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The 5-HT_{1A} Agonist 8-OH-DPAT Increases Attachment Maintenance but Decreases Suckling-Related Intake in 17–18-Day-Old Rat Pups

LINDA PATIA SPEAR,[1] NANCY A. FRAMBES, GREGORY A. GOODWIN AND CAROLE A. MOODY

Department of Psychology and Center for Developmental Psychobiology, Binghamton University, State University of New York, Binghamton, NY 13902-6000

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SPEAR, L. P., N. A. FRAMBES, G. A. GOODWIN AND C. A. MOODY. *The 5-HT_{1A} agonist 8-OH-DPAT increases attachment maintenance but decreases suckling-related intake in 17–18-day-old rat pups.* PHARMACOL BIOCHEM BEHAV 47(1) 133–139, 1994.—Deprived and nondeprived preweanling (17–18 days of age) Sprague–Dawley rat pups were injected with 0, 0.03, 0.06, 0.1, or 0.5 mg/kg of the 5-HT_{1A} agonist 8-hydroxy-2-(di-*n*-propylamino)tetralin (8-OH-DPAT) and observed in a suckling test using a milk replete anesthetized dam, with milk let-downs being intermittently precipitated via IV infusions of oxytocin. In experiment 1, the 0.5 mg/kg dose of 8-OH-DPAT was observed to increase the proportion of nondeprived animals which attached to a nipple; no dose effect was seen in deprived animals, who generally all attached. Deprived pups given the 0.5-mg/kg dose exhibited a lower frequency of nipple disattachment/reattachment following milk let-downs and had significantly lower percent body weight gains when compared with saline controls. In experiment 2a, the 0.5-mg/kg dose of 8-OH-DPAT was observed to decrease the overall incidence of nipple disattachment/reattachment as well as to suppress nipple shifting per se in both deprived and nondeprived 17–18-day-old rat pups; this dose also suppressed body weight gains in both the deprived and nondeprived pups. The suppression in weight gain by 8-OH-DPAT does not appear to be primarily related to a drug-induced reduction in nipple shifting. In experiment 2b, where pups were given access to only one nipple, an 8-OH-DPAT-related reduction in body weight gain was still evident. These experiments, which demonstrate that attachment maintenance and suckling ingestion are altered in opposite ways by 8-OH-DPAT, provide strong evidence that these two suckling-related phenomena are subject to different physiological controls.

8-OH-DPAT 5-HT_{1A} agonist Ontogeny Suckling Intake Nipple shifting Suckling maintenance

THE serotonergic (5-HT) system has been implicated not only in the control of ingestion in adulthood [e.g., see (1)], but also in the control of suckling as well as suckling-independent ingestion throughout the neonatal to weanling age period (7,9,11,12,15,19). For instance, low doses (0.03–1.0 mg/kg) of the 5-HT_{1A} agonist 8-hydroxy-2-(di-*n*-propylamino)tetralin (8-OH-DPAT) (18) have been reported to increase oral movements and ingestion in adulthood, presumably due to the selective stimulation of 5-HT_{1A} autoreceptors located on the cell bodies of serotonergic neurons (6,8). Higher doses have been reported to stimulate both 5-HT_{1A} autoreceptors as well as postsynaptic 5-HT_{1A} receptors; stimulation of these postsynaptic receptors typically induces the "serotonergic syndrome," which may compete with ingestion, sometimes to the point of decreasing ingestion below control levels (4,5). In ontogenetic studies in which rat pups were tested for suckling-independent ingestion by giving isolated pups access to both mash and liquid diets, both a low dose stimulatory effect and a high dose suppressant effect of 8-OH-DPAT on mash-related ingestive behaviors were observed in late preweanling (17–18-day-old) and postweanling (28–29-day-old) animals (16), findings reminiscent of those reported in adulthood (4,5,6,8). However, there was a marked ontogenetic shift in the dose–response curve to 8-OH-DPAT, with late preweanling pups exhibiting greater sensitivity to the drug than postweanlings. In contrast, only a suppressant effect on milk-related mouthing and ingestion was observed following a wide range of doses of 8-OH-DPAT when administered to neonatal (3–4-day-old) rat pups

[1] Requests for reprints should be addressed to Linda Spear, Department of Psychology, Box 6000, Binghamton University, State University of New York, Binghamton, NY 13902-6000.

(16), data suggesting the possibility that 5-HT_{1A} autoreceptors may not be functionally active in the control of ingestion early in life.

The effects of 5-HT_{1A} receptor stimulation on ingestion and ingestion-related behaviors previously have not been examined in a suckling situation, although the 5-HT system has been implicated in the control of suckling throughout the neonatal to weanling age period, with the 5-HT system apparently facilitating suckling maintenance early in life [e.g., see (15) for review] but conversely inhibiting suckling during the weaning process (15,19). Little is known regarding the role of different 5-HT subtypes in the ontogenetic transitions seen in the 5-HT modulation of suckling during the neonatal to weanling age period. There is substantial evidence to suggest that suckling and ingestion independent of the dam are not homologous behaviors [see (10) for review]. Early forms of independent ingestion appear to be a precursor of later adult ingestion, whereas suckling seems to be a behavior unique to infancy and for the sole purpose of infantile consumption (10). Indeed, the physiological controls of these two forms of ingestion appear to differ significantly throughout the preweanling period [see (10) for review]. Consequently, the purpose of the present experiments was to determine whether 8-OH-DPAT would influence body weight gain and ingestion-related behaviors in late preweanling rat pups ingesting milk in a suckling situation in a manner similar to that previously observed in testing of ingestion independent of the dam.

EXPERIMENT 1

In this study, the effects of the 5-HT_{1A} agonist 8-OH-DPAT on ingestion and ingestion-related behaviors was examined in 17–18-day-old rat pups, using the same dose range of 8-OH-DPAT that was previously found to reveal both low dose stimulatory and high dose inhibitory effects on ingestion independent of the dams in animals of this age (16).

Methods

Subjects were 80 male and female rat pups derived from established Charles River Sprague–Dawley (CD-COBS) breeding pairs in our colony room. Animals were tested on postnatal day 17-18 (P17-18) with the day of birth being designated as P0. Only litters containing 8–10 pups after culling were used in this study. All pups were housed with parents and littermates in a colony room maintained on a 12/12 light/dark cycle with lights on at 0700.

Six hours prior to testing (at 0700), nonexperimental pups were removed from two maternal test dams (postpartum day 5–20) to allow for milk repletion in these dams. These dams were anesthetized 30 min before testing via an IM injection of 0.5 ml/kg of a ketamine–xylazine mixture (18 mg xylazine in 1 ml of a 100 mg ketamine solution) and were given supplemental doses of the mixture as necessary to maintain levels of anesthesia during the 1-h test. Following anesthetization, each dam was implanted with an IV cannula in the lateral vein of the tail for administration of oxytocin to precipitate milk let-downs during the suckling test [e.g., see (17)] and subsequently placed in a testing apparatus consisting of a clear Plexiglas cage (48 × 26 cm) with a layer of clean shavings on the floor. A clear Plexiglas divider was used to allow the tail of the dam to be placed in a portion of the cage where the pups could not disturb the cannula. Each test dam was placed in a supine position with both nipple lines exposed.

Five hours prior to testing, half of the pups in each test litter (deprived pups) were removed from the dam and placed together in a holding apparatus maintained at 32°C (± 1°C) by a heating pad. During this period of time the pups were deprived of the dam and food but allowed access to water via a drinking tube. The remaining pups in each test litter (nondeprived pups) remained with the dam until testing, except for weighing and voiding. One hour prior to testing, all of the animals from the litter were voided via gentle stroking of the anogenital region with a dampened cotton swab. All animals were weighed immediately before the onset of testing.

At the time of testing, one pup from each deprivation condition was injected SC with 0 (0.9% saline), 0.03, 0.06, 0.1, or 0.5 mg/kg/5 ml of 8-OH-DPAT (Research Biochemicals, Inc) given in a volume of 5 ml/kg. Immediately following injection, five pups were placed with each dam, with one saline animal and at least two animals from each deprivation condition in each set of five animals. The latency to attach to a nipple was recorded for each pup. Beginning 10 min after the onset of the test session, and every 5 min thereafter for a total duration of 60 min (10 milk let-downs), 0.0015 IU oxytocin was delivered in a volume of 0.10 ml/infusion. During the 5-min period beginning at the onset of each milk let-down, each pup was observed for the presence or absence of a stretch response and/or nipple-switching behavior. In addition, instances of "activation" on the nipple were also recorded during each 5-min test period; this response was characterized by a sudden tugging at the nipple while simultaneously exhibiting forepaw treading of the dam's ventrum, as well as hindpaw paddling.

At the end of testing, all pups were weighed and the percent body weight gain calculated. Data were discarded for any group of test pups in which none of the pups gained more than 2% body weight, suggesting that the mother may have had an inadequate supply of milk [see (17)]. The final sample sizes consisted of eight pups in each test condition, with only one pup per litter being assigned to each of the 5 (Drug Dose) × 2 (Deprivation) test conditions. Experimenters conducting the testing were not informed as to the contents of any given test solution.

Results

Only in two cases was the weight gain in a group of test pups less than 2% per pup; these data were discarded from the analyses.

Frequency of attachment. The percentage of animals attaching in each group was calculated and analyzed via a chi-square analysis. This analysis revealed significant differences, $\chi^2(4, 80) = 17.13$, $p \leq .01$. Simple chi-square analyses revealed that a significantly greater proportion of nondeprived pups given a dose of 0.06 or 0.5 mg/kg attached when compared with nondeprived saline controls, 0.06 mg/kg vs. saline: $\chi^2(1) = 10.22$, $p < .01$; 0.5 mg/kg vs. saline: $\chi^2(1) = 16.66$, $p < .01$]. As can be seen in Fig. 1, whereas generally all deprived pups attached, only half of the nondeprived saline animals attached, with the higher doses of 8-OH-DPAT increasing attachment frequency. Due to the limited number of nondeprived saline animals that attached during the suckling test, the remaining data were analyzed only in deprived animals using a one-way analysis of variance (ANOVA) across dose, with Dunnett's tests used for post hoc comparisons across dose.

Disattachment and reattachment (nipple shifting). The ANOVA on the data for the total number of times that each pup disattached and reattached to nipples revealed a significant dose effect, $F(4, 35) = 2.761$, $p < .05$. Dunnett's test

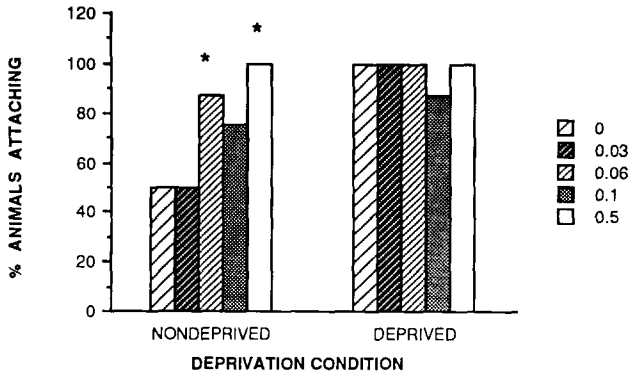

FIG. 1. Percentage of nondeprived and deprived preweanling rat pups that attached to a nipple during a suckling test following administration of various doses of 8-OH-DPAT in experiment 1.

revealed that animals given 0.5 mg/kg 8-OH-DPAT exhibited significantly less disattachment and reattachment than saline controls, as can be seen in Fig. 2A. When these data were separately analyzed for nipple shifting (attachment to a different nipple) as well as reattachment to the same nipple, dose effects approached but did not reach significance. As can be seen in Figs. 2B and C, a trend for a dose-related decrease in both of these attachment-related behaviors was observed.

Other behaviors. ANOVAs of attachment latency and frequency of "activation" and stretch responses revealed no significant effects of dose.

Percent body weight gain. A one-way ANOVA of percent body weight gain in deprived rats revealed a significant effect of dose, $F(4, 34) = 3.370$, $p < .05$. Dunnett's tests showed that animals given 0.5 mg/kg 8-OH-DPAT gained significantly less weight than did saline controls, as shown in Fig. 3.

Discussion

In this experiment, the 5-HT_{1A} agonist 8-OH-DPAT was observed to increase the probability of attachment in nondeprived 17–18-day-old pups and to increase attachment maintenance (i.e., decrease the rate of nipple disattachment and reattachment) in deprived pups at this age. In contrast to this facilitation of attachment and attachment maintenance by the drug, 8-OH-DPAT suppressed suckling intake as indexed by body weight gains in deprived pups of this age.

From the results of this study, it is not clear whether 8-OH-DPAT would also suppress nipple disattachment and reattachment and alter weight gain in nondeprived pups, as many nondeprived pups did not attach (other than those given the higher doses of 8-OH-DPAT). For this reason, experiment 2a was conducted to extend these findings, using sample sizes sufficient to allow for assessment of the effects of 8-OH-DPAT on suckling-related behaviors and intake in nondeprived as well as deprived animals.

One of the major ways that older preweanling rat pups regulate intake during suckling is via nipple shifting, which allows the pup to obtain a greater volume of milk by consuming milk stores available from nonsuckled nipples (3). Given that 8-OH-DPAT induced a dose-dependent decrease in nipple disattachment/reattachment in deprived pups, it is possible that it is primarily by this means that 8-OH-DPAT decreases ingestion during suckling in these animals. This possibility was addressed in experiment 2b.

EXPERIMENT 2

To explore further the findings of experiment 1, in experiment 2a both deprived and nondeprived 17–18-day-old rat pups were given doses of 0, 0.05, 0.1, and 0.5 mg/kg 8-OH-DPAT and tested in a manner identical to experiment 1, with the constraint that sample sizes were increased as necessary to insure that data from at least eight pups that attached during the suckling test were obtained within each combination of drug and deprivation condition. In experiment 2b, deprived 17–18-day-old rat pups were given either saline or 0.5 mg/kg prior to a suckling test in which only a single nipple was available. If the suppression in ingestion induced by 8-OH-DPAT is a result of a drug-induced decline in nipple shift-

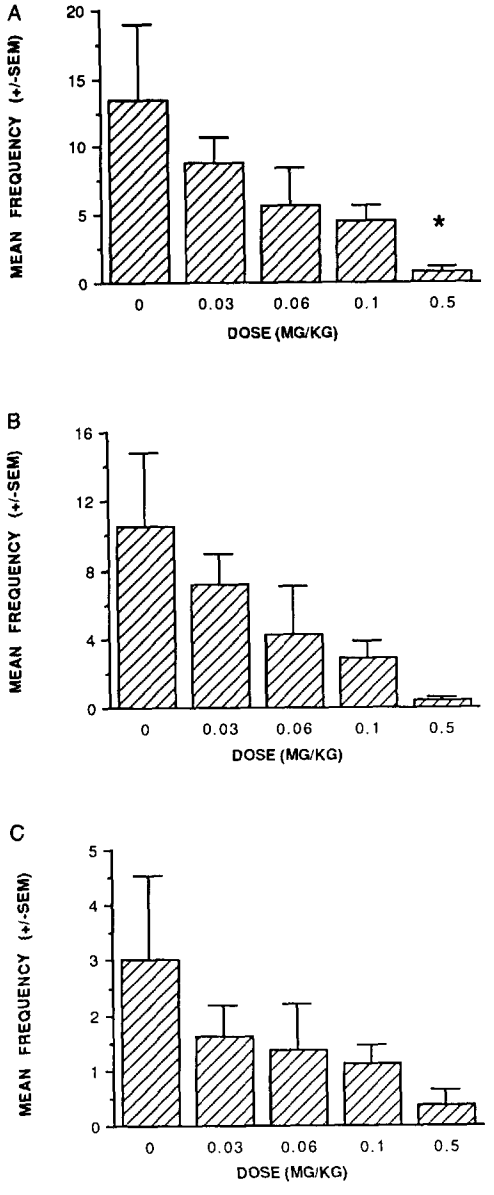

FIG. 2. Mean frequency of (A) nipple disattachment and reattachment, (B) nipple shifting, and (C) reattachment to the same nipple during a suckling test of deprived preweanling rat pups following administration of various doses of 8-OH-DPAT in experiment 1.

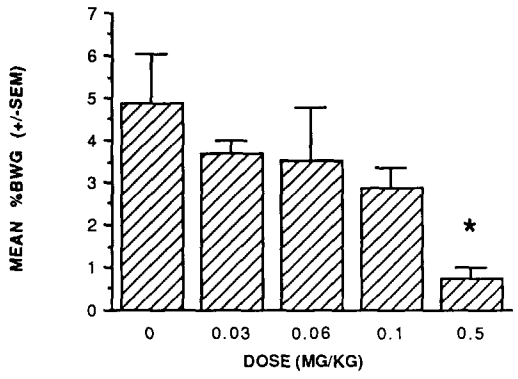

FIG. 3. Mean percent body weight gain (BWG) during a suckling test of deprived preweanling rat pups following administration of various doses of 8-OH-DPAT in experiment 1.

ing, then saline- and 8-OH-DPAT-treated pups should show similar intakes when restricted to only a single nipple during testing.

Methods

Experiment 2a. Subjects were 82 male and female 17–18-day-old rat pups derived from established Charles River (Wilmington, MA) Sprague–Dawley (CD-COBS-VAF) breeding pairs. The procedure used to prepare the dams and pups for testing were identical to those used in experiment 1 except that six pups were deprived 5 h prior to testing and four pups were left with their dam until test onset. At the time of testing, one pup from each deprivation condition was injected SC with 0 (0.9% saline), 0.05, 0.1, or 0.5 mg/kg/5 ml of 8-OH-DPAT (Research Biochemicals, Inc., Natick, MA). Two pups from the deprived group and two pups from the nondeprived group were placed with each stimulus dam and behavioral measures recorded in the same manner as in experiment 1 with the addition of one behavioral measure—time spent attached. The remaining two deprived pups in each litter were tested in experiment 2b.

Experiment 2b. Subjects were 19 deprived 17–18-day-old rat pups derived as outlined above. To determine whether the decrease in nipple shifting was responsible for the decrease in weight gain seen at the highest dose of 8-OH-DPAT, the two remaining deprived pups from each litter as described in experiment 2a were given access to only one teat so that nipple shifting could not occur. Dams were prepared in exactly the same manner as those in experiment 1, and in addition had all but two teats covered with gauze. A Plexiglas partition was placed against the dam's body such that one teat was exposed on each side of the partition. One deprived pup was placed on each side of the partition immediately after receiving an injection of either saline or 0.5 mg/kg 8-OH-DPAT. The same behavioral measures were taken from each pup as in experiment 1 with the exception that, of course, the pups had no opportunity to demonstrate nipple shifting. In addition, the time spent attached by each pup during the test session was recorded. The inclusion criterion of 2% minimal weight gain was not used in this experiment, as preliminary findings revealed that pups spent substantially less time attached in this test situation than in the more typical suckling test situation where groups of pups are tested simultaneously with multiple available nipples.

Results

Experiment 2a. In no instance was the weight gain in a group of test pups less than 2%; hence, data from all test groups were included in the data analysis.

Frequency of attachment. A chi-squared analysis on the percentage of animals attaching in each group revealed no significant differences. All deprived animals attached during the suckling test, and percentage of nondeprived animals who attached was also high in all groups (saline: 80%; 0.05 mg/kg: 100%; 0.1 mg/kg: 82%; 0.5 mg/kg: 100%). Pups that did not attach during the test were eliminated from further data analysis. Final sample sizes after eliminating pups that did not attach ranged from 8 to 11 pups for each of the eight (4 [Dose] × 2 [Deprivation]) test conditions.

Disattachment and reattachment (nipple shifting). A 2 (Deprivation Condition) × 4 (Dose) ANOVA on the data for the total number of times that each pup disattached and reattached to nipples revealed a significant dose effect, $F(3, 67) = 6.675$, $p < .001$, but no main effect or interaction involving deprivation condition. Dunnett's tests revealed that pups given the 0.5 mg/kg dose of 8-OH-DPAT disattached and reattached to nipples significantly less often than control ani-

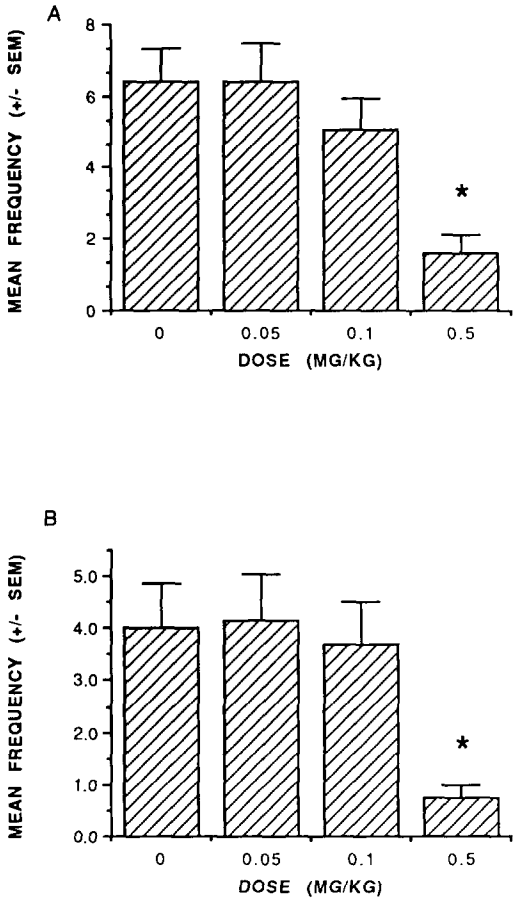

FIG. 4. Mean frequency of (A) nipple disattachment and reattachment and (B) nipple shifting following administration of various doses of 8-OH-DPAT in experiment 2a.

mals (see Fig. 4A). When the data were separately analyzed for nipple shifting (attachment to a different nipple) as well as reattachment to the same nipple, only the analysis of nipple shifting revealed a significant effect of dose, $F(3, 67) = 4.857$, $p < .005$, with pups given the 0.5-mg/kg dose of 8-OH-DPAT exhibiting significantly less nipple shifting than saline controls (see Fig. 4B). A similar trend was seen in the data for disattachment and reattachment to the same nipple, although this was not significant (data not shown). Again, no main effects or interactions of deprivation condition were seen in these ANOVAs.

Other behaviors. The 2 (Deprivation Condition) × 4 (Dose) ANOVAs on the latency to attach, time spent attached, and frequency of "activation" on the nipple revealed only significant main effects of deprivation condition: $F(1, 67) = 13.559$, $p < .001$; $F(1, 67) = 4.961$, $p < .05$; $F(1, 67) = 4.026$, $p < .05$, respectively. Deprived pups attached more rapidly (mean ± SE: 4.7 ± 0.9 min) than nondeprived pups (13.0 ± 2.0 min), spent more time attached (50.3 min ± 1.4 min) than nondeprived pups (44.5 ± 2.3 min), and exhibited more incidences of "activation" following milk let-downs (8.6 ± 0.4 min) than nondeprived pups (7.4+0.5). The ANOVA of the incidence of stretch responses revealed no significant effects.

Percent body weight gain. In both this experiment and experiment 2b, posttest body weights inadvertently were not collected for several animals, reducing the amount of data available for calculation of percent weight gain. A 2 (Deprivation Condition) × 4 (Dose) ANOVA on percent body weight gain revealed significant main effects of Deprivation, $F(1, 58) = 9.479$, $p < .005$, and Dose, $F(3, 58) = 3.866$, $p < .05$. Deprived pups gained more weight than their nondeprived counterparts, and the 0.5-mg/kg dose of 8-OH-DPAT significantly suppressed weight gain relative to saline controls. Although there was no significant interaction of Deprivation and Dose, as can be seen in Fig. 5, the effects of deprivation condition were largely evident only at the higher doses of 8-OH-DPAT, with the suppressant effect of 8-OH-DPAT on body weight gain tending to be more pronounced in nondeprived animals.

Experiment 2b.

Frequency of attachment. A chi-squared analysis on the percentage of animals attaching in the two groups revealed no significant differences, with only one saline-treated deprived animal failing to attach during the single nipple test. This pup was eliminated from further analysis, reducing the sample size to nine subjects in each of the two dose (saline vs. 8-OH-DPAT) test groups.

Other behaviors. A one-way ANOVA revealed a significant effect of dose for nipple disattachment and reattachment, $F(1, 16) = 12.094$, $p < .005$, with animals given 8-OH-DPAT exhibiting significantly less nipple disattachment and reattachment (1.7 ± 0.8) than saline control animals (6.2 ± 1.0). No effect of dose was seen in the ANOVAs for latency to attach, time spent attached, or frequency of stretch or "activation" responses.

Percent body weight gain. The one-way ANOVA of percent body weight gain revealed a significant effect of dose, $F(1, 15) = 10.118$, $p < .01$, with saline-treated animals exhibiting significantly greater percent weight gain (1.38 ± 0.54) than 8-OH-DPAT-treated animals (−0.96 ± 0.50).

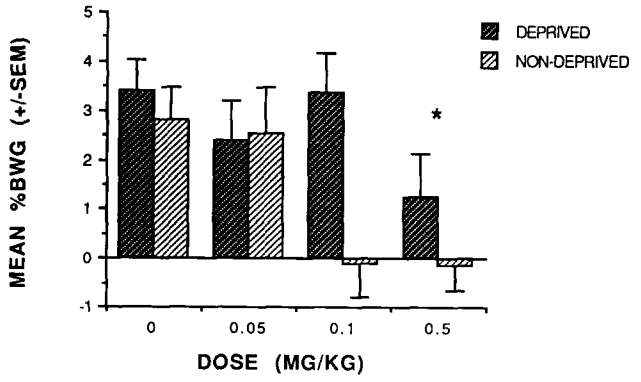

FIG. 5. Mean percent body weight gain (BWG) of both deprived and nondeprived rat pups following administration of various doses of 8-OH-DPAT in experiment 2a.

DISCUSSION

The results of experiment 2a confirm the findings in experiment 1 that 8-OH-DPAT decreases suckling intake and conversely increases suckling maintenance via suppressing nipple disattachment and reattachment. In addition, 8-OH-DPAT was observed to significantly suppress nipple shifting per se in experiment 2a, whereas only a trend for this effect was seen in experiment 1. These effects of 8-OH-DPAT on suckling intake and maintenance in experiment 2a were seen in both deprived and nondeprived pups.

In contrast to experiment 1, 8-OH-DPAT was not observed to increase the probability of attachment per se in nondeprived animals in experiment 2a. This lack of facilitation of attachment may be a result of the higher baseline levels of attachment in this experiment; whereas only 50% of the nondeprived, saline-treated pups in experiment 1 attached, 80% did so in this experiment. There are several possible explanations for the difference in baseline levels of attachment between the two experiments. Charles River Sprague-Dawley CD-COBS rats were used in the first experiment, whereas the animals from experiment 2 were derived from our colony, which now contains only specific pathogen-free Sprague-Dawley-derived CD-COBS-VAF animals from Charles River. A number of differences have recently been noted between these variant strains, including significantly greater food consumption and growth in the CD-COBS-VAF variant that results in distinct body weight differences between the variants by three months of age (the youngest age examined) (14). Whether this increased food consumption evident in adult CD-COB-VAF animals would also be evident in terms of suckling propensity during the late preweanling period is not clear. Alternatively, we previously have shown that maternal pariety influences suckling propensity at least in older, weanling age animals (15), and pariety was not specifically manipulated or controlled in these experiments. In addition, it should be noted that the two experiments were also conducted at temporally different times in our laboratory, and hence it is possible that some seasonal rhythm could have influenced these differences across experiments in the baseline suckling propensity of nondeprived preweanling rat pups.

In experiment 2b, 8-OH-DPAT was observed to significantly attenuate suckling intake relative to saline controls, even though the pups did not have the opportunity to nipple shift. As discussed further in the General Discussion section below, these data suggest that the reduction in intake on the nipple seen following 8-OH-DPAT is not predominantly related to the reduction in nipple shifting seen in these animals.

It should be noted that the levels of ingestion seen in both the saline- and 8-OH-DPAT-treated pups in experiment 2b were lower than those seen in the other experiments. Indeed, the 8-OH-DPAT animals tended to lose weight during the test, presumably because weight loss associated with micturation and defecation exceeded the weight gain associated with milk intake. In rat pups of this age, it is not possible to seal the anogenital region to prevent elimination; thus, in all experiments, net weight gain in the pups reflects a combination of both intake and elimination. The reduced intake in experiment 2b relative to the other two experiments may be a function of the abnormal nature of the one-nipple suckling situation. Indeed, *t* tests comparing saline-treated deprived pups from experiments 2a and 2b revealed that pups in the one-nipple test (experiment 2b) spent less time on the nipple (32.3 ± 7.1 min) than their counterparts in experiment 2a (49.6 ± 3.1 min) ($t(17) = 2.32, p < .05$) and exhibited fewer "activation" [4.3 ± 1.4 vs. 8.4 ± 0.9; $t(17) = 2.52, p < .05$] and stretch [3.6 ± 1.2 vs. 8.2 ± 1.0; $t(17) = 3.01, p < .01$] responses. Given these data, it is not surprising that the intake of the saline-treated deprived pups in the one-nipple test was less (1.4 ± 0.5%) than the intake of their counterparts in the more typical suckling situation of experiment 2a [3.4 ± 0.6%; $t(15) = 2.42, p < .05$].

GENERAL DISCUSSION

The 5-HT_{1A} agonist 8-OH-DPAT was observed to increase attachment maintenance in 17–18-day-old rat pups, while conversely decreasing suckling intake in pups at this age as indexed by percent body weight gain. This 8-OH-DPAT-induced decrease in body weight gains during suckling in preweanlings is reminiscent of previous findings that this agonist suppresses intake of wet mash at this age (16). Therefore, in both a suckling situation and in a test of ingestion independent of the dam, a modest dose of 8-OH-DPAT (0.5 mg/kg) was observed to attenuate weight gain in late preweanling rat pups. Consequently, although there is evidence that the neural substrates regulating suckling differ from those modulating ingestion independent from the dam (10), 5-HT_{1A} receptor stimulation is nevertheless effective in inhibiting weight gains with both types of ingestion in the late preweanling pup.

Whereas 8-OH-DPAT had similar suppressant effects on body weight gains during suckling and when examining ingestion independent of the dam in late preweanling rat pups, the effect of 8-OH-DPAT at this age on behaviors related to ingestion varied with the type of ingestion under investigation. A moderate dose of 8-OH-DPAT (0.5 mg/kg) has been previously observed to decrease both milk-induced mouthing (9) and the number of feeding bouts at wet mash food source (16) exhibited by 17–18-day-old rat pups. Yet, in pups of the same age tested in the present study, this dose of 8-OH-DPAT consistently was observed to increase attachment maintenance. This finding was unexpected, and it is not clear why 8-OH-DPAT should consistently decrease the likelihood of disattachment following milk let-downs, thereby increasing attachment maintenance.

Although pups exhibited a higher rate of attachment maintenance following a dose of 0.5 mg/kg 8-OH-DPAT, this dose of 8-OH-DPAT decreased ingestion, as indexed by percent body weight gain. There are two methods by which pups control milk intake on the nipple: through nipple shifting (disattachment/reattachment) to obtain a larger volume of milk by depleting available stores of milk from nonsuckled nipples (3), and through altering the amount of negative pressure exerted on the nipple and hence the volume of milk extracted (2,10). Although 8-OH-DPAT induced a dose-dependent decrease in nipple disattachment/reattachment, the results of experiment 2b suggest that the suppression in nipple disattachment/reattachment is not a primary factor leading to the attenuation in weight gain in these pups. In experiment 2b where pups had access to only one nipple, a reduction in weight gain still was evident in 8-OH-DPAT-treated pups. This raises the possibility that the observed 8-OH-DPAT-induced reduction in milk intake while suckling may be related to reduced suckling vigor, although negative pressure per se was not examined in this study. It appears unlikely, however, that the drug-induced decrease in intake is indirectly related to incapacitation of the pup. Animals given 8-OH-DPAT exhibited no signs of sedation, behaving like saline control animals with regard to time spent attached, frequency of active tugging at the nipple, and frequency of elicitation of the stretch response following milk let-downs.

The inhibition of ingestion induced by 8-OH-DPAT during the late preweanling period in both the present suckling study and in independent ingestion testing (16) is reminiscent of the decrease in ingestion observed in adult animals following administration of relatively high doses of 8-OH-DPAT (4). It should be noted, howver, that the 8-OH-DPAT-induced suppression of ingestion in adulthood is thought to be due to the induction of the "serotonergic syndrome" which competes with ingestion-related behavior (4,5), whereas the attenuated ingestion seen in the preweanlings in the present experiments was seen without overt behavioral consequences (other than the increase in attachment maintenance). In contrast to the high dose suppression of ingestion, lower doses of 8-OH-DPAT have been observed to have a stimulatory effect on ingestion in adulthood, an effect that is presumably due to preferential stimulation of 5-HT_{1A} autoreceptors (5,6). Whereas a low dose (0.03 mg/kg) stimulation of ingestion by 8-OH-DPAT has also been observed in testing of ingestion independent of the dam in 17–18-day-old animals (16), no such increase in ingestion was observed in the present suckling test. The lack of a low dose 8-OH-DPAT-induced increase in ingestion could perhaps merely reflect a ceiling effect, with levels of ingestion possibly being already maximal in these animals. Alternatively, it is possible that the doses of 8-OH-DPAT used in these experiments were not appropriate to reveal a low dose stimulation of suckling ingestion. Nevertheless, at present there is no evidence for a low dose, presumably autoreceptor-mediated, stimulation of feeding in late preweanling animals tested in a suckling situation.

Taken together, the results of the present study show that 5-HT_{1A} receptor stimulation has opposite influences on attachment maintenance and ingestion as indexed by body weight gains in late preweanling pups tested in a suckling situation. These data support the conclusion that suckling-related ingestion and attachment maintenance per se are differentially regulated processes, a conclusion previously based largely on variations in the ontogeny of the influence of privation status and degree of stomach fill on these two suckling-related phenomena [e.g., (2,13)]. The present findings, which demonstrate that attachment maintenance and ingestion are altered in opposite ways by 8-OH-DPAT, provide strong evidence that these two suckling-related phenomena are subject to differential physiological controls. Such psychopharmacological assessments may provide a valuable means to examine the similarities and differences in the ontogeny of the neural regulation of attachment behavior and intake in both suckling situations and when ingesting food independent of the dam.

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