Evidence from the present study supports a learning interpretation. In the intravenous experiment, the mean number of infusions increased by about 30 on each successive food-deprivation day, and this effect was even more pronounced (more than 100) in a subsequent replication of this experiment with cocaine (*13*). These increases are not explained by tolerance since there were no increasing trends in infusions (for either drug) on food-satiation days. Thus, the increase in drug intake on food-deprivation days may have been a result of the repeated pairing of food deprivation with the reinforcing effects of the drugs. There are also data from an extension (*16*) of the present oral etonitazene experiment showing more rapid increases in etonitazene intake as a result of repeated exposures to food deprivation and etonitazene access. At the end of phase 4, group E-FD was deprived of food a second time. Mean etonitazene intake increased to previous food deprivation levels within 1 or 2 days. By contrast, in phase 3 it initially took 17 days for etonitazene intake to reach maximum levels and stabilize.

Food deprivation is routinely used in many areas of behavioral research, including animal tests employed in the initial screening of psychoactive drugs to classify them and to evaluate their abuse liability. An implication of the present research is that food deprivation, and possibly other deprivational states, may have a substantial effect on the outcome of preclinical drug research, and this variable should be controlled in the design of such experiments. In more general terms, feeding condition or deprivational state appears to represent a major class of variables controlling drug-reinforced behavior in laboratory animals.

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References and Notes

1. W. S. Verplanck and J. R. Hayes, *J. Comp. Physiol. Psychol.* **46**, 327 (1958).
2. K. Oatley and D. A. Tonge, *Q. J. Exp. Psychol.* **21**, 162 (1969).
3. F. D. Scheffield and T. B. Roby, *J. Comp. Physiol. Psychol.* **43**, 471 (1950); M. Smith and M. Duffy, *ibid.* **50**, 65 (1957); S. R. Hursch and R. C. Beck, *Psychol. Rep.* **29**, 419 (1971).
4. J. Mendelson, *Physiol. Behav.* **5**, 1225 (1970).
5. J. Olds, *J. Comp. Physiol. Psychol.* **51**, 320 (1958); R. H. Carey, E. Goodall, S. A. Lorens, *ibid.* **88**, 224 (1975).
6. L. Paul, W. M. Miley, R. Baenninger, *ibid.* **76**, 242 (1971); J. B. Malik, *Physiol. Behav.* **14**, 171 (1975).
7. J. L. Falk, H. H. Samson, G. Winger, *Science* **177**, 811 (1972); J. D. Leander, D. E. McMillan, L. S. Harris, *J. Pharmacol. Exp. Ther.* **195**, 279 (1975); R. A. Meisch and L. J. Stark, *Pharmacol. Biochem. Behav.* **7**, 195 (1977).
8. R. A. Meisch and T. Thompson, *Psychopharmacologia* **28**, 171 (1973); *Pharmacol. Biochem. Behav.* **2**, 589 (1974).
9. A. Wikler, W. R. Martin, F. T. Pescor, C. G. Eades, *Psychopharmacologia* **5**, 55 (1963).
10. H. I. Chernov, F. G. Ambrose, A. J. Plummer, *Arch. Int. Pharmacodyn. Ther.* **175**, 309 (1968).
11. A. Randrup and J. Munkvad, *J. Psychiatr. Res.* **11**, 1 (1974); S. D. Iverson and L. L. Iverson, *Behavioral Pharmacology* (Oxford, New York, 1975), p. 275.
12. J. R. Weeks, in *Methods in Psychobiology*, R. D. Meyers, Ed. (Academic Press, New York, 1972).
13. M. E. Carroll, J. E. Henningfield, R. A. Meisch, paper presented at the Symposium on Substance Abuse: Behavioral Aspects, American Psychological Association Meeting, Toronto, August 1978.
14. M. E. Carroll and R. A. Meisch, paper presented at a conference entitled Technical Review on the Chemistry and Pharmacology of PCP and Its Analogues, sponsored by the Research Division of the National Institute on Drug Abuse, Rockville, Md., 14 to 15 March 1979.
15. W. J. Lang, A. A. Latiff, A. McQueen, G. Singer, *Pharmacol. Biochem. Behav.* **7**, 65 (1977); R. N. Takahashi, G. Singer, T. P. S. Oei, *ibid.* **9**, 857 (1978).
16. M. E. Carroll and R. A. Meisch, *ibid.* **10**, 155 (1979).
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Sucrose Consumption Early in Life Fails to Modify the Appetite of Adult Rats for Sweet Foods

Abstract. *Male rats consumed a diet containing 0, 12, or 48 percent sucrose on days 16 to 30 of life. Thereafter, they had simultaneous access to all three diets until day 63. No relationship was detected between sucrose consumption early in life and subsequent preference for sucrose. The onset of puberty was associated with a decreased appetite for sucrose among animals of both sexes.*

It is widely believed that the consumption of sucrose during infancy and early childhood is associated with a preference for sweet foods later in life. Although there is considerable evidence that a preference for sweet flavors can be detected in many mammals (including humans) during the first days of life (*1*), we are unaware of any published data concerning the effect of sucrose consumption by infants on their food preferences as adults. In the present report we examine the relationship between the amount of sucrose provided to nursing and immature rats and their elective consumption of sucrose later in life.

In order to choose the amounts of sucrose to include in the test diets and the ages at which to examine feeding behavior, we had first to characterize the ontogenesis of sucrose preference in our experimental animals (Sprague-Dawley rats; Charles River Breeding Laboratories). We therefore measured the quantities of sucrose consumed by male and female rats, from 21 to 63 days of age, given a choice of isocaloric diets with or without sucrose (*2*). On each day, food intake was measured and the position of the food cups was rotated. Sexual maturation was identified in males by the descent of the testes and in females by vaginal opening. The study was repeated three times.

Both male and female rats showed a significant preference for the sucrose-containing diet prior to sexual maturation (Table 1). The appearances of testicular descent (at days 37 to 38) and of spontaneous vaginal opening (at days 39 to 41) both coincided with marked decreases in elective sucrose consumption ($P < .001$) to levels that persisted for the duration of the experiments.

Earlier studies, in which the consumption of a saccharin solution as an index of preference for sweets was used, were interpreted as indicating that immature rats of both sexes reject sweet foods and that mature female rats have a greater

Table 1. Effect of age and sexual maturation on sucrose consumption by rats given choice of 0 and 24 percent sucrose diets. Male and female rats were housed singly at weaning and given access simultaneously to 0 and 24 percent sucrose diets. The diets were isocaloric and contained similar amounts of protein, fat, vitamins, and minerals (*2*). Food intake was measured daily. The percentage of sucrose consumed was determined by dividing the grams of sucrose (× 100) by the total grams of food consumed. Sexual maturation was noted by testicular descent (in a 36-hour period on days 37 to 38) and by spontaneous vaginal opening (days 39 to 41). Data are presented as means and standard errors of the mean.

Age (days)	Percentage of sucrose consumed	
	Male rats	Female rats
21 to 28	21 ± 1.2	22 ± 1.0
29 to 35	19 ± 1.9	21 ± 1.2
36 to 42	11 ± 0.5*	18 ± 1.9
43 to 49	12 ± 1.0	14 ± 0.7*
50 to 56	12 ± 1.7	15 ± 1.2
57 to 63	14 ± 2.2	14 ± 1.0

*$P < .001$ compared to prepubertal sucrose intake.

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Table 2. Relationship between sucrose consumption between days 16 and 30 of life and subsequent sucrose preference in rats. Male rats were given access to a diet containing 0, 12, or 48 percent sucrose at 16 to 30 days of age. Thereafter, they were allowed to choose among all three diets. Daily food consumption was measured until day 63. Sucrose consumption as the percentage of total food intake was determined by dividing the grams of sucrose eaten (× 100) by the total grams of food consumed. Data are presented as means and standard errors of the mean. During days 30 to 36, rats that had initially eaten 0, 12, or 48 percent sucrose consumed totals of 12 ± 0.5, 12 ± 0.6, or 12 ± 0.6 g of food (dry weight) per day, respectively. At all other intervals, until the end of the experiment, there continued to be no significant differences in the total quantities of food consumed daily by animals in the three experimental groups.

Preweaning diet (percent sucrose)	Percentage of sucrose consumed		
	Prepuberty (days 30 to 36)	Postpuberty	
		Days 37 to 40	Days 40 to 63
0	22 ± 3.1	7 ± 1.2*	13 ± 1.0†
12	24 ± 2.5	12 ± 1.1*	14 ± 0.7*
48	31 ± 2.8	9 ± 1.6*	14 ± 0.8*

*$P < .001$ compared to prepubertal sucrose intake. †$P < .01$ compared to prepubertal sucrose intake.

preference for sweet foods than do males (*3*). The discrepancy between our findings and these earlier studies might be explained by postulating that the effect of consuming a sweet constituent in food is different from the effect of consuming it in solution. Thus Mook found that adult rats that preferred a saccharin solution over water failed to exhibit a clear preference for a food flavored with the same concentration of saccharin (*4*). Alternatively, the difference between our results and those of earlier investigators may reflect the ability of sucrose to produce metabolic effects that are absent after saccharin consumption.

To examine this latter possibility, we gave immature male rats simultaneous access to a diet flavored with saccharin and a nonsweet diet or to a saccharin-containing diet and a sucrose-containing diet. In the first set of experiments, rats chose among three sucrose-free diets containing 0, 0.1, or 0.25 percent saccharin; in the second set, rats chose among a sucrose-containing (24 percent) diet and two sucrose-free diets containing 0 or 0.25 percent saccharin. Food intake was measured daily for 8 days. Rats failed to choose saccharin-containing over nonsweet diets; however, they did show a significant preference for the sucrose-containing diets over those containing saccharin: 58 ± 3.1 percent of the total food consumed was the sucrose-containing diet, 19 ± 1.7 percent was the 0.1 percent saccharin diet, and 23 ± 3.4 percent was the 0.25 percent saccharin diet.

These observations agree with findings that rats prefer solutions of sucrose over saccharin (*5*) and that the availability of a saccharin solution does not reduce subsequent sucrose consumption (*6*). Our results raise the possibility that the appetite of immature rats for sucrose (Table 1) reflects a desire for its metabolic and neurochemical consequences and not just for its sweet taste (*7*). Such consequences might include the insulin-mediated changes in plasma amino acid patterns and brain serotonin synthesis that follow consumption of particular carbohydrates (*8*). Crapo *et al.* found that the consumption by human volunteers of sucrose or starch elicited different plasma glucose and insulin patterns (*9*).

To examine the relationship between early postnatal sucrose consumption and subsequent preference for this sweet nutrient, we gave animals diets containing 0, 12, or 48 percent sucrose between days 16 and 30 of life and then examined their choice of food when given simultaneous access to all three diets between days 30 and 63. The separate experiments yielded similar results; data from one are described below. (Prior to day 16, dams had free access to Purina Rat Chow. The strain of animals that we used normally starts to consume solid food at day 16 of life.) Two litters, each containing a dam and eight male pups, were given access to each of the three test diets. All test diets were isocaloric and contained similar amounts of protein, fat, vitamins, and minerals. They were semisoft, and thus could be pushed through the grids covering the cage so that they were accessible to the pups as well as to the dams. On day 22, the animals were weaned, but pups from the same litter were kept together and continued to receive their particular test diets until day 30. Thereafter, they were housed in suspended cages that contained three food pans with each of the test diets.

No relationship was noted between the sucrose content of the diet consumed prior to day 30 and the amount of sucrose eaten thereafter, when animals had simultaneous access to the three diets (Table 2). As noted previously (Table 1), sucrose consumption declined with puberty; however, at no time was the elective sucrose intake of adults affected by the amount of sucrose they had consumed between days 16 and 30 (Table 2). These observations provide no support for the view that the consumption of sucrose-rich foods early in childhood causes prolonged increases in preference for sucrose.

These studies thus demonstrate (i) a preference for sucrose-containing diets among sexually immature male and female rats, (ii) a significant decrease in elective sucrose consumption coincident with the onset of puberty, (iii) that the change in sucrose preference with puberty may relate to the metabolic consequences of its consumption, and (iv) that the amount of sucrose consumed during the early postnatal period bears no clear relationship to the amount consumed electively during subsequent development and maturation.

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References and Notes

1. J. A. Desore, O. Mallor, R. E. Turner, *J. Comp. Physiol. Psychol.* **84**, 496 (1973); R. Nisbett and S. Gurwitz, *ibid.* **73**, 245 (1970); H. Jacobs, *Psychonom. Sci.* **1**, 195 (1964).
2. The diets contained 23 percent casein, 5 percent fat (Mazola oil), 2.2 percent Vitamin Mix (ICN Pharmaceuticals, Cleveland), and 4.0 percent Harper-Rogers Mineral Mix (Tekland Test Diets, Madison). One contained 24 percent sucrose, 24 percent dextrose, and 24 percent dextrin, while the other contained 24 percent dextrose, 48 percent dextrin, and no sucrose. Although dextrose is somewhat sweet, it is considerably less so, on a molar basis, than sucrose [G. H. Nowlis and W. Kessen, *Science* **191**, 865 (1976)], which also contains equal amounts of the highly sweet fructose.
3. I. Zucker, *Physiol. Behav.* **4**, 595 (1969); G. Wade and I. Zucker, *J. Comp. Physiol. Psychol.* **69**, 291 (1969); G. Wade, *Physiol. Behav.* **8**, 523 (1972); L. Hamilton and C. R. Timmons, *ibid.* **17**, 221 (1976).
4. D. Mook, *Psychol. Rev.* **81**, 475 (1974).
5. G. Collier and K. Novell, *J. Comp. Physiol. Psychol.* **64**, 404 (1967).
6. J. Kenney and R. Collier, *J. Nutr.* **106**, 388 (1976).
7. In support of this hypothesis, we have also observed that 45-day-old male rats given simultaneous access to diet pairs (for example, 25 versus 75 percent dextrin; 50 versus 75 percent sucrose) containing different proportions of dextrose, dextrin, or sucrose choose roughly equal total amounts of each carbohydrate, independently of whether it happens to be sweet or nonsweet [J. J. Wurtman and R. J. Wurtman, *Life Sci.* **24**, 895 (1979)].
8. J. D. Fernstrom and R. J. Wurtman, *Sci. Am.* **230**, 84 (Feb. 1974).
9. P. Crapo, G. Reaven, J. Olefsky, *Diabetes* **25**, 741 (1976).
10. We thank Dr. W. Rand for his statistical analysis of the data. These studies were supported in part by a grant from the National Institutes of Health; J.J.W. was supported in part by a postdoctoral fellowship from the U.S. Public Health Service.

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