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Food Deprivation Increases the Etonitazene-reinforced Performance of Rats

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ABSTRACT

Etonitazene-reinforced performance of rats was increased by food deprivation and decreased by food satiation. These changes were not due to general increases in either activity or liquid intake.

Etonitazene is an opioid qualitatively similar to morphine in its behavioral effects but about 1000 times as potent (Dykstra, Wharton & McMillan, 1977; Shannon & Holtzman, 1977; Wikler, Martin, Pescor, & Eades, 1963). Etonitazene has been used in studies of drug dependence, since it can function as a reinforcer for rats (Carroll & Meisch, 1979a; Leander & McMillan, 1975; Lewis, Margules & Ward, 1975; McMillan & Leander, 1976; Meisch & Stark, 1977a). Also, the drug is readily consumed in amounts that produce physiological dependence (Carroll & Meisch, 1979a; McMillan, Leander, Wilson, Wallace, Fix, Redding & Turk, 1976).

This report confirms and extends earlier findings from our laboratory, viz. that food deprivation increases etonitazene drinking and etonitazene-reinforced lever pressing. Such a finding was unexpected, for it is widely known that food deprivation decreases water intake of rats (for example, see Falk, 1964; Hursh & Beck, 1971; Strominger, 1946). Apart from findings in our laboratory (Carroll & Meisch, 1979b; Carroll, France & Meisch, 1979; Meisch & Stark, 1977b), we are not aware of previous reports of increased drug-reinforced behavior due to food deprivation with the exception of ethanol -- a drug which also has caloric value.

Food deprivation also increases behavior maintained by other non-caloric reinforcers. Intracranial self-stimulation (Carey, Goodall, & Lorens, 1975; Olds, 1958), muricidal behavior (Malick, 1975; Paul, Miley, & Baenninger, 1971), schedule-induced behaviors (Falk, 1971), and lever pressing that produces a brief duration of light onset (Davis, 1958; Segal, 1959), all occur with greater frequency when animals are food deprived. Food deprivation also facilitates certain consumatory behaviors such as saccharin drinking (Hursh & Beck, 1971; Sheffield & Roby, 1950; Smith &

Duffy, 1957), drinking produced by injections of hypertonic saline (Oatley & Tonge, 1969), and hypothalamic drinking (Mendelson, 1970). The relation, if any, of increases in etonitazene intake due to food deprivation to increases in behavior maintained by other reinforcers is not clear.

METHOD

Subjects. Six experimentally naive male albino Wistar rats (Bio-lab Corporation, St. Paul, MN) were approximately five months old at the onset of the experiment. They were individually housed in wire mesh cages in a continuously illuminated room and maintained at 24 degrees C. Their weights were: 409 g (K-1), 447 g (K-2), 381 g (K-3), 413 g (K-4), and 422 g (K-5). Water was always available in the home cages except during the initial training period when lever pressing was being established with water.

Apparatus. Three identical operant conditioning chambers were used (Lehigh Valley Electronics No. 143-25). Each chamber was contained in a sound--attenuating cubicle (LVE No. 132-02). On one end of the chamber were two levers (LVE No. 121-05), a pellet receptacle, an opening for a liquid dipper cup attached to a solenoid-driven arm (LVE No. 114-02), 6 cue lights (lever lights), a speaker, a Sonalert (2.9 KHz, Mallory & Co.), and a house light. A light was also mounted 3.0 cm above the opening for the dipper cup. The force requirement for the lever switch closures was approximately 0.3 N.

The 0.1 ml dipper cup was constantly available in the up position, except during the 0.8 sec refilling operation when it was lowered into the reservoir. Liquid was contained in partially covered reservoirs to

minimize evaporation. Masking white noise was constantly present, and an exhaust fan provided ventilation. Automatic data recording and programming equipment were located in an adjacent room. The temporal pattern of lever presses and dipper presentations was continuously recorded by a cumulative recorder and by a counter which printed every 5 min.

Procedure.

Establishment of water-reinforced lever pressing. Each rat was placed in an operant conditioning chamber for 2 hr a day at a regular starting time. Initially, the rats were deprived of water for 24 hr, and Purina Rat Chow was placed in wire mesh food hoppers in the experimental chambers prior to each session. The food was placed in the chambers to increase the frequency of water responding, since rats usually drink after eating (cf. Verplank & Hayes, 1953). The rats were trained to press a lever for water. Each press on the right-hand lever resulted in a refilling operation, during which a Sonalert tone sounded and the light above the dipper opening went off. After the lever-press response was established, water bottles were restored to the home cages. Presses on the left-hand lever were recorded as activity responses but produced no programmed consequence. General illumination was provided by the three lever lights (4.76 W each) located above each lever and by the house light (4.76 W).

Establishment of etonitazene as a reinforcer: First procedure. The weight of each rat was reduced to 80% of the free-feeding weight (as determined at age 5 months) by limiting the amount of Purina Rat Chow to 12 g a day. Prior to each session the food was placed in wire mesh hoppers in the operant chambers to induce water drinking. When the 80%

body weight was reached, the amount of food in the operant chambers was increased by approximately 5 g in order to prevent further weight loss. After five sessions of stable lever pressing, water was replaced first by 1.25 and then by 2.5 µg/ml etonitazene HCl. Subsequently, the daily feeding was shifted from the operant chamber to the home cage where the food was given immediately after the session. In the next phase, the number of lever presses required per dipper presentation was increased from 1 to 2 to 4. Each condition was held constant until performance was stable for at least 5 sessions.

This food-induced drinking procedure resulted in mean intakes at 0 (water), 1.25 µg/ml and 2.5 µg/ml of 15.4, 20.8, and 22.2 ml, respectively (n=25; 5 rats x 5 sessions). However, when food was no longer available in the operant chamber, the volume consumed of 2.5 µg/ml etonitazene decreased to 10.1 ml, and when the number of lever presses required per dipper presentation was increased to 4, the volume consumed decreased still further. These findings indicate the etonitazene had not been established as a reinforcer. Other investigators have also found it difficult to obtain etonitazene-reinforced lever pressing (Lewis et al., 1975).

Establishment of etonitazene as a reinforcer: Second procedure. Since the first procedure was not successful, a second acquisition procedure was employed. This procedure differed from the first procedure in three ways: (1) the rats were reduced to 70% instead of 80% of their free-feeding weights; (2) they received the ascending series of drug concentrations during the period of weight loss (i.e., while their weights were decreasing to the 70% value); and (3) the concentration was increased

to 5 µg/ml instead of 2.5 µg/ml.

Specifically, the rats were given unlimited access to food until free-feeding body weights were regained. Subsequently, daily feedings were limited to 8 g of Purina Rat Chow available in the operant chambers. The rats received 0 (water), 1.25, 2.5 and 5 µg/ml etonitazene in that order, with each concentration present for 5 consecutive sessions and each lever press resulting in a dipper presentation. When body weights had decreased to 70% of free-feeding values, supplemental feedings were given in the home cages. At concentrations of 0, 1.25, 2.5, and 5 µg/ml the rats drank mean volumes of 8.8, 13.0, 13.0 and 7.3 ml, respectively. (See Tables 1, 2, and 3 of the Appendix for data of individual rats).

At 5 µg/ml, when lever pressing was stable, the in-session feedings of 8 g were discontinued, and food was given only in the home cages after the sessions; the rats continued to drink a mean volume of 3.1 ml.

The number of lever presses required per dipper presentation was increased in the sequence 2, 4, 8, and 16 (fixed-ratio or FR schedules). Rat K-4's FR size was increased to 8, but not to 16. Each increase in ratio size occurred after performance was stable for 5 consecutive sessions. Performance was judged to be stable if there were no increasing or decreasing trends over the 5 sessions. Response rate increased as a function of ratio size. (Tables 1, 2, and 3 of the Appendix present data for individual rats).

Effects of food deprivation and food satiation on etonitazene-reinforced performance. After etonitazene-reinforced FR performance was established, the rats were exposed to a sequence of sessions alternating between water and etonitazene, 5 µg/ml. Water and etonitazene sessions were correlated

with illumination of the lever lights and house light, respectively. FR size was held at 8 for rat K-4 and at 16 for the other rats, and body weights were maintained at 70% of their free-feeding values. After this food deprivation phase, the rats were given unlimited access to food in their home cages. Finally, the rats' body weights were again reduced to 70% of their free-feeding values by limiting home cage food intake to 7 g. Once 70% weights were reached, home cage feedings were increased to maintain the rats at this reduced weight. The alternating 2-hr water and etonitazene sessions continued throughout the three phases of food deprivation, satiation, and re-deprivation. Within each phase, sessions were continued until body weights and water and drug-maintained performances showed no trend across 10 consecutive sessions.

Drug solutions. All etonitazene solutions were prepared using etonitazene HCl and tap water at least 24 hr prior to the daily session. Concentrations are expressed in terms of the salt.

Volume consumed. The volume of solution remaining in the reservoir was measured immediately after each daily session. During the initial acquisition phase, the mean numbers of dipper presentations correlated 0.91 with mean volumes of solution delivered (n=25 pairs of means; 5 rats x 5 means each; each mean was based on data from 5 sessions). A regression equation was then calculated in order to estimate the actual volume consumed. This equation was subsequently employed to correct for losses due to evaporation and handling.

RESULTS

Figure 1 and Table 1 show that when the rats were food-deprived they obtained substantially more dipper presentations of etonitazene than of water. Since drug-maintained response rates exceeded vehicle-maintained rates, etonitazene functioned as a positive reinforcer. Number of etonitazene dipper presentations obtained declined markedly when the rats were food-satiated (Figure 1 and Table 1). However, when the rats were redeprived, drug-reinforced behavior generally increased above the original values (Figure 1 and Table 1). Volumes of water and etonitazene solution consumed paralleled the numbers of dipper presentations (Table 2).

Mean rates of drug intake under conditions of food deprivation, food satiation, and redeprivation were 66, 4, and 62 µg per kg of body weight per 2-hr session, respectively (n = 25; 5 rats x 5 sessions). Table 3 presents drug intake values for each rat.

When the rats were food-satiated, lever-pressing gradually decreased across approximately 16 days (Figure 2). The total number of days the rats were food-satiated ranged from 20 to 37; note that the last 10 days constituted the phase of stable behavior. Over the first 16 days of food satiation, body weights increased a mean of 157 g. The mean stable weight was 530 g. When the rats were restricted to seven g of food, lever-pressing rates increased abruptly, and after two to three drug sessions (or four to six days) these rates were often within the range of final values. The number of days food-deprived that occurred prior to reaching the stable phase ranged from 15 to 23. Body weights reached 70% values after 20 days of restriction to seven g.

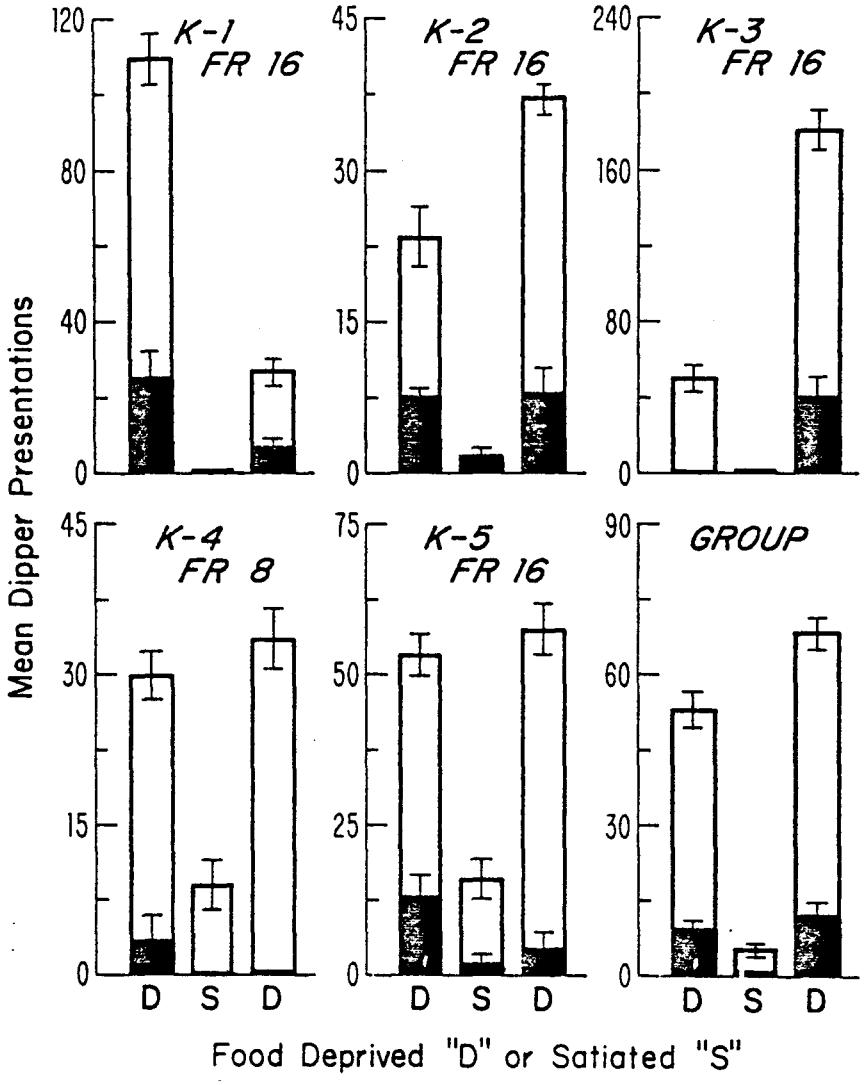

Figure 1. Mean dipper presentations as a function of liquid (5 µg/ml etonitazene HCl or water) and food condition ("D":deprived or "S":satiated). Dipper presentations followed every eighth or sixteenth lever press (FR 8 or FR 16). Total height of bars represents etonitazene values, and filled portions represent water values. Each bar is a mean of the last 5 sessions during each phase. Brackets indicate the standard error of the mean. Group bars are means of 25 observations (5 rats x 5 sessions each), and the brackets indicate the median standard error of the mean (n = 5; 5 rats x 1 S.E. each).

Table 1

Dipper presentations per 2-hr session as a function of liquid (5 µg/ml etonitazene or water) and food condition (deprived or satiated). Values are means with the standard error of the mean in parentheses.

		Food Deprived		Food Satiated		Food Deprived (retest)	
Rats	Liquid Schedule	5.0 µg/ml	0 µg/ml	5.0 µg/ml	0 µg/ml	5.0 µg/ml	0 µg/ml
		n=5	*n=5*	*n=5*	*n=5*	*n=5*	*n=5*
K-1	FR 16	109.9(5.8)	24.3(6.3)	0	0	25.0(3.1)	5.8(2.6)
K-2	FR 16	23.4(3.0)	7.6(0.8)	1.6(0.7)	1.6(0.8)	37.2(1.5)	7.8(2.6)
K-3	FR 16	51.4(3.6)	0	0	0	183.2(10.8)	40.4(10.6)
K-4	FR 8	29.9(2.6)	3.6(2.4)	9.0(2.5)	0	33.4(3.1)	0
K-5	FR 16	51.4(3.2)	12.2(5.0)	15.2(3.9)	1.8(1.6)	61.6(4.6)	4.2(3.0)
		n=25	*n=25*	*n=25*	*n=25*	*n=25*	*n=25*
Group		53.2(3.6)[a]	9.5(2.9)[a]	5.2(1.4)[a]	0.7(0.5)[a]	68.1(4.6)[a]	11.6(3.8)[a]

[a]Mean S.E.M. (n = 5; 5 rats X 1 S.E.M. each)

Table 2

Milliliters consumed per 2-hr session as a function of liquid (5 µg/ml etonitazene or water) and food condition (deprived or satiated). Values are means with the standard error of the mean in parentheses.

		Food Deprived		Food Satiated		Food Deprived (retest)	
Rats	Liquid Schedule	5.0 µg/ml	0 µg/ml	5.0 µg/ml	0 µg/ml	5.0 µg/ml	0 µg/ml
		n=5	*n=5*	*n=5*	*n=5*	*n=5*	*n=5*
K-1	FR 16	10.0(0.5)	1.7(0.4)	0	0	2.7(0.3)	0.5(0.2)
K-2	FR 16	2.1(0.3)	0.6(0)	0.1(0)	0.2(0)	3.4(0.1)	0.7(0)
K-3	FR 16	4.7(0.3)	0	0	0	8.4(1.1)	3.7(0.9)
K-4	FR 8	2.7(0.2)	0.3(0.2)	0.8(0.2)	0	3.1(0)	0
K-5	FR 16	4.7(0.3)	1.1(0.4)	1.4(0.3)	0.1(0)	5.6(0.4)	0.4(0.2)
		n=25	*n=25*	*n=25*	*n=25*	*n=25*	*n=25*
Group		4.8(0.3)[a]	0.7(0.2)[a]	0.5(0.1)[a]	0.6(0)[a]	4.6(0.4)[a]	1.1(0.3)[a]

[a]Mean S.E.M. (n = 5; 5 rats X 1 S.E.M. each)

Table 3

Quantity of etonitazene consumed (μg/kg body wt./2-hr session) as a function of liquid (5 μg/ml etonitazene or water) and food condition (deprived or satiated). Values are means with the standard error of the mean in parentheses.

Rats	Liquid Schedule	Food Deprived	Food Satiated	Food Deprived (retest)
		n=5	*n=5*	*n=5*
K-1	FR 16	132.6	0	36.4
K-2	FR 16	25.6	0.95(0)	40.9
K-3	FR 16	67.3	0	120.1
K-4	FR 8	38.3	7.9	43.0
K-5	FR 16	62.2	13.3	73.6
		n=25	*n=25*	*n=25*
Group		65.2(18.5)	4.4 (2.6)	62.8(15.8)

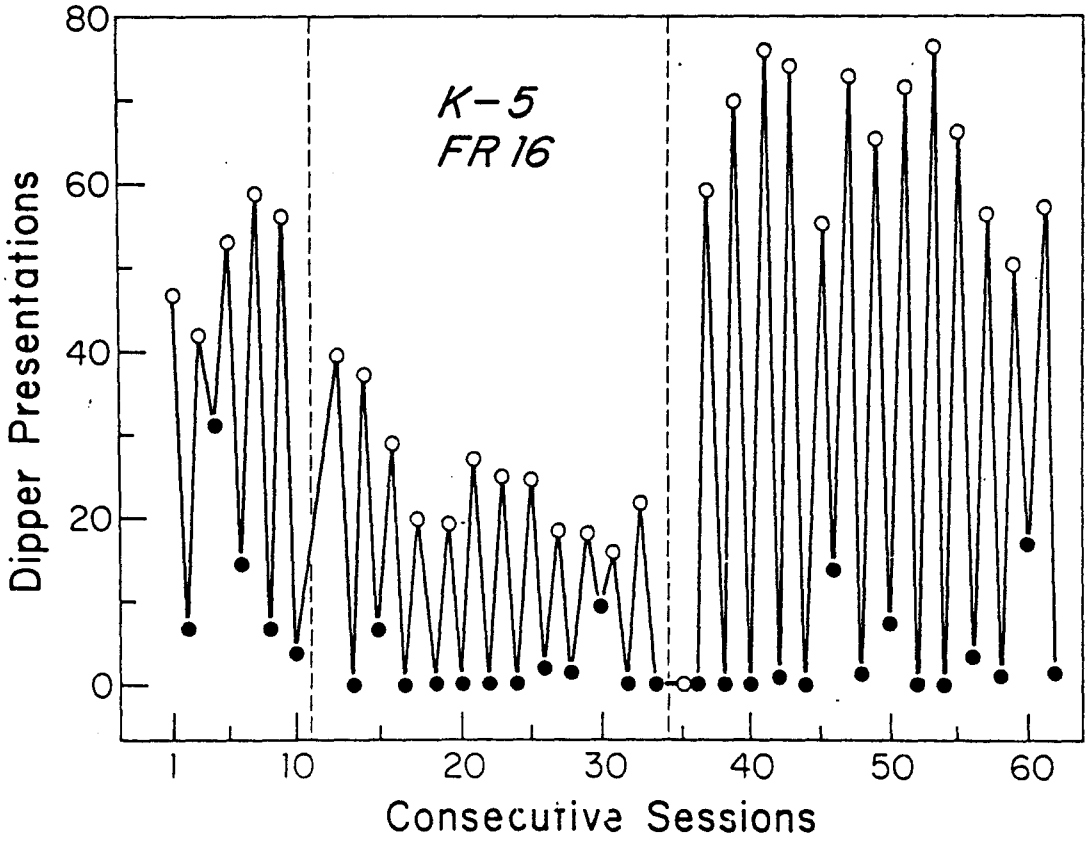

Figure 2. Rat K-5's dipper presentations per 2-hr session as a function of liquid (5 µg/ml etonitazene HCl or water) and food condition (deprived or satiated). Unfilled circles: etonitazene sessions; filled circles: water sessions. Between session 1 to 10 the rat was fed 15 g of Purina Rat Chow immediately after each session, and thereby it was maintained at 70% of its free-feeding weight (383 g). Between sessions 11 to 34 the rat had unlimited access to food in its home cage. By session 25 the rat reached a stable weight of 527 g. Between sessions 35 to 54, the rat was limited to 7 g of food until it reached its 70% weight (381 g). Subsequently, the rat was maintained at this weight by feedings of 12 g. Data from this rat were selected on the basis of their being the closest of any rat to mean data for the group.

Table 4 shows that presses on the second lever that had no scheduled consequence did not vary with the food condition and occurred at a far lower rate than did drug-reinforced presses. Thus, the increase in etonitazene-reinforced performance during food deprivation is not due to a nonspecific increase in lever pressing (cf. Meisch & Stark, 1977b). Another possible explanation for increased etonitazene intake during food deprivation is that the increase is secondary to an increased liquid requirement. However, the substantially lower levels of water-maintained behavior rule out this explanation (See Figure 1 and Tables 2 and 3).

DISCUSSION

These findings confirm earlier results that food deprivation increases and food satiation decreases etonitazene-reinforced performance (Meisch & Stark, 1977b). In the earlier study etonitazene was available during daily 4-hr sessions, and intervening water control sessions were not employed (Meisch & Stark, 1977b). The present study utilized water sessions on alternate days to evaluate the possibility that increases in etonitazene intake simply reflected more general increases in liquid intake. The present results rule out this possibility since when food deprived, the rats drank greater volumes of etonitazene solution than of water.

Rates of water-reinforced lever pressing were often greater when rats were food deprived than when they were food satiated. Since water intake of rats has been consistently reported to be decreased by food deprivation (Falk, 1964; Hursh & Beck, 1971; Morrison, 1968; Oatley & Tonge, 1969; Strominger, 1946), the increases in water responding probably reflect generalization of lever pressing that occurred during the intervening

Table 4

Activity responses per 2-hr session as a function of liquid (5 µg/ml etonitazene or water) and food condition (deprived or satiated). Values are means with the standard error of the mean in parentheses.

Rats	Liquid Schedule	Food Deprived		Food Satiated		Food Deprived (retest)	
		5.0 µg/ml	0 µg/ml	5.0 µg/ml	0 µg/ml	5.0 µg/ml	0 µg/ml
		n=5	*n=5*	*n=5*	*n=5*	*n=5*	*n=5*
K-1	FR 16	6.6(1.7)	5.2(1.3)	1.4(0.9)	0	0.6(0.2)	0.4(0.4)
K-2	FR 16	0	0.4(0.2)	1.8(1.0)	0	1.0(0.3)	0.9(0.5)
K-3	FR 16	0.2(0.2)	0	2.9(0.9)	0	56.4(17.2)	19.0(8.2)
K-4	FR 8	2.2(1.2)	0	5.6(5.1)	0	6.6(2.7)	0.2(0.2)
K-5	FR 16	5.2(2.7)	3.0(2.3)	3.6(2.9)	0	3.2(1.4)	1.0(0.8)
		n=25	*n=25*	*n=25*	*n=25*	*n=25*	*n=25*
Group		2.8(1.3)[a]	1.7(1.0)[a]	3.1(0.8)[a]	0	13.6(10.8)[a]	4.3(3.7)[a]

[a]Mean S.E.M. (n = 5; 5 rats X 1 S.E.M. each)

drug session.

Food deprivation also markedly increases the etonitazene-reinforced performance of rats under conditions very different from those employed in the present study (Carroll & Meisch, 1979a). Different groups of rats were given continuous access (24 hr per day) in their home cages to bottles containing either water or etonitazene 5 µg/ml. Half of the rats receiving water and half of the rats receiving etonitazene were reduced to 75% of their free-feeding weights. Only the group that was food deprived and received etonitazene showed marked increases in liquid intake. In contrast, the food-deprived water control group reduced its liquid intake.

Increases in etonitazene consumption during food deprivation are not limited to the oral route, since food deprivation increases rats' intravenous self administration of etonitazene (Carroll, France, & Meisch, 1979). The magnitude of the increase grew with repeated periods of food deprivation. Since the magnitude of the successive increases was not accompanied by increases in drug intake on intervening food satiation days, some type of learning may be involved (Carroll et al., 1979).

Food deprivation also increases rats' intravenous self administration of cocaine and phencyclidine under conditions where these drugs serve as reinforcers (Carroll & Meisch, 1979b; Carroll et al., 1979). Also, Singer and colleagues have reported that the frequency of intravenous nicotine and amphetamine self administration is increased when rats are food deprived (Lang, Latiff, McQueen, & Singer, 1977; Singer, Simpson, & Lang, 1978; Takahashi, Singer, & Oei, 1978). Additionally, food deprivation increases behavior of rhesus monkeys that is reinforced by the opportunity to drink solutions of phencyclidine and pentobarbital (Carroll & Meisch, 1979b; Kliner

& Meisch, unpublished observations). Thus, food deprivation produces increases in drug-reinforced performance with several different types of drugs, species of animals, and routes of administration. Any proposed explanations of the food deprivation produced increases in drug-reinforced behavior will have to take into account the range of conditions under which such increases occur.

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APPENDIX

List of Tables

Table 1

Dipper presentations per 2-hr sessions as a function of etonitazene HCl concentration and fixed-ratio (FR) size. Values are means with the standard error of the mean in parentheses.

Liquid Schedule	Etonitazene Concentration (µg/ml)	Grams of Food in Session	Rats					GROUP
			K-1	K-2	K-3	K-4	K-5	
			n=5	*n=5*	*n=5*	*n=5*	*n=5*	*n=25*
FR 1	0	8	93.8(3.7)	92.0(11.2)	63.3(7.3)	116.0(3.7)	117.7(2.3)	96.6(5.6)[a]
FR 1	1.25	8	257.5(13.8)	108.1(5.8)	116.5(3.4)	156.8(9.5)	251.7(19.9)	178.0(10.5)[a]
FR 1	2.5	8	319.3(5.2)	65.8(10.6)	133.7(14.1)	118.7(7.1)	203.7(12.8)	168.0(10.0)[a]
FR 1	5.0	8	139.5(9.0)	35.9(2.4)	76.6(2.3)	101.0(7.9)	196.4(19.9)	110.0(8.3)[a]
FR 1	5.0	0	55.2(8.8)	19.4(1.0)	43.2(3.4)	33.0(5.6)	943.4(50.3)	219.0(13.8)[a]
FR 2	5.0	0	66.2(6.6)	23.4(1.2)	58.4(2.2)	36.6(3.2)	339.8(28.1)	105.0(8.3)[a]
FR 4	5.0	0	52.8(2.4)	19.8(2.4)	47.2(2.6)	38.6(6.1)	230.4(14.6)	78.0(5.6)[a]
FR 8	5.0	0	35.4(2.4)	19.8(2.7)	39.0(2.5)	23.0(1.7)	82.8(3.3)	40.0(2.5)[a]
FR 16	5.0	0	21.6(1.4)	17.0(1.2)	20.6(0.8)	------	43.8(1.7)	26.0(1.3)

[a]Mean S.E.M. (n = 5; 5 rats X 1 S.E.M. each)

Table 2

Milliliters consumed per 2-hr session as a function of etonitazene HCl concentration and fixed-ratio (FR) size. Values are means with the standard error of the mean in parentheses.

Liquid Schedule	Etonitazene Concentration (µg/ml)	Grams of Food in Session	Rats					
			K-1	K-2	K-3	K-4	K-5	GROUP
			n=5	*n=5*	*n=5*	*n=5*	*n=5*	*n=25*
FR 1	0	8	8.3(0.3)	8.5(1.0)	6.0(0.7)	10.0(0.3)	11.1(0.2)	8.8(0.5)[a]
FR 1	1.25	8	22.1(1.3)	9.7(0.5)	10.7(0.3)	15.7(0.9)	7.3(1.8)	13.0(1.0)[a]
FR 1	2.5	8	29.0(0.5)	8.1(1.0)	11.5(1.3)	11.6(0.7)	3.7(1.2)	13.0(1.0)[a]
FR 1	5.0	8	13.6(0.8)	3.5(0.2)	7.0(0.2)	9.8(0.7)	2.6(1.8)	7.3(0.7)[a]
FR 1	5.0	0	5.1(0.8)	1.8(0.1)	4.0(0.3)	3.0(0.5)	1.5(0.4)	3.1(0.4)[a]
FR 2	5.0	0	6.1(0.6)	2.1(0.1)	5.3(0.2)	3.3(0.3)	3.4(2.5)	4.0(0.7)[a]
FR 4	5.0	0	4.8(0.2)	1.8(0.2)	4.3(0.2)	3.5(0.6)	3.6(1.3)	3.6(0.5)[a]
FR 8	5.0	0	3.2(0.2)	1.8(0.2)	3.6(0.2)	2.1(0.2)	3.3(0.3)	2.8(0.2)[a]
FR 16	5.0	0	2.0(0.1)	1.6(0.1)	1.9(0.1)	------	3.0(0.2)	2.1(0.1)

[a]Mean S.E.M. (n = 5; 5 rats X 1 S.E.M. each)

Table 3

Quantity of etonitazene consumed (µg/kg body wt./2-hr session) as a function of etonitazene HCl concentration and fixed-ratio (FR) size. Values are means with the standard error of the mean in parentheses.

Liquid Schedule	Etonitazene Concentration (µg/ml)	Grams of Food in Session	Rats					GROUP
			K-1	K-2	K-3	K-4	K-5	
			n=5	*n=5*	*n=5*	*n=5*	*n=5*	*n=25*
FR 1	1.25	8	61.3	25.3	32.1	46.0	20.5	37.0(7.4)[a]
FR 1	2.5	8	169.4	45.0	72.5	71.6	22.0	76.1(25.1)[a]
FR 1	5.0	8	168.4	42.0	93.1	125.8	31.8	92.2(25.6)[a]
FR 1	5.0	0	69.2	23.1	57.7	44.1	20.5	42.9(9.5)[a]
FR 2	5.0	0	81.0	25.7	76.5	46.8	45.2	55.0(10.4)[a]
FR 4	5.0	0	63.7	22.1	61.2	49.0	46.8	48.6(7.4)[a]
FR 8	5.0	0	42.4	21.9	51.2	29.7	42.8	37.6(5.2)[a]
FR 16	5.0	0	26.7	19.4	27.2	----	39.1	28.1(4.1)[a]

[a]Mean S.E.M. (n = 5; 5 rats X 1 S.E.M. each)