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Opioid Regulation of Parental Behavior in Juvenile Rats

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KINSLEY, C. H., J. C. WELLMAN, D. B. CARR, AND A. GRAHAM. *Opioid regulation of parental behavior in juvenile rats.* PHARMACOL BIOCHEM BEHAV 44(4) 763–768, 1993.—When exposed to young rats for a period of days, juvenile rats will respond with full parental behavior (FPB: retrieval and grouping of, and crouching over, pups). Because the parental behavior of juveniles is so robust, and because opiates have been shown to be involved in the regulation of parental behavior in adult animals, we examined morphine's ability to disrupt the display of parental behavior in the juvenile animal. In Experiment 1, 25-day-old males and females were administered one of three injection regimens of morphine (MOR), saline (SAL), or naloxone (NAL)—[MOR (5.0 mg/kg) + SAL; MOR + NAL (0.5 mg/kg); or SAL + SAL]—and 1 h later were exposed to three 1- to 6-day-old neonates. Behavior was scored over a 60-min period and animals were considered parental if they responded with FPB for 2 consecutive testing days. Whereas the SAL + SAL and MOR + NAL were not different, MOR + SAL virtually failed to respond to young over a 10-day period. Experiment 2 exposed juveniles to young for a period of days until they displayed 2 consecutive days of FPB. Next, separate groups of juveniles were treated with the same regimen as above. Again, SAL + SAL and MOR + NAL responded rapidly to young, whereas MOR + SAL did not. These data suggest that the display of parental behavior, both its onset (Experiment 1) and maintenance (Experiment 2), appears to be regulated by opiates.

Development Juvenile rats Naloxone Opioids Parental behavior Play behavior Sex differences

A number of laboratories have reported that juvenile rats (20–25 days postnatal) are especially responsive to neonates (2–5,9,14,20). This increased responsiveness resembles those behaviors displayed toward young by postpartum, lactating females (14,15). The juvenile expression differs primarily in the latency with which the behaviors are expressed [cf. (30)] and the facility with which the smaller juveniles can maneuver the relatively large neonates. An interesting feature of the parental behavior shown by juvenile rats is the reversal of the normal sex difference observed in response latencies in the adult rat (viz., male > female), as juvenile males respond more quickly than juvenile females (2,9,14).

The juvenile animal undergoes a tremendous amount of maturation in the 20- to 30-day window, during which previous work has demonstrated significant effects on both behavioral and physiological/endocrinologic indices. For instance, gonadal steroid profiles (6–8) and regulatory systems (25) and opioid and neurotransmitter systems (12,13) change markedly during this time.

Recently, Kinsley and Bridges (14) reported that the anterior pituitary hormone prolactin (Prl) was involved in the parental behavior displayed by juvenile rats, especially males. Thus, both juvenile males and females resemble, in part, postpartum females in their behavior toward young and in a reliance upon exposure to Prl for the exhibition of the behavior. Because the maternal behavior of postpartum, lactating females is significantly disrupted following injections of morphine (1,10,15), we asked whether or not, and to what extent, morphine [in a dosage (5.0 mg/kg) known to disrupt the behavior in adult females], and blockade of morphine's effects with the narcotic antagonist naloxone, would affect the parental behavior exhibited by juvenile rats.

METHOD

Animals

Female nulliparous Sprague-Dawley rats (Crl : CD[SD]BR) purchased from Charles River Laboratories, Inc. (Wilmington, MA) were timed-mated, and vaginally smeared daily. The day that sperm was observed in the vaginal lavage was designated day 0 of pregnancy, at which time females were isolated in 20 × 45 × 25-cm polypropylene cages, the floors of which were covered with pine shavings. Food (Purina Rat Chow) and water were available ad lib and all animals were housed

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in light- (0500–1900 h) and temperature-(21–24°C) controlled testing rooms for the duration of the present work. Animals used in this study were maintained in accordance with the guidelines of the Institutional Animal Care and Use Committee of the University of Richmond and those prepared by the Committee on Care and Use of Laboratory Animal Resources, National Research Council (DHHS publication No. [NIH] 85-23, Revised, 1985).

Upon delivery (day 0), litters were culled to eight pups (four male, four female) and remained with their mothers until weaning on day 21, at which time they were singly housed. No more than two males and two females from each litter were used in either of the two experiments to follow.

Experiment 1: Initiation of Parental Behavior

Procedure. Experiment 1 examined the onset of parental behavior following morphine exposure in pup-naive juvenile rats. Beginning on day 25 of life, both male and female juveniles were randomly divided into three groups of 9–10/group and injected with one of the following treatments: morphine (5.0 mg/kg) + saline (MOR + SAL); morphine (5.0 mg/kg) + naloxone (0.5 mg/kg) (MOR + NAL); or saline + saline (SAL + SAL). (The dosages of morphine and naloxone were chosen based upon their usage, in body weight-corrected fashion, in work with adult females and in a pilot study.) Sixty minutes following injections, animals were exposed to 1- to 7-day-old rat pups (provided by a separate group of donor mothers bred exclusively for this purpose). Pups were placed into the juvenile's cage at a point opposite the location of the nest and the behavior was then scored. The behaviors we examined [and hereafter refer to as full parental behavior (FPB)] consisted of retrieving and grouping and crouching over pups during a 1-h test session. Juveniles were scored as fully parental if they retrieved, grouped, and crouched within 60 min of exposure to the young, following which pups remained in the cage until testing the following day. The latency of the animal (in days) to display FPB was based upon the first day (and test session) of two consecutive test sessions in which FPB was observed. For example, at the initiation of each testing session pups from the previous day's testing were removed (from test day 2 onward) and juveniles were injected with the respective treatments. Sixty minutes later, three freshly suckled pups obtained from the donor mothers were proffered to subjects whose behavior was scored. Testing continued for 10 days or until 2 consecutive days of FPB were observed. All testing took place between 1000 and 1300 h.

Experiment 2: Maintenance of Parental Behavior

Procedure. Whereas in Experiment 1 we investigated the onset of parental behavior in juvenile rats, Experiment 2 examined the maintenance of the behavior and its susceptibility to disruption by morphine. Therefore, we used behaviorally sensitized animals. On day 25 of life, a separate group of both male and female juveniles were randomly divided into three groups of 9–11/group and exposed to three 1- to 7-day-old rat pups. Using the testing regimen described above for the initiation phase, we continued to test for FPB in all juveniles until they displayed 2 consecutive days of FPB. On the morning of day 3 (following the second day of the display of FPB), animals were injected with one of the three treatments detailed above (MOR + SAL, MOR + NAL, or SAL + SAL) and next were exposed to the three pups. Behavioral testing for this maintenance phase consisted of a single test on the day following each animal's second day of FPB responding. Thus, repeated tests were not conducted because the aim in this second experiment was to attempt to disrupt—as demonstrated in postpartum females—the established behavior. We emphasize that the assignment to groups in this study was random. Therefore, the number of quick responders in the MOR + NAL and SAL + SAL groups and the number of slow responders in the MOR + SAL group were roughly equivalent in an effort to avoid biasing the direction of the posttreatment effects.

Statistical Analysis

For the analyses of behavioral differences among the groups in Experiment 1, a Kruskal–Wallis (KW), the nonparametric equivalent of the one-way analysis of variance (ANOVA), was employed. In those cases where overall differences were detected with the KW, a Mann–Whitney U was used for single comparisons between separate pairs. In Experiment 2, a χ^2 analysis was used. In all cases, statistical significance was considered to be $p < 0.05$.

RESULTS

Experiment 1: Initiation

Figure 1 displays the median latencies for the three treatment groups (MOR + SAL, MOR + NAL, or SAL + SAL) to exhibit full parental behavior for Experiment 1. It is evident that morphine had a significant effect on the parental behavior displayed by juvenile rats. The overall KW revealed a significant effect of morphine treatment on the latency to display 2 consecutive days of FPB, the primary criterion ($H = 13.4$, $p < 0.002$). Further, latencies to display 1 day of FPB ($H = 15.4$, $p < 0.001$), retrieve one ($H = 9.7$, $p < 0.002$), two ($H = 12.5, p < 0.002$), and three pups ($H = 7.4, p < 0.05$), group ($H = 14.2$, $p < 0.001$), and crouch ($H = 15.3$, $p < 0.001$) were significantly extended by morphine treatment in juvenile males.

The follow-up with the MW U showed that, in males, latencies to display 2 consecutive days of FPB were significantly protracted in the MOR + SAL group vs. the SAL + SAL group ($U = 16.0$, $p < 0.01$; see Fig. 1), as were latencies to exhibit 1 day of FPB ($U = 16.0$, $p < 0.01$), retrieve one ($U = 12.0$, $p < 0.01$), two ($U = 10.5$, $p < 0.05$), and three pups ($U = 14.5$, $p < 0.01$; see Table 1). Further, latencies to group pups ($U = 7.5$, $p < 0.001$), and crouch ($U = 2.5$, $p < 0.001$) were significantly longer for the MOR + SAL group relative to the SAL + SAL group. Moreover, MOR + SAL required significantly longer than the MOR + NAL group to display 2 consecutive days of FPB ($U = 20.0$, $p < 0.01$) display 1 day of FPB ($U = 14.0$, $p < 0.01$), retrieve three pups ($U = 22.0$, $p < 0.01$), group pups ($U = 15.3$, $p < 0.005$), and crouch over pups ($U = 24.0$, $p < 0.01$) (see Table 1). Importantly, the only significant difference in any behavioral measure between the MOR + NAL and SAL + SAL groups was the latency to display 1 day of FPB ($U = 23.0$, $p < 0.05$), which demonstrates that naloxone was mostly capable of antagonizing the disruptive effects of morphine on the parental behavior displayed by juveniles.

In juvenile females, the KW revealed that morphine treatment was similarly disruptive of 2 consecutive days of FPB ($H = 6.0$, $p < 0.05$), as were the latencies to display 1 day of FPB ($H = 6.4$, $p < 0.05$) and crouch over pups ($H = 13.6$, $p < 0.002$). For females, the KW indicated that there were no significant effects of morphine treatment on latencies to retrieve one, two, and three pups or group pups.

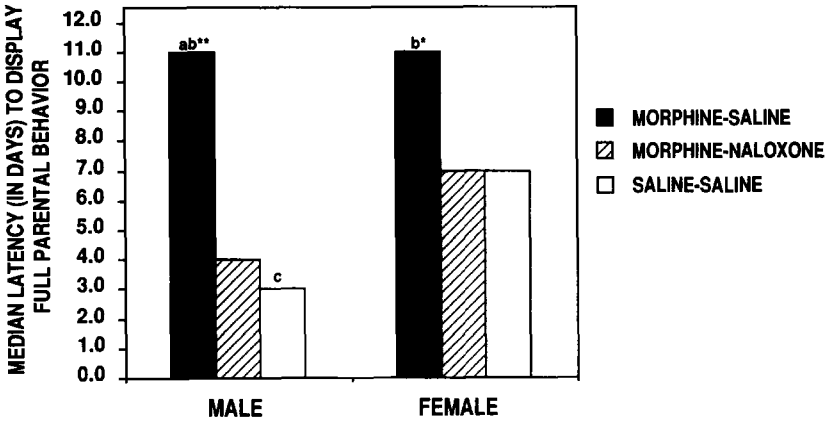

FIG. 1. The latencies (in days) to display 2 consecutive days of full parental behavior (FPB; retrieving, grouping, and crouching over three neonates in a 60-min period) for juvenile males and females treated with morphine (5.0 mg/kg) + saline (MOR + SAL, $n = 11$), morphine (5.0 mg/kg) + naloxone (0.5 mg/kg; MOR + NAL, $n = 10$), or saline + saline (SAL + SAL, $n = 9$). [a]Significantly different from MOR + NAL. [b]Significantly different from SAL + SAL. [c]Significant sex difference, same treatment group, at $p < 0.05$. *$p < 0.05$; **At least $p < 0.01$.

Individual comparisons within the female groups (see Fig. 1) showed that MOR + SAL took significantly longer than SAL + SAL to display 2 consecutive days of FPB ($U = 20.5$, $p < 0.05$), display 1 day of FPB ($U = 20.5$, $p < 0.05$), and crouch ($U = 10.0$, $p < 0.01$) (see Table 1). There were no significant differences between MOR + SAL and MOR + NAL. The only significant difference between MOR + NAL and SAL + SAL was for crouching ($U = 25.0$, $p < 0.01$).

Individual sex differences in behavior were also informative. The MW revealed that whereas there were no significant differences in any behavior between the male and female MOR + SAL groups there were significant differences between male and female MOR + NAL groups for 1 day of FPB ($U = 17.5$, $p < 0.01$), to retrieve one ($U = 24.0$, $p < 0.05$), two ($U = 24.0$, $p < 0.05$), and three ($U = 27.0$, $p < 0.05$) pups, to group pups ($U = 25.0$, $p < 0.05$), and to crouch over pups ($U = 24.0$, $p < 0.05$). Between SAL + SAL males and females, the differences consisted of significant latencies to display 2 consecutive days of FPB ($U = 16.0$, $p < 0.05$), and 1 day of FPB ($U = 16.0$, $p < 0.05$), retrieve one pup ($U = 15.0$, $p < 0.05$), retrieve two pups ($U = 17.0$, $p < 0.05$), retrieve three pups ($U = 16.0$, $p < 0.05$), and group pups ($U = 15.0$, $p < 0.05$; see Table 1).

Experiment 2: Maintenance

Experiment 1 demonstrated that morphine disrupted, and naloxone could reverse, the initiation of parental behavior displayed by male and female juvenile rats. Experiment 2 sought to examine how morphine would affect the established

TABLE 1

MEDIAN LATENCIES (IN DAYS) FOR JUVENILE MALE AND FEMALE RATS TO EXHIBIT THE VARIOUS COMPONENTS OF FULL PARENTAL BEHAVIOR FOR EXPERIMENT 1, INITIATION

	Juvenile Males			Juvenile Females		
	MOR + SAL	MOR + NAL	SAL + SAL	MOR + SAL	MOR + NAL	SAL + SAL
1-day FPB	10*†‡	4†‡§	3§	11†¶	7	7
Retrieve 1 pup	6†‡	3§	2§	4	5	5
Retrieve 2 pups	9†‡	4§	3§	7	6	5
Retrieve 3 pups	10*†‡	5§	3§	8	6	5
Latency to group	9*†‡	4§	3§	8	6	5
Latency to crouch (on at least 1 pup)	8*†‡	4§	2	7†‡	6†‡	2
n	11	10	9	11	10	9

Overall data were analyzed with the Kruskal-Wallis *H*, with individual comparisons performed with a Mann-Whitney *U*. See the Results section for individual significance levels and details.

*Significantly different from MOR + NAL.

†Significantly different from SAL + SAL.

‡At least $p < 0.01$.

§Significantly sex difference, same treatment group, at $p < 0.05$.

¶$p < 0.05$.

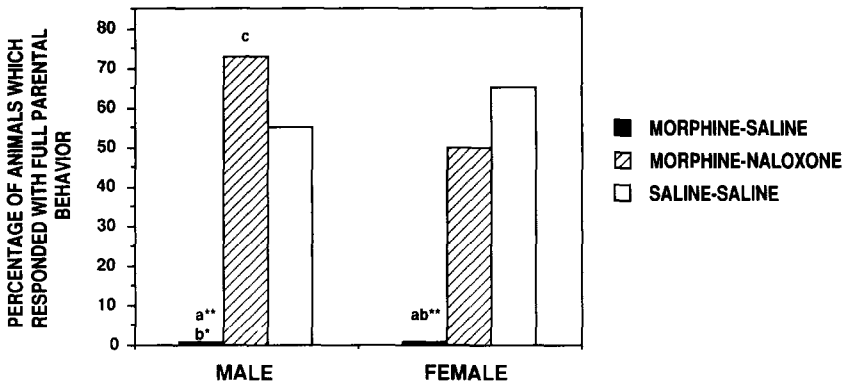

FIG. 2. The percentages of animals displaying full parental behavior (FPB; retrieving, grouping, and crouching over three neonates in a 60-min period) for juvenile males and females treated with morphine (5.0 mg/kg) + Saline (MOR + SAL, $n = 11$), morphine (5.0 mg/kg) + naloxone (0.5 mg/kg; MOR + NAL, $n = 10$), or saline + saline (SAL + SAL, $n = 9$). [a]Significantly different from MOR + NAL. [b]Significantly different from SAL + SAL. [c]Significant sex difference, same treatment group, at $p < 0.05$. *$p < 0.05$; **At least $p < 0.01$.

behavior in sensitized juvenile males and females (Fig. 2, Table 2). For males, following 2 consecutive days of FPB in the absence of treatment significantly fewer of the MOR + SAL group displayed FPB on the first day of injection compared to either MOR + NAL or SAL + SAL (MOR + SAL vs. MOR + NAL, $\chi^2 = 11.5, p < 0.01$; vs. SAL + SAL, $\chi^2 = 6.3, p < 0.05$). There were no significant differences between MOR + NAL and SAL + SAL males.

For females, significantly fewer MOR + SAL-treated females displayed FPB compared to both MOR + NAL and SAL + SAL animals (vs. MOR + NAL, $\chi^2 = 8.0, p < 0.01$; vs. SAL + SAL, $\chi^2 = 9.0, p < 0.01$). There were no significant differences between MOR + NAL and SAL + SAL females.

For males, additional analyses revealed that fewer MOR + SAL than MOR + NAL animals retrieved one ($\chi^2 = 9.8$, $p < 0.01$), two ($\chi^2 = 9.8, p < 0.01$), and three pups ($\chi^2 = 9.0, p < 0.01$), grouped pups ($\chi^2 = 4.5, p < 0.05$), and crouched ($\chi^2 = 7.2, p < 0.05$) on this first day of injection. For MOR + SAL vs. SAL + SAL, there were significant differences for retrieving one ($\chi^2 = 8.1, p < 0.01$), two ($\chi^2 = 11.5, p < 0.01$), and three pups ($\chi^2 = 11.5, p < 0.001$), grouping ($\chi^2 = 4.0, p < 0.05$), and crouching ($\chi^2 = 5.5, p < 0.05$).

For females, significantly fewer MOR + SAL than MOR + NAL retrieved one pup ($\chi^2 = 6.4, p < 0.05$), grouped ($\chi^2 = 4.4, p < 0.05$), and crouched ($\chi^2 = 9.0, p < 0.01$). For MOR + SAL vs. SAL + SAL, there were significant differences for retrieving two pups ($\chi^2 = 5.6, p < 0.05$), retrieving three pups ($\chi^2 = 4.4, p < 0.05$), grouping ($\chi^2 = 5.6, p < 0.05$), and crouching ($\chi^2 = 10.9, p < 0.001$). For MOR + NAL vs. SAL + SAL, the only significant difference was for retrieving one pup ($\chi^2 = 15.0, p < 0.001$).

There were no significant sex differences between MOR + SAL males and females; in both groups, parental behavior was equally disrupted. For MOR + NAL, there were sex dif-

TABLE 2

PERCENTAGES OF JUVENILE MALE AND FEMALE RATS EXHIBITING THE VARIOUS COMPONENTS OF FULL PARENTAL BEHAVIOR FOR EXPERIMENT 2, MAINTENANCE

	Juvenile Males			Juvenile Females		
	MOR + SAL	MOR + NAL	SAL + SAL	MOR + SAL	MOR + NAL	SAL + SAL
Retrieving 1 pup	22*†‡	91	89	22*¶	80†‡	100
Retrieving 2 pups	22*†‡	91	100	22†¶	60	78
Retrieving 3 pups	22*†‡	91	100§	22†¶	60	56
Grouping	44*†¶	100§	89	22*†¶	70	78
Crouching (over at least 1 pup)	22*†¶	82	78	11*†‡	80	89
n	11	11	9	11	10	9

Data were analyzed with the χ^2 test. See the Results section for details and individual significance levels.
*Significantly different from MOR + NAL.
†Significantly different from SAL + SAL.
‡At least $p < 0.01$.
§Significant sex difference, same treatment group, at $p < 0.05$.
¶$p < 0.05$.

terences for FPB ($\chi^2 = 4.5$, $p < 0.05$) and grouping ($\chi^2 = 3.9$, $p < 0.05$). For SAL + SAL, there was a sex difference only for retrieving three pups ($\chi^2 = 5.1$, $p < 0.05$).

DISCUSSION

Our data demonstrate that the display of parental behavior in the juvenile animal is under the influence of the endogenous opioid system. Morphine disrupts and naloxone restores the behavior in both males and females. The effects are seen during both initial exposure to offspring (Experiment 1, Initiation), as well as in animals that have been sensitized to young and were responding parentally prior to morphine treatment (Experiment 2, Maintenance). In both experiments, when animals were treated with either saline plus saline (SAL + SAL) or the combination of morphine plus naloxone (MOR + NAL), a potent narcotic antagonist, there was no effect on the display of the behavior; males and females continued to exhibit retrieving, grouping, and crouching toward the three pups. In the morphine plus saline (MOR + SAL) condition, however, juveniles were active in their cages and would investigate pups but not attempt to be parental.

For each treatment condition, a typical behavioral bout usually took the form of the following sequence: As pups were placed in the cages, there would be initial investigation by the juvenile, involving sniffing, and nudging and prodding. The juvenile would next retreat to the back of the cage, where it would begin to dart rapidly to and fro. This elevated activity would give way to the juvenile's apparent attempts to engage the pup as a coactor [much like the reports of play behavior discussed below; cf. (14)] but, failing this, control (SAL + SAL and MOR + NAL) juveniles would begin to drag the pup(s) around the cage, more often than not, back to the nest, whereupon they would be grouped and the juvenile would attempt to crouch. We say "attempt" because the juvenile does not dwarf the pup as its adult counterpart and hence has difficulty perching over all three pups concurrently. Nevertheless, the behavior displayed toward the grouped pups was clearly a crouch. Together, the behavior possesses components of both play and parental behavior, with the emphasis placed on the latter.

In the MOR + SAL condition, juveniles would continue to be active in the presence of pups but would rarely retrieve, group, and crouch. We did notice, however, that this group was more likely to spend much of the test period eating from the food bin. Morphine has facilitatory effects on food intake (18), and this may explain in part our casual observation. We have not, however, observed a similar phenomenon in our previous work on maternal behavior in the morphine-treated *adult*.

One feature that lends itself to examinations of morphine's effects on parental behavior at this age is the relative ease and quickness with which the behavior can be established. Juvenile animals are very parental. In fact, the developmental events underlying the decrease in parental responsiveness between the juvenile and adult animal are not clear. Adult animals, in particular males, require a number of days (about 4–8) to initiate parental behavior (2,14,20,30). The influences underlying this developmental difference may relate to a variety of factors, some of which were discussed in (14), and may involve the steady rise of gonadotropin surges and testicular hormones and a diminution in, and/or increased sensitivity to, Prl levels (6–8,14).

One possible factor responsible for this developmental difference, and for mediation of endocrine regulatory systems, may be the maturation of various neurotransmitter and neuropeptide systems. For example, there is functional maturation of the endogenous opioid system that is ongoing from before birth (11), during the neonatal period (16) and beyond, through the juvenile (12,13) and prepubertal (17) periods. Further, there are changes in other neurotransmitter systems across early developmental stages in male and female rats (28). In the caudate nucleus of neonates (~birth) to juveniles (30 days), dopamine and serotonin and their metabolites displayed temporal increases, suggesting a dynamic and maturing system throughout the early developmental period of the rat.

That sex differences in developmental profiles of opioid systems have been reported may be of relevance to the present work. We observed sex differences in the behavioral responses in both Experiments 1 and 2, with males responding more quickly than females in the MOR + NAL and SAL + SAL conditions; interestingly, following treatment with MOR + SAL the sex differences were no longer evident. The results for sex differences, indicating that males in general responded more quickly than females (in particular in the SAL + SAL conditions), replicate and extend other work that has reported sex differences in juvenile parental responding (2,9,14). The sex difference in Experiment 1, however, was greater than that observed in Experiment 2 [and follows from our previous findings (14)] because the latter experiment utilized subjects that were already sensitized to pups, whereas the former experiment examined latencies (in days) to respond to young. One might expect to observe differential parental responding if, for example, there were sex differences in either opioid receptor systems [in particular μ-opioid receptors (19)] or opioid ligand levels. Perhaps baseline differences in opioid "tone" or in the maturation of opioid systems (or both) affect parental responding in juvenile animals.

There is some discussion of the parental behavior of juveniles either resembling, or in fact being, an expression of play behavior (4,5,20). This accounts for our occasional use of the term "parental-like" [cf. (14)]. As mentioned above, the behavior of the juvenile possesses components of what appear to be both parental and play responses, a complement that makes for a robust (and entertaining) behavioral response. That opiates play a significant role in the expression of both parental behavior (1,10) and play behavior (26,27) indicates an interesting relationship between these two major juvenile behaviors.

Numan and colleagues both elegantly investigated (21, 22,24) and discussed (23) the neural requirements for the exhibition of maternal behavior. The primary region involved in the response is the basal forebrain structure, the medial preoptic area (MPOA), and its various projections. It is not known to what extent the immature MPOA regulates the results of the current work, although other regions involved in endocrine and behavioral regulation mature apace at this time. The median eminence (ME) of the juvenile female markedly increases its capacity to secrete luteinizing hormone-releasing hormone (LHRH) between days 22–34 (25). It is reasonable to presume that parallel maturation may be occurring in regions of the brain underlying juvenile parental responsiveness and the change in same that occurs with advancing age. Recent work also suggests that synaptic area densities in the MPOA and hypothalamic arcuate nucleus are sensitive to both sex differences and treatment with estradiol (29). Thus, the maturing brain may be different between males and females and may undergo site-specific temporal development.

In conclusion, the present data demonstrate that the enhanced parental responsiveness of juvenile animals, in particu-

lar males, is susceptible to the disruptive effects of morphine. In juveniles exposed to morphine in advance of exposure to pups, the initiation of parental responsiveness fails to be expressed. When antagonized with naloxone, morphine's disruptive effects are blocked and the behavior is displayed. In juveniles that are allowed prior exposure to young, and are all responding parentally, morphine again will disrupt the responsiveness, the effect of which is antagonized with naloxone. Collectively, the data point to a developmental stage or open 7- to 10-day window in the juvenile animal during which responsiveness to young is high and following which (~30 days of age) responsiveness declines. The extent to which opioid tone functions to affect baseline behavioral, especially parental, responses is not clear. The present work, however, suggests that it is a factor that merits further consideration.

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REFERENCES

1. Bridges, R. S.; Grimm, C. T. Reversal of morphine disruption of maternal behavior by concurrent treatment with the opiate antagonist naloxone. Science 218:166–168; 1982.
2. Bridges, R. S.; Zarrow, M. X.; Goldman, B. D.; Denenberg, V. H. A developmental study of maternal responsiveness in the rat. Physiol. Behav. 12:149–151; 1974.
3. Brunelli, S. A.; Hofer, M. A. Parental behavior in juvenile rats: Environmental and biological determinants. In: Krasnegor, N. A.; Bridges, R. S., eds. Mammalian parenting: Biochemical, neurobiological and behavioral determinants. New York: Oxford University Press; 1990:372–399.
4. Brunelli, S. A.; Shindledecker, R. D.; Hofer, M. A. Development of maternal behaviors in prepubertal rats at three ages: Age-characteristic pattern of responses. Dev. Psychobiol. 18:309–326; 1985.
5. Brunelli, S. A.; Shindledecker, R. D.; Hofer, M. A. Behavioral responses of juvenile rats (*Rattus norvegicus*) to neonates after infusion of maternal blood plasma. J. Comp. Psychol. 101:47–59; 1987.
6. Dohler, K. D.; Wuttke, W. Serum LH, FSH, prolactin and progesterone from birth to puberty in female and male rats. Endocrinology 94:1003–1008; 1974.
7. Dohler, K. D.; Wuttke, W. Changes with age in levels of serum gonadotropins, prolactin, and gonadal steroids in prepubertal male and female rats. Endocrinology 97:898–907; 1975.
8. Dohler, K. D.; Wuttke, W. Circadian fluctuations of serum hormone levels in prepubertal male and female rats. Acta Endocrinol. 83:269–276; 1976.
9. Gray, P.; Chesley, S. Development of maternal behavior in nulliparous rats (*Rattus norvegicus*): Effects of sex and early maternal experience. J. Comp. Psychol. 98:91–99; 1984.
10. Grimm, C. T.; Bridges, R. S. Opiate regulation of maternal behavior in the rat. Pharmacol. Biochem. Behav. 19:609–616; 1983.
11. Hammer, R. P., Jr. The sex hormone-dependent development of opiate receptors in the rat medial preoptic area. Brain Res. 360: 65–72; 1985.
12. Ieiri, T.; Chen, H. T.; Meites, J. Effects of morphine and naloxone on serum levels on luteinizing hormone and prolactin in prepubertal males and females. Neuroendocrinology 29:288–294; 1979.
13. Johnston, C. A.; Negro-Vilar, A. Maturation of the prolactin and proopiomelanocortin-derived peptide responses to ether stress and morphine: Neurochemical analysis. Endocrinology 118:797–804; 1986.
14. Kinsley, C. H.; Bridges, R. S. Prolactin modulation of the maternal-like behavior exhibited by juvenile rats. Horm. Behav. 22:49–65; 1988.
15. Kinsley, C. H.; Bridges, R. S. Parity associated reductions in behavioral sensitivity to opiates. Biol. Reprod. 39:270–278; 1988.
16. Kornblum, H. I.; Hurlbut, D. E.; Leslie, F. M. Postnatal development of multiple opioid receptors in rat brain. Dev. Brain Res. 37:21–41; 1987.
17. Limonta, P.; Dondi, D.; Maggi, R.; Martini, L.; Piva, F. Neonatal organization of the brain opioid systems controlling prolactin and luteinizing hormone secretion. Endocrinology 124:681–686; 1989.
18. Mann, P. E.; Arjune, D.; Romero, M. T.; Pasternak, G. W.; Hahn, E. F.; Bodnar, R. J. Differential sensitivity of opioid-induced feeding to naloxone and naloxonazine. Psychopharmacology (Berl.) 94:336–341; 1988.
19. Mann, P. E.; Kinsley, C. H.; Bridges, R. S. Opioid receptor subtype involvement in maternal behavior in lactating rats. Neuroendocrinology 53:487–492; 1991.
20. Mayer, A. D.; Rosenblatt, J. S. Ontogeny of maternal behavior in the laboratory rat: Early origins in 18- 27-day-old young. Dev. Psychobiol. 12:407–424; 1979.
21. Numan, M. Brain mechanisms of maternal behaviour in the rat. In: Balthazart, J.; Prove, E.; Gilles, R., eds. Hormones and Behaviour in higher vertebrates. New York: Springer-Verlag; 1983: 69–85.
22. Numan, M. Maternal behavior. In: Knobil, E.; Neill, J.; Ewing, L. L.; Greenwald, G. S.; Markert, C. L.; Pfaff, D. W., eds. The physiology of reproduction. New York: Raven Press; 1988:1569–1645.
23. Numan, M. Neural control of maternal behavior. In: Krasnegor, N. A.; Bridges, R. S., eds. Mammalian parenting: Biochemical, neurobiological and behavioral determinants. New York: Oxford University Press; 1990:69–85.
24. Numan, M.; Rosenblatt, J. S.; Komisaruk, B. R. Medial preoptic area and onset of maternal behavior in the rat. J. Comp. Physiol. Psychol. 91:146–164; 1977.
25. Ojeda, S. R.; Urbanski, H. F.; Katz, K. H.; Costa, M. E. Activation of estradiol-positive feedback at puberty: Estradiol sensitizes the LHRH-releasing system at two different biochemical steps. Neuroendocrinology 43:259–265; 1986.
26. Panksepp, J.; Jalowiec, J.; DeEskinazi, F. G.; Bishop, P. Opiates and play dominance in juvenile rats. Behav. Neurosci. 99:441–453; 1985.
27. Panksepp, J.; Siviy, S.; Normansell, L. The psychobiology of play: Theoretical and methodological perspectives. Neurosci. Biobehav. Rev. 8:465–492; 1984.
28. Restani, P.; Corsini, E.; Galimberti, R.; Galli, C. L. Postnatal ontogenesis of dopaminergic and serotonergic systems in rat caudate nucleus. Pharmacol. Res. 22:343–350; 1990.
29. Rodriguez-Sierra, J. F.; Clough, R. W. Sexual dimorphism in the synaptic effect of estradiol in prepuberal female rats. Synapse 1: 258–264; 1987.
30. Rosenblatt, J. S. Nonhormonal basis of maternal behavior in the rat. Science 156:1512–1514; 1967.