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BRIEF COMMUNICATION

Effects of Phenobarbital on Saccharin and Citric Acid Intake in Fluid Deprived Rats[1,2]

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WAYNER, M. J., D. B. RONDEAU, F. B. JOLICOEUR AND E. A. WAYNER. *Effects of phenobarbital on saccharin and citric acid intake in fluid deprived rats.* PHARMAC. BIOCHEM. BEHAV. 4(3) 335–337, 1976. – Rats were adapted to a 23 hr fluid deprivation schedule. Every third day animals were offered either 0.125 percent Na saccharin or 0.2 percent citric acid solutions in place of water during the 1 hr drinking session. Sodium phenobarbital was administered subcutaneously, 40 mg/kg, 15 min prior to drinking. Results indicate that the drug increases saccharin and citric acid consumption following the injections. No decreases in intakes of saccharin and citric acid occurred on subsequent postdrug days and the amounts of fluid consumed on these days were comparable to the baseline predrug days intakes.

Sodium phenobarbital Fluid deprivation Saccharin intake Citric acid intake Taste aversion

THE effects of sodium phenobarbital on periodic ethanol consumption in rats on a 23 hr fluid deprivation schedule have been reported recently [7]. Results of this experiment indicated that phenobarbital administered subcutaneously 15 min prior to a 1 hr drinking session significantly increased the consumption of 3 percent and 7 percent ethanol solutions. The enhancement in the ingestion of these ethanol solutions to which the animals had been previously exposed occurred only with phenobarbital treatment. Significant decreases in fluid consumption were observed upon subsequent presentation of the ethanol solutions two days following the phenobarbital administration. The fact that some barbiturates were reported to induce aversions to saccharin solutions [2] and sometimes to milk [1,10] suggested that the postdrug depression in ethanol intake could have resulted from a taste aversion produced by the barbiturate. Indeed, it has been demonstrated recently that sodium phenobarbital can induce a classical taste aversion for sapid ethanol solutions and saccharin [11]. It should be noted that the aversions which occurred on the subsequent presentation of the ethanol or saccharin solutions were obtained in rats which had no prior exposure to these fluids before the phenobarbital treatment.

The purpose of the present experiment was to determine the effects of sodium phenobarbital in a dose of 40 mg/kg on periodic forced 0.125 percent Na saccharin and 0.2 percent citric acid consumption in fluid deprived rats with limited prior exposure to these sapid fluids. Results demonstrate a clear increase in the drinking of saccharin and citric acid solutions by sodium phenobarbital and no subsequent postdrug decrease in intake of the same solutions.

METHOD

Animals

Twelve male hooded rats from our colony, approximately 75 days of age with mean body weights of 261 g were used. The rats were housed in individual cages in a constantly illuminated room as used previously [7]. The rats were separated into 2 groups of 6 animals each. They were weighed and handled daily throughout the experiment. Purina Lab Chow blocks and tap water were continuously available for 4 days.

General Procedure

Tap water, 0.125 percent w/v Na saccharin or 0.2

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percent w/v citric acid solutions were presented in 100 ml calibrated Richter drinking tubes clipped to the front of each cage. Saccharin and citric acid solutions were prepared every 2 or 3 days and were offered at room temperature. Distilled water was used to prepare the solutions to the desired concentrations. Sodium phenobarbital was dissolved in physiological saline and stock solutions of the drug were kept in the dark and under refrigeration. The dosage of sodium phenobarbital used was 40 mg/kg. All injections were administered subcutaneously. None of the injection volumes exceeded 0.3 ml.

Drinking Schedule and Drug Procedure

Animals were adapted to a 23 hr fluid deprivation schedule. The amounts of fluid consumed during the 1 hr drinking sessions were measured. Except for the first 10 days of the experiment, food was available during the 23 hr fluid deprivation period and removed just prior to the presentation of fluid. Food was removed from the floor of the cages while animals were weighed. Food was replaced immediately upon termination of the drinking session. Drinking sessions occurred at approximately the same time every day.

On Days 1–4, water was presented during the 1 hr drinking session. On Day 5, the animals were injected subcutaneously with 0.9 percent NaCl after being weighed. Fifteen minutes later each group of animals received its respective drinking solution. On Day 5, the saccharin and citric acid solutions offered during the drinking session were at half the concentrations to be used later in the experiment. This procedure was used to familiarize the animals with the taste and flavor of the solutions before drug treatments. On Days 6 and 7, tap water was the only fluid presented to both groups. Every 3 days from Day 8–32 the two groups of animals were respectively provided with 0.125 percent Na saccharin and 0.2 percent citric acid for the 1 hr drinking session. Tap water was offered on the 2 days in between each presentation of the sapid solutions. Consequently, animals were forced to drink either saccharin or citric acid solutions on Days 8, 11, 14, 17, 20, 23, 26, 29, and 32. The rats received 0.9 percent NaCl injections on Days 8, 11, 14, 20, 26, and 32 and injections of sodium phenobarbital on Days 17, 23, and 29. On Days 8, 11, and 14, the animals were injected with 0.9 percent NaCl 15 min prior to drinking. The data, expressed in terms of milliliters of fluid imbibed, obtained on Days 11 and 14 constituted predrug day baseline intakes for each solution. Drug administration took place on Days 17, 23, and 29. Sodium phenobarbital in a dose of 40 mg/kg was administered 15 min prior to drinking. On Days 20, 26, and 32, treatments of both groups of rats were identical to those of the predrug days 11 and 14, on which 0.9 percent NaCl injections preceded drinking. This procedure provided postdrug fluid intake measures with which it was possible to compare predrug and drug day intakes.

RESULTS

The results are based on the consumption data during the 1 hr drinking sessions on predrug days, drug days and postdrug days. Saccharin and citric acid solutions were the fluids offered on these days. Water intakes on all the inter-days were found to be of small variance and were not included in the analysis of the data. The results are illustrated in Fig. 1 where the mean intakes of saccharin and citric acid solutions are presented for the combined predrug days 11 and 14, for the combined drug days 17, 23, and 29, and for the combined postdrug days 20, 26, and 32. A one-way ANOVA with repeated measures [12] was carried out for each of the two groups. The main effect for the saccharin solution intake data was significant, $F(7,35) = 8.38$, $p<0.01$ as was the main effect for the citric acid solution intake data, $F(7,35) = 7.6$, $p<0.01$. A Tukey Type A analysis revealed that for both solutions the amounts of

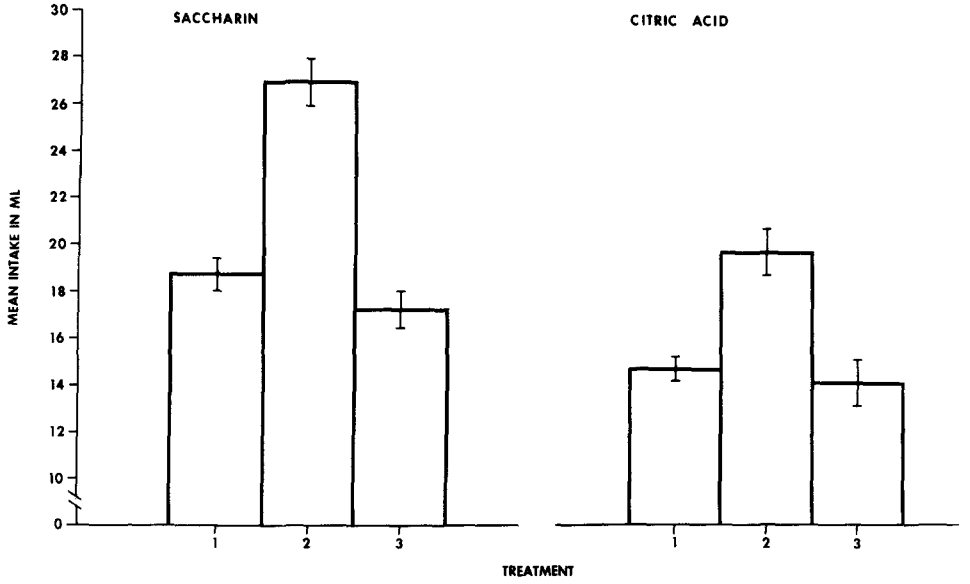

FIG. 1. Effects of sodium phenobarbital, 40 mg/kg, on saccharin and citric acid intake. Treatment 1: mean of the combined intakes for the predrug days 11 and 14. Treatment 2: mean of the combined intakes for the drug days 17, 23 and 29. Treatment 3: mean of the combined intakes for the postdrug days 20, 26 and 32. All means ± standard errors.

fluid ingested were significantly increased by sodium phenobarbital administration when compared to the amounts consumed on predrug and postdrug days. No difference was found between the intakes obtained on the predrug days 11 and 14 and those obtained on the postdrug days 17, 23, and 29. The amounts of fluid consumed on each of the drug days 20, 26, and 32, did not differ significantly. Also, there was no difference between the intakes on each of the postdrug days.

DISCUSSION

The observed increases in saccharin and citric acid consumption during the drinking sessions 15 min following subcutaneous administration of sodium phenobarbital confirm that this barbiturate enhances consumption of palatable and mildly aversive solutions [4, 7, 8, 9]. An interesting finding of the present experiment is that postdrug decreases in saccharin and citric acid intake did not occur upon subsequent presentation of the fluids two days following the phenobarbital treatment. The animals did not show taste aversions for the saccharin and citric acid solutions on the postdrug days. The fact that the postdrug depression in saccharin and citric acid consumption did not occur can be attributed to the effects of the limited prior exposure the animals had to these sapid fluids. This is plausible since several reports have indicated that familiarization or preexposure to the fluids used as taste stimuli attenuate the magnitude of the taste aversions to the fluids [3, 5, 6]. Although it has been unequivocally demonstrated that phenobarbital induces taste aversion to a saccharin solution presented as a novel taste stimulus [11], it appears from the present results that limited previous exposure to the saccharin solution can prevent the establishment of a taste aversion. However, a postdrug depression in 3 percent and 7 percent ethanol intake was observed in fluid deprived rats which had been previously exposed to these ethanol solutions [7]. In view of the results of the present experiment it seems that the reported decrease in ethanol consumption cannot be explained adequately as a nonspecific induced taste aversion by phenobarbital but indicates a specific effect of this barbiturate on ethanol intake.

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