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CHANGES OF RATS BEHAVIOURAL REACTIONS UNDER INTOXICATION BY NDMA WITH THE CORRECTION BY THE «CYTAFAT» PREPARATION

Мақалада нитрозодиметиламиннің орталық жүйке жүйесінің қызметіне әсер етуінің сипаттамасы берілген. Қазіргі кезге дейін зерттелген және өз талдаулар нәтижесін салыстырмалы қарастыра отырып, нитрозодиметиламиннің орталық жүйке жүйесінің қызметін бұзатыны анықталған.

В данной статье рассмотрено влияние нитрозодиметиламина на центральную нервную систему. Представлены результаты исследований в сравнительном аспекте и доказано нарушение деятельности нервной системы под воздействием нитрозодиметиламина.

The lab rodents` behavior under the N-nitrosodimethylamine (NDMA) action with the application of the hepatoprotector «Cytafat» has been researched. The received models can be successfully used in ecology, pathology, psychopharmacology areas and in the behavior modification.

The research of the laboratory rodents` behavior is a convenient method for screening of various toxic substances, and it is a topical biological problem. Besides the theoretical importance, it is important for human beings for better self-recognition — the biological origin of human mentality, and for understanding animals etology as well. The prospects of the research are based on a possibility of the successful using of new models for the basic problems of ecology, pathologies, psychopharmacology, and for behavior modification as well [1].

The experiments were underdone with 150 white, not purebred rats 250–300 gr heavy, which were divided into 5 groups. The first group (n=30) was consisted of the control animals; the second group (n=30) — of the animals who received 40 mg/kg of N-nitrosodimethylamine (NDMA) intrastomach once; the third group (n=30) — of the animals who recieved a new hepatoprotector — «Cytafat» (100 mg/kg doze) [15, 16] intrastomach and then, in an hour, they received 40 mg/kg of NDMA once; the fourth group (n=30) — of the animals who received 4 mg/kg of (NDMA) intrastomach within three months; the fifth group (n=30) — of the animals who received 4 mg/kg of NDMA intrastomach within three months and then, within the last two months of a priming they recieved a preparation «Cytafat» (100 mg/kg doze).

The isolated smooth muscle preparations from an aortic arch, a chest lymphatic channel, visceral lymph nodes (hepatic, kidney, intestinal), an ileum were used for the contraction activity studying. Blood of a carotid artery was taken for cytologic, biochemical and cytogenetic research

During the experiment the sequence and the duration of each act was registered in seconds. The simultaneous analysis of:

- a) quantities (frequency)

b) duration of the behavioral acts of rodents seemed much more demonstrative with the fixed timing, as it allows to differentiate the behavior under stress (rare but longer in duration acts) from the opposite comfort behavior. In the experiment, the behavior of the animals in a new, strange situation («open field») is characterized by research/trying to find the direction motivation and by negative emotional condition (e.g. anxiety, fear). The research/trying to find the direction behavior includes the specific poses and movements, using to get information from the environment. They are the evidences like vertical and horizontal activity, sniffing around.

Grooming is a widespread form of rodent behavior which is carrying out some important functions in an organism — taking care of skin and fur, thermoregulation, distribution of chemical substances, etc. [2, 3]. Besides the direct biological function, grooming is often a very important element of rodents behavior in natural conditions, it represents the specific ritual with the certain sequence of behavioral patterns [4, 2]. Alongside with bathing, yawning and stretching grooming is traditionally determined as a category of comfort behavior [5]. On the other hand, the rodents grooming is specifically activated under the stress and thus it is considered as one of their behavioral markers [2]. For example, the strong stress leads to the decrease of moving and research activity of the rodents, while their grooming is noticeably increases [6,7]. Also, the rodents grooming is activated when an animal refuses to solve an excessively difficult problem [8], under the action of weak sound-light stress or after the placing the animal in unfamiliar environment [9].

The emotional level эмоциональности is determined by the amount of fecal boluses and urination.

The results received during our experiments are represented in table 1.

Table 1

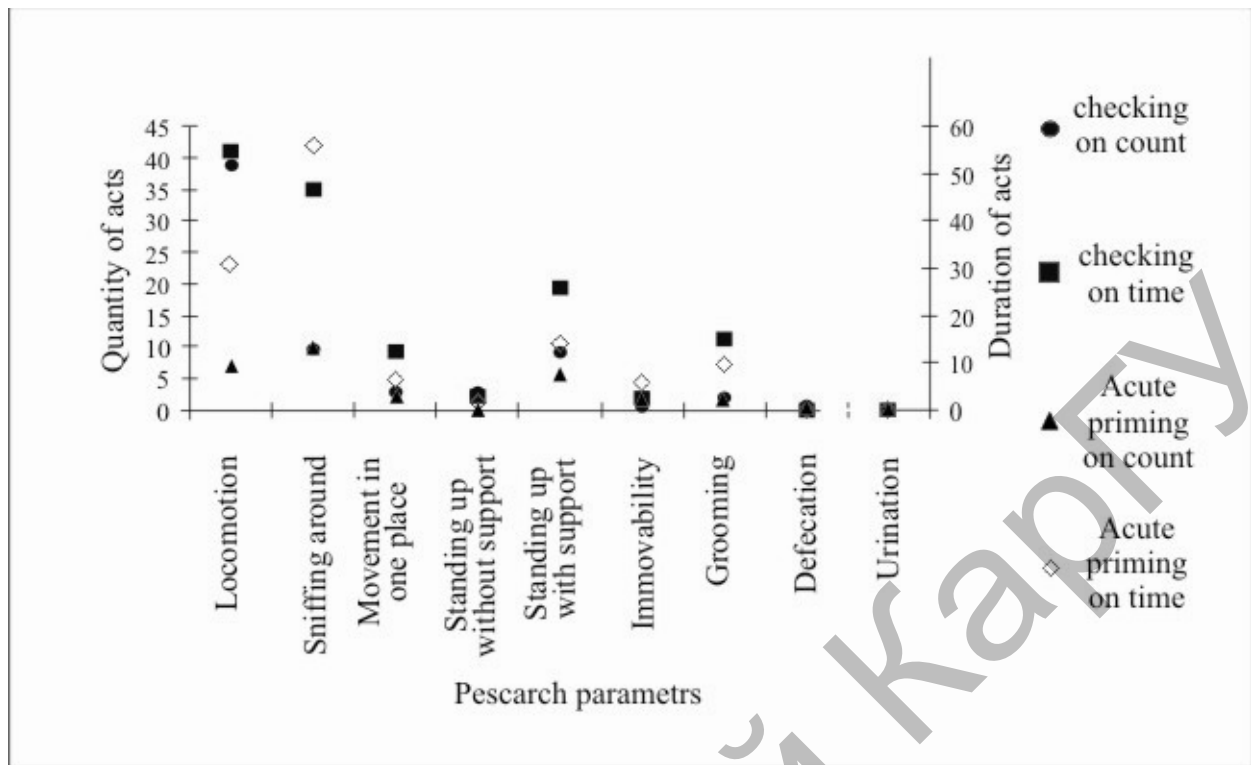
Parameters of the functional condition of CNS for the white rats of the control group

Researched parameters		Quantity	Duration, sec
Horizontal activity	Locomotion	39,2±0,98	41±2
	Movement in one place	3,0 ±0,5	9,3± 1,5
Vertical activity	Standing up with support	9,2 ±0,8	19,2±1,5
	Standing up without support	2,5±0,2	2,3±0,12
Grooming		2,0± 0,1	11,2 ±0,9
Sniffing around		9,5± 0,5	35,0 ±1,1
Immovability		0,50±0,04	2,0±0,1
Defecation		0,20 ±0,02	-
Urination		-	-

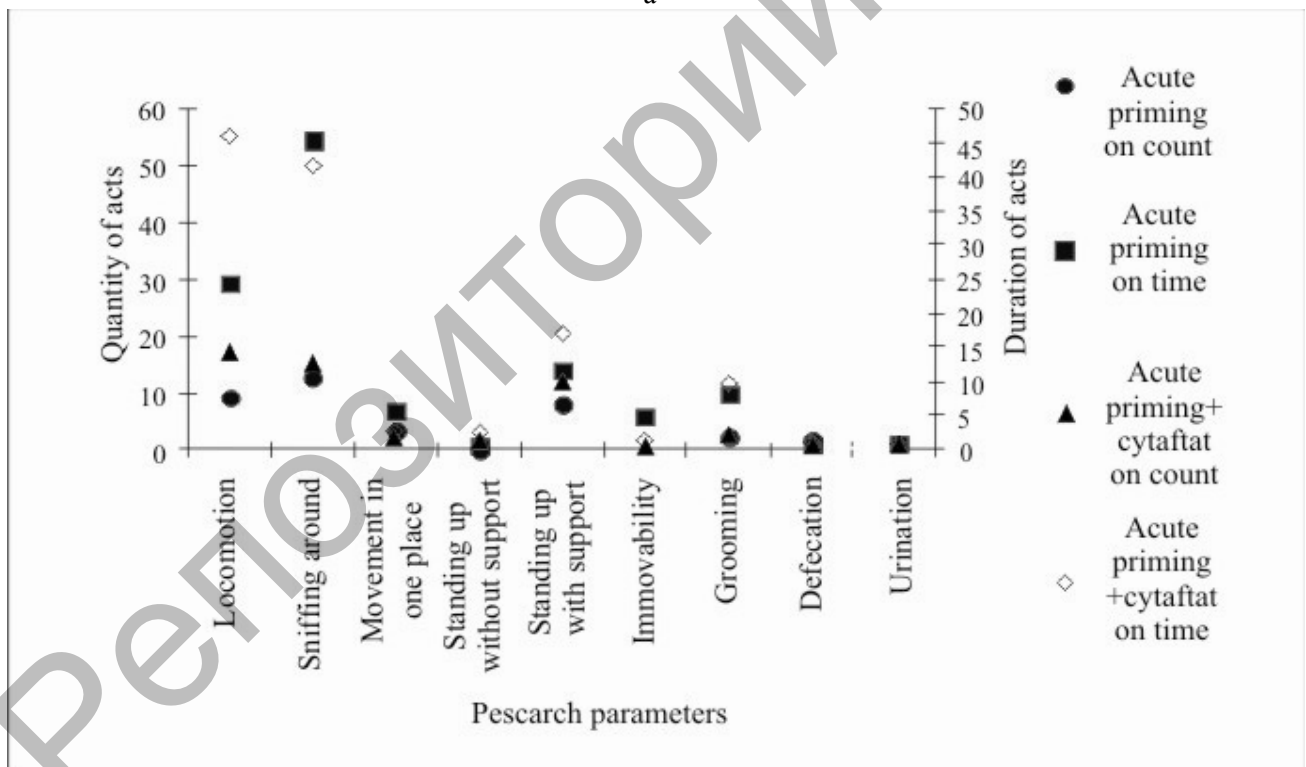
The biggest number of the behavioral acts was represented by locomotion and, correspondingly, more time in the control experiments was spent on it.

During the acute intoxication number of the locomotion acts reduces at 76,04 % ($p < 0,01$), and their duration reduces at 28,29 %. After introduction of «Cytafat» preparation to the third group of the animals, the reduction of locomotion acts number was observed at 63,77 % ($p < 0,01$) in comparison with the control data, but in comparison with the data of the second group, this parameter is 51,06 % more ($p < 0,05$). The duration of this act is not much longer than the parameter of the control animals; and in comparison with the data of the second group of the animals it is 55,78 % longer, which demonstrates the activity of the animals of the given group (drawing 1 a, b).

Under the chronic intoxication by NDMA the acts number of this parameter reduces at 69,65 % ($p < 0,001$), the duration at 8,29 % in comparison with the control animals. And after introduction of «Cytafat» preparation to the fifth group, number of the acts of this behavior parameter was 70,15 % less ($p < 0,01$) than the control data, which is insignificantly less than the fourth group data. The locomotion duration of the fifth group was 2,68 % less than the control group data and 8,24 % more than the fourth group data. This is the evidence of the motor activity suppression under chronic intoxication by NDMA and after correction by «Cytafat» preparation, but in a case of «Cytafat» preparation application the animals began to spend more time for locomotion acts and became more active (drawing 2 a, b.).



a



b

Drawing 1 — Average amount of the basic elements of rats species-specific behavior under acute intoxication by NDMA (a) and under introduction of «Cytatfat» preparation (b). The reliability of the distinctions for the average amount of behavioral reactions at compared groups is given in the text.

Sniffing around, vertical activity, movements at one place, grooming, immobility, defecation and urination are the next, referring to a number and duration of the behavioral acts of the control animals.

Sniffing around takes the first place at the second group — referring to the structure of the behavioral acts. This parameter is 36,84 % ($p < 0,01$) higher in number and 54,85 % ($p < 0,01$) longer than the same parameter for the control animals.

Sniffing around (its number and duration) takes the second place at the third group, similar to the control animals. This behavior reaction which characterizes the research component of the CNS activity was 30,53 % ($p < 0,01$) higher in number, and its duration was 18,86 % ($p < 0,05$) more compare to the control group. In comparison with the data of the second group, the number of this act was insignificantly less (4,6 %) and its duration was 22,99 % ($p < 0,01$) lower as well.

Sniffing around takes the first place at the fourth group, its number and duration were accordingly 40 % ($p < 0,01$) and 28,57 % ($p < 0,01$) higher compare to the control group. Sniffing around dominates at the fifth group as well — number of the acts is 38,95 % ($p < 0,01$) higher, the duration is 18,28 % higher compare to the control animals. The fourth group data do not differ significantly.

The first kind of the vertical activity (standing up with the support) was less in number in duration than the control data — 15,21 % and 28,2 % correspondingly. The second kind of the vertical activity (standing up without a support) was lower in number in duration — 96 % ($p < 0,001$) and 73,91 % ($p < 0,01$) correspondingly.

At the introduction of «Cytafat» preparation at the third group the first kind of the vertical activity has changed insignificantly compare to the control data, and compare to the second group data it is 25,64 % ($p < 0,05$) higher in number, and 18,57 % longer in duration. The second kind of the vertical activity for the third group is 44 % ($p < 0,001$) less in number compare to the control group data and is the same in duration. Compare to the second group data it is 33,33 % ($p < 0,01$) higher in number, and 300 % ($p < 0,001$) longer.

The first kind of the vertical activity for the fourth group is 30,43 % less in number and 46,86 % ($p < 0,01$) less in duration than the control group. The second kind of the vertical activity is less compare to the control group — 80 % ($p < 0,01$) less in number and 60,86 % ($p < 0,001$) less in duration. At the fifth group the second kind of the vertical activity is also less in both number and duration — 42,39 % ($p < 0,05$) and 50,52 % correspondingly — compare to the control group; compare to the fourth group this parameter is 17,19 % ($p < 0,05$) less in number and its duration differs slightly. In comparison with the data of the fourth group, this parameter is 200 % ($p < 0,001$) higher in both — number and duration.

The grooming act was higher in number at the fourth group — 45 % ($p < 0,01$) and its duration was not changed. The fifth group changes (referring grooming) were not significant compare to the control data, and compare to the fourth group data this parameter was 37,94 % ($p < 0,01$) less in number and 13,4 % longer.

The act varies slightly at the second and third groups in comparison with the control animals.

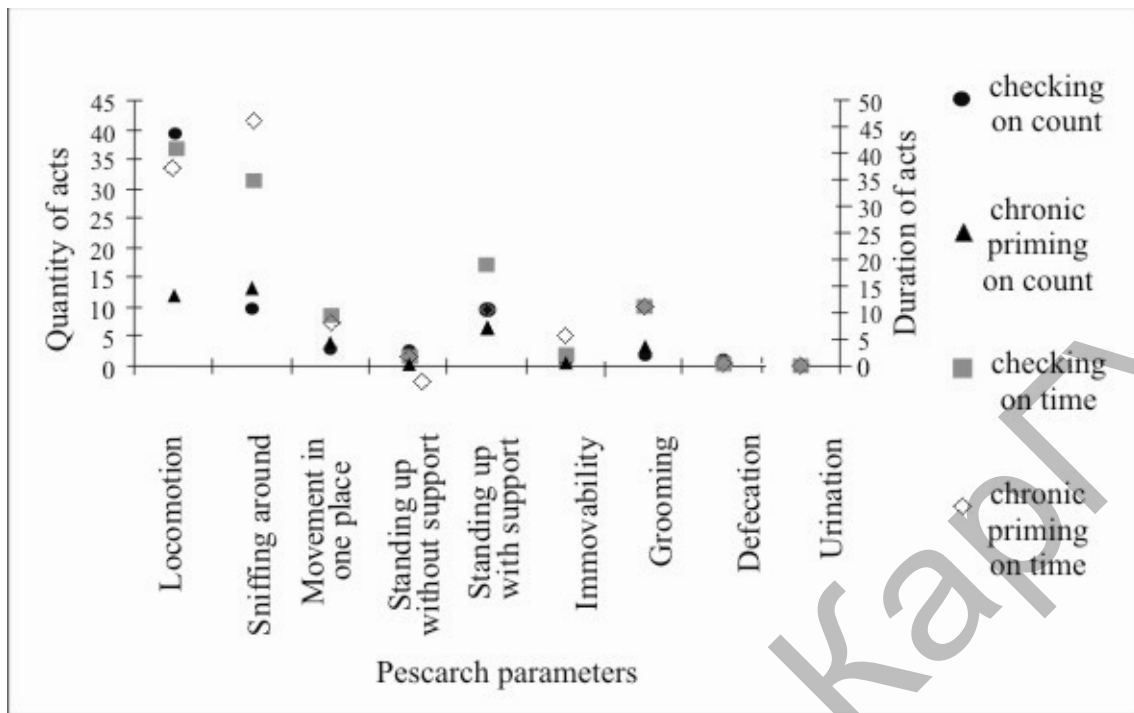
In the second group the immovability has increased at 220 % ($p < 0,01$) referring to quantity and at 180 % ($p < 0,05$) referring to duration; and at introduction of «Cytafat» preparation in the third group of the animals this parameter was 60 % ($p < 0,01$) less referring to quantity and 50 % ($p < 0,05$) less referring to duration in comparison with the control group data. It is 87,5 % ($p < 0,01$) less in quantity and 82,14 % less in duration in comparison with the second group data.

The immovability act was increasing under intoxication by NDMA in the fourth group — 80 % referring to quantity, 165 % ($p < 0,05$) referring to duration; in the fifth group this parameter was also increasing - 20 % ($p < 0,05$) referring to quantity, 25 % ($p < 0,05$) referring to duration compare to the control animals data. At comparison with the fourth group data it was 33 % ($p < 0,01$) less referring to quantity and 72 % ($p < 0,01$) less referring to duration. Defecation and urination acts of the tested animals were shown poorly.

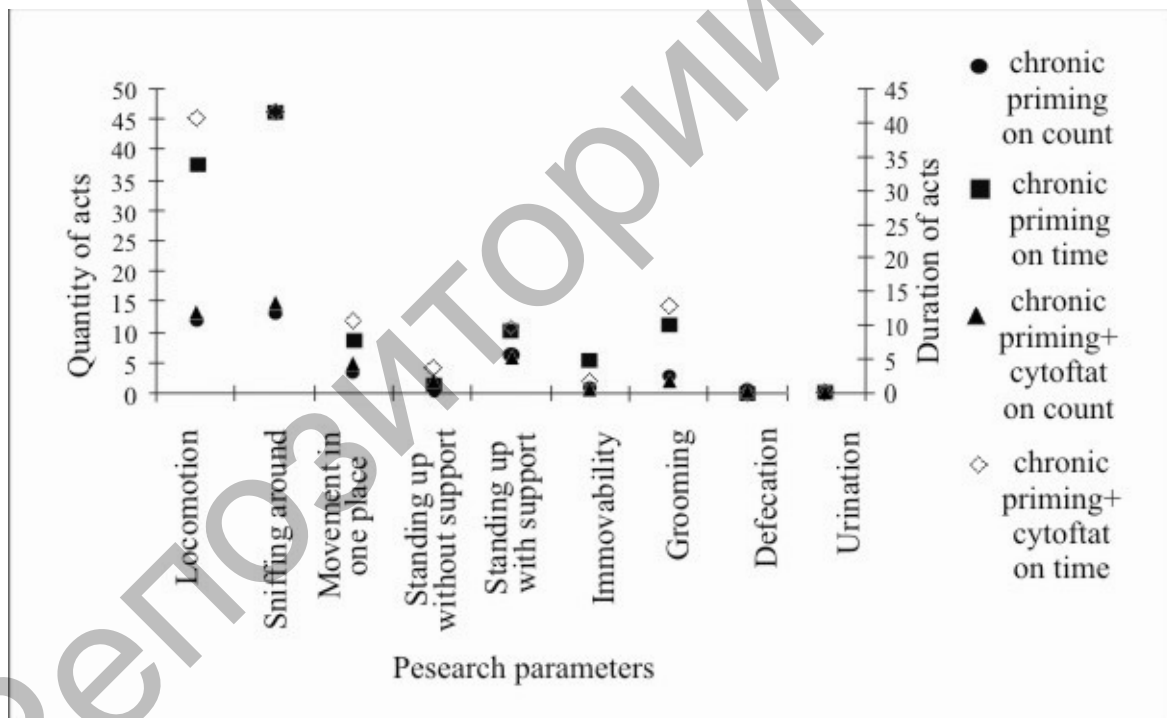
The analysis of rodents behavior in experimental model «Open field» and under stress factor (acute and chronic intoxication by NDMA) influence led to the several conclusions on how the animal behavior under stress differs etologically from the behavior in normal (comfortable) conditions.

Thus, the above mentioned changes lead to the conclusion that the motor component (horizontal — locomotion, movement in one fixed area; vertical — standing up with the support, standing up without a support) is suppressed by the NDMA priming, the more is the doze the more is suppression.

The research component of both group behavior is increased due to the high parameters of sniffing around.



a



b

Drawing 2 — Average amount of the basic elements of rats species-specific behavior under acute intoxication by NDMA (a) and under introduction of «Cytatfat» preparation (b). The reliability of the distinctions for the average amount of behavioral reactions at compared groups is given in the text.

The suppression of motor acts number and the increasing of the immovability acts confirm, that under the long application of the moderate dozes of NDMA various nervous system dysfunctions take place. Those changes are more distinctive under the acute intoxication. It is possible to admit, that the stress causes animals general motor deficiency. The interesting detail of the analysis of relationship in «behavior-stress» system is that the increasing of the research activity can take place at the same time.

Fear or anxiety can be the other important factors under the stress, they often cause «hiding» as a defense reaction (increasing immovability and sniffing around — in number and time characteristics — of the animals who received «Cytafat».

Perhaps, the motivation of the animals to the interaction is decreasing under the stress which leads to the excessive self — accent.

Grooming activation by the stress at the forth group of the animals who have received NDMA for 3 months, might be connected to the adoption need to decline the level of hyper-stimulation caused by stress. According to other authors, the biological meaning of the grooming stress activation can be explained as classical displaced activity [6, 10, 11]. This behavior form is often observed as manipulation of rodents with their bodies — such as appearance improvement, which is not adequate in the given situation [12]. The explanation of such nonsense care is that it may ease tension and help to output of nervous energy [12, 11].

Socially-adaptive value of the grooming increasing, registered under the stress, might mean that the grooming is provoked by stress until more adequate in the situation behavior forms (aggression or escape) are shown. Alternatively, grooming can replace some other behavior forms (e.g. research activity), being suppressed by fear, anxiety or other reasons [8]. Therefore it is possible to assume, that similar social factor has an important meaning in the natural conditions (perhaps, it was evolutionally fixed as a «stress-grooming-behavior» cluster).

Despite the often definition of grooming as «un-featured», non-specific behavior, it is the whole combination of heterogenic, extremely complicated to interpret but very informative behavior reactions [14].

Motor component has been insignificantly changed by «Cytafat» introduction, but based on the other parameters it is possible to assume that «Cytafat» positively influences the central nervous system.

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