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Food Deprivation and Cocaine Self-Administration

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DE LA GARZA, R., J. BERGMAN AND C. R. HARTEL. *Food deprivation and cocaine self-administration*. PHARMAC. BIOCHEM. BEHAV. 15(1) 141–144, 1981.—The effects of food deprivation on the self-administration of cocaine were assessed in three rhesus monkeys under different schedules of reinforcement. In one subject, decreasing body weight to 80% of free-feeding weight (ffw) resulted in increased response rates and number of cocaine infusions taken. The same effects were observed in a second subject when restricted food intake resulted in 88% ffw. When schedule contingencies limited the number of infusions available, reduction to 90% ffw in the third subject resulted in increased response rates. These data suggest that food deprivation can be a potent variable in responding maintained by cocaine self-administration.

Cocaine self-administration   Food deprivation   Rhesus monkeys

FOOD deprivation has been shown to increase ethanol consumption [10,11]. Recently, the self-administration of drugs with no caloric value has also been shown to increase under conditions of food deprivation. For instance, Takahashi, Singer and Oei [14] reported that food deprivation increased the probability of amphetamine self-administration in rats. Carroll, France and Meisch [3], Meisch and Kliner [9], and Carroll and Meisch [4] found that food deprivation increased oral and intravenous etonitazine intake in rats. A recent report shows that food deprivation will also increase oral phencyclidine intake in rhesus monkeys [5]. The present report extends these findings to responding maintained by intravenous cocaine delivery in rhesus monkeys *(Macaca mulatta)*. These data are of particular interest since we were able to collect them using several schedules of reinforcement in the context of other on-going experiments.

METHOD

Animals

One female (7086) and two male (7801 and 6097) rhesus monkeys were used. Each monkey was equipped with a single lumen silicone venous catheter which was protected by a stainless steel harness as described by Johanson [8].

All monkeys had continuous access to water. Food availability (Purina Monkey Chow biscuits) was restricted as described below. Each animal received a sugar cube saturated with liquid vitamins every day. When necessary, antibiotics were administered intramuscularly to arrest catheter tract infection.

Apparatus

Each monkey was housed in a sound-attenuated wooden cubicle (inside dimension: 70×80×70 cm) that served as the experimental space. Each cubicle was equipped with a fan for ventilation and masking extraneous sounds. In addition, a convex lens inserted into the door allowed visual observation of the monkey. Mounted on the door of the cubicle were two metal boxes (12.5×15 cm) located 23 cm apart. Each box contained a response lever (PRL-001, BRS/LVE, Beltsville, MD). For monkey 7801, there were four Dialco stimulus lights above the levers. Two of these lights were covered with white lens caps and two were covered with red lens caps. Monkeys 6097 and 7086 had translucent plates above the levers that were transilluminated with red and green (No. 6097) or amber and green (No. 7086) stimulus lights. The cubicles also contained red and white ceiling lights. Cables connected the experimental cubicles to solid state or electromechanical programming and recording equipment located in an adjacent room.

Procedure

The terminal schedule for drug delivery and the deprivation procedure varied for each animal.

For monkey 7801, responding on the right lever was maintained under a fixed ratio 10 schedule of 0.1 mg/kg cocaine delivery (FR 10; ten responses for each infusion) in the presence of an illuminated white ceiling light and white stimulus lights above both levers. Responding on the left lever had no programmed consequences but was recorded. During each 10 sec infusion, which delivered 1 ml in volume, the white

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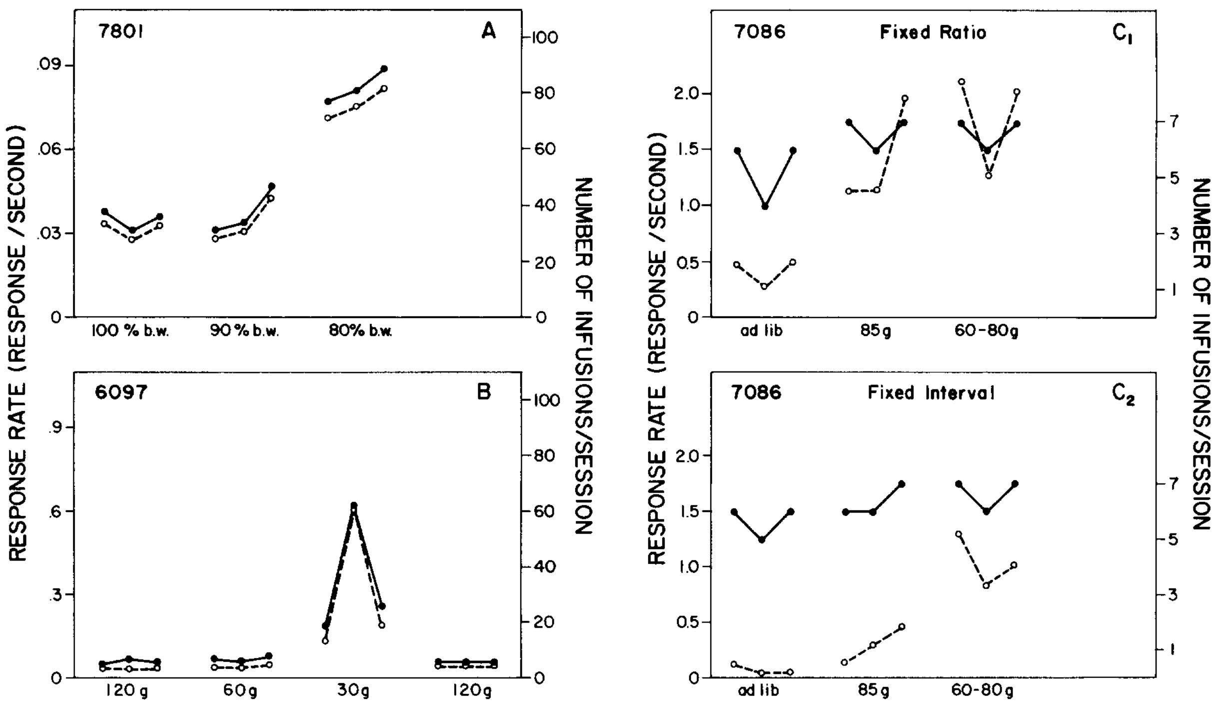

FIG. 1. Response rate in resp/sec (left ordinate: open circles connected by dotted lines) and number of infusions per session (right ordinate: filled circles connected by solid lines) as a function of body weight (animal 7801, panel A) or of food intake (animals 6097 and 7087, panels B and C). The last three days under each condition are shown for each animal. For animal 7086, Panel C_1 shows FR data and C_2 shows FI data.

lights were extinguished and the red ceiling light and the red lights above the levers were illuminated. During each daily 3 hr session, the number of infusions delivered and the total number of responses on each lever were recorded every 30 min. Deprivation procedures for this animal involved first restricting food availability to 0 g for two days. Thereafter, beginning with access to 100 g, food availability was steadily decreased to 60 g/day until the monkey's body weight was reduced to 80% free-feeding weight (ffw). Food availability was then increased to 80 g/day to maintain this body weight. The animal was fed 12 hr before the daily session.

Monkey 6097 responded under a 2 component multiple schedule. Responding in the first component was maintained by a 0.4 mg/kg cocaine infusion under an FR 10 schedule. The component lasted one-half hour and was associated with a red stimulus light above the right lever. Reinforcement was accompanied by a change in ceiling lights as described for animal 7801. Responding in the second component was maintained by delivery of 1 g banana-flavored Noyes pellets under an FR 30 schedule. Reinforcement was accompanied by an audible click. This component lasted one hour and was associated with a green stimulus light above the right lever. Responses on the left lever were not recorded and had no programmed consequences. Each daily session consisted of one presentation of the multiple schedule. When the sessions were completed during the baseline conditions, 120 g of food were added to the number of pellets obtained during the session. During the deprivation condition, the supplementary food was reduced to 60 g for 13 days, then to 30 g for 28 days, and then the baseline condition, 120 g, was reinstated. During the last 3 days of the 60 g condition, the animal's body weight was 96% ffw and reached 88% ffw during the last 3 days of the 30 g condition.

Monkey 7086 responded under a multiple schedule of 0.1 mg/kg cocaine delivery. In the first component, the completion of 30 responses on the right lever within 60 sec (FR 30, LH 60 sec) resulted in the delivery of drugs as described for animal 6097. This component was associated with amber stimulus lights above both levers. A 6 min time out (TO 6 min) followed whether or not the animal completed the ratio. In the second component, signalled by a green stimulus light, the first response after 5 min elapsed produced the delivery of cocaine followed by a 6 min TO. If no response occurred within 30 sec, the 6 min TO went into effect (FI 5 min; LH 30 sec). Responses on the left lever had no programmed consequences and were not recorded. Each session consisted of 7 presentations of this multiple schedule and lasted about 2 hr. Originally, the animal received ad lib food. The deprivation procedure began with one day of no food availability, followed by 6 days of access to 40 g/day. Then the animal was given 85 g/day for 2 weeks during which time body weight reached 90% ffw. This period was followed immediately by a period of access to 60–80 g/day. The animal was fed immediately after each session.

Drug

Cocaine HCL was dissolved in physiological saline and doses refer to the salt. Concentrations were altered as animals' weights changed to maintain the doses specified above for 7801 and 6097. The concentration for animal 7086 was not adjusted and varied from 0.1 mg/kg to 0.11 mg/kg.

RESULTS

Figure 1 shows the total number of infusions per session and the response rate for each of the animals used in this study. The data shown are from the last three sessions in each condition. In panel A, number of infusions and the response rate are shown as functions of body weight for animal 7801. While a reduction to 90% ffw had little effect, a further reduction to 80% ffw resulted in substantial increases in both the number of infusions taken and the rate of responding. Cocaine intake increased from a mean of 33 inf/session at ffw to 84 at 80% ffw. Correspondingly, response rate increased from 0.03 to 0.11 resp/sec. No responses were made on the non-operant (left) lever either before or after food deprivation procedures were instituted.

Panel B shows the number of infusions and response rate for animal 6097 as a function of the total amount of food (g) provided daily. In the baseline condition, the subject was given access to 120 g food. The mean number of infusions and the response rate (resp/sec) for that condition were 6 and 0.04, respectively. When food was limited to 60 g, there were virtually no changes in the number of inf/session, 7, or in resp/sec, 0.04. However, when food was limited to 30 g, the total number of cocaine infusions increased to an average of 35.6 and the rate increased to 0.31 resp/sec, although great variability was seen from one session to the next. Both number of infusions and response rate increased five-fold over baseline levels. A return to baseline feeding conditions produced a corresponding return to baseline levels of infusions (6 inf/session) and response rate (0.05 resp/sec).

Panel C shows the number of inf/session, the FR response rates (C_1), and the FI rates (C_2) for animal 7086 as a function of daily food intake. Because of schedule contingencies, the maximum number of infusions available in each session was 14. Under baseline conditions with ad lib access to food, FR rates averaged 0.41 resp/sec; FI rates were much lower, 0.07 resp/sec. While the monkey was maintained on 85 g food/day, FR response rates for cocaine increased over three-fold to 1.44 resp/sec from the ad lib food period; FI rates increased almost five-fold to 0.32. Further food deprivation (60–80 g/day) further increased FR rates to 1.83 resp/sec, while FI rates increased three-fold (1.05 resp/sec) over those of the previous condition. During the three conditions, the average number of infusions per session taken by animal 7086 rose only slightly from 11 (ad lib) to 13 (85 g/day) to 13.3 (60–80 g/day). The animal's death, due to unrelated causes, precluded further manipulations.

DISCUSSION

Food deprivation has been shown to affect a variety of behaviors. For example, exploratory behavior increases when food intake is restricted [15]. Increases have also been reported for responding maintained by events such as food delivery [13], intracranial stimulation [2], and light presentation [6, 7, 12]. In some instances, responding maintained by food but suppressed by punishment has been found to increase following food deprivation [1]. In studies using drug self-administration procedures, investigators have reported that food intake is an important determinant of rate of drug intake in rats [3, 4, 8, 14].

Our data extend these findings to a primate species self-administrating intravenous cocaine. Although the procedure for limiting access to food was different for each animal, food deprivation increased response rates in each of three animals regardless of drug dose. Since these data were collected in the course of other ongoing studies it was not possible to institute appropriate controls for general activity effects, e.g., saline substitution for cocaine. It is worth noting, however, that food deprivation caused no increases in non-operant (left) lever responding by the animal for which it was recorded.

It is unclear whether food deprivation altered the reinforcing efficacy of the response-maintaining event or whether it directly affected the response rate. In two of the animals (7801 and 6097), restricting food intake resulted in increases in the amount of cocaine self-administered and in the rates of responding. In the third animal (7086), cocaine intake, limited by schedule contingencies, did not increase greatly, although response rates increased several-fold. Further experiments are necessary to confirm the relationship between food deprivation and response rate when reinforcement density is held constant.

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