Pharmacology Biochemistry & Behavior, Vol. 20, pp. 145–151, 1984. © Ankho International Inc. Printed in the U.S.A.

Self-Administration of Orally-Delivered Methohexital in Rhesus Monkeys with Phencyclidine or Pentobarbital Histories: Effects of Food Deprivation and Satiation

MARILYN E. CARROLL,[1] DANA C. STOTZ, DALE J. KLINER AND RICHARD A. MEISCH

Psychiatry Department, Mayo Box 392, University of Minnesota, Minneapolis, MN 55455

Received 13 May 1983

CARROLL, M. E., D. C. STOTZ, D. J. KLINER AND R. A. MEISCH. *Self-administration of orally-delivered methohexital in rhesus monkeys with phencyclidine or pentobarbital histories: Effects of food deprivation and satiation.* PHARMACOL BIOCHEM BEHAV **20**(1)145–151, 1984.—Orally-delivered methohexital was demonstrated to function as a reinforcer for rhesus monkeys with either phencyclidine or pentobarbital self-administration histories. The effects of food deprivation and food satiation were compared across a wide range of methohexital concentrations. Initially, three monkeys were trained to orally self-administer phencyclidine (0.25 mg/ml) and water, and three were trained to orally self-administer pentobarbital (0.5 mg/ml) and water under concurrent fixed-ratio (FR) schedules during daily 3-hr sessions. Liquid deliveries during the session (drug and water) and intersession (water) were contingent upon lip contact responses on solenoid-operated drinking spouts. The monkeys were first tested while food deprived by maintaining them at 85% of their free-feeding body weights. Methohexital concentrations were presented in the following order, and each concentration was held constant until at least five or six sessions of stable behavior were obtained: 2, 2.8, 4, 2 (retest), 1, 0.5, (plus 0.25 and 0.125 in monkey M-W) and 2 (retest) mg/ml. The monkeys were then food satiated by allowing them unlimited access to food, and the methohexital concentration series was repeated. During food deprivation, the concentration-response functions generally resembled an inverted U. Concurrent water-maintained responding was generally low, but it increased in some monkeys as methohexital concentrations increased in some monkeys. During food satiation, methohexital-maintained responding was not different from water-maintained responding in some monkeys, but in others it was substantially higher than water-maintained responding. Maximum drug intake ranged from 20.4 to 93.8 mg/kg during food deprivation and from 6.4 to 64.2 during food satiation among the six monkeys. During food deprivation, most methohexital-maintained responding occurred during the first half of the 3-hr session; however, during food satiation, responding was evenly distributed throughout the 3-hr session. The time course of water-maintained responding was not altered as a result of changes in the feeding condition. Generally it appeared that methohexital was more easily substituted for pentobarbital than it was for phencyclidine, and higher rates of performance were maintained in the pentobarbital-trained monkeys.

Drug history Food deprivation Food satiation Lip-contact response Methohexital
Oral drug self-administration Pentobarbital Phencyclidine Rhesus monkeys

IN recent years oral drug self-administration in nonhuman primates has been extended from ethanol [23] to opioids [9], dissociative anesthetics [2, 3, 12], barbiturates [1,26] and psychomotor stimulants [12]. Initially, schedule-induced polydipsia [9,10] and other food-induced drinking procedures [23] were used to generate drinking and establish drugs as reinforcers. Later studies demonstrated the effectiveness of training monkeys with ethanol [26] or phencyclidine [2], and then substituting a drug with similar pharmacological properties.

In the present experiment, a substitution procedure was used as a means to rapidly produce oral methohexital self-administration in rhesus monkeys and to evaluate the importance of drug history in establishing a new drug as a reinforcer. Methohexital was substituted for phencyclidine in one group of monkeys and for pentobarbital in another group. Methohexital self-administration has previously been demonstrated via the intravenous route in rats [30] and monkeys [34] and via the oral route in baboons [1]. Substitution procedures have been extensively used in intravenous self-administration studies [18] and to a limited extent in oral self-administration studies [1, 2, 12]. There is recent evidence that intravenous self-administration of a particular drug may depend on the pharmacological class of the substituted drug [19,35].

Another objective of the present study was to compare the effects of food deprivation and satiation on methohexital-reinforced behavior over a wide range of drug concentrations. Food deprivation has been shown to dramatically increase self-administration of ethanol [14, 22, 27, 31], opiates [4, 5, 25, 28], stimulants [5, 12, 13, 28, 33], dissociative anesthetics [3, 10, 12] and barbiturates [20].

[1]Requests for reprints should be addressed to M. E. Carroll.

METHOD

Animals

Six adult male rhesus monkeys (*Macaca mulatta*) served as subjects. At the start of the experiment they were maintained at 85% of their free-feeding body weights by restricting their access to food (Purina High Protein Monkey Chow No. 5045). The monkeys were housed individually in their experimental chambers in rooms illuminated from 7:00 to 19:00 hr. Three monkeys (M-B, M-M1 and M-R) had previously been trained to self-administer orally-delivered phencyclidine. Two monkeys (M-B and M-R) had previous experience with etonitazene self-administration [9], and all three monkeys had also received phencyclidine analogs and quinine [2]. Their 85% weights ranged from 6.3 to 9.4 kg. The other three monkeys (M-BL, M-P1, and M-W) had previously been trained to self-administer pentobarbital [26], and they also had oral self-administration experience with ethanol [17,24]. Their 85% weights ranged from 8 to 13.7 kg.

Drugs

Methohexital sodium (Brevital®) was supplied by Lilly Research Laboratories (Indianapolis, IN). Phencyclidine HCl was obtained from the National Institute on Drug Abuse (Research Triangle Institute: Research Triangle Park, NC). Pentobarbital HCl was purchased from the Ganes Chemical Co. (Pennsville, NJ). Methohexital solutions were prepared with room temperature distilled water, and phencyclidine and pentobarbital solutions were prepared with room temperature tap water.

Apparatus

The experimental chambers were stainless-steel Hoeltge (No. HB-108) or Labco (No. ME-1305) primate cages, equipped with a work panel on one wall. The work panel contained two liquid spouts, spaced 30 cm from each other, and corresponding stimulus lights that signaled experimental events. The brass drinking spouts were 2.7 cm long and 1.2 cm in diameter. A drinkometer circuit was operated when the monkey placed his lip on the spout. The lip contact response operated a solenoid for approximately 120 msec and released 0.55 ml of liquid from the spout. The drinking spout contained no moving parts that would provide auditory feedback for each response; therefore, feedback stimuli were provided by one of two pairs of small lights mounted directly behind a Plexiglas plate supporting the spout. When a drug solution was available from a spout, two small green lights were illuminated for the duration of each lip contact. Similarly, when water was available from a spout, two small white lights were illuminated for the duration of each lip contact. In addition to these feedback lights, larger green lights 12 cm above the drinking spouts were illuminated when water was available during sessions and intersession periods. This light blinked (10 cycles/sec) on the side where a drug solution was available during the session. Liquids were contained in covered stainless-steel reservoirs, and there was no measurable evaporation. Experimental sessions were controlled automatically, and data were recorded and printed by microcomputers or solid state programming and recording equipment located in an adjacent room. Liquid responses and deliveries were also recorded on Gerbrands cumulative recorders. Complete details of the control and recording equipment, drinking devices, and experimental chambers, have been described elsewhere ([11, 15, 23], respectively).

Procedure

Daily 3-hr experimental sessions took place between 9:30 a.m. and 12:30 p.m. or between 10:00 a.m. and 1:00 p.m. Each session was preceded and followed by a 1-hr timeout when solutions were changed and data were recorded. During the timeout, stimulus lights were not illuminated, and behavior had no programmed consequences. During the sessions, drug and water were simultaneously available from the two drinking spouts under a concurrent fixed-ratio (FR) schedule. Side positions of drug and water were reversed daily. During the 19-hr intersession periods, water was available ad lib from either one or both drinking spouts under an FR 1 schedule. Throughout this experiment, stability was defined as no steadily increasing or decreasing trend in the number of liquid deliveries and no change in the overall pattern of responding. Typically, there were only about 5 to 7 sessions at each concentration, since behavior rapidly changed with changes in concentration, and the number of sessions required to obtain stability did not vary as a function of concentration. The monkeys were weighed every 7–10 days throughout the experiment.

At the start of this experiment five sessions of stable behavior were obtained at the 0.5 mg/ml pentobarbital or the 0.25 mg/ml phencyclidine concentration (while the monkeys were food deprived and maintained under a concurrent FR 16 schedule). Monkey M-P1 was tested at FR 64 during the pentobarbital baseline procedure and with methohexital. The high FR was used to produce a separation between drug- and water-maintained responding to demonstrate that the drugs were functioning as reinforcers. The following methohexital concentration series was subsequently tested: 2, 2.8, 4, 2 (retest), 1, 0.5 (plus 0.25 and 0.125 in M-W) and 2 (retest) mg/ml. For monkey M-B methohexital (1 mg/ml) was initially substituted for phencyclidine; however, behavior was not well-maintained even after the FR was reduced from 16 to 8. Phencyclidine (0.25 mg/ml) was reinstated at FR 8, and after ten sessions of stable behavior were obtained, methohexital was added to phencyclidine solution and then phencyclidine was gradually removed from the drug solution. Initially, this monkey received a combination containing 0.125 mg/ml phencyclidine and 1 mg/ml methohexital. After four sessions, the phencyclidine concentration was reduced to 0.0625 mg/ml, and after two sessions it was further reduced to 0.0312 mg/ml. After two additional sessions, methohexital (1 mg/ml) was presented alone. The concentration was subsequently raised to 2 mg/ml and the concentration series described above was tested. Monkey M-R's FR was also decreased to 8, since his responding was not well-maintained at FR 16.

After the food deprivation phase was completed, the monkeys were food satiated by allowing them unlimited access to food. They continued to receive concurrent access to methohexital and water under their respective FR schedules during the daily 3-hr sessions. When their behavior stabilized (after about 20 to 30 sessions), an identical methohexital concentration series was run. Subsequently, four of the six monkeys were again food deprived and retested at the 2 mg/ml methohexital concentration. They were given 75 g of food per day until they reached their 85% body weights and then an amount necessary to maintain them at those weights. Again, they continued to receive methohexital and water during daily sessions while the weights stabilized. The 85% weights were based upon the weights taken at the end of the food satiation phase. The monkeys continued to receive

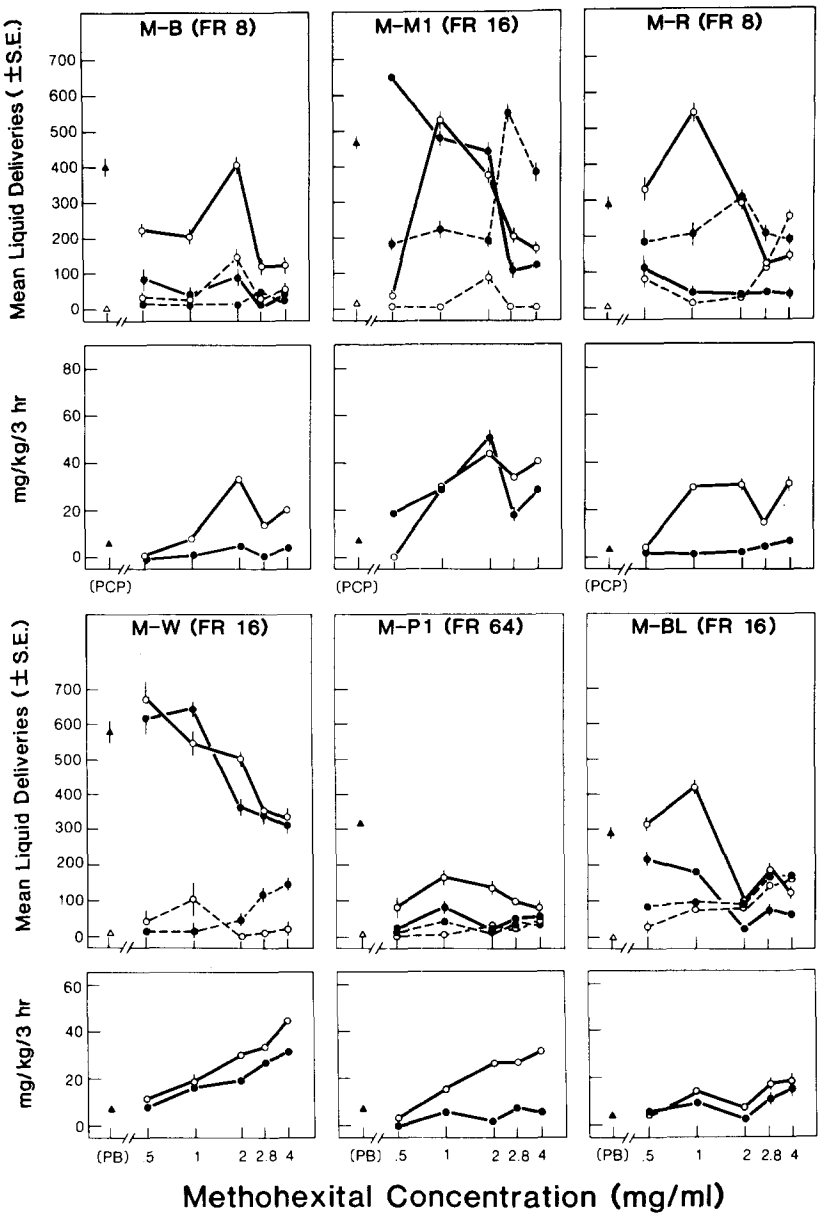

FIG. 1. Mean liquid deliveries and drug intake (mg/kg) are presented as a function of methohexital concentration for six monkeys. Concentrations were presented in the following order 2, 2.8, 4, 2 (retest, not shown), 1, 0.5 and 2 (retest, not shown) mg/ml. The FR schedule parameters for liquid deliveries are indicated in parentheses. In the upper frames, filled triangles refer to phencyclidine deliveries for M-B, M-M1 and M-R, and to pentobarbital deliveries for M-W, M-P1 and M-BL under food deprivation conditions. Open triangles indicate the concurrent water deliveries. The FRs for methohexital were 16 in all monkeys except M-P1 whose FR was 64 and M-B and M-R whose FRs were 8; open circles refer to food deprivation sessions, and filled circles refer to food satiation sessions. Solid lines represent methohexital deliveries, and dotted lines refer to concurrent water deliveries. In the lower frames for each monkey, open circles indicate methohexital intake during food deprivation and filled circles refer to methohexital intake during food satiation. Each point is a mean (±S.E.) of the last five sessions of stable behavior at each concentration.

concurrent methohexital and water until their behavior stabilized (10 to 20 sessions), and then they were given their original drug (pentobarbital or phencyclidine).

RESULTS

When methohexital was substituted for phencyclidine or pentobarbital, it was consumed in excess of water, indicating that the drug was functioning as a reinforcer. Figure 1 shows mean methohexital and water deliveries and drug intake (mg/kg) per 3-hr session for the five methohexital concentrations during food deprivation and food satiation.

Food Deprivation

Methohexital deliveries followed an inverted U-shaped function as drug concentration increased, except for monkey M-W who did not show decreased methohexital-maintained responding even when the concentrations were lowered to 0.25 and 0.125 mg/ml (not shown). Water deliveries did not change systemically as a function of drug concentration, except there was an increase at higher concentrations for monkeys M-R and M-BL. Drug intake (mg/kg) generally increased as concentration increased.

Food Satiation

The number of methohexital deliveries decreased (from food deprivation values) to near water levels in four monkeys, and remained about the same as food deprivation levels in two monkeys. Monkeys that did not show a decrease in methohexital-maintained responding (M-M1 with a phencyclidine history and M-W with a pentobarbital history) during food satiation were also the ones with the highest methohexital intake. Water-maintained responding did not change systematically as a function of drug concentration except for monkeys M-M1, M-BL and M-W who showed increased responding at the higher concentrations. Except for monkeys M-M1 and M-W, drug intake increased only slightly as concentration was increased. During food satiation body weights gradually increased and eventually exceeded preexperimental free-feeding weights.

Retest points obtained at the 2 mg/ml concentration were not plotted, as both drug and water retest values were very similar to the initial values. For instance, when the 2 mg/ml concentration was retested before the food satiation portion of the experiment, mean methohexital deliveries for the last five sessions of stable behavior for the six monkeys, M-B, M-M1, M-R, M-W, M-P1 and M-BL were 294.6, 324, 295.6, 481, 157.4 and 234.4, respectively. When the monkeys were returned to the food deprivation condition and the 2 mg/ml concentration was retested, the means for the last five sessions for monkeys M-B, M-M1, M-R and M-BL were 146.7, 286, 229.7 and 299.6, respectively. Body weights were not as low as during the previous food deprivation phase, and new 85% weights were recalculated based upon the most recent free-feeding weights. When the original drugs (phencyclidine or pentobarbital) were reinstated at the end of the experiment, the monkeys readily self-administered them at rates that were comparable to those originally reported.

Figure 2 illustrates the mean time course of liquid deliveries over the 3-hr sessions. During food deprivation, methohexital deliveries followed a negatively accelerated pattern, with almost all drinking occurring during the first half of the session. This negatively accelerated pattern was more pronounced at the higher concentrations. During food

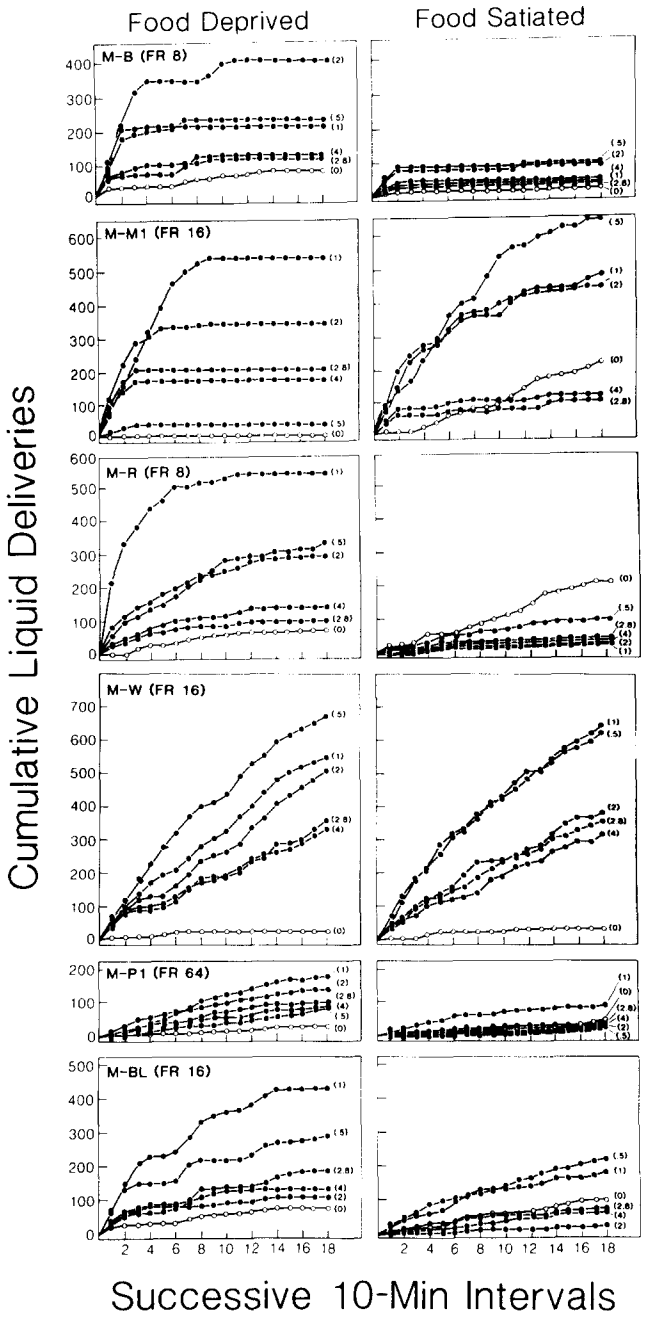

FIG. 2. Mean liquid deliveries cumulated at 10-min intervals over 3-hr sessions are presented for the five methohexital concentrations and water. The curve that is shown for water deliveries represents the median number of methohexital deliveries (of the five concentrations tested). Frames on the left illustrate the food deprivation condition, and frames on the right illustrate the food satiation condition. The FR schedule parameters are indicated in parentheses after each monkey's initials. Filled circles refer to methohexital deliveries, and open circles refer to water deliveries. Each point is the mean of the last five sessions of stable behavior under each condition.

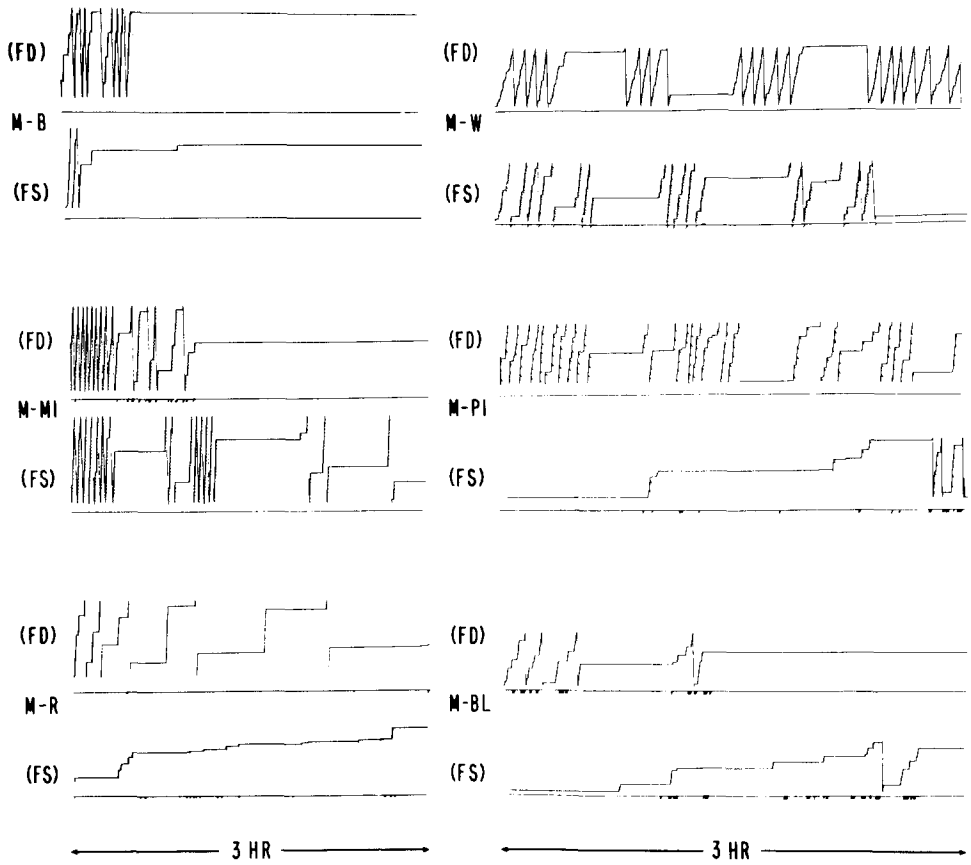

FIG. 3. Two cumulative records are presented for each of the six monkeys representing a 3-hr food deprivation session (upper record) and a 3-hr food satiation session (lower record) at the 2.0 mg/ml methohexital concentration. The first three monkeys (M-B, M-M1 and M-R) were initially trained with phencyclidine, and the last three monkeys (M-W, M-P1 and M-BL) were initially trained with pentobarbital. Each record was selected as the one with the total number of liquid deliveries closest to the mean of the last five sessions of stable behavior. The pen stepped across the record with each response, and downward deflections of the stepping pen represent methohexital deliveries. The pen reset at approximately 350–400 responses. Downward deflections of the lower event pen represent water deliveries. Methohexital and water were available under a concurrent FR 16 schedule for all monkeys except M-B (FR 8), M-R (FR 8) and M-P1 (FR 64). Note that the recorder speeds for the monkeys on the right were twice as fast as those on the left; thus, the scales for monkeys on the left differ from those on the right.

satiation, methohexital deliveries were more evenly distributed throughout the session. There were no differences in the time course of water deliveries between the food deprivation and food satiation conditions.

Figure 3 shows representative cumulative response records for each monkey at the 2 mg/ml methohexital concentration. The records were selected from those sessions with the total number of liquid deliveries closest to the mean for the last five sessions of stable behavior at that concentration. Methohexital-maintained responding during food deprivation was characterized by long drinking bouts during the early part of the session. During food satiation, methohexital drinking often did not begin until several minutes of the session had elapsed, and drinking bouts were distributed throughout the 3-hr session. It appeared that local response rates within each FR were not altered by the feeding condition.

DISCUSSION

Oral methohexital self-administration was rapidly established in six rhesus monkeys, and the drug was functioning as a reinforcer. Drug self-administration in excess of the vehicle (e.g., water) has been used a criterion for identifying a drug (or drug dose) as reinforcing. In earlier studies of oral drug self-administration, food-induced drinking procedures were used to establish orally-delivered ethanol [23], etonitazene [9], methohexital [1], pentobarbital [26] and phencyclidine [3,10] as reinforcers. These procedures required substantially more time than the present substitution method because the drug was introduced at a low concentration and gradually increased, then concurrent food was systematically withdrawn from the drug session. In previous oral drug self-administration studies, substitution procedures have been successfully used with drugs from within the same pharmacological class [1, 2, 12, 26]. The results with methohexital in the phencyclidine-trained monkeys demonstrated the feasibility of substituting drugs from different pharmacological classes. It was also recently shown that *d*-amphetamine can substitute for phencyclidine as a reinforcer in rhesus monkeys [12].

A problem with using substitution procedures for establishing self-administration of orally-delivered drugs is that it is unclear whether the new drug is self-administered for its intrinsic reinforcing effects or whether behavior persists due to similar taste properties, discriminative stimulus properties (interoceptive or exteroceptive), or a combination of factors. Control conditions have been implemented in previous substitution studies which suggest that generalization due to taste and exteroceptive discriminative stimuli may not account for all of the drug-maintained behavior [2]. It was shown that behavior was not maintained for long periods by these stimuli alone. In the present experiment, responding maintained by methohexital did not diminish during several months of testing. Furthermore, retest values (for 2 mg/ml methohexital) during the initial food-deprivation concentration series and the second food-deprivation phase (after the food satiation phase) were similar to the original determinations.

The effect of training history (phencyclidine vs. pentobarbital) is difficult to assess in the present experiment. Comparisons are limited because the length of the training history varied with each monkey and different FR values were used in the present study to optimize each monkey's drug-reinforced performance. However, the optimal FR values suggest methohexital was a more effective reinforcer for the pentobarbital-trained monkeys than it was for the phencyclidine-trained monkeys. Two phencyclidine-trained monkeys did not maintain stable methohexital self-administration at FR 16, while the pentobarbital-trained monkeys performed at conditions of FR 16 or higher. Additionally, with one of the phencyclidine-trained monkeys (M-B) it was necessary to add methohexital to phencyclidine and then to gradually reduce the phencyclidine concentration, as the direct substitution method was not successful. Further research is needed to determine whether substitution of orally-delivered drugs is more easily accomplished with drugs from the same or different pharmacological classes. Using intravenous self-administration procedures with rhesus monkeys, Young and Woods [35] demonstrated phencyclidine maintained responding when the drug was substituted for ketamine but not when it was substituted for codeine.

The present study extended the generality of methohexital self-administration to the oral route with rhesus monkeys. A recent study demonstrated self-administration of orally-delivered methohexital in food-deprived baboons [1]. Across the range of concentrations used in the present study, maximum drug intake among the six monkeys (20.4 to 93.8 mg/kg) was nearly identical to that reported earlier by Ator and Griffiths [1] (approximately 15 to 80 mg/kg). However, in the baboon study a preference for methohexital over water was shown only with the higher concentrations (e.g., 0.8 to 6.4 mg/ml). This difference in results may have been modulated by schedule contingencies. In the earlier baboon study, an FR 1 contingency was used, and it has been previously shown that differences in concurrent drug and water intake are enhanced by increasing the FR value [10,16]. The present results were also similar to those previously reported in a study of intravenous methohexital self-administration in food satiated rhesus monkeys [34]. In the IV study total session drug intake ranged from approximately 20 to 40 mg/kg and responding occurred in evenly spaced bursts throughout the 3-hr sessions.

The present results also extend the generality of the food-deprivation effect to methohexital. With four monkeys food deprivation greatly enhanced the reinforcing effects of methohexital at the lower concentrations. The increases in water intake at the higher methohexital concentrations were not characteristic of previous research with phencyclidine [10], pentobarbital [20] or *d*-amphetamine [12]; however, such increases were found with ketamine [12]. In two of the monkeys (M-R and M-BL), water deliveries were within the range of methohexital deliveries at the higher concentrations during food deprivation. It is unlikely that the drug was no longer functioning as a reinforcer as the drug intake (mg/kg) remained high. Instead, it is possible that aversive taste properties limited drug intake and increased water intake. The interaction between concentration and feeding condition in the present experiment illustrated a limitation of the generality of the food-deprivation effect. Other variables that have been shown to interact with food deprivation-satiation are percent decrease in body weight [7, 10, 20], and method of food satiation [6].

Food deprivation has generally increased self-administration of all drugs that are known to function as reinforcers via the intravenous route, for example, *d*-amphetamine [12,33], cocaine [5,13], ethanol [14, 22, 27, 31], etonitazene [4, 6–8, 25], heroin [28], ketamine [12], pentobarbital [20] and phencyclidine [5,9]. There are no data concerning the effects of food deprivation on psychotropic drugs or other drugs that have not been shown to function as reinforcers (due to difficulties in obtaining self-administration) to conclude that food deprivation selectively affects the reinforcing properties of a drug. There is some evidence that food deprivation does not enhance self-administration of drugs that are not easily established as intravenously-delivered reinforcers for rats, such as methadone [28], nicotine [21] and THC [32]. In contrast, when drugs that are known to function as reinforcers via the IV route, such as, phencyclidine [5] and cocaine [29], are presented at doses too low to maintain responding, subsequent food deprivation produces high rates of self-administration. These studies suggest that the food deprivation effect may be limited to self-administration of reinforcing substances.

Changes in the patterns of responding are also of interest, since they may represent more subtle behavioral processes that are not evident from overall means. The patterns of responding found in the present experiment under both food-deprivation and -satiation conditions were similar to those previously reported with orally-delivered phencyclidine [3], *d*-amphetamine and ketamine [12]. During food deprivation, drinking began immediately at the start of the session and continued at a high rate for 60–90 min. During food satiation, there was a long latency before drinking began and smaller drinking bouts were spaced throughout the 3-hr session, separated by long pauses. Taken together, the results of the present experiment, such as the abrupt decrease in responding and the lower rates of responding at session onset during food satiation, and the diminished effect of food deprivation at higher drug concentrations suggest that food deprivation serves to increase the reinforcing efficacy of a drug.

ACKNOWLEDGEMENTS

We thank Greg Lemaire, Kathy Manion, Heidi Noetzel, Jim Pederson, David Sauter, Ignatius Tan and Jane Wright for their technical assistance and G.L. and I.T.'s critical comments on the manuscript. The gift of methohexital from the Lilly Research Laboratories is greatly appreciated. This research was supported by NIDA grants DA 02486 and 03240 to M.E.C. and a NIDA grant DA 00944 and a Research Scientist Development Award (DA 00007) to R.A.M.

REFERENCES

1. Ator, N. A. and R. R. Griffiths. Oral self-administration of methohexital in baboons. *Psychopharmacology (Berlin)* **79:** 120–125, 1983.
2. Carroll, M. E. Oral self-administration of phencyclidine (PCP) and PCP analogs PCE and TCP by rhesus monkeys: Conditioned reinforcing effects of taste and visual stimuli. *Psychopharmacology (Berlin)* **78:** 116–120, 1982.
3. Carroll, M. E. Rapid acquisition of oral phencyclidine self-administration in food-deprived and food-satiated rhesus monkeys: Concurrent phencyclidine and water choice. *Pharmacol Biochem Behav* **17:** 341–346, 1982.
4. Carroll, M. E., C. P. France and R. A. Meisch. Food deprivation increases oral and intravenous drug intake in rats. *Science* **205:** 319–321, 1979.
5. Carroll, M. E., C. P. France and R. A. Meisch. Intravenous self-administration of etonitazene, cocaine and phencyclidine in rats during food deprivation and satiation. *J Pharmacol Exp Ther* **217:** 241–247, 1981.
6. Carroll, M. E. and R. A. Meisch. Determinants of increased drug self-administration due to food deprivation. *Psychopharmacology (Berlin)* **74:** 197–200, 1981.
7. Carroll, M. E. and R. A. Meisch. Effects of feeding conditions on drug reinforced behavior: Maintenance at reduced body weights vs. availability of food. *Psychopharmacology (Berlin)* **68:** 121–124, 1980.
8. Carroll, M. E. and R. A. Meisch. Effects of food deprivation on etonitazene consumption in rats. *Pharmacol Biochem Behav* **10:** 155–159, 1979.
9. Carroll, M. E. and R. A. Meisch. Etonitazene as a reinforcer: Oral intake of etonitazene by rhesus monkeys. *Psychopharmacology (Berlin)* **59:** 225–229, 1978.
10. Carroll, M. E. and R. A. Meisch. Oral phencyclidine (PCP) self-administration in rhesus monkeys: Effects of feeding conditions. *J Pharmacol Exp Ther* **214:** 339–346, 1980.
11. Carroll, M. E., P. A. Santi and R. L. Rudell. A microcomputer system for the control of behavioral experiments. *Pharmacol Biochem Behav* **14:** 415–417, 1981.
12. Carroll, M. E. and D. C. Stotz. Oral *d*-amphetamine and ketamine self-administration by rhesus monkeys: Effects of food deprivation. *J Pharmacol Exp Ther* in press, 1983.
13. de la Garza, R., J. Bergman and C. R. Hartel. Food deprivation and cocaine self-administration. *Pharmacol Biochem Behav* **15:** 141–144, 1981.
14. Henningfield, J. E., N. A. Ator and R. R. Griffiths. Establishment and maintenance of oral ethanol self-administration in the baboon. *Drug Alcohol Depend* **7:** 113–124, 1981.
15. Henningfield, J. E. and R. A. Meisch. Drinking device for rhesus monkeys. *Pharmacol Biochem Behav* **4:** 609–610, 1976.
16. Henningfield, J. E. and R. A. Meisch. Ethanol as a positive reinforcer via the oral route for rhesus monkeys: Maintenance of fixed-ratio responding. *Pharmacol Biochem Behav* **4:** 473–475, 1976.
17. Henningfield, J. E. and R. A. Meisch. Ethanol drinking by rhesus monkeys as a function of concentration. *Psychopharmacology (Berlin)* **57:** 133–136, 1978.
18. Johanson, C. E. and R. L. Balster. A summary of the results of a drug self-administration study using substitution procedures in rhesus monkeys. *Bull Narc* **30:** 43–54, 1978.
19. Johanson, C. E., J. Bergman and R. de la Garza. Effects of behavioral and pharmacological variables on drug self-administration. A paper presented at the 90th annual meeting of the American Psychological Association, Washington, D.C., 1982.
20. Kliner, D. J. and R. A. Meisch. The effects of food deprivation and satiation on oral pentobarbital self-administration in rhesus monkeys. *Pharmacol Biochem Behav* **16:** 579–584, 1982.
21. Lang, W. J., A. A. Latiff, A. McQueen and G. Singer. Self-administration of nicotine with and without a food delivery schedule. *Pharmacol Biochem Behav* **7:** 65–70, 1977.
22. Meisch, R. A. Ethanol self-administration: Infrahuman studies. In: *Advances in Behavioral Pharmacology*, vol 1, edited by T. Thompson and P. B. Dews. New York: Academic Press, 1977, pp. 35–84.
23. Meisch, R. A. and J. E. Henningfield. Drinking of ethanol by rhesus monkeys: Experimental strategies for establishing ethanol as a reinforcer. In: *Alcohol Intoxication and Withdrawal: Experimental Studies IIIb*, edited by M. M. Gross. New York: Plenum Press, 1977, pp. 443–463.
24. Meisch, R. A., J. E. Henningfield and T. Thompson. Establishment of ethanol as a reinforcer via the oral route: Initial results. In: *Alcohol Intoxication and Withdrawal II*, edited by M. M. Gross. New York: Plenum Press, 1975, pp. 323–342.
25. Meisch, R. A. and D. J. Kliner. Etonitazene as a reinforcer for rats: Increased etonitazene-reinforced behavior due to food deprivation. *Psychopharmacology (Berlin)* **63:** 97–98, 1979.
26. Meisch, R. A., D. J. Kliner and J. E. Henningfield. Pentobarbital drinking by rhesus monkeys. Establishment and maintenance of pentobarbital-reinforced behavior. *J Pharmacol Exp Ther* **217:** 114–120, 1981.
27. Meisch, R. A. and T. Thompson. Ethanol as a reinforcer: Effects of fixed-ratio size and food deprivation. *Psychopharmacologia* **28:** 171–183, 1973.
28. Oei, T. P. S., G. Singer, D. Jeffreys, W. Lang and A. Latiff. Schedule-induced self-injection of nicotine, heroin and methadone by naive animals. In: *Stimulus Properties of Drugs: Ten Years of Progress*, edited by F. C. Colpaert and J. A. Rosecrans. Amsterdam: North Holland, 1978, pp. 506–516.
29. Papasava, M., T. P. S. Oei and G. Singer. Low dose cocaine self-administration by naive rats: Effects of body weight and a fixed-time one minute food delivery schedule. *Pharmacol Biochem Behav* **15:** 485–488, 1981.
30. Pickens, R., D. Muchow and V. DeNoble. Methohexital-reinforced responding in rats: Effects of fixed-ratio size and injection dose. *J Pharmac Exp Ther* **216:** 205–209, 1981.
31. Roehrs, T. A. and H. H. Samson. Relative responding on concurrent schedules: Indexing ethanol's reinforcing efficacy. *Pharmacol Biochem Behav* **16:** 393–396, 1982.
32. Takahashi, R. N. and G. Singer. Effects of body weight levels on cannabis self-injection. *Pharmacol Biochem Behav* **13:** 877–881, 1980.
33. Takahashi, R. N., G. Singer and T. P. S. Oei. Schedule-induced self-injection of *d*-amphetamine by naive animals. *Pharmacol Biochem Behav* **9:** 857–861, 1978.
34. Winger, G., M. L. Stitzer and J. H. Woods. Barbiturate-reinforced responding in rhesus monkeys: Comparisons of drugs with different durations of action. *J Pharmacol Exp Ther* **195:** 505–514, 1975.
35. Young, A. M. and J. H. Woods. Maintenance of behavior by ketamine and related compounds in rhesus monkeys with different self-administration histories. *J Pharmacol Exp Ther* **218:** 720–727, 1981.