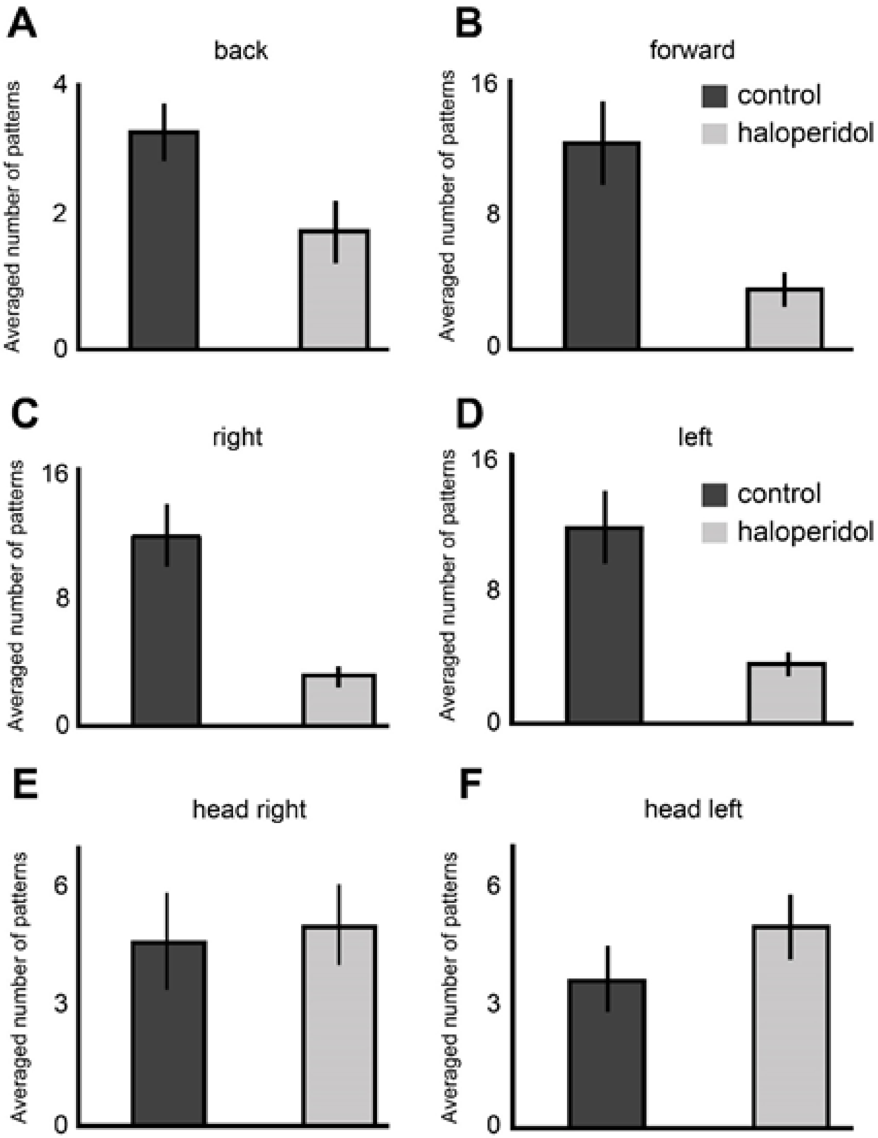

Fig. 2. Comparison of the average number of dynamical patterns between control (dark gray) and haloperidol (light gray) groups.

A, 180º, back; B, forward movement; C, turns right; D, turn left; E, head turned right; E, head turned left

The position of the tail as a predictive criterion was not justified. Using the t-test, we found that only the head and torso were predictive for the four selected patterns. Indeed, we recorded a rather high probability that haloperidol-injected rats increased the predictive power of head and/or trunk position compared to control group ($p<0.008$). In addition, it was noted that in the haloperidol group there were fewer failures in predictions.

The color coding method used here has shown its effectiveness in data analysis and processing. The results obtained are consistent with data from various sources, in which both traditional imaging methods and modern ones were used. This concerned the factor of the side effect of haloperidol on the decrease in motor activity, orienting-exploratory behavior, and features of the trajectory of motor activity. Thus, the color coding method opens up new perspectives in working with biological images using a relatively simple technique. For the efficient operation of neural networks, the creation of a larger database is required. We hope that in the near future, the combination of traditional methods for studying the brain and the effect of drugs on it, with modern methods of machine learning and computer vision will make it possible to identify motor disorders and other neurological disorders in patients at the early stages of pathology development. It may also help in the search for new drugs and methods for the treatment and prevention of brain diseases in humans.

Список источников

1. Дроздов А.Л. и др. Влияние психотропных лекарственных средств на спонтанную поведенческую активность белых крыс // Вісник Дніпропетровського університету. Біологія. Медицина. 2011. Т. 1, вип. 2. С. 47–53.

2. Звездочкина Н.В., Муранова Л.Н., Андрианов В.В. Локомоторные реакции и возбудимость нейронов в условиях блокады дофамина галоперидолом у беспозвоночных и позвоночных животных // Российский физиологический журнал им. И.М. Сеченова. 2004. Т. 90, № 11. С. 1381–1392.

3. Сысоев Ю.И. и др. Метод регистрации биоэлектрической активности коры головного мозга у крыс в условиях хронического эксперимента // Российский физиологический журнал им. И.М. Сеченова. 2022. Т. 108, № 2. С. 279–290.

4. Amtage J., Schmidt W.J. Context-dependent catalepsy intensification is due to classical conditioning and sensitization // Behavioural pharmacology. 2003. Vol. 14, № 7. P. 563–567. DOI: 10.1097/00008877-200311000-00009.

5. Carola V. et al. Evaluation of the elevated plus-maze and open-field tests for the assessment of anxiety-related behaviour in inbred mice // Behavioural brain research. 2002. Vol. 134, № 1–2. P. 49–57. DOI: 10.1016/s0166-4328(01)00452-1.

6. de Souza Caetano K.A., de Oliveira A.R., Brandao M.L. Dopamine D2 receptors modulate the expression of contextual conditioned fear: role of the ventral tegmental area and the basolateral amygdala // Behavioural pharmacology. 2013. Vol. 24, № 4. P. 264–274. DOI: 10.1097/FBP.0b013e32836356c4.

7. Harris L.W. et al. Schizophrenia: metabolic aspects of aetiology, diagnosis and future treatment strategies // Psychoneuroendocrinology. 2013. Vol. 38, № 6. P. 752–766. DOI: 10.1016/j.psyneuen.2012.09.009.

8. Irving C.B., Adams C.E., Lawrie S. Haloperidol versus placebo for schizophrenia // Cochrane Database of Systematic Reviews. 2006. № 4. DOI: 10.1002/14651858.CD003082.

9. Molodij G. et al. Time-space Fourier κω′ filter for motion artifacts compensation during transcranial fluorescence brain imaging // Physics in Medicine & Biology. 2020. Vol. 65, № 7. DOI: 10.1088/1361-6560/ab7631.

10. Prut L., Belzung C. The open field as a paradigm to measure the effects of drugs on anxiety-like behaviors: a review // European journal of pharmacology. 2003. Vol. 463, № 1–3. P. 3–33. DOI: 10.1016/S0014-2999(03)01272-X.

11. Strange P.G. Antipsychotic drug action: antagonism, inverse agonism or partial agonism // Trends in pharmacological sciences. 2008. Vol. 29, № 6. P. 314–321. DOI: 10.1016/j.tips.2008.03.009.

12. Tecott L.H., Nestler E.J. Neurobehavioral assessment in the information age // Nature neuroscience. 2004. Vol. 7, № 5. P. 462–466. DOI: 10.1038/nn1225.

13. Wahlsten D. Mouse behavioral testing. How to use mice in behavioral neuroscience. Elsevier: Academic Press, 2011. 304 p.

References

1. Drozdov A.L., Demchenko E.M., Ejjyad A., Nerush O.P. [Influence of psychotropic drugs on spontaneous behavioral activity of albino rats]. *Visnyk of Dnipropetrovsk University. Biology. Medicine.* V. 1, No 2 (2011): pp. 47-53. (In Russ.).

2. Zvezdochkina N.V., Muranova L.N., Andrianov V.V., Arkhipova S.S., Gainutdinov Kh.L., Golubev A.I., Pleshchinskii I.N. [Locomotor reactions and excitability of neurons during the blockade of dopamine by haloperidol in vertebrate and invertebrate animals]. *Rossijskij fiziologičeskij žurnal imeni I.M. Sečenova.* Vol. 90, No 11 (2004): pp. 1381-1392. (In Russ.). DOI: 90(11):1381-92.

3. Sysoev Yu.I., Prikhodko V.A., Idiyatullin R.D., Chernyakov, R.T., Karev V.E., Okovitiy S.V. [A Method for Chronic Registration of Brain Cortical Electrical Activity in Rats]. *Rossijskij fiziologičeskij žurnal imeni I.M. Sečenova.* Vol. 108, No 2 (2022): pp. 279-290. (In Russ.).

4. Amtage J., Schmidt W.J. Context-dependent catalepsy intensification is due to classical conditioning and sensitization. *Behavioural pharmacology.* Vol. 14, No 7 (2003): pp. 563-567. DOI: 10.1097/00008877-200311000-00009.

5. Carola V., D'Olimpio F., Brunamonti E., Mangia F., Renzi P. Evaluation of the elevated plus-maze and open-field tests for the assessment of anxiety-related behaviour in inbred mice. *Behavioural brain research.* Vol. 134, No 1-2 (2002): pp. 49-57. DOI: 10.1016/s0166-4328(01)00452-1.

6. de Souza Caetano K. A., de Oliveira A. R., Brandao M. L. Dopamine D2 receptors modulate the expression of contextual conditioned fear: role of the ventral tegmental area and the basolateral amygdala. *Behavioural pharmacology*. Vol. 24, No 4 (2013): pp. 264-274. DOI: 10.1097/FBP.0b013e32836356c4.

7. Harris L.W., Guest P.C., Wayland M.T., Umrania Y., Krishnamurthy D., Rahmoune H., Bahn S. Schizophrenia: metabolic aspects of aetiology, diagnosis and future treatment strategies. *Psychoneuroendocrinology.* Vol. 38, No 6 (2013): pp. 752-766. DOI: 10.1016/j.psyneuen.2012.09.009.

8. Irving C.B., Adams C.E., Lawrie S. Haloperidol versus placebo for schizophrenia. *Cochrane Database of Systematic Reviews*. No 4 (2006). DOI: 10.1002/14651858.CD003082.

9. Molodij G., Sdobnov A., Kuznetsov Y., Harmelin A., Meglinski I., Kalchenko V. Time-space Fourier κω′ filter for motion artifacts compensation during transcranial fluorescence brain imaging. *Physics in Medicine & Biology*. Vol. 65, No 7 (2020). DOI: 10.1088/1361-6560/ab7631.

10. Prut L., Belzung C. The open field as a paradigm to measure the effects of drugs on anxiety-like behaviors: a review. *European journal of pharmacology*. Vol. 463, No 1-3 (2003): pp. 3-33. DOI: 10.1016/S0014-2999(03)01272-X.

11. Strange P.G. Antipsychotic drug action: antagonism, inverse agonism or partial agonism // Trends in pharmacological sciences. Vol. 29, No 6 (2008): pp. 314-321. DOI: 10.1016/j.tips.2008.03.009.

12. Tecott L.H., Nestler E.J. Neurobehavioral assessment in the information age. *Nature neuroscience.* Vol. 7, No 5 (2004): pp. 462-466. DOI: 10.1038/nn1225.

13. Wahlsten D. Mouse behavioral testing. How to use mice in behavioral neuroscience. Elsevier, Academic Press, 2011. 304 p.

Статья поступила в редакцию 18.10.2022; одобрена после рецензирования 09.11.2022; принята к публикации 29.11.2022.

The article was submitted 18.10.2022; approved after reviewing 09.11.2022; accepted for publication 29.11.2022.

Информация об авторах

М. К. Гузенко – магистрант кафедры фармакологии и фармации;

Э. А. Коркотян – доктор философии, зав. лабораторией конфокальной микроскопии.

Information about the authors

M. K. Guzenko – master of the Department of Pharmacology and Pharmacy;

E. A. Korkotian – Doctor of Philosophy, Head of Confocal Microscopy Division.

Вклад авторов:

Гузенко М. К. – развитие методологии; создание базы данных; статистическая обработка данных; написание исходного текста; создание иллюстраций.

Коркотян Э. А. – научное руководство; концепция исследования; создание методологии; оформление иллюстраций; написание окончательного текста.

Contribution of the authors:

Guzenko M. K. – development of methodology; database creation; statistical data processing; writing the initial draft; creating illustrations.

Korkotian E. – scientific management; research concept; creation of methodology; illustration design; writing the final text.