NOVELTY-SEEKING BEHAVIOUR AND OPERANT ORAL ETHANOL SELF-ADMINISTRATION IN WISTAR RATS

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Abstract — The aim of the present study was to investigate the relationship between novelty-seeking behaviour and operant oral ethanol self-administration in Wistar rats. The open field and novel object test was used to assess novelty-seeking. Ethanol self-administration was initiated in an operant procedure where ethanol was introduced in the presence of sucrose. Eighteen out of 32 rats were successfully initiated to lever-press for 8% (v/v) ethanol. None of the parameters assessed in the open field (horizontal activity, rearings) or novel object test (number of contacts with an object, exploration time) differed between the initiated and non-initiated subjects. In addition, correlational analysis revealed that response to novelty did not predict individual differences in ethanol intake in the initiated rats. These results suggest that there is no relationship between novelty-seeking and operant ethanol self-administration in Wistar rats.

INTRODUCTION

There is a large body of evidence that certain personality traits may contribute to development of drug misuse and dependence in humans (Rosenthal et al., 1990; Nestadt et al., 1992; Wills et al., 1994). For example, it has been repeatedly reported that high novelty-seeking may predict increased vulnerability to drug misuse in different human populations (Cloninger et al., 1988; Teichman et al., 1989; Masse and Tremblay, 1997; Gabel et al., 1999). It seems that the positive correlation between novelty-seeking and drug-seeking behaviour may also exist in laboratory animals. It has been shown that rats with the highest locomotor response to novel environment (high responders, HR) acquire operant responding for amphetamine more readily than low responders (LR) (Piazza et al., 1989, 1990; Exner and Clark, 1993; for review, see Bardo et al., 1996). In the case of alcohol (ethanol), the situation is less clear. Several laboratories (Bisaga and Kostowski, 1993; Samson and Chappelle, 1995; Koros et al., 1998, 1999a), using non-selected Wistar rats, have reported no correlation between spontaneous locomotor activity in a novel open field arena and non-operant ethanol drinking. Similarly, no consistent relationship between locomotor activity in a novel environment and ethanol intake has been observed for genetically selected lines of alcohol-prefering and alcohol-non-prefering rats (Päivärinta and Korpi, 1993; Badishtov et al., 1995; Nowak et al., 2000). All pairs of lines used in these latter studies had been selected for differences in non-operant ethanol drinking in a classic two-bottle choice procedure.

Comparing the results of the amphetamine and ethanol studies cited in the previous paragraph, one should be aware that different behavioural procedures were used for assessment of ethanol (non-operant drinking) and amphetamine self-administration (operant responding). The relationship between non-operant and operant ethanol self-administration is not clear. For example, it has been reported that rats avoiding alcohol in the two-bottle choice test may be successfully initiated to respond for alcohol in an operant oral self-administration procedure (George and Ritz, 1993; Ritz et al., 1994; Koros et al., 1999b).

Given the above, we aimed to investigate the possible relationship between response to novelty and operant oral ethanol self-administration in Wistar rats. It has been argued that individual differences in novelty-seeking may be more accurately assessed by using various behavioural procedures (Bevins et al., 1997; Robinet et al., 1998). In the present study, response to novelty was measured in two standard procedures: the open field and novel object test (Bardo et al., 1996; Koros et al., 1998; Robinet et al., 1998).

MATERIALS AND METHODS

Subjects

Thirty-two male Wistar rats (320–350 g at the beginning of the study) were used. They were housed two per cage in a temperature-controlled colony room at 22 ± 1°C, 60% relative humidity, and 12-h light/12-h dark cycle (lights on at 07:00). The rats were obtained from a breeder (HZL, Warsaw, Poland) 14 days before the onset of the investigation. During this time, the animals were weighed and handled several times. The subjects had free access to standard laboratory chow (‘Labofeed H’; WPIK, Keynia, Poland) and tap water (except as noted below). Treatment of the rats in the present study was in full accordance with the ethical standards laid down in respective European and Polish regulations. All procedures were reviewed and approved by a local Ethics Committee on Animal Studies.

Open field test

The open field test was done as described by Koros et al. (1998). The open field apparatus consisted of four identical, dimly lit (10 lux), computer-controlled cages (60 × 60 × 40 cm; COTM, Białystok, Poland) located in an air-conditioned enclosure with a background white noise of 60 dB. Each cage was transected by two perpendicular, co-planar arrays of 16 infra-red photocells (located 3 cm above floor level) which were intended to measure forward locomotion by determining the rat’s position every 100 ms. The forward locomotion was defined as the distance (in cm) travelled by the rat during the...
20-min test session. Another set of photocells located 15 cm above the cage floor measured the number of rearings. After an initial habituation of 20 min to the test room, each rat was introduced to the test cage for another 20 min. The cages were carefully cleaned between the recordings. The test sessions were conducted between 10:00 and 14:00 to avoid errors attributable to the variation in motor activity of the day activity cycle (File and Day, 1972).

Novel object test

The novel object test (Robinet et al., 1998) was performed in the colony room 1 week after completion of the open field test. Novel object exploration was assessed in standard plastic cages (32 × 60 × 19 cm). On the first day of the procedure, the subjects were habituated individually to the test cages for 30 min. On the second day, an opaque glass jar of irregular shape (diameter: 13 cm; height: 15 cm) was placed in one corner of the test cage. The jar could not be moved by the rat. The number of approaches to the object (the animal’s nose within 2.5 cm of the jar) and the duration of contact with the object (nose, mouth and/or front paw touching the jar) were recorded for 5 min by using a video camera connected to a TV screen located in an adjacent room. The cages and jars were carefully cleaned between the recordings. All procedures were conducted between 10:00 and 14:00.

Operant oral ethanol self-administration

Apparatus. Ethanol-reinforced behaviour was studied in standard operant chambers (Coulbourn Instruments, Inc., Allentown, PA, USA). The chambers consisted of modular test cages enclosed within sound-attenuating cubicles with fans for ventilation and background white noise (for details, see Bienkowski et al., 1999). A white house light was centred near the top of the front of the cage. The start of training or test sessions was signalled by turning the house light on. The cage was also equipped with two response levers, separated by a liquid delivery system (a liquid dipper, E14-05; Coulbourn). Only one lever (‘active’ lever) activated the liquid dipper. Presses on the other lever (‘inactive’ lever) were recorded but not reinforced. The liquid delivery system presented 8% (v/v) ethanol in a 0.1-ml portion for 5 s.

Acquisition of operant oral ethanol self-administration. The self-administration procedure was started 7 days after completion of the novel object test. The rats were trained to respond for 8% (v/v) ethanol according to the sucrose-fading procedure (Samson, 1986) with some minor modifications (for details, see Bienkowski et al., 1999; Koros et al., 1999b). The animals were deprived of water for 22 h/day during the first 4 days of training and trained to lever-press for 10% (w/v) sucrose solution on a fixed ratio 1 (FR1) schedule of reinforcement. As soon as lever-pressing was established, water started to be freely available in the home cages. All training sessions were 30 min long and one session was given each day. Starting on day 5, the animals received 2.5% ethanol–10% sucrose. Then, over the next 14 sessions, ethanol concentrations were gradually increased from 2.5 to 8%, and sucrose concentrations decreased from 10 to 0%. The detailed sequence of ethanol–sucrose concentrations was: 2.5% ethanol–10% sucrose (2 days), 5% ethanol–10% sucrose (2 days), 8% ethanol–10% sucrose (2 days), 2.5% ethanol–10% sucrose (2 days), 8% ethanol–5% sucrose (2 days), 8% ethanol–2.5% sucrose (2 days), 8% ethanol–7.5% sucrose (2 days), 8% ethanol–1.25% sucrose (3 days).

The rats were allowed to respond for 8% ethanol for the next 20 days (a maintenance phase). It was assumed that the subjects consistently responding more than 30 times on the active lever were initiated to respond for 8% ethanol.

Statistics

Student’s t-test was used to study differences between the ‘initiated’ and ‘non-initiated’ subjects. Pearson product-moment correlation test was employed to assess correlations between response to novelty and operant behaviour. The ‘Statistica’ software package for Windows (StatSoft Inc., Tulsa, OK, USA) was used to analyse all data. P < 0.05 was considered significant.

RESULTS

The rats (n = 18) consistently responding more than 30 times on the active lever were classified as initiated to self-administer ethanol. Other subjects (n = 14) were classified as non-initiated. All behavioural parameters are summarized in Table 1. During the first five ethanol self-administration sessions (the maintenance phase), the initiated subjects gave more responses and consumed more ethanol (0.61 g/kg/30 min) than the non-initiated subjects (0.15 g/kg/30 min). Alcohol intake in the initiated rats remained stable. The mean alcohol consumption in this group averaged across days 6–20 of the maintenance phase was 0.68 g/kg/30 min. During the same period, responding for ethanol in the non-initiated subjects dropped to non-significant levels (ethanol intake: 0.04 g/kg/30 min; Table 1).

In general, forward locomotion and rearings in the open field arena were not correlated with the parameters derived from the novel object test (−0.07 < r < 0.18, P > 0.3). The only exception was a significant positive correlation between the total number of rearings and the exploration time (r = 0.44, P < 0.02).

There were no significant relationships between the number of days required to learn operant responding and the measures of novelty-seeking (−0.28 < r < 0.06, P > 0.11). The number of days required to learn operant behaviour did not differ between the non-initiated (mean ± SEM: 2.8 ± 0.3 days) and initiated subjects (2.4 ± 0.3 days; t = 1.16, P = 0.25; Student’s t-test).

There were no differences between the groups in terms of open field activity or novel object exploration (P > 0.4; Table 1). In addition, neither locomotor activity nor object exploration predicted ethanol-taking behaviour in the initiated rats (−0.16 < r < 0.32, P > 0.18).

DISCUSSION

Our recent experiments (Koros et al., 1998, 1999a) have demonstrated that locomotor response in a novel open field arena (measured before and after the ethanol-drinking phase) was not correlated with either initiation or maintenance of long-term non-operant ethanol drinking in Wistar rats. In line with the above, locomotor activity in a novel environment failed to predict operant oral ethanol self-administration in
the present study. Thus, it seems that there is no positive correlation between novelty-seeking and either operant (present study) or non-operant ethanol-taking behaviour in the rat (Bisaga and Kostowski, 1993; Fahlke et al., 1995; Samson and Chappelle, 1995). Moreover, it has been found that the rewarding effects of ethanol measured in the conditioned place preference (CPP) procedure were not associated with individual differences in open field or hole board exploration (Nadal et al., 1992). Similar results have been obtained for BXD Recombinant Inbred (RI) mice. Using 20 RI mouse strains, Cunningham (1995) found that locomotor activity in a novel environment did not predict ethanol-induced CPP. At least two groups have reported a negative correlation between locomotor response to novelty and ethanol consumption in the rat. Gingras and Cools (1995) have shown that their HR rats drank significantly less alcohol than LR rats. Nadal et al. (1996) have reported that rats exhibiting more rearing during exposure to a novel open field arena tended to drink less ethanol in a subsequent two-bottle choice test. No association between locomotor activity in a novel environment and ethanol intake has also been observed for genetically selected lines of alcohol-prefering and alcohol-non-prefering rats (Päivärinta and Korpi, 1993; Badishtov et al., 1995).

It is assumed that locomotor activity in an inescapable open field reflects both stress and the rewarding component of novelty. In contrast, free choice exploration of novel stimuli may reflect mainly the rewarding effects of novelty (Exner and Clark, 1993; Robinet et al., 1998). In the present study, no consistent relationship was found between locomotor activity in the open field test and novel object exploration. Thus, the two tests may be measuring different aspects of novelty-seeking behaviour. In this respect, our findings supports previous studies (Bevins et al., 1997; Robinet et al., 1998) and further underscores the importance of using more than one behavioural procedure to assess novelty-seeking in the rat (Nowak et al., 2000). In agreement with the results cited in the previous paragraph, the rats which acquired ethanol self-administration did not differ from the non-initiated subjects in terms of propensity to explore the novel object. Recently, Nowak et al. (2000) have tested alcohol-prefering (P, HAD) and alcohol-non-prefering (NP, LAD) lines of rats in several tests of novelty-seeking behaviour. Presentation of novel odours in a novel or familiar environment produced greater locomotor activation in alcohol-prefering subjects. However, when nose-poking for novel odours and preference for a novel versus a familiar compartment were assessed, the behaviour of the preferring lines did not differ from that of the non-prefering lines. The above authors concluded that the relationship between novelty-seeking and alcohol consumption is rather moderate and is observed only under specific experimental conditions (Nowak et al., 2000).

It is noteworthy that Goeders and Guerin (1996) have shown no association between the locomotor response to a novel environment and cocaine self-administration. In addition, Erb and Parker (1994), as well as Robinet et al. (1998), reported that locomotor response in a novel environment did not predict amphetamine-induced CPP. Accordingly, even in the case of psychostimulants, the positive correlation between response to novelty and a drug’s rewarding effects may not be as robust as originally suggested by Piazza and colleagues (Piazza et al., 1989, 1990).

In conclusion, the present findings together with several previous reports indicate that individual differences in response to novelty may not predict ethanol self-administration in Wistar rats. This conclusion seems to be at variance with several human studies showing that high novelty-seeking is a risk factor for developing alcohol misuse and dependence (Teichman et al., 1989; Bardo et al., 1996; Galen et al., 1997; Gabel et al., 1999).

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Table 1. Parameters of ethanol self-administration, open field activity and novel object exploration in rats initiated or non-initiated to lever-press for 8% ethanol

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Initiated subjects (n = 18)</th>
<th>Non-initiated subjects (n = 14)</th>
<th>Student’s t-test</th>
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<tr>
<td>OPERANT SELF-ADMINISTRATION OF 8% (v/v) ETHANOL IN A 20-DAY MAINTENANCE PHASE</td>
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<tr>
<td>DAYS 1–5</td>
<td></td>
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<tr>
<td>Lever-presses</td>
<td>43.7 ± 3.9</td>
<td>13.4 ± 4.4</td>
<td>t = 5.09, P &lt; 0.001</td>
</tr>
<tr>
<td>Ethanol consumption (g/kg/30 min)</td>
<td>0.61 ± 0.06</td>
<td>0.15 ± 0.04</td>
<td>t = 5.01, P &lt; 0.001</td>
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<tr>
<td>DAYS 6–20</td>
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<tr>
<td>Lever-presses</td>
<td>49.7 ± 2.6</td>
<td>3.9 ± 1.0</td>
<td>t = 13.98, P &lt; 0.0001</td>
</tr>
<tr>
<td>Ethanol consumption (g/kg/30 min)</td>
<td>0.68 ± 0.05</td>
<td>0.04 ± 0.02</td>
<td>t = 11.39, P &lt; 0.0001</td>
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<tr>
<td>OPEN FIELD TEST</td>
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<tr>
<td>Forward locomotion (cm)</td>
<td>430.7 ± 30.2</td>
<td>414.6 ± 18.9</td>
<td>t = 0.43, P = 0.66</td>
</tr>
<tr>
<td>0–5 min</td>
<td>1116.5 ± 88.2</td>
<td>1046.5 ± 57.1</td>
<td>t = 0.65, P = 0.53</td>
</tr>
<tr>
<td>Rearings</td>
<td>25.5 ± 2.0</td>
<td>26.1 ± 2.2</td>
<td>t = 0.21, P = 0.83</td>
</tr>
<tr>
<td>0–20 min</td>
<td>66.1 ± 5.7</td>
<td>67.2 ± 7.7</td>
<td>t = 0.12, P = 0.90</td>
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<tr>
<td>NOVEL OBJECT EXPLORATION</td>
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<tr>
<td>Number of contacts</td>
<td>10.2 ± 0.7</td>
<td>11.2 ± 1.1</td>
<td>t = 0.81, P = 0.42</td>
</tr>
<tr>
<td>Exploration time (s)</td>
<td>79.5 ± 9.1</td>
<td>87.7 ± 11.1</td>
<td>t = 0.57, P = 0.58</td>
</tr>
</tbody>
</table>

Values are means ± SEM.

*aValues were calculated for the first 5 min of the 20-min open field session.*
REFERENCES


