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Research Article

The effect of acute swimming stress, corticosterone, dexamethasone, and fludrocortisone on anxiety-like behavior in mice

Nikita V. Kudryashov[1,2], Alexander A. Gorbunov[1], Sergey E. Mironov[1], Dmitriy A. Tikhonov[1], Andrey A. Nedorubov[1], Olga Yu. Arshinova[1], Maria A. Simukhina[1], Vera N. Busol[1], Vladimir P. Fisenko[1]

1 Sechenov First Moscow State Medical University (Sechenov University), 8-2 Trubetskaya str., Moscow, 119991, Russia
2 Federal State Budgetary Scientific Institution "Federal Research Center for Innovator and Emerging Biomedical and Pharmaceutical Technologies", 8 Baltijskaya str., Moscow, 125315, Russia

Corresponding author: Nikita V. Kudryashov (kudryashov_n_v@staff.sechenov.ru)

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Abstract

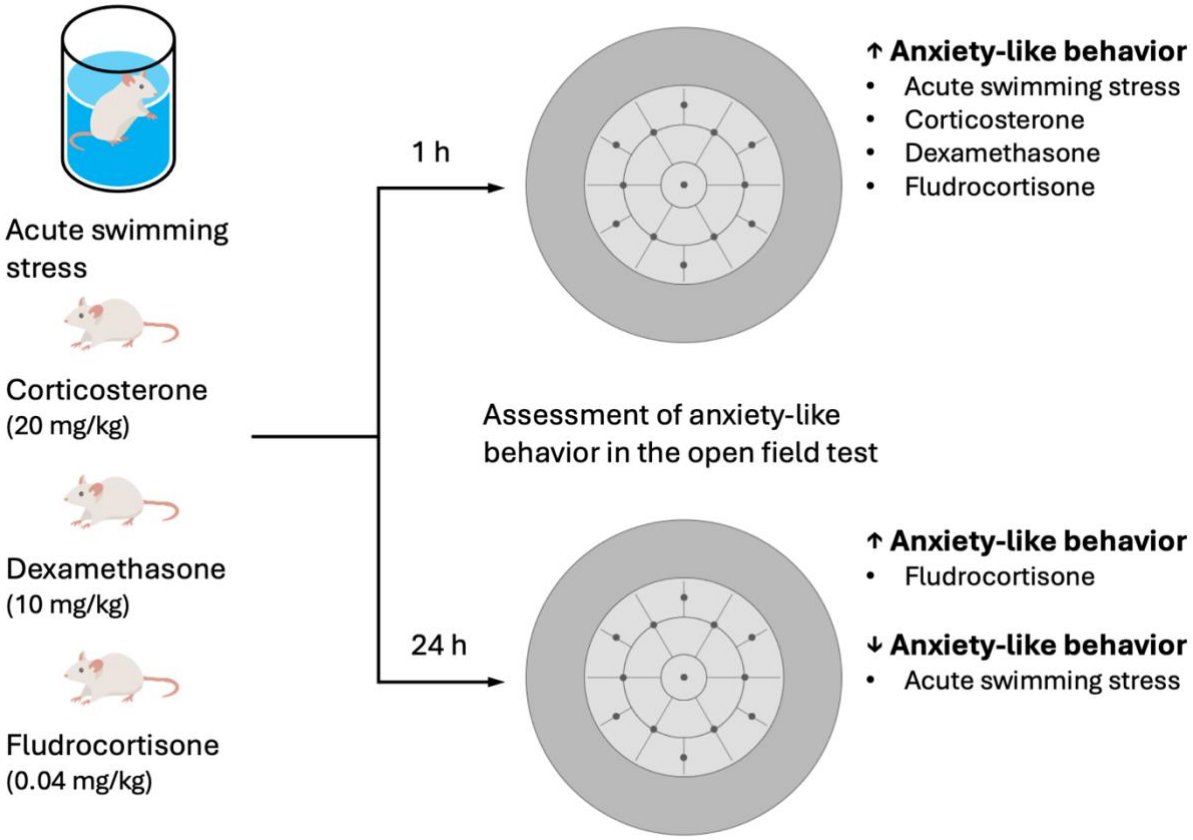
Introduction: Acute swimming stress (ASS) exerts a biphasic effect on anxiety-like behavior (ALB) in mice, inducing an enhancement and a subsequent decrease in ALB 1 h and 24 h after exposure, respectively. Presumably, this effect may be caused by the activation of mineralocorticoid and glucocorticoid receptors, both during the immediate response to acute stress and after its termination at the phase of adaptive changes. **Aim of the Research**: Comparative study of the effects of acute swimming stress, corticosterone, dexamethasone, and fludrocortisone on ALB in mice 1 h and 24 h after stress exposure or administration of the studied substances.

Materials and Methods: To model ASS in adult male ICR mice, the forced swimming test (FST) was employed. ALB was assessed in mice in the open field test 1 h and 24 h after FST or systemic administration of corticosterone (20 mg/kg), dexamethasone (10 mg/kg), and fludrocortisone (0.04 mg/kg).

Results: Central activity and anxiety index were increased 1 h after exposure to FST, while an increase in the anxiety index was observed 24 h after exposure to FST in the open field test compared to the non-stressed mice. Corticosterone, dexamethasone, and fludrocortisone decreased central activity and anxiety index 1 h after the administration, compared to the control group. However, fludrocortisone decreased central activity and total locomotor activity 24 h after administration compared to the control group.

Conclusion: A similar pattern of enhancement of anxiety-like behavior was observed in mice 1 h after FST or the administration of corticosterone (single dose 20 mg/kg, i.p.), dexamethasone (single dose 10 mg/kg, i.p.), and fludrocortisone (single dose 0.04 mg/kg, i.p.). Nonetheless, 24 h after exposure to stress or administration of the studied substances, FST decreased ALB, fludrocortisone enhanced ALB, while corticosterone and dexamethasone showed no effect on ALB in mice 24 h after exposure to stress or administration of the studied substances.

Graphical abstract



Keywords

acute swimming stress, anxiety, corticosterone, dexamethasone, fludrocortisone, mouse, open field test

Introduction

The forced swimming test (FST) is one of the most frequently employed tests for the evaluation of antidepressant-like activity of pharmacological substances in preclinical studies. FST was developed and first described by R.D. Porsolt et al. (1977). Subsequently, numerous modifications of FST have been reported. In this test, rats or mice are placed into transparent cylinders filled with water, from which the animals cannot escape. Depressive-like behavior is manifested by a progressive increase in animal's immobilization time after the initial attempt to escape from the cylinder. During repeated testing, the total immobilization time increases, while the latent period until the first episode of immobility decreases (Kloet de and Molendijk 2016; Pesarico et al. 2020). The increase in immobilization time is interpreted as a state of despair and a depression-like behavioral phenotype (Can et al. 2012; Pesarico et al. 2020).

It was hypothesized that the increase in immobilization time should be considered as an adaptive response to acute stress (Molendijk and Kloet de 2022) mediated by corticosteroids and implemented through the stimulation of mineralocorticoid (MR) and glucocorticoid receptors (GR) (Kloet de and Molendijk 2016; Ruiz-Sánchez et al. 2021). This mechanism ensures the selection of behavioral strategies in acute stress situations, as well as the consolidation and retention of information on the stress event (Kloet de and Molendijk 2016; Commons et al. 2017). Consequently, FST can be considered as an acute stress paradigm. Furthermore, it has been established that acute swimming stress (ASS) differentially affects anxiety-like behavior

(ALB) in mice in the open field test, depending on the time elapsed after exposure to acute stress. In particular, ALB increases 1 h after the ASS, followed by paradoxical anxiolysis 24 h after exposure (Kudryashov et al. 2022). Presumably, the described dynamics of ALB in mice exposed to ASS are mediated by the balance between MR and GR activation by corticosteroids.

The aim of our research was to conduct a comparative study of the effects of exposure to ASS and administration of corticosterone, dexamethasone, and fludrocortisone on ALB in mice using the open field test. Behavioral assessments were performed 1 h and 24 h after acute stress exposure or administration of the studied substances.

Materials and Methods

Animals

The experiments were conducted on 120 adult male ICR mice weighing 20-22 g (the breeding station "Andreevka" of the Federal State Budgetary Scientific Institution "Scientific Center for Biomedical Technologies" of the Federal Medical and Biological Agency of Russia). The animals were kept in standard conditions with natural day/night light cycles and free access to water and food. The experiments were performed in accordance with the European Community Council Directive 2010/63/EEC and the Decision of the EEC Council dated 03.11.2016 No. 81 "On Approval of the Rules of Good Laboratory Practice of the Eurasian Economic Union in the Field of Circulation of Medicinal Products". All the procedures with animals were considered and approved by the Local Ethics Committee (Minutes № 24-22 of 12 November 2024).

Substances

In the present research, the following substances were employed: corticosterone (20 mg/kg, Sigma Aldrich, USA), dexamethasone (10 mg/kg, JSC "Production Pharmaceutical Company Renewal", Russia), and fludrocortisone (0.04 mg/kg, Sigma Aldrich, USA). Corticosterone and fludrocortisone were used as an emulsion with Tween-80 (Sigma Aldrich). The equivalent volume (0.1 mL per 10 g of animal body weight) of 0.9% sodium chloride solution with the addition of Tween-80 (Sigma Aldrich) was used as a control. The studied substances were administered intraperitoneally 1 h and 24 h before the open field test. The doses of the substances were selected in accordance with the earlier published data (Zhao et al. 2007; Vafaei et al. 2008; Laviolle et al. 2014).

Acute swimming stress

To model acute stress, mice were placed for 10 min in plastic cylinders for the FST (30 cm height, 10 cm in diameter, OpenScience, Russia), which were filled with water to the height of 20 cm at a temperature of 22°C. The mice were then gently dried and returned to their boxes (Kudryashov et al. 2022).

Open field test

To assess ALB, a circular "Open Field" set was used (inner set diameter 63 cm, wall height 32 cm, floor hole diameter 1 cm, OpenScience, Russia). The illumination of the set was 300 lux, and before being placed in the set, the mice were kept in darkness for 30 minutes in a chamber with 5 lux illumination. During the test, the following parameters were registered over a 2-min period: peripheral activity near the walls of the set, central activity, vertical activity, and the number of floor holes examined. Total locomotor activity was measured by the sum of all the activity types. The anxiety index was assessed by the ratio of central activity to the sum of central and peripheral activity multiplied by 100%. An increase in the anxiety index was a correlate of decreased anxiety reactions (Kudryashov et al. 2022).

Experimental design

The study consisted of two experiments. In Experiment 1, the mice were divided into 5 groups (12 mice per group): control; ASS 1 h after exposure; ASS 24 h after exposure; corticosterone 1 h after administration; corticosterone 24 h after administration. In Experiment 2, there were 5 groups of the animals, each group consisted of 12 mice: control; dexamethasone 1 hour after administration; dexamethasone 24 hours after administration; fludrocortisone 1 hour after administration; fludrocortisone 24 hours after administration.

Statistical analysis

The assessment of the collected data was performed using GraphPad Prism 8.0 software (GraphPad Software, Inc., USA). The normality of distribution was tested by the Shapiro-Wilk normality test, after which the data was presented as Me (Q1; Q3). The differences between the

groups were determined using the Kruskal-Wallis test with Benjamini-Hochberg correction for multiple comparisons. The results were considered significant at $p<0.05$.

Results and Discussion

Experiment 1

The peripheral activity in the control group in the open field test was 53.0 (49.5; 61.5), central activity – 6.0 (4.0; 12.3), vertical activity – 1.5 (0; 3.0); total locomotor activity – 63.0 (55.5; 73.0), the number of examined holes – 2.0 (1.0; 4.0) and anxiety index – 12.1 (6.3; 16.4) (Fig. 1). According to the results of the Kruskal-Wallis test, significant effects of ASS and corticosterone on the anxiety index ($H(4) = 27.66$, $p<0.0001$) and central activity ($H(4) = 22.53$, $p=0.0002$) in the open field test were revealed. In subsequent multiple comparisons, it was found that 1 h after ASS the anxiety index (3.9 (0; 6.5), $p<0.05$) and central activity (2.5 (0; 4.0), $p<0.05$) decreased, and after 24 h the anxiety index increased (22.8 (16.0; 30.6), $p<0.05$), while corticosterone decreased central activity (1.0 (0; 4.8), $p<0.05$) and anxiety index (2.1 (0; 7.5)) 1 h after administration compared to the control group.

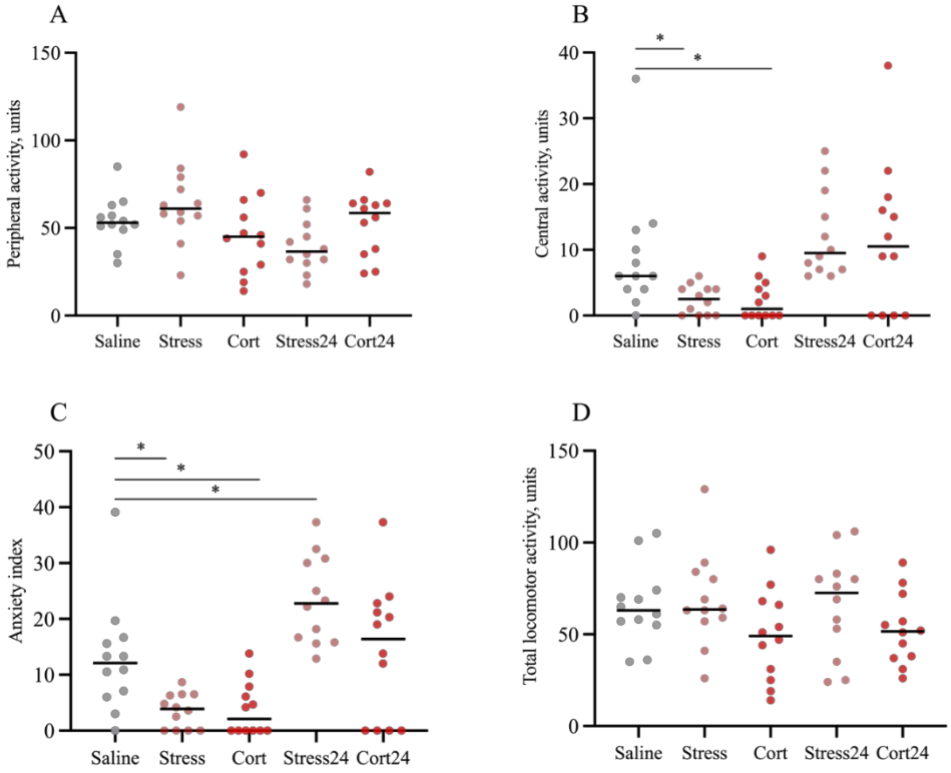


Figure 1. The effect of acute swimming stress and corticosterone on anxiety-like behavior in mice in the open field test. ***Note:*** **A** – peripheral activity; **B** – central activity; **C** – anxiety index' **D** – locomotor activity; Cort – corticosterone 1 h after administration; Cort24 – corticosterone 24 h after administration; Stress – 1 h after acute swimming stress; Stress24 – 24 h after acute swimming stress; black line – median; * – $p<0.05$ compared to saline group.

Experiment 2

The peripheral activity of animals in the control group in the open field test was 42.0 (35.5; 55.5), central activity – 7.5 (3.5; 8.8), vertical activity – 0.5 (0; 4.3), motor activity – 53.0 (39.8; 62.0), number of investigated holes – 1.0 (0; 2.0), and anxiety index – 13.2 (8.0; 17.4) (Fig. 2). In accordance with the Kruskal-Wallis test results, significant effects of the studied substances on central activity ($H(4) = 35.2$, $p <0.0001$), anxiety index ($H(4) = 30.0$, $p <0.0001$) and total locomotor activity ($H(4) = 18.74$, $p = 0.0009$) of mice in the open field test were revealed. In subsequent multiple comparisons, it was established that dexamethasone (10 mg/kg, i.p.) decreased central activity (0.5 (0; 1.8), $p <0.01$) and anxiety index (0 (0; 0.8), $p <0.01$) 1 h after administration compared to animals in the control group. Meanwhile, fludrocortisone (0.04 mg/kg, i.p.) decreased central activity (0 (0; 2.8), $p <0.01$) and anxiety index (0 (0; 9.3), $p <0.01$) and reduced central activity (0 (0; 0), $p <0.01$), anxiety index (0 (0; 0), $p <0.01$) and

total locomotor activity (31.0 (9; 39.8), p <0.01) 24 h after administration compared to animals in the control group.

In the present study, we focused on the comparative examination of the effects of ASS, corticosterone, dexamethasone, and fludrocortisone on ALB in mice. Previously, it was revealed that ASS is characterized by a biphasic effect on ALB in mice in the open field test: an increase in ALB is observed in mice 1 h after stress exposure, while a decrease in ALB occurs 24 h after the stress event compared to intact animals (Kudryashov et al. 2022). ASS leads to an increase in immobility time during repeated exposure to the stressor, which is interpreted as the development of a passive coping strategy for inescapable stressful situations. This adaptive reaction develops as a result of the activation of the hypothalamic-pituitary-adrenal (HPA) axis and the stimulation of both MR and GR by corticosterone, implying the balance between MR and GR activation in this process (Kloet de and Molendijk 2016; Commons et al. 2017).

We reproduced the previously obtained results in the present study; however, the pattern of behavioral disturbances induced by ASS in outbred mice possesses several peculiarities. Twenty-four hours after ASS exposure, we detected a selective increase in the anxiety index, which more closely resembles the response to ASS observed in C57BL/6 mice than that of BALB/c mice in which an increase in all the evaluated parameters was reported. This finding can be explained by strain differences in adaptive responses to acute stress exposure (Kudryashov et al. 2022).

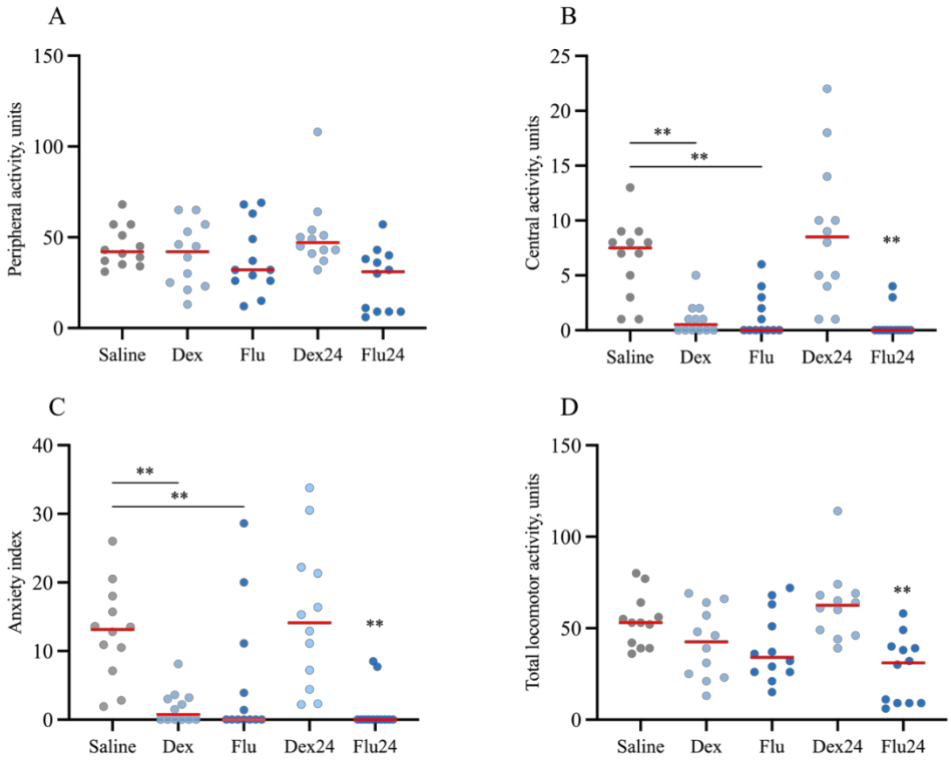


Figure 2. The effect of dexamethasone and fludrocortisone on anxiety-like behavior in mice in the open field test. ***Note:*** **A** – peripheral activity; **B** – central activity; **C** – anxiety index; **D** – locomotor activity; Dex – dexamethasone 1 h after administration; Flu – fludrocortisone 1 h after administration; Dex24 – dexamethasone 24 h after administration; Flu24 – fludrocortisone 24 h after administration; red line – median; ** – p<0.01 compared to saline group.

The enhancement of ALB in mice 1 h after ASS exposure appears to be caused by the immediate response to acute stress. The underlying mechanism involves activation of the HPA axis, increased corticosterone secretion, as well as changes in the activity of monoaminergic systems in the brain structures responsible for anxiety regulation – the prefrontal cortex and amygdala (Christianson et al. 2013; Browne et al. 2014; Atrooz et al. 2021; Pesarico et al. 2020). The anxiolytic effect observed 24 h after ASS may be associated with the activation of adaptive neurobiological mechanisms, which include decreased HPA axis activity, reduced corticosterone levels (Fediuc et al. 2006; Hoeijmakers et al. 2014) and, possibly, the desensitization of 5-HT_{2C} receptors in the hypothalamus activated by serotonin during the immediate response to acute stress (Christianson et al. 2013), as well as the elevated activity of the endogenous neuroactive steroid system due to the increased density of the mitochondrial translocator protein 18 kDa (TSPO) (Avital et al. 2001).

Since the stimulation of GR and MR by endogenous corticosteroids plays one of the principal roles in the mechanisms of the immediate response to acute stress and the phase of adaptive changes (Kloet de et al. 2016; Hartmann et al. 2021; Kloet de 2022; Oakley et al. 2023), we additionally studied the effects of various ligands of the above-mentioned receptors during the same time periods (1 h and 24 h after administration) as ASS. Particularly, we examined the effects of the GR and MR ligand corticosterone, the GR ligand dexamethasone, and the MR ligand fludrocortisone on ALB in mice in the open field test 1 h and 24 h after administration.

One hour after administration of corticosterone, which is frequently employed in animal models of stress (Dieterich et al. 2019; Bertholomey et al. 2022), an increase in ALB was detected in mice, characterized by the same behavioral pattern seen 1 hour after FST – a decrease in central activity and anxiety indexes (Fig. 1).

Nonetheless, 24 h after corticosterone administration, no behavioral changes were observed compared to the control group. Similar results were obtained in relation to dexamethasone, which is consistent with the earlier published data regarding the effect of dexamethasone at a dose of 10 mg/kg on anxiety reactions in mice (Vafaei et al. 2008). On the one hand, these effects may result from the stimulation of central GR. Firstly, this is confirmed by a similar behavioral pattern observed after the administration of both corticosterone and dexamethasone, and, secondly, by the role of GR in the formation of an anxious phenotype in transgenic mice with the overexpression of GR in the forebrain (Wei et al., 2004).

On the other hand, there is evidence of the involvement of amygdala MR in enhancing ALB in rodents when aldosterone is directly injected into the amygdala of rats (Myers et al. 2010).

Simultaneously, different data was collected regarding the effects of fludrocortisone. In particular, 1 h after fludrocortisone administration, an increase in anxiety reactions was observed similar to that after FST exposure and administration of corticosterone and dexamethasone. Twenty-four hour after fludrocortisone administration, the observed effect persisted, but it was accompanied by a decrease in total locomotor activity compared to the intact control. To our knowledge, this is the first study of the effect of systemically administered fludrocortisone on ALB in mice. The obtained results are consistent with the earlier published data on the enhancement of ALB in rats after the administration of aldosterone to the amygdala (Myers et al. 2010). Interestingly, this effect was not only present 24 h after administration, but also accompanied by a decrease in total locomotor activity. Presumably, in the present case we deal with a biphasic action of fludrocortisone. The effects observed 1 h after fludrocortisone administration may be primarily linked to non-genomic mechanisms, while the effects, which occurred 24 h after administration, can be explained by genomic mechanisms. Given the determining role of MR in selecting the behavioral strategy for overcoming a stressful situation (Kloet de et al. 2016), it can be assumed that the administration of fludrocortisone, which has a high affinity for MR, leads to the formation of a behavioral phenotype characterized by a passive strategy for coping with stress, which is manifested not only by a decrease in central, but also total locomotor activity in the open field test. In any case, the effect of fludrocortisone on anxiety-like behavior in rodents and the underlying neurobiological mechanisms require further study.

Conclusion

FST is characterized by opposite effects on ALB in mice in the open field test, which depends on the time elapsed after the stress exposure – increased anxiety reactions 1 h after exposure and decreased anxiety reactions 24 h after exposure. Corticosterone (single dose 20 mg/kg, i.p.), dexamethasone (single dose 10 mg/kg, i.p.), and fludrocortisone (single dose 0.04 mg/kg, i.p.), which possess different affinities for GR and MR, only partially replicated the behavioral pattern observed after FST exposure. Corticosterone and dexamethasone increased ALB in mice only 1 h after administration, while the effect of fludrocortisone persisted even 24 h after administration, but it was accompanied by a decrease in total locomotor activity. Consequently, the effect of FST on anxiety-like behavior in mice is based not only on a certain balance between MR and GR activation, but also on other mechanisms dependent on the nature, intensity, and duration of the stressor.

Additional information

Conflict of interest

The authors declare the absence of a conflict of interests.

Funding

The authors have no funding to report.

Data availability

All of the data that support the findings of this study are available in the main text.

Ethics Statements

All the procedures with animals were considered and approved by the Local Ethics Committee, Sechenov University (Minutes № 24-22 of 12 November 2024).

References

- Atrooz F, Alkadhi KA, Salim S (2021) Understanding stress: Insights from rodent models. Current Research in Neurobiology 2: 100013. https://doi.org/10.1016/j.crneur.2021.100013 [PubMed] [PMC]
- Avital A, Richter-Levin G, Leschiner S, Spanier I, Veenman L, Weizman A, Gavish M (2001) Acute and repeated swim stress effects on peripheral benzodiazepine receptors in the rat hippocampus, adrenal, and kidney. Neuropsychopharmacology 25(5): 669–678. https://doi.org/10.1016/S0893-133X(01)00286-X [PubMed]
- Bertholomey ML, Nagarajan V, Smith DM, Torregrossa MM (2022) Sex- and age-dependent effects of chronic corticosterone exposure on depressive-like, anxiety-like, and fear-related behavior: Role of amygdala glutamate receptors in the rat. Frontiers in Behavioral Neuroscience 16: 950000. https://doi.org/10.3389/fnbeh.2022.950000 [PubMed] [PMC]
- Browne CA, Hanke J, Rose C, Walsh I, Foley T, Clarke G, Schwegler H, Cryan JF, Yilmazer-Hanke D (2014) Effect of acute swim stress on plasma corticosterone and brain monoamine levels in bidirectionally selected DxH recombinant inbred mouse strains differing in fear recall and extinction. Stress 17(6): 471–483. https://doi.org/10.3109/10253890.2014.954104 [PubMed] [PMC]
- Can A, Dao DT, Arad M, Terrillion CE, Piantadosi SC, Gould TD (2012) The mouse forced swim test. Journal of Visualized Experiments 59: e3638. https://doi.org/10.3791/3638 [PubMed] [PMC]
- Christianson JP, Drugan RC, Flyer JG, Watkins LR, Maier SF (2013) Anxiogenic effects of brief swim stress are sensitive to stress history. Progress in Neuro-Psychopharmacology & Biological Psychiatry 44: 17–22. https://doi.org/10.1016/j.pnpbp.2013.01.011 [PubMed] [PMC]
- Commons KG, Cholanians AB, Babb JA, Ehlinger DG (2017) The rodent forced swim test measures stress-coping strategy, not depression-like behavior. ACS Chemical Neuroscience 8(5): 955–960. https://doi.org/10.1021/acschemneuro.7b00042 [PubMed] [PMC]
- Dieterich A, Srivastava P, Sharif A, Stech K, Floeder J, Yohn SE, Samuels BA (2019) Chronic corticosterone administration induces negative valence and impairs positive valence behaviors in mice. Translational Psychiatry 9(1): 337. https://doi.org/10.1038/s41398-019-0674-4 [PubMed] [PMC]
- Dinel AL, Guinobert I, Lucas C, Blondeau C, Bardot V, Ripoche I, Berthomier L, Pallet V, Layé S, Joffre C (2019) Reduction of acute mild stress corticosterone response and changes in stress-responsive gene expression in male Balb/c mice after repeated administration of a Rhodiola rosea L. root extract. Food Science & Nutrition 7(11): 3827–3841. https://doi.org/10.1002/fsn3.1249 [PubMed] [PMC]
- Fediuc S, Campbell JE, Riddell MC. (2006) Effect of voluntary wheel running on circadian corticosterone release and on HPA axis responsiveness to restraint stress in Sprague-Dawley rats. Journal of Applied Physiology 100(6): 1867–1875. https://doi.org/10.1152/japplphysiol.01416.2005 [PubMed]
- Hartmann J, Bajaj T, Klengel C, Chatzinakos C, Ebert T, Dedic N, McCullough KM, Lardenoije R, Joëls M, Meijer OC, McCann KE, Dudek SM, Sarabdjitsingh RA, Daskalakis NP, Klengel T, Gassen NC, Schmidt MV, Ressler KJ (2021) Mineralocorticoid receptors dampen glucocorticoid receptor sensitivity to stress via regulation of FKBP5. Cell Reports 35(9): 109185. https://doi.org/10.1016/j.celrep.2021.109185 [PubMed] [PMC]
- Hoeijmakers L, Harbich D, Schmid B, Lucassen PJ, Wagner KV, Schmidt MV, Hartmann J (2014) Depletion of FKBP51 in female mice shapes HPA axis activity. PLoS One 9(4): e95796. https://doi.org/10.1371/journal.pone.0095796 [PubMed] [PMC]

- Kloet de ER, Molendijk ML (2016) Coping with the forced swim stressor: Towards understanding an adaptive mechanism. Neural Plasticity 2016: 6503162. https://doi.org/10.1155/2016/6503162 [PubMed] [PMC]
- Kloet de ER (2022) Brain mineralocorticoid and glucocorticoid receptor balance in neuroendocrine regulation and stress-related psychiatric etiopathologies. Current Opinion in Endocrine and Metabolic Research 24: 100352. https://doi.org/10.1016/j.coemr.2022.100352 [PubMed] [PMC]
- Kudryashov NV, Naplekova PL, Volkova AV, Kasabov KA, Narkevich VB, Kudrin VS, Kalinina TS, Voronina TA (2022) Effects of acute swimming stress on the behavioral and neurochemical effects of pyrazolo[c]pyridine derivative GIZh-72 and diazepam in BALB/c and C57BL/6 mice. Neuroscience and Behavioral Physiology 52: 135–149. https://doi.org/1007/s11055-022-01215-5
- Laviolle B, Nesseler N, Massart C, Bellissant E (2014) Fludrocortisone and hydrocortisone, alone or in combination, on in vivo hemodynamics and in vitro vascular reactivity in normal and endotoxemic rats: a randomized factorial design study. Journal of Cardiovascular Pharmacology 63(6): 488–496. https://doi.org/10.1097/FJC.0000000000000072 [PubMed]
- Molendijk ML, Kloet de ER (2022) Forced swim stressor: Trends in usage and mechanistic consideration. The European Journal of Neuroscience 55(9-10): 2813–2831. https://doi.org/10.1111/ejn.15139 [PubMed] [PMC]
- Myers B, Greenwood-Van Meerveld B (2010) Divergent effects of amygdala glucocorticoid and mineralocorticoid receptors in the regulation of visceral and somatic pain. American Journal of Physiology. Gastrointestinal and Liver Physiology 298(2): G295–G303. https://doi.org/10.1152/ajpgi.00298.2009 [PubMed]
- Oakley RH, Riddick NV, Moy SS, Cidlowski JA (2023) Imbalanced glucocorticoid and mineralocorticoid stress hormone receptor function has sex-dependent and independent regulatory effects in the mouse hippocampus. Neurobiology Stress 28: 100589. https://doi.org/10.1016/j.ynstr.2023.100589 [PubMed] [PMC]
- Pesarico AP, Birmann PT, Pinto R, Padilha NB, Lenardão EJ, Savegnago L (2020) Short- and long-term repeated forced swim stress induce depressive-like phenotype in mice: Effectiveness of 3-[(4-chlorophenyl)selanyl]-1-methyl-1h-indole. Frontiers in Behavioral Neuroscience 14: 140. https://doi.org/10.3389/fnbeh.2020.00140 [PubMed] [PMC]
- Porsolt RD, Le Pichon M, Jalfre M (1977) Depression: A new animal model sensitive to antidepressant treatments. Nature 266(5604): 730–732. https://doi.org/10.1038/266730a0 [PubMed]
- Ruiz-Sánchez E, López-Ramírez AM, Ruiz-Chow Á, Calvillo M, Reséndiz-Albor AA, Anguiano B, Rojas P (2021) Variability in behavioral phenotypes after forced swimming-induced stress in rats is associated with expression of the glucocorticoid receptor, nurr1, and IL-1β in the hippocampus. International Journal of Molecular Sciences 22(23): 12700. https://doi.org/10.3390/ijms222312700 [PubMed] [PMC]
- Vafaei AA, Rashidy-Pour A, Taherian AA. (2008) Peripheral injection of dexamethasone modulates anxiety related behaviors in mice: an interaction with opioidergic neurons. Pakistan Journal of Pharmaceutical Sciences 21(3): 285–289. [PubMed]
- Wei Q, Lu XY, Liu L, Schafer G, Shieh KR, Burke S, Robinson TE, Watson SJ, Seasholtz AF, Akil H (2004) Glucocorticoid receptor overexpression in forebrain: a mouse model of increased emotional lability. Proceedings of the National Academy of Sciences of the United States of America 101(32): 11851–11856. https://doi.org/10.1073/pnas.0402208101 [PubMed] [PMC]
- Zhao Y, Ma R, Shen J, Su H, Xing D, Du L (2008) A mouse model of depression induced by repeated corticosterone injections. European Journal of Pharmacology 581(1-2): 113–120. https://doi.org/10.1016/j.ejphar.2007.12.005 [PubMed]

Author Contribution

- **Nikita V. Kudryashov,** PhD in Biology, Associate Professor at the Department of Pharmacology of the Institute of Biodesign and Complex System Modelling, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; Senior research scientist at the Department of Neuropsychopharmacology, Federal Research Center for Innovator and Emerging Biomedical and Pharmaceutical Technologies, Moscow, Russian Federation; e-

mail: kudryashov_n_v@staff.sechenov.ru; **ORCID ID:** https://orcid.org/0000-0002-1819-1867. Development of the idea of the study, carrying out behavioral tests, and writing the manuscript.

- **Alexander A. Gorbunov,** PhD in Biology, Associate Professor at the Department of Pharmacology of the Institute of Biodesign and Complex System Modelling, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; e-mail: gorbunov_a_a@staff.sechenov.ru; **ORCID ID:** https://orcid.org/0000-0002-5773-5177. Carrying out behavioral tests and writing the manuscript.
- **Sergey E. Mironov**, PhD in Pharmacy, Associate Professor at the Department of Pharmacology of the Institute of Biodesign and Complex System Modelling, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; e-mail: mironov_s_e@staff.sechenov.ru; **ORCID ID:** https://orcid.org/0009-0008-2427-2736. Carrying out behavioral tests.
- **Dmitriy A. Tikhonov,** PhD in Medicine, Associate Professor at the Department of Pharmacology of the Institute of Biodesign and Complex System Modelling, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; e-mail: tikhonov_d_a@staff.sechenov.ru; ORCID ID: https://orcid.org/0009-0004-6310-973X. Statistical analysis and editing the manuscript.
- **Andrey A. Nedorubov**, Head of the Center for Preclinical Studies of the Institute for Translational Medicine and Biotechnology, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; e-mail: nedorubov_a_a@staff.sechenov.ru; **ORCID ID:** https://orcid.org/0000-0002-5915-7999. Carrying out behavioral tests and editing the manuscript.
- **Olga Yu. Arshinova**, PhD in Pharmacy, Senior Lecturer at the Department of Pharmacology of the Institute of Biodesign and Complex System Modelling, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; e-mail: arshinova_o_yu@staff.sechenov.ru; **ORCID ID:** https://orcid.org/0009-0005-4110-0467. Carrying out behavioral tests.
- **Maria A. Simukhina**, PhD in Medicine, Senior Lecturer at the Department of Pharmacology of the Institute of Biodesign and Complex System Modelling, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; e-mail: simukhina_m_a@staff.sechenov.ru; **ORCID ID:** https://orcid.org/0000-0003-1099-9447. Carrying out behavioral tests and editing the manuscript.
- **Vera N. Busol**, undergraduate student, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; e-mail: verafbmusik@yandex.ru; **ORCID ID:** https://orcid.org/0009-0001-3785-374X. Search and analysis of literature and writing the manuscript.
- **Vladimir P. Fisenko**, Doctor Habilit. of Medicine, Professor, RAS academician, Head of the Department of Pharmacology of the Institute of Biodesign and Complex System Modelling, Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; e-mail: vpfisenko@mail.ru; **ORCID ID:** https://orcid.org/0000-0002-9080-5763. Development of the idea of the study and editing the manuscript.