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Effects of Isoproterenol and Chlordiazepoxide on Drinking and Conflict Behaviors in Rats

J. B. PATEL AND J. B. MALICK

Biomedical Research Department, Stuart Pharmaceuticals Division of ICI Americas Inc., Wilmington, DE 19897

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PATEL, J. B. AND J. B. MALICK. *Effects of isoproterenol and chlordiazepoxide on drinking and conflict behaviors in rats*. PHARMAC. BIOCHEM. BEHAV. 12:(5) 819–821, 1980.—Isoproterenol, a beta-adrenergic agent, induced drinking in water-satiated rats. Isoproterenol exhibited significant anti-conflict activity in water-deprived rats in the Shock-induced Suppression of Drinking (SSD) procedure. Chlordiazepoxide (CDP), at the highest dose tested, also increased drinking in non-deprived naive rats. As expected, CDP demonstrated highly significant anti-conflict activity in thirsty rats (SSD test). These results suggest that in conflict procedures, where food or water is used as a reward, agents that affect the consumatory drive mechanisms could show up as "false positives." Moreover, agents that affect primary drives (e.g., CDP), in addition to their anti-anxiety activity, could show additive activity in such conflict procedures.

Isoproterenol Chlordiazepoxide Drinking Conflict Behavior Rats

SEVERAL preclinical methods that are used routinely to evaluate potential psychotropic agents make use of primary drives (e.g., hunger or thirst) to manipulate a subject's behavior. Obviously, agents that affect the primary drive states could alter the subject's behavior.

Isoproterenol, a beta-adrenergic agent, when administered peripherally in small doses, has been shown to induce water consumption and vasopressin release [4, 8, 9]. In addition, chlordiazepoxide, a benzodiazepine anxiolytic agent, has been reported to increase food consumption in rats [3, 7, 10] and, to some extent, water consumption [1, 2, 6]. The present study investigated the effects of isoproterenol and chlordiazepoxide on water consumption in naive rats as well as their effects in a conflict procedure in which thirsty rats were punished periodically for licking a water tube.

METHOD

Animals and Apparatus

Male Wistar (HLA) rats, weighing 200–220 g, were used throughout these studies. The rats were housed 3–4 per cage with food and water continuously available. Separate groups of rats (minimum of 8 subjects per drug or vehicle treatment) were used for each procedure; rats were used once and discarded. The apparatus consisted of a clear Plexiglas box (40×40×45 cm) with a small black Plexiglas chamber (13×13×13 cm) attached to one wall and a stainless steel grid floor throughout. An opening (5.5×11 cm) permitted access from the large box to the small chamber. A water bottle was attached to a metal drinking tube that extended 2 cm into the small chamber; the drinking tube was located 1.5 cm above the grid floor. A drinkometer (Coulburn Model S26-01) was used to record the number of licks (responses) the subjects made during the session. During conflict testing, a 0.225 mA shock (solid state shocker, Coulburn Model E13-16) could be automatically administered to each animal through the drinking tube (tongue) and grid floor (feet) as the subject licked the tube. The entire apparatus was contained in a (70×50×62 cm) sound attenuated chamber. Both isoproterenol and chlordiazepoxide were dissolved in saline and the volume of each injection was 1 ml/kg of body weight. Drugs were administered 30 min prior to either the drinking session or conflict test.

Drinking Behavior

Drinking behavior can be measured by the volume of water consumed or the number of licks in a given time interval. In the present study the number of licks during a 60-min period was measured. There was no shock delivered during this testing.

Anti-Conflict Activity

A modification of the method of Vogel *et al.* [11] was used; this procedure is referred to as the Shock-induced Suppression of Drinking (SSD) test in our laboratory. Briefly, rats were deprived of water (48hr) and food (24 hr) prior to testing. Upon being placed into the black Plexiglas chamber, each animal was allowed to locate the drinking tube and complete 20 licks before the onset of the first grid-shock (0.225 mA). A 3-min timer was started at the termination of the first shock. During the 3-min period, shocks were delivered following each twentieth lick, and the number of shocks received during a 3-min session was recorded for each subject.

RESULTS

Figure 1 presents the mean number of licks during a 60-min drinking session. Isoproterenol treated animals

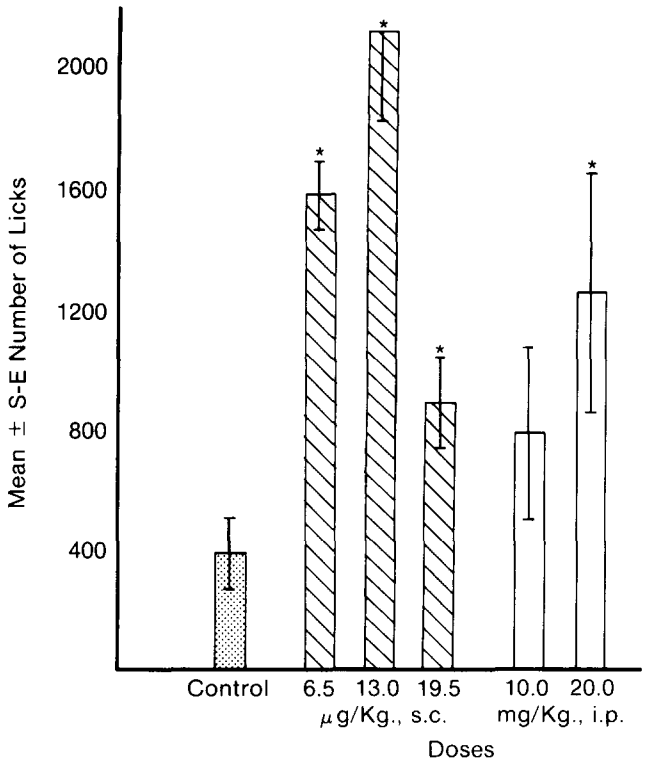

FIG. 1. Effects of isoproterenol (striped bar) and chlordiazepoxide (open bar) on water consumption in satiated rats. *$p<0.05$, t-test, (N=8).

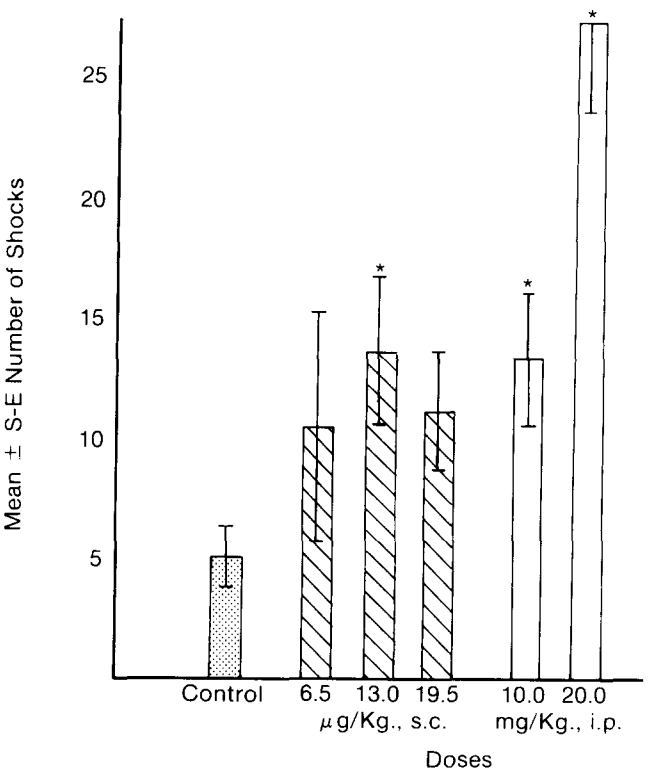

FIG. 2. Effects of isoproterenol (striped bar) and chlordiazepoxide (open bar) on conflict responding water deprived rats. *$p<0.05$, t-test, (N=8).

showed a significant ($p<0.05$) dose-related increase in mean number of licks in naive rats. As seen in Fig. 1, the mean number of licks increased by 4 and 5 times greater than controls following isoproterenol at doses of 6.5 and 13.0 μg/kg, respectively. Chlordiazepoxide also produced an increase in the mean number of licks; however, only the highest dose (20.0 mg/kg) tested produced significant ($p<0.05$) increase over the saline-treated controls. The mean number of licks was 2 and 3 times greater than the appropriate control group with CDP at 10.0 and 20.0 mg/kg, respectively.

The mean number of shocks taken in the conflict test are presented in Fig. 2. Saline-treated animals took an average of 5 shocks during the 3-min session. As expected, chlordiazepoxide produced a dose-related, statistically significant ($p<0.05$) increase in the number of shocks received. Isoproterenol also produced increases in the mean number of shocks taken and, in fact, at a dose of 13.0 μg/kg, it produced a significant ($p<0.05$) anticonflict effect.

DISCUSSION

The present investigation demonstrated that isoproterenol, when administered peripherally in small doses, caused a dose-related increase in drinking. Chlordiazepoxide also caused a significant increase in drinking behavior at the highest dose tested. These data are in accordance with those of previous investigators who reported that isoproterenol [4, 8, 9] and chlordiazepoxide [1, 2, 7] increased drinking behavior.

Having found that isoproterenol induced drinking, it was decided to study the effects of isoproterenol in conflict behavior under similar conditions. To our knowledge, isoproterenol does not have any anti-conflict or disinhibitory activity; in fact, very little is known about its actions on the central nervous system. In this study, isoproterenol exhibited significant anti-conflict activity at the highest dose tested. Thus, these data support the hypothesis that agents that affect the consumatory drive mechanisms could show up as "false positives" in procedures where behavior is manipulated by such drives. We next sought to determine the effects of a well-known anti-conflict agent, chlordiazepoxide, on drinking. CDP also exhibited a significant increase in water consumption in non-conflict situations. As expected, CDP produced a dose-related significant anti-conflict activity in the SSD procedure; benzodiazepines are used routinely as reference standards in such conflict tests. The procedures described in this report provide a ready means of quantifying the effect of drugs on both water consumption and conflict behavior in the same experimental environment.

Based on these findings, it is reasonable to assume that with agents which affect primary drives at least part of their activity in conflict procedures can be attributed to their effects on the primary drive states themselves; i.e., although it is clear that agents such as CDP have anti-conflict activity, their effects in procedures involving water or food consumption might be additive in that part of their activity is due to their effects on the anxiety state. Thus, anxiolytic agents that do not affect the primary drive states might be equipotent as anxiolytics but might very well appear to be weaker than

agents with both activities in such procedures. In addition, drugs which increase either food or water consumption might appear to be anxiolytics in conflict procedures (e.g., SSD, Geller-Seifter Conflict [5]) using these reinforcers; however, such agents may be "false positives" in these tests. Thus, procedures which do not make use of primary drives should be developed to confirm anxiolytic activity that has been discovered in procedures which use food or water as reinforcers.

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