Effects of food deprivation on cocaine base smoking in rhesus monkeys

Abstract Studies have shown that both food deprivation and response cost have important influences on the magnitude of self-administration of a wide variety of psychoactive drugs. In an attempt to extend these findings to the smoked route of drug self-administration, the effects of food allotment and fixed-ratio (FR) value were evaluated in four male rhesus monkeys trained to smoke cocaine base. In the first phase of the experiment, monkeys were trained to self-administer smoked cocaine base under a chained progressive-ratio (PR), fixed-ratio (FR) schedule during daily experimental sessions. Monkeys were required to make 20 lever-press responses and then five inhalations on a smoking spout to obtain the first smoke delivery. The lever ratio then increased to 60, 140, 300, 620, 1260, 2540, and 4940 for each successive smoke delivery. The initial lever ratio value was reset to 20 at the beginning of each daily session. The body weights of three monkeys were determined under free-feeding conditions. Monkeys were then restricted to 100 g food and, when body weights had stabilized, the daily food allotment was increased to 150 g, approximately 210 g, or greater than 400 g (satiation). As the daily food allotment and body weight increased, the mean number of smoke deliveries decreased in two of three monkeys. In the second phase of the experiment, three monkeys were maintained under either food-satiated or food-restricted conditions. Body weights were maintained at approximately 90% of their free-feeding weights under food-restricted conditions. Fixed-ratio values were increased from 128 to 256, 512, 1024, and 2048. Monkeys were required to complete the lever FR value and then to make five inhalations on the smoking spout to gain access to 1.0 mg/kg per delivery cocaine base. The mean number of smoke deliveries increased at FR 256, 512, and 1024 when monkeys were food-restricted as opposed to food-satiated. Correspondingly, the mean number of responses increased under food-restricted conditions. Responding continued to increase over a wider range of FR values, and the peak number of responses was higher under food-restricted, as opposed to food-satiated conditions. These results, using the smoking route of administration, are consistent with the hypothesis that food deprivation increases the self-administration of reinforcing drugs.

Key words Cocaine base • Crack • Drug self-administration • Fixed ratio • Food deprivation • Food satiation • Progressive ratio • Reinforcing efficacy • Rhesus monkeys • Smoking

Introduction

Food deprivation has a marked effect on a number of behaviors that are associated with positively reinforcing events, such as wheel-running, intracranial self-stimulation, and saccharin consumption (see Carroll and Meisch 1984 for a review). Several studies have also shown that during food deprivation, the consumption of commonly abused substances in both humans and non-humans increases. For example, coffee and cigarette intake increased in humans maintained under semi-starvation conditions (Franklin et al. 1948). A group of normal, control women also spent more time working for cigarettes under food deprivation conditions (Bulik and Brinded 1994). And finally, weight loss has been associated with increased relapse to cigarette smoking (Hall et al. 1986) and increased...
cotinine levels in smokers (Niaura et al. 1992). In the laboratory, it has been demonstrated that consumption of a wide variety of psychoactive drugs increases under food deprivation conditions. For example, phencyclidine, ketamine, pentobarbital, methohexitol, cocaine, and d-amphetamine self-administration increased in rhesus monkeys (Carroll 1982, 1987; Carroll and Stotz 1983; Carroll et al. 1984; de la Garza and Johanson 1987) and etonitazene, alcohol, cocaine, and phencyclidine self-administration increased in rats (Carroll and Meisch 1978; Carroll et al. 1981; Files et al. 1993) during food deprivation. Thus, in a number of different species, the self-administration of drugs from a wide variety of pharmacological classes increases under food deprivation conditions.

Although the increase in self-administration occurred across drugs from many different pharmacological classes (Carroll and Meisch 1984), the magnitude of this increase may vary depending on the reinforcing efficacy of the drug that is self-administered (de la Garza and Johanson 1987). In a study examining the effects of food deprivation on IV self-administration of amphetamine, cocaine, nicotine, diazepam, and perphenazine, de la Garza and Johanson (1987) showed that food deprivation increased self-administration only when the drug of interest was self-administered above saline levels. For example, nicotine, cocaine and amphetamine self-administration significantly increased in food-deprived rhesus monkeys. In contrast, diazepam and perphenazine self-administration increased only slightly at some doses in some monkeys. Monkeys that did not self-administer either diazepam or perphenazine above saline levels also did not show an increase in drug self-administration under food deprivation conditions. Thus, these investigators found that food deprivation had minimal effects on the self-administration of drugs that did not consistently maintain responding above saline levels. In addition to drug, route of administration may also be an important variable in the effects of food deprivation on drug self-administration. When rats self-administered etonitazene, cocaine or phencyclidine intravenously, large, rapid increases in drug self-administration occurred when rats were food-deprived, compared to when they were food-satiated (Carroll et al. 1981; Carroll and Boe 1984). In contrast, when rats self-administered etonitazene by the oral route, the magnitude of the increase in drug self-administration was smaller, and a significant increase in self-administration only occurred over a period of several weeks (Carroll and Meisch 1979). Thus, drug and route of administration appear to be important variables in the effect of food deprivation on drug self-administration.

Although cocaine abuse by the smoked route of administration has risen dramatically within the last decade, very little research has been conducted to evaluate smoked cocaine self-administration in laboratory animals. Recently, investigators in this laboratory developed a model of cocaine base smoking in rhesus monkeys (Carroll et al. 1990a) and showed that when cocaine base was available, lever-press responding was maintained at higher levels than when lidocaine was available (Carroll et al. 1990a; Comer et al. 1994). Furthermore, cocaine base self-administration showed the classic inverted U-shaped curve as a function of cocaine dose (Carroll et al. 1990b). Also, cocaine smoking decreased after pretreatment with the partial mu opiate agonist buprenorphine and when the alternative reinforcer, saccharin, was concurrently available (Carroll et al. 1992; Comer et al. 1994). The purpose of the current study was to extend earlier findings by evaluating the effects of food deprivation on cocaine base smoking in rhesus monkeys. Food restriction versus satiation and lever FR requirement for access to cocaine base smoke were manipulated. In the first experiment, cocaine base smoking was examined as body weight was manipulated in monkeys maintained under a chained progressive-ratio (PR), FR schedule. The ratio value for each smoke delivery was progressively increased within each experimental session. In the second experiment, cocaine base smoking was examined as the cost (FR) of cocaine base was manipulated in monkeys maintained under either food restricted or satiated conditions. In this experiment, the lever FR value, which remained constant within each experimental session, was only increased after several days of stable responding at that particular FR value. Conditions in the second experiment more closely approximate the human situation in which prices of cocaine are relatively stable over time, rather than changing after each administration.

Materials and methods

Subjects

Four adult male rhesus monkeys (Macaca mulatta) were housed in individual chambers in a temperature (23.3°C) and humidity controlled room (lights on at 6:00 a.m. and off at 6:00 p.m.). All of the monkeys had been used in previous experiments and were experienced with the cocaine base smoking procedures (see Carroll et al. 1990a for a description of the training procedure). Water was freely available throughout the day except for a 1-h period just prior to the start of the session. During this time, data from the previous day were collected and fresh water was made available. Purina high-protein monkey chow and fresh fruit were given at the end of the experimental session each day. Monkeys were weighed once every 2 weeks during the first phase of the experiment and once a week during the second phase of the experiment. The daily food allotment was adjusted to maintain body weights at the experimentally determined level.

Apparatus

Subjects were housed in custom-made stainless-steel experimental chambers (Carroll et al. 1990a). Vertical bars were located at the front of each chamber so that the monkeys could see each other. Each chamber was equipped with a work panel located on one side