PHARMACOLOGY AND TOXICOLOGY

Acute Extinction of Exploratory Behavior in Mice: Role of the Zoosocial Factor and the Effects of Pyracetam and Scopolamine

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An important role of the zoosocial factor in the acute extinction of exploratory behavior (habituation) is demonstrated by showing that habituation of mice to the new environment of a testing chamber occurs more rapidly and is more strongly marked when a group of animals is placed in the chamber than when animals are placed there singly. The nootropic drug Pyracetam, which improves cognitive functions, accelerated the habituation process only in grouped mice, whereas the amnesia-promoting drug scopolamine inhibited this process in both grouped and single mice.

Key Words: *exploratory activity; zoosocial factor; pyracetam; scopolamine*

Habituation, which is regarded as one of the elementary forms of learning [4], consists in inhibition rather than acquisition of new behavioral responses and for this reason is also called "negative learning" [2,10].

One manifestation of habituation is the attenuation (extinction) with time of exploratory behavior in a new environment as a result of its rating as biologically insignificant. The behavioral aspects of habituation are usually studied with single animals which are repeatedly placed for short periods (up to 5 min) in the testing chamber or box of the recording instrument [8]. If the interval of time between tests is large enough, the animal forgets the information received, and this is manifested in the absence of extinction. In such a situation, the original habituation response can be restored by the nootropic drug pyracetam. A test for acute inhibition of exploratory behavior was proposed originally [1] as a simple screening test for evaluating substances that facilitate cognitive functions. The main feature of this test distinguishing it from the testing method mentioned above is that a group of animals is placed in the chamber only once but for a more extended period (30-40 min); in this case, the inhibition of exploratory behavior is accelerated by nootropic agents [1].

In a group of animals placed in the testing chamber, inhibition of exploratory behavior (movements of animals seeking to orient themselves in the new environment) can be determined at least by two factors: habituation of the animals to the new environment [1,8] and their habituation to each other (zoosocial factor) [6].

The objectives of the present study were to analyze the role of those two factors in the acute extinction of exploratory behavior and evaluate the effects on this process of two compounds, one of which improves mnestic (cognitive) functions and the other deteriorates them.

MATERIALS AND METHODS

Random-bred white male mice (body weight 18-22 g) maintained under standard vivarium condi-

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tions, 50-100 mice per cage, were used. Habituation (acute extinction of exploratory behavior) was studied in mice injected intraperitoneally with either pyracetam, a nootropic drug improving cognitive functions and thus learning (50 mg/kg) [1]; scopolamine, an M-cholinergic receptor blocker interfering with cognitive functions (0.5 mg/kg) [3,7,9]; or 0.9% isotonic NaCl solution (for the control tests). Immediately postinjection, all mice were placed in plastic boxes, one animal per box, where they remained until their motor activity was recorded. In the tests for acute extinction in grouped animals, 10 mice were placed together in the chamber of a motor activity recorder (Opto-varimex) 30 min postinjection; tests for acute extinction in single animals were conducted in the motor activity recorder's chamber to which only one mouse had been transferred at a time 30 min postinjection. Records of motor activity in the chamber over each 5-min intervals of the 30 min recording period were obtained (all recordings were done between 10:00 and 13:00).

As the indicator of habituation, an extinction coefficient K was used, defined by the formula: $K=MA_2/MA_1\times100\%$, where MA_1 is the motor activity recorded over the first 5 min and MA_2 is the total motor activity recorded over each of the subsequent 5-min intervals of the 30-min recording period. The lower the value of this indicator, the greater the degree of habituation. The effects of pyracetam and scopolamine on the extinction of exploratory behavior were compared by calculating the difference (ΔK) between the extinction coefficients in the control and main (drug-treated) groups ($\Delta K=K_{cont}-K_{main}$). ΔKs with positive values indicated increased habituation and those with negative values, decreased habituation.

The mean values obtained for motor activity (at least from three series in tests with grouped mice and 10 series in tests with single mice) were analyzed by the Mann—Whitney U test.

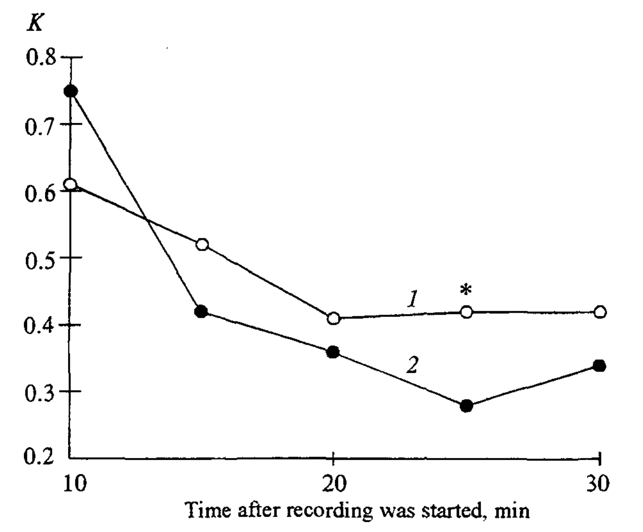

Fig. 1. Extinction of exploratory activity with time in single and grouped control mice injected with isotonic NaCl solution. *1*) single mice; *2*) grouped mice. *$p<0.05$ by the Mann—Whitney U test in comparison with the grouped mice over the same period.

RESULTS

As follows from the K values shown in Figure 1, habituation in grouped mice developed more rapidly and was more strongly marked than in single mice.

Pyracetam facilitated habituation in grouped mice, as was evidenced by positive ΔK values which indicated that the K coefficient in the pyracetam-treated mice was significantly lower ($p<0.05$) than in the control animals; in contrast, pyracetam had no significant influence on the extinction of exploratory behavior in single mice (Table 1).

Scopolamine, unlike pyracetam, significantly delayed the habituation process in both the grouped and single mice ($p<0.05$ relative to the control mice), as is evidenced by the negative ΔK values in Table 1. This effect could be due not only to the

TABLE 1. Extinction with Time of Exploratory Activity in Single and Grouped Mice under the Influence of Pyracetam and Scopolamine. The values are those of ΔK

Treatment	No. of tests	No. of mice	Time after recording was started, min				
			10	15	20	25	30
Pyracetam							
single mice	10	10	6	-12	-15	18	-8
grouped mice	3	30	22	34	44	44*	42*
Scopolamine							
single mice	11	11	-15	-38	-58	-18	-10
grouped mice	5	50	-28	-25	-45	-24	-40

Note. *$p<0.05$ by Mann—Whitney's U test in comparison with single mice over the same interval.

interference of scopolamine with habituation ("negative learning"), but also with its stimulatory action on motor activity. In the dose used (0.5 mg/kg), however, scopolamine was found not to alter the initial motor activity, which agrees with the results reported by other investigators [3,5]. Hence, the effect of scopolamine on the behavior of animals in the testing chamber was attributed to the weakening of extinction with time.

As can be seen from the results of this study, the habituation process in grouped animals proceeds more intensively than in single animals, which testifies to an important role of the zoosocial factor in the phenomenon of motor activity inhibition. Our study also indicates that habituation will be accelerated by a drug improving cognitive functions (pyracetam) and inhibited by one deteriorating them (scopolamine). However, scopolamine influenced habituation in both grouped and single mice, whereas pyracetam did so only in grouped mice. This suggests that pyracetam acts predominantly on the zoosocial component of "negative learning" which involves adaptation of animals to each other, while scopolamine also influences their habituation to the new surroundings. Hence it may be concluded that only the method of acute motor activity inhibition in a group [1] is suitable for use as a screening test in the evaluation of nootropic substances, whereas the above-mentioned method proposed by Platel [8] and involving repeated exposures is best suited for use with single animals in evaluating substances improving cognitive functions.

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