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Effects of Body Weight Reduction and Food Deprivation on Cocaine Self-Administration

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OEI, T. P. S. *Effects of body weight reduction and food deprivation on cocaine self-administration.* PHARMACOL BIOCHEM BEHAV 19(3) 453–455, 1983.—The present experiments attempted to study the effects of food deprivation and body weight reduction on cocaine self-administration. Rats whose body weight was reduced to 80% free feeding weight (FFW) with 23 hours' food deprivation increased cocaine intake by 30-fold compared to 100% FFW animals. The results demonstrated that, in rats, body weight reduction and the state of food deprivation interact to further enhance self-administration of cocaine. From the practical point of view, the results suggest that there may be an increased risk of drug dependence with patients taking stimulants to control body weight.

Cocaine Drug Self-administration Body weight Food deprivation

A CONSIDERABLE number of studies have shown that when animals are reduced to 80% of their free feeding weight (FFW), self-administration of a wide range of drugs increases [2, 3, 4, 5, 6, 7, 10]. Recently, we [6] reported that self-administration of a low dose of cocaine (0.1 mg/kg) which was not self-administered by rats at free-feeding weight, was enhanced by body weight reduction. De la Garza *et al.* [3] working with monkeys supported this finding. One of the problems with using 80% reduced body weight animals is the confounding effect of food deprivation. Body weight reduction is normally achieved by restricted food intake and thus animals are food deprived at the same time. It is therefore very difficult to separate the effects of body weight reduction from the effects of food deprivation on the enhancement of drug self-administration. Furthermore, the published reports (e.g., [1,2]) imply that food deprivation has a general effect in enhancing self-administration of drugs. It is possible, and indeed likely, that food deprivation only has an enhancing effect on body weight reduced animals but has no similar effect on animals kept at 100% free feeding weight (FFW). The present experiment, therefore, was designed to investigate the separate effects of food deprivation and of body weight reduction on low dose cocaine self-administration.

METHOD

Twenty-eight male Wistar albino rats weighing approximately 400 g were used. All animals were housed individually in a temperature controlled room with a 12 hr light/dark cycle. Water was available freely in home cages. Animals were given restricted food intake in order to maintain their body weights at 100% and 80% free feeding weight.

Apparatus

The experimental apparatus used was similar to that described earlier by Oei *et al.* [5,6]. Briefly, animals were tested in a modified operant box with a bar situated 5 cm, and a pellet dispensing unit 3 cm, from the grid floor. The bar, when triggered, operated a syringe infusion pump (Saga Instruments, Model 341) which delivered 0.07 ml of cocaine or saline solution.

Drugs

Solutions of cocaine hydrochloride (Macfarlane Smith Ltd, Edinburgh) were prepared for intravenous administration prior to each testing session in 0.9% sterile saline at a dose of 0.1 mg/kg infusion. The anaesthetic used for the surgery consisted of a combination of pentobarbital sodium and chloral hydrate and the solution was injected IP.

Procedure

Rats were randomly divided into 100% and 80% FFW groups. Each group was then divided into Fed and Hungry conditions and tested for 15 days. All animals were weighed, anaesthetised and surgically implanted with an SP 28 polythene cannula through the jugular vein. The cannulae were maintained in position by leather jackets and were also connected to a flexible swivel system which allowed animals relatively free movement. (For details see Oei *et al.* [5].)

Three days after surgery, they were placed on a fixed time 1 min (FT1) food delivery schedule. One hour testing sessions with FT1 were repeated at the same time each day for the three phases of the experiment. Each phase lasted 5

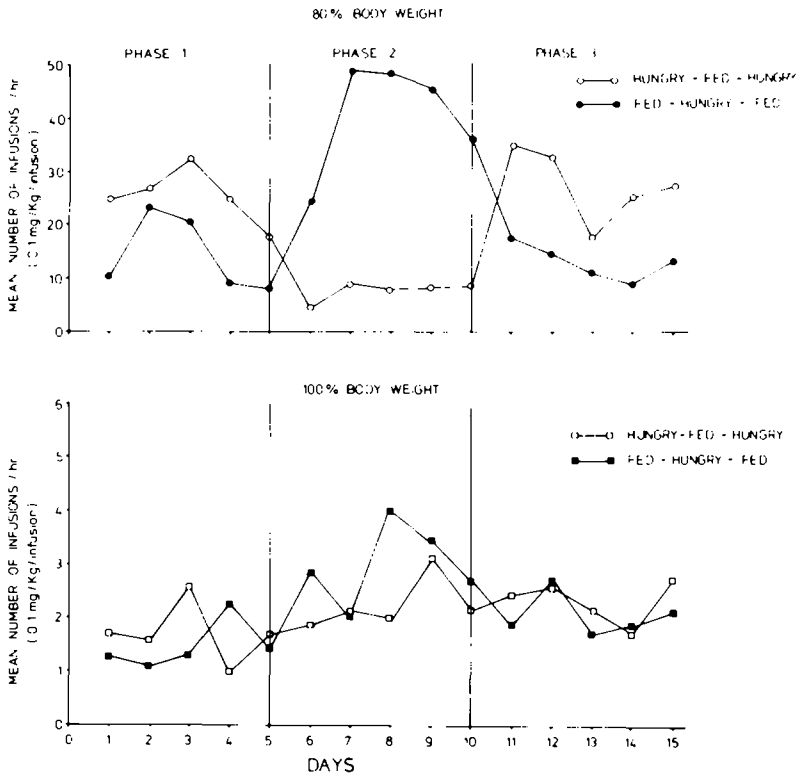

FIG. 1. The mean number of cocaine infusions/hr over the three phases of the experiment for the 80% (top panel) and 100% (bottom panel) Free Feeding Weight animals. The scale for the top panel is different from that of the bottom panel.

days. Each experimental session commenced by priming the animal with an initial infusion of cocaine. The cannulae were flushed each day with saline to prevent blockage. During Phase I, one group of rats (FED condition) were fed for an hour before the experimental session and therefore had 0 hours of food deprivation. A second was fed for an hour immediately after the experimental session. Therefore, this group (HUNGRY condition) was food deprived for 23 hours. Food was therefore only available for one hour in 24 hours. In Phase II, the experimental conditions of the two groups were reversed, i.e., the FED animals now received 23 hours' food deprivation whereas the HUNGRY animals received 0 hours. In Phase III, the treatment conditions reverted back to those in Phase I.

RESULTS

80% FFW Group

The mean number of infusions of cocaine per hour over the three phases for FED and HUNGRY conditions is presented in Fig. 1 (upper panel). A two-way analysis of variance with repeated measures was applied to Phases I and II data and the results showed only one significant interaction effect between experimental conditions and phase, $F(1,108)=39.45$, $p<0.001$, showing that the amount of cocaine intake for the FED or HUNGRY group was dependent on the treatment phase. Animals with 23 hours' food deprivation increased cocaine intake when compared to 0 hours' deprivation (see Fig. 1). When the data for Phases II and III were analysed, the results showed a significant interaction effect for Experimental Conditions and phase, $F(1,108)=26.04$, $p<0.001$, again suggesting that the mean amount of cocaine intake for animals in Phase II was reversed from that of Phase III (see Fig. 1). The results clearly demonstrated that 23 hour food deprivation enhanced cocaine self-administration.

100% FFW Group

The mean number of infusions/hr over the three phases for the FED and HUNGRY animals at 100% FFW are depicted in Fig. 1 (lower panel). The statistical analysis used was similar to that of Experiment 1. The results showed no significant difference between Phases I and II data and Phases II and III data. So the amount of cocaine intake in these 100% FFW animals was not influenced by their state of food deprivation. These findings suggest that self-administration of a low dose of cocaine was not influenced simply by the state of deprivation of the animals (see Fig. 1, lower panel).

Table 1 presents the overall mean cocaine, water and food intake for the 100% and 80% FFW animals over the FED and HUNGRY conditions. As can be seen from Table 1, overall cocaine self-administration was increased by tenfold in animals at 80% as compared to 100% FFW. Twenty-three hour food deprivation further enhanced the cocaine intake by another threefold in the 80% FFW animals. However, no such enhancement was observed with the 100% FFW animals, i.e., deprivation state only affects animals whose body weight has been reduced to less than the Free Feeding Weight.

TABLE 1

THE OVERALL MEAN COCAINE, WATER, AND FOOD INTAKE FOR THE 80% AND 100% FREE FEEDING WEIGHT ANIMALS OVER THE 0 AND 23 HOUR DEPRIVATION STATE CONDITIONS

	Fed 0 hr Deprivation			Hungry 23 hr Deprivation		
Body Weight Conditions	Cocaine mg/kg/hr	Water ml/24 hr	Food g/1 hr	Cocaine mg/kg/hr	Water ml/24 hr	Food g/1 hr
80% FFW	1.1*	24.98	12.34	3.14*	24.11	13.53
100% FFW	0.19	26.73	11.07	0.25	25.07	14.89

*$p < 0.01$.

It should be noted that comparison of the data from 80% body weight (upper frame, Fig. 1) with 100% body weight (lower frame, Fig. 1) confirms the results from earlier studies [1, 3, 6] that body weight reduction is sufficient for increases in drug self-administration to occur. There were, however, no significant differences between the amount of food and water intake for the 80% and 100% FFW animals and between the FED and HUNGRY conditions.

DISCUSSION

The present findings clearly showed that body weight reduction and the state of food deprivation interact to enhance the intake of cocaine significantly; in some cases the cocaine intake was increased by thirtyfold. These findings partially support our earlier work [6, 7, 9] and the work of other researchers [1, 2, 3] who showed that both body weight reduction and food deprivation enhanced drug self-administration. More importantly, the current results further extend the literature on self-administration of drugs by separating out the effects of food deprivation and body weight reduction. It seems that the food deprivation state has an added effect of increasing drug self-administration only on reduced body weight animals.

It has been suggested that food deprivation and body weight reduction interact with stimulants, e.g., amphetamine, to give rise to different rates of self-administration of these drugs [9]. The present findings support such a contention. However, they do not agree with Carroll and Meisch's [1] hypothesis that "the interoceptive stimuli related to food deprivation become partially associated with the reinforcing properties of the drugs." If this hypothesis were correct then an increase in cocaine intake for the 100% FFW animals in the present study would be expected. No such increase of cocaine intake was observed. A more parsimonious hypothesis is that food deprivation interacts with body weight reduction to give rise to differential sensitivity of the reinforcing properties of the drugs.

From a practical point of view, these findings and the work of previous investigators suggest that patients who are taking such drugs for weight control tend to put themselves into a state of food deprivation. This state combined with body weight reduction could result in patients taking more drugs, and thus increase the risk of drug dependence although the drug at an initial stage may have no significant effect on the patient. Our data showed that rats increased their intake of cocaine by thirtyfold under the conditions of 23 hour food deprivation and 80% FFW. It is hoped that such a thirtyfold increase would not be generalized to patients taking stimulant anorectics to reduce body weight. In any event, the findings from this and other studies strongly suggest that it would be wise to carry out experimental clinical trials to explore the relations between food deprivation, body weight reduction and drug dependence.

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