THE EFFECTS OF COCAINE AND MORPHINE ON AVOIDANCE RESPONDING AT DIFFERENT LEVELS OF FOOD DEPRIVATION

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(ABSTRACT)

Three rats deprived to 80% of free-feeding weight pressed a bar to avoid electric shock in a Sidman avoidance procedure (20 s R-S interval, 5 s S-S interval). Once responding became stable, two of the rats were reduced to 70% of free-feeding weight and one rat's weight was increased to 95%. Cocaine (10.0, 17.0, 30.0, 40.0 mg/kg), morphine (5.6, 10.0, 17.0, 30.0, 40.0) and saline were tested in a random series with multiple determinations. Rate of responding and avoidance proficiency were recorded. When the injection series was completed the rats were free-fed and their weights redetermined so that the two rats that were at 70% of free-feeding weight were increased to 95% and the rat at 95% was reduced to 70%. Then the rats were tested again. Morphine produced little systematic change in rate or proficiency. Cocaine produced a dose-dependent increase in responding, but little change in proficiency. Economic versus stress hypotheses are discussed.

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LIST OF FIGURES

page

LIST OF TABLES

page

TABLE OF CONTENTS

Introduction

In the experiment reported in this Thesis, the effects of the abused drugs cocaine and morphine were tested on the shock avoidance behavior of rats maintained under conditions of extreme food deprivation (established by maintaining rats at 70% of free-feeding weights) and minimal food deprivation (90% of free-feeding). Alterations in levels of food deprivation have been shown to change the effects of these and other abused drugs on positively reinforced behavior, such as drug-reinforced (Carroll & Meisch, 1984) and food-reinforced (Odum, Haworth, & Schaal, 1998; Schaal, Miller, & Odum, 1995) behavior. The goal of the present study, then, was to determine whether food deprivation levels influence the effects of drugs on negatively reinforced, shock-avoidance behavior. If avoidance behavior is differentially sensitive to drug effects under different levels of food deprivation, then it may be concluded that food deprivation alters drug effects *in general*, regardless of whether positive or negative reinforcement controls the behavior. A failure to find that food deprivation alters drug effects, however, would suggest that this interaction is specific to positively reinforced behavior.

In order to establish the rationale for the present research, I will review research from several areas. First, changes due to food deprivation in the effects of drugs on food- reinforced behavior and in the reinforcing effects of

drugs will be reviewed to establish the scope and reliability of the "food-deprivation effect." The effects of drugs on motor activity, which are also altered by food deprivation, will also be reviewed. The goal of this section is to show that drug effects are often robustly altered by changes in food deprivation.

Second, the effects of morphine and cocaine (and pharmacologically similar drugs) on free-operant (i.e., Sidman) shock-avoidance behavior will be reviewed. Sidman avoidance was selected as the behavioral procedure in this experiment for two reasons; first, it is a negative-reinforcement procedure, and second, previous research has shown that it produces behavior that is sensitive to the effects of a variety of drugs, including cocaine and morphine.

Third, the pharmacology of cocaine and morphine will be briefly reviewed. Although morphine and cocaine differ considerably in pharmacology, these drugs were selected for study because they are both abused drugs whose effects have been shown to depend on food deprivation levels. Thus, the pharmacological distinctness of the drugs is of less concern to this study than their behavioral similarities.

Finally, I will speculate briefly on behavioral mechanisms that could account for the experiment's outcomes. If food deprivation does not alter the effects of these

drugs (i.e., if dose-response functions are similar regardless of body weight), then food deprivation may alter drug effects in a manner that is specific to behavior maintained by positive reinforcement. In this case a "reinforcer substitution model," based on behavioral economics, may be applicable. If food deprivation does change the effects of drugs in this procedure, however, then a more general model, perhaps focusing on food deprivation as a stressor, is more appropriate.

Literature Review

Food Deprivation

The effects of cocaine and morphine on behavior maintained by food reinforcement have been shown to depend on levels of food deprivation (Odum et al., 1998; Schaal & Branch, 1992; Schaal et al., 1995). When food deprivation is kept constant, the effects of the drugs on the food-reinforced behavior of several species depend primarily on the baseline rate of the behavior; at low-to-moderate doses, low response rates tend to be increased and higher response rates tend to be decreased or are less affected (Dews, 1958; Goldberg, Morse, & Goldberg, 1976; Heifetz & McMillan, 1971; Katz & Goldberg, 1986; McKearney, 1974, 1980; Rhodus, Elmore, & Manning, 1974; Schaal et al., 1995; Schaal & Branch, 1992; Slifer, 1982; Taskin, 1986; Woolverton, Kandel & Schuster, 1978). At the highest doses, response rates are

generally suppressed regardless of the baseline rate. Severe food deprivation, however, arranged by maintaining pigeons at 70% of their free-feeding weights, lessens the rate-reducing effects of high doses (i.e., larger doses are required to suppress response rates) and enhances the rate-increasing effects of lower doses of both cocaine (Schaal & Branch, 1992; Schaal et al., 1995) and morphine (Odum et al., 1998). These rate- and deprivation-dependent effects were studied in pigeons using fixed-ratio (FR) schedules to maintain high baseline rates and fixed-interval (FI) schedules to maintain baseline rates that range from low early in the interval to high as the moment of reinforcement approached. The combination of severe food deprivation (70% of free-feeding weights) and low-to-moderate doses of cocaine and morphine produced robust rate increases early in the FI, which were larger and more likely than when pigeons were maintained at higher body weights. High baseline rates late in the FI and during the FR were decreased by lower doses of the drugs when pigeons were less food-deprived. Thus, severe food deprivation altered the rate-increasing and rate-decreasing effects of cocaine and morphine across the entire dose range.

While alterations by food deprivation of drug effects on food-reinforced behavior are interesting, some may not find them all that surprising. Food deprivation should be

an important variable determining the effects of drugs on *food-reinforced behavior*. Such effects might simply be attributed to changes in the reinforcing value of food; food-reinforced responding is more greatly enhanced by drug when animals are hungrier, and animals are more likely to continue to responding for food in the presence of behaviorally disruptive effects of high doses when they are hungrier. The “food deprivation effect” becomes more curious, and explanations such as this one becomes less tenable, however, when one considers the fact that changes in food deprivation also alter levels of operant behavior reinforced by drug self-administration. Experimental animals self-administer more drug and respond for lower doses of drug when they are food deprived compared to when they are not (Carroll, 1985; Carroll, France & Meisch, 1979; Carroll, France, & Meisch, 1981; Carroll & Meisch, 1979; Carroll & Meisch, 1980; Carroll & Meisch, 1981; de la Garza, Bergman, & Hartel, 1981; de la Garza & Johanson, 1987; Kliner & Meisch, 1982; Meisch & Kliner, 1979; Meisch & Thompson, 1973, 1974; Oei, Singer, Jeffreys, Lang, & Latiff, 1978; Papasava & Singer, 1985; see review by Carroll & Meisch, 1984). This finding has suggested to some (e.g., Kliner & Meisch, 1989) that food deprivation actually enhances the reinforcing value of drugs. Schaal and colleagues (Odum et al., 1998; Schaal et al., 1995) have

proposed a different explanation, that is, that food deprivation may alter other effects of self-administered drugs. In particular, food deprivation may enhance the rate-increasing effects of self-administered drug in a manner similar to food deprivation's effects on food-reinforced behavior. Food deprivation may also lessen the rate-decreasing effects of large, cumulative doses of self-administered drug. Both of these effects would result in animals self-administering more drug whether or not the drug's reinforcing effects had been altered by food deprivation. Regardless of the mechanisms by which food deprivation increases drug-taking in experimental animals, however, this finding suggests that the effects of food deprivation are not limited to behavior reinforced by food. They may, in fact, be considerably more general.

The generality of the food-deprivation effect is established also by data showing that, in the absence of experimenter-arranged contingencies of reinforcement, food deprivation enhances the activity-increasing effects of both cocaine, and other psychomotor stimulants and morphine. In such studies rats are allowed to move freely within a chamber equipped to measure their movement. Campbell and Fibiger (1971) showed that a moderate dose of amphetamine (which is pharmacologically similar to cocaine) increased the number of line-crossings in such a chamber from 250 to

1200 in 5 hours when rats had been deprived of food for one to four days, respectively. Non-deprived rats only crossed lines about 100 times. In a similar study Deroche, Marinelli, Maccari, Le Moal, Simon & Piazza (1995) used a device that automatically measured large-body movements of rats to investigate the effects of food restriction on movements enhanced by morphine. Their results showed that 60 min after an inter-cranial injection of morphine food-restricted rats (90% of free feeding body weight) showed an increased number, 300 compared to 175 in 30 minutes, of large-body movements over non-food-restricted controls. Thus, food deprivation and drug seem to have interactive effects on several types of behavior, which suggest that food deprivation may alter the behavioral effects of cocaine and morphine regardless of the conditions under which they are studied. The goal of the present study is to determine whether the food deprivation effect will be observed in another, very different, behavioral situation, that is, negative reinforcement by shock avoidance.

Avoidance

In Sidman avoidance (Sidman, 1953a) shocks are distributed regularly over time and responses postpone shock for a certain amount of time. The interval between a response and the next shock is called the “response-shock” (R-S) interval, and is reset after each response. Once a

shock has been delivered, shocks continue according to another schedule, the “shock-shock” or S-S, interval, until the subject responds. Thus, each response postpones the next shock, and, with a sufficiently high rate of response, shocks can be avoided entirely. Responding controlled by this type of avoidance procedure has been shown to be remarkably stable (Sidman, 1960) and the effects of many different drugs have been assessed using this procedure (Heise & Boff, 1962; Scheckel & Boff, 1964; Verhave, 1957). In general, cocaine at doses lower than 30.0 mg/kg has been shown to increase lever pressing by rats responding to avoid shock (Heise & Boff, 1962; Scheckel & Boff, 1964; Pearl, Aceto & Fitzgerald, 1968) and morphine at doses above 2.0 mg/kg decreased responding using the same procedure (Heise & Boff, 1962; Holtzman & Jewett, 1971, 1972).

It is unknown how or whether food deprivation will alter the effects of cocaine and morphine on shock avoidance. Increasing food deprivation alone has been shown to decrease response rates and subsequently increase the number of shocks received on a Sidman avoidance schedule with rats (Leander, 1973). This is in contrast to the typical effect of increased food deprivation on food-reinforced behavior (e.g., Clark, 1958), which is to increase its rate. These findings plus the data regarding food deprivation, and the effects of drugs on food

reinforced behavior raises the question of how food deprivation may alter the effects of drugs on avoidance responding. Answers to questions such as these may give us insight not only into the behavioral mechanisms of drugs, but also provide information about the pharmacology of these drugs.

Pharmacology of Cocaine and Morphine

Pharmacology is the study of the effects of drugs on the functioning of organisms at multiple levels, from cellular to behavioral. Currently, predominant theories in pharmacology account for drug effects by specifying the types of receptors (i.e., proteins located on neurons) to which drug molecules bind. This binding initiates neuronal activity that leads, eventually, to the multiple effects of drugs. Cocaine exerts most of its effects on the central nervous system by blocking reuptake of dopamine, norepineprhrine and serotonin thus prolonging and intensifying the effects of these neurotransmitters. Morphine acts as an agonist on the μ and to some extent the 6 opioid receptor subtypes, thus mimicking effects of some endogenous opioids. Cocaine and other psychomotor stimulants produce increases in locomotor activity, stereotypy, perseveration, and anorexia (Evenden & Ryan, 1990). Morphine and other opioids produce analgesia, drowsiness, respiratory depression, decreased

gastrointestinal motility, nausea, vomiting, and alterations of the endocrine and autonomic nervous system (Martin, 1983).

Cocaine and morphine obviously have very dissimilar neurochemistries, receptor sites, and behavioral effects, but they do have important similarities. They have both functioned as reinforcers (Pickens & Thompson, 1968; Weeks & Collins, 1964; for a review, see Schuster & Thompson, 1969), they both have rate-dependent effects on food-reinforced behavior (Sanger & Blackman, 1976), and they both increase locomotor activity (Babbini & Davis 1972; Evenden & Ryan, 1990). Stewart and Badiani (1993) demonstrated that both morphine and amphetamine produced sensitization (i.e., the long-lasting increment in response upon repeated presentation of a stimulus) of locomotor activity to subsequent injections of both drugs. Furthermore, sensitization to one of these drugs led to cross-sensitization to the other. This result is not surprising since cocaine and morphine have sites of action in both the nucleus accumbens and the ventral tegmental area in the brain and both drugs increase supplies of dopamine, a neurotransmitter involved in both movement and reinforcement, in those areas (Fibiger, Phillips, & Brown, 1992; Leone, Pocock, & Wise, 1991). Similarities or differences notwithstanding, these drugs were selected for

this study because they are drugs of abuse that have been studied extensively and both drugs' effects are altered by food deprivation. In this respect, the pharmacology of these drugs is not as important as the behavioral outcomes that may be obtained from their use in this experiment.

Given these pharmacological mechanisms as a starting point, it is possible to look at the interaction of these mechanisms with behavioral processes. Cocaine and morphine may interact with the reinforcing events of operant behavior and produce a situation that can be viewed as an economic system. Both morphine and cocaine have reinforcing effects, and food deprivation increases the likelihood and the amount of self-administration of these drugs. Increases in drug self-administration due to food deprivation have been interpreted to reflect increases in the reinforcing efficacy of drugs (Carroll & Stotz, 1983; Carroll & Stotz, 1984; Carroll, Stotz, Kliner, & Meisch, 1984; Kliner & Meisch, 1989). If these drugs are related by a sort of reinforcer interaction (Carroll, Carmona, & May, 1991) they may act as substitutes. That is, as consumption of one increases the demand for the other decreases (Samuelson & Nordhaus, 1985). Drugs may readily substitute not only for other drugs (Bickel, DeGrandpre, & Higgins, 1995), but also for non-drug reinforcers (Carroll, 1987; DeGrandpre, Bickel, Higgins, & Hughes, 1995; Higgins, Bickel, & Hughes, 1994). Possibly,

when these drugs are administered prior to an experimental session they act by providing response independent or free “artificial” reinforcement that competes with “natural” food reinforcement, thereby devaluing the food reinforcement. Increasing the food deprivation of an organism may then revalue the reinforcer and produce the effects noted, e.g., the rate suppressing effects of cocaine are lessened by food deprivation. This type of economic substitution does not seem to be relevant to avoidance responding where there is no “commodity” to devalue. If this is the case, level of food deprivation may have little or no influence on drug effects on behavior maintained by shock avoidance.

If food deprivation alters the effects of drugs on shock avoidance behavior, however, then the stress inherent in food deprivation might be implicated. Food deprivation may be conceptualized as a stress-producing event as shown by the increased levels of corticosterone (a stress-related hormone) found in food-deprived animals. Serum levels of corticosterone have been shown to increase during fasting, starvation or food restriction (Leakey, Chen, Manjgaladze, Turturro, Duffy, Pipkin, & Hart, 1994). The application of stress increases perseveration and locomotor excitation in rats (Hahn, Zacharko, Anisman, 1986). In regard to the effects of stress on drug influenced behavior Deroche, Piazza, Le Moal and Simon (1994) showed that stress produced

by social isolation sensitized rats to the locomotor effect of morphine and that this psychomotor sensitization was reduced by lowering levels of corticosterone. Campbell and Fibiger (1971) showed that amphetamine-induced arousal and subsequent psychomotor excitation was enhanced by food deprivation. The sensitivity to the psychomotor effects of both morphine and amphetamine that is created by food restriction depend on the secretion of corticosterone, i.e., when corticosterone levels are reduced this sensitivity is reduced (Deroche, Piazza, Casolini, Le Moal & Simon, 1993; Deroche et al., 1995).

This may mean that food deprivation acts as a stressor to enhance arousal thus altering the effects of cocaine and morphine regardless of the type of reinforcement used. This suggests that the present study should yield results similar to the results found in studies where food is the reinforcing event.

Statement of the Problem

This experiment was designed as a starting point for addressing these two alternative explanations for the interaction of food deprivation and drug administration. The lever pressing of rats was maintained by a Sidman shock avoidance procedure. The rats were maintained at different body weights across phases of the experiment and different doses of both morphine and cocaine were tested to determine

the effects of the combination of drug and food deprivation on avoidance responding. If the rats' avoidance responding is unchanged by food deprivation then this would provide some support for the economic view that deprivation alters drug effects only when the reinforcers are substitutable for each other. If changes in responding occur similar to the changes seen when food is the reinforcer this would provide evidence that the stress produced by food deprivation is what alters the effects of drugs irrespective of the maintaining event.

Method

Subjects

Four experimentally naive male Sprague-Dawley rats (Rattus Norvegicus), approximately 200 days old at the start of the experiment, were used. All rats were housed individually in a temperature controlled colony room on a reversed 12-hr light/dark cycle (lights off from 5:00 a.m. to 5:00 p.m.).

Apparatus

Two custom-built operant chambers, 28.5 cm long, 25 cm wide, and 20 cm high were used. The side walls and ceiling were made of plexiglass, and the front and rear walls were made of aluminum. The grid floor (Coulbourne Instruments, Model E10-10SF) was constructed of stainless steel rods 0.5 cm in diameter and spaced 1.5 cm apart. Two aluminum levers

were mounted on the front wall. The levers were 13.5 cm apart, 5 cm from the floor, and required approximately .25 N to depress. Two 28-V dc lights, covered with white plastic caps were located 5 cm above each lever. A 28-V dc houselight was mounted between the two levers 2 cm above the chamber and 3 cm from the front panel. The grid floor, aluminum walls and levers were wired to conduct shock supplied by a shocker (Med Associates, Model ENV-410) and grid scrambler (Med Associates, Model ENV-412). The chambers were housed in sound-attenuating cabinets equipped with ventilation fans. A white noise generator was used to mask extraneous sound. Contingencies were programmed and data recorded by a MS-DOS-based 80386 microcomputer using the Smart Cumulative Recorder® and a 80486 microcomputer programmed under Medstate Notation® software using a Med-PC computer interface system.

Procedure

Training. Preliminary training and baseline procedures were conducted with the rats reduced to 80% of their free-feeding weight. Sessions were run daily with the animals being fed in their home cages immediately after the session. Lever pressing was shaped by reinforcing successive approximations to the lever press using two hand switches (Courtney & Perone, 1992). One hand switch caused stimulus lights above the levers, houselight and white noise to be

turned off and the schedule of shock delivery to be suspended. The second hand switch controlled the delivery of shock. Throughout the experiment shock intensity was 1 mA. Movements away from the lever were punished by shock delivery. Movements toward the left lever, contacting the lever and pressing the lever were reinforced by the termination of light, sound and the shock schedule. The termination of light, sound and shock schedule lasted 20 s during the initial part of training and was reduced to 0.5 s. Once lever pressing had been reliably established on the left lever the computer controlled shock on a 20 s R-S interval and 5 s S-S interval avoidance schedule was introduced. The right lever had no programmed consequence. The 0.5 s termination of light and sound continued to provide feedback for each lever press. If for any reason the subject did not avoid 50 continuous shocks, as a safeguard against injury, the session ended automatically and all lights shut off and shock was terminated.

Baseline. Experimental sessions lasted 100 min and were conducted daily at approximately the same time. Overall rates of lever pressing and total number of shocks delivered were recorded.

Subjects responding on a Sidman avoidance schedule are at times prone to emitting bursts of responses (Sidman, 1953b) but if the bursts of responding are followed by long

periods of no responding shocks may ensue. Rate of responding is often not the best datum for determining shock avoidance proficiency. The measure that is commonly used is a computation of the number potential shocks the subject avoided during a session (Dworkin, Pitts & Galizio, 1993). This is done by subtracting the time spent in the shock-shock interval from the total session length and dividing this number by the length of the response-shock interval. For example, if a session lasted 100 min (6000 s) and a subject received 40 shock-shocks at 5 s shock-shock interval and the response-shock interval was 20 s the number of potential shocks is 290 as shown in Equation 1.

Equation 1

$$= \frac{\text{session length} * (\text{shock-shocks} * \text{shock-shock interval})}{\text{response-shock interval}}$$

$$\frac{6000 - (40 * 5)}{20} = 290$$

Proficiency is calculated by subtracting the number of shocks obtained from the number of potential shocks. This number is then divided by the number of potential shocks to produce a percentage. Equation 2 shows the calculations for a subject who received 50 response-shocks and 40 shock-shocks in a 100 m session.

Equation 2

$$\text{proficiency} \quad \frac{\text{potential shocks - response shocks}}{\text{potential shocks}} = \text{avoidance}$$

$$\frac{290 - 50}{290} = 83\% \text{ or } .83$$

A proficiency criterion of avoiding at least 70% of potential shocks was established. One rat, M4, did not meet the proficiency criterion and was removed from the study. M2 (randomly selected by a coin toss) was initially maintained at 95% of free-feeding body weight (FFW). The other two were maintained at 70% of FFW. When proficiency did not vary by more than 10% for five consecutive sessions with no upward or downward trend and no daily session of less than .70 proficiency was recorded drug tests began. The number of sessions before the stability criterion was met and drug administration had begun varied between subjects. The top panel in Table 1 shows the number of 100 min sessions during training and baseline for the three subjects at the various weight conditions.

Drug Administration. Cocaine and morphine (generously supplied by the National Institute on Drug Abuse) were dissolved in sterile 0.9% saline and injected intraperitoneally in a volume of 1.0 ml/kg 10 min before the

start of a test session. Rats were placed in the darkened test chamber during this 10 min period. Cocaine was administered in doses of 10.0, 17.0, 30.0, and 40.0 mg/kg. Morphine was injected in doses of 5.6, 10.0, 17.0, 30.0, and 40.0 mg/kg. The highest doses, 40.0 mg/kg of both cocaine and morphine, were added to the dose regime when little

Table 1

Number of Sessions at Each Weight Before Drugs Were Administered for Each Series of the Study. A Series Began When Weights Were Changed and a New Baseline Was Established.

Series 1

Subject	Training sessions at 80% FFW[1]	Sessions during wt. Change	Baseline Sessions at new wt. (70% or 95%)[2]	Total sessions before 1st drug admin.
M1	56	14	55	125
M2	69	14	61	130
M3	30	14	16	60

Series 2

Subject	Sessions at FFW	Sessions during wt. Change	Baseline sessions at new wt. (70% or 95%)[3]	Total sessions before 2nd drug admin.
M1	19	4	18	41
M2	19	20	2	41
M3	13[4]	5	16	34

[1]FFW indicates Free Feeding Weight.
[2]M1 and M3 were reduced to 70% of their FFW. M2 was maintained at 95% of its FFW.
[3]M1 and M3 were maintained at 95% of their FFW. M2 was reduced to 70% of its FFW.
[4]M3 became ill during this period and was not run for one week.

effect was seen at the smaller doses. Tests of doses of both drugs were conducted in a mixed order. Each dose was tested two or three times to ensure each condition was replicated with accuracy. During these redeterminations a new random order of drug doses was used (see Table 2 for dose order).

Weight redetermination. At the end of testing the subjects were allowed free access to food and continued to participate in daily avoidance sessions until a new free-feeding weight was obtained. At that time the animals' weights were reduced again, based on the new free-feeding weights. The rat that was maintained at 95% of its free-feeding body weight in the first part of the study was reduced to 70% of its feeding weight and the rats that were maintained at 70% initially were reduced to 95% (see the bottom panel in Table 1). Once the subjects' weights and behavior had stabilized another series of dose-effect tests were conducted as before. Several determinations were conducted for both drugs and saline (see Table 2).

Results

Figure 1 shows the average response rate for the last five days at each of the various body weight manipulations before drug administrations began for all three subjects. The dotted line refers to the beginning of an injection

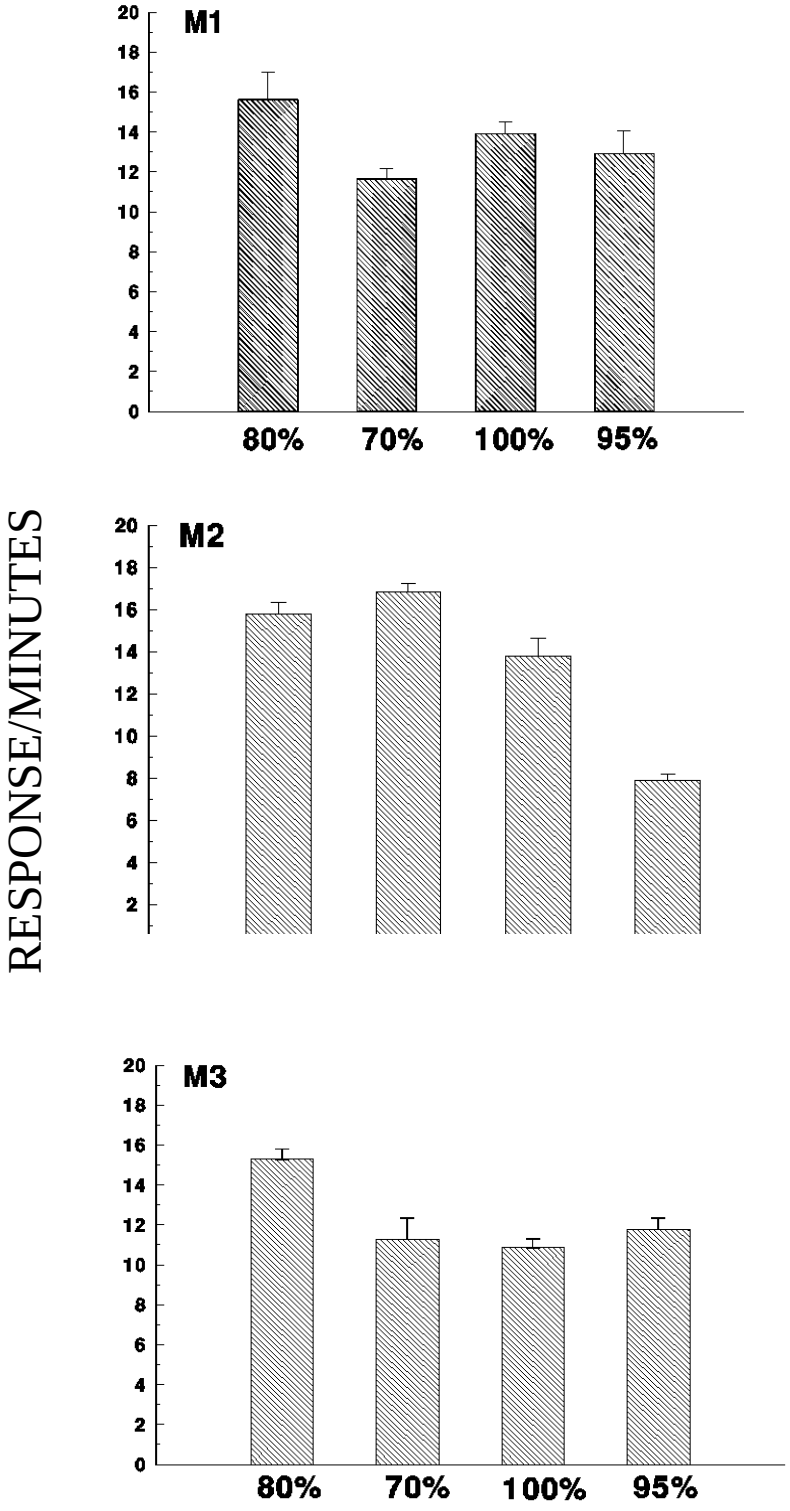
Table 2

Dosing Order in mg/kg. "C" Indicates Cocaine and "M" Indicates Morphine.

Dosing Order Series 1 (M1 and M3 at 70% FFW, M2 at 95% FFW)	10 C,10 M,17 M,17 C, SAL,5.6 M,30 C,17 C,17 M,10 M,30 C,5.6 M, SAL,10 C,5.6 M,17 C,30 M, 30 C,10 M,10 C,SAL,17 M,40 C, SAL,30 M,30 M,40 C,40 M,40 M
Dosing Order Series 2 (M1 and M3 at 95% FFW, M2 at 70% FFW)	10 C,10 M,SAL,17 M,10 M,17 M, 30 M,SAL,30 M,17 C,10 C,17 C, 30 C,30 C,40 M,40 M[1]

[1]All animals received all doses of drug in the above specified order except M3. M3 died before receiving the last two doses of 40 mg/kg M.

Figure 1 (next page). Responses per minute averaged for the last 5 days for each weight condition for each rat before the injection series began. Error bars are standard error of the mean. Dotted lines represent the start of an injection series.


RESPONSE/MINUTES
M1
M2
M3
0
2
4
6
8
10
12
14
16
18
20
80%
70%
100%
95%

series. No data was used from these sessions because drugs that affect rate of responding were administered to the rats. In every instance except one, the change in weight corresponds to a change in rate of responding. Although the effect was very small, when weight was increased rate of avoidance responding increased and when weight was decreased rate of responding decreased. It should be noted that in the one instance that did not follow this rule (M3 - 100% to 95%) the animal had been removed from the study for a week because of an unknown illness. In all of the other instances rate of responding increased as body weight increased and rate of responding decreased as body weight decreased.

Figure 2 and Figure 3 show the rate of responding for all three subjects under both body weights for both drugs tested (Figure 2 shows the effects of cocaine, Figure 3 shows the effects of morphine). Rate of responding was increased by cocaine in a dose dependent manner. Morphine did not produce clear effects on rate across the dose range. For rats M2 and M3, morphine reduced rates, but in rat M1 morphine both increased and decreased rates.

There was no systematic differential effect on rates

in regard to the deprivation level of the subjects at any

Figure 2 (next page). Responses per minute for each rat for each dose of cocaine and saline (Marked S). Solid lines with circle indicates the 70% FFW condition. Dotted lines with a square indicates the 95% FFW condition. Each point is an average of the number of determinations done at that particular dose. Range bars have been added to all points that are an average of two or more points. To obtain the actual number of determinations made at each dose see table 2. The weight condition that was determined first is indicated on each graph.

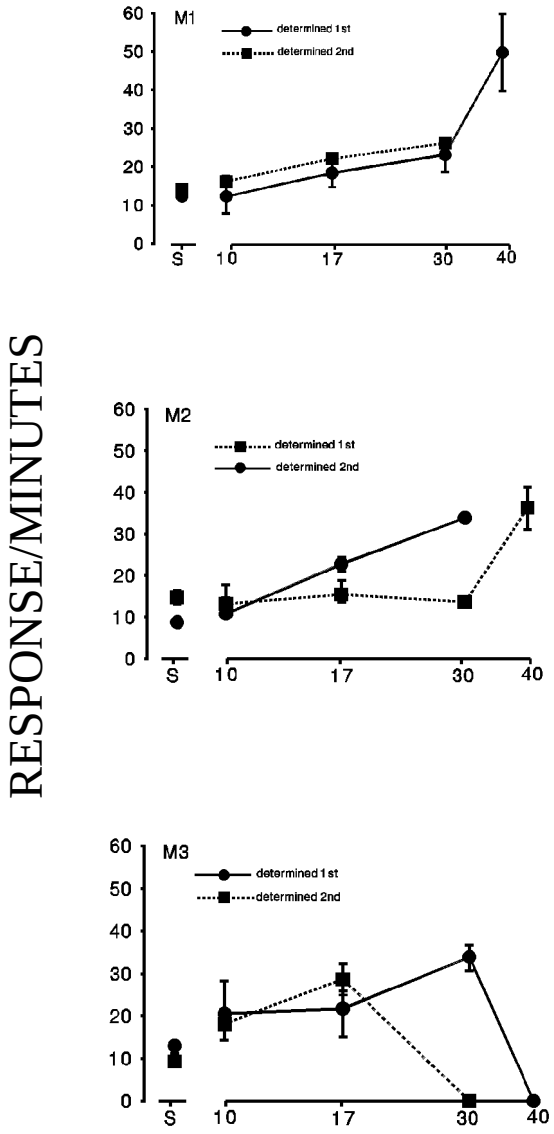
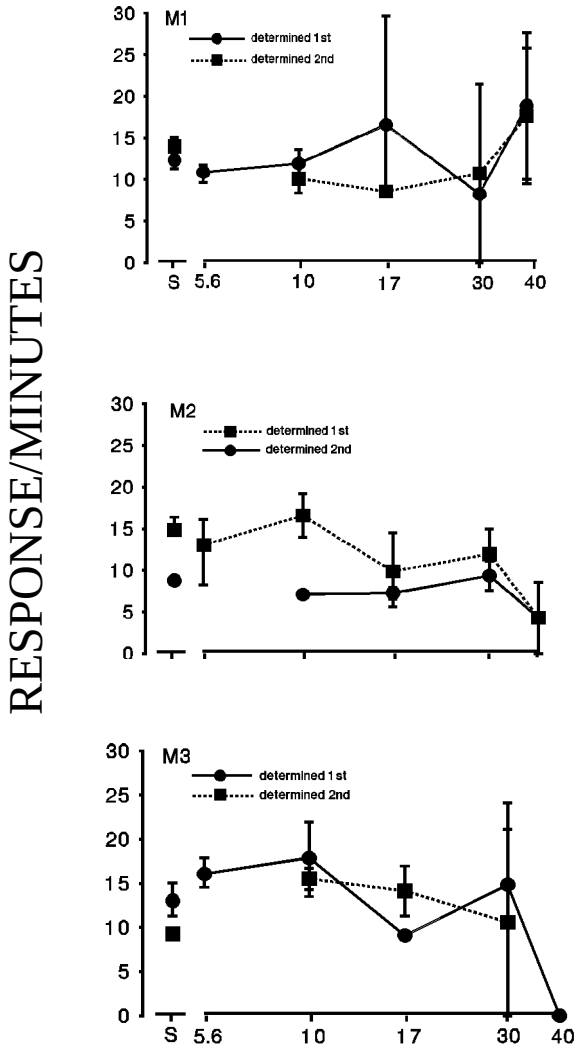

M1
determined 1st
determined 2nd
M2
determined 1st
determined 2nd
M3
determined 1st
determined 2nd
60
50
40
30
20
10
0
S
10
17
30
40
RESPONSE/MINUTES
MG/KG COCAINE

Figure 3 (next page). Responses per minute for each rat for each dose of morphine and saline (Marked S). Solid lines with circle indicates the 70% FFW condition. Dotted lines with a square indicates the 95% FFW condition. Each point is an average of the number of determinations done at that particular dose. Range bars have been added to all points that are an average of two or more points. To obtain the actual number of determinations made at each dose see table 2. The weight condition that was determined first is indicated on each graph.


M1
determined 1st
determined 2nd
M2
determined 1st
determined 2nd
M3
determined 1st
determined 2nd
30
25
20
15
10
5
0
S
5.6
10
17
30
40
RESPONSE/MINUTES
MG/KG MORPHINE

dose of cocaine or morphine. Only at the 30.0 mg/kg dose for animals M2 and M3 was there seen a differential effect of food deprivation (see Figure 2). The rate-enhancing effects of cocaine appeared to be reduced at this dose for these two rats when they were maintained at 95% of free-feeding weight. Rate increases are only seen in those two rats at the 70% body weight condition.

Figures 4 and 5 show avoidance proficiency for all three subjects at both body weights for both drugs (Figure 4 shows the effects of cocaine, Figure 5 shows the effects of morphine).

Except at the highest doses of drug there appears to be very little effect on avoidance proficiency throughout the experiment. At these high doses, 30.0 to 40.0 mg/kg of both drugs, the effect was similar. Either the drug had very little effect on proficiency or the subject was so debilitated by the drug injection that responding was completely disrupted and proficiency fell to zero (see Figures 4 and 5). The 30.0 mg/kg dose of cocaine, once again, seemed to be the only point at which there may have been a differential effect that appeared to be related to body weight. At this dose for both M2 and M3 proficiency

was relatively unchanged for the 95% condition and reduced

Figure 4 (next page). Proficiency avoiding shocks for each rat for each dose of cocaine and saline (Marked S). Solid lines with circle indicates the 70% FFW condition. Dotted lines with a square indicates the 95% FFW condition. Each point is an average of the number of determinations done at that particular dose. Range bars have been added to all points that are an average of two or more points. To obtain the actual number of determinations made at each dose see table 2. The weight condition that was determined first is indicated on each graph.

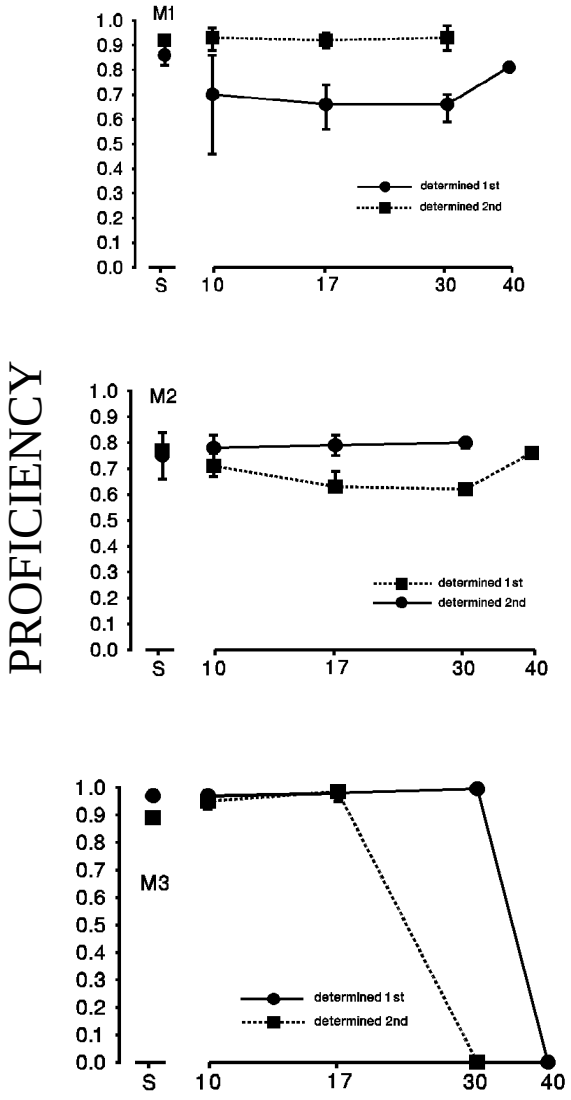
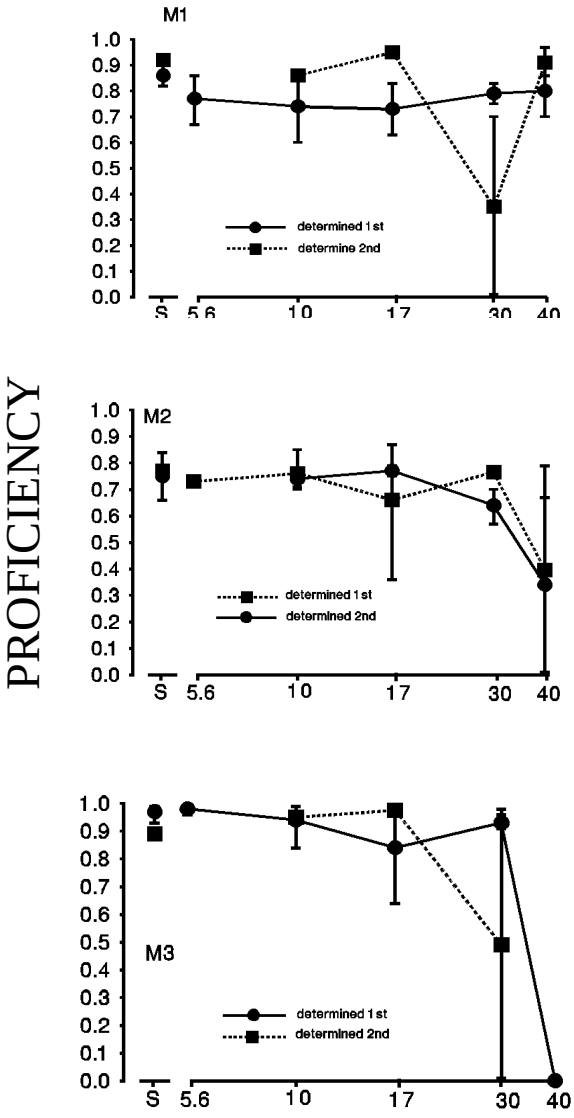

M1
M2
M3
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
S
10
17
30
40
determined 1st
determined 2nd
PROFICIENCY
MG/KG COCAINE

Figure 5 (next page). Proficiency avoiding shocks for each rat for each dose of morphine and saline(Marked S). Solid lines with circle indicates the 70% FFW condition. Dotted lines with a square indicates the 95% FFW condition. Each point is an average of the number of determinations done at that particular dose. Range bars have been added to all points that are an average of two or more points. To obtain the actual number of determinations made at each dose see table 2. The weight condition that was determined first is indicated on each graph.


M1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
determined 1st
determine 2nd
S
5.6
10
17
30
40
M2
determined 1st
determined 2nd
M3
determined 1st
determined 2nd
PROFICIENCY
MG/KG MORPHINE

for the 70% condition.

Discussion

The effects of the drugs on response rates generally support previous studies in this area. Cocaine generally produced dose-dependent increases in response rates (Heise & Boff, 1962) while morphine most often either had no effect or decreased rates (Holtzman & Jewett, 1971). Proficiency was not systematically altered by either drug except at the highest doses where rats sometimes failed to avoid shocks. Altering food deprivation did little to alter morphine's effects, but it appeared that the rate-enhancing effects of higher doses of cocaine were potentiated by severe food deprivation in the two subjects, M2 and M3. An effect of food deprivation may have been detected in rat M1 as well had we been able to test the 40.0 mg/kg dose in this rat.

Firm conclusions regarding the interaction of food deprivation and drugs on shock-avoidance behavior are premature owing to difficulties encountered in conducting these tests on a small number of subjects. Therefore, much of this discussion will focus on differences between the current experiment and previous ones in which food deprivation clearly altered the effects of these drugs that may account for the differences in results. Generally, it will be concluded that "shock avoidance vs. food

reinforcement" was not the only important difference.

One possible reason why this study did not produce clear results similar to past studies simply may be that negative and positive reinforcement may work by different mechanisms and food deprivation may not produce the same effect on the two procedures. Barrett (1987) has shown that changes in responding after drug administration may depend on the type of maintaining event (e.g., food versus shock). The question then arises, does the current study support the notion that these two variables, drug and level of deprivation, only interact when a positive reinforcer is involved?

Reinforcer Substitution

Responding on an avoidance schedule, in most instances, was not altered by food-deprivation in the same way as seen in other studies that used food as a reinforcer. This lends some support for the idea that the reinforcers involved in this interaction must substitute for one another. Substitution, as mentioned earlier, means that the reinforcers must have an interchangeable value. Shock and food may not have this interchangeability. Thus, rate of responding may not be affected by revaluing the reinforcer. Because of this one of these events may have little effect

on other.

Does this mean that an interpretation of these effects in terms of arousal is not supported by this evidence? Little can be deduced from a negative result such as this one, but there was at least one dose of cocaine that did produce the same effect that was seen when food was used as a reinforcer.

Arousal

Because both shock and drug produce stress it may be that these two factors produce increases in activity that is generally seen in stressful situations. The arousal produced by these two events may jointly produce higher rates of responding. This increase in rate of responding was only noted at the 30 mg/kg dose, a large dose. Rate effects on the behavior of rats and pigeons maintained by food-reinforcement occur at much lower doses (Dews, 1958; Woolverton, 1978; see review by Sanger & Blackman, 1976). This suggests that in order to produce this effect on behavior maintained by an avoidance schedule particularly large doses are necessary. This means that an avoidance schedule may produce responding that is less sensitive to the variables studied here.

If these drugs act on behavior through directly increasing arousal and it is conceded that very little

difference was seen in the effects of drugs on behavior at different body weights, then possibly these systems are independent. This may mean that stress produced by deprivation does not produce additional arousal that may summate with drug arousal, thus these effects in some sense, act separately.

Response rates also changed when body weights were manipulated before and between weight conditions (see Figure 1). Leander (1973) reported reduced avoidance responding by rats with reduced body weights. This finding makes it clear that weight manipulations can produce differential effects on avoidance responding. If body weight manipulations produced changes in response rates but little differential effects of drug administration were obtained, this would appear to be evidence that these two variables act independently. There are several additional interesting aspects of this investigation that may shed some light on these questions.

Other Factors that may Influence Drug Effects

Rats versus Pigeons.

Another possible reason for current findings differing from previous ones might be that prior studies used pigeons and this study used rats as subjects. Pigeons regulate their weights fairly well on a free-feeding schedule, but

rats' weights increase throughout their lives. That makes it more difficult to establish and maintain a "70%" verses a "95%" body weight. Rats that have not eaten in 22 hours may, in some sense, be equally food deprived, regardless of current body weight. A clearer test may be to pit rats at a low body weight against rats that are free-feeding or to compare the responding of rats that have eaten an hour ago versus rats that have not eaten for 22 hours.

Reinforcer Type and Reinforcer Schedule.

It is probably necessary to take into account other factors besides reinforcer type to understand the effects of deprivation on avoidance responding. Barrett (1987) states:

> Since the type of reinforcing or punishing event can be an important factor in determining drug effects, it would appear that the processes of reinforcement and punishment are not unitary phenomena. (p. 1494)

In regard to schedule effects Barrett (19879 states:

> Drugs that produce one effect depending on the type of maintaining event presented under fixed interval schedules may produce different effects under fixed ratio schedules. (p. 1494)

Possibly the reinforcing event is not the key variable in the present study. Other variables such as the schedule of reinforcement may be more important. The process of

reinforcement consists of many different classes of variables that must be taken into consideration when an analysis of this type is being attempted. It may be premature to conclude that body weight and drug effects are unconnected variables in regard to avoidance responding until these other factors have been investigated.

One of the factors that may need to be investigated is the rate and temporal pattern of behavior produced by a particular schedule. Barrett and Katz (1981) state:

> ...The development of similar performances is now almost generally acknowledged to be a crucial initial phase in examining whether the type of event influences the effects a drug will have on behavior. (P. 125)

When we wish to compare drug effects on behavior with different reinforcers, it is desirable to hold constant the rates and patterns of the different performances. In this analysis we are generally comparing the work of Schaal et al. (1995) and Odum et al. (1998) with the current project. Both of these studies used interval and ratio performance to assess drug effects. The current study used an interval-based avoidance procedure that produced responding that does not resembles “ratio runs” or “FI scallops”. Thus, it may be premature to attribute differences in effects of drugs and food deprivation in these studies to the reinforcers.

Shock avoidance procedures that generate FR-like and FI-like performances provide the more appropriate comparison (Morse & Kelleher, 1966).

Behavioral Momentum.

Finally, Table 1 shows the large number of sessions run before drug administration began (mean = 105), and before the second phase of the experiment was started (mean = 38.67). Strength of responding might have been so great by the time the injection series began that it might prove difficult for the manipulations used (or any manipulations) to create a noticeable change (Nevin, 1974). This lack of overall effect may be due to what has been termed "behavioral momentum" (Nevin, Mandell, & Atak, 1983), i.e., persistence in behavior following a change in experimental conditions. This would include conditions where a large dose of morphine (30.0 mg/kg), a dose that normally produces deep analgesia (Jaffe & Martin, 1990) was administered with little effect, a result that on the surface appears counterintuitive given that the stimulus being avoided was "painful" shock. This argument seems plausible except that in the pigeon studies where clear effects of food deprivation were seen on food-maintained responding the pigeons were also run for many sessions. That would mean that momentum on an avoidance schedule must differ from

momentum seen on a food-reinforced schedule.

In summary, the hypothesis that reinforcer substitution may be the process that produces the effect seen with a food-maintained schedule at different body weights is supported because no systematic differential effect between weight conditions was seen using an avoidance schedule. There was a small differential effect seen at the 30 mg/kg dose of cocaine for rats M2 and M3. That evidence may provide some support for the notion that animals injected with cocaine, but not morphine, may respond similarly on both food-reinforced schedules and avoidance schedules, thus supporting the hypothesis that summation of arousal maybe the important variable here. In actuality, little can be concluded from a negative effect or from the small effect seen here.

Future experimentation might include procedures that minimize behavioral momentum, such as, beginning the injection series earlier in the experimental regime. As mentioned above, rate and temporal patterns of responding appears to be important. Perhaps future experiments should also attempt to produce avoidance rates and temporal patterns that are more similar than those seen in food-maintained responding. Since very little difference was seen between the smaller doses of either drug perhaps it is

advisable to give larger doses. In any event, enough questions remain concerning the food deprivation and avoidance responding that continued experimentation in this area appears to be warranted.

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