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Enhancement of Pseudoconditioning and Retardation of Escape by Low Doses of Ethanol [1]

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DI GIUSTO, E. L. AND N. BOND. *Enhancement of pseudoconditioning and retardation of escape by low doses of ethanol.* PHARMAC. BIOCHEM. BEHAV. 6(2) 175–177, 1977. – Independent groups of mature Wistar rats were injected intraperitoneally with 0.9% NaCl solution or 0.5 g/kg, 1 g/kg or 2 g/kg ethanol prepared from a 30% ethanol solution in 0.9% NaCl. Thirty min later each animal was placed in a two compartment shuttlebox and given 25 trials during which footshock was presented every 60 sec and tones of 8 sec duration were randomly programed. Shock-escape latencies and frequencies of intercompartmental (pseudoconditioned) responses to the tone were measured. The results showed that 1 g/kg and 2 g/kg ethanol significantly retarded escape performance but 2 g/kg ethanol significantly enhanced pseudoconditioning. These findings have implications for the design of experiments concerned with the effects of drugs on learning processes, and for theories of the effects of ethanol on behavior.

Ethanol Escape performance Pseudoconditioning Activating effects

WHILE it is well established that high doses of ethanol have a marked depressant effect on behavior, the role of low doses of the drug has not been completely clarified. In fact, several recent animal experiments together provide evidence that ethanol administered in low quantities has a significant stimulant, activating or disinhibitory effect on behavior in a variety of species and environmental contexts. For example, it has been demonstrated that doses of ethanol ranging from 1 to 3 g/kg increased motor activity in rats and mice [3], retarded the rate of habituation of a consummatory response (prey-catching) in frogs [7], increased low rates of lever-pressing for food in squirrel monkeys [6], enhanced acquisition of shuttlebox avoidance responding in rats [5] and retarded extinction of active avoidance responding in rats and mice [1,2]. Further, there is evidence that acute doses of ethanol stimulate the synthesis of brain catecholamines [4], and that α-methyl-p-tyrosine, which inhibits catecholamine synthesis at the tyrosine hydroxylase step, blocks both ethanol-induced motor activity [3] and ethanol-caused enhancement of avoidance responding [5]. These studies suggest a close relationship between ethanol-induced behavioral activation and the catecholamine system.

In a separate series of studies using rats, Izquierdo [8,9] reported that drugs which influence the catecholamine system (e.g. amphetamine) also influence pseudoconditioning in the shuttlebox. Pseudoconditioning was obtained by programing footshocks and tones independently of one another during a single test session. The frequency of intercompartmental crossings to the tones served as the response index. As Izquierdo [8] has pointed out, pseudoconditioning is a neglected but potentially interesting phenomenon in that although pseudoconditioned responses are topographically similar to conditioned responses, they occur in the absence of a contingency between tones, responses and shocks, they decrease rather than increase in frequency with repetition, they show no evidence of retention and they have different neurochemical correlates to conditioned responses [9]. Pseudoconditioned responses thus appear to reflect a temporary, nonassociative, activation process which may act as a potential contaminant of associative learning such as avoidance conditioning.

The above experiments appear to establish a close relationship between small doses of ethanol, increased catecholamine synthesis and behavioral activation in a variety of contexts on the one hand, and the catecholamine system and pseudoconditioning on the other. This relationship suggested an experiment examining the effect of small doses of ethanol on pseudoconditioning. In addition,

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the effect of ethanol on escape performance in the shuttlebox was studied.

METHOD

Animals

A total of 80 male Wistar rats approximately 130 days old at testing were used. On each of 3 days prior to testing the rats were individually handled for several minutes. Animals were maintained two to a cage in 12 hr:12 hr light on: light off conditions with ad lib food and water. Testing always occurred during the light on phase.

Apparatus

The major piece of apparatus consisted of a conventional two compartment shuttlebox identical to that described in detail by Chesher [5]. The shuttlebox was fully automated and escape latencies to shock and frequency of intercompartmental responses were recorded by means of automatic printout timers. All equipment was situated in a darkened, temperature controlled, sound attenuated cubicle.

Procedure

Each rat was assigned randomly to one of the four groups, each of which consisted of 20 animals. Thirty min prior to testing animals were injected intraperitoneally with either 0.9% NaCl solution or 0.5 g/kg, 1 g/kg or 2 g/kg ethanol prepared from 30% ethanol solution in 0.9% NaCl. The saline control group received an injection volume equivalent to that received by the 1 g/kg ethanol group as it was considered unnecessary to control for saline volume across all three experimental groups.

During testing each rat was placed in the same side of the shuttlebox and allowed a 5 min adaptation period with the guillotine door separating the two compartments raised. The rat was subsequently removed briefly from the shuttlebox while the apparatus was activated and the animal was then replaced. A 1.5 mA scrambled footshock began each of 25, 60 sec trials. On every trial the shock remained on until the rat escaped to the other compartment. Within each 60 sec interval a 2800 Hz tone of 8 sec duration was randomly programed with the restriction that no tone occurred within 10 sec prior to or following shock. This restriction ensured that no close forward or backward pairing of tone and shock occurred.

RESULTS

The dependent variables for each animal were mean shock-escape latency, frequency of intercompartmental responses to the tone (pseudoconditioning) and frequency of intercompartmental responses during the absence of tones and shocks during the 25 test trials. Since none of the animals responded in the absence of tones and shocks, following the first shock, this category was omitted from the data analysis. A summary of the results is included in Table 1.

An analysis of variance conducted on mean shock-escape latencies showed that significant differences occurred among the saline control and ethanol treatments, $F(3,76) = 3.39$, $p<0.05$. Planned comparisons revealed that both 2 g/kg ethanol ($p<0.02$) and 1 g/kg ethanol ($p<0.05$) but not 0.5 g/kg ethanol ($p>0.05$) retarded escape performance when compared to the control group.

TABLE 1

SUMMARY OF MEANS ± STANDARD ERRORS OF MEANS FOR ESCAPE LATENCIES AND PSEUDOCONDITIONED RESPONSES FOR EACH OF THE FOUR GROUPS

Treatment	Dependent Variable	
	Escape latencies in sec	Frequency of pseudoconditioned responses
saline solution	1.6 ± 0.21	3.1 ± 0.84
0.5 g/kg ethanol	1.7 ± 0.26	4.2 ± 0.82
1 g/kg ethanol	2.3 ± 0.22	3.1 ± 0.77
2 g/kg ethanol	2.5 ± 0.26	6.1 ± 0.84

An analysis of variance conducted on frequency of pseudoconditioned responses confirmed that significant differences also occurred on this dependent variable among the saline control and ethanol treatments, $F(3,76) = 2.93$, $p<0.05$. Planned comparisons revealed that only the 2 g/kg ethanol dose increased pseudoconditioning ($p<0.02$), while the 1 g/kg and 0.5 g/kg ethanol doses had no significant effect ($p>0.05$).

DISCUSSION

The major conclusion from the present study is that a relatively low dose of ethanol significantly increased the frequency of pseudoconditioned responses. This result provides additional experimental support for the hypothesis that low doses of ethanol have stimulant properties, probably mediated by the catecholamine system, and is consistent with the results of the experiments summarized earlier. However, it seems unlikely that a simple motor activation mechanism is sufficient to explain all the reported data. In the present study for example, escape responding was retarded by ethanol at a dose which facilitated pseudoconditioning (2 g/kg). In fact, escape responding was also significantly disrupted by a dose of ethanol which was too low to affect pseudoconditioning (1 g/kg). Also, Pliner and Cappell [10] demonstrated that affective responses to alcohol in humans are significantly influenced by the social environment. The latter result suggests that there is no simple correspondence between an ethanol-induced biochemical manipulation and its behavioral consequences, which is independent of the environmental context.

The effects of ethanol and of other drugs [9] on nonassociative processes linked to activation strongly suggest that additional controls should be included when studying the effects of such drugs on learning. For example, avoidance acquisition studies [5] have rarely included a pseudoconditioning control group despite the fact that use of aversive stimulation makes such pseudoconditioning a likely contaminant of performance, and thus makes correct interpretation of the data less probable.

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