AGE PECULIARITIES OF THE COGNITIVE FUNCTIONS OF RATS IN TERMS OF VIOLATIONS OF THYROID BALANCE

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Annotation. *In experiments on animals of three age groups, the cognitive activity of the central nervous system was investigated under dysfunction of the thyroid gland. With experimental hyperthyroidism in juvenile (5-6 weeks) rats, there was an improvement in the process of formation of conditional protective reaction and anxiolytic effect in a cross-shaped elevated labyrinth, accumulation of the inhibitory neurotransmitter amino acid - GABA in the cortex of 38.5% (anxiolytic action), as well as excitatory amino acids - glutamate in the hippocampus by 45.6% (mnastic activity). In young (5-6 months) animals to a lesser extent anxiolytic effect and cognitive activity were observed. In neocortex, significant accumulation of inhibitory neurotransmitter amino acids - GABA at 49.3%, glycine by 17.5%, serotonin by 33%, total NO synthase by 59.6%. In older rats there was a pronounced inhibition of cognitive function, a decrease in the content of GABA by 46.1%, serotonin by 17.3%, NO synthase activity by 37%, and an increase in glutamate by 61.5%. The condition of hypothyroidism of the thyroid gland was accompanied by inhibition of cognitive function, to a greater extent in the old rats. In juvenile individuals, memory decline occurred on the background of increased anxiety. In young rats, inhibition of mestizal activity was accompanied by a sharp decrease in emotional and anxiety. This condition is ensured by an increase in the neocortex content of serotonin and glycine by 37.1% and 17.5%, respectively, of total NO synthase by 36.8% in this brain structure. In older animals, hypothyroidism caused an increase in glutamate levels in the cortex of 84.6% and a 109.6% hippocampus, which is possibly causative exitotoxic effect.*

Key words: *experimental hyperthyroidism, hypothyroidism; ontogenesis; cognitive function; neurotransmitter amino acids.*

Introduction. Higher brain functions are determined by the activity of the neurohumoral regulatory mechanism. Among the hormones that influence the cognitive activity of the central nervous system (CNS), the important role belongs to the thyroid hormones (TH) [11,20,24]. Due to the maintenance of the proper level of energy and plastic exchange of neuroglial structures, the modulation of neurotransmitter diffusion systems and the autonomic catecholamine pressor effect, these hormones provide organization of the psycho-emotional status of the organism [8,22]. Thyroid dysfunction, which today is

one of the most common endocrine pathologies, is accompanied by a significant range of CNS disorders, from increased susceptibility and stenotic reactions to depression and psychosis [13,27]. Therefore, the appointment of one substitution hormonal therapy is often insufficient and does not eliminate the thyroid disease mental syndrome, especially in relation to the cognitive function [7]. According to the statistics of the last decades, the most vulnerable to thyroid dysfunction was the childhood and adolescence period, as well as the age of the elderly [10,23]. Perhaps this is due to the fact that in early postnatal and prepubertal age, need for TH increases and with age comes their shortage. Despite numerous scientific data on the influence of TH on higher brain functions, their mechanism of action remains unclear [3,6]. One of the important but controversial aspects of the TH effect on the central nervous system's cognitive function is the regulation of the brain's main inhibitory GABA, serotonin, glycinergic and stimulating glutamatergic mediation activity [16,21 , 36]. Therefore, the study of the role of neurotransmitter amino acids in the formation of psycho-emotional status, the mnestic activity of the rats of different age in conditions of dysfunction of the thyroid will make it possible to better correct substitution hormonal therapy in children, adolescents and the elderly in this pathology.

Materials and methods. Studies were conducted on white Wistar rats of three age groups: I - juvenile (4-5 weeks) II - young (5-6 months); III - old (18-24 months). The experiments were carried out in accordance with the European Convention for the Protection of Vertebrate Animals used for research and other scientific purposes (Strasbourg, 1986) and the Law of Ukraine “On the Protection of Animals Against Cruel Treatment” (dated 21.02.2006, No. 3447 - IV).

The hyperthyroid state was modeled by administering powdered L-thyroxine tablets (Berlin-Chemie AJ, Germany) with food for two weeks in doses that were gradually increased due to inactivation of exogenous thyroxine. At the beginning of the experiment, the dose was higher than the daily production of thyroxine (3-5 μg / animal) and amounted to 10 μg / day. Daily concentration of thyroxine was increased by 5 μg compared with the previous one. A hypothyroid state was created by administering mercazolil in a dose of 10 mg / kg for two weeks with food. The probability of the created model was confirmed by determining the concentrations of thyroxine and thyroid-stimulating hormone in the blood plasma of experimental rats and assessing the clinical status of the animals: body weight, heart rate, mobility, excitability, and emotionality.

A study of the behavioral activity of rats was performed in a cruciform sublime maze [4]. The cross-shaped labyrinth is represented by four sleeves 40 cm long. Two corridors were open and two closed side walls 20 cm wide. The labyrinth was fixed at a height of 80 cm from the floor. The animal was placed in the central area. For 3 minutes, the following behavioral indicators were recorded: the number of transitions to the light and dark corridors, the duration of stay in them, the number of racks, acts of defecation, the duration of grooming.

Spatial memory was studied by developing a conditional reaction to finding a place in the water maze of Morris [32], from which the animal could be saved using a stand. A pool with a diameter of 2.8 m and a depth of 60 cm was filled with water (21°C) to a

level of 40 cm. A platform-stand was placed in a specific place, which was 3-5 cm deep under water. The animal was placed in the central sector of the pool. Watched 5 min. The training was conducted once daily for 4 days. The following indicators were determined: the duration of stay and placement on the rescue site from which the animal was taken, the number of boluses of defecation, the number and duration of fading (hang-ups), the number of laps that the animal overcame to finding a stand. The concentration of glycine, GABA, glutamate in the brain homogenate was determined by chromatographic method based on the separation of glycine, GABA and glutamate in the system n-butanol: acetic acid: water in a thin layer of sorbent, followed by quantitative determination by reaction with alloxan [5]. On the starting line of the plate "Silufol" put 0.2 ml of tissue extract and chromatograph in the system n-butanol: acetic acid: water in a ratio of 8: 2: 1. Then the plate was dried and developed with a 1% alloxan solution in dimethylformamide at 100 ° C. Spots corresponding to GABA, glycine, glutamate were cut out and were sulphurised in 3 ml of dimethylformamide for 3:00. Then the samples were centrifuged at 2500 rpm for 30 minutes (at a temperature of 15 ° C), after which their spectrophotometers at a wavelength of 540 nm. The contents of GABA, glycine, and glutamate were calculated from the calibration curve with reference to the weighed tissue.

The method for determining the total activity of NO synthase is based on the oxidation of NADPH during the reaction of the formation of NO from L-arginine. A decrease in NADPH, an equimolar amount of NO formed, which was recorded spectrophotometrically at a wavelength of 340 nm. The reaction was started by adding 0.1 ml of cytosol in the incubation mixture (37 ° C) in a quartz cuvette (1 cm). Optical density was measured immediately and then after 4 minutes. The activity of NO synthase was calculated by the corresponding formula.

The research results were processed using parametric statistical methods using Student's t-test for small samples [14]. Changes in the indices were considered significant at $p < 0.05$.

Results. The study of the age aspect of the role of thyroid hormones in the organization of spontaneous behavioral activity of rats, which was carried out by us earlier, revealed far from the "classical" view of the stimulating effect of these hormones on the reproduction of innate - mobility research instincts. On the contrary, the inhibition of certain components of behavior in the "open field", whose degree was determined by the thyroid status and age of animals, was observed. The most pronounced behavioral deficit, which is completely logical, was observed in conditions of hypothyroidism. In the youngest age of rats, the inhibitory effect was the most significant, which can be interpreted as a depressive state: a sharp decrease in mobility, a research link of behavior and an increase in anxiety. Hypothyroid and hyperthyroid conditions in young animals were a limitation of emotionality. In the old rats there was a decrease in motor and emotional activity while maintaining research activity. That is, the presence in animals of motor, emotional and cognitive deficits in conditions of thyroid dysfunction explains the relevance and importance of the next stage of research. The most informative method for detecting and studying the state of depression is the method of observing spontaneous

behavior in a cross-bearing elevated labyrinth.

The study of behavioral activity of rats of three age groups in a cross labyrinth under conditions of hyperthyroidism revealed the same type of behavioral changes in juvenile and young animals, which related to an increase in the length of stay in the illuminated part of the labyrinth. In juvenile rats, the number of transitions in the light of the sleeve was 1,63± 0,15 on average, which is 103.8% more than control.

In the group of young animals, this indicator increased by 87.7%. The duration of stay in light compartments also increased: in the I age group - almost 3.5 times, in II - in 2.3 times. The predominance of finding in the illuminated space is estimated by researchers as an anxiolytic effect [35]. The emotional component of behavior in juvenile rats has not changed. Unlike the younger age group, in young animals, the number of acts of defecation decreased by 66.7%, which characterizes the presence of emotional deficiency. The opposite reaction of the CNS to elevated thyroid status was found in the old rats. The number of transitions in the light of the hallway of the labyrinth and the length of stay in them significantly decreased - by 74.2% and 85.5% respectively. In addition, the number of racks decreased by 75% and acts of defecation by 39.1% relative to control. That is, in the old rats, hyperthyroid dysfunction was accompanied by a significant inhibitory effect in the CNS.

The state of hypothyroidism was accompanied by a decrease in the behavioral activity of animals of three age groups, especially in young rats. In juvenile rats, the number and length of stay of animals in the bright part of the labyrinth decreased by 40.9% and 26.5%, according to the control group. Also, the time of grooming decreased by 82.8%. In young animals, there was a pronounced inhibitory effect, which spread on all components of behavior, except for the number of racks. The most significant was the suppression of the rate of transitions in the illuminated sleeves and the duration of their stay in them - by 63.2% and 85.5% respectively. The mating response from the open sites of the plant was almost absent, when in the control group, this indicator amounted to an average of 2.57 ± 0.58. The autonomic component of emotionality, the number of acts of defecation, was also absent. The duration of the grooming reflexes was 5.57 ± 0.65 s, which is 71.3% less than in the control. That is, the hypothyroid condition was accompanied by a significant emotional and motor deficiency. In older animals to a greater extent than in young rats, mobile activity was inhibited: the number of measures in the dark and in the light of the labyrinth's arms was almost not detected. Emotion also decreased by 26.8%. The duration of the grooming was suppressed by 67.4% relative to the control group. The number of hatching has increased significantly - by 3.4 times. Thus, a defective thyroid condition caused inhibition, primarily, of mobile activity, to a large extent in young and old rats.

The emotional state actively influences the formation of the cognitive function of animals. It is known that the development of a reflex reaction with positive reinforcement occurs with the participation of serotonin mediation; with negative reinforcement - with the participation of cholinergic [1]. That is, conditioned reflex activity is provided by the activity of specific mediator systems of the brain [12,18]. In turn, TH has a significant modulating effect in the activity of these mediators of the CNS. Interesting and logical

was the next stage of research - the study of age characteristics of the process of forming a spatial protective response against the background of the changed thyroid status of animals.

In juvenile rats, in the background of a hyperthyroid state, the process of developing a conditional protective reflex for finding the site among the water space was accelerated.

Thus, during the first training session, the time of finding the "rescue" stand in the control animals group was 187.20 ± 15.02 sec. In comparison with the group "hyperthyroidism", where this index was on average 132.21 ± 12.84 s, the time of the defense reflex reaction was 29.4% lower. Experimental rats more likely found a place with a stand. The average number of visits to the right sector was 4.19 ± 0.48, which was 36.6% lower than control. At the same time, in rats with elevated thyroid status, emotionality and anxiety increased - the number of acts of defecation and the time of freezes in water increased by 45.3% and 2.2 times respectively. After the second session, the development of a protective reaction in juvenile rats with elevated thyroid status, the time of finding the "rescue" stand was on average 77.21 ± 12.43 s, which was almost twice less than control, where this figure was 138.10 ± 14, 82 s. Along with the gradual improvement of spatial memory there was an increase in anxiety and depression. The proof of the formation of such a state was an increase in the time of the first fading when the animal was exposed to water by 88.2% compared to intact rats. The third training session also revealed an enhanced mental effect in rat with increased thyroid status. The latent period of the defense response to avoidance of water space was reduced by 38.3% relative to the control group. The number of rats swallowed in search of the site was reduced by almost twice. The time of the first hangers in the water, as in previous sessions, was significantly increased - almost twice.

In young individuals with hyperthyroidism training in the water labyrinth of Morris was less effective. In particular, after the first session of spatial memory development in search of a "rescue" site, the time of its location was 56,42 ± 6,52 s on average, which practically did not distinguish this group of animals from the group "hyperthyroidism", where this indicator was 53.62 ± 7.03 sec.

Hyperthyroid condition in young rats was accompanied by an emotional deficit - a decrease in acts of defecation by 31.4%, a lack of first fading, and a significant decrease in the duration of general fading by 70%. The production of the conditioned reflex during the second session revealed a significant reduction in the latent period of finding the place from which you can exit the pool: in the experimental group, this figure decreased by 23,4%. As in the previous session, in rats with elevated levels of thyroid hormones, the number of acts of defecation decreased and the duration of the first freezes decreased by 36.7% and 56%, respectively. During the third session, the development of a protective reaction avoided without significant differences in control. The emotional deficit remained unchanged, that is, the reduction of defecation boluses and the absence of first fading by 33%.

In the old rats of the group "hyperthyroidism" training was biphasic. At the first presentation of the water space, the rats of the group "hyperthyroidism" found a rescue stand at 72.58 ± 12.04 sec on average, while sailing more than 4 laps in search of the site.

At the same time, the animals showed anxiety, in relation to the control, the duration of the first floodgates was three times greater, and the time of the general fading period

was 3.8 times longer. During the second session of the development of the conditional protective reflex, the time of finding the "conditional" site was reduced, both in the "control" group and in the group "hyperthyroidism" and was 32.58 ± 6.26 s and 26.75 ± 6.82 s respectively , which did not differ significantly, as in the first training. The third session revealed a significant deterioration in mnestic activity in animals with elevated thyroid status. The implementation time of the conditional reaction avoided prolonged by 80.6%. The number of rats swallowed by rats in search of the site significantly increased to 4.20 ± 0.91 on average, which was 2.5 times greater than control (1.67 ± 0.42). Thus, the condition of hyperthyroidism contributed to the improvement of the formation of spatial memory in juvenile rats and, on the contrary, caused a deterioration of training in young and especially in older animals.

According to the majority of authors of scientific and clinical studies, the state of hypothyroidism reduces mental activity, intellectual development, worsens memory [30,31]. In earlier studies conducted by us, a decrease in the process of spatial memory formation in rats was established, which was supported by a positive stimulus - food. At the same time, the development of the conditional reaction of passive avoidance, supported by a negative stimulus - a pain, did not reveal significant deviations. Therefore, the study of spatial memory when reinforced by a rigid negative protective reaction, deprivation of the water space, is an important informative moment.

In young rats, the state of hypothyroidism at the beginning of the development of a conditional protective response to avoidance of the water space was accompanied by an improvement in the formation of spatial memory. So, the time of finding a rescue stand was reduced by 24%. The number of acts of defecation, the time of the first freezes and general fading also decreased by 38.9%, 34.3%, and 35.5%, respectively, according to control. With increased mnestic activity, the emotional nature of animals was reduced. The second training session was characterized by similar changes. The latent period of the protective reaction was less than control by 30.1%.

Emotional activity, which manifested itself in terms of acts of defecation and duration of the first fading, was also inhibited by 91.1%, 61.3% respectively. The third session of developing a conditioned reflex finding a rescue stand showed the opposite effect. The latent period of the protective reaction increased by 21.5%, with a further reduction in emotionality and anxiety, which was 80% and 38.7% relative to the control.

In the old rats, the hypothyroid state was accompanied by a deterioration of the cognitive function. In particular, during the first training session, the duration of finding the right place of water in animals in the experimental group was 104.75 ± 8.86 s on average, which is 41.6% more than control. The duration of freezing was also increased by 48.9%.

Even more significantly, an increase in anxiety and depression in older rats with hypothyroidism was noted on the second day of the development of a protective reaction. In particular, the reflex of the first fading was observed only in the experimental group, and in general the duration of freezes was 1.00 ± 0.22 s, on average, which was three times greater than the control value. The third session of training was accompanied by

even more significant inhibition of conditioned reflex activity. The time for the protective reaction was 42.00 ± 6.01 s on average, which is 58% longer than in the control group. The number of visits to the faithful sector also increased by 56.9%. Thus, the lowered level of thyroid hormones caused a decrease in cognitive activity, which was more pronounced in the old and juvenile animals.

Discussion. Thyroid dysfunction is the most common endocrine disorder, which is almost inferior to only diabetes mellitus, which is in the first position in this system of pathologies. The results of epidemiological studies have shown that the prevalence of manifested and subclinical hyper-and hypothyroidism is 7-10% among women and 2-3% among men. In elderly women, the incidence of hypothyroidism is 14-15%. Widespread clinical symptoms of thyroid disturbance that accompany the development of neuropsychiatric disorders, namely increased nervousness, irritability and excitability, anxiety, depression, attention deficit and memory, psychotic behavior, tremor, stupor, polyneuropathy, etc., are widely known. [4]. The authors of the paper believe that in hyperthyroidism, the damage to the nervous system is associated with the toxic effects of TH, acceleration of metabolism and increased sensitivity to catecholamines. One of the causes of mental disorders in hypothyroidism is encephalopathy [29]. All this points to significant violations of the integrative activity of the brain, which is the result of the interaction of molecular, biochemical, neurochemical mechanisms of the functioning of the CNS. Numerous studies have shown that TH influence their effects on higher nervous activity through direct direct action on brain metabolism, and by modulating the activity of its neurotransmitter systems. This is due to changes in synthesis, tourner and reverse mediator seizure, brain amino acid composition, sensitivity and number of receptors [9]. The most known mechanism of action of TH for higher nervous activity is through activation of the noradrenergic system of the brain, which leads to increased excitability of the organism. Less common data on the modulatory effect of hormones on the glutamatergic system of the brain. It is anticipated that the activating effect of TH on higher functions is associated with an increase in glutamate levels in neocortex and other structures. Today, another, opposite mechanism of the implementation of the action of hormones on the functioning of the CNS - through the braking systems of the brain [13]. It is envisaged that the activation of mediator systems data is a reversible protective response, through which excessive excitation is limited. In particular, the concept that the main effect of TH on higher brain functions is mediated through GABA- ergic synaptic transmission is proposed. In the light of these representations, hormones are involved in the pathophysiology of anxiety and depression. But the contradictory data that exists today on this issue is large enough and needs to be clarified. The connection of TH with another braking system - serotoninergic, most presented in the scientific literature [25]. Moreover, there is a critical period in the life of rats, during which TH are necessary for optimal development of the serotoninergic system in the developing brain (the ripening brain). The modeling of hypothyroidism in adult rats caused the accumulation of serotonin in the brain. In this case, hyperthyroid animals showed an increase, as well as a decrease in the population of serotonin receptors. Most authors noted the inverse relationship between

serotonin metabolism in the brain and thyroid status. Despite the fact that over the last decades enough material on the influence of TH on the body has been collected, the age-old peculiarities of their mechanism of action on the integrative activity of the CNS have not been clarified and contain significant contradictions.

Investigation of the functional state of the CNS under conditions of thyroid dysfunctions in rats of all ages showed that emotionality, mobile activity, mnestic function of animals is formed depending on the age and content of TH. Interestingly, the changes we have discovered in our system of behavioral of animals do not fall under the classical idea - an elevated level of TH causes the activation of the CNS , and diminished - on the contrary, inhibition of activity. Taking into account the significant modulating effect of TH on the activity of brain neurotransmitter systems, it can be predicted that one of the possible mechanisms for the formation of a cognitive function of animals is the regulation of the content of certain neurotransmitter amino acids of inhibitory and exciting nature. Therefore, the next stage of the work was an analysis of changes in the content of free amino acids of the neurotransmitter nature in the cortex and the hippocampus, in the structures responsible for the formation of long-term spatial memory [28].

The study of behavioral activity and the formation of spatial memory of juvenile rats in conditions of hyperthyroidism showed the most classical characteristic of changes - activation of the cognitive function [2,11,24]. At the same time, the non-classical component was determined - anxiolytic effect, which in most scientific papers the authors associate with the accumulation of inhibitory mediators in the brain [17]. Determination of the content of amino acids in neocortex has indeed shown an increase in the concentration of GABA by 38.5% and simultaneously reduction of glycine by 25.7%.

Perhaps anxiolytic effect is provided by a more substantial accumulation of GABA. The participation of GABA-A and GABA-B receptors in the formation of anxiolytic and antidepressant effects in the CNS was confirmed by many studies [34,35]. The activation of the cognitive function is evidently due to a decrease in the concentration of inhibitory amino acids - glycine by 17.9% and GABA by 31.6% and, at the same time, increased glutamate by 45.6%. Hyperthyroid condition in young animals also caused anxiolytic effect, and unlike juvenile rats, deterioration in the production of conditional protective response. These behavioral changes were accompanied by an increase in the cerebral cortex of the amount of inhibitory amino acids. In particular, serotonin content increased by 33%, GABA by 51%, glycine by 17.5%. In addition, significant activation of NO-synthase was noted at 59.6%, possibly leading to an increase in NO, which also plays a role of the inhibitor in the CNS. Such, too significant accumulation of inhibitory mediators in the neocortex may cause emotional deficits, anxiolytic effects and, as a result, a deterioration in the process of developing a protective avoidance response. Over the past few decades, researchers have collected a wealth of materials to determine the influence of TH on higher brain functions, but the interpretation of these data is different [18,29]. The old rats showed the most inhibitory effect - emotional, motorized and, more significantly, cognitive deficits than young rats. Such effects were observed in the level of neurotransmitter amino acids. In the neocortex, accumulation of glutamate by 61.5% and reduction of serotonin by 17.3%

and GABA by 46.1% were noted. Such a redistribution of neurotransmitter amino acids in the direction of neurotransmitters of excitatory nature in the neocortex will cause inhibition of subcortical structures, in particular, limbic, including the hippocampus. In addition, in the hippocampus there was a significant increase in the content of glycine - by 113.6%. In general, increasing the excitation process in the neocortex and inhibition in the hippocampus may cause a general depressing effect in the functioning of the CNS of the old rats.

The state of hypothyroidism caused a unidirectional inhibitory effect in the CNS, which was noted in numerous studies by scientists [30,31]. This was reflected by a decrease in motor and emotional activity, as well as a weakening of the cognitive function. Juvenile rats developed anxiety and depression in the background of deteriorating memory. At the same time, in the cerebral cortex, the serotonin content was significantly increased by 51.7%, which is possibly due to these changes in behavior. The participation of serotonin in the formation of the state of anxiety and depression has been repeatedly emphasized in scientific sources [9,32,34,35]. In young animals, there was even more pronounced accumulation of inhibitory neurotransmitters in neocortex - serotonin by 37.1% and glycine by 17.5%. Perhaps this would cause a deterioration in the process of forming spatial memory engrams and a decrease in motor and emotional activity. In older animals, the inhibitory effect of the CNS on the background of hypothyroidism was most pronounced. As with hyperthyroidism, the neocortex reduced the content of GABA by 36.8%, as well as increased glutamate by 86.4%. That is, there was a shift in the balance of neurotransmitter compounds in the direction of excitation processes.

Thus, the neocortex as a braking structure, in a state of increased excitability, can have a significant inhibitory effect on subcortical structures, in particular, the limbic system, brain stem nuclei, and the hippocampus. In the hippocampus, an elevated glycine content was determined by 31.8%. Perhaps such a redistribution of neurotransmitter amino acids led to a general depressing state of the CNS of the old rats. Probably another assumption. Extremely significant increases in the concentration of glutamate in the cortex (by 85%) and the hippocampus (by 109%) can simultaneously lead to an excitotoxic effect, which was observed by other researchers [15].

Conclusions. Thus, TH play a significant role in the formation of cognitive function of rats of different ages. Significance of hormones in the early postnatal period, activating the mnestic function, may be due to lower serotonin and glycine levels, as well as a moderate increase in the concentration of glutamate in the hippocampus. In the cortex, as an inhibitory structure, there was an increase in the content of gamma-aminobutyric acid, which can be considered as a process of reducing inhibition of subcortical structures, in particular, the hippocampus. In young rats, hormones of the thyroid gland support mnestic function at the proper level, apparently, also due to reduced inhibition of subcortical structures with an increase in the level of neurotransmitter amino acids of inhibitory nature - glycine, gamma-aminobutyric acid and serotonin in the neocortex. In the old rat, an imbalance of TH negatively affected cognitive function. The hyperthyroid state was accompanied by an excessive excitation process in the cerebral cortex, which caused an increase in the content of glutamate with a significant decrease in serotonin mediators,

gamma-aminobutyric acid and NO-synthase activity. In addition, a significant increase in the concentration of glycine in the hippocampus was also able to significantly suppress activity of this structure.

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