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Immediate and delayed voluntary ethanol effects on motor performance, learning and inhibition in rats

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Abstract

The effects of prolonged voluntary ethanol consumption on psychomotor performance, operant conditioning and inhibition were examined in adult male Wistar rats. Animals were food deprived and alcohol or control solution was available 1 h/day during 15 days, with free water for the rest of the day. Then, rats were tested in a two-bottle paradigm (solution and water available) for 1 h/day during 19 days, and subjects were tested daily for psychomotor performance and operant conditioning immediately or 6 h after (delayed) the solution access. Psychomotor performance was tested in an 80°-inclined screen. Successive conditioning phases were: free shaping (FS), continuous reinforcement (CRF), operant extinction (EXT), successive discrimination (DIS) and two-stimuli test (TST). Alcohol consumption deteriorated psychomotor performance and improved the animal's ability to learn simple associations between stimuli and responses (free shaping and extinction), in immediate and delayed groups. Finally, alcohol deteriorated behavioral inhibition (DIS and TST) tested immediately after drinking. Taken together, results suggest that prolonged voluntary ethanol intake could induce permanent psychomotor impairment and associative learning facilitation, and also an impairment of the inhibition related to the intoxication state.

Keywords: Voluntary prolonged alcohol intake; Operant conditioning; Inhibition; Free shaping; Successive discrimination; Two-stimuli test; Psychomotor performance; Wistar rats

1. Introduction

Forced chronic ethanol administration induces learning and memory deterioration in shock avoidance tasks (File and Mabbutt, 1990; Freund and Walker, 1971; Walker and Freund, 1971), maze tests (Beatty et al., 1984; Beracochea et al., 1987; Bond and Di Giusto, 1976) and temporal discrimination (Smith et al., 1979; Walker and Freund, 1973), although no effects in spatial and temporal discrimination have also been reported (Blokland et al., 1993). Conversely, sensory-mediated radial arm maze tasks may be transiently enhanced by chronic forced exposure to ethanol (Steigerwald and Miller, 1997). Nevertheless, most of these results have been obtained using forced oral or intraperitoneal ethanol administrations. There is little information available about the effects of voluntary oral self-administration of ethanol on learning tasks. Self-ingestion of alcohol, rather than injection by the investigator, is the best procedure to study the effects of alcohol on the behavior because alcoholic humans always self-administer alcohol orally. Therefore, after voluntary chronic oral ethanol consumption, different results have been reported: facilitation of lever-press acquisition, extinction (Pallarès et al., 1992) and active avoidance acquisition (Pallarès et al., 1997) in nonselected rats, or no disturbances on spatial learning in radial-arm maze and on passive avoidance learning in alcohol-preferring rats (P) (Fadda et al., 1999). In addition, it has been proposed that P rats could have higher associative learning abilities than alcohol-nonpreferring (NP) rats (Slawecki et al., 1999).

On the other hand, several studies of ethanol effects on learning that implies alternation of response, for example in mazes, have reported that alcohol deteriorates the ability to modify the learned response (Beracochea et al., 1987; Davenport et al., 1989; Maier and Pohorecky, 1986). This

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impairment in the flexibility of the response (persistence) has also been reported in runway (Lobaugh et al., 1991; Wigal and Amsel, 1990) and in Pavlovian eye-blink conditioning when rabbits were submitted to an extinction of a previous conditioning (Hernandez and Powell, 1986; Hernandez et al., 1986). The lack of inhibition and error perseveration in alcoholic humans has also been well described (Dougherty et al., 1999; Finn et al., 1999; Mello, 1972). We have previously reported that, in rats drinking toxic amounts of ethanol, the worsening of inhibition has only been found in tasks signalled by exteroceptive stimuli that require the development of excitatory and inhibitory stimulus control. Thus, we have proposed that prolonged oral self-administration of ethanol induces a specific impairment of the subjects' capability to inhibit responses previously reinforced (Pallarès et al., 1992, 1997).

In the present study, the inhibitory learning was tested by means of operant extinction (EXT), successive discrimination (DIS) and two-stimuli tests (TSTs) in the Skinner box. Behavior has been tested following alcohol intake but also after a delay of 6 h postdrinking in order to differentiate state from permanent effects of alcohol in ethanol drinker rats. EXT can be considered as an inhibition process of a previously learned response, in which the differential cue from previous experience is the absence of reinforcement (Mackintosh, 1974). Operant DIS (S^+/S^-) involves a positive stimulus indicating the reinforcing schedule and a negative stimulus, which indicates the extinction schedule. The TST was proposed the first time by Pavlov (1927) as a test for inhibitory stimulus control, was adapted to the operant conditioning (Rescorla, 1969) and may be considered a good measure of the inhibitory control of a stimulus paired with the extinction (Hearst et al., 1970).

We have used our intake induction procedure described in previous studies (Nadal et al., 1992, 1996; Pallarès et al., 1992, 1997) based on the limited access to the alcohol solution and the addition of glucose to increase palatability and reward. Limited access (Linseman, 1988; Marcucella and Munro, 1987; Meisch and Thompson, 1974) and palatable solutions (Goodwin and Amit, 1998; Linseman, 1988, 1989) have been employed by several other investigators. Sweetened solutions were used in order to avoid taste aversion, and to ensure a rapid, high, and stable ethanol consumption. Likewise, restricted food-access situation was applied since food deprivation has been shown to increase self-administration of drugs with rewarding properties in animals, not only those with caloric content, such as ethanol, but also those lacking caloric content such as phencyclidine (Carroll, 1982; Meisch, 1987). Moreover, food deprivation was necessary for operant conditioning. In addition, recent studies in P and NP rats show that food consistently fails to substitute for alcohol (Heyman, 2000). The use of sweet ethanol solutions in animal models of alcoholism is appropriate since it has been shown that taste factors, such as sweetness, are not the primary factors in controlling ethanol consumption in Wistar rats (Goodwin and Amit, 1998; Samson et al., 1996). In addition, it seems that caloric contents of solution do not play a significant role in the determination of ethanol consumption regulation in Wistar rats (Samson et al., 1996). Finally, we have evaluated the effects of alcohol on psychomotor performance by means of an 80° inclined screen test (IS) just before the start of each operant conditioning session (immediately after the period of alcohol access), but also 6 h after drug intake, in order to observe any time course-dependent motor impairment.

2. Method

2.1. Animals

Eighty 5-month-old male Wistar rats were individually housed in a temperature-controlled environment on a 12L:12D cycle with lights on at 0800 h. The subjects had continuous access to food and water in their home cage, except where otherwise noted. All experiments were approved by the ethical committees of the Autonomous University of Barcelona and Departament d'Agricultura, Ramaderia i Pesca (DARP) of the Generalitat de Catalunya (Catalonian Government: number of protocol N-977), and they were carried out in accordance with the European Communities Council Directive of 24 November 1986 (86/609/EEC).

2.2. Drugs

The alcohol solution for the experimental groups consisted of 10% v/v absolute extra pure ethanol (Normasolv, Barcelona, Spain) and 10% w/v anhydrous D(+)-glucose (Panreac, Barcelona, Spain) dissolved in distilled water. Control solution consisted of 10% w/v anhydrous D(+)-glucose (Panreac) dissolved in distilled water.

2.3. Apparatus

The experiments were conducted in two operant chambers (Ralph Gerbrands, Arlington, MA) encased in sound-attenuation cubicles. The chambers were fitted with a center lever placed 7.5 cm from the floor. The food cup was connected to a pellet dispenser that delivered 45 mg food pellets (Noyes). A 12-V light was situated 3 cm above the lever and 4 cm to the right. A 6-V buzzer (60 db) was situated 3 cm above the lever and 4 cm to the left. Psychomotor performance was evaluated by means of an inclined screen apparatus. This was a 45×65 cm locally manufactured screen, located with an angle of 80°. The screen area was covered by grating (1×1 cm). This test was adapted from the original description (Joseph et al., 1983).

2.4. Procedure

All rats were food deprived for 10 consecutive days using the procedure previously described (Pallarès et al., 1995). During this period, they reached values between 75% and 80% of the free-feeding weight. After this period, subjects were assigned at random to four experimental groups: immediate effects of alcohol self-administration (IALC: $n=26$), delayed effects of alcohol self-administration (DALC: $n=19$), immediate glucose (IGLU: $n=24$), and delayed glucose (DGLU: $n=16$), and were submitted to two consecutive phases: (1) intake induction and (2) two bottle. The total length of the procedure was 44 consecutive days. There were no weekend pauses in order to avoid possible withdrawal effects.

2.4.1. Intake induction phase

Alcohol subjects (IALC, DALC) received a bottle containing the sweetened alcoholic solution and control subjects (IGLU, DGLU) received the sweet solution in their home cages for a period of 1 h per day. After the 1 h of access, solutions were removed, and subjects received tap water and the daily maintenance food for the rest of the day (23 h). Body weight prior to the 1 h of access, solution intake (milliliters), and water intake (milliliters) were recorded daily. Ethanol doses were computed as ethanol (grams) divided by body weight (kilograms). This phase lasted for 15 consecutive days.

2.4.2. Two-bottle phase

All subjects received the alcohol or the control solution (depending on the group) and tap water for 1 h per day. The two bottles were situated at random each day in order to avoid place effects. Tap water was freely available for the rest of the day. Subjects were weighted after operant sessions and maintenance food was added if necessary. Body weights prior to the 1 h of access, solution intake (milliliters), and water intake (milliliters) were recorded daily. Ethanol doses were expressed as grams EtOH per kilogram body weight per hour. Immediately after the 1 h of access, the behavior of IALC and IGLU was tested. For delayed groups (DALC, DGLU), behavior was tested 6 h after the end of the ethanol-access period. Behavioral tests were carried out in the same order every day: (1) psychomotor test, (2) operant learning program. This phase lasted for 19 consecutive days.

2.4.3. Psychomotor test

The rat was lowered by the tail and placed in the middle of the IS, with the head oriented towards the top of the apparatus. The IS was cleaned at the end of each trial. The measure was the total length of stay in the apparatus (in seconds) until the animal fell down, with a maximum of 1 min allowed. IS test was carried out during the 19 days of the two-bottle phase, just before each operant conditioning session.

2.4.4. Operant learning program

The conditioning schedule consisted of: free shaping (FS: one session), continuous reinforcement schedule (CRF: four sessions), EXT (two sessions), DIS (10 sessions) and TST (two sessions). FS was performed using an automatic procedure (Ferré and García-Sevilla, 1987; Pallarès et al., 1992, 1995). If the subject did not emit 10 responses (acquisition criterion) in the first session, it underwent a second one (this session replaced the first one of CRF). CRF was conducted in order to stabilize lever-press performance in subjects before the start of the extinction phase. CRF sessions were stopped after 30 min or when the subjects had obtained 120 pellets. FS and CRF were performed with the light on. EXT sessions (30 min/session) were conducted with the light off. DIS schedule alternated successively continuous reinforcement periods (positive stimuli = light on + buzzer off) with extinction periods (negative stimuli = light off + buzzer on). The 10 sessions were always started and finished with the positive stimulus, and their duration ranged between 22 and 48 min. The positive discriminative stimulus duration range was between 48 s and 5 min 16 s, and the negative discriminative stimulus between 2 min 26 s and 7 min 6 s. The ratio between the two situations ranged from (S+/S−): 60−40% to 43−57%. TST sessions lasted for 30 min. In this test, the two discriminative stimuli (positive: light on; negative: buzzer on) were simultaneously presented and there was no reinforcement (extinction situation).

2.5. Statistical analyses

The STATISTICA package (StatSoft, Tulsa, USA) was used for data analyses. The normality of the data was assessed by means of the Kolmogorov−Smirnov test. To analyze the level of performance across sessions, analyses of variance (ANOVA) with repeated measures were used: Group (IALC, DALC, IGLU, DGLU) × Sessions, or Treatment (alcohol, control) × Delay (delayed, nondelayed) × Sessions. Post hoc Newman−Keuls tests and polynomial contrast analyses were used when necessary.

3. Results

3.1. Alcohol consumption

In the intake induction phase, the average dose of alcohol (g EtOH/kg body weight/h) computed was (mean ± S.D.): IALC = 3.06 ± 0.76, DALC = 2.57 ± 0.87. There were no global differences between IALC and DALC in the alcohol dose [$F(1,42)=3.9$, $P>.05$]. Ethanol intake increased significantly over the 15 days of this phase in the two groups [polynomial (linear), IALC: $F(1,42)=44.47$, $P<.001$, DALC: $F(1,42)=18.34$, $P<.001$]. See Table 1a for the means of the last four sessions.

Table 1

	Group			
	IALC		DALC	
Sessions	Mean	S.D.	Mean	S.D.
a. Ethanol dose (g/kg/h) in induction phase				
12	3.71	0.94	2.92	1.30
13	3.72	1.35	3.01	1.43
14	3.77	1.09	3.03	1.14
15	3.85	1.16	3.6	1.43
b. Ethanol dose (g/kg/h) in two-bottle phase				
1	3.81	1.16	3.25	1.46
2	3.69	1.05	3.01	0.87
3	3.75	1.23	3.16	1.16
4	3.56	1.09	3.3	1.12
5	3.65	1.17	3.38	0.91
6	3.63	1.19	3.41	1.03
7	3.74	0.81	3.7	1.25
8	4.15	1.18	5.22	1.71
9	3.16	1.04	3.07	1.13
10	3.58	1.23	3.5	1.06
11	3.81	1.29	3.55	1
12	3.88	1.32	3.44	1.08
13	4.16	1.18	3.6	1.15
14	4.17	0.92	3.85	0.83
15	3.89	1.24	3.73	0.88
16	4.06	1.17	4.03	1.29
17	4.02	1.17	3.73	0.98
18	4	1.22	3.55	0.85
19	3.61	1.08	3.61	1.21

In the two-bottle period, the average dose of alcohol computed was (mean ± S.D.): IALC = 3.81 ± 0.79, DALC = 3.57 ± 0.75. There were no global differences between IALC and DALC in the alcohol dose [$F(1,42) = 0.95$, $P > .05$]. Ethanol intake remained steady throughout the 19 sessions of this period in the two groups. See Table 1b for the means of the 19 sessions.

Globally, there were no significant differences [$F(1,36) = 1.604$; $P > .05$] between the two control groups in the glucose solution intake (g glucose/kg body weight) (mean ± S.D.: IGLU = 9.24 ± 2.04; DGLU = 8.51 ± 1.19).

3.2. Psychomotor performance

Mixed ANOVA showed a significant effect of the treatment factor [$F(1,75) = 41.23$, $P < .001$]: the alcohol drinker rats spent less time in the IS than controls. Also, a significant effect of the delay factor was detected [$F(1,75) = 5.36$, $P < .05$]: delayed groups remained more time in the apparatus. Results showed global significant differences between the four groups [$F(3,75) = 15.89$, $P < .001$]. Post hoc Newman–Keuls analyses indicated that the DGLU group spent more time in the apparatus than the rest of the groups: DALC ($P < .001$), IGLU ($P < .05$) and IALC ($P < .001$). Also, psychomotor performance was lower in DALC than in IGLU ($P < .01$), and greater in IGLU than in IALC ($P < .001$). The evolution across sessions was only different depending on treatment factor [$F(18,1350) = 3.3$, $P < .001$]. In control groups (IGLU, DGLU), contrast analysis showed no differences [$F(1,75) = 0.02$, $P > .05$] between psychomotor performance in Session 10 and in the mean of Sessions 1 and 19. Nevertheless, in alcohol treatment groups, the time in the apparatus in Session 10 was significant higher [$F(1,75) = 28.11$, $P < .001$] than the mean time of Sessions 1 and 19. These results indicate the existence of a U-shaped curve. Results of the four experimental groups are presented in Fig. 1.

3.3. Operant learning conditioning

3.3.1. Free shaping

The learning acquisition criterion was computed as the time (in seconds) required to perform the first 10 responses minus the time to perform the first response (Ferré and García-Sevilla, 1987; Pallarès et al., 1995). ANOVA revealed a significant effect of the treatment factor [$F(1,81) = 5.95$, $P = .017$], with the time to acquire the operant learning lower in alcohol drinker rats. The effects of the delay factor [$F(1,81) = 0.29$, $P > .05$] and the Delay × Treatment interaction [$F(1,81) = 0.004$, $P > .05$] were not statistically significant. See Fig. 2 for the means of the four experimental groups.

3.3.2. Continuous reinforcement schedule

This phase was performed in order to obtain a stabilization of the lever-press response before EXT phase. Therefore, only the response rate in the last session of CRF was analyzed. Response rate was computed as the number of responses divided by the session duration in seconds. ANOVA showed no differences [$F(3,81) = 1.8$, $P > .05$] in the response rate between the four groups (mean ± S.D.: IALC = 0.19 ± 0.04; DALC = 0.16 ± 0.05;

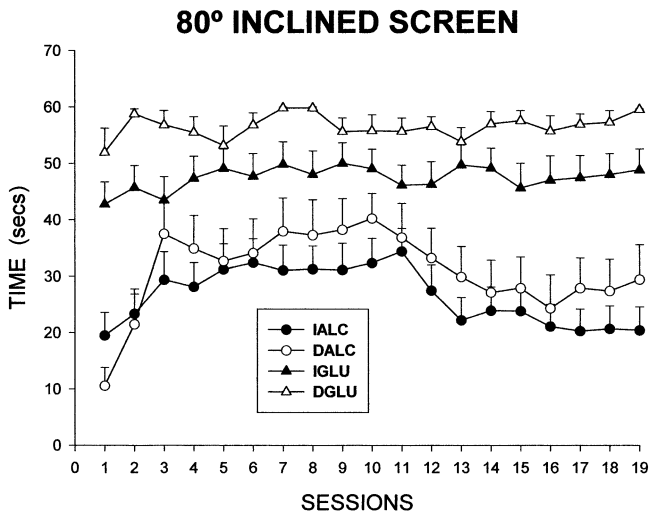

Fig. 1. Time (in seconds) in the 80°-inclined screen in the 19 sessions, with a maximum of 60.

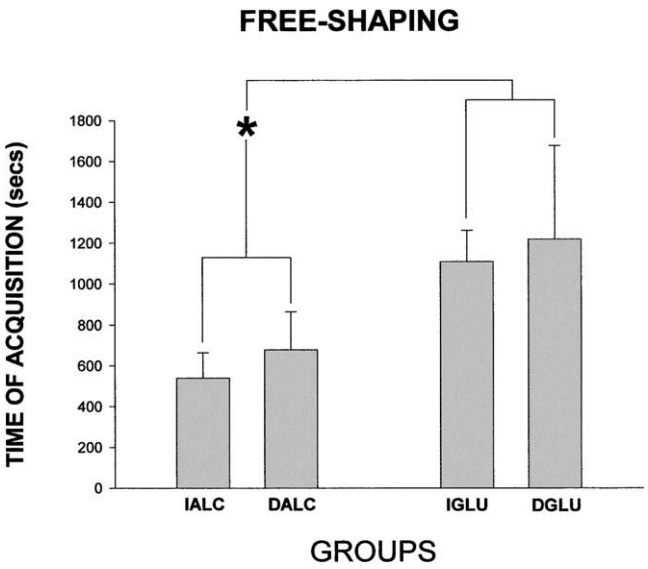

Fig. 2. Time (in seconds) of learning acquisition in free-shaping conditioning, computed as: time required to perform the first 10 responses minus time required to perform the first response. *$P<.05$.

IGLU = 0.18 ± 0.06; DGLU = 0.19 ± 0.02) in the last session of this phase.

3.3.3. Operant extinction

Results showed a global significant effect of the treatment factor [$F(1,79)=15.3$, $P<.001$], with the number of responses lower in alcohol drinker rats. The effects of the delay factor [$F(1,79)=2.82$, $P>.05$] and the Delay × Treatment interaction [$F(1,81)=0.33$, $P>.05$] were not statistically significant. Also, results indicated a significant decrease in the number of responses across sessions [$F(1,79)=72.94$, $P<.001$] in all groups. See Fig. 3 for the means of the four groups. We calculated the caloric value of the solutions ingested by subjects in the two extinction sessions, considering that ethanol has 7 kcal/g and glucose 3.87 kcal/g. ANOVA showed no differences [$F(3,81)=1.44$, $P>.05$] in the averaged caloric intake (kilocalories) between the four groups (mean ± S.D.: IALC = 12.28 ± 3.44; DALC = 12.81 ± 2.99; IGLU = 11.53 ± 3.28; DGLU = 13.53 ± 2.36).

3.3.4. Successive discrimination learning

The discrimination index (DI) was obtained from the following formula: DI = [total responses in the presence of the positive stimulus/total responses] × 100, as previously reported (Pallarès et al., 1992).

In the sixth session of DIS phase, all groups reached DI values up to 75% (mean ± S.D.: IALC = 78.18 ± 9.61; DALC = 77.73 ± 12.36; IGLU = 82.29 ± 7.09; DGLU = 76.79 ± 10.84), so DIS was divided in a first slot of six sessions (stimuli control acquisition) and in a second slot of four sessions (stimuli control consolidation) and they were analyzed separately. In the first six sessions, there were no global differences between the four experimental groups [$F(3,81)=1.53$, $P>.05$]. ANOVA revealed a significant evolution in the DI across the five sessions [$F(5,405)=54.71$, $P<.001$] that was the same in all groups, an increase of DI. The analysis of the last four sessions showed significant effects of treatment [$F(1,81)=7.4$, $P<.01$] and delay [$F(1,81)=4.16$, $P<.05$] factors, but the Treatment × Delay interaction was not statistically significant [$F(1,81)=0.001$, $P>.05$]. Control groups (IGLU, DGLU) presented higher DI levels than alcohol drinker groups (IALC, DALC). Also, delayed groups (DALC, DGLU) presented higher DI levels than nondelayed (IALC, IGLU). Post hoc Newman–Keuls analysis indicated the existence of significant differences ($P<.01$) only between IALC and DGLU groups. The average values of the 4 days were (mean ± S.D.): IALC = 77.81 ± 11.21; DALC = 82.07 ± 10.98; IGLU = 83.51 ± 8.09; DGLU = 87.91 ± 6.56.

3.3.5. Two-stimuli test

There were no significant differences between groups in the global number of responses [$F(3,81)=0.72$, $P>.05$]. However, there was a significant evolution of the number of responses across the two sessions [$F(1,81)=43.74$, $P=.001$] that was different between groups [Group × Sessions: $F(3,81)=4.1$, $P<.01$]. Posterior contrast analysis showed a significant decrease in the number of responses across sessions in DALC ($P<.001$), IGLU ($P<.01$) and DGLU ($P<.001$). In the IALC group, contrast analysis indicated no differences in the number of responses between first and

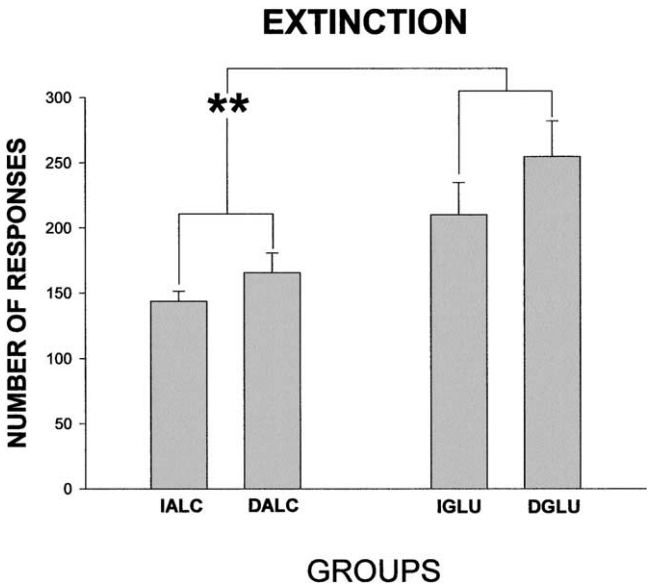

Fig. 3. Number of responses in extinction (mean of the two sessions). **$P<.01$.

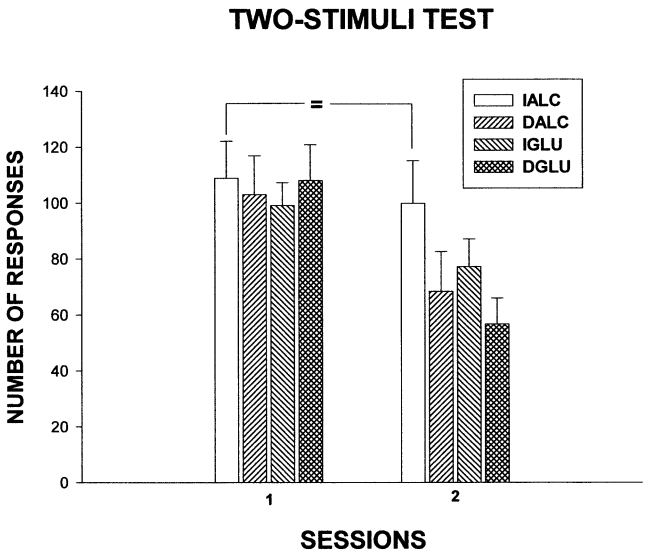

Fig. 4. Number of responses in the two sessions of two stimuli test. =: no statistical differences.

second sessions. See Fig. 4 for the means of the four experimental groups.

4. Discussion

The ethanol doses ingested by the subjects were comparable to those obtained in previous experiments using the same concentrations of glucose and alcohol (Pallarès et al., 1992) but higher than those obtained using lower concentrations of glucose (3%) (Nadal et al., 1992, 1996; Pallarès et al., 1997). By using this method, in previous studies we obtained a significant positive correlation between the ethanol dose ingested and the blood ethanol levels recorded immediately after the 1 h of ethanol access in the last day of the intake induction phase (1 g ETOH/kg body weight corresponded to 0.15 g ETOH/l blood) (Pallarès et al., 1997). In the present experiment, the estimated blood ethanol levels in the last day of the intake induction phase were (mean ± S.D.): 0.56 ± 0.19 g ETOH/l blood.

Ethanol consumption was increasing across the days in the intake induction phase and remained steady in the two-bottle phase. The doses recorded in the two-bottle phase were similar to those obtained in the last days of the intake induction phase. IALC rats showed ataxic effects as activity decrease, muscular relaxation, and loss of fine motor control, effects that were directly observable during the animal manipulation for behavioral testing. Nevertheless, these effects were not directly observable in DALC rats, and this suggests that ethanol ingested 6 h before testing was partially metabolized.

Prolonged oral self-administration of alcohol impaired psychomotor performance measured in the IS when rats were tested immediately after alcohol intake, but also at 6 h after consumption. State-dependent deficits in psychomotor performance induced by acute (Middaugh et al., 1992; Pohorecky, 1977; Prunell et al., 1987) and chronic (Lister, 1987; Ward and Jones, 1987) alcohol administration are well documented. The present data indicates that prolonged voluntary alcohol intake induces also a permanent psychomotor deterioration in alcohol drinker rats. Moreover, the two alcohol groups presented a U-shaped curve in the evolution across the days of the psychomotor performance. The ascending part of the curve could be related to the development of tolerance to the sedative effects of alcohol, and the descending part to a later sensitization to this effect. However, this curve can indicate the probable existence of a learning process, especially because of the repetition of testing across sessions. Thus, psychomotor disturbed animals could learn that falling down the apparatus does not imply negative consequences. Finally, the increase of psychomotor performance in delayed groups could be due to motivational differences with regard to nondelayed groups.

The learning of the lever-press response in the FS phase, measured as the time spent between the first and the 10th response, was facilitated by alcohol consumption. Thus, alcohol drinker rats presented shorter latencies to acquire a regular rate of response than control rats. These results indicate that prolonged voluntary ethanol consumption can facilitate the animal's ability to learn simple associations between reinforcing stimuli and responses. Moreover, this learning facilitation was observed in the two alcohol groups, and these data indicate the existence of a permanent alcohol facilitation in the acquisition of the lever-press response in alcohol drinker rats.

In the CRF schedule, there were no differences in the response rate between the four groups in the last session of this program. Therefore, all subjects reached the same level of lever-press performance before the start of the EXT phase. In EXT, rats had to inhibit the response reinforced in a preceding session. Considering the extinction resistance, results showed a significant effect of treatment, with alcohol drinker rats showing less number of responses than controls. Alcohol facilitated the extinction processes in the IALC group, as previously reported (Pallarès et al., 1992), and also in delayed alcohol drinker rats (DALC). This data indicates the existence of permanent effects of alcohol on the extinction of the lever-press response in ethanol drinker rats. Although the decrease in the number of responses in EXT shown in the IALC group could be partially explained by the well-documented depressing effects of ethanol (Keane and Leonard, 1983; Lister, 1987; Prunell et al., 1987; Sonderegger et al., 1984), alcohol did not decrease the number of lever-press responses neither in FS nor in CRF sessions. Also, we stated a recovery of the muscular tone in the delayed alcohol group when subjects were handled for testing (6 h after ethanol intake). On the other hand, it is well known that preloading reduces extinction responding for food. Nevertheless, the caloric intake was statistically the same in the four groups, thus extent of the preload effect can be rejected.

EXT results are in accordance with those obtained in FS: the extinction of the lever-press response also implies the capability to learn simple associations between reinforcing stimuli and responses. The accordance between FS and EXT results could indicate that we have tested the effects of alcohol on the same learning process (stimulus–response association) by using two different contingencies of reinforcement. Thus, voluntary chronic alcohol consumption seems to induce permanent improvement of simple associative learning.

Alcohol learning facilitation has been documented after acute administration at low doses in active avoidance in rats (Colbern et al., 1986; Matthews et al., 1999; Prunell et al., 1987, 1994) and in Pavlovian eye-blink conditioning in rabbits at mild doses (Hernandez and Powell, 1986; Hernandez and Valentine, 1989; Hernandez et al., 1986). Learning facilitation in rats has also been observed in conditioned avoidance after chronic ethanol treatment (Criswell and Breese, 1989), and after prolonged voluntary alcohol intake in lever-press conditioning (Pallarès et al., 1992) and in active avoidance (Pallarès et al., 1997). Besides, P rats seem to have greater associative learning abilities than NP rats (Slawecki et al., 1999). Moreover, in humans, several studies have documented a retrograde facilitation of memory by alcohol (Alkana and Parker, 1979; Bruce et al., 1999; Hewitt et al., 1996; Lamberty et al., 1990; Parker et al., 1980, 1981; Tyson and Schirmuly, 1994) and a positive effect of moderate alcohol consumption on cognitive performance (Eckardt et al., 1998; Elias et al., 1999).

In the DIS phase, the discrimination index was greater in control than in alcohol groups. However, results also showed a significant effect of the delay, with DI levels higher in delayed groups. This effect could be due to motivational differences between delayed and nondelayed groups. Alcohol intoxication deteriorated inhibitory stimulus control in successive discrimination, measured by the discrimination index, as previously reported (Pallarès et al., 1992). This impairment of the inhibition seems to be state-dependent, because DI levels were statistically the same in DALC and control rats. These results are different from those obtained in the EXT phase, and this difference could be due to the stimuli control. It seems that the negative effects of ethanol intoxication on the response inhibition only appear in tests that involve control by exteroceptive stimuli. Extinction can be considered a process not involving exteroceptive stimulus control. Discriminative stimulus control must be acquired by means of a conditioning process (Hearst, 1972) that requires the presentation of the negative stimulus paired with the contingency of no reinforcement (Honing et al., 1972), as well as the successive or simultaneous presentation of the positive stimulus paired with the contingency of reinforcement.

TSTs involve the presence of both discriminative stimuli (positive and negative) in an extinction schedule. In this test, there were no significant differences between groups in the number of responses, but the groups presented a different evolution across the two sessions. The number of responses in rats under the effects of alcohol (IALC) was steady across sessions, whereas the rest of the groups showed a significant decrease in the number of responses, as expected from the normal learning process. Thus, alcohol intoxication deteriorated behavioral inhibition measured by the TST, as previously reported (Pallarès et al., 1992). Comparing EXT and TST, it can be observed that the presence of the two exteroceptive stimuli inverted alcohol effects. Therefore, as showed in DIS, the impairment of behavioral inhibition could be a specific effect of the intoxication state. As proposed for FS and EXT for the learning of simple associations, with DIS and TST we have tested the effects of ethanol consumption on the same general process (inhibition) using two different tests, so this accordance between DIS and TST results.

5. Summary and conclusions

Alcohol intoxication improved the animal's ability to learn simple associations between reinforcing stimuli and responses, as observed in free shaping and extinction. This learning facilitation has also been observed in the delayed alcohol group, thus this effect seems to be permanent. Alcohol deteriorated behavioral inhibition, and this could be a specific effect of intoxication. Prolonged voluntary alcohol consumption disturbed psychomotor performance in alcohol drinker rats (IALC and DALC) when the inclined screen test was used. Taken together, results suggest that chronic alcohol drinking could induce permanent changes in psychomotor and simple associative learning abilities, and that the impairment of inhibition could be a state-dependent effect, so induced by ethanol intoxication.

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