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Reduction of Heroin Intake in Baboons by an Economic Constraint[1,2,3]

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ELSMORE, T. F., G. V. FLETCHER, D. G. CONRAD AND F. J. SODETZ. *Reduction of heroin intake in baboons by an economic constraint.* PHARMAC. BIOCHEM. BEHAV. 13(5) 729–731, 1980.—Baboons earned their total food ration in a situation where they were periodically given an opportunity to choose between food and an intravenous infusion of heroin. As the number of daily choices was restricted, food intake remained relatively constant, while heroin intake decreased dramatically.

Heroin Food intake Choice Drug abuse Economics Baboon

RECENT investigations of the reinforcing properties of drugs have emphasized conditions necessary to demonstrate similarities between drug- and food-reinforced behavior [8, 9, 13, 15]. While such investigations attest to the power of intermittent schedules of reinforcement in the control of behavior, and perhaps suggest some reasons why drug-seeking behavior appears to be so persistent, they have been conducted in laboratory situations that may preclude the operation of some variables that are present in the natural environment. [1, 7, 12]. For example, individuals rarely find themselves with a single alternative and must allocate resources among available commodities. Two commodities of interest are food and heroin. Heroin use is typically attributed to its potent reinforcing and dependence-producing properties [11, 14, 16, 18], and food has the important biological property of being required for the survival of the organism, which can be viewed as choosing between these two potent reinforcers. Herrnstein [4,5] and others have suggested that the relative frequency of choices of an alternative will match the relative frequency of reinforcement for that alternative. Another view suggests that economic variables may play an important part in the control of choice behavior [6, 7, 10], emphasizing the relationship between consumption and cost. The present experiment, therefore, examines the effect of restricting available resources upon the daily intake of two potent reinforcers, food and heroin, under conditions where the subjects must choose between the two.

METHOD

Subjects and Apparatus

Two sexually mature baboons [2] weighing 16.3 kg (P363) and 25.0 kg (P241) were restrained for the duration of the experiment in chairs similar to those described by Findley *et al.* [3]. The animals earned their total daily food ration, with the exception of a piece of fruit each day, working under the experimental procedures. Water was continuously available.

The animals were prepared with indwelling venous catheters (Dow-Corning "Silastic", 0.64 mm ID and 1.19 mm OD) under sterile conditions. The catheters were placed *via* one of the femoral veins into the vena cava to a point above the diaphragm and distally, subcutaneously to the midpoint of the back, where the exit point was reinforced with a subcutaneous piece of "Marlex" mesh which was cemented to the catheter and served to minimize infection of the wound by providing a secure mechanical anchor. Infusions were made by a piston pump (Harvard "Lambda" Model No. 1302) delivering 0.01 ml from a reservoir per operation. Each infusion cycle consisted of 10 operations of the pump, spaced at 0.5-sec intervals.

The restraint chairs were housed in isolation booths such that an aluminum intelligence panel was located flush with the front of the chair. Two circular press plates (keys), 4.5 cm in diameter were centered 12.5 cm apart directly in front of the animal's left hand, and a food cup was located near the

[1]This material has been reviewed by the Walter Reed Army Institute of Research, and there is no objection to its presentation and/or publication. The opinions or assertion contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

[2]In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care", as promulgated by the Committee of the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences, National Research Council.

[3]Heroin HCl was obtained from the Drug Enforcement Agency with the cooperation of the joint NIDA/DEA Psychotomimetic Agents Advisory Committee. The material was from batch A1OOD and was assayed to be in excess of 90% pure by the Division of Biochemistry of the Walter Reed Army Institute of Research.

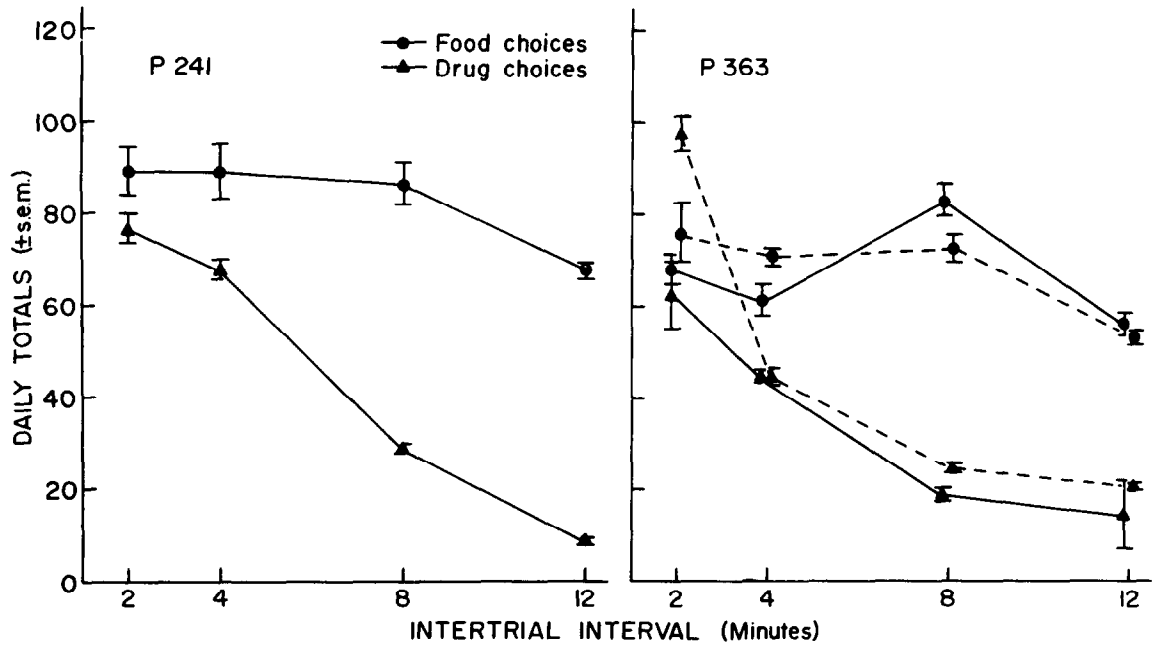

FIG. 1. Throughout the day, baboons were given the opportunity to choose between 3.0 g of food or a 0.1 mg/kg intravenous infusion of heroin. Effects on total daily choices are shown as a function of the interval between choice-trial onsets. The solid lines connect the points for an ascending sequence of intertrial intervals, and the dashed line for baboon P363 is for a descending sequence.

animal's right hand. The keys operated with a force of about 0.2 N and could be illuminated from behind with different colors. General illumination was provided by a fluorescent light behind a slit at the top of the panel which was illuminated from 0800-2400 hr daily.

Procedure

Prior to surgery, the animals were adapted to the restraint and housing conditions for 30 days, and earned their entire food ration by pressing on the two keys, only one of which was illuminated white and produced food pellets under a fixed-ratio (FR) schedule [2] which was gradually increased to five responses. The active key was changed daily. Following surgery the animals were immediately placed on the final procedure, providing them with periodic opportunities to choose between a heroin infusion and food. Choice opportunities were signalled by illumination of the two keys with white light. Completion of five presses on the left key resulted in an intravenous infusion (0.1 mg/kg heroin HCl in 0.9% saline in a volume of 0.1 ml, accompanied by a red key light for five seconds. The right key was not illuminated during infusions. Similarly, five presses on the right key when it was white changed it from white to green for five seconds, extinguished the left key light and delivered 3 g of food (four 750 mg Noyes pellets at 0.5-sec intervals). Both key lights were extinguished following either drug infusion or food delivery. If five presses were not made on either key within 100 sec from the start of a trial, it terminated automatically. Initially, the interval between choice-trial onsets was 2 min. After about 60 days of acquisition during which heroin intake stabilized, the interval between choice-trial onsets was varied between 2 and 12 min, with a minimum of 14 days at each intertrial interval. Both baboons were exposed to an ascending sequence of intertrial intervals, and baboon P363 was also exposed to a descending sequence.

RESULTS

Figure 1 shows choices per day of food and heroin as a function of the interval between choice trials. As the interval was increased, choices of heroin decreased much more rapidly than food choices. Increasing the intertrial interval from 2 to 12 min reduced food intake about 23%, while heroin intake was decreased an average of 83%. These reductions were accompanied by an increase in the percentage of trials on which the animals responded from an average of 22% at the 2-min intertrial interval to 63% at the 12-min intertrial interval. Thus, heroin intake was reduced even though the animals could have responded on 37 percent more of the trials and maintained heroin intake at near-baseline levels.

DISCUSSION

Numerous attempts have been made to compare the reinforcing efficacy of different events. With respect to homogeneous reinforcing events (e.g. different amounts of the same kind of food), these efforts have been markedly successful, and have led to the formulation of the matching law which states that the relative distribution of behavior among alternatives matches the relative amounts of reinforcement supplied by the alternatives [4,5]. In the present case, as in all cases involving ratio schedules of reinforcement this relationship remains true, although perhaps trivial. When the reinforcing events are heterogeneous, however, the relationship does not appear to apply [6], and alternative theories may be required.

Economic theory supplies a particularly attractive framework [6,10]. The demand for commodities is evaluated by the slope of the curves relating consumption to price or to income. In the present case, the available income (i.e. number of choice opportunities per day) was manipulated, and the demand curve for heroin was demonstrated to be

steeper or more "elastic" [7] than that for food. Thus, the distribution of choices between food and heroin depends upon the economic context in which the choice situation is imbedded. If resources are plentiful, intake of both commodities is maintained. If resources are more scarce, food intake is maintained [1], while heroin intake decreases. Similarly, Wurster *et al.* [17] showed that heroin intake could be reduced by providing alternative sources of food and drug reinforcement.

These results show that through the use of appropriate environmental manipulations, it is possible to reduce heroin intake. A thorough understanding of the elimination of drug-maintained behavior as well as its acquisition and maintenance, will require further exploration of conditions resulting in the reduction of drug intake in experimental situations that mimic important aspects of the natural environment. For example it will be important to determine the generality of the present results across different unit doses of heroin. Within this framework, the concepts of "addiction" and "dependence" appear to have little utility, with attention being focused upon observable and manipulable variables that control drug-taking behavior.

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