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The Effects of Amphetamine and Chlorpromazine on Independent Ingestion of Milk in Preweanling Rats

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CAPUANO, C. A., G. A. BARR AND S. F. LEIBOWITZ. *The effects of amphetamine and chlorpromazine on independent ingestion of milk in preweanling rats.* PHARMACOL BIOCHEM BEHAV **33**(3) 567–572, 1989.—To assess the effects of catecholaminergic drugs on independent feeding during development, preweanling rats were administered amphetamine (AMPH) or chlorpromazine (CPZ) and were allowed to ingest milk through anteriorly located intra-oral cannulas. In 1-hr milk-deprived rat pups, AMPH stimulated milk intake at 3, 7 and 10 days of age and suppressed intake at 15 days. In 22-hr-deprived pups, AMPH had no effect at 3, 7 and 10 days, but reliably suppressed intake at 15 days. CPZ stimulated intake in 3-, 10- and 15-day-old milk-satiated pups. In 22-hr-deprived pups, CPZ had no effect at 3 and 10 days, but stimulated intake at 15 days. While AMPH produced pronounced nonappetitive behavioral activation in conjunction with enhanced intake in 1-hr-deprived pups, AMPH-induced activation occurred without enhanced intake in 22-hr-derived pups. Thus, there was a dissociation between AMPH's effect on milk intake and AMPH-induced nonappetitive behavioral activation. Collectively, the present results support the following conclusions. First, a catecholaminergic system(s) that enhances independent feeding is present very early in postnatal development of the rat. Second, level of food deprivation is an important state-dependent variable when assessing the effects of AMPH and CPZ on independent feeding in preweanling rats.

Ontogeny Catecholaminergic drugs Amphetamine Chlorpromazine Independent feeding
Food deprivation level Nonappetitive behavioral activation Development Preweanling rats

THE ontogeny of physiological mechanisms regulating feeding behavior has been a topic of much attention in recent years. Investigations examining the development of feeding behavior in the rat have provided evidence that in addition to the suckling system, there exists another form of ingestion in infant rats, ingestion independent of the mother. It has been argued that suckling, the primary form of ingestion in newborn mammals, and 'independent feeding,' ingestion away from the mother, differ with respect to: the motor pattern involved in appetitive responding; external controls; internal controls; experiential determinants; availability of food; and neural substrates (7,9). Moreover, in mediating ingestion of milk off the nipple, this independent feeding system in preweanling rats appears to be developmentally continuous with feeding in adult rats, and while it is not used by the infant during normal development, it does seem to represent an appropriate starting point for developmental analysis of adult feeding behavior in the rat (7–9).

Although it appears that the physiological mechanisms regulating independent feeding in preweanling rats serve as developmental precursors to those for adult feeding, they are not fully mature. This argument is supported by evidence suggesting that certain neural substrates mediating drug-induced suppression of feeding in the adult rat do not appear to be functionally mature until 2 weeks postpartum. Naloxone, an opiate antagonist, has been shown to suppress milk intake via suckling, self-feeding and intra-oral cannulas in 8-hr-deprived pups 14 and 19 days of age, but not in similarly deprived pups 3, 10 and 12 days of age (1). Cholecystokinin, a putative satiety peptide, has also been shown to suppress milk intake via tongue cannulas in 24-hr-deprived 15- and 20-day-old pups, but not in similarly deprived 5- and 10-day-old pups (2).

Studies of the neuropharmacology of feeding behavior have provided considerable evidence for the involvement of amines in the regulation of feeding in adult rats. Specifically, two separate ascending catecholaminergic systems have been identified (10,14). The first is a noradrenergic (and/or adrenergic) system that stimulates feeding through interaction with alpha-adrenergic receptors located in the medial (paraventricular) hypothalamic region and the second is a system that suppresses feeding through interaction with beta-adrenergic and dopaminergic receptors lo-

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cated in the lateral (perifornical) hypothalamic region.

Previous studies with amphetamine (AMPH), a catecholaminergic agonist, have shown AMPH to suppress independent ingestion of milk via intra-oral cannulas in deprived pups as young as 3 and 5 days of age (9,16). A more recent investigation has reported AMPH to suppress or enhance independent ingestion of milk in deprived 9-day-old pups as a function of dose, ambient temperature and method of milk presentation (18). Together, these findings suggest that both catecholaminergic systems may be functional in regulating independent ingestion of milk in infant rats. Yet, the organization of these systems in development is not clear.

The present study was undertaken to investigate further the changes in the organization of catecholaminergic regulation of feeding in the developing rat. In doing so, the effects of AMPH and chlorpromazine (CPZ) on independent ingestion of milk in preweanling rats were assessed. AMPH was chosen since it has been demonstrated to suppress feeding in adult rats following systemic administration on numerous occasions. Enhancement of feeding has also been reported with medial hypothalamic injection of AMPH, a finding that is in direct contrast with the anorectic effect produced by lateral hypothalamic injection of AMPH (13). CPZ was chosen since it has been shown to stimulate feeding in adult rats when administered either systemically (17) or centrally (10, 14, 15). Like AMPH, CPZ is believed to act via hypothalamic catecholaminergic systems (10,14).

GENERAL METHOD

Subjects

A total of 464 male and female offspring from 122 different litters of Long-Evans hooded rats, bred and reared in the laboratory colony, were used as subjects. Mothers were checked for birth twice daily, at 0800 and 1800 hr, and rat pups found at either of these times were designated 0 days of age. All litters were culled to a maximum of 10 pups three days after birth and were otherwise left undisturbed until the time of testing. Pups 3, 7, 10 and 15 days of age were used and each pup was tested only once at one of the four ages.

Apparatus and Procedure

On the day of testing, pups from the same litter were removed from their mother and placed individually in small, clear plastic containers ($10 \times 12.2 \times 12.7$ cm) that contained a small amount of the same type of bedding material (pine shavings) found within their litter cage. The individual containers were then secured within a water bath (Precision Scientific Co., Thelco Model 83) that maintained the ambient temperature within each container at 32–34°C throughout each individual test period. At this time, an intra-oral cannula was implanted in the anterior portion of the mouth of each pup (6). In doing so, a piece of polyethylene tubing (PE 10, Clay Adams) was flanged at one end by a flame and its other end was passed through the mouth of the unanaesthetized pup just behind the root of the lower incisors with the aid of a piece of 30-gauge needle that was cut and angled to approximately 45°. The free end of the cannula was then attached, through a larger piece of polyethylene tubing (PE 50, Clay Adams), to a 5 or 10 cc syringe that was placed in a dual infusion/withdrawal pump (Harvard Apparatus Co. Inc., Model 600-910). The pump infused milk continuously at rates of 0.6, 2.9, 2.9 and 4.5 cc per hr for 3-, 7-, 10- and 15-day-olds respectively. In each case, the rate of infusion was approximately equal to 10% of the pup's body weight per hr, which slightly exceeded intake. A continuous infusion was chosen as opposed to a pulsating infusion so that when pups were ready to eat milk was available. With a pulsating infusion, milk is restricted and when pups are ready to eat milk may not be available. The diet used for this study was commercially available Half-and-Half (milk and cream), which has certain similarities to rat's milk (6).

After voiding the pup's bladders by gently stroking their anogenital area with a moist Q-tip swab, the urogenital and anal openings were sealed with a drop of nonirritating self-curing acrylic (Silverman's) to minimize weight loss through excretion. The pups were then weighed and either milk-satiated for a 1-hr period by infusing milk at the appropriate rate or milk-deprived for a 1- or 22-hr period. Following the period of satiation or deprivation, the pups were reweighed and injected intraperitoneally with one dose of either d-AMPH sulfate (0.5, 1.0, 2.0 mg/kg salt weight), CPZ hydrochloride (0.5, 1.0, 2.0 mg/kg salt weight) or an equivalent volume (1 ml/100 g) of the 0.9% saline vehicle. Immediately following the injections, the pump was started and a continuous milk infusion was delivered for a 2-hr test period. In all cases, littermates were regarded as an experimental unit and thus received identical manipulations with the exception of the experimental conditions (IP injections).

Weight gain was used as a measure of milk ingested, since it has been shown that weight gain is a valid measure of intake in suckling rats (11). For each test, increases in body weight of the drug-injected pups were compared to that of their littermate given the saline vehicle.

Statistical Evaluation

Statistical analyses were performed on weight gain in grams and on its conversion to a percentage of postsatiation or postdeprivation weight for the data of Experiments 1 and 2. These data were evaluated for each experiment by an appropriate two-way (Age × Dose) factorial analysis of variance (ANOVA). Subsequently, post hoc comparisons were made using tests for simple main effects (12).

Statistical analyses were also performed on interval and cumulative weight gain and on interval and overall nonappetitive behavioral activity for the data of Experiment 3. These data were evaluated for this experiment by an appropriate two-way (Drug × Time Interval) factorial ANOVA.

EXPERIMENT 1: AMPHETAMINE FEEDING

In this first experiment, AMPH's effect on milk intake was assessed by measuring weight gain at the end of each individual test period. Both 1-hr and 22-hr deprivation periods were employed using 3-, 7-, 10- and 15-day-old pups.

Animals were deprived in this experiment in order to assess AMPH's suppressive effect on deprivation-induced feeding. Two levels of deprivation were used for comparison.

Results

Figure 1 shows weight gain for the 2-hr test period as a function of age, dose and deprivation level. In 1-hr-deprived pups, AMPH stimulated intake (as measured by weight gain in grams or its conversion to a percentage of postdeprivation weight) at 3, 7 and 10 days of age and suppressed intake at 15 days. Analysis of weight gain showed a significant age-effect, $F(3,32) = 36.15$, $p<0.001$, in grams, and, $F(3,32) = 15.65$, $p<0.001$, as percent; dose-effect, $F(3,96) = 3.34$, $p<0.05$, in grams, and, $F(3,96) = 3.73$, $p<0.05$, as percent; and age-by-dose interaction, $F(9,96) = 8.35$, $p<0.001$, in grams, and, $F(9,96) = 9.70$, $p<0.001$, as percent. Subsequent analyses for simple main effects (12) confirmed that AMPH significantly enhanced intake at 3 ($p<0.05$ in

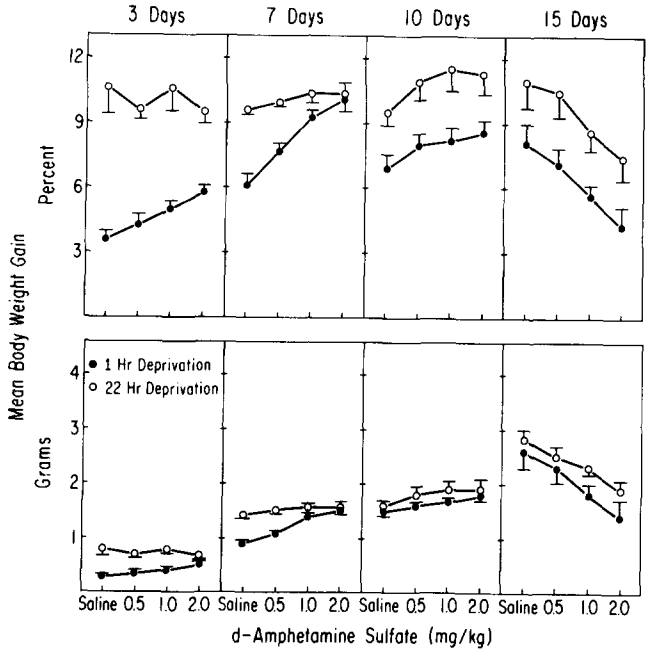

FIG. 1. Amphetamine's effect on milk intake as a function of age, dose and deprivation level. The bottom panel represents weight gain in grams for pups that received milk infusions through intra-oral cannulas during the 2-hr test period; the top panel represents its conversion to a percentage of postdeprivation weight. The error bars are one standard error of the mean.

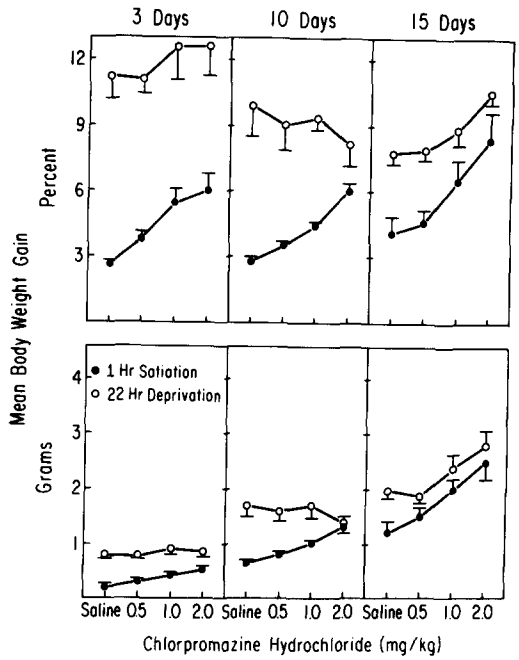

FIG. 2. Chlorpromazine's effect on milk intake as a function of age, dose and satiation or deprivation level. The bottom panel represents weight gain in grams for pups that received milk infusions through intra-oral cannulas during the 2-hr test period; the top panel represents its conversion to a percentage of postsatiation or postdeprivation weight. The error bars are one standard error of the mean.

grams and $p<0.001$ as percent), 7 ($p<0.001$ for both measures) and 10 days of age ($p<0.01$ in grams and $p<0.001$ as percent) and significantly suppressed intake at 15 days ($p<0.001$ for both measures).

In 22-hr-deprived pups, AMPH had no effect at 3, 7 and 10 days of age, but reliably suppressed intake at 15 days. Analysis of weight gain showed a significant age-effect, $F(3,24)=45.43$, $p<0.001$, in grams, and, $F(3,24)=3.04$, $p<0.05$, as percent; dose-effect, $F(3,72)=3.97$, $p<0.05$, in grams, and, $F(3,72)=3.59$, $p<0.05$, as percent; and age-by-dose interaction, $F(9,72)=4.44$, $p<0.001$, in grams, and, $F(9,72)=2.07$, $p<0.05$, as percent. Subsequent tests for simple main effects (12) confirmed that AMPH had no effect at 3, 7 and 10 days of age ($p>0.05$ for both measures), but significantly suppressed intake at 15 days ($p<0.001$ for both measures).

EXPERIMENT 2: CHLORPROMAZINE FEEDING

In this experiment, CPZ's effect on milk intake was assessed by measuring weight gain at the end of each individual test period. Both 1-hr satiation and 22-hr deprivation periods were employed using 3-, 10- and 15-day-old pups.

Animals were satiated in this experiment in order to clearly assess CPZ's stimulative effect on feeding. Severely deprived animals were tested for comparison.

Results

Weight gain for the 2-hr test period as a function of age, dose and satiation or deprivation level is depicted in Fig. 2. In 1-hr-satiated pups, CPZ stimulated intake (as measured by weight gain in grams or its conversion to a percentage of postsatiation weight) at 3, 10 and 15 days of age. Analysis of weight gain showed a significant age-effect, $F(2,21)=28.0$, $p<0.001$, in grams, and, $F(2,21)=3.48$, $p<0.05$, as percent; dose-effect, $F(3,63)=89.16$, $p<0.001$, in grams, and, $F(3,63)=47.04$, $p<0.001$, as percent; and age-by-dose interaction, $F(6,63)=11.67$, $p<0.001$, in grams, and, $F(6,63)=2.31$, $p<0.05$, as percent. Enhancement of intake by CPZ increased over age. Subsequent analyses for simple main effects (12) confirmed that CPZ significantly enhanced intake at 3, 10 and 15 days of age ($p<0.001$ for both measures).

In 22-hr-deprived pups, CPZ had no effect at 3 and 10 days of age, but stimulated intake at 15 days. Analysis of weight gain showed a significant age-effect, $F(2,19)=42.52$, $p<0.001$, in grams, and, $F(2,19)=6.03$, $p<0.01$, as percent; dose-effect, $F(3,57)=2.80$, $p<0.05$, in grams, and, $F(3,57)=2.86$, $p<0.05$, as percent; and age-by-dose interaction, $F(6,57)=3.14$, $p<0.01$, in grams, and, $F(6,57)=3.25$, $p<0.01$, as percent. Subsequent tests for simple main effects (12) confirmed that CPZ had no effect at 3 and 10 days of age ($p>0.05$ for both measures), but significantly enhanced intake at 15 days ($p<0.001$ in grams and $p<0.01$ as percent).

EXPERIMENT 3: AMPHETAMINE FEEDING AND ACTIVITY AS A FUNCTION OF TIME

In this final experiment, AMPH's effect on milk intake was more closely examined by measuring weight gain at 10- and 20-min intervals throughout each individual test period. In addition, AMPH's effect on nonappetitive behavioral activity was also recorded and scored for each individual test period.

As detailed elsewhere (6), the frequencies of 14 behaviors (probing, rooting, rolling over, curling, reaching into the air, walling, crawling, burrowing, climbing, grooming, posturing,

TABLE 1

AMPHETAMINE'S EFFECT ON MILK INTAKE AS A FUNCTION OF TIME AND DEPRIVATION LEVEL

	Time Interval (min)							
	0–10	10–20	20–40	40–60	60–80	80–100	100–120	0–120
1 Hr Deprivation								
Saline	0.28 ± 0.04	0.11 ± 0.03	0.13 ± 0.03	0.16 ± 0.02	0.08 ± 0.03	0.10 ± 0.04	0.04 ± 0.02	0.91 ± 0.13
d-Amphetamine Sulfate (1 mg/kg)	0.46 ± 0.04	0.23 ± 0.05	0.21 ± 0.02	0.19 ± 0.03	0.08 ± 0.02	0.11 ± 0.03	0.10 ± 0.03	1.38 ± 0.11
22 Hr Deprivation								
Saline	0.34 ± 0.01	0.29 ± 0.01	0.24 ± 0.01	0.23 ± 0.01	0.16 ± 0.00	0.13 ± 0.00	0.07 ± 0.00	1.46 ± 0.03
d-Amphetamine Sulfate (1 mg/kg)	0.36 ± 0.01	0.31 ± 0.01	0.24 ± 0.01	0.23 ± 0.01	0.17 ± 0.00	0.14 ± 0.01	0.07 ± 0.01	1.54 ± 0.02

Entries in the body of the table are mean ± SEM body weight gain in grams for 1- and 22-hr-deprived 7-day-old pups that received milk infusions via intra-oral cannulas during the 2-hr test period. Entries for 0–120 min represent cumulative weight gain for the 2-hr test period. The most pronounced amphetamine-enhanced intake occurred during the first 40 min of the test period for 1-, but not 22-hr-deprived pups.

twitching, tail flicking and stretching) were recorded for 20-min intervals and each interval was scored according to seven behavioral categories that ranged from an activity score of 0 (no movement except for occasional twitches) to an activity score of 6 (extreme, vigorous locomotion). CPZ's effect on nonappetitive behavioral activity was similarly examined. Only two experimental conditions [AMPH (1 mg/kg) vs. saline vehicle] were used in this final experiment with 1- and 22-hr-deprived 7-day-old pups tested. This age group was chosen since significant enhancement of intake by AMPH occurred at 7 days of age for 1-hr, but not 22-hr-deprived pups in Experiment 1. Furthermore, behavioral activity in 7- vs. 3-day-old pups is easier to assess, thus making a dissociation between AMPH-enhanced intake and AMPH-induced nonappetitive behavioral activation easier to discern.

Results

Intake. Table 1 presents the data for AMPH's effect on milk intake as a function of time and deprivation level. In verification of the results of Experiment 1, AMPH stimulated intake in 1-, but not 22-hr-deprived 7-day-old pups. Analysis of weight gain revealed a significant drug-effect, $F(1,12)=7.82$, $p<0.05$; time-effect, $F(6,72)=27.54$, $p<0.001$; and drug-by-time interaction, $F(6,72)=2.42$, $p<0.05$, for the data of 1-hr-deprived 7-day-olds. Closer inspection of the data indicates that the most pronounced AMPH-enhanced intake occurred during the first 40 min of the test period.

For 22-hr-deprived 7-day-olds, analysis of weight gain revealed no drug-effect, $F(1,8)=3.54$, $p>0.05$; a significant time-effect, $F(6,48)=344.56$, $p<0.001$; and no drug-by-time interaction, $F(6,48)=0.76$, $p>0.05$.

Activity. Nonappetitive behavioral activity as a function of time and deprivation level was scored as a composite of seven behavioral categories [see (6) for details regarding scoring procedure]. AMPH produced nonappetitive behavioral activation in both 1- and 22-hr-deprived 7-day-old pups (Table 2). Analysis of behavioral activity revealed a significant drug-effect, $F(1,12)=199.18$, $p<0.001$; time-effect, $F(5,60)=3.97$, $p<0.01$; and drug-by-time interaction, $F(5,60)=13.40$, $p<0.001$, for the data of 1-hr-deprived 7-day-olds. The same results were obtained for 22-hr-deprived 7-day-olds [drug-effect, $F(1,8)=118.5$, $p<0.001$; time-effect, $F(5,40)=5.74$, $p<0.001$; drug-by-time interaction, $F(5,40)=8.32$, $p<0.001$]. Inspection of the data indicates that AMPH produced pronounced nonappetitive behavioral activation during the first 100 min of the test period for both 1- and 22-hr-deprived pups.

CPZ did not produce any observable nonappetitive behavioral activation in 1- or 22-hr-deprived 7-day-old pups. Therefore, nonappetitive behavioral activity was not scored for these animals.

GENERAL DISCUSSION

The results of this study show stimulation of milk intake by AMPH and CPZ in mildly milk-deprived (1 hr) and milk-satiated rat pups as young as 3 days of age. By 15 days, AMPH began to exert its well-known anorectic effect. In addition, severe milk deprivation (22 hr) disrupted both AMPH- and CPZ-induced stimulation of intake at ages earlier than 15 days postpartum, but did not alter AMPH anorexia or CPZ-induced stimulation of intake at 15 days. The present results suggest that a catecholaminergic system(s) that enhances independent feeding is present very early in postnatal development of the rat.

In discussing the results in relation to behavioral activity, it is possible that stimulation of milk intake by AMPH may have been a direct result of the pronounced AMPH-induced activation of nonappetitive behavior depicted in Table 2. However, this possibility appears to be unlikely in light of the finding that severely deprived pups, who also showed pronounced AMPH-induced nonappetitive behavioral activation, failed to exhibit any enhancement of intake. The stimulative effect of CPZ on intake also occurred without any pronounced CPZ-induced nonappetitive behavioral activation. Thus, while a link between nonappetitive behavioral activation and increased intake may exist, increased activation does not necessarily lead to increased intake. Furthermore, a dissociation between AMPH's effect on milk intake and AMPH-induced nonappetitive behavioral activation has also recently been reported in 24-hr-deprived 9-day-old pups (18).

The possibility that AMPH and CPZ failed to enhance intake in young, severely deprived pups due to a ceiling effect is apparent in that perhaps no further drug-induced intake was able to occur. In regard to this possibility, a more recent investigation in our laboratory has shown stimulation of milk intake in 22-hr-deprived pups at 2 days of age following direct administration of epinephrine, a catecholaminergic agonist, into the anterolateral hypothalamus (3,4). The data from this study showed a significant increase in intake (mean = 7.4%; $p<0.01$) for the group having received

TABLE 2

AMPHETAMINE'S EFFECT ON NONAPPETITIVE BEHAVIORAL ACTIVITY AS A FUNCTION OF TIME AND DEPRIVATION LEVEL

	Time Interval (min)						
	0–20	20–40	40–60	60–80	80–100	100–120	0–120
1 Hr Deprivation							
Saline	1.7 ± 0.3	2.0 ± 0.3	2.0 ± 0.2	3.0 ± 0.0	2.6 ± 0.4	2.7 ± 0.3	2.4 ± 0.1
d-Amphetamine Sulfate (1 mg/kg)	5.1 ± 0.1	5.1 ± 0.1	5.1 ± 0.1	4.7 ± 0.2	3.6 ± 0.4	3.1 ± 0.3	4.5 ± 0.2
22 Hr Deprivation							
Saline	2.4 ± 0.2	2.6 ± 0.2	2.6 ± 0.2	3.2 ± 0.2	2.8 ± 0.5	2.8 ± 0.4	2.7 ± 0.1
d-Amphetamine Sulfate (1 mg/kg)	5.6 ± 0.2	5.6 ± 0.2	5.4 ± 0.2	4.8 ± 0.2	3.6 ± 0.5	2.8 ± 0.4	4.6 ± 0.1

Entries in the body of the table are mean ± SEM activity scores for 1- and 22-hr-deprived 7-day-old pups that received milk infusions via intra-oral cannulas during the 2-hr test period. Entries for 0–120 min represent overall activity scores for the 2-hr test period. Amphetamine produced pronounced nonappetitive behavioral activation during the first 100 min of the test period for both 1- and 22-hr-deprived pups.

the highest dose tested relative to the control group (mean = 6.9%) following a 1-hr period of continuous milk infusion. As indicated, this study employed a 1-hr test period. Pilot data from the present study showed percent intake ranging from 6.7 to 6.9% across all conditions following 1 hr of milk infusion. These findings suggest that young pups are not necessarily at ceiling following this level of milk deprivation and 1 hr of continuous milk infusion. That is, they are able to consume more milk following drug stimulation. Unfortunately, we do not have 2-hr data from our central administration studies. Thus, within the limitations discussed above, these findings support the view that severe milk deprivation disrupts both AMPH- and CPZ-induced stimulation of milk intake in pups at ages prior to 15 days postpartum.

As summarized previously, studies have shown that AMPH suppresses intake via independent ingestion in severely deprived pups at early ages (9,16). The present results suggest that AMPH and CPZ stimulate intake in young, mildly deprived and satiated pups, but that severe deprivation disrupts AMPH- and CPZ-induced stimulation of intake prior to 15 days of age. Together, these findings suggest that level of food deprivation is an important state-dependent variable in assessing the effects of AMPH and CPZ on intake via independent ingestion in preweanling rats prior to 15 days postpartum. In contrast, by 15 days, the effects of AMPH and CPZ on intake do not appear to be as sensitive to deprivation level as they do prior to this age. Alternatively, 22–24-hr deprivation may not be as severe for rat pups 15 days or older as it appears to be for pups younger than this age.

Variables other than deprivation level may also play a significant role in assessing AMPH's effect on independent feeding. Recently, both AMPH-induced stimulation and suppression of intake have been reported in 24-hr-deprived 9-day-old pups (18). AMPH's effect was found to vary with drug dose, ambient temperature and method of milk presentation. Methodological differences such as these suggest that deprivation level may be only one of several variables that influence the effects of AMPH and perhaps other catecholaminergic drugs on independent feeding in preweanling rats.

In review of present and previous results, the evidence also suggests that co-existing catecholaminergic systems mediating stimulation and suppression of intake via independent ingestion are functional very early in development. This view is further supported by results showing an early onset of catecholaminergic regulation of feeding in rats as demonstrated by hypothalamic administration of catecholaminergic drugs (3–5). In addition, while independent feeding in preweanling rats appears to be developmentally continuous with adult feeding (7–9), it is not fully mature, as indicated by differences in deprivation level and pharmacological effects prior to and after 15 days of age when the preweanling rat begins to acquire independent, adult ingestive controls.

In summary, there is considerable evidence that AMPH and CPZ exert their effects on feeding in the adult rat through two separate ascending catecholaminergic systems that innervate the hypothalamus (10,14). Earlier studies have indicated that these systems may reach functional maturity at very early ages in development (9,16). The present results of deprivation-dependent AMPH and CPZ effects on independent feeding in preweanling rats prior to 15 days of age support this hypothesis and may also provide a model for studying the functional maturity of catecholaminergic systems as well as other neurochemical systems regulating independent feeding in the developing rat.

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