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BRIEF COMMUNICATION

Suppression of Saccharin-Induced Drinking in the Nondeprived Rat by Low Dose Diazepam Treatment

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COOPER, S. J. *Suppression of saccharin-induced drinking in the nondeprived rat by low dose diazepam treatment.* PHARMACOL BIOCHEM BEHAV 18(5) 825–827, 1983.—Access to a highly palatable 0.005 M sodium saccharin solution resulted in considerable overdrinking in nondeprived rats over a 6 hr observation period. Contrary to previous reports documenting benzodiazepine-induced hyperdipsia in animals challenged with thirst stimuli or in animals exhibiting schedule-induced drinking, diazepam (0.1–3.0 mg/kg) had no effect to enhance the intake of the saccharin solution. Instead, diazepam produced a significant suppression of fluid consumption, in a manner not monotonically related to dose. Thus, diazepam (0.3 mg/kg) produced maximal suppression which did not dissipate over a 6 hr period, while diazepam (3.0 mg/kg) had no effect. Possible behavioral mechanisms by which low dose diazepam treatment might reduce the drinking are briefly considered.

Diazepam Drinking Saccharin Taste

THERE is consistent evidence that benzodiazepines enhance the consumption of water in water-deprived rats [3, 5, 7, 8, 10, 16], and in animals challenged with an osmotic or a hypovolemic thirst stimulus [4]. In many instances, although not all, benzodiazepines also increase schedule-induced licking and water consumption in the rat and monkey [1, 2, 12–15]. There are data indicating that benzodiazepine treatment can enhance the consumption of saccharin-flavored solution in water-deprived rats [8], an effect which can also be obtained with phenobarbital treatment [17].

It is well established that rats in water balance will consume excessive quantities of fluid in response to palatable flavors [6]. Sweet taste can operate as a powerful dipsogenic stimulus to produce considerable overdrinking. Physiological measures indicate that rats will avidly consume large quantities of a particularly palatable 0.005 M sodium saccharin solution, and, as a result, go into positive water balance [11]. The kidneys excrete the excess water load which is generated. The purpose of the present study was to determine whether or not diazepam treatment would enhance the copious drinking induced by saccharin flavor in nondeprived rats. A dose range of 0.1–3.0 mg/kg was employed, since there were no previously available data concerned with the effects of diazepam at low doses on ingestive responses.

METHOD

Animals and Procedure

Subjects were 40 experimentally naive male, hooded rats (General strain) bred in our laboratory. They were housed in pairs in stainless steel cages, with free access to food pellets (modified Diet 41B, Heygate and Sons, U.K.) and water. They were maintained under a 12 hr light–12 hr dark cycle (lights on at 7:00 a.m.) and room temperature was kept constant at 21°C. The animals weighed 250–380 g at the time of the study. They were all first familiarised with 0.005 M sodium saccharin (B.D.H.) solution by clipping a burette containing the solution at the front of the cage, and disconnecting the water supply from 9:00 a.m. on two consecutive days during the week prior to the drug study.

On the test day, animals were transferred to a rack of cages, identical to the home cages, and were housed singly. Diazepam was administered between 9:30 a.m. and 10:00 a.m., and 30 min after drug injection, a 50 ml calibrated cylinder containing 0.005 M sodium saccharin solution was clipped to the front of each cage. Latency to begin drinking was noted by an observer, and the intake of the solution was noted to the nearest 0.5 ml at hourly intervals over a 6 hr period. The rats were weighed before and after the test period. Food was not available during the test.

The 40 animals were allocated to 5 equal groups (N=8), and received the following injections 0, 0.1, 0.3, 1.0 and 3.0 mg/kg diazepam respectively, administered intraperitoneally. The drug vehicle was propylene glycol and water (48:52% by volume).

The saccharin intake data were analysed using a *t*-test for independent groups.

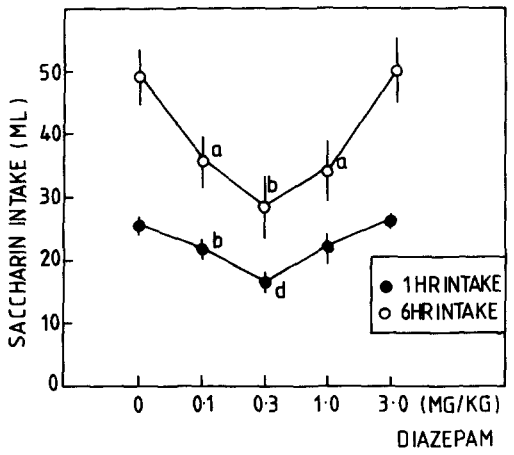

FIG. 1. Maximal suppressant effect of diazepam on the consumption of 0.005 M sodium saccharin solution in the nondeprived rat occurred at 0.3 mg/kg. No suppression occurred at a higher dose (3.0 mg/kg). First hour intakes (●) and total 6 hr intakes (○) are shown. Results are shown as mean (±SEM). Significant departures from control intake: $^{a}p<0.05$, $^{b}p<0.025$, $^{c}p<0.01$, $^{d}p<0.005$.

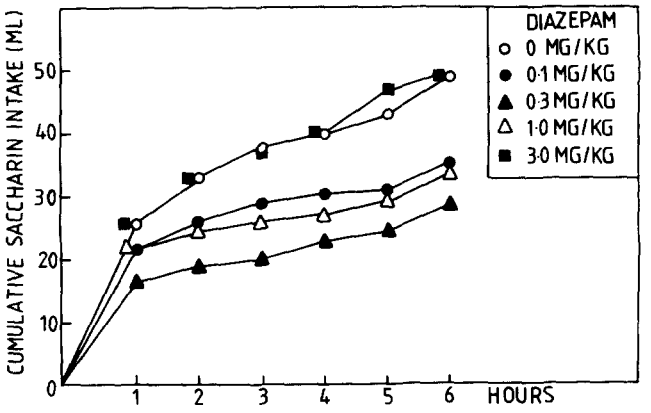

FIG. 2. Cumulative saccharin solution consumption (ml) over 6 hr test period after injection of diazepam (0.1–3.0 mg/kg) or diazepam vehicle. Low dose suppression of intake was not reversed by the end of the session.

RESULTS AND DISCUSSION

Figure 1 indicates that control animals treated with diazepam vehicle consumed 25.4 ml sodium saccharin solution within the first hour of the test, and this had risen to 49 ml by the end of the 6 hr period of observation. These results replicate earlier findings [11]. Diazepam did not enhance saccharin solution consumption at any dose level. Instead, diazepam (0.1 and 0.3 mg/kg) significantly reduced first hour intake. The most marked suppressant effect occurred with diazepam (0.3 mg/kg), when animals consumed only 65% of the control level of intake. The suppression was not due to a delay in the initiation of drinking, since all animals were observed to begin drinking immediately. There was no indication that the animals were showing signs of sedation after diazepam (0.1 or 0.3 mg/kg). At higher doses, diazepam (1.0 and 3.0 mg/kg) had no significant effect on first hour saccharin solution intake.

The low dose diazepam suppression of fluid consumption was not dissipiated over the course of the 6 hr test session (Fig. 2). In fact, by the end of the 6 hr period, saccharin solution intake in the 0.3 mg/kg diazepam group was only 58.6% of the control level of intake. Diazepam (3.0 mg/kg) had no overall effect on saccharin solution ingestion. Body weight changes after the 6 hr session were slightly negative, and not related to the diazepam-induced suppression of intake. Thus, mean body weight changes were −0.7 g, −1.4 g, −2.7 g for diazepam vehicle, 0.3 mg/kg diazepam, and 3.0 mg/kg diazepam groups, respectively. The rats were efficient in excreting all excess fluid load.

The striking aspect of the present data is that at a specific low dose (0.3 mg/kg), diazepam produced a marked suppression of saccharin solution consumption which did not dissipate over the course of a 6 hr test session. At slightly lower or higher doses (0.1 and 1.0 mg/kg) the suppression was less pronounced, and it was entirely absent at 3.0 mg/kg. The suppression cannot be attributed to either a drug-induced sedation or taste-aversion since there is no reason to expect that such effects would diminish with increasing diazepam dose. The suppression can also not be accounted for in terms of baseline dependency, since benzodiazepines enhance water consumption in water-deprived rats that exhibit high baseline levels of water ingestion [3, 5, 7, 10].

Furthermore, it is not clear how the suppression of saccharin solution consumption could be attributed to the anxiolytic properties of diazepam. The animals were tested under conditions of familiarity, and were nondeprived. Indeed, benzodiazepines have been shown to enhance the consumption of a novel, palatable, fluid diet, as a consequence of a proposed antineophobic action [9]. The present data do not, however, rule out the possibility that low dose treatment with diazepam might produce anxiogenic effects. Additional behavioral experimentation using animal models of anxiety is required in order to examine this notion. Alternatively, the diazepam-induced suppression may depend on drug-induced effects on taste responsivity, taste reward in nondeprived animals, or on drinking satiety. Further work is necessary in order to distinguish amongst these mechanisms, and to determine whether or not the low dose suppression applies specifically to drinking, or more generally to other behavioral categories, including feeding and general activity.

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