ACTION OF METRAZOL ON DEFENSIVE BEHAVIOR IN RATS

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Individual sensitivity of organisms to drugs modifying the functional properties of systems controlling the level of emotional reactivity is an extremely urgent problem. The action of anxiety-inducing agents on learning has been inadequately studied [2], and individual differences in this matter remain virtually unstudied. Accordingly the comparative study of differences in the action of drugs inducing anxiety states is very interesting.

In the investigation described below dependence of changes in defensive behavior arising in rats under the influence of the anxiety-inducing drug metrazol on individual differences in animals was investigated.

EXPERIMENTAL METHOD

Male Wistar rats were used. The animals were trained in a shuttle box, using the "Reflex 16" experimental computerized system (Colombus Instruments, USA). With this system it is possible to use three stimuli – photic, acoustic, nociceptive (footshock). Each stimulus lasted 10 sec. Each experiment included 20 presentations, 60 sec in duration (interval between them 30 sec). The photic stimulus was neutral, the acoustic was accompanied by an electric shock. The animal could respond in four ways: to the conditioned stimulus, to the nociceptive stimulus, with no change of position, (passive defensive method of response), and intertrial response. After 200 presentations and after scalping of the animals an injection of metrazol (10 μg/5 μl) was given into the lateral ventricle (according to data in the literature [2, 4] metrazol induces a marked degree of anxiety). Control animals were given 5 μl of physiological saline. Before training, the individual differences in behavior of the rats were studied on an "Opto-Varimex" apparatus (Colombus Instruments, USA). The results were subjected to statistical analysis by Wilcoxon's test [1].

EXPERIMENTAL RESULTS

Preliminary investigation in the open field test revealed great differences in the level of motor activity of the experimental animals. As a result, three groups, each of 21 rats, were selected: with low activity ("passive"), with high activity ("active"), and with intermediate activity ("average"). The criteria of selection were elaborated beforehand: they were the points of inflexion on the curve of the normal distribution describing the rats' motor activity in the open field. Rats whose motor activity was on the part of the curve before the first point of inflexion were considered to be "passive," those after the second point of inflexion were "active," and animals whose motor activity fell on the middle part of the curve were "average."

These differences had no effect on the learning process in the shuttlebox – in all three groups two main strategies of avoidance behavior were detected: predominance of running away either in response to the conditioned acoustic stimulus (type 1 strategy) or directly in response to electric shock (type 2 strategy). Behavior of the type 1

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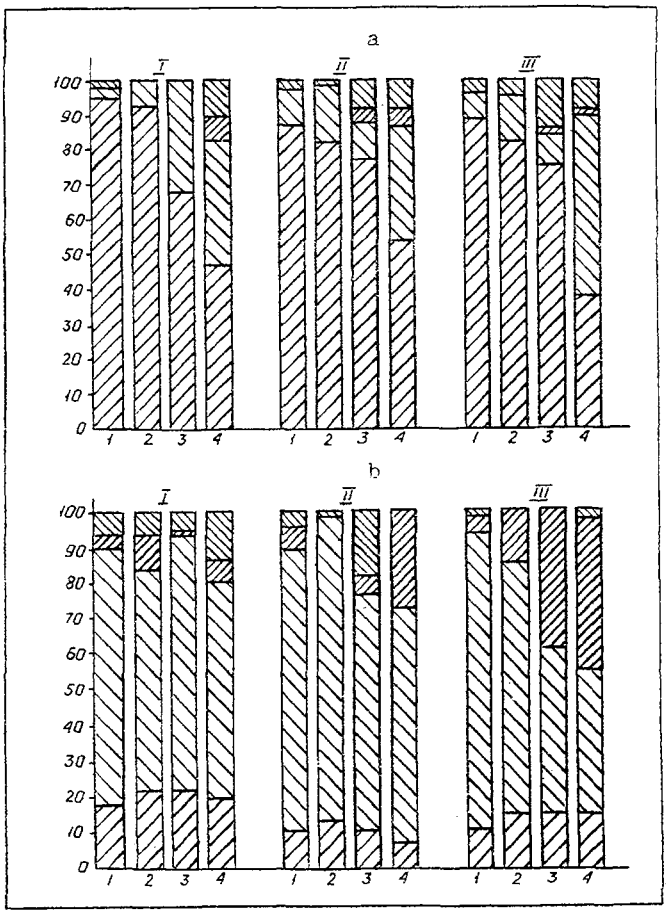

Fig. 1. Changes in conditioned defensive reflect formed in rats with type 1 (a) and type 2 (b) strategies of behavior in response to different types of stimulation: I) "active"; II) "average"; III) "passive" rats; 1) last experiment; 2) experiment after scalping; 3) injection of physiological saline; 4) injection of metrazol; oblique shading sloping to the right – response to conditioned stimulus, oblique shading sloping to the left – response to electric shock; close oblique shading with sloping to the right – no change of position; close oblique shading sloping to the left – intertrial reactions. Ordinate, representation of different methods of response in experiment.

strategy was characterized by the virtually complete absence of the passive defensive component, which was clearly manifested in the rats of type 2.

The procedure of scalping itself is undoubtedly stress-inducing. Nevertheless, on the day after the operation the rats demonstrated about the same level of conditioned-reflex activity as on the last day before the operation. Only a small increase can be noted in the number of intertrial and passive-defensive reactions (Fig. 1).

Control injection of physiological saline, which did not change the general strategy of behavior, i.e., running away in response either to the acoustic or the nociceptive stimulus, predominated, significantly increased the number of intertrial reactions (which may be an indicator of the restless state of the animals) in rats of the passive and average groups (Fig. 1), whereas in the passive rats with type 2 strategy, it increased the passive defensive component.

Metrazol had the strongest action on the groups of active rats with both types of strategy (Fig. 1): the number of passive defensive and intertrial reactions in these animals was considerably and significantly increased. In the passive and average rats, which preferred the type 1 strategy, the number of reactions to electric shock increased significantly at the expense of a decrease in the number of reactions to the conditioned stimulus (Fig. 1a).

It can accordingly be concluded that rats with the type 1 strategy, responding preferentially to the conditioned acoustic stimulus, were most sensitive to the action of the anxiety-inducing drugs. It is interesting to note that the individual level of motor activity, while not significantly affecting adaptive behavior in a situation usual for the animal, is significant after injection of metrazol: animals with the greatest motor and investigative activity were the most vulnerable. Metrazol, however, in low doses, is on the one hand known to be anxiety-inducing, whereas on the other hand, it can provoke paroxysmal states [3]. This fact is reflected in the increased reactivity of rats with high levels of open field activity to it.

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