

EVALUATION OF ANXIOLYTIC ACTIVITY IN A NUMBER OF DERIVATIVES OF DIPHENILGLYCOLIC ACID IN "OPEN FIELD" TEST

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The active pace of modern life, the continuous development of information technology, and also adverse social situations have a considerable influence on the humans nervous system and their mental health. Such a state inevitably leads to a significant decrease in efficiency and vitality, and also to strong quality of life and social inclusion. In many cases, a certain level of anxiety is a quite normal thing, which is a natural reaction to a stressful situation. It develops into a problem only when the level of anxiety is not proportional to its cause or if there is no objective external cause for anxiety. In the end of 50-ies last century tranquilizers were the basic medicines that were used to treat such diseases. But it later turned out, along with certain medicinal properties, these drugs have a number of serious side effects such as – effect dependence, drowsiness, impaired memory and some lethargy.

The search for new compounds which have an anxiolytic activity and don't cause addiction, is an urgent problem of medicine and pharmacy to improve the human condition.

The purpose of this study was the search substances that have an anxiolytic activity in a number of derivatives of diphenilglycolic acid and the study of their effect on behavioral responses of animals to test "open field".

The evaluation of anxiolytic activity was conducted among 7 new biologically active substances - derivatives of diphenilglycolic acid. Its N-heterylamidy (N-heterylamides) (KMS-10, KMS-282, KMS-284) products of intramolecular cyclization (KMS-303, KMS-229), and on the basis amides (KMS-68, KMS-70) were studied. Study substances were administered orally in the form of aqueous solutions in doses 12 mg/kg in 60 minutes before the experiment start. The animals of control group were injected with the corresponding volume of saline.

The study of behavioral reactions was performed using "open field" test. Using "open field" influence of study drugs on orientation motive reaction and locomotor activity was studied and anxiety model was created. Exploratory activity is an important adaptive mechanism facilitating the probability of individuals survival. "Open field" test recorded the following parameters: rear onto its hind legs number – vertical component of estimated response, number of crossed squares – horizontal component; number of scuttles in the holes – hole exploratory behavior that reflects exploratory activity, and the number of defecation, urination and grooming acts – indicator of animal emotion. During the test exploratory activity appears as central coming out and increased number of explored holes. Test duration was 3 minutes.

The main manifestations of orientation exploratory behavior study included rashes on the surface of the field that are measured by the number of crossed squares and vertical racks.

Analysis of orientation exploratory behavior of rats in "open field" test in terms of horizontal motion and vertical motor activity reveals motivational part of animals. The number of squares crossed at the surface of open field of the experimental animals injected by 3-(2-Hydroxy-2 2-diphenyl-acetylamino) -thiophene-2-carboxylic acid methyl ester (KMS-10) were decreased, the activity decreased significantly to 13.43, which is 43% less than in the group of control animals. At the same time, an increase of the number of vertical racks (34%) was observed. After administration of 6- (Morpholine-4-carbonyl) -3,3-diphenyl-1H, 3H-thieno [3,4-b] pyrrol-2-one (KMS-70) horizontal activity of animals grew by 75%, N-3-indolyl amide of diphenilglycolic acid (KMS-282) - 40% of six-members thienolactames (KMS-303) – to 26.43%. The vertical

component of the estimated response increased in experimental animals injected with seven-members thienolactames (KMS-229) and 3- (2-Hydroxy-2,2-diphenyl-acetylamino) -5methoxy-1-methyl-1H-indole-2-carboxylic acid ethyl ester (KMS-284), but the result is not statistically significant. After administration of [2- (1H-imidazol-4-yl) -ethyl] amide (KMS-68), KMS-70, KMS- 282 and KMS-303 index decreased significantly by 27%, 34%, 63% and 47% respectively.

Number of explored holes characterizes cognitive activity of rats. The administration of substances didn't cause significant changes.

Level of rats emotional state is measured by the number of defecations and urination. Number of defecation after administration of test substances significantly reduced. Urination number after administration of KMS-10 slightly reduced, but the results are not significant. After administration of remaining substances, such as KMS-70, KMS-229, KMS-284, KMS-303, urination was absent what is significant. Number of grooming with the introduction of KMS-10 in experimental group of rats was significantly increased by 133%. Changes of characteristics, such as lack of grooming were observed in the group of experimental animals after administration of KMS-70, KMS-284, KMS-303, which is not statistically significantly compared with the control.

The sum of all activities, which were registered during the "open field" test after administration of KMS-70 and KMS-282 significantly increased by 15,5% та 7,9% respectively, and administration of KMS-68 significantly reduced the parameter by 9,5%. The administration of substance KMS-10 significantly reduced the amount of activities that were recorded during the test, in a group of experimental animals by 15,5% compared to the control group.

Color of "open field" arena influences on the behavior of experimental animals. In white open field there is stress behavior caused by the effect of novelty and open space. Individual rats resistance to emotional stress depends on the nature of their behavior in the test: motor and exploratory activity, emotional state that is manifested by the number of defecation, urination and grooming acts.

In case of absent of any shelter animals feel more protected being at the wall of the field. Attempts to escape in "holes" on the surface of the field become more frequent. Rare coming-outs in the center of the field suggest the prevalence of protective type of exploratory behavior.

Horizontal (motor) activity shows the level of anxiety in experimental animals: the higher the activity compared with the control group, the lower the level of anxiety. Number of vertical racks reflects the exploratory rat activity.

After administration of KMS-10 the group of experimental animals experienced a significant decrease in physical activity. A lower number of desertions evidence of suppression of emotional status, which is reflected in the reduction of motor activity. Given the fact that the introduction of this compound in animals has increased the number of vertical posts, we can conclude that this substance has anxiolytic action with muscle-relaxant activity. the administration of substances didn't cause significant changes.

The number of crossed squares and sum of activity were significantly increased after administration of KMS-70 and KMS-282.

Among 7 new biological substances the test substances – derivatives of diphenylglycolic acid two substances, namely KMS-10 and KMS-68, characterized anxiolytic activity. After administration of KMS-10 a significant decrease motor activity and increase the number of vertical racks were observed. Thus, substance KMS-10 acts as an anxiolytic with muscle-relaxant of action.