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The Effects of Cocaine on Food Intake of Baboons Before, During, and After a Period of Repeated Desipramine

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FOLTIN, R. W., M. W. FISCHMAN AND C. NAUTIYAL. *The effects of cocaine on food intake of baboons before, during, and after a period of repeated desipramine*. PHARMACOL BIOCHEM BEHAV 36(4) 869–874, 1990.—Food intake of five adult male baboons (*Papio c. anubis*) was monitored during daily 22-hr experimental sessions. Food was available under a chain schedule with two components. Following completion of the "procurement" component, the first response requirement, access to food, i.e., a meal, became available under the second, "consumption" component, during which each response produced a 1 g food pellet. After a 10-min interval in which no response occurred, the consumption component was terminated. Complete dose-response functions for cocaine (0.50–4.0 mg/kg, IM) and desipramine (0.50–4.0 mg/kg, IM), were determined before, during, and after a period of repeated administration of desipramine. Cocaine produced dose-dependent increases in the latency to initiate feeding and decreases in food intake during the first eight hr of the session. Compensatory feeding occurred later in the session so that cocaine had no effect on total daily intake. There was no interaction between repeated desipramine and the acute effects of cocaine. Desipramine produced dose-dependent decreases in intake during the first two hr of the session, the size of the first meal and intake during the entire session. These measures, as well as number of meals and second meal size, remained below baseline during repeated desipramine. Thus, repeated desipramine, while having significant effects on feeding behavior itself, did not influence the effects of cocaine administration on food-maintained responding.

Cocaine Desipramine Stimulant Tricyclic antidepressant Food intake Drug interaction Baboon

THERAPY with the tricyclic antidepressant desipramine (DMI) has been suggested as a pharmacological adjunct for the treatment of cocaine (COC) abuse (10, 20, 22, 23). In a double-blind clinical trial (21), about three times as many patients maintained on DMI remained abstinent for three to four weeks than those patients maintained on placebo. We have reported that under controlled laboratory conditions, DMI maintenance alters the subjective effects of COC, but not its reinforcing effects, in healthy volunteers who were not seeking treatment (11). Gawin and Kleber (20) have proposed that repeated COC use results in noradrenergic and dopaminergic receptor changes that are similar to those seen in depression. Thus, the utility of antidepressants, particularly tricyclic antidepressants, may be as therapeutic adjuncts rather than as pharmacological antagonists of cocaine's effects.

Desipramine and COC share some neuropharmacological effects. Desipramine inhibits the reuptake of norepinephrine and serotonin (24), while COC inhibits the reuptake of norepinephrine and dopamine (18,26). Data from several sources support the notion that acute DMI administration enhances the effects of acute COC administration in laboratory animals. For example, DMI prolongs and increases some of the behavioral effects of amphetamine, a drug which shares many effects with COC [e.g., (7, 9, 31)] including a food-intake decreasing effect (33). Desipramine pretreatment results in higher brain levels of COC (1), while imipramine, the metabolic precursor to DMI, enhances the effects of COC on intracranial self-stimulation (17) and Sidman avoidance responding (30).

The purpose of the present report was to investigate the interaction between the acute effects of COC and repeated administration of DMI using a different behavioral measure and species than has been previously studied. Recently we have been studying the effects of acute and repeated administration of anorectic drugs on feeding in baboons [e.g., (13)]. While parenteral DMI (5,27) and COC (2, 3, 16) produce dose-dependent decreases in food intake in rats, systematic studies on the effects of these drugs on responding maintained by food delivery in primates have not been

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conducted. In the present study, dose-response functions for COC and DMI were determined before, during, and after a period of repeated DMI administration in baboons who were given relatively continuous access to food.

METHOD

Animals and Apparatus

Five adult male baboons (*Papio cynocephalus anubis*), ranging in weight from 26.4 to 39.9 kg, were housed in standard primate cages (approximately $0.94 \times 1.21 \times 1.52$ m high for the three larger baboons, and $0.82 \times 0.94 \times 1.2$ m high for the smaller baboons). The light-dark cycle was controlled by natural light. Chewable vitamins (Goldline, Ft. Lauderdale, FL) and a piece of fresh fruit (80–100 kcal) were given daily. Water was available ad lib. Due to the necessity of sedating baboons in order to determine body weight, animals were weighed once every three months. Attached to the front of each cage was a panel consisting of a food hopper, two stimulus lights, a Lindsley lever (Gerbrands, Arlington, MA), and a pellet dispenser (BRS-LVE model PDC-005, Beltsville, MD). All schedule contingencies were programmed using an Apple IIe computer located in an adjacent room.

Feeding Schedule

Food was available 22 hours/day, from 11:00 a.m. to 9:00 a.m. the following morning. The remaining two hours of the day were used for cage and animal maintenance. Illumination of a red stimulus light indicated the availability of the initial component of a two-component chain schedule of food delivery. This procurement component required completion of a fixed number of responses. Upon completion of the ratio requirement, the red stimulus light was extinguished, and a green stimulus light was illuminated to indicate the availability of the second component of the chain schedule. During the second, or consumption component, each lever pull resulted in the delivery of a single one g banana-flavored pellet (3.7 kcal/g, Noyes Co., Inc., Lancaster, NH) into the food hopper. After a ten-minute interval in which no responses occurred, the consumption component was terminated, the green light extinguished, and the red light illuminated. All pellets earned during each consumption component were defined as occurring within a single meal. In order to gain access to another meal, the baboon was required to complete the ratio requirement of the procurement component again. Initially, 10 responses on the lever were required to complete the ratio requirement of the procurement component. This response requirement was in effect until responding stabilized (less than 10% variation in the number of meals and less than 20% variation in food intake for three consecutive days). The procurement component response requirement was then systematically increased for each baboon until the number of meals stabilized between two and four per session. This resulted in different response requirements among baboons: the response requirement was 100 responses for R-82, 200 responses for A-33 and O-02, 400 responses for A-22, and V-3. Although differences in response requirements were required to equate meal numbers across baboons, these procedures engendered similar patterns, intermeal intervals and intake during meals across baboons (14).

Procedure

Complete desipramine (0.50–4.0 mg/kg, courtesy of Merrell Dow Research Institute, Cincinnati, OH) and cocaine hydrochloride (0.50–4.0 mg/kg, Mallinckrodt, St. Louis, MO) dose-response functions were determined for each baboon before, during, and after periods of repeated administration of DMI. All doses were administered in the thigh muscle 15 min prior to the start of the session on Tuesdays and Fridays. Each dose was administered once. Immediately following the determination of the initial dose-response functions ("Before"), baboons experienced two ten-day periods of repeated drug administration. During the first ten-day period, each baboon was given a dose of DMI that decreased its food intake to 60–80% of baseline during the Before dose-response function. During the next ten-day period the next larger dose of DMI was given on a daily basis. The initial DES dose was 0.5 mg/kg for O-02, 1.0 mg/kg for A-33, R-82, and V-3, and 2.0 mg/kg for A-22. Following 20 days of repeated DMI baboons were maintained on the daily DMI dose given during the second period of repeated administration, and dose-response functions for both DMI and COC were redetermined by substituting a test dose of drug on Tuesdays and Fridays ("During" dose-response functions). Repeated drug administration was then terminated. After 20 drug-free days a third set of dose-response functions for DMI and COC were determined ("After" dose-response functions). Dose-response functions were determined by first injecting a dose in the middle of the projected dose range and then adjusting subsequent doses in accordance with the effectiveness of the first dose. The dose-response functions for DMI were determined before COC dose-response functions in three baboons, while for the other baboons, COC dose-response functions were determined before DMI dose-response functions.

Data Analysis

Separate baselines were calculated for each dose-response determination for each drug based on three days of stable intake prior to the start of the determination of each dose-response function. Measures included intake during the first 2, 4 and 8 hr of the session and the entire 22-hr session, latency to the first consumption component (including the time required to complete the first procurement component), and number of meals. Although, following some doses, baboons did not have two meals, it was sufficiently common for baboons to consume at least two meals to allow analysis of the effects of drugs on the first two meals of the session. Data were analyzed using a linear regression model of analysis of variance (ANOVA; Systat, Evanston, IL). The significance of the following variables were tested: dose (a continuous variable), dose-response function (before, during, and after repeated administration), and a dose by dose-reponse function interaction. Separate ANOVAs were calculated for each dependent measure and drug. Eating behavior during the 20 days of repeated drug administration and the 20-day drug-free period were also analyzed to determine changes over time. The significance of the period (first ten days, second ten days), and day within period was tested. All dependent variables during the periods of repeated administration were compared to predrug baseline. No corresponding baseline was available for the analyses of the drug-free periods. Effects were considered statistically significant if $p<0.05$.

RESULTS

Effects of COC and DMI Before, During and After Repeated DMI

Four of the five baboons developed necrotic lesions in the thigh muscle during the period of repeated DMI administration. The lesions were severe enough in two baboons to require antibiotics, and DMI was discontinued in A-22 after 20 days, therefore, no dose-response functions for COC or DMI could be determined during the period of repeated DMI in this baboon. The top panel

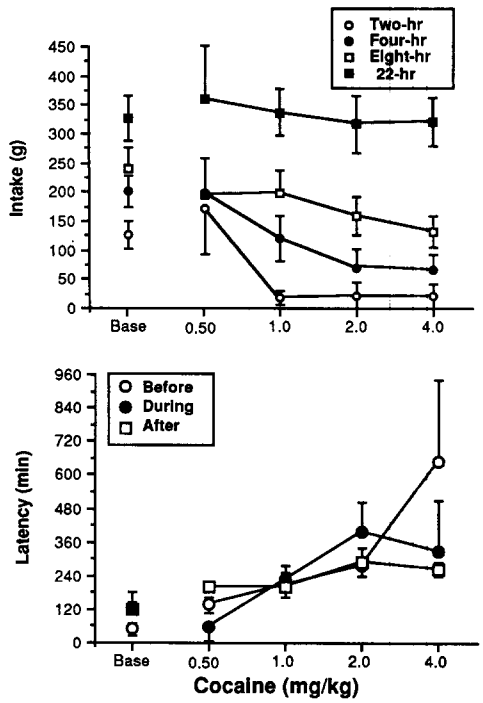

FIG. 1. Top panel: Food intake as a function of time within experimental session and dose of cocaine. Bottom panel: Latency to the first meal as a function of dose of cocaine and dose-response function (Before, During, and After repeated desipramine). Error bars represent SEMs.

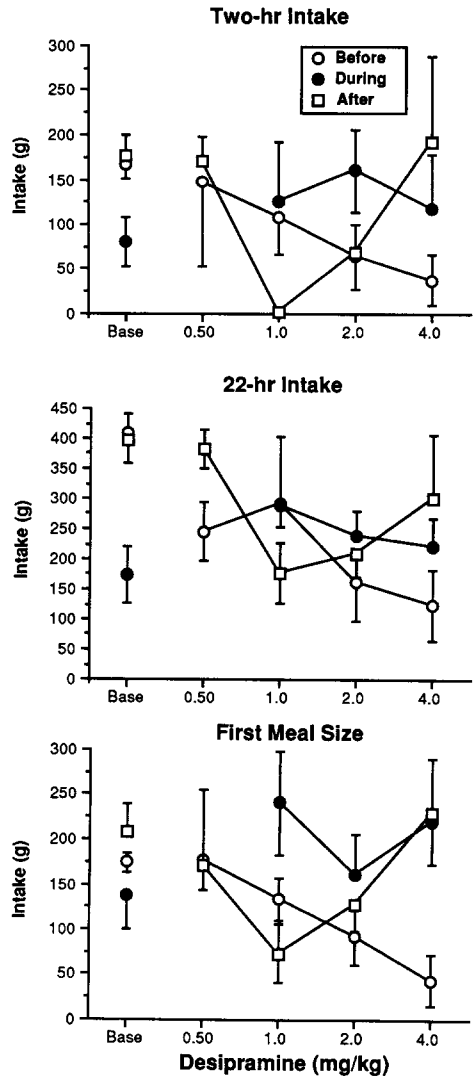

FIG. 2. Food intake during the first two hr of the session (top panel), the entire 22-hr session (middle panel), and the first meal of the session (bottom panel) as a function of dose of desipramine and dose-response function. Error bars represent SEMs.

of Fig. 1 presents intake during experimental sessions as a function of dose of COC. Cocaine produced dose-dependent decreases in food intake during the first two hr, $F(1,52)=7.71$, $p<0.008$, four hr, $F(1,52)=12.48$, $p<0.001$, and eight hr, $F(1,52)=6.55$, $p<0.013$ of the session which were unaffected by desipramine administration. Once feeding began during each session, however, compensatory intake occurred so that total intake was not significantly decreased by COC administration ($p<0.097$). The bottom panel of Fig. 1 compares the latency to the first meal of the session as a function of dose of COC before, during, and after repeated DMI. Cocaine produced dose-dependent increases in the latency to the first meal of the session, $F(1,52)=38.98$, $p<0.0001$. There was a significant interaction between COC dose and the presence of DMI, $F(2,52)=4.91$, $p<0.011$, resulting from the longer baseline latencies observed during and after repeated DMI compared to before repeated DMI, and the longer latencies observed after 0.50 mg/kg COC before and after repeated DMI compared to during repeated DMI. Cocaine had no significant effects on any other dependent measure.

The top panel of Fig. 2 presents intake during the first two hr of the session as a function of dose of DMI before, during, and after repeated DMI. There was a significant DMI dose by dose-reponse function interaction for intake during the first two hr of the session, $F(2,54)=3.32$, $p<0.044$. Initially, DMI produced dose-dependent decreases in intake during the first two hr of the session. During repeated DMI two-hr intake was lower than before, or after DMI, and when the DMI dose-response function was determined during repeated DMI there were no dose-dependent changes in two-hr intake. The response to DMI was especially variable when tested after the period of repeated administration. Such large variability was common when testing the effects of DMI. A similar pattern of results and significant dose by dose-response function interaction, $F(2,54)=3.56$, $p<0.035$, was also observed for intake during the entire 22-hr session as shown in the middle panel of Fig. 2. Prior to repeated DMI, acute DMI administration produced dose-dependent decreases in food intake. During the period of repeated aministration, total intake was decreased, and dose-dependent decreases in food intake were not observed. As shown in the bottom panel of Fig. 2, there was also a significant interaction between DMI dose and dose-response function with respect to the effects of DMI on the size of the first meal of the session, $F(2,54)=4.03$, $p<0.023$. Similar to those effects described above, initially DMI produced dose-dependent decreases in the size of the first meal, first meal size was smaller during the period of repeated DMI compared to before, or after DMI, and during repeated DMI dose-dependent changes in first meal size were not evident.

There were significant effects of dose-response function on the

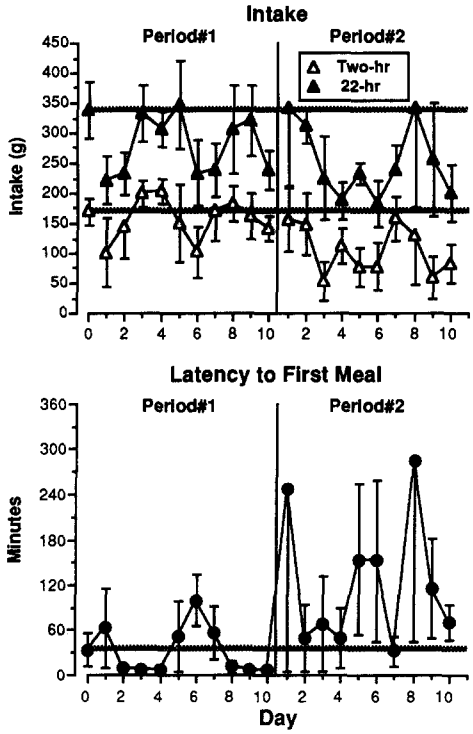

FIG. 3. Top panel: Food intake during the first two hr of the session and the entire 22-hr session as a function of period and day of repeated desipramine administration. Bottom panel: Latency to the first meal of the session as a function of period and day of repeated desipramine administration. For four baboons, the desipramine dose was doubled during Period No. 2 compared to Period No. 1, while for the remaining baboon desipramine dose was the same during both periods. Stippled lines represent baseline values determined prior to repeated desipramine. Error bars represent SEMs.

number of meals, $F(2,54)=3.74$, $p<0.03$, and size of the second meal, $F(2,54)=3.11$, $p<0.053$. There were fewer meals and the second meal size was smaller during repeated DMI compared to before and after repeated DMI. The number of meals, averaged across baseline and DMI test days, were 2.03 ± 0.20, 1.51 ± 0.14, and 2.17 ± 0.20 (mean with SEM), before, during, and after repeated DMI, respectively. Second meal sizes, averaged across baseline and DMI test days, were 93.4 ± 14.0 g, 53.8 ± 18.0 g, and 84.4 ± 17.1 g, before, during, and after repeated DMI, respectively.

Period of Repeated DMI

The top panel of Fig. 3 compares intake during the first two hr of each session, and during the entire 22-hr session as a function of day and period of repeated DMI administration. Dose of drug given during the second period of DMI administration was twice that given during the first period for all baboons with one exception. Due to consistent low daily intake under the first DMI dose conditions, DMI dose was not increased for one baboon. On the first day of DMI administration, total intake was reduced to 70% of baseline. Total intake rapidly returned to baseline levels by day 3, and fluctuated at, or below baseline, throughout the periods of repeated DMI. Total intake was variable with no significant difference between intake during the two periods of daily DMI dosing. Intake during the first two hr of the session was significantly less during the second period of repeated DMI than during the first period, $F(1,92)=6.29$, $p<0.014$. The bottom panel of Fig. 3 compares the latency to the first meal as a function of day and period of repeated DMI administration. Latency to the first meal was significantly longer during the second period of repeated DMI administration than during the first period, $F(1,92)=4.86$, $p<0.03$.

Feeding Behavior After Repeated DMI

When the first ten days of food intake after the termination of repeated DMI were compared to the tenth through 20th days of food intake after the termination of repeated DMI, several significant differences were observed. Mean food intake during the first two hr of the session was 121.9 ± 14.5 g during the first ten days, which significantly increased to a mean of 173.5 ± 15.8 g for the next ten days, $F(1,86)=5.81$, $p<0.018$. Food intake during the first four hr of the session showed a similar pattern averaging 234.5 ± 18.6 g during the first ten days, and 280.1 ± 17.1 g for the next ten days, $F(1,86)=6.04$, $p<0.016$. Finally, total intake also had the same pattern, increasing to 403.1 ± 20.2 during the second ten days compared to 332.5 ± 15.9 during the first ten days after repeated DMI, $F(1,86)=8.03$, $p<0.006$.

Body Weight

Baboons lost an average of 2.02 ± 0.74 kg over the four months of the study. A-22 lost 3.4 kg from a starting weight of 26.4 kg, A-33 gained 0.5 kg from a starting weight of 29.8 kg, O-02 lost 3.6 kg from a starting weight of 32.2 kg, R-82 lost 1.9 kg from a starting weight of 27.9 kg, and V-3 lost 1.7 kg from a starting weight of 39.9 kg.

DISCUSSION

Cocaine administration disrupted responding maintained by food delivery in baboons by decreasing food intake during the first two, four, and eight hr of a 22-hr feeding session. This decrease in food intake was a consequence of an increase in the latency to initiate feeding. Once feeding began, however, compensatory feeding was evident so that intake during the entire session was not significantly affected by COC administration. There were no significant differences between the effects of COC when compared before, during and after a period of repeated DMI administration. Similar transient decreases in food intake of rats at the beginning of a 4-hr feeding session has also been reported following cocaine administration (2). When given before or during operant-responding sessions, cocaine also produces pauses in responding in rats (36,29), pigeons (32), and primates (35). While other longer-acting stimulant drugs, e.g., amphetamine, diethylpropion, mazindol (12,14), increase latency to the first meal under these feeding conditions, little compensatory feeding occurs so that food intake is still decreased over the 22-hr session. Cocaine's effects are more like another short-acting drug, phencyclidine, in that compensatory feeding ameliorates the short-term reductions in food intake (12). The conditions under which compensatory feeding occurs under free-feeding conditions are unclear (15).

The effects of COC on food intake of baboons were similar across DMI maintenance conditions. The absence of an interaction between COC and DMI using food intake as a dependent measure accentuates the importance of measuring drug interactions under a wide range of conditions. Clinical reports indicate that DMI maintenance increases the number of patients remaining cocaine-free during short-term drug treatments involving multiple treatment components (20,21). In a controlled laboratory study assessing the interaction between DMI and COC in human volunteers using multiple dependent measures (11), the interactive effects of these

two drugs were dependent upon the behavioral measures. Clearly, the interactive effects of DMI and COC are critically dependent upon concurrent environmental conditions and dependent measures.

Desipramine inhibits the reuptake of norepinephrine and serotonin (24), while cocaine inhibits the reuptake of dopamine and norepinephrine (18,26), suggesting that the coadministration of these drugs may increase their behavioral activity. Since the effects of both drugs were independent, multiple neurotransmitters are likely involved in feeding behavior (13). Single dose pretreatment with DMI increases the disruption of Sidman avoidance behavior induced by COC (30), and increases brain levels of COC (1) in rats. In addition, many reports indicate that single dose pretreatment with DMI or imipramine increases the behavioral effects of amphetamine in rats [e.g., (7, 9, 31)] including its effect in decreasing food intake (33). Although there is a species difference between the previous reports (rats) and the current paper, the critical difference among these studies may be that the interactive effects of COC and DMI vary as a function of DMI treatment, i.e., acute vs. repeated DMI maintenance conditions. Willner and Montgomery (34) have indeed reported that acute DMI increases the food-intake decreasing effects of amphetamine, but during repeated DMI administration no such interactive effects of the two drugs were observed.

The clinical efficacy of antidepressant medication is only observed following a period of repeated, rather than acute administration, and complaints of weight gain are often concomitant with clinical improvement [e.g., (4,19)]. Desipramine differs from other antidepressants in that the weight gains are smaller with repeated administration (25). In the current paper, acute DMI produced dose-dependent decreases in food intake during the first two hr of the session, the size of the first meal, and the entire session in free-feeding baboons. Dose-dependent decreases in food intake have also been observed in rats maintained under shorter feeding schedules (5,27). During repeated DMI there was little evidence for the development of tolerance: a) intake during the first meal, the first two hr of the session and the entire session remained below levels observed before repeated DMI, b) the number of meals and size of the second meal were decreased when dose-response functions determined during DMI were compared to those determined before repeated DMI, c) total intake was greater ten to twenty days after the cessation of repeated DMI compared to the first ten days after repeated DMI, and d) four of the five baboons lost weight during the study. During the period of repeated DMI, however, dose-dependent decreases in intake during the first meal, the first two hr of the session and the entire session were not evident when the DMI dose-response function was redetermined, indicating a change in sensitivity to acute DMI. These findings support earlier studies demonstrating that there is little development of tolerance to the food-intake decreasing effects of DMI (27) or imipramine (6) when given repeatedly to rats. [One study has, however, reported tolerance to the water intake decreasing effect of DMI when given repeatedly to rats (28).]

In summary, cocaine produced dose-dependent decreases in food intake during the early part of a 22-hr session which were unaffected by repeated DMI. Desipramine produced dose-dependent decreases in total food intake, and there was little evidence of tolerance development during repeated DMI. The absence of an interaction between repeated DMI and COC suggest that their effects on feeding behavior are mediated by different neurochemical systems, and when compared with previous studies on such interactions, indicates the importance of measuring drug interactions using a variety of dependent measures.

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REFERENCES

1. Angel, C.; Roberts, A. J. Effect of electroshock and antidepressant drugs on cerebrovascular permeability to cocaine in the rat. J. Nerv. Ment. Dis. 142:376–380; 1966.
2. Balopole, D. C.; Hansult, C. D.; Dorph, D. Effects of cocaine on food intake in rats. Psychopharmacology (Berlin) 64:120–121; 1979.
3. Bedford, J. A.; Borne, R. F.; Wilson, M. C. Comparative behavioral profile of cocaine and norcocaine in rats and monkeys. Pharmacol. Biochem. Behav. 13:69–75; 1980.
4. Berken, G. H.; Weinstein, D. O.; Stern, W. C. Weight gain: A side-effect of tricyclic antidepressants. J. Affect. Disord. 7:133–138; 1984.
5. Blavat, N.; DeFeudis, F. V. Inhibition of food intake in the rat by antidepressants. Pharmacol. Res. Commun. 14:663–669; 1982.
6. Broitman, S. T.; Donoso, A. O. Effects of chronic imipramine and clomipramine oral administration on maternal behavior and litter development. Psychopharmacology (Berlin) 56:93–101; 1978.
7. Carlton, P. L. Potentiation of the behavioral effects of amphetamine by imipramine. Psychopharmacologia 2:364–376; 1961.
8. Davidson, R. A.; Smith, B. D. Arousal and habituation: Differential effects of caffeine, sensation seeking and task difficulty. Person. Indiv. Diff. 10:11–119; 1989.
9. Dolfini, E.; Tansella, M.; Valzelli, L.; Garattini, S. Further studies on the interaction between desipramine and amphetamine. Eur. J. Pharmacol. 5:185–190; 1969.
10. Extein, I. L.; Gold, M. S. The treatment of cocaine addicts: Bromocriptine or desipramine. Psychiatry Ann. 18:535–537; 1988.
11. Fischman, M. W.; Foltin, R. W.; Nestadt, G.; Pearlson, G. D. Effects of desipramine maintenance on cocaine self-administration in humans. J. Pharmacol. Exp. Ther. 253:760–770; 1990.
12. Foltin, R. W. Effects of anorectic drugs on the topography of feeding behavior in baboons. J. Pharmacol. Exp. Ther. 239:101–109; 1989.
13. Foltin, R. W. Differential development of tolerance to the effects of d-amphetamine and fenfluramine on food intake in baboons. J. Pharmacol. Exp. Ther. 252:960–969; 1990.
14. Foltin, R. W.; Fischman, M. W. Food intake in baboons: Effects of d-amphetamine and fenfluramine. Pharmacol. Biochem. Behav. 31: 585–592; 1988.
15. Foltin, R. W.; Fischman, M. W. Effect of caloric manipulations on food intake in baboons. Appetite; in press.
16. Foltin, R. W.; Woolverton, W. L.; Schuster, C. R. Effects of psychomotor stimulants, alone and in pairs, on milk drinking in the rat after intraperitoneal and intragastric administration. J. Pharmacol. Exp. Ther. 226:411–418; 1983.
17. Frank, R. A.; Pommering, T.; Nitz, D. The interactive effects of cocaine and imipramine on self-stimulation train-duration thresholds. Pharmacol. Biochem. Behav. 30:1–4; 1988.
18. Furchgott, R. F.; Kirpekar, S. M.; Rieker, M.; Schwab, A. Actions and interactions of norepinephrine, tyramine and cocaine on aortic strips of rabbit and left atria of guinea pig and cat. J. Pharmacol. Exp. Ther. 142:39–58; 1963.
19. Garland, E. J.; Remick, R. A.; Zis, A. P. Weight gain with antidepressants and lithium. J. Clin. Psychopharmacol. 8:322–330; 1988.
20. Gawin, F. H.; Kleber, H. D. Cocaine abuse treatment. Open pilot trial with desipramine and lithium carbonate. Arch. Gen. Psychiatry 41:903–909; 1984.
21. Gawin, F. H.; Kleber, H. D.; Byck, R.; Rounsaville, B. J.; Kosten, T. R.; Jatlow, P. I.; Morgan, C. Desipramine facilitation of initial cocaine abstinence. Arch. Gen. Psychiatry 46:117–121; 1989.
22. Giannini, A. J.; Billett, W. Bromocriptine-desipramine protocol in

treatment of cocaine addiction. J. Clin. Pharmacol. 27:549–554; 1987.
23. Giannini, A. J.; Malone, D. A.; Giannini, M. C.; Price, W. A.; Loiselle, R. H. Treatment of depression in chronic cocaine and phencyclidine abuse with desipramine. J. Clin. Pharmacol. 26: 211–214; 1986.
24. Glowinski, J.; Axelrod, J. G. Effects of drugs on the disposition of H{3}-norepinephrine in the rat brain. Pharmacol. Rev. 18:775–785; 1966.
25. Levitt, A. J.; Joffee, R. T.; Esche, I.; Sherret, D. The effect of desipramine on body weight in depression. J. Clin. Psychiatry 48:27–27; 1987.
26. Muscholl, E. Effect of cocaine and related changes on the uptake of noradrenaline by heart and spleen. Br. J. Pharmacol. 16:352–361; 1982.
27. Nobrega, J. N.; Coscina, D. V. Effects of chronic amitriptyline and desipramine on food intake and body weight in rats. Pharmacol. Biochem. Behav. 27:105–112; 1987.
28. O'Donnell, J. M.; Rider, D. P.; Somani, S.; Seiden, L. S. The effect of repeated desipramine administration on water intake in rats. Psychopharmacology (Berlin) 77:128–133; 1982.
29. Pickens, T.; Thompson, T. Cocaine-reinforced behavior in rats: Effects of reinforcement magnitude and fixed-ratio. J. Pharmacol. Exp. Ther. 161:122–129; 1968.
30. Scheckel, C. L.; Boff, E. Behavioral effects of interacting imipramine and other drugs with d-amphetamine, cocaine, and tetrabenazine. Psychopharmacologia 5:98–208; 1964.
31. Sulser, F.; Owens, M. L.; Dingell, J. V. On the mechanism of amphetamine potentiation by desipramine (DMI). Life Sci. 5:2005–2010; 1966.
32. Thompson, D. M. Development of tolerance to the disruptive effects of cocaine on repeated acquisition and performance of response sequences. J. Pharmacol. Exp. Ther. 203:294–302; 1977.
33. Towell, A.; Willner, P.; Booth, D. A. Central and peripheral contributions to the enhancement of amphetamine anorexia by desmethylimipramine. Pharmacol. Biochem. Behav. 22:57–60; 1985.
34. Willner, P.; Montgomery, T. Behavioral changes during withdrawal from desmethylimipramine. I. Interactions with amphetamine. Psychopharmacology (Berlin) 75:54–59; 1981.
35. Wilson, M. C.; Hitomi, M.; Schuster, C. R. Psychomotor stimulant self administration as a function of dosage per injection in the rhesus monkey. Psychopharmacologia 22:271–281; 1971.
36. Woolverton, W. L.; Kandel, D.; Schuster, C. R. Effects of repeated administration of cocaine on schedule-controlled behavior of rats. Pharmacol. Biochem. Behav. 9:327–337; 1978.