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Assessment of Exploratory Activity and Anxiety in Rats with Different Levels of Impulsive Behavior

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Selection of a pedal to obtain reinforcement depending on its value and delay time was used to divide rats into three groups. Animals selecting the valuable but delayed reinforcement in more than 70% of cases were assigned to the self-controlled groups, while those making this choice in fewer than 30% of case were assigned to the impulsive group and rats showing no preference in choosing reinforcement were members of the ambivalent group. The levels of orientational-exploratory activity and anxiety in rats with different types of behavior were then assessed in an elevated plus maze, on acquisition of a conditioned fear reaction (fear conditioning), and in a neophagophobia test (novelty suppressed feeding). The animals which were least active and most anxious in all tests were those of the self-controlled group. Ambivalent rats were the least anxious in the elevated plus maze test and produced the greatest number of successful trials in terms of finding and eating food in the novel context, as compared with rats of the other groups. Impulsive animals demonstrated more marked freezing reactions on acquisition of the conditioned fear reaction in the fear conditioning test and found food more quickly in the novel context.

Keywords: impulsivity, rats, anxiety, behavioral study, elevated plus maze, acquisition of conditioned fear reaction, feeding behavior in a novel context.

Impulsivity is characterized by a wide spectrum of behavioral reactions, including risky actions performed without the appropriate consideration and executed on the spur of the moment [5, 7]. At the same time, impulsivity is a feature of normal behavior and can be a useful characteristic in certain circumstances. However, excessive impulsivity is often pathological in nature and is manifest as a variety of mental disorders, including psychopathy, suicide, attention deficit hyperactivity disorder in children, etc. [14, 18]. Impulsivity is linked with weakness of behavioral inhibition, ill-considered decision-taking, and intolerance of delay in reinforcement [21, 22, 28, 29]. In laboratory conditions, impulsive behavior is studied in animals. One such model is known in the English-language literature as the "delay-discount" model, which provides for studies of subjective changes in the value of reinforcement depending on the duration of the delay before its presentation.

A significant focus in animal studies of impulsivity is placed on the link between this behavior and various types of dependence on chemical substances [15, 20, 26, and others]. Little is known about the relationship between impulsivity and other behavioral manifestations, such as anxiety, emotional states, and exploratory behavior. Gray [10] suggested that the level of anxiety can have significant influence on the occurrence of impulsivity and in some conditions is involved in regulating the behavioral inhibition mechanism. However, there have only been a few studies of the extent to which anxiety and novelty-seeking coexist and influence impulsive behavior [18]. We have previously [1, 3] reported studies of the behavior of animals with different levels of impulsivity in the open field and light-dark chamber tests. The results of these experiments showed that impulsive animals adapt to a novel context more rapidly and display more marked exploratory activity than self-controlled animals.

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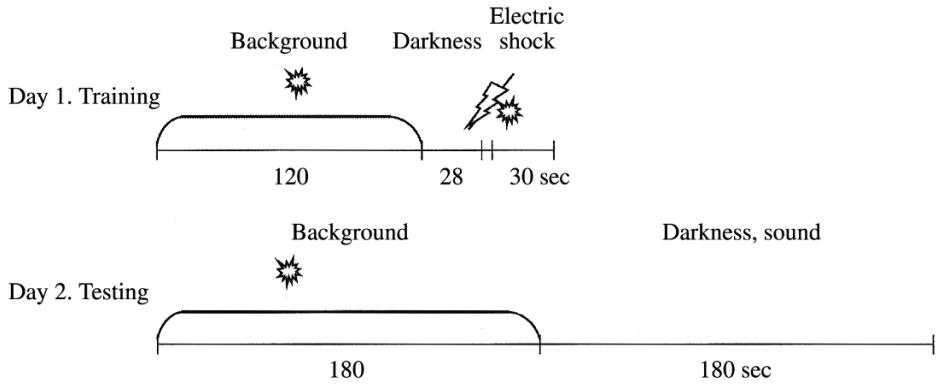

Fig. 1. Scheme of conditioned fear acquisition experiment.

Self-controlled rats had higher levels of anxiety [1]. However, the open field test is not particularly suitable for assessing anxiety, as a number of the parameters used for evaluating this state can reflect not only anxiety, but also general emotional arousal. More precise assessment of anxiety levels in rats and further development of our view of the orientational-exploratory behavior of impulsive and self-controlled animals can be obtained using tests with greater specificity for identifying these characteristics. Methods for studying behavior in the elevated plus maze (EPM) [4] and training to a conditioned fear reaction in a test for neophagophobia meet these needs entirely.

We report here studies using a method based on selection of reinforcement value depending on the time delay from presentation, which divided the animals into groups based on the level of impulsivity. The behavior of rats in groups with different levels of impulsivity was then studied using tests for anxiety in the elevated plus maze and training to a conditioned-reflex fear reaction (fear conditioning) by investigating feeding behavior in a novel context and in a neophagophobia test.

Methods

Experiments were performed on male Wistar rats weighing 350–450 g and aged 4–6 months. Experiments were conducted in compliance with the humanitarian principles laid down in the Directives of the European Community (86/609/EC) and approved by the Medical Ethics Committee in accordance with the positions of the Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences in relation to studies using experimental animals.

Rats were kept in cages in groups of five animals with free access to water. The quantity of food supplied was controlled to keep weight at about 80% of the weight with free access to food. Rats were initially trained in an experimental apparatus to press a pedal, reinforced with standard 45-mg pellets (Bio-Serv, USA). Animals were given a choice between a scanty reinforcement (one pellet) delivered immediately after pressing the pedal and a more valuable reinforcement (four pellets) delivered 5 sec after pressing. The experimental scheme has been described in more detail in [2, 3]. Animals selecting the valuable but delayed reward in more than 70% of trials were assigned to the "self-controlled" group, while those selecting this reward in fewer than 30% of trials formed the "impulsive" group and those lacking preference in reward selection were regarded as "ambivalent." The behavior of rats of different groups was studied using training to a conditioned-reflex fear reaction, in the EPM, and in a neophagophobia test.

Elevated plus maze. Studies used a EPM constructed from plywood (3 mm thick) and painted black. The arms were 10 cm wide and 50 cm long, and the walls of the closed arms were 40 cm high. A central platform of size 10×10 cm was located at the crossing point. A modified EPM was used in which there were no closing walls at the ends of the closed arms (some authors believe that looking down from (hanging from) the closed arms reflects risk-assessing behavior) [24, 26]. The maze was mounted on four supports (legs) at a height of 80 cm above the floor. Such parameters as the number of excursions and the durations of time spent in the open and closed arms, the number of hangings from the open arms and terminal parts of the closed arms, the number of rearings, the number and durations of grooming reactions, and the numbers of defecation and urination reactions were monitored. Rats were tested once in sessions lasting 5 min for each rat. Data recording and analysis were performed using the Noldus EthoVision 3.1 program. Differences between groups of animals with different levels of impulsivity were compared.

Training to a conditioned-reflex fear reaction. The conditioned fear reaction was developed in an experimental chamber from Panlab (Startle and Fear Combined System, USA). The apparatus consisted of a chamber of size $250 \times 250 \times 250$ mm, which was placed in a soundproofed chamber of size $670 \times 530 \times 550$ mm. An original platform with a pressure probe was used for quantitative determination of

the level of the animal's freezing. A program from the same company was used to analyze the data obtained. Rats were tested over a two-day period and the experimental scheme is shown in Fig. 1. Animals were trained on day 1: an animal was placed in a soundproofed chamber, which it explored for 2 min with the light switched on. The light was then switched off and a sound signal (60 dB) was presented for 28 sec; an electric shock (2 mA) was delivered immediately after the sound and the animal was left in the chamber without any further events for 30 sec with the light on. On day 2, the rat was kept in the chamber with the light on for 3 min, after which the light was switched off and the sound signal was delivered after a further 3 min. The proportions of freezing reactions during the training and testing of the animals with different levels of impulsivity were analyzed and compared.

Studies of feeding behavior in a novel context (neophagophobia, novelty-suppressed feeding test). Animals were subjected to 24-h food deprivation, after which they were placed in a novel context for 5 min, this being an unfamiliar open field (a chamber of size 100 × 100 × 40 cm) with food in the center. Success levels in the test were evaluated in terms of finding and consuming food in the novel context and, when trials were successful, latent periods of the onset of food consumption were measured.

Double-blind monitoring during testing of behavioral characteristics was achieved on the basis that the typology of each animal was determined after recording of behavioral parameters, the experimenter not knowing the results of the behavioral tests.

Data were analyzed statistically in Statistica. Distributions were confirmed as normal using the Kolmogorov–Smirnov test. Groups were compared using the one-way ANOVA test and the nonparametric Mann–Whitney test (U test) and the 2 × 2 Fisher test (the F test). Differences were regarded as statistically significant at $p < 0.05$.

Results

Behavior of rats in the elevated plus maze test. On the basis of the rats' choice of a valuable delayed or a small but immediate reinforcement, 28 animals were assigned to the group of impulsive rats and 30 to the self-controlled group; 12 animals showed no preference in selecting the pedals and were assigned to the ambivalent group.

The most interesting parameter in the EPM was the comparison of the behavior of the animals when placed in the open and closed arms. We assessed behavioral activity in terms of the ratio of concrete behavioral parameters (frequency of visits, their duration, the distance covered, and speed) in the open arms to mean values in the open and closed arms. In terms of the number of excursions into the open arms, self-controlled rats were statistically significantly behind animals of the ambivalent ($p < 0.05$, U test) group; in the open arms, they covered a statistically significantly shorter distance than ambivalent animals ($p < 0.01$, U test) and impulsive animals ($p < 0.05$, U test). The time spent in the open arms by self-controlled rats was also shorter than that of ambivalent animals ($p < 0.05$, U test; Fig. 2, *A*). Thus, ambivalent animals were the most active on testing in the EPM – they visited the open arms of the maze more than other animals, spent longer in them, and moved more, as indicated by the distance covered and the rate of movement. All these parameters had the smallest values in self-controlled animals, while impulsive rats occupied the intermediate position. A further important measure for assessment of anxiety levels was provided by the latent period of excursions into the open arms, where difference were also found between the study groups ($F_{2,67} = 3.5769$, $p = 0.03215$) (Fig. 2, *B*). In this case, the duration of the first visit to an open arm in self-controlled rats was statistically significantly greater than that in the ambivalent group of animals ($p < 0.05$).

Our evaluation of the behavior of animals in the EPM included analysis of the number and duration of reactions such as vertical rearings, hangings, grooming, and glances from the closed arms of the maze during the whole of the test period (Fig. 3, *A*, *B*). In terms of the number of rearings, there were no statistically significant differences between rats of the different typological groups, though the time spent by the animals on these reactions showed a trend to more time taken for these reactions in self-controlled animals than ambivalent animals ($p = 0.08$). In terms of the number and duration of hanging reactions, self-controlled rats also lagged behind ambivalent animals, though here there was only a tendency ($p = 0.08$, $p = 0.05$, respectively). The number of grooming reactions in self-controlled animals was statistically significantly ($p < 0.05$) smaller than that in ambivalent rats. In terms of the duration of grooming reactions and the number and duration of glancing reactions, there were no significant differences between groups of rats. Counting of defecation reactions also revealed statistically significant ($p < 0.05$, U test) differences between rats of the self-controlled and ambivalent groups, these reactions being greater in self-controlled rats.

Behavior of rats in the apparatus during training to the conditioned fear response. Rats of the three study groups (28 impulsive, 30 self-controlled, 12 ambivalent) were trained to a conditioned fear reaction. There were no significant differences between groups in the durations of episodes (reactions) of freezing in baseline conditions on the training day before delivery of the conditioned stimulus. There was only a tendency to a difference in this parameter between impulsive and self-controlled rats ($p = 0.08$), U test). A statistically significantly ($p < 0.05$, U test) greater duration of freezing episodes in impulsive rats was seen on the day after testing (Fig. 4, *A*). Freezing reactions after delivery of the sound signal on the training day were less marked in self-controlled rats than in rats of the other groups, differences compared with impulsive animals being statistically significant ($p < 0.05$, U test) and compared with ambivalent animals trending towards being different ($p = 0.07$, U test).

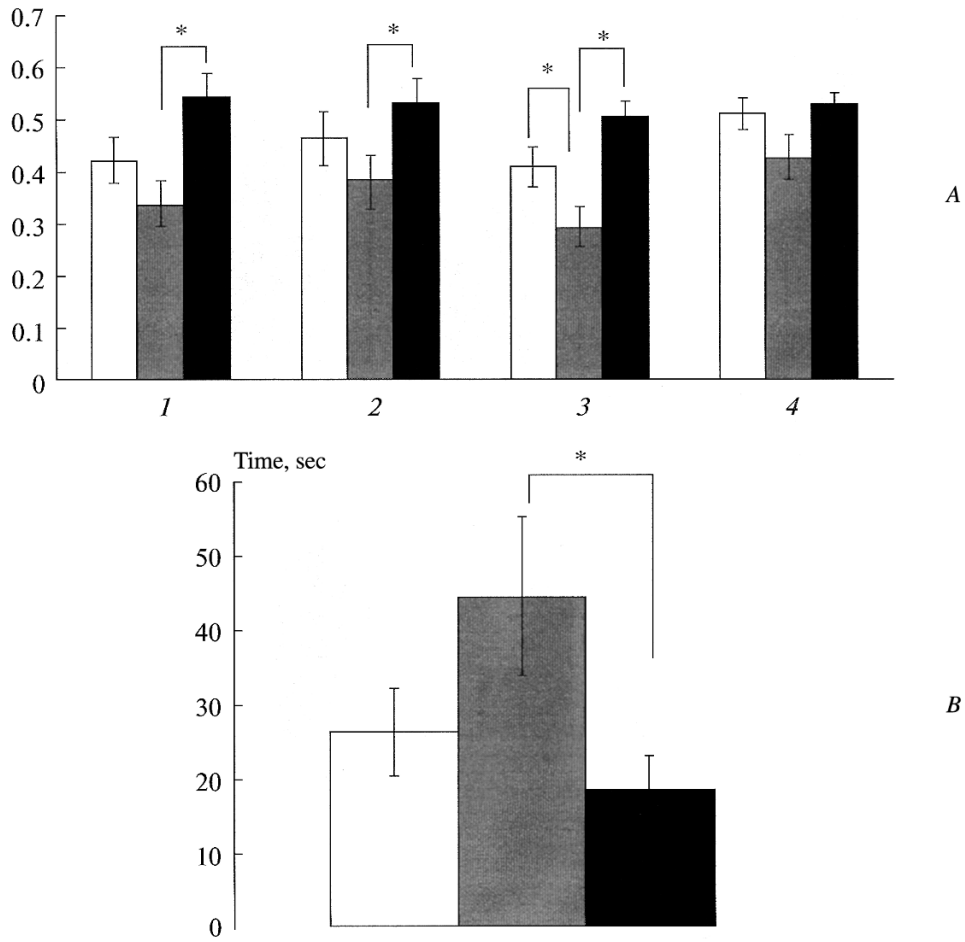

Fig. 2. Activity of rats in the open arms of the EPM. *A*) Motor activity of rat; *1*) number of excursions; *2*) duration of visits (sec); *3*) distance covered (cm); *4*) rate of movement (cm/sec). The vertical axis shows the ratio of measures of activity in the open arms to mean measures of activity in the open and closed arms. *B*) Mean latency of first excursion into the open arms. White columns show impulsive rats; gray columns show self-controlled rats; black columns show ambivalent rats. *Statistically significant differences, $p < 0.05$.

On the following (test) day, there were no differences between rats of the various groups in the extent of freezing reactions in response to the conditioned stimulus (10.92 ± 4.93, 3.00 ± 2.02, and 13.79 ± 8.92) (Fig. 4, *B*).

A difference was seen in emotional parameters between self-controlled and ambivalent animals. On day 1, the number of defecation reactions in self-controlled rats was significantly ($p < 0.05$, *U* test) greater than that in ambivalent rats (Fig. 4, *C*), while the number of urinations was greater in ambivalent rats than self-controlled animals ($p < 0.05$, *U* test) (Fig. 4, *D*).

Assessment of feeding behavior in a novel context (novelty-suppressed feeding). Experiments were performed on 64 animals (27 impulsive, 25 self-controlled, 12 ambivalent). The results of these experiments showed that self-controlled rats had fewer successful trials (i.e., trials in which they found and ate the food) in a novel context as compared with rats of other groups. These differences were statistically significant as compared with ambivalent animals ($p < 0.05$, *F* test) (Fig, 5, *A*). Comparison of the latent periods of finding the food revealed statistically significant differences between groups ($F_{2,31} = 4.1475$, $p = 0.02534$), impulsive rats having the shortest food-finding and -eating times. Differences were statistically significant compared with ambivalent animals ($p < 0.05$, *U* test) and tended to be different compared with self-controlled animals ($p = 0.08$) (Fig. 5, *B*).

Discussion

The elevated plus maze is a widely used method for assessing anxiety in animals. The characteristic features of the elevated plus maze which allow levels of anxiety in animals to be assessed are that it has open and closed arms. Rodents such as rats and mice are known to prefer dark, protected places, which in this case are provided by the closed arms of the maze, and they avoid visiting the open arms. The number of excursions to and the total time spent

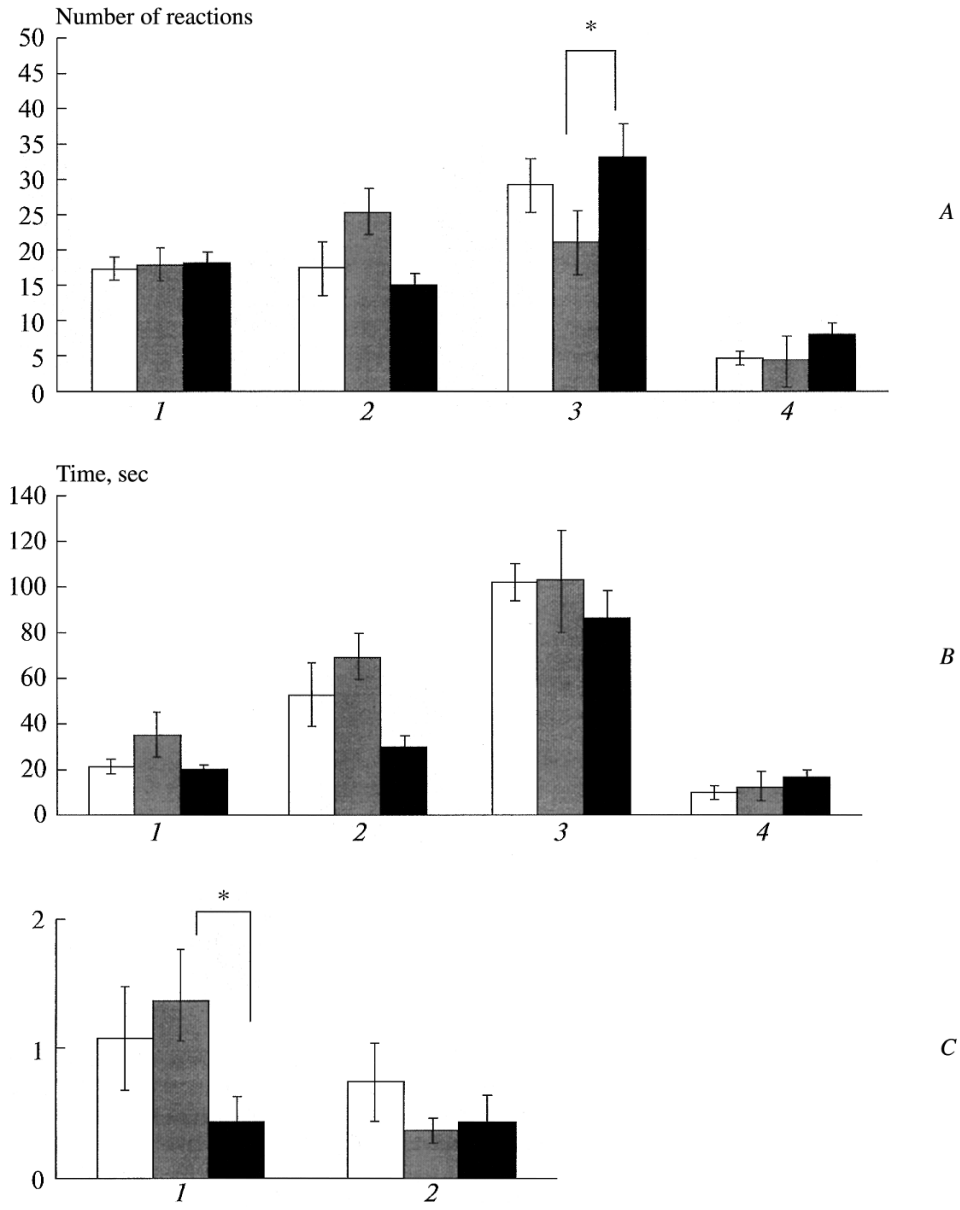

Fig. 3. Emotional reactions in the elevated plus maze. *A*) Number of behavioral reactions. *B*) Duration of behavioral reactions. *1*) Rearings; *2*) hanging reactions; *3*) grooming reactions; *4*) glancing reactions. *C*) Numbers of defecation (*1*) and urination (*2*) reactions. For further details see caption to Fig. 2.

in the open arms, as well as the latency of the first visit, are reliable measures for assessment of levels of anxiety and exploratory behavior [6, 22, 25]. The EPM test also provides some degree of assessment of the locomotor activity of the study animals, as evaluated from the distances covered and the rate of motion.

Our studies identified differences in these behavioral parameters between groups of animals with different levels of impulsive behavior. It should be noted that in the present studies we identified a quite large number of animals whose behavior in selecting reinforcement value did not allow them to be assigned either to the impulsive group or to the self-controlled group, as they made equal proportions of choices of the immediate scanty reinforcement and the delayed but more valuable reinforcement. These animals constituted a separate group – ambivalent rats. These rats were the most active and least anxious in the elevated plus maze test in terms of virtually all measures, with greater values than seen in all other groups. Self-controlled rats, conversely, had the greatest level of anxiety and were char-

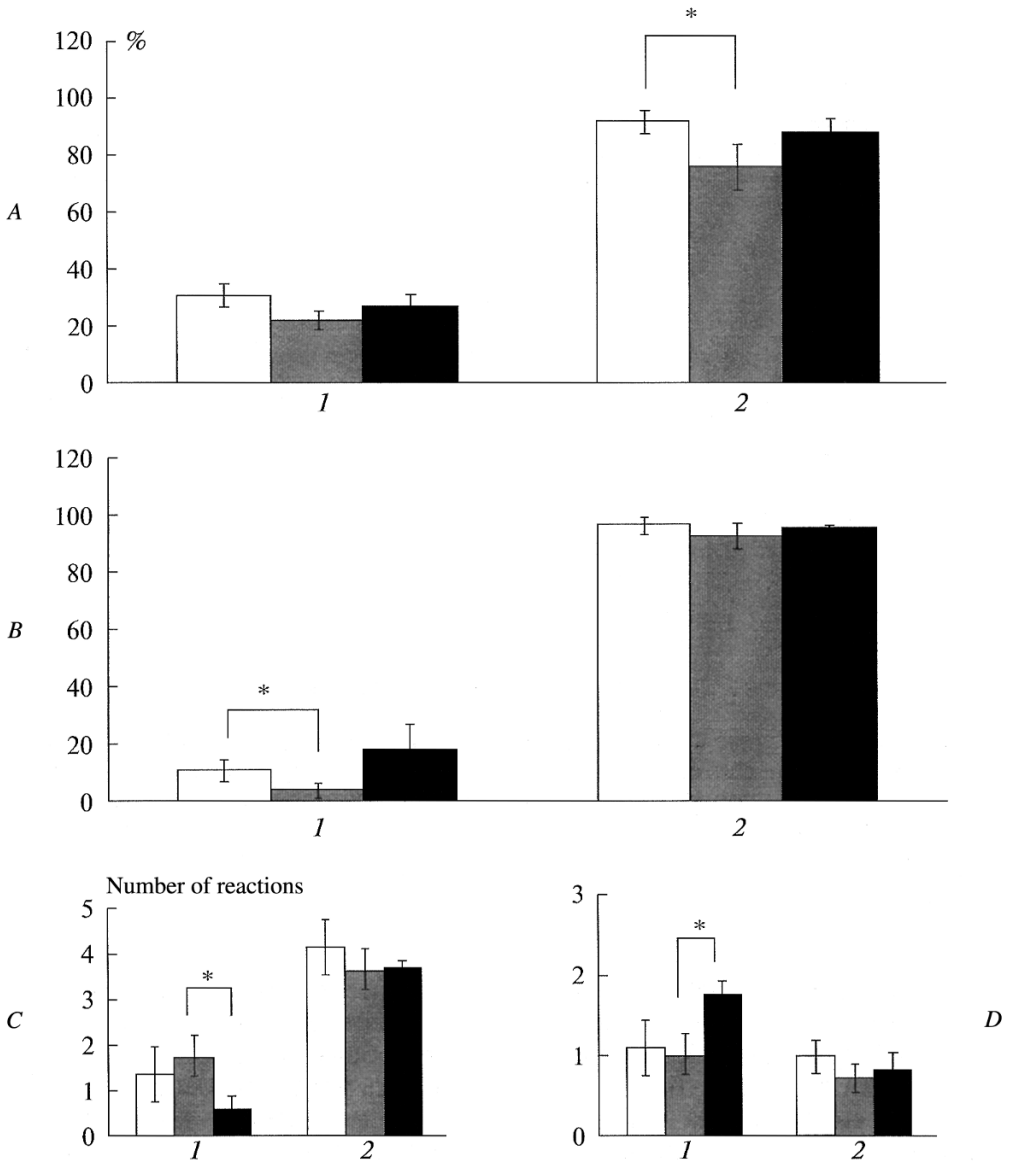

Fig. 4. Acquisition of conditioned fear reaction. *A*) Durations of freezing reactions in background and on the training (*1*) and test (*2*) days. *B*) Duration of freezing reactions to the conditioned stimulus (sound). The vertical axis shows the duration of freezing reactions (% of total test time). *C*) Numbers of defecation reactions . *D*) Numbers of urination reactions on the training (*1*) and test (*2*) days. For further details see caption to Fig. 2.

acterized by decreased exploratory activity. In terms of these behavioral parameters, impulsive animals occupied an intermediate position.

Analysis of reactions such as vertical activity, hanging, grooming, glancing from the closed arms, defecation, and urination was performed to supplement the behavioral profiles of the groups of animals studied here. Vertical activity, apparent in these studies as rearing, correlated closely with horizontal activity [8]. Rearing is an element of species-specific exploratory behavior, which is considered an indicator of anxiety supplementing traditional indexes [23–25]. The present experiments showed no differences in the numbers of rearings between rats of the different typological groups, though their duration in self-controlled rats was significantly greater than in impulsive and ambivalent animals. This may be evidence the exploratory behavior is different in nature in these rats. Rats of the self-controlled group are evidently characterized more by so-called distant investigation [17], i.e., obtaining a significant proportion of their information on the environment from afar, resulting in lower exposure to risk. Our previous study on the behavior of rats in an "emotional resonance" test also showed that the

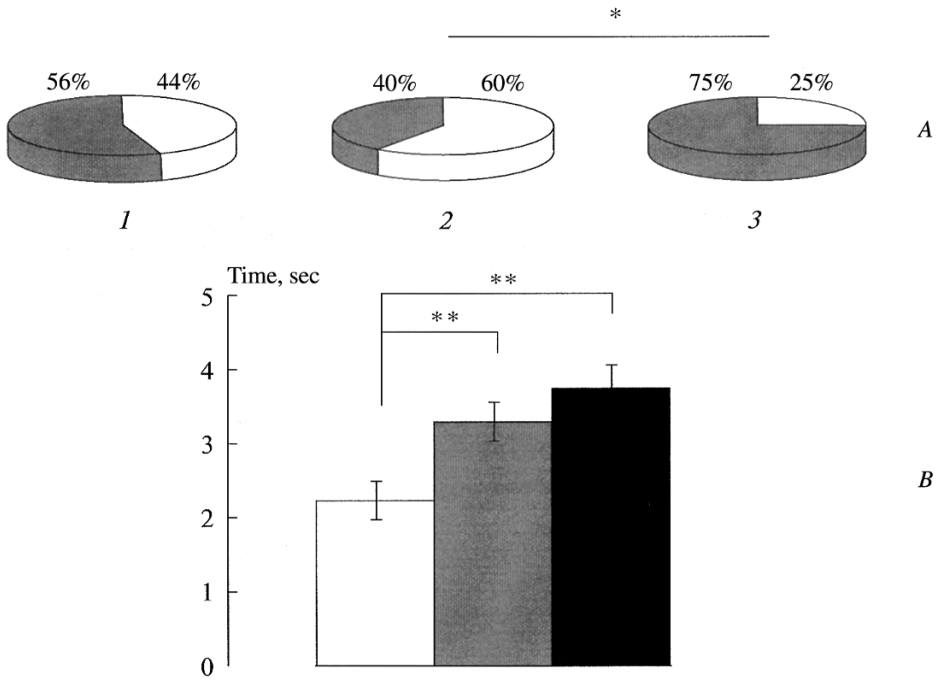

Fig. 5. Feeding behavior of rats in a novel environment (novelty-suppressed feeding). *A*) Proportions of successful (gray sectors) and unsuccessful (light sectors) food-finding trials. *B*) Latent period of finding food, sec. **Statistically significant differences ($p < 0.01$). For further details see caption to Fig. 2.

sense of self-preservation is more developed in rats of the self-controlled group [3].

Many authors link the hanging reaction with such cognitive properties of the nervous system as evaluation of risk prior to decision-taking. Animals found themselves faced with choosing between competing desires: to escape the open space of the arm and the fear of heights. Self-controlled rats also demonstrated larger numbers and longer durations of hanging reactions than animals of the other groups. Thus, the evaluation function is more characteristic of self-controlled rats.

Interpretation of the functional significance of grooming reactions is not always unambiguous. Many authors are of the view that during the first few minutes of being in an unfamiliar environment, grooming is a displacement reaction related to the conflict between the exploratory motivation and fear. As the rats acclimate to the novel context, grooming becomes a reflection of a comfort situation. Our results showed that more marked grooming reactions were demonstrated by ambivalent animals. Fewer of these reactions were seen in self-controlled rats than in ambivalent and impulsive rats.

Defecation and urination are significant factors determined by fear and anxiety states [9, 11, 26–28]. Stress and anxiety are linked with activation of the sympathetic nervous system and increase the intensity of defecation, thus allowing the intensity of emotional stress to be assessed [12]. The greater number of defecation reactions in self-controlled rats is also evidence that they have a greater level of anxiety.

Freezing reactions during acquisition of conditioned fear reactions were more intense in impulsive animals, which may indicate not only the greater intensity of fear reactions in these animals, but also that they have better learning ability.

Studies of feeding behavior in rats in a novel context (novelty-suppressed feeding) also suggested a higher level of anxiety in self-controlled rats than animals of other groups. Impulsive rats were the most active in seeking food, as indicated by the latent period of finding food, though the effectivenesds of seeking behavior was greater in ambivalent animals, as evidenced by the greater proportion of successful trials in which food was found.

These results point to a greater level of anxiety in self-controlled rats than in rats of other groups. The literature contains few data on forms of behavior such as exploratory activity and anxiety in rats with different levels of impulsivity. Our previous studies of behavior of such rats in an open field test demonstrated lower levels of exploratory activity and greater levels of anxiety in self-controlled rats than impulsive rats [1]. This is indirectly supported by data showing greater impulsivity in animals with high levels of exploratory behavior [16].

Studies using rats with different levels of reactivity and hyperactivity (sometimes linked with impulsivity) are also

of interest. Rats with greater reactivity were more active and less anxious than less reactive animals [22]. The same characteristics were also seen with hyperactive rats [27]. Administration of diazepam had no influence on impulsive animals but produced dose-dependent alterations in the selection of the valuable reinforcement in self-controlled animals, pointing to a link between self-control and anxiety [13]. One study on impulsivity and assessment of anxiety was reported by Molander et al. [19], in which the extent of impulsivity in rats was measured in terms of the number of premature reactions in a place differentiation test (5-CSRT, five-choice serial reaction time task). Spontaneously highly impulsive rats entered the open arms of the elevated plus maze significantly more quickly than rats with low levels of impulsivity. The results reported in [19] did not identify any difference in exploratory activity in the open field test or anxiety levels between high- and low-impulsivity rats (on testing in the 5-CSRT). The present studies also found no significant differences in these measures between self-controlled and impulsive animals, though ambivalent animals were significantly different from self-controlled animals in terms of a number of measures.

Conclusions

The results obtained here provide evidence of greater levels of passivity and anxiety in self-controlled animals able to tolerate a delay in order to receive a more valuable reward. Our study is the first on rats whose behavior could be termed neither self-controlled nor impulsive. These animals showed equal proportions of choices of the immediate scanty reward and the more valuable but delayed reward. These animals were the most active and least anxious on testing in the elevated plus maze. This group is evidently the group best adapted to changing environmental conditions and with the least difficulty in correcting their behavior in relation to these conditions.

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