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Mothering begets mothering: The transmission of behavior and its neurobiology across generations

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Abstract

Early experiences exert their effects on adult parental behavior in part by altering the development of neurobiological mechanisms that initiate or support the initiation and sustenance of adult parental behavior. The effects of parental behavior on sensory, perceptual and emotional mechanisms in offspring constitute an experientially based mechanism by which neurobiological factors regulating behavior can be transferred from generation to generation somewhat independently of genetic endowment.

Keywords: Maternal behavior; Affiliation; Mother–infant interactions; Rats; Monkeys; Development

1. Introduction

In rodents and primates, acquired experiences between birth and weaning can have profound effects on the quality and intensity of parenting behavior that is expressed toward neonates in adulthood (Berman, 1990; Fairbanks, 1996; see Fleming et al., 1999). Mammalian offspring are born relatively plastic physiologically. Many of their hormonal and neuronal systems organize their long-term functions and regulatory capacity in relation to interactions that the infant has with a caregiver and later on with peers (Fleming et al., 1999; Hofer, 1972; Kraemer, 1992). Some of the neurobiological changes that result in adequate caregiving in adulthood are predicated on earlier social experiences that range from patterns of somatosensory stimulation to complex and reciprocal stimulus–response interactions involving olfactory, auditory and visual mechanisms. For example, if the primate neonate does not have early attachment experiences or is isolated or abused, then typically the ability to exhibit normal social behavior and social problem solving fails to develop (Kraemer, 1992). One cause of abnormal behavior in adulthood appears to be related to changes in brain neurotransmission and neuroendocrine regulation in systems that usually regulate fear responses, aggressive and affiliative behavior, and responses to stressors per se (Clarke et al., 1998; Kraemer, 1997; Kraemer and Bachevalier, 1998; Kraemer and Clarke, 1996; Kraemer et al., 1989, 1991, 1997). The generality of negative cognitive, emotional and social behavioral effects of disruption or alteration of early rearing experience has been studied in primates and perhaps received the most attention because of the parallels that seem to apply to human development (Harlow et al., 1971; Kraemer, 1992; Kraemer et al., 1991). The mechanisms of the effect of environmental influences per se on psychobiological development, however, have been and are best studied in rodents (Fleming et al., 1999; Meaney et al., 1994).

1.1. Effects of early environmental influences in the nest on adult maternal behavior

The mother rat and maternal nest provide a host of stimuli that the young can learn about and that can form

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the basis of their later responsiveness to stimuli and behavior. Newborn pups preferentially approach and then learn to recognize the mother and the nest site based on their unique odors (Polan and Hofer, 1998). Their first attachments to the teats are guided and activated by the odor and taste of amniotic fluid first experienced by the young in utero (Pedersen and Blass, 1981; see also Goursaud and Nowak, 1999). Antecedent factors are the compression of labor, the decline in ambient temperature with the birth and the postpartum licking stimulation provided by the mother (Abel et al., 1998). The subsequent attraction to mothers' odors enables the infant to orient to the mother (Leon, 1978) and, in some species, locate a nipple position (Rosenblatt, 1971). Later, food preferences arise as a result of the pairing of mothers' diet and odors with licking stimulation provided by the mother prior to a nursing bout (Galef, 1990; Wilson and Sullivan, 1994).

The neurobiology of this early perception-recognition conditioning is now well understood and involves neural and neurochemical systems that are also involved in later learning (see Wilson and Sullivan, 1994). Until recently, however, the long-term effects of this acquired attraction to mother's odors on female offspring were not known. In a recent study, we found that if female rat pups are exposed to mothers scented with an artificial odorant prior to weaning, then when they grow up and give birth, they in turn are more responsive to pups scented with that same odorant (licking them more) by comparison to unscented control pups (Shah et al., in press).

Subjects were female rat pups reared by mothers who had been scented either with lemon extract or with distilled water (not scented), applied daily from Days 1 to 18 postpartum to their ventral surfaces. Control animals received preweaning exposure to lemon scent or no scent on a daily basis but not in associated with the mother. Pups were given odor preference tests as juveniles and in adulthood, were mated and were tested for their maternal behavior toward foster pups that were scented with lemon extract or not scented. Maternal behavior tests were conducted daily using six 2–6-day-old recently fed foster pups. In this and other studies, testing involved the continuous observation of the different behaviors exhibited by the mother using a computer-based event recorder. Behaviors that were recorded included body licking, anogenital licking, crouching over pups in nursing posture or hovering over them, retrieving pups to the nest, building the nest, and self-grooming. Tests involved removing pups from the subject's cage for a 2–5-min period and returning them to the quadrant of the cage opposite the female's nest. These 10-min tests were followed by 2-min spot-checks every 1/2 h over the subsequent 2-h period.

Exposure to lemon in association with mother (but not in the absence of mother) enhanced lemon preferences during the juvenile period, consistent with the results of Sullivan and Leon (1986) (see Wilson and Sullivan, 1994). Once animals had exhibited postpartum maternal behavior as adults, offspring-turned mothers showed higher levels of licking and of crouching when tested with pups that had the same (lemon-lemon or natural-natural) as opposed to different (lemon-natural or natural-lemon) odor characteristics as they had experienced on their own mothers (scented or unscented) (see Fig. 1). Most importantly, simple exposure to odorants early in life, not in association with mother or licking, produced no such preference after weaning. Fig. 1 shows all behaviors exhibited on Day 5 of test toward same and differently scented pups.

That these findings reflect a normal ongoing process and not some artifact of the use of artificial odorants is suggested by our recent findings that if pups are raised without mothers altogether but in cups with their own bedding and olfactory environment [see below, artificially reared (AR) animals], then at weaning they do not show the typical pattern of preference for the maternal nest odor normally shown by mother-reared (MR) animals. Instead, they come to prefer their own nest and milk odor on which they had been raised (Levy et al., in preparation). This reinforces the finding that olfactory systems of the pup encode odors that

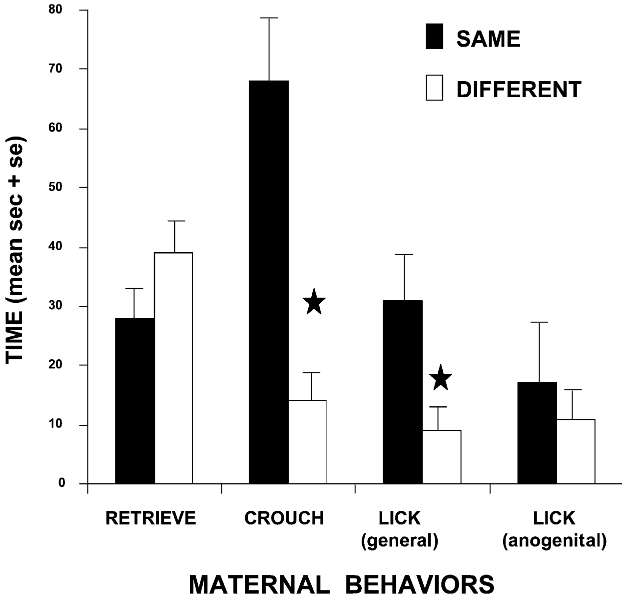


Fig. 1. Durations of maternal behaviors exhibited on the last day of testing were analyzed using one-way ANOVAs, comparing groups that were exposed to the SAME odors in adulthood as they experienced earlier in the nest with those experiencing a DIFFERENT odorant. Animals exposed to pups with the same scent as they had experienced earlier in the nest licked [$F(1,42)=9.6$, $P<.003$] and crouched over [$F(1,42)=5.1$, $P<.028$] the pups more than did females exposed to a different scent at the two time points. There were no same–different effects for the other maternal behaviors. Similar effects were found if only animals that had retrieved pups were included in the analyses. To control for the effects of exposure to an odor, independent of the mother, a second experiment exposed preweaning pups daily to artificial scents independent of the nest and the mother and then tested them in adulthood for postpartum maternal behavior toward pups with the same and different scents. Unlike the first experiment, in the second there was no preferential licking or crouching over pups scented with experienced odor, indicating that for the preference to develop the scent must be associated with the mother.

become associated with their own nests and simulated "licking," even if these odorants are very different from the natural lactating nest odors.

These experiments indicate that olfactory experiences acquired by rat pups have a long-term influence on how they subsequently make discriminations and exhibit maternal behavior in adulthood. Therefore, if rats are exposed to an unusual rearing experience in one generation (like a lemon-smelling mother), then they can be referred to as "carrying or holding" the responsiveness to lemon into adulthood. Now, there is an experiential selection factor operating because the "same-smelling" pups that may receive increased licking, for example, are not selected for increased maternal attention by their probable "fitness" in the face of environmental odds but are rather selected by the sensory "set" and preferences of the mother. Hence, an environmental effect in one generation could lead to a variation in maternal care that in turn may affect the fitness of the pups.

If one replays this effect over many generations, then we can see how a within-species perception of a cue and attraction to it, ultimately related to experiences of ancestors and propagated through successive mothers, could ultimately affect the genotypic variance in relation to the environment. The neural substrate that supports this propagation appears to be operating at sensory and perceptual levels of brain function. Beyond this, there appear to be mechanisms by which experiences in one generation can modulate emotional responsiveness to cues, so that attraction or aversion is more or less likely to be exhibited when the mother is exposed to infant cues.

1.2. Effects of being licked

The early experiences of being mothered have long-term effects on the quality of mothering offspring will show toward their offspring when they grow up. The experience of receiving more somatosensory stimulation and a more varied nest experience, while in the presence of the natural mother and nest odor, may directly contribute to the animals' physiology and maturational processes, and active associative processes may be involved as well.

In a recent series of studies, Meaney et al. demonstrated that young that receive more licking from their mothers grow up to show higher levels of licking toward their own offspring in comparison to those that received low licking (Francis et al., 1999a,b). This effect was also found if the young from high- and low-licking mothers were cross fostered to a mother showing the opposite pattern of licking than their biological mothers. Hence, if offspring from low-licking mothers are cross-fostered to high-licking mothers, they show a high-licking pattern when they grow up and vice versa (Francis et al., 1999a,b).

These licking effects can also be demonstrated experimentally by altering the characteristics of the mother and nest to enhance or reduce the amount of licking the offspring will receive. The amount of licking experienced by pups is reduced if the mother is rendered anosmic through olfactory bulbectomy or if pups are raised in a large litter (Fleming et al., 1979; Jans and Woodside, 1987).

During their pregnancies, mother rats were either olfactory bulbectomized by aspiration (OBX) or sham operated (SHAM) and they raised either a small litter of six pups (three males, three females) or a large litter of 12 pups (six males, six females). After weaning, animals were raised socially, in same sex pairs derived from the same condition or group. One female pup from each of the litters was tested for maternal behavior with her own medium-sized litter of eight pups (four males, four females) after giving birth in adulthood. Analyses of all maternal behaviors (including retrieving, crouching and nest building) indicated that primarily pup licking was affected. The pup licking behavior of the original mothers was affected by bulbectomy and litter size and there was a significant interaction between the two treatments. OBX mothers licked pups less than SHAM mothers. Small litters were licked more than large litters. The most intense licking received by pups in the first generation was delivered by the SHAM small litter mothers and the least by the OBX large litter mothers (see Fig. 2).

In the second generation, the same pattern of licking behavior was recapitulated by the daughters of mothers in each group. Among these adult offspring, those who grew up in a small litter licked pups more than those growing up in a large litter and those raised in large litters by OBX mothers crouched over and licked their pups the least. Moreover, total licking by mothers on Day 6 postpartum and total licking by their adult offspring on Day 6 postpartum were positively and significantly correlated ($r = .48$). Hence, differential experiences of being licked had effects on expression of that behavior in offspring when they became mothers. This result occurred even though the daughters could smell their litters and had litters of intermediate size.

Most importantly, the "reasons" or causes for more or less licking demonstrably changed across the two generations. In the first generation, the effect was caused by an intervention affecting the mother. In the second generation, the effect was caused by prior interactions of the new mother with her own mother. The most effective period for transmission of these kinds of intergenerational effects seems to be during the very early postpartum period. Significant correlations between mother and daughter behavior occurred when comparing behaviors exhibited during the first postpartum week but not after that period.

This cross-generational effect of licking provides a nongenomic neurobiological mechanism for the transmission of behavioral phenotypes (see also Gonzalez et al., 2001). This transfer is almost certainly mediated through mechanisms that are involved with modulation of emotional and/or perceptual responses rather than those involved with learning and memory. There is no indication that pups exhibit licking behavior themselves while they are being licked.

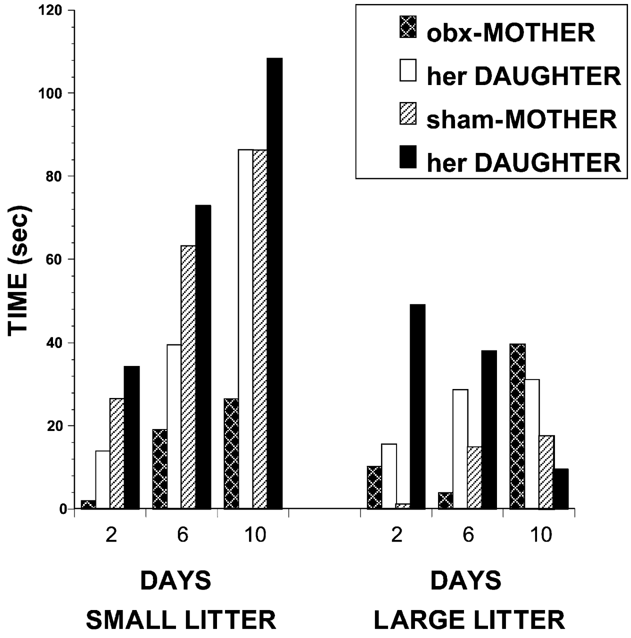


Fig. 2. Durations of maternal behaviors shown in mothers and their offspring when mothers were either bulbectomized (OBX) or SHAM operated and when litters in which offspring were either raised in LARGE (12 pups) or SMALL (6 pups) litters. The 2 (OBX–SHAM) × 2(SMALL–LARGE) ANOVAs were performed on duration of maternal behavior during tests on Days 2, 4, 6 and 10 postpartum (averaged). For mothers' behaviors, mothers raising SMALL as opposed to LARGE litters licked pups more [$F(1,16)=5.99$, $P<.026$] and SHAM mothers licked their pups more than OBX mothers [$F(1,16)=3.8$, $P<.069$]. In fact, the animals licking least were OBX LARGE litter mothers [interaction $F(1,16)=7.1$, $P<.017$]. Among the daughters, those raised in SMALL litters engaged in pup licking [$F(1,14)=5.1$, $P<.04$] and genital licking [$F(1,14)=7.5$, $P<.016$] more than did those raised in SMALL litters and females who were raised in LARGE litters by OBX mothers crouched over their young the least [interaction $F(1,14)=3.07$, $P<.05$].

Hence, there is no way for this behavior to be reinforced or conditioned in relation to the prevailing stimuli. Indeed, these same stimuli are not present later in life when the adult licking behavior is exhibited. When the pup matures and becomes a mother, there is no indication that she has "learned to lick" more or less from her mother or that there is a previously conditioned somatosensory reflexive response that leads to more or less licking in response to pup cues, although this latter idea has yet to be tested. Instead, how much licking occurs depends on the mother's past experience with being licked as a pup and at least the olfactory characteristics of her own pups later.

1.3. Disruption of usual early rearing experience

A third way of manipulating the maternal system to assess the effects on adult maternal behavior of early nest experiences is to alter the consistency and reliability of the mother's behavior toward her pups. This can be done by separating mothers and offspring during the nesting period (Gonzalez et al., 2001; Lovic et al., 2001; Rees and Fleming, 2001).

In different studies, pups were either left with their own mothers for the entire preweaning period (controls) or separated from their mothers for 3 h daily (Days 2–9), 5 h daily (Days 2–18) or 24 h daily (Days 4–20). In animals experiencing 3 or 5 h of maternal deprivation daily, the litters were culled to 12 pups (6 males and 6 females) on PND 1. From PND 2 to 9 or 18, three females from each litter were maternally deprived for 3 or 5 h daily (Lovic et al., 2001; Rees and Fleming, 2001). The deprived pups (D) were individually placed into plastic containers maintained at 30 °C. The other pups were kept with the dam and were not deprived (ND). On PND 21, all female offspring were weaned. All the animals were pair weaned until adulthood when they were mated and gave birth. Mothers were separated from pups at parturition. Foster pups were returned to the mothers starting 4 days after parturition and maternal behavior was assessed for 5 consecutive days.

Under conditions where animals were maternally deprived for 24 h daily, their litters were culled to 10 pups, four males and six females at parturition. On PND 4 and 5, four females were removed from the nest, three of the females underwent a gastrostomy to enable milk delivery and a fourth was marked and returned to nest (intact control, mother reared). Two of the three females that underwent surgery were raised artificially (experimental, AR minimally stimulated and AR maximally stimulated) and the third had the gastrostomy tube cut off just outside the skin and was returned to the nest after being marked with a different color (surgical control, mother reared).

AR pups were housed individually in open-top plastic cups with corn-cob bedding, which fit into a second weighted cup floating in a temperature-controlled water bath (36–40 °C). The gastrostomy tubing was connected to syringes containing Messer milk formula mounted in a Harvard Apparatus Syringe Pump programmed to infuse the diet (volume calculated as a function of pup's body weight) for 10 min every hour, 24 h daily. Experimental rats were artificially reared from PND 4 to 20, with the exception of a suckle control and a sham surgery group, which were reared with the dams and weighed daily. The offspring of the AR females (F1 generation) were themselves reared to adulthood, mated and tested with their own offspring (F2 generation).

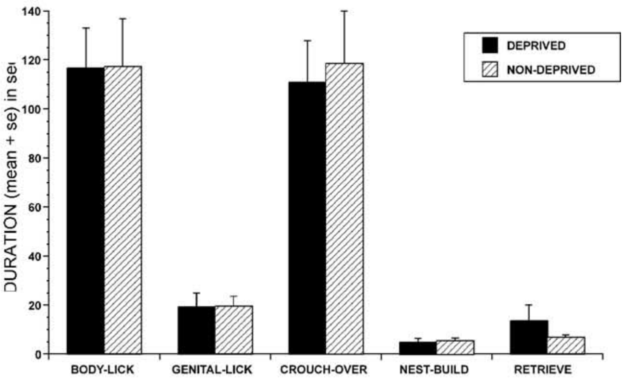
Maternal behavior deficits in the offspring were related to the degree of earlier maternal deprivation (Fig. 3a and b). Offspring that had experienced the least deprivation (3 h daily) showed no deficits in adult maternal behavior in comparison to controls (Fig. 3a). Offspring that experienced somewhat longer 5-h daily periods of deprivation and over a longer preweaning period showed initial deficits in licking behavior compared with controls, and once they were fully maternal these deficits persisted in both licking and crouching by comparison to controls (see Fig. 3b for the average across 5 test days).

Mothers experiencing, as pups, the most extreme periods of maternal deprivation (24 h daily) exhibited even greater reductions in pup body licking, genital licking and crouching as adults (Fig. 3c) (Gonzalez et al., 2001). These animals were also unlike MR animals by showing deficits in their ability to gain lasting benefits from their postpartum interactions with pups. If MR animals were exposed to pups during the first few postpartum hours and then separated from them, they showed enhanced responsiveness to pups when tested after a 15-day separation from them. Maternally deprived animals seemed less affected by a similar experience, taking significantly longer to respond maternally to foster pups (Melo and Fleming, in preparation). Hence, their ability to learn from their pup-related experiences was compromised through this 15-day separation.

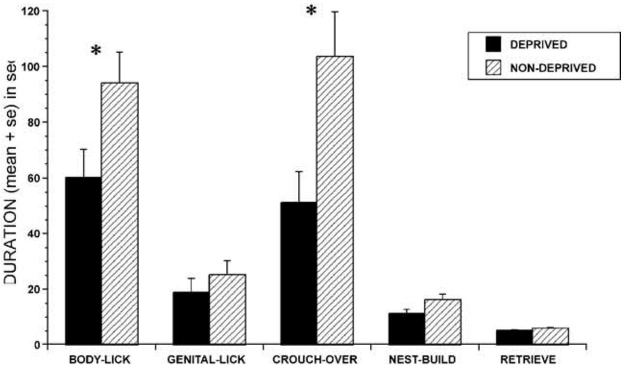
1.3.1. Behavior of mothers of deprived pups on reunion

If pups have access to their mothers for most of the day, then short periods of deprivation during their preweaning lives are not detrimental to their adult maternal behavior. In fact, if these periods of deprivation are very brief (15 min) (also known as the “handling” regime), when deprived pups are returned, the mother licks them more than she would normally, both on their reunification with the mother and 24 h later (and these pups, in turn, as mothers will lick their own pups more) (Caldji et al., 1998, 2000; Fleming et al., 1999; Francis and Meaney, 1999; Francis et al., 1999a,b; Liu et al., 1997; Pryce et al., 2001). If separations are somewhat longer in duration, on the order of 5 h or more, on reunion with their litters, the dams of the deprived pups will respond maternally to their offspring, but their behavior is by no means normal. While the return of the litter may result in elevated licking on their replacement in the nest, this elevation is short lived and is no longer apparent the next morning (Pryce et al., 2001). Moreover, the pups from separated litters experience lengthy periods when they are not receiving all the usual somatosensory, thermal, olfactory and possibly auditory stimuli they would normally experi-

(a) 3-hour Daily Separation



(b) 5-hour Daily Separation



(c) 24-hour Daily Separation

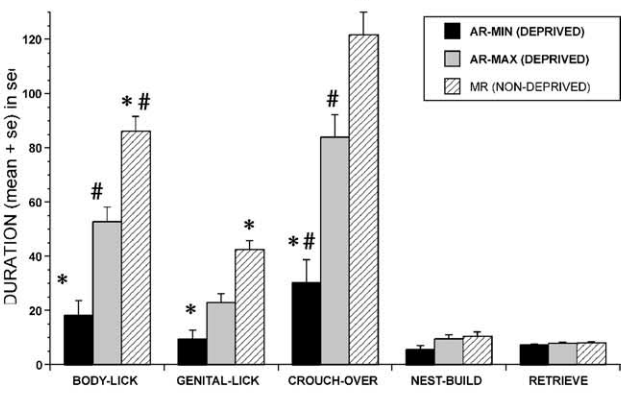


Fig. 3. Durations of different maternal behaviors averaged across 5 test days in mothers tested postpartum that had been separated from their own mothers (DEPRIVED) or not separated (NOT DEPRIVED) for 3 (a) or 5 (b) h daily during the preweaning period. ANOVA comparisons between deprived and nondeprived animals in both 3- and 5-h deprived groups in latencies to first show different maternal behaviors were not different. All animals expressed maternal behavior on the first or second test day. The 2 (neonatal condition) × 5 (time, days) ANOVAs on durations of behavior were performed for both deprivation conditions. There were no differences between groups in comparisons of nondeprived and 3-h deprived groups (a). However, in comparisons with the 5-h deprived conditions, deprived animals showed lower levels of body licking and crouching than did nondeprived animals (b) [$F(1,40)=3.78-5.7$, $P<.05-.02$]. (c) Durations of different maternal behaviors were averaged across 5 test days in mothers tested postpartum that had been reared without mother (artificial, AR-DEPRIVED) or by mother (MR-NONDEPRIVED). AR animals either had received six additional strokings daily (AR-MAX) or two strokings daily (AR-MIN). Repeated-measures (2 × 2 design) rearing (AR vs. MR) × time (early, Days 2+4 postpartum vs. late, Days 6+10 postpartum) were done on durations of all the maternal behaviors for cohorts one and two combined. For all the statistical analyses performed, there were 22 AR animals and 31 MR animals. For pup licking, genital licking and crouching, there were significant effects of rearing condition, with MR animals showing higher levels than AR animals [pup licking $F(1,51)=36.96$, $P<.000$; genital licking $F(1,51)=15.44$, $P<.000$; crouching: $F(1,51)=20.4$, $P<.000$]. For licking measures, there were also time effects, with licking increasing over time. Repeated-measures (2 × 2 design) rearing (MAX vs. MIN) × time (early, Days 2+4 postpartum vs. late, Days 6+10 postpartum) were done on durations of all maternal behaviors. For all statistical analyses performed, there were 11 MAX and 11 MIN animals. There were significant stimulation condition for pup licking [$F(1,20)=14.74$, $P<.001$], genital licking [$F(1,20)=7.20$, $P<.020$] and crouching [$F(1,20)=7.86$, $P<.020$]. In all cases, MAX animals showed a higher level of these behaviors than did MIN animals.

ence when with their mothers. These stimulation deficits result in progressive dysregulation of physiological processes in the offspring, which affect a wide range of behaviors, including their responses to stressors (Hofer, 1987; Kraemer, 1992; Kuhn and Schanberg, 1998; Lovic et al., 2001; Hall, 1998; Panksepp et al., 1997). As well, these deficits affect brain mechanisms that mediate maternal behavior.

1.4. Deprivation of mother and her "replacement"

To determine whether the effects of more extended preweaning maternal deprivation (24-h separation) could be remedied or reversed by providing additional licking-like somatosensory stimulation, we reared pups artificially and then determined the effects of more or less stimulation during the preweaning period (Gonzalez et al., 2001).

Pups that are artificially reared require a minimum of two anogenital swabbings a day to facilitate urination and defecation. Without this amount of stimulation, pups will not survive. One group of AR animals (MIN group) were stroked twice a day (the required minimum) with a warm, wet paintbrush that wiped their anogenital regions for approximately 45 s to stimulate urination and defecation. A second group of AR pups (MAX group) was stroked five times a day with both anogenital and overall body stimulation, the stimulation lasted 2 min per pup. This stimulation was carried out from the day the pups were placed on the pumps (PND 4) to the day of weaning (PND 20). Animals were assessed for their pup-directed behaviors as adults, with their own litters, culled to eight pups, starting on the day of parturition and through Day 18 postpartum.

Complete deprivation of mothering resulted in reductions in many maternal behaviors but not in the motivation to respond maternally. All groups retrieved young. However, reduced body licking, genital licking and crouching produced by complete deprivation of mothering were partially reversed by giving AR pups maximum brushing stimulation as they were growing up (Fig. 3c). This indicates that licking-like stimulation reduces deficits in a number of maternal behaviors. Whether the early experiences affect the expression of the adult maternal behaviors by altering the appetitive components of behavior (as in the hedonic or salience value of pup stimuli that elicit or maintain licking behavior) or by altering the strictly consummatory responses (as in the peripheral and central mechanisms mediating the movements associated with licking behavior) is currently not known. It seems, however, most likely that some aspect of the perception of the pup cues and not the motor response itself is affected by early deprivation because we have not observed a change in the quality of behaviors exhibited, only in their intensity.

With respect to the nature of the effective early experiences, other as yet undefined aspects of maternal stimulation must contribute to the development of maternal licking and crouching behaviors. In fact, there is every likelihood that a "combination" replacement regime (simulating mothers' odors, temperature, movement and other somatosensory characteristics) would result not only in more complete maternal responding in adult offspring but also would likely result in the reductions in deficits in many of the other emotional and social deficits that follow early maternal deprivation (Fleming and Blass, 1992; Kraemer, 1992; Moore, 1995; Najbauer and Leon, 1995; Wilson and Sullivan, 1994). Indeed, stimulation by conspecifics and by their movement, warmth and tactile characteristics likely also contribute to the normal development of behavior. In a recently completed study, we have found that rearing AR-MAX animals with one other conspecific (AR-SOCIAL or peer rearing) ameliorates some of the behavioral deficits seen during the juvenile period. As juveniles, these animals are less erratic and engage in more licking and crouching when placed with pups (Melo et al., in preparation) (see Fig. 4). To date, these animals have not been tested on other tasks.

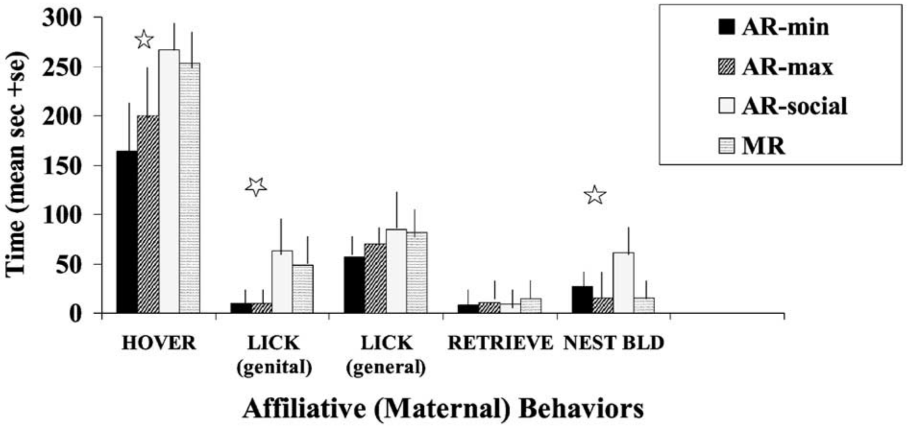


Fig. 4. Social peer rearing reverses the negative effects of AR. 24-h Maternal deprivation on maternal behaviors in juvenile female rat comparisons among the three groups [AR (MAX and MIN, combined) vs. AR-SOCIAL vs. MR] were done using one-way ANOVAs on all the maternal behaviors. Overall differences were found for crouching [$F(2,40)=3.44$, $P<.042$], genital licking [$F(2,40)=5.66$, $P<.007$], nest building [$F(2,40)=3.35$, $P<.050$] and marginally for general licking [$F(2,40)=2.32$, $P<.110$]. No difference was found between AR-SOCIAL and MR for crouching or licking behaviors.

However, if these studies play out as with prior studies in rhesus monkeys (Kraemer et al., 1991), the eventual finding may be that one can experimentally "replace" the quantity of maternal stimulation in a variety of ways but not quite the quality. It is the contingent pattern of maternal stimuli in relation to infant behavior that seems to be critical once the quantity of stimulation is within the normal range.

1.5. Deprivation effects on the maternal behavior of granddaughters

AR and MR dams whose maternal behavior was described above had offspring who were themselves reared to adulthood (F2 generation). These animals were mated and were then observed for their maternal behavior in response to their own offspring.

The offspring of AR mothers licked their pups and crouched over them less than did offspring of MR mothers (not shown). As shown in Fig. 5, the correlation between the pup licking of MR and AR mothers and these same behaviors in their daughters was positive and significant (Gonzalez et al., 2001).

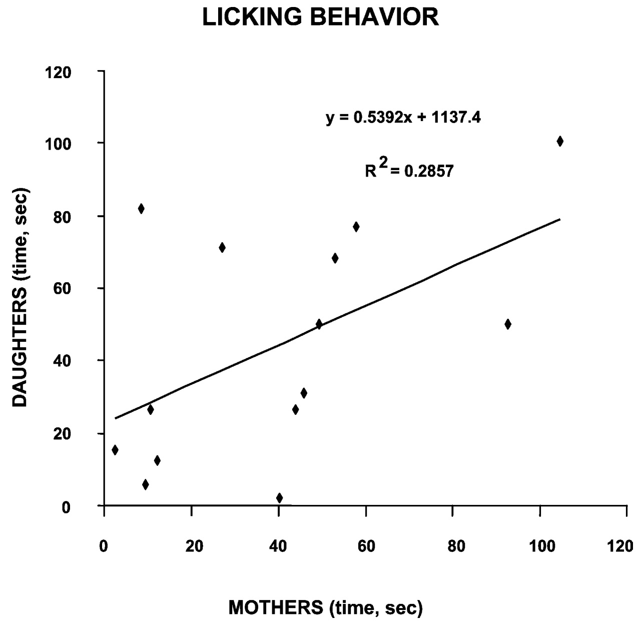


Fig. 5. Regression line relating pup licking by MR and AR female offspring toward their offspring (daughters) in adulthood and by their female offspring towards their offspring (granddaughters). Repeated-measures (2 × 2 design) mother's rearing condition (AR vs. MR) × time (early, Days 2 + 4 postpartum vs. late, Days 6 + 10 postpartum) were done on all maternal behaviors. For all statistical analyses performed, there were 11 AR and 14 MR offspring. There was a significant main effect of mother's rearing condition with offspring of MR mothers showing higher levels of the behaviors than offspring of AR mothers [pup licking $F(1,24) = 5.59$, $P < .050$; crouching $F(1,24) = 3.93$, $P < .050$; nest building $F(1,24) = 16.42$, $P < .001$]. There was no significant effect for pup genital licking, body sniffing, grooming and digging. There were no differences among offspring of AR mothers as a function of level of stimulation (MAX vs. MIN) that their mothers received.

1.6. Other behavioral changes produced by maternal deprivation that influence mother's responses to her offspring

As indicated earlier, AR animals are less able to gain from their mothering experiences than are MR animals (Melo and Fleming, in preparation). This learning deficit seems not to be restricted to the maternal context but seems to extend to other social experiences. For instance, artificially raised animals were worse than MR animals in their ability to recognize familiar conspecifics and hence showed deficits in a social learning task. When exposed on 2 consecutive days to either the same juvenile or two different juveniles, on the first day of exposure the two groups sniffed the novel juvenile equally. On the second day of exposure, however, MR animals approached and sniffed the familiar juvenile less than the nonfamiliar juvenile, whereas AR animals sniffed the two equally, as though both were novel (Levy et al., in preparation). In contrast to social tasks, as long as the tasks were easy enough, deficits did not extend to other kinds of learning tasks. AR animals showed no deficits in either a discriminative fear conditioning task, the Morris water maze or the radial arm maze (Levy et al., in preparation).

Recent evidence from our laboratory shows, however, that artificial rearing may disrupt sensorimotor gating and ability to inhibit responses and these may well affect an animal's sustained attention to her own litter (Fleming et al., 2001). In a novel open-field test AR, animals are more active than are MR animals (Gonzalez et al., 2001). In tests of prepulse inhibition, AR animals, in comparison to MR animals, show reduced inhibition of the acoustic startle response after a prepulse. In an attentional set shifting task, they also show slower learning when relevant cues (the CS+) for learning are changed. As well, these animals seem to perseverate in their responses and to have difficulty shifting strategies, as in reversal learning (Fleming et al., 2001). In many cases, these deficits are partially reversed by providing AR animals with preweaning "replacement" licking-like stimulation.

To describe the rationale and details of the prepulse task in more detail, prepulse inhibition of the startle response is used as an operational measure of sensorimotor gating or involuntary preattentive inhibition of responses to sensory stimuli. It is hypothesized that successful completion of goal-directed behavior is optimized by inhibition of competing cognitive or motor processes, that is, good sensorimotor gating. Moreover, the prepulse inhibition task is a task that is known to be affected by early experiences (Geyer et al., 1993; Ellenbroek et al., 1998) and is dependent on many of the same neurochemical and neural mechanisms known to mediate maternal behavior (see below).

In the present context, AR-MIN, AR-MAX and MR animals were place in a grid floor animal holder, which was secured onto the startle platform. The session started with a 7-min acclimation period followed by a period in which baseline startle responses were established. Animals were then given 90 trials each which consisted of 15 startle trials (120 dB, 10 kHz tone, 30 ms long), 60 prepulse and startle trials that assessed prepulse inhibition (15 for each prepulse intensity), 12 prepulse alone trials (3 for each prepulse intensity) and 3 no stimulus trials. The prepulse inhibition trials consisted of prepulses of 72, 74, 80 and 86 dB (10 kHz, 20 ms long) followed by startle pulses of 120 dB. The pulses started 100 ms after the onset of prepulses. Prepulse inhibition was calculated according to the following formula: 100−[(startle amplitude on prepulse+startle trials/startle amplitude on pulse alone trials)×100]=percent inhibition.

As shown in Fig. 6, there were no significant group differences in initial startle amplitudes (first four trials) or in their baseline startle responses. However, in comparisons between MR and AR-MIN animals, MR animals showed substantial inhibition of the acoustic startle response when it was preceded by a prepulse, whereas the AR-MIN animals did not. Extrasomatosensory licking-like stimulation of the AR-MAX animals during development reversed some of these inhibition deficits seen in the AR-MIN animals. What is interesting in the present context is that animals who showed the largest deficits in response inhibition as assessed by these tasks also showed the lowest levels of maternal licking and crouching when with their pups (Fleming et al., 2001). In fact, the level of maternal licking and crouching shown was highly correlated with responses on the prepulse inhibition task. The greater the inhibition shown, the higher the levels of these maternal behaviors in the home cage.

1.7. Neurobiological mechanisms affected by early experience

1.7.1. The maternal circuit

The "maternal circuit" has been conceptualized as a set of brain structures that are genetically mandated to express maternal behavior. This circuit in turn is viewed as interfacing with brain mechanisms that mediate emotion, sensation, perception, recognition and memory and cognitive functions more generally (Fleming et al., 1999). It is not known whether early maternal stimulation or its deprivation alters adult maternal responsiveness to offspring by altering the formation of the maternal neural circuit directly (Numan, 1994) or possibly by altering its plasticity, which underlies postpartum experience effects acquired in adulthood (Fleming and Korsmit, 1996; Fleming et al., 1994, 1996; Walsh et al., 1996; Numan and Numan, 1994). It is possible that early deprivation from the mother alters the development of the medial preoptic system or its afferent (amygdala, bed nucleus of stria terminalis) or efferent (midbrain tegmentum) connections (Numan, 1994). It is also likely that it alters the development of receptor systems normally activated by the parturitional hormones that reside in this maternal circuit (see below).

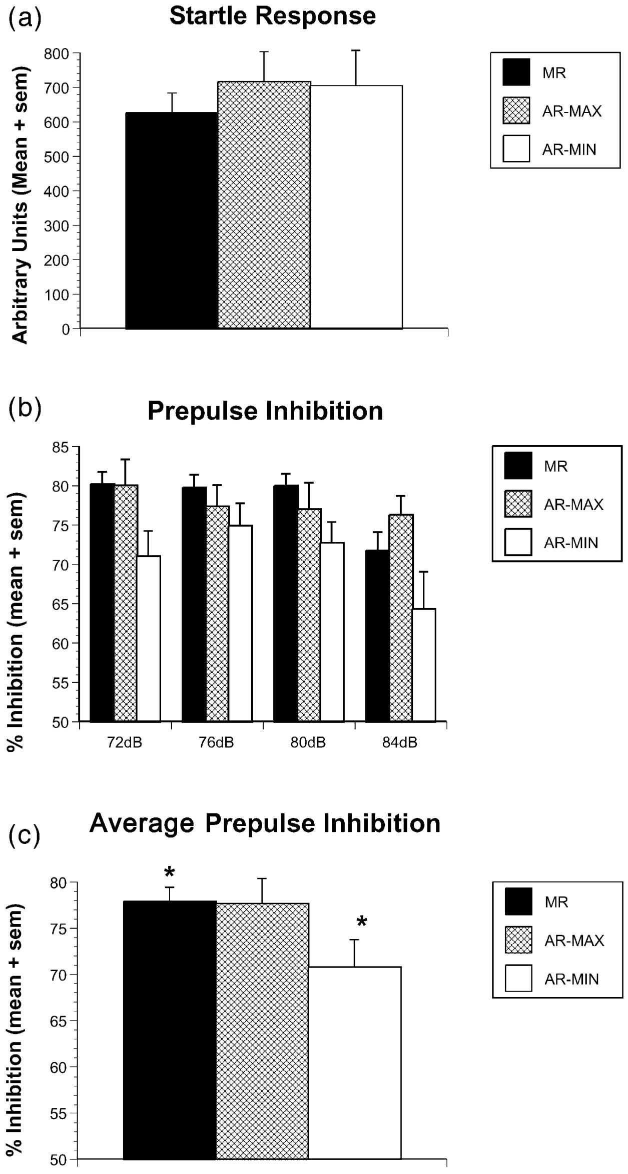


Fig. 6. Bar graphs show average±S.E.M. startle responding in second block of startle trials (a). Percentage prepulse inhibition for four prepulse intensity levels (b) and averaged prepulse inhibition (c) are also depicted. Compared to MR rats, AR-MIN rats showed reduced levels of prepulse inhibition. Prepulse inhibition analyses were carried out using repeated-measures ANOVA [$F(2,47)=2.7$, $P<.08$] followed by Dunnett's post hoc tests. Dunnett's post hoc tests indicated that MR rats showed greater prepulse inhibition than AR-MIN rats ($P<.031$). Importantly, there were no differences between groups with respect to their responses in prepulse alone trials. This indicates that PPI deficits in AR-MIN rats are not due to differential hearing sensitivities to the four different prepulses.

Consistent with this notion are recent data by Gonzalez and Fleming (in preparation) showing that in comparison to mother rearing, early maternal deprivation by artificial rearing results in juvenile female animals that show reduced pup-related c-*fos* activation in the "maternal circuit" and especially in the medial preoptic area in animals interacting maternally with rat pups (see Fig. 7). AR and MR animals were placed into one of four juvenile conditions: exposed to

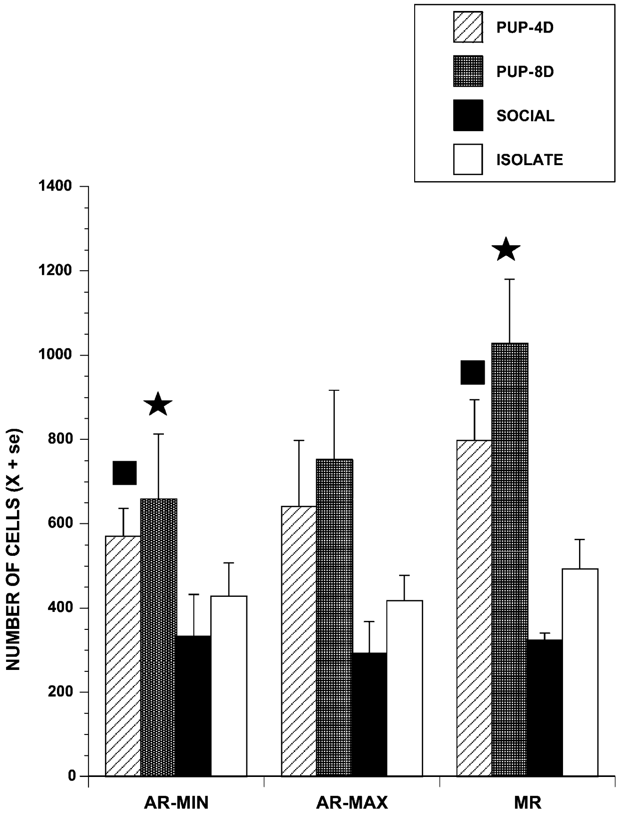


Fig. 7. Number of cells showing fos-like immunoreactivity in the MPOA of the juvenile rat (AR-MAX, AR-MIN and MR) within each of the juvenile conditions: exposure to pups for 4 days (PUPS-4); exposed to pups for 8 days (PUPS-8); exposed to a social conspecific for 4 or 8 days (SOCIAL) and left alone in isolation (CONTROL). ANOVA comparisons between the three rearing conditions (MAX vs. MIN vs. MR) show that there were main effects for the MPOA, with MR animals within the pup groups (PUPS-4 and PUPS-8) having the highest cell densities and the MIN having the lowest. There was also a significant main effect for juvenile condition within the MPOA [$F(1,94)=19.12$, $P<.001$], with the two pup groups, regardless of early rearing condition, having the highest cell densities compared to the social and isolated control groups. Post hoc comparisons show that for the MPOA both pup groups were significantly different from the social and isolated controls.

pups for 4 days (PUPS-4) (PND 22–25, sacrificed on PND 26, $n=20$), exposed to pups for 8 days (PUPS-8) (PND 22–29, sacrificed on PND 30, $n=20$), exposed to a social playmate for 4 or 8 days (SOC-4 and SOC-8) ($n=35$) or left alone in isolation (CONTROL) ($n=20$). A distinction was made between 4 and 8 days of exposure to pups because it was assumed that the 4-day group would be on the threshold of becoming maternal (where 15–20% retrieve pups), whereas the 8-day group would exhibit the full repertoire of maternal behaviors including, retrieval, pup licking and hovering (where >90% retrieve pups). Animals were separated from pups at the end of the stimulation period and then exposed to pups on the next day for a 2-h period prior to sacrifice. As shown in Fig. 7, groups exposed to pups licked and crouched over them and had higher c-*fos* expression in the MPOA than those not exposed to pups. Animals that showed maternal behaviors, particularly retrieval behavior, had the highest levels of Fos-lir in MPOA. As well, with respect to the effects of preweaning experiences, among those exposed to pups, AR-MIN animals had significantly lower c-*fos* counts in the MPOA than did MR animals. Not surprisingly, replacement with extra stimulation (AR-MAX condition) reversed some of these c-*fos* effects of deprivation.

In a recent study, we have found that these effects persist into adulthood and can be revealed during the postpartum period (Gonzalez et al., in preparation). In comparison to MR animals, AR animals, when tested with their own offspring postpartum, showed lower levels of licking and crouching as well as lower levels of c-*fos* expression in the MPOA. Again, the AR-MIN animals had the lowest number of Fos-lir cells in the MPOA and the AR-MAX animals had levels similar to, if not higher than, levels seen in MR animals (see Fig. 8).

Although these results suggest a brain change associated with early maternal deprivation, we do not know what the underlying molecular and physiological "causes" of the reduction in c-*fos* activation are. In light of these considerations, it would be interesting to know whether manipulations of maternal odors, vocalizations and/or thermal cues in conjunction with stroking stimulation, in the artificial rearing "pup-in-the-cup" paradigm, would affect animals' subsequent responses to their pups and their cues and whether there occurs an associated change in olfactory, limbic and hypothalamic mechanisms.

1.7.2. General neurochemistry

Deprivation of maternal behavior is known to induce a variety of physiological, behavioral, metabolic and neuro-

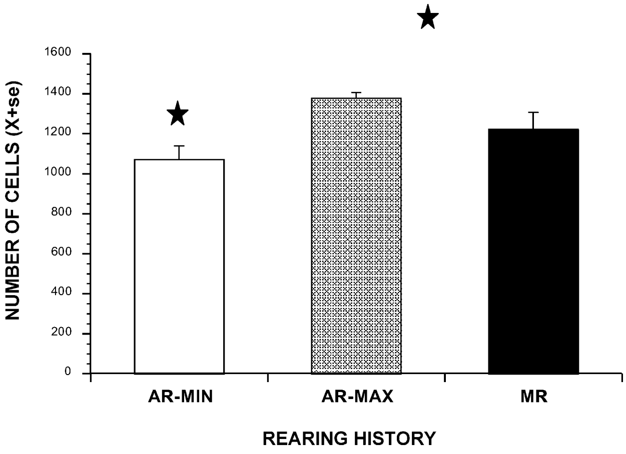


Fig. 8. Number of cells showing fos-like immunoreactivity in the MPOA of the adult female rat (AR-MAX, AR-MIN and MR). ANOVA comparisons between the three rearing conditions (MAX vs. MIN vs. MR) show that there were main effects for the MPOA, with AR-MIN animals having the lowest number of cells showing FOS-lir in the MPOA when exposed to pups postpartum. Extra stimulation provided during the neonatal period reverses these effects [$F(2,16)=3.968$, $P<.05$].

chemical changes that are differentially regulated by environmental and social stimuli and that could influence a mother's responsiveness to her offspring (Hall, 1998). For instance, there are changes in the oxytocin system (Boccia and Pedersen, 1999; Francis et al., 2000; Noonan et al., 1994), important for affiliation and postpartum maternal behavior (Insel, 1997; Noonan et al., 1994; Panksepp et al., 1994; Uvans-Moberg, 1998). There are also changes in the dopamine system (Hall et al., 1999; Kehoe et al., 1998), also known to be important for maternal behavior (Hansen, 1994; Hansen et al., 1993; Keer and Stern, 1999; Stern and Keer, 1999) as well as for processes of reinforcement, stimulus salience, attentional function, prepulse inhibition and learning in a biologically relevant context (Fleming et al., 1994; Varty and Higgins, 1995; Matthews et al., 1996). Associated with changes in the dopamine system, there may also be changes in prolactin and other hormones that are important for the expression of maternal behavior at parturition (Bridges, 1990).

1.7.3. Sensory-perceptual mechanisms

There is now substantial evidence that the experience of exposure to mothers' odors in association with her licking is encoded in and produces long-lasting changes in the olfactory bulb and in the brain. Formation of the association between licking and maternal odor produces changes in the olfactory bulbs, altering their neurochemical and structural properties (Najbauer and Leon, 1995; Wilson and Sullivan, 1994), and depends on the activation of the noradrenergic system that originates in the midbrain locus coeruleus and terminates in the olfactory bulbs (Wilson and Sullivan, 1994). In fact, infusions of norepinephrine agonists into the olfactory bulbs of neonates during odor exposure mimics the reinforcing effects of stroking stimulation and induces olfactory conditioning (Sullivan et al., 2000). It would be interesting to see if this manipulation would also enhance an animal's later responsiveness to pups scented with the same odor stimulus that had been associated with noradrenergic agonists earlier during the neonatal period.

1.7.4. Recognition-response mechanisms

In addition to olfactory mechanisms, there are substantial data that additional environmental manipulations during the preweaning period (including somatosensory "licking" stimulation) produce changes in cortex, hippocampus and other limbic areas (Cramer, 1988; Pascual and Figueroa, 1996; Post et al., 1998; Rosenzweig and Bennett, 1996). Given the importance of pup odors in the regulation of normal pup identification and licking by maternal animals (Brouette-Lahlou et al., 1999; Fleming and Rosenblatt, 1974a,b; Moore, 1995), tactile stimulation from the pups for normal mouthing, retrieving and high arched crouching (Stern and Johnson, 1990; Stern and Kolunie, 1991; Stern, 1996) and infant ultrasounds in the regulation of search and retrieval (Brunelli et al., 1994), it remains to be seen whether or not the behavioral deficits seen in maternally deprived animals are due to the absence of normal early social recognition and response patterns and hence disruptions in brain systems that mediate these experience effects.

1.7.5. Emotional-motivational mechanisms: hypothalamic–pituitary–adrenal (HPA) axis

1.7.5.1. Emotional behavior. Maternal deprivation also affects the development of fear and emotionality (Francis et al., 1999a,b; Gonzalez et al., 2001), albeit in complex ways. These emotional changes could clearly influence how a mother responds to her offspring (Fleming and Luebke, 1981). Females who are reared artificially seem not to show the usual consistent pattern of neophobia that characterizes MR animals, although they are somewhat hyperreactive in novel contexts. In comparison to MR animals, they are more agonistic with unfamiliar conspecifics (Gonzalez and Fleming, in preparation) and show enhanced activity in a novel environment (Gonzalez et al., 2001). In a somewhat different deprivation paradigm, Francis et al. (1999a,b) report that animals that were briefly separated from their mothers early on (in comparison to those that were handled but not in relation to nonhandled animals) show reduced exploration in the open-field test of emotionality (Francis et al., 1999a,b). Using similar lengths of deprivation as Francis et al. (1999a,b) during the first postnatal week, Rees and Fleming (2001) did not find any effects of separation or handling, when compared with undisturbed controls, on emotionality in the open-field test (Rees and Fleming, 2001). Clearly, the effect on emotionality of early deprivation is not a simple or unitary one and merits further analysis.

1.7.5.2. HPA axis. However, there is a large body of research indicating that maternal deprivation alters the output and feedback regulatory responsiveness of the HPA axis, both following an acute preweaning deprivation period (a single 24-h deprivation) and following chronic deprivations of 3 (or 5) or more h daily, as described in this report (see Suchecki et al., 1995). While the role of the HPA system in the normal expression of postpartum maternal behavior is ambiguous, recent results suggest that it may be involved in licking and crouching, although not in the initial retrieval behaviors (Panesar et al., submitted for publication; see below).

Chronic daily separations from mother and nest across the preweaning period usually encompasses the first 2 weeks of stress hyporesponsiveness (the SHRP). This form of deprivation produces long-term changes in the responsiveness of the HPA axis, although these are often not straightforward. In comparison to animals who are "handled" (either with a 15-min separation or without), animals experiencing chronic and longer deprivations, similar to those described in this report, in general have higher levels of basal corticosterone (Biagini et al., 1998) as well as higher concentrations of CRH mRNA and CRH in the median eminence (Plotsky and Meaney, 1993). These animals are also reported to exhibit higher levels of "stress"-induced corticosterone and ACTH in adulthood (Liu et al., 2000; Plotsky and Meaney, 1993; Wigger and Neumann, 1999).

While long periods of chronic deprivation create detrimental changes in the HPA axis, short periods of chronic deprivation (15 min or what is referred to as "handling") have beneficial effects on the stress system through increased licking by the mother after handled pups are returned to the nest (Meaney et al., 1989; O'Donnell et al., 1994; Plotsky and Meaney, 1993). During adulthood, handled rats have lower levels of both corticosterone and ACTH following the presentation of a stressor and they also show a faster hormonal return to basal levels than non-handled rats (Meaney et al., 1989). Handled rats also show lower levels of CRH mRNA than both deprived and non-deprived/handled rats (Plotsky and Meaney, 1993). These alterations in the HPA axis are thought to be due to a more efficient negative feedback system, which is characterized by increased glucocorticoid receptors (GRs) but stable mineralocorticoid receptors MRs in the hippocampus (O'Donnell et al., 1994).

In light of our behavioral effects, it is interesting that the increased activation of the HPA axis found in acutely deprived rats can be reversed by feeding and stroking rats during the deprivation period (Suchecki et al., 1993; van Oers et al., 1998). Feeding during the deprivation period can prevent the increase in corticosterone (van Oers et al., 1998). Stroking can prevent the increase in ACTH (Suchecki et al., 1993) and reverse the deprivation-induced depression in GRs in the hippocampus but not in the PVN (van Oers et al., 1998). Stroking has also been found to normalize growth hormone secretion and ornithine decarboxylase activity (Evoniuk et al., 1979; Suchecki et al., 1993). Hence, by reinstating critical components of the dams' nurturing behavior, some of the negative physiological responses due to maternal deprivation can be reversed.

Alterations seen in HPA activity not only occur as a function of maternal deprivation and "stroking" stimulation, but also have been found with normal variations in maternal care (Caldji et al., 1998; Francis and Meaney, 1999; Francis et al., 1999a,b; Liu et al., 1997). Variations in maternal licking and grooming of rat pups produce differences in the regulation of HPA activity in the pups. Offspring from mothers that received high, as opposed to low, amounts of licking in the nest show decreased plasma ACTH and corticosterone response to stress, increased hippocampal glucocorticoid receptor expression, decreased levels of hypothalamic expression of CRF, increases in the density of receptor binding of central benzodiazepine receptor and $\alpha 2$ adrenoreceptor and increases in CRH binding in the amygdala and locus coeruleus (Caldji et al., 1998; Liu et al., 1997).

1.8. Transgenerational propagation

How the complement of biological effects associated with variation in maternal behavior might be transmitted partially or in totality is not understood. There are at least two mechanisms that can be defined. The first is the propagation of behavioral phenotypes that lead to variation in preferences for and responsiveness to pup cues. After an environmental change (lemon odor) as a pup, the grown-up pup-as-new mother is "set" to respond to pups having stimulus properties characteristic of her own mother. Intergenerational variation in how mothers identify and respond to pups appears to depend on experience, because pups reared with mothers who are scented with one type of odorant ultimately come to prefer pups scented with the same odorant when they become maternal. In terms of its proximal control, we know that the elicitation of different components of maternal behavior is dependent on sensory inputs from the pups that usually activate expression of behavior in the mother and this would feed back to the pup through a different modality (Alberts and Gubernick, 1990; Brouette-Lahlou et al., 1999; Brunelli et al., 1994; Lonstein and Stern, 1997; Stern, 1996; Stern and Kolunie, 1991). That is, a particular smell of the pup would lead to more or less retrieval and then more or less somatosensory stimulation (licking) of the pup. Perceptual and perhaps recognition systems underlying maternal behavior are affected by early experience and these changes may be propagated in the form of altered pup care and perhaps survival if the environment permits it (Fleming and Blass, 1992; Kraemer, 1992; Moore, 1995; Najbauer and Leon, 1995; Wilson and Sullivan, 1994). On the other hand, the lemon scented, and perhaps more licked pup, may transfer that aspect of behavior as well through changes in a second mechanism.

The second mechanism is the propagation of behavioral phenotypes in emotional or stress responsiveness to stimuli in general. This emotional "responsiveness" is then reflected in maternal practices. The idea would be that, because she is less fearful and timid, the more-licked-as-a-pup mother is more likely to exhibit increased licking to her own pups. This is a modulation or expansion of a behavioral theme that is normally expressed. Thus, by comparison to non-mothers, typical new mother rats are less emotional, respond with less avoidance to novel cues, learn more rapidly about their pups as well as other olfactory and social stimuli and rapidly develop an attraction to pups and their cues (Fleming et al., 1996). Stimulation of the perioral region around the mothers' mouth by contact with pups facilitates maternal mouthing of pups and their retrieval into the nest (Alberts and Gubernick, 1990; Brunelli et al., 1994; Brouette-Lahlou et al., 1999; Lonstein and Stern, 1997; Stern, 1996; Stern and Kolunie, 1991). Stimulation of the mothers' mammary gland region by pups located underneath her belly facilitates pup attachment to the teats and the adoption of a nursing crouch over the young. Odors in the form of pup body, urine and nest odors stimulate the mother to lick the pups, and pup ultrasound vocalizations cause the mother to leave the nest in search of the pups and to orient toward them (Alberts and Gubernick, 1990; Brunelli et al., 1994; Brouette-Lahlou et al., 1999; Lonstein and Stern, 1997; Stern, 1996; Stern and Kolunie, 1991). These behavioral changes in the new mother are dependent on the hormonal and neurochemical profile that activates maternal behavior (Fleming et al., 1996).

Hence, the endocrine state associated with motherhood induces enhanced sensitivity and/or hedonic responses, but the degree to which this is itself expressed behaviorally appears to be modulated by actions of the HPA axis in addition to changes in the animals' reinforcement, memory and sensory systems (Fleming and Corter, 1995). Supporting a role of the HPA axis in the regulation of postpartum maternal responding, in a recent study, we have found that adrenalectomy results in a reduction in maternal licking and crouching, whereas high concentrations of corticosterone in the drinking water has opposite effects (Panesar et al., submitted). Clearly, these effects of corticosterone are opposite to what one would predict by what we know at present about the effects of deprivation on both the HPA axis and the maternal behavior. What we do not know is what the optimal levels and patterns of HPA activation might be for the normal expression of adult behavior. Establishing the clear links and lawful (possible U-shaped) relations between the effects of deprivation on the HPA axis and of the HPA axis on subsequent maternal behavior has yet to be established.

If the mother-related stimuli are not experienced by the young, then these recognition and stress mechanisms may not develop in the usual fashion and the behavioral phenotype of the next generation will be disrupted. When deprivation or additional stimulation in one modality (somatosensory) is given to offspring, either in the nest as a consequence of brief deprivation or experimentally in the form of simulated licking (brushing), the granddaughters have a different experience than they would have had otherwise, and cross-generational transmission effects may be exhibited.

2. Discussion

The quality of maternal behavior propagated in young adult mother rats is affected by the nature of mothering they received as neonates. This factor appears to overshadow factors directly attributable to parent–offspring lineage within a restricted breeding population. Thus, via cross-fostering studies, transmission of maternal behavior quality has been shown to be independent of degree of relatedness of mothers and the offspring they nurtured in colony-housed rats. Licking of the young is a predominant but not singular feature of this transmission process in rats. Rat mothers who are more maternally responsive to their infants in multiple domains of sensation and behavioral response produce infants who are in turn more maternally responsive to their infants. These effects could be propagated and maintained across generations under the appropriate environmental circumstances and generally are assumed to have adaptive value.

Conversely and logically, patterns of seemingly less adaptive maternal characteristics, such as reduced licking and so forth, can also be propagated across generations in rats. Seemingly deficient practices also propagate across generations in groups of nonhuman primates (Berman, 1990; Fairbanks, 1996) and again under the appropriate environmental circumstances (Maestripieri et al., 1997). More specifically, in human and nonhuman primates, patterns of maternal behavior characterized as "harsh," "insensitive" or "rejecting" are known to propagate across generations. Some aspects of the behavior are related to lineage/inheritance (Maestripieri et al., 1997; Skarr and McCartney, 1993; Skarr and Weinberger, 1983), but there is clear evidence for experiential transfer as well (Berman, 1990; Fairbanks, 1996).

Why, one wonders, is the mammalian nervous system set up so that both more or less adaptive or deficient maternal care practices can be propagated with some fidelity across generations (within limits)? Seemingly "deficient" rearing practices may produce offspring that are better able to survive and procreate in some environments, and some genotypes may be better able to withstand harsh rearing practices. Overall, the most parsimonious explanation of the results of animal studies, both rat and nonhuman primate, is that the effects of insensitive and neglectful parenting may not be demonstrably deleterious in many of the "natural" environments where these practices arise and are yet another example of plasticity in the mammalian nervous system. In primates, if the period of early deprivation prevents later sexual behavior or care of offspring to weaning, then the one generation deprivation/isolation effect will die out (Kraemer, 1992). It will not propagate because there will be no living individuals carrying the behavioral phenotype of the past experience to pass on to their offspring. At lesser levels of neglect/deprivation, where procreation and care of offspring remains successful in terms of survival, offspring are less canalized in terms of their acquired social behavior, and there is an increased probability for expression of behavior that would not have occurred otherwise.

Hence, in rhesus monkeys, the more general effects of maternal deprivation on adolescent and adult behavior are an increase in intraspecific aggressive behavior, "impulsiveness," meaning both exaggerated approach and withdrawal responses to environmental change and an increased ability to solve cognitive problems that depend on responding to novelty (Kraemer and Bachevalier, 1998). There is also a propensity to rear offspring in a "rejecting" or "harsh" manner (as we may define that culturally), which in all likelihood leads to propagation of these characteristics, or similar ones, to offspring. Ongoing studies will probably establish that a similar propagation of the effects of maternal deprivation in one generation to the next generation can also be observed in groups of rats procreating in a protected (laboratory) environment. That is, the effect is not specific to primates and may be more characteristic of mammals in general. Disruption of social rearing in one generation generally appears to lead to the production of offspring that are neurobiologically less responsive to social cues and hence less responsive to a social structure present in the previous generation for their behavioral regulation. The result is an expanded expression of behavior beyond the previously observed and socially defined limits. Whether this effect is successful in a larger context depends on the interaction of the next generation with the prevailing environment. Whether a phenotypic expression is "adaptive" has to stand the test of reality, that is, whether its bearer survives and rears offspring to reproductive maturity.

3. Conclusion

Transfer of maternal phenotypes is not peculiar to humans and nonhuman primates but can be demonstrated in rats as well. There is a neurobiological mechanism that appears to support this effect more generally in mammals. The core theme of this paper is that while many aspects of maternal behavior are propagated from generation to generation through genetic mechanisms, maternal behavioral phenotypes are also propagated through the effects of early experiences on maternal sensory, perceptual and recognition mechanisms that affect later responsiveness to offspring. If the transmission of the "maternal phenotype" is disrupted in one generation (via deprivation for example), then previously improbable phenotypic themes, neurobehavioral expressions, which may be proven to be more or less successful, emerge in the next generation. Therefore, understanding function and malfunction of the sensory, perceptual and recognition mechanisms by which parental behavioral responsiveness to offspring is transferred, or fails to transfer, from one generation to the next generation constitutes the next challenge.

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