Taste and Diet Preferences as Predictors of Drug Self-Administration

Blake A. Gosnell and Dean D. Krahn

Several observations suggest that there may be specific, important relationships between taste/diet preferences and drug self-administration. These include reports of: (a) differences in drug self-administration in rats with differing baseline taste or diet preferences, (b) correlations between the intake of saccharin and the intake of alcohol, and (c) changes in drug self-administration when sweet-tasting solutions are provided as alternative reinforcers. In humans, there is a high comorbidity between eating disorders and drug and alcohol abuse. Further, this relationship extends to subclinical levels of each behavior. With a better under-standing of these relationships, it may be possible to use measures of diet and taste preferences, along with dietary manipulations, to predict and reduce vulnerability to drug abuse, as well as to monitor and improve current treatments for drug abuse. Animal and human studies relevant to the relationship between diet and taste preferences and drug abuse will be reviewed below, followed by a brief discussion of the possible mechanism underlying the relationship.

ANIMAL STUDIES

Through selective breeding, lines of rats have been developed that display relatively high or low levels of drug self-administration or drug preference (Li et al. 1979; Schechter 1992; Sinclair et al. 1989). Some inbred strains have also been found to differ from one another in drug self-administration (George and Goldberg 1988; Suzuki et al. 1988, 1992). In many cases, the differences in drug intake are paralleled by differences in the self-administration of other substances. For example, Nichols and Hsiao (1967) selectively bred rats for high or low suscepti-bility to morphine addiction. The groups subsequently displayed corresponding high and low susceptibility to alcohol addiction. Rats of the ALKO Alcohol-Accepting (AA) strain consumed more etonitazene (ETZ) than those of the ALKO Alcohol Non-Accepting (ANA) strain (Hyyatiä and Sinclair 1993) and were also found to self-select a diet higher in fat than that selected by ANA rats (Forsander 1988).

Marks-Kaufman and Lipeles (1982) found that those rats that eventually drank a morphine solution consumed more dietary fat than those that would not drink the morphine solution.

Based on the findings that AA rats eat more fat than ANA rats (Forsander 1988), Krahn and Gosnell (1991) performed a study to determine whether rats with differing diet preferences would differ in their voluntary consumption of alcohol. After measuring macronutrient self-selection in a large group of rats, two subgroups were selected: one group had self-selected a diet containing a large amount of carbohydrate and little fat, and the other consumed large amounts of fat and little carbohydrate; protein intake was similar in the two groups (N = 8 per group). All rats were then placed on a standard lab chow diet, and subsequent alcohol intake was determined. The rats were given daily sessions in which alcohol (4 to 12 percent, v/v) or water was available. Initially, sessions were conducted with rats on a food restriction schedule; in later sessions, food was available ad libitum. During restriction, alcohol was available for only the first hour of the 4-hour daily feeding session. On the final 6 days of the experiment (no feeding restriction), water and 8 percent ethanol (EtOH) were alternated as the fluid presented during daily 1-hour sessions. Non-deprived, fat-preferring rats tended to consume more alcohol than carbohydrate-preferring rats at nearly every opportunity over approximately 4 weeks of repeated exposures to alcohol (4 to 12 percent). When the intake of 8 percent alcohol was compared to the intake of water, fat-preferring rats consumed significantly more alcohol than water (figure 1). Furthermore, they consumed more alcohol than carbohydrate- preferring rats. This study provided evidence for a relationship between fat preference and alcohol intake. It is important to note that when rats were tested for alcohol intake, both groups were maintained on the same diet (i.e., lab chow). Therefore, the observed differences in alcohol intake cannot be attributed to differences in the composition of the maintenance diet, but are more likely to be related to baseline differences in preference.

In contrast to the experiment described earlier, Prasad and colleagues (1993) found no relationship between macronutrient preference and alcohol preference in Sprague-Dawley rats, as measured in tests in which alcohol (6 percent v/v) and water were available continuously for 5 days. They did find, however, that rats of the alcohol-preferring (P) line displayed a significantly greater preference for protein and a decreased preference for carbohydrate than rats of the alcohol-nonpreferring (NP) line. This contrasts with the observation that AA rats consume more fat

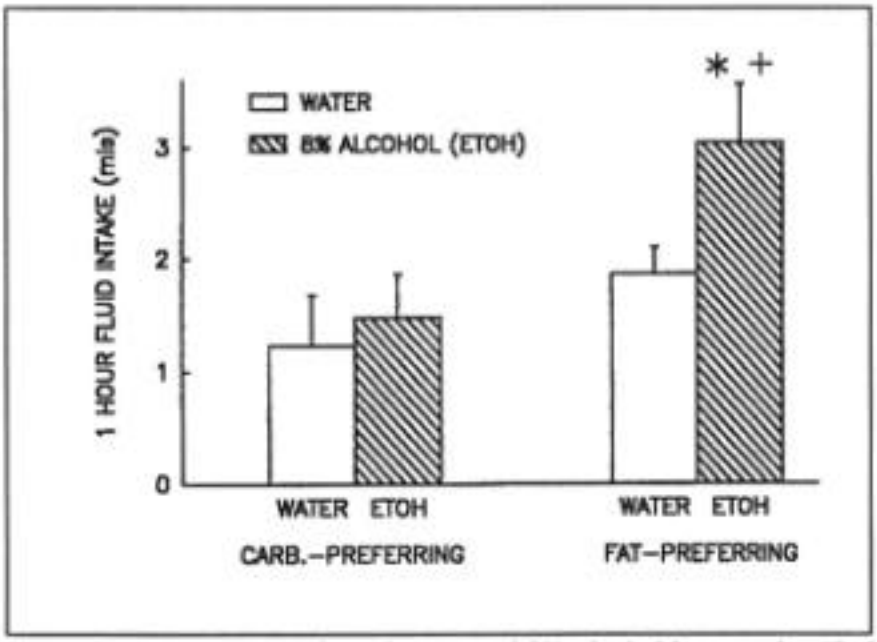

FIGURE 1. *Average intakes of water and 8% alcohol by rats classified as carbohydrate-preferring or fat-preferring. The means are the average of three 1-hr sessions with each fluid for each rat. Fat-preferring rats consumed significantly more alcohol than water (*$p < 0.01$) and significantly more alcohol than carbohydrate-preferring rats (+ $p < 0.05$).*

SOURCE: Krahn and Gosnell 1991, Copyright 1991, Pergamon Press.

than ANA rats (Forsander 1988). Differences between these results and those of Forsander (1988) and Krahn and Gosnell (1991) may be related to methodological differences, particularly the composition of the test diets, the methods for measuring alcohol intake and preference, and the strains of P and NP rats tested.

Sweet taste is another attribute that appears to have some relationship to drug self-administration beyond the fact that sweeteners are frequently added to EtOH solutions to make them more palatable. In alcohol preference studies, the provision of saccharin, sucrose, or fat solutions as options to EtOH caused a decrease in EtOH consumption (Lester and Greenberg 1952). Similarly, the availability of a saccharin-glucose (sac-gl) solution decreased the acquisition and maintenance of cocaine self-administration in rats (Carroll and Lac 1993; Carroll et al. 1989), while the deprivation of a sac-gl solution increased the self-administration of ETZ (Carroll and Boe 1982) and cocaine (Carroll et

al. 1989). In rhesus monkeys, the provision of a saccharin solution as an alternative reinforcer to smoked cocaine base led to a small but nonsignificant decrease in cocaine intake; the decrease was most noticeable at high fixed-ratio (FR) values (Comer et al. 1994). As the FR value was increased, the number of cocaine deliveries decreased, and the intake of saccharin increased.

In rats selected or bred for high and low alcohol self-administration, corresponding high and low intakes of sucrose and saccharin have been noted (Kampov-Polevoy et al. 1990; Sinclair et al. 1992; Stewart et al. 1994). Gosnell and Krahn (1992) tested whether this relationship was reciprocal by measuring EtOH intake in rats selected for differing amounts of saccharin intake. Groups of rats with low, intermediate, or high intake of saccharin were formed on the basis of voluntary saccharin intake in daily 1-hour sessions (N = 8 per group). These rats were then given daily sessions in which alcohol (2 to 8 percent , v/v) or water was available. Initially, sessions were conducted with rats on a food restriction schedule; in later sessions, food was available ad libitum. When food restricted, the groups did not differ in alcohol or water intake. When the food restriction schedule was discontinued, alcohol intake in the intermediate and high saccharin groups was generally higher than that of the low saccharin group (figure 2). On the final series of alcohol sessions, the high saccharin group consumed significantly more 2 and 6 percent alcohol than the low saccharin group and tended to consume more of the other concentrations as well. A paper by Overstreet and colleagues (1993) confirms this positive relationship between saccharin and alcohol preference across several rat strains.

A more indepth study of the saccharin-alcohol relationship was conducted by Bell and associates (1994). From a large group of rats (N = 40), groups representing high, intermediate, and low saccharin preferences were selected (N = 6 per group). These rats were reduced to 80 percent of their free-feeding weights, and EtOH was established as a reinforcer by use of a food-induced drinking procedure in which rats learned to press a lever to obtain water or EtOH solutions. Response rates were measured across acquisition sessions, an FR1-8 series, and a concentration series. There was considerable variability within groups, such that the group means were not significantly different. However, a striking pattern emerged. In nearly all conditions, the mean number of responses for EtOH was higher for the high saccharin group than for the low.

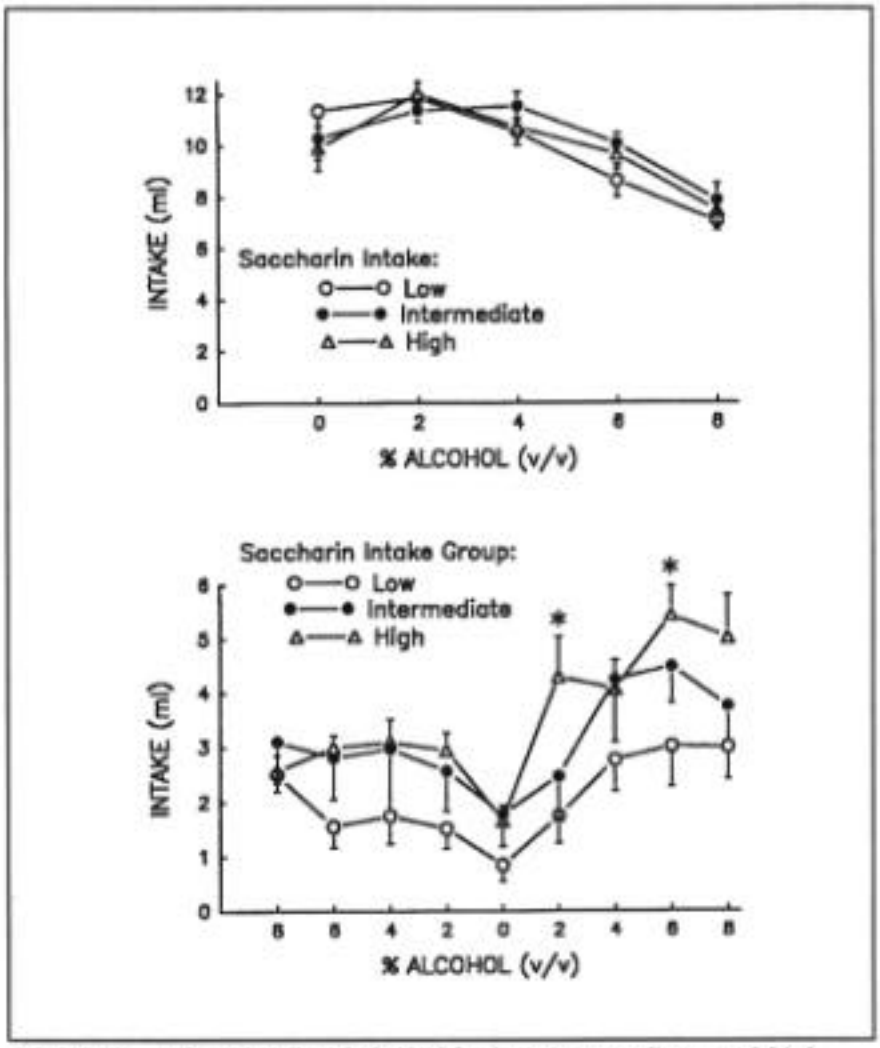

FIGURE 2. *(Top) Intake of alcohol by low, intermediate, and high saccharin-consuming rats (means±SEM, N = 8/group). Each point represents the average of the final 3 sessions at the indicated concentration. Rats were on a food-restricted schedule, and the test session coincided with the first hour of food availability each day. (Bottom) Intake of alcohol by the same groups when food was available ad libitum, except during the test session. Each point represents the average of 2 to 4 sessions. Asterisks indicate significant differences from the low saccharin group ($p < 0.05$, one-tailed Bonferroni t test).*

SOURCE: Gosnell and Krahn 1992, Copyright 1992, Pergamon Press.

Results for the concentration series (at FR1) are shown in figure 3. Under a null hypothesis of no relationship between saccharin and EtOH intake, such a consistent pattern over an extended series of conditions would not be expected. These results, then, offer some support for a relationship between the factors mediating EtOH self-administration and those involving ingestion of palatable foods and fluids.

A positive relationship between the oral intakes of two substances may be related to individual differences in the general propensity to consume any distinctively flavored solutions that are presented. The results of Stewart and colleagues (1994), however, argue against this possibility, at least for the P and alcohol NP rat lines. They found that rats of the P strain consumed more sucrose solution than NP rats, but that the strains did not differ in the intakes of sour (citric acid) or bitter (sucrose octa-acetate) solutions. With sodium chloride solutions, NP rats displayed a higher preference than P rats. They interpret these results as evidence that these rat strains do not simply differ in their acceptance of all flavored fluids.

Gosnell and associates (1995) recently conducted a study that examined the relationship between saccharin preference and intravenous (IV) morphine self-administration. The IV route eliminates the oral route for one of the substances and should minimize the influence of drug taste on self-administration. Rats with a high (N = 8) or low (N = 8) preference for saccharin were selected from a larger group (N = 31). The oral consumption of morphine (0.5 mg/mL) was then measured in these rats with a procedure identical to that used for measuring saccharin preference. In both groups, oral morphine intake was low, and the groups did not differ. Catheters were then implanted in all rats. After recovery from surgery, rats were placed in operant chambers for daily 1-hour sessions. During the sessions, each press of the right lever caused an infusion of 0.04 mg/kg of morphine sulfate. A 30-second timeout period followed the start of each infusion; during this time, lever-presses were counted but did not activate the infusion pumps. No training in the operant chambers was provided. After 10 daily sessions at 0.04 mg/kg/infusion, the dose was increased to 0.08 mg/kg/infusion for 22 sessions, then to 0.16 mg/kg/infusion for 10 sessions. There were 14 rats that completed the study through day 20 of the sessions with the infusion dose at 0.08 mg/kg; 10 rats completed the entire study.

The groups did not differ in the number of infusions obtained at 0.04 mg/kg/infusion. Over the course of the 0.08 mg/kg sessions,

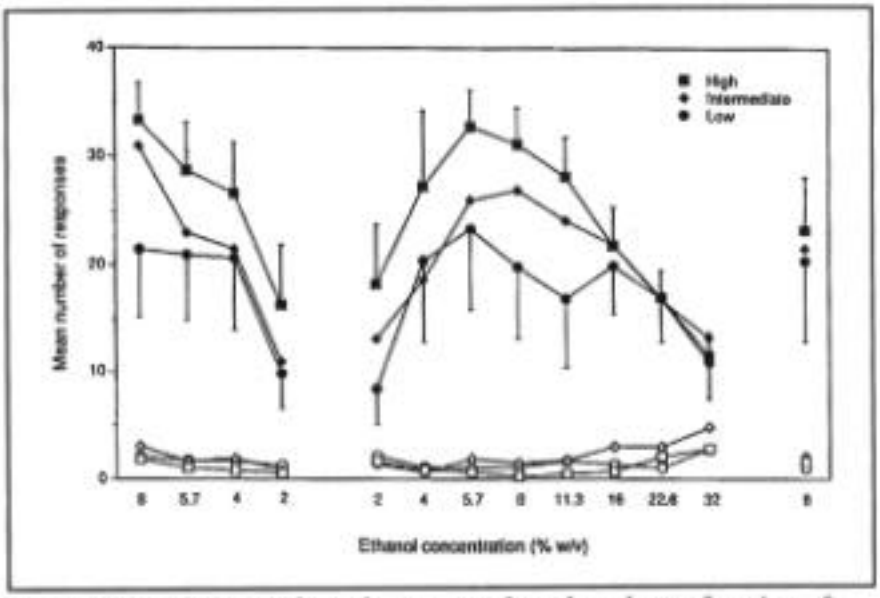

FIGURE 3. *Mean number of responses for ethanol as a function of concentration (% w/v). Each point represents the group mean (N = 6) over the six sessions at each condition; groups represent high, intermediate, and low saccharin preference. Closed symbols represent responses for ethanol, and open symbols represent responses for concurrently available water. SEMs are shown for high and low saccharin groups but, for visualization purposes, not shown for the intermediate group.*

SOURCE: Bell et al. 1994.

saccharin-preferring rats began to self-administer significantly more morphine than rats with a low saccharin preference. For example, averaged over sessions 16 through 20 at this dose, the high-saccharin rats obtained 10.5Å2.3 infusions per session, whereas the low-saccharin rats obtained 4.1Å0.8 infusions ($p < 0.05$). When the dose was increased to 0.16 mg/kg/infusion, rats in the low-saccharin preference group began to self-administer more morphine than they did at the lower dose. In the high-saccharin preference group, there was a decrease in the number of infusions obtained per session. The groups did not significantly differ at this dose. This study suggested that the threshold dose for morphine self-administration may be higher in rats with a low saccharin preference when compared to those with a high saccharin preference. The decreases in self-administration by the high-saccharin group when the dose was

increased to 0.16 mg/kg may represent a compensatory response to the greater amount of drug obtained per infusion. This study supports the hypothesis that saccharin preferences are related to drug self-administration and suggests that the relationship is not due simply to similarity of tastes.

There is also evidence that ingestion of palatable fluids may alter the effects of a drug. For example, chronic or acute intake of a sweet solution (a 10 percent sucrose-0.1 percent saccharin solution) enhanced the rewarding effect of morphine, as measured by the conditioned place preference procedure (Lett 1989). With the "hotplate" procedure for measuring pain sensitivity, Lieblich and associates (1983) have reported that chronic access to a palatable sac-gl solution reduced the analgesic effect of morphine in a line of rats selectively bred for high rates of hypothalamic self-stimulation. This effect, however, may not be specific to sweet tastes or this particular line of rats, as a reduction in morphine analgesia was also observed in Sprague-Dawley rats after 48-hour exposure to solutions of quinine, sac-gl, or sodium chloride (Holder 1988). With the tailflick assay, morphine analgesia increased after long-term access to sweet solutions (> 20 days) (Kanarek et al. 1991; Roane and Martin 1990) and decreased after a shorter period of access to a sweetened solution (3 to 24 hours) (Fidler et al. 1993; Klein and Green 1988). Because the effects of a drug may be related to the likelihood of self-administration of the drug, these results, too, suggest a relationship between palatable tastes and self-administration.

The studies described earlier suggest that drug self-administration may be predictable from diet or taste preferences. A potentially important area for future research is the determination of whether procedures that alter taste or diet preferences have a concomitant effect on drug intake. It is well known, for example, that saccharin preference can be altered through preexposure and/or conditioning; macronutrient preference can also be experimentally manipulated (Gerardo-Gettens et al. 1991; Matsuo et al. 1984; Reed et al. 1992). Measurements of the acquisition or maintenance of drug self-administration after such manipulations will provide some indication of whether vulnerability to drug abuse in humans may be reduced through efforts to improve dietary habits and preferences.

HUMAN STUDIES

There is increasing evidence from human studies that supports the hypothesis that eating behavior and alcohol and other drug use are related. As many as 55 percent of bulimic patients are reported to have alcohol and other drug use problems (Beary et al. 1986; Hudson et al., 1988; Mitchell et al. 1985, 1990; Weiss and Ebert 1983). Conversely, 15 to 40 percent of females with alcohol or other drug abuse problems have been reported to have eating disorder syndromes, usually involving binge eating (Beary et al. 1986; Hudson et al. 1992; Jonas et al. 1987). It is important to note that during binge episodes, bulimics typically ingest large amounts of sweet and/or high-fat foods (Abraham and Beumont 1982; Mitchell et al. 1981; Weltzin et al. 1991). In standardized taste tests with mixtures of sugar and dairy products, however, bulimics were found to have an optimal sweetness preference that was higher than controls and an optimal fat preference lower than controls (Drewnowski et al. 1987).

Krahn and colleagues studied the relationship between dieting and bulimic behaviors and alcohol use and abuse in women entering their freshman year of college (Krahn et al. 1992). Subjects responded to questionnaires regarding a variety of health issues including dieting and bulimic behaviors and alcohol and other drug abuse. On the basis of their responses, subjects were categorized into one of six dieting severity groups ranging from nondieter to bulimic. There was a significant, positive relationship between the frequency and intensity of alcohol consumption and the severity of dieting and bulimic behaviors (figure 4). In a subsequent study with questionnaires and semistructured interviews, it was found that the more severely dieting and binge eating women were more likely to have experienced negative consequences from their drinking and to have met criteria for substance abuse or dependence (Krahn, unpublished observations). The reported likelihood of responding to stress by binge eating, drinking alcohol, using other drugs, going shopping, and exercising were all positively, significantly related to dieting severity, which suggests that these immediately gratifying coping mechanisms may be linked, at least in certain subgroups of young women.

Another study (Bohn and Krahn, unpublished observations) assessed the relationship between self-deprivation of alcohol by alcoholics in their first 6 months of sobriety and their self-reported change in likelihood of binge-eating. Of the 242 men in the study, 37 percent reported at least

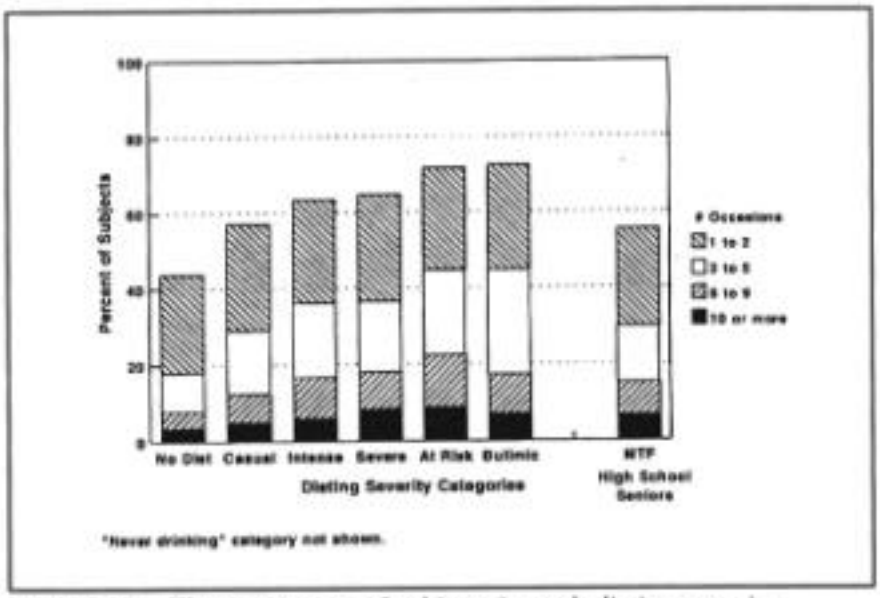

FIGURE 4. *The percentage of subjects in each dieting-severity category who reported each frequency of alcohol use over the last month. The relationship between dieting-severity categories and frequency of alcohol use is significant (γ = 0.21, t = 8.24, $p < 0.001$). Data on the same question from the 1989 Monitoring the Future (MTF) study, obtained from a national sample of high school senior girls with probable or definite plans to graduate from a 4-year college, are included for comparison (Johnston et al. 1990).*

SOURCE: Krahn et al. 1992, Copyright 1992, Ablex Publishing Corporation.

some binging, and 17 percent reported at least weekly binging. Of the 109 alcoholic women, 62 percent reported a history of binge-eating, and 32 percent reported weekly binges. Of those who reported any previous history of binge-eating, more than 50 percent reported an increase in the likelihood of binging associated with a cessation of alcohol use, while about 20 percent reported a decrease in the propensity to binge. Further, 50 percent of all subjects reported that eating caused a decrease in desire for alcohol while only 7 percent reported that eating increased their desire for alcohol. Understanding the interaction of these two appetites may improve treatment for the large number of women alcoholics with comorbid eating disorders and the large number of bulimics with comorbid alcoholism.

In addition to studies of the comorbidity of substance abuse and "pursuit of thinness" disorders, intriguing relationships between drug use and food intake have been reported. For example, sweet cravings and high intakes of sweet foods have been reported for opiate addicts (Morabia et al. 1989; Weiss 1982; Willenbring et al. 1989). In a sample of recovering alcoholics, Yung and colleagues (1983) found that those who achieved the longest periods of postdetoxification sobriety reported increased intake of sugar in beverages. In a study of bulimic female smokers, cessation of smoking caused a selective increase in fat intake (Bulik et al. 1991). Interestingly, in the treatment community, alcoholics are being told to follow one of two conflicting paths: Some are told to avoid sweets, as the use of these foods is viewed as an alternative addiction that primes the alcoholic for relapse (Ketcham and Mueller 1983); others are told to use sweets to decrease the urges for alcohol (Alcoholics Anonymous 1975). Neither of these recommendations, however, has received rigorous scrutiny in treatment trials. Finally, the ability to taste the bitter compound propylthiouracil (PROP) has been linked to both alcoholism and the hedonic response to sweet tastes. Children of alcoholics are more likely to be nontasters of PROP than children of nonalcoholics (Pelchat and Danowski 1992). In a study that classified subjects as likers or dislikers of sweet taste, Looy and Weingarten (1992) found that PROP non-tasters were generally sweet likers. Conversely, sweet dislikers were generally PROP tasters. These studies indicate that the interactions between preference for sweet/fat substances and the preference for and intake of drugs may have a genetic basis.

PARALLELS BETWEEN FACTORS AFFECTING DRUG SELF-ADMINISTRATION AND TASTE/DIET PREFERENCES

In many cases, stress or drug preexposure increases subsequent behavioral responses to a drug and/or self-administration of the drug (Horger et al. 1990; Piazza et al. 1989; Robinson 1993). For example, food deprivation, which may be viewed as a form of stress, is well known to increase the self-administration of a number of drugs (see Carroll and Meisch 1984 for a review). Tailpinch stress increases vulnerability to the acquisition of amphetamine self-administration (Piazza et al. 1990). Immobilization stress was found to increase the oral self-administration of morphine and fentanyl (Shaham et al. 1992), and footshock stress increased the IV self- administration of heroin in rats on a progressive ratio reinforcement schedule (Shaham

and Stewart 1994). Some aspects of taste and diet preferences also appear to be stress-sensitive and/or subject to "sensitization." Although chronic stress generally causes a decreased intake or preference for sweetened solutions (Katz 1982; Pucilowski et al. 1993; Willner et al. 1987), one mild stressor, tailpinch, is known to cause a short-term increase in feeding (see Morley et al. 1983 for a review). When given a choice of four fluids (milk, sweetened milk, sucrose solution, and water), Bertiere and colleagues (1984) observed that mild tailpinch stress caused a preferential increase in sucrose intake. Prenatal exposure to nicotine (in male rats) and cocaine (in humans) has been shown to increase sweet taste preference (Lichtensteiger and Schlumpf 1985; Maone et al. 1992). It should be noted that the effects of prenatal nicotine were observed in adult rats, thus indicating a long-term change (Lichtensteiger and Schlumpf 1985). Food deprivation increases preferences for saccharin (Hursh and Beck 1971; Valenstein 1967), and the intake of dietary fat is preferentially increased after food deprivation or food restriction (Gerardo-Gettens et al. 1991; Matsuo et al. 1984; Reed et al. 1988). Finally, bulimia (a disorder that has many characteristics of addictive behavior) has been found to be related to the amount and severity of previous dieting (Abraham and Beumont 1982; Fairburn and Cooper 1984). As noted earlier, women with anorexia or bulimia have increased preferences for sweet tastes and have increased rates of alcoholism and other substance abuse. Thus, taste and diet preferences appear to be related to subsequent drug self-administration, and may be sensitive to some of the same factors that have been shown to affect drug self-administration.

A POSSIBLE MECHANISM

Correlations in the intakes of two orally self-administered substances may be attributable in part to common taste properties of the substances. For example, EtOH appears to have a taste similar to solutions with a combination of sweet and bitter tastes (Kiefer and Lawrence 1988). It might be expected, then, that the preference for one substance would correlate with the preference for a similar-tasting substance. However, Sinclair and others (1992) have argued that the relationship they observed between saccharin and EtOH intake in P versus NP rats was related to the postingestive effects of EtOH. Hyyatiä and Sinclair (1993) observed that alcohol-preferring AA rats consumed more cocaine and ETZ than did the alcohol nonpreferring ANA line. They suggested that the differences in cocaine intake may be due to differences in sensitivity to bitter tastes, but that strain

differences in ETZ self-administration could not be completely explained on the basis of taste sensitivity. In the study described earlier on the relationship of saccharin preference to IV morphine self-administration (Gosnell et al. 1995), the use of the IV route minimized the influence of morphine taste. These findings suggest that the relationships between diet/taste preferences and drug self-administration are not simply due to taste similarities.

A more likely explanation for the observed positive relationships between the intakes of diverse substances is that they have in common the ability to activate the same neural pathways. The pathway that has received the most attention in regard to reward circuits is the mesolimbic dopaminergic system. Most drugs of abuse activate this system (see Di Chiara et al. 1992 and Wise 1987 for reviews) and differences in drug self-administration have been linked to differences in mesolimbic dopamine (DA) levels, either in the basal or stimulated state (Glick et al. 1992; Hooks et al. 1992). There is much evidence that the mesolimbic DA system is also involved in intracranial electrical self-stimulation (see Phillips and Fibiger 1989 for a review), and it is interesting to note that rats that have been selectively bred for high or low rates of lateral hypothalamic self-stimulation also display relative high and low saccharin consumption (Ganchrow et al. 1981).

Measures of DA release in the nucleus accumbens also support a role for dopamine in the mediation of taste palatability. Mark and colleagues (1991) found that the intraoral application of saccharin increased DA levels in the nucleus accumbens, as measured by microdialysis. A more recent study did not find significantly increased DA release after saccharin ingestion, but did report an anticipatory increase just prior to saccharin intake (Weiss et al. 1993). Dopaminergic antagonists were found to reduce the intake of sucrose solutions (at low concentrations) and to reduce sham-feeding of corn oil and sucrose solutions (Muscat and Willner 1989; Weatherford et al. 1990). The dopaminergic antagonist SCH 23390 also reduced lever-pressing for food, water, and saccharin solutions (see Nakajima 1989). In taste reactivity tests, the antagonist pimozide was found to reduce the hedonic response to intraoral infusions of sucrose (Leeb et al. 1991). The common ability to activate the mesolimbic dopaminergic system, therefore, may underlie the observed relationships between the diet and taste preferences and drug self-administration.

Caine and Koob (1994) have reported that depletion of mesolimbic DA reduced cocaine self-administration but did not affect operant responding for food. While this finding appears to cast doubt upon the hypothesis that food reward and drug self-administration are mediated by a common system, it is important to note that the animals were tested when food restricted. A number of studies suggest there may some critical differences between food ingestion in the deprived state and that which occurs in the nondeprived state. For example, naloxone was found to be more effective in reducing the intake of palatable chow or a sweet solution in nondeprived rats than in reducing intake in food-deprived rats (Levine et al. 1995; Segall and Margules 1989). Morphine had opposite effects on food intake in food-satiated and food-deprived rats (Sanger and McCarthy 1980). Based on studies of conditioned place preference in rats, Bechara and van der Kooy (1992) have argued that deprivation- and nondeprivation-induced motivation may be mediated by different neural systems. This possibility should be kept in mind when assessing the relationships between feeding and drug self-administration, particularly since food deprivation and food restriction are sometimes used to facilitate the intake of both food and drugs.

Compulsive, repetitive consumption of substances of abuse and/or palatable foods in the pursuit of an improved affective state is a core behavior in the syndromes of drug abuse and drug dependence as well as eating disorders such as bulimia or compulsive overeating. If, as suggested by the studies reviewed earlier, a common neural system is involved in mediating taste preferences as well as the reinforcing effects of drugs, then it is not surprising that certain characteristics of substance use and palatable food consumption are similar and correlated. A better understanding of the relationship between drug use and taste and diet preferences may provide new insights into the etiology of eating disorders and substance abuse. It is possible that a test could be developed based on responses to “natural” reinforcers such as palatable foods that would predict vulnerability to alcohol and other drug abuse and drug dependence in humans. Further, monitoring and/or manipulating dietary intake and diet preferences may be useful adjuncts to other treatment programs and may offer a means of predicting the likelihood of a favorable treatment response in certain groups of substance abusers. Finally, it is possible that pharmacological interventions effective in the treatment of eating disorders may prove to be of some value in the treatment of substance use disorders as well. These potential applications, however, will first require additional investigation at the basic and preclinical levels on

both the acquisition and maintenance of drug self-administration and taste preferences.

REFERENCES

Abraham, S.F., and Beumont, P.J. How patients describe bulimia or binge eating. *Psychol Med* 12:625-635, 1982.

Alcoholics Anonymous. *Living Sober*. New York: Alcoholics Anonymous World Services, 1975. p. 23.

Beary, M.D.; Lacey, J.H.; and Merry, J. Alcoholism and eating disorders in women of fertile age. *Br J Addict* 81:685-689, 1986.

Bechara, A., and van der Kooy, D. A single brain stem substrate mediates the motivational effects of both opiates and food in nondeprived rats but not in deprived rats. *Behav Neurosci* 106:351-363, 1992.

Bell, S.M.; Gosnell, B.A.; Krahn, D.D.; and Meisch, R.A. Ethanol reinforcement and its relationship to saccharin preference in Wistar rats. *Alcohol* 11:141-145, 1994.

Bertiere, M.C.; Mame Sy, T.; Baigts, F.; Mandenoff, A.; and Apfelbaum, M. Stress and sucrose hyperphagia: Role of endogenous opiates. *Pharmacol Biochem Behav* 20:675-679, 1984.

Bulik, C.M.; Dahl, R.E.; Epstein, L.H.; and Kaye, W.H. The effects of smoking deprivation on caloric intake in women with bulimia nervosa. *Int J Eat Disord* 10:451-459, 1991.

Caine, S. B., and Koob, G.F. Effects of mesolimbic dopamine depletion on responding maintained by cocaine and food. *J Exp Anal Behav* 61:213-221, 1994.

Carroll, M.E., and Boe, I.N. Increased intravenous drug self-administration during deprivation of other reinforcers. *Pharmacol Biochem Behav* 17:563-567, 1982.

Carroll, M.E., and Lac, S.T. Autoshaping i.v. cocaine self-administration in rats: Effects of nondrug alternative reinforcers on acquisition. *Psychopharmacology* 110:5-12, 1993.

Carroll, M.E., and Meisch, R.A. Increased drug-reinforced behavior due to food deprivation. In: Thompson, T.; Dews, P.B.; and Barrett, J.E., eds. *Advances in Behavioral Pharmacology*. Vol. 4. New York: Academic Press, 1984. pp. 47-88.

Carroll, M.E.; Lac, S.T.; and Nygaard, S.L. A concurrently available nondrug reinforcer prevents the acquisition or decreases the maintenance of cocaine-reinforced behavior. *Psychopharmacology* 97:23-29, 1989.

Comer, S.D.; Hunt, V.R.; and Carroll, M.E. Effects of concurrent saccharin availability and buprenorphine pretreatment on demand

for smoked cocaine base in rhesus monkeys. *Psychopharmacology* 115:15-23, 1994.

Di Chiara, G.; Acquas, E.; and Carboni, E. Drug motivation and abuse: A neurobiological perspective. *Ann N Y Acad Sci* 654:207-219, 1992.

Drewnowski, A.; Bellisle, F.; Aimez, P.; and Remy, B. Taste and bulimia. *Physiol Behav* 41:621-626, 1987.

Fairburn, C.G., and Cooper, P.J. The clinical features of bulimia nervosa. *Br J Psychiatry* 144:238-246, 1984.

Fidler, P.; Kalman, B.A.; Ziemer, H.E.; and Green, K.F. Early onset of reduced morphine analgesia by ingestion of sweet solutions. *Physiol Behav* 53:167-171, 1993.

Forsander, O.A. The interaction between voluntary alcohol consumption and dietary choice. *Alcohol Alcohol* 23:143-149, 1988.

Ganchrow, J.R.; Lieblich, I.; and Cohen, E. Consummatory responses to taste stimuli in rats selected for high and low rates of self-stimulation. *Physiol Behav* 27:971-976, 1981.

George, F.R., and Goldberg, S.R. Genetic differences in responses to cocaine. In: Clouet, D.; Asghar, K.; and Brown, R., eds. *Mechanisms of Cocaine Abuse and Toxicity*. National Institute on Drug Abuse Research Monograph 88. DHHS Pub. No. (ADM)88-1588. Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1988. pp. 239-249.

Gerardo-Gettens, T.; Miller, G.D.; Horwitz, B.A.; McDonald, R.B.; Brownell, K.D.; Greenwood, M.R.C.; Rodin, J.; and Stern, J.S. Exercise decreases fat selection in female rats during weight cycling. *Am J Physiol* 260:R518-R524, 1991.

Glick, S.D.; Merski, C.; Steindorf, S.; Wang, S.; Keller, R.W.; and Carlson, J.N. Neurochemical predisposition to self-administer morphine in rats. *Brain Res* 578:215-220, 1992.

Gosnell, B.A., and Krahn, D.D. The relationship between saccharin and alcohol intake in rats. *Alcohol* 9:203-206, 1992.

Gosnell, B.A.; Lane, K.E.; Bell, S.M.; and Krahn, D.D. Intravenous morphine self-administration by rats with low vs. high saccharin preferences. *Psychopharmacology* 117:248-252, 1995.

Holder, M.D. Responsivity to pain in rats changed by the ingestion of flavored water. *Behav Neural Biol* 49:45-53, 1988.

Hooks, M.S.; Colvin, A.C.; Juncos, J.L.; and Justice, J.B., Jr. Individual differences in basal and cocaine-stimulated extracellular dopamine in the nucleus accumbens using quantitative microdialysis. *Brain Res* 587:306-312, 1992.

Horger, B.A.; Shelton, K.; and Schenk, S. Preexposure sensitizes rats to the rewarding effects of cocaine. *Pharmacol Biochem Behav*

37:707-711, 1990.
Hudson, J.I.; Pope, H.G., Jr.; Wurtman, J.; Yurgelun-Todd, D.; Mark, S.; and Rosenthal, N.E. Bulimia in obese individuals: Relationship to normal-weight bulimia. *J Nerv Ment Dis* 176:144-152, 1988.
Hudson, J.I.; Weiss, R.D.; Pope, H.G., Jr.; McElroy, S.K.; and Mirin, S.M. Eating disorders in hospitalized substance abusers. *Am J Drug Alcohol Abuse* 18:75-85, 1992.
Hursh, S.R., and Beck, R.C. Bitter and sweet preferences as a function of food deprivation. *Psychol Rep* 29:419-422, 1971.
Hyyatiä, P., and Sinclair, J.D. Oral etonitazene and cocaine consumption by AA, ANA and Wistar rats. *Psychopharmacology* 111:409-414, 1993.
Johnston, L.D.; Bachman, J.G.; and O'Malley, P.M. *Monitoring the Future: A Continuing Study of the Lifestyles and Values of Youth, 1989* [Computer file]. Ann Arbor, MI: Interuniversity Consortium for Political and Social Research. Conducted by University of Michigan, Survey Research Center, 1990.
Jonas, J.M.; Gold, M.S.; Sweeney, D.; and Pottash, A.L.C. Eating disorders and cocaine abuse: A survey of 259 cocaine abusers. *J Clin Psychiatry* 48:47-50, 1987.
Kampov-Polevoy, A.B.; Kasheffskaya, O.P.; and Sinclair, J.D. Initial acceptance of alcohol: Gustatory factors and patterns of alcohol drinking. *Alcohol* 7:83-85, 1990.
Kanarek, R.B.; White, E.S.; Biegen, M.T.; and Marks-Kaufman, R. Dietary influences on morphine-induced analgesia. *Pharmacol Biochem Behav* 38:681-684, 1991.
Katz, R.J. Animal model of depression: Pharmacological sensitivity of a hedonic deficit. *Pharmacol Biochem Behav* 16:965-968, 1982.
Ketcham, K., and Mueller, L.A. *Eating Right to Live Sober*. New York: Penguin Books, 1983.
Kiefer, S.W., and Lawrence, G.J. The sweet-bitter taste of alcohol: Aversion generalization to various sweet-quinine mixtures in the rat. *Chem Senses* 13:633-641, 1988.
Klein, S.P., and Green, K.F. Tolerance to morphine analgesia from brief exposure to a palatable solution. *Brain Res Bull* 21:963-965, 1988.
Krahn, D.D., and Gosnell, B.A. Fat-preferring rats consume more alcohol than carbohydrate-preferring rats. *Alcohol* 8:313-316, 1991.
Krahn, D.; Kurth, C.; Demitrack, M.; and Drewnowski, A. The relationship of dieting severity and bulimic behaviors to

alcohol and other drug use in young women. *J Subst Abuse* 4:341-353, 1992.

Leeb, K.; Parker, L.; and Eikelboom, R. Effects of pimozide on the hedonic properties of sucrose: Analysis by the taste reactivity test. *Pharmacol Biochem Behav* 39:895-901, 1991.

Lester, D., and Greenberg, L.A. Nutrition and the etiology of alcoholism: The effect of sucrose, saccharin and fat on the self-selection of ethyl alcohol by rats. *Q J Stud Alcohol* 13:553-560, 1952.

Lett, B.T. Ingestion of sweet water enhances the rewarding effect of morphine in rats. *Psychobiology* 17:191-194, 1989.

Levine, A.S.; Weldon, D.T.; Grace, M.; Cleary, J.P.; and Billington, C.J. Naloxone blocks that portion of feeding driven by sweet taste in food restricted rats. *Am J Physiol* 268:R248-R252, 1995.

Li, T.-K.; Lumeng, L.; McBride, W.J.; and Waller, M.B. Progress toward a voluntary oral consumption model of alcoholism. *Drug Alcohol Depend* 4:45-60, 1979.

Lichtensteiger, W., and Schlumpf, M. Prenatal nicotine affects fetal testosterone and sexual dimorphism of saccharin preference. *Pharmacol Biochem Behav* 23:439-444, 1985.

Lieblich, I.; Cohen, E.; Ganchrow, J.R.; Blass, E.M.; and Bergmann, F. Morphine tolerance in genetically selected rats induced by chronically elevated saccharine intake. *Science* 221:871-873, 1983.

Looy, H., and Weingarten, H.P. Facial expressions and genetic sensitivity to 6-n-propylthiouracil predict hedonic response to sweet. *Physiol Behav* 52:75-82, 1992.

Maone, T.R.; Mattes, R.D.; and Beauchamp, G.K. Cocaine-exposed newborns show an exaggerated sucking response to sucrose. *Physiol Behav* 51:487-491, 1992.

Mark, G.P.; Blander, D.S.; and Hoebel, B.G. A conditioned stimulus decreases extracellular dopamine in the nucleus accumbens after the development of a learned taste aversion. *Brain Res* 551:308-310, 1991.

Marks-Kaufman, R., and Lipeles, B.J. Patterns of nutrient selection in rats orally self-administering morphine. *Nutr Behav* 1:33-46, 1982.

Matsuo, T.; Shimakawa, K.; Ikeda, H.; and Suzuoki, Z. Relation of body energetic status to dietary self-selection in Sprague-Dawley rats. *J Nutr Sci Vitaminol* 30:255-264, 1984.

Mitchell, J.E.; Hatsukami, D.; Eckert, E.D.; and Pyle, R.L. Characteristics of 275 patients with bulimia. *Am J Psychiatry* 142:482-485, 1985.

Mitchell, J.E.; Pyle, R.L.; and Eckert, E.D. Frequency and duration of binge-eating episodes in patients with bulimia. *Am J Psychiatry* 138:835-836, 1981.

Mitchell, J.E.; Pyle, R.; Eckert, E.D.; and Hatsukami, D. The influence of prior alcohol and drug abuse problems on bulimia nervosa treatment outcome. *Addict Behav* 15:169-173, 1990.

Morabia, A.; Fabre, J.; Chee, E.; Zeger, S.; Orsat, E.; and Robert, A. Diet and opiate addiction: A quantitative assessment of the diet of non-institutionalized opiate addicts. *Br J Addict* 84:173-180, 1989.

Morley, J.E.; Levine, A.S.; and Rowland, N.E. Stress-induced eating. *Life Sci* 32:2169-2182, 1983.

Muscat, R., and Willner, P. Effects of dopamine receptor antagonists on sucrose consumption and preference. *Psychopharmacology* 99:98-102, 1989.

Nakajima, S. Subtypes of dopamine receptors involved in the mechanism of reinforcement. *Neurosci Biobehav Rev* 13:123-128, 1989.

Nichols, J.R., and Hsiao, S. Addiction liability of albino rats: Breeding for quantitative differences in morphine drinking. *Science* 157:561-563, 1967.

Overstreet, D.H.; Kampov-Polevoy, A.B.; Rezvani, A.H.; Murrelle, L.; Halikas, J.A.; and Janowsky, D.S. Saccharin intake predicts ethanol intake in genetically heterogeneous rats as well as different rat strains. *Alcohol Clin Exp Res* 17:366-369, 1993.

Pelchat, M.L., and Danowski, S. A possible genetic association between PROP-tasting and alcoholism. *Physiol Behav* 51:1261-1266, 1992.

Phillips, A.G., and Fibiger, H.C. Neuroanatomical bases of intracranial self-stimulation: Untangling the Gordian knot. In: Liebman, J.M., and Cooper, S.J., eds. *The Neuropharmacological Basis of Reward*. New York: Oxford University Press, 1989. pp. 66-105.

Piazza, P.V.; Deminière, J.M.; Le Moal, M.; and Simon, H. Factors that predict individual vulnerability to amphetamine self-administration. *Science* 245:1511-1513, 1989.

Piazza, P.V.; Deminière, J.M.; Le Moal, M.; and Simon, H. Stress- and pharmacologically-induced behavioral sensitization

increases vulnerability to acquisition of amphetamine self-administration. *Brain Res* 514:22-26, 1990.

Prasad, A.; Abadie, J.M.; and Prasad, C. Can dietary macronutrient preference profile serve as a predictor of voluntary alcohol consumption? *Alcohol* 10:485-489, 1993.

Pucilowski, O.; Overstreet, D.H.; Rezvani, A.H.; and Janowsky, D.S. Chronic mild stress-induced anhedonia: Greater effect in a genetic rat model of depression. *Physiol Behav* 54:1215-1220, 1993.

Reed, D.R.; Contreras, R.J.; Maggio, C.; Greenwood, M.R.C.; and Rodin, J. Weight cycling in female rats increases dietary fat selection and adiposity. *Physiol Behav* 42:389-395, 1988.

Reed, D.R.; Friedman, M.I.; and Tordoff, M.G. Experience with a macronutrient source influences subsequent macronutrient selection. *Appetite* 18:223-232, 1992.

Roane, D.S., and Martin, R.J. Continuous sucrose feeding decreases pain threshold and increases morphine potency. *Pharmacol Biochem Behav* 35:225-229, 1990.

Robinson, T.E. Persistent sensitizing effects of drugs on brain dopamine systems and behavior: Implications for addiction and relapse. In: Korenman, S.G., and Barchas, J.D., eds. *Biological Basis of Substance Abuse*. New York: Oxford University Press, 1993.
pp. 373-402.

Sanger, D.J., and McCarthy, P.S. Differential effects of morphine on food and water intake in food deprived and freely-feeding rats. *Psychopharmacology* 72:103-106, 1980.

Schechter, M.D. Rats bred for individual differences in preference to cocaine: Other behavioral measurements. *Pharmacol Biochem Behav* 43:1015-1021, 1992.

Segall, M.A., and Margules, D.M. Central mediation of naloxone-induced anorexia in the ventral tegmental area. *Behav Neurosci* 103:857-864, 1989.

Shaham, Y., and Stewart, J. Exposure to mild stress enhances the reinforcing efficacy of intravenous heroin self-administration in rats. *Psychopharmacology* 114:523-527, 1994.

Shaham, Y.; Alvares, K.; Nespor, S.M.; and Grunberg, N.E. Effects of stress on oral morphine and fentanyl self-administration in rats. *Pharmacol Biochem Behav* 41:615-619, 1992.

Sinclair, J.D.; Kampov-Polevoy, A.; Stewart, R.; and Li, T.K. Taste preferences in rat lines selected for low and high alcohol consumption. *Alcohol* 9:155-160, 1992.

Sinclair, J.D.; Lê, A.D.; and Kiianmaa, K. The AA and ANA rat lines, selected for differences in voluntary alcohol consumption. *Experientia* 45:798-805, 1989.

Stewart, R.B.; Russell, R.N.; Lumeng, L.; Li, T.-K.; and Murphy, J.M. Consumption of sweet, salty, sour, and bitter solutions by selectively bred alcohol-preferring and alcohol-nonpreferring lines of rats. *Alcohol Clin Exp Res* 18:375-381, 1994.

Suzuki, T.; George, F.R.; and Meisch, R.A. Differential establishment and maintenance of oral ethanol reinforced behavior in Lewis and Fischer 344 inbred rat strains. *J Pharmacol Exp Ther* 245:164-170, 1988.

Suzuki, T.; George, F.R.; and Meisch, R.A. Etonitazene delivered orally serves as reinforcer for Lewis but not Fischer 344 rats. *Pharmacol Biochem Behav* 42:579-586, 1992.

Valenstein, E.S. Selection of nutritive and nonnutritive solutions under different conditions of need. *J Comp Physiol Psych* 63:429-433, 1967.

Weatherford, S.C.; Greenberg, D.; Gibbs, J.; and Smith, G.P. The potency of D-1 and D-2 receptor antagonists is inversely related to the reward value of sham-fed corn oil and sucrose in rats. *Pharmacol Biochem Behav* 37:317-323, 1990.

Weiss, G. Food fantasies of incarcerated drug users. *Int J Addict* 17:905-912, 1982.

Weiss, F.; Lorang, M.T.; Bloom, F.E.; and Koob, G.F. Oral alcohol self-administration stimulates dopamine release in the rat nucleus accumbens: Genetic and motivational determinants. *J Pharmacol Exp Ther* 267:250-258, 1993.

Weiss, S.R., and Ebert, M.H. Psychological and behavioral characteristics of normal-weight bulimics and normal-weight controls. *Psychosom Med* 45:293-303, 1983.

Weltzin, T.E.; Hsu, L.K.G.; Pollice, C.; and Kaye, W.H. Feeding patterns in bulimia nervosa. *Biol Psychiatry* 30:1093-1110, 1991.

Willenbring, M.L.; Morley, J.E.; Krahn, D.D.; Carlson, G.A.; Levine, A.S.; and Shafer, R.B. Psychoneuroendocrine effects of methadone maintenance. *Psychoneuroendocrinology* 14:371-391, 1989.

Willner, P.; Towell, A.; Sampson, D.; Sophokleous, S.; and Muscat, R. Reduction of sucrose preference by chronic unpredictable mild stress, and its restoration by a tricyclic antidepressant. *Psychopharmacology* 93:358-364, 1987.

Wise, R.A. The role of reward pathways in the development of drug dependence. *Pharmacol Ther* 35:227-263, 1987.

Yung, L.; Gordis, E.; and Holt, J. Dietary choices and likelihood of abstinence among alcoholic patients in an outpatient clinic. *Drug Alcohol Depend* 12:355-362, 1983.

ACKNOWLEDGMENTS

Research in the authors' laboratory was supported by National Institute on Drug Abuse grant nos. DA05471, DA06827, and DA06791.

AUTHORS

Blake A. Gosnell, Ph.D.
Assistant Professor

Dean D. Krahn, M.D.
Associate Professor

Department of Psychiatry
University of Wisconsin-Madison
B6/210 Clinical Science Center
600 Highland Avenue
Madison, WI 53792

Click here
to go to
next section