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BRIEF COMMUNICATION

Chlordiazepoxide and Preference for Free Food in Rats

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TYE, N. C., D. J. NICHOLAS AND M. J. MORGAN. *Chlordiazepoxide and preference for free food in rats.* PHARMAC. BIOCHEM. BEHAV. 3(6) 1149–1151, 1975. – Rats continued to lever press for food when a bowl of free food was placed in the experimental chamber. Chlordiazepoxide increased the amount of free food consumed, and tended to reduce the amount of lever pressing. It is argued that the drug decreased container neophobia in the animals, rather than acting like an increase in food deprivation.

Chlordiazepoxide Food consumption Lever pressing Free food Hunger

THERE has been much speculation about the increases in eating behaviour elicited by benzodiazepines [6, 15, 16]. More specifically, it is not clear whether the increased eating reflects the reduction of anxiety, previously suppressing food intake [11], or is a result of a more specific action on hunger or satiety mechanisms [9]. Wise and Dawson [19] concluded that neither explanation could account for all their experimental results.

The problem could probably be resolved by a test that dissociated the effects of hunger and reduced anxiety on eating behaviour in the rat. A possibility is lever pressing in the presence of free food [7,13]. If rats are trained to lever press for pellets, they will continue to press to a certain extent even when a bowl of identical pellets is introduced into the apparatus. Typically, the animals begin each session by sampling the free food and then return to an extended bout of lever pressing [13,18]. An increase in food deprivation raises the consumption both of free and earned pellets [14] but it has a relatively greater enhancing effect upon lever pressing [14,18]. Thus, if a drug has an effect analogous to that of food deprivation, one would expect it to increase both the amount of lever pressing, and the consumption of free food; and to increase the ratio of earned to free pellets. On the other hand, there is no reason why anxiety reduction should have such an effect, and a certain amount of evidence suggests that it might have the opposite effect. It has been suggested [10,11] that lever pressing in the presence of free food is related to container neophobia in the rat [3]. The greater the animals' familiarity with the free food container the more they will eat from it [11]; also, those rats that show the greatest timidity in eating from a novel container in their home cage, show the least eating of free food in the operant situation. Further evidence for the neophobia interpretation is that rats reared in social isolation eat less free food than socially-reared animals [14]. Isolates are also more timid than social rats in an emergence test of exploration [12] and speed of emergence in social and isolated rats is differentially affected by chlordiazepoxide [5]. This is just one example of the well-established change in responsivity to a number of drugs following long-term isolation in rodents [1, 2, 8, 17]. If a drug reduces timidity in rats, it might be expected to increase the consumption of food from a novel container. We therefore studied the effects of chlordiazepoxide upon lever pressing in the presence of free food, in the hope that the results might decide between the hunger and anxiety interpretations of drug-induced eating.

METHOD

Animals

Ten male Wistar rats weighing between 250 and 275 g, housed in pairs and kept at 85 percent free-feeding weight were used in Experiment 1. The animals of Experiment 2 were 16 male Lister hooded rats (Animal Suppliers Ltd.) weighing between 250 and 350 g, and kept on an ad lib diet of laboratory chow. In both experiments water was available in the home cages throughout.

Apparatus

The operant chambers in both experiments were 4 Campden Instruments CI-410 2-lever rat boxes with an automatic magazine delivering 45 mg Noyes Sucrose pellets. Rewards were delivered into a recess between the 2 levers, in front of which was a 5 cm wide transparent flap which the rat had to push open with its head to collect pellets. General illumination came from a 2.8 W houselight on the

ceiling. The food tray was illuminated with a 2.8 W light when a pellet was delivered, the light going off again when the pellet had been collected. Each chamber was enclosed in a ventilated, sound-resistant housing; programming equipment was located in a different room. The sucrose pellets used as rewards (3.9 Kcal/g) are highly palatable to the laboratory rat, and have the following composition: Sucrose (92.4 percent), Starch (4.7 percent), Calcium Stearate (2.3 percent), Water (0.6 percent). In the first experiment the free food was placed in earthenware bowls (6.0 cm dia.); and in the second experiment in tobacco tins (10.5 × 8.0 × 2.5 cm; tins were substituted in the second experiment to permit electrical recording of contacts, for the purpose of another experiment).

Procedure

In both experiments, animals were trained to press the left-hand lever for single-pellet rewards. Each lever press switched off the houselight, switched on the food-tray light, and delivered a single pellet into the tray. Further presses on the lever had no effect until the rat pushed open the flap in front of the food tray, at which point the tray light went off and the houselight came back on again. Session length was 20 min in Experiment 1 and 30 min in Experiment 2. When responding had stabilized, the free food bowl (Experiment 1) or tin (Experiment 2), containing 75–100 g of the reward pellets was placed against the back wall of the chamber. In Experiment 1, 5 of the rats were injected intraperitoneally an hour before testing with chlordiazepoxide HCL (Librium, Roche; 7.5 mg/kg in saline); the other 5 rats received control saline injections (1 ml/kg). The dosage was chosen on the basis of previous work on the effects of chlordiazepoxide upon emergence in rats [5]. At the end of the 20 min session the bowl of free food was weighed to determine how many pellets had been consumed. The procedure in Experiment 2 was the same except that the rats were divided into 4 groups of 4, and received injections of saline, 4, 8 and 12 mg/kg of chlordiazepoxide respectively.

RESULTS

Experiment 1

The mean free food consumed from the bowl was 5.5 g in the drug group and 3.1 in the controls. This enhancing effect of the drug was highly significant (Analysis of variance; $F(1,9) = 10.5$, $p = 0.01$). The drug, however, caused a non-significant decrease in the number of pellets earned by lever pressing (1.0 g in the drug group; 1.89 g in the controls, $F(1,9) = 1.25$, $p = 0.29$). Thus the relative amount of free food eaten was increased by the drug, in marked contrast to the effects of an increase in food deprivation [14,18]. To investigate this further, we carried out a study using non-deprived rats, and several doses of the drug.

Experiment 2

The mean data and standard errors are shown in Fig. 1. The drug increased consumption of free food at all doses. An analysis of variance showed that the differences between the 4 groups in free food consumption were highly significant, $F(3,12) = 11.2$, $p = 0.00085$. As in the first experiment, however, the effect upon the number of earned pellets was non-significantly in the reverse direction, $F(3,12) = 1.276$, $p = 0.3$. Thus the proportion of free pellets taken increased with each dose of the drug.

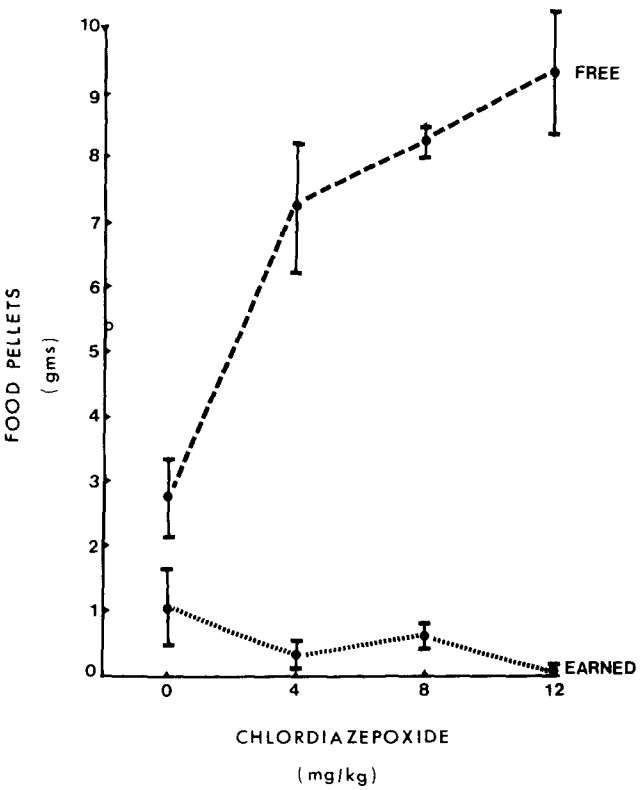

FIG. 1. Results of Experiment 2, which investigated the effects of different dosages (abscissa) of chlordiazepoxide upon consumption of sucrose pellets (ordinate) from two different sources in the same operant chamber. Free pellets were available from a container; earned pellets were available by pressing a lever. The data show that the drug selectively enhanced consumption of the free food.

GENERAL DISCUSSION

In both experiments the drug increased consumption of the free food, but had a non-significant effect in the reverse direction upon lever pressing. The reliability of the phenomenon is attested to by the fact that the two experiments employed different strains of animals under different conditions of food deprivation. Comparison between the two saline control groups in the two experiments reinforces the point that deprivation has a very different effect from that of the drug. The deprived rats in the first experiment consumed 3.1 g of free food and earned 1.89 g; the non-deprived animals of the second experiment ate 2.7 g of free food and earned only 1.1 g. If these small differences are due, at least in part, to deprivation conditions, it agrees with previous reports [14,18] that deprivation selectively enhances lever pressing. The drug, on the other hand, selectively enhanced consumption of free food. This cannot be reconciled with the view that the drug causes an increase in hunger. The results are consistent with an anxiety or timidity explanation. Verification of our hypothesis that chlordiazepoxide reduces neophobia, or reluctance to eat in a novel situation,

will demand study of the interactions between the drug and other treatments thought to affect timidity. We are currently investigating the effects of the drug upon differences between social and isolated rats in the free food situation. Another approach would be to investigate effects of the drug upon behaviour thought to be related to work in the presence of free food. One such behaviour is transport of food in mazes from unfamiliar to familiar locations [4]. A recent investigation by Cohen-Salmon (unpublished Ph.D. thesis) suggests that chlordiazepoxide does indeed reduce the tendency to transport in a way that would be predicted by our hypothesis.

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