

BRIEF COMMUNICATIONS

Opioids and Attachment in Rhesus Macaque (*Macaca mulatta*) Abusive Mothers

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This study investigated the role of the endogenous opioid system in maternal and affiliative behavior of group-living rhesus macaque (*Macaca mulatta*) mothers with a history of abusive parenting. Eighteen mothers received an injection of the opioid antagonist naltrexone or saline for 5 days per week for the first 4 weeks of the infant's life. After treatment, mother–infant pairs were focally observed. Naltrexone did not significantly affect infant abuse or other measures of maternal behavior. Naltrexone increased the amount of grooming received by mothers from other group members and reduced the mothers' rate of displacement activities such as scratching, yawning, and self-grooming. These results concur with previous primate studies in suggesting that opioids mediate the rewarding effects of receiving grooming and affect anxiety-related behaviors.

Attachment is an emotional bond to another individual that is characterized by proximity-seeking and proximity-maintaining behavior as well as intense distress in response to separation (Bowlby, 1969). Different forms of attachment are usually recognized in both animals and humans, including offspring–parent attachment, parent–offspring (parental) attachment, and attachment between adults (adult attachment). Although these different forms of attachment are characterized by similar behaviors, it is not clear whether they share underlying neurobiological substrates because of the lack of relevant data or the inconsistency of the findings, particularly with regard to parental attachment (Carter, 1998; Maestriperieri, 2001; Mason & Mendoza, 1998; Nelson & Panksepp, 1998; see the following).

The endogenous opioid system is one putative neurochemical substrate of attachment that may be shared by different forms of bonding (other putative substrates include, for example, the neu-

ropeptides oxytocin and vasopressin; Carter, 1998; Insel, 1997; Nelson & Panksepp, 1998). Based on similarities between attachment and opiate addiction, it has been hypothesized that a release of endogenous opioids mediates the rewarding properties of attachment, whereas a reduction in endogenous opioids results in emotional distress and drives the need to seek and maintain proximity with the attachment object (Panksepp, 1981). According to this hypothesis, exogenous opiates such as morphine should create a feeling of social comfort and reduce the motivation to seek social contact, whereas opiate receptor blockers such as naltrexone or naloxone should increase the motivation to seek social contact. This hypothesis has been supported by many studies of nonprimate animals such as rats, voles, guinea pigs, and chicks (Nelson & Panksepp 1998; Panksepp, Herman, Vilberg, Bishop, & DeEskenazi, 1980; Panksepp, Nelson, & Siviy, 1994). For example, work with rats has shown that physical contact and other types of social stimuli are associated with opioid release, and that opioid agonists are effective in decreasing isolation-induced vocalizations (see Nelson & Panksepp, 1998, for a recent review). On the basis of this research, Panksepp and colleagues suggested that the motivation for attachment may be dependent on specific brainstem and limbic circuits in the mammalian brain that originally subserved basic physiological needs such as energy balance, thermoregulation, or pain perception (e.g., Nelson & Panksepp, 1998).

Studies of nonhuman primates have supported the hypothesis that the opioid system is implicated in adult attachment as well as in offspring–parent attachment. However, the role of opioids in parental attachment is less clear. Research by Keverne and colleagues showed that adult talapoin monkeys treated with naltrexone or naloxone increased grooming solicitations of their social partners and received more grooming (Fabre-Nys, Meller, & Keverne, 1982; Keverne, Martensz, & Tuite, 1989; Meller, Keverne, & Herbert, 1980). Conversely, treatment with morphine resulted in a reduction of grooming solicitations and grooming

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time (Keverne et al., 1989). When socially isolated adults were allowed access to a conspecific, there were increases in the amount of time spent grooming as well as in the cerebrospinal fluid (CSF) levels of β -endorphin (Keverne et al., 1989). Finally, in rhesus macaques, naloxone increased the number of grooming solicitations and the amount of grooming received by adult females from other individuals (Martel, Nevison, Simpson, & Keverne, 1995). Taken together, the findings of these studies are consistent with the hypothesis that endogenous opioids may mediate the rewarding properties of affiliative interactions between adults.

Studies manipulating the opioid system of immature monkeys have produced results consistent with the hypothesized relation between opioids and attachment (Kalin, Shelton, & Barksdale, 1988; Kalin, Shelton, & Lynn, 1995; Martel et al., 1995; Schino & Troisi 1992). Thus, infant attachment and adult attachment appear to share a common neurochemical substrate (Nelson & Panksepp, 1998). The role of the opioid system in mediating maternal attachment to the infant has been investigated in only two primate studies that reported conflicting results. In one study, the opioid system was pharmacologically manipulated after mother–infant separation and reunion in rhesus macaques (Kalin et al., 1995). Morphine decreased clinging with the infant during the first 30 min of reunion, whereas naltrexone increased clinging. In a study of socially living rhesus mothers and infants, however, naloxone reduced both maternal grooming and maternal restraining of the infant, suggesting decreased rather than increased attachment to the infant (Martel, Nevison, Rayment, Simpson, & Keverne 1993). The effects of naloxone on affiliative interactions between mothers and other adults, however, were also contrary to the expectations. In fact, the mothers treated with naloxone showed reduced number of grooming solicitations and reduced amount of grooming received from other individuals. Because the study by Martel et al. (1993) contradicted findings that are well established in the primate literature on opioids and grooming behavior (previously mentioned), the results of that study are generally difficult to interpret. Clearly, further research on opioids and maternal behavior is needed before any firm conclusions can be drawn regarding the role of opioids in mediating maternal attachment.

In the present study, we investigated the effects of naltrexone on the behavioral interactions of rhesus macaque mothers with their infants and other group members. Consistent with the opioid hypothesis of attachment, we predicted that the effects of naltrexone on affiliative interactions between mothers and other group members would be similar to those reported by most previous primate studies. In other words, we predicted that naltrexone-treated mothers would increase the number of grooming solicitations and the amount of grooming received from other individuals (no specific prediction was made about grooming performed). We also predicted that the effects of naltrexone on maternal attachment to the infant would be similar to those on adult attachment. In other words, we predicted that mothers would increase their contact-seeking and contact-maintaining behavior with their infants.

In this study, we also investigated the possible role of the opioid system in abusive parenting. The rhesus macaque mothers used in this study were specifically selected for their propensity to display abusive parenting with their infants (Maestripieri, 1998; Maestripieri & Carroll, 1998b). Because abusive parenting may reflect lower maternal attachment to the infant, we hypothesized that if the treatment with naltrexone is effective in increasing maternal

attachment, it should also reduce or eliminate infant abuse. Finally, in this study we also investigated the effects of naltrexone on macaque mothers' anxiety, as reflected in their rates of displacement activities such as scratching, self-grooming, body shaking, and yawning (Maestripieri, Schino, Aureli, & Troisi, 1992; Schino, Perretta, Tagliani, & Troisi, 1996). In macaques, maternal anxiety plays an important role in both individual differences in parenting style and in the etiology of infant abuse (Maestripieri, 1993a; Maestripieri & Carroll, 1998a; Troisi & D'Amato, 1984; Troisi et al., 1991). For example, treatment of a Japanese macaque mother with diazepam reduced both anxiety and infant abuse (Troisi & D'Amato, 1991). Previous studies of primates reported that naloxone or naltrexone reduced the frequency of scratching (Fabre-Nys et al., 1982; Martel et al., 1995) and self-grooming (Schino & Troisi, 1992). On the basis of such studies, we predicted that the administration of naltrexone to macaque mothers would affect their rates of displacement activities and perhaps contribute to the reduction or elimination of anxiety-related infant abuse.

Method

Subjects and Housing

Subjects were 18 rhesus macaque (*Macaca mulatta*) mothers and their infants living in five large social groups at the Field Station of the Yerkes Regional Primate Research Center in Lawrenceville, Georgia. All macaques were housed in outdoor compounds (measuring 38×38 m) with adjacent indoor housing. The five groups averaged 103 members consisting of 1–3 adult males and 26–57 adult females with their subadult and juvenile offspring. Water was available ad libitum. Macaques received monkey chow (Ralston-Purina, St. Louis, MO) twice daily and were supplemented with oranges once per day. Dominance relationships among the adult females in each group were assessed with observations of aggressive and submissive behavior made prior to this study. Adult females in each group were ranked along a linear dominance hierarchy that remained stable during the course of the study. Adult females were classified as high ranking or low ranking depending on whether they ranked in the top half or bottom half of their group's hierarchy.

In the population of rhesus macaques housed at the Yerkes Field Station, 20–25 adult females have been identified who physically abuse their offspring (Maestripieri & Carroll, 1998b; definitions of infant abuse are described later). Infant abuse is clearly distinguishable from any other behavior in the maternal repertoire, and abusive mothers abuse their offspring with similar rates over the years (Maestripieri, Tomaszycki, & Carroll, 1999). The 18 adult females used as study subjects had been observed in previous years and determined to be abusive mothers. Abusive mothers were recruited into the study as they gave birth. All subjects were born and raised by their biological mothers in the groups in which they were observed. They were all multiparous and had successfully raised at least one offspring prior to this study. Information about their age, rank, and the sex of their infants is provided in the Results section.

Procedure

As soon as they gave birth, abusive mothers were randomly assigned to one of two experimental groups ($n = 9$ per group): Mothers in the first group (subjects) received a daily injection of naltrexone (1 mg/kg im) 5 days per week during the first 4 weeks of infant life, whereas mothers in the second group (controls) received an equivalent volume of saline with a similar schedule. Preliminary analyses indicate that subjects and controls did not differ significantly in their rates of infant abuse with their previous offspring. The dose of naltrexone was chosen on the basis of previous studies of macaques showing that such a dose can affect behavior without

Table 1
Mean (\pm SEM) Hourly Rates of Mother–Infant Interactions in
Subjects and Controls

Behavior	Subjects	Controls
M makes contact	1.76 \pm 0.33	1.69 \pm 0.26
M breaks contact	1.56 \pm 0.27	1.65 \pm 0.44
I makes contact	0.75 \pm 0.25	0.59 \pm 0.19
I breaks contact	3.49 \pm 0.51	3.54 \pm 0.40
M restrains	0.60 \pm 0.19	0.73 \pm 0.38
M rejects	0.41 \pm 0.12	0.82 \pm 0.36
M grooms	1.90 \pm 0.39	3.13 \pm 0.69
I screams	1.18 \pm 0.38	1.39 \pm 0.72
M abuses	0.34 \pm 0.11	0.82 \pm 0.36

Note. M = mother; I = infant.

any significant side effects (Kalin et al., 1988; Schino & Troisi, 1992). Drug treatment began the 1st day after parturition. Mothers were trained to be captured and receive injections and were never separated from their infants during the procedures. Shortly after the mothers received the injection and were released into their social group, mother and infant were focally observed for 1 hr. The observations were made from a platform that provided unobstructed viewing of the entire compound. Data were collected with IBM laptop computers.

The following maternal behavior patterns were included into the infant abuse category: (a) dragging (the mother drags her infant by its tail or leg while walking or running), (b) crushing (the mother pushes her infant against the ground with both hands), (c) throwing (the mother throws her infant at a short distance with one hand while standing or walking), (d) hitting (the mother violently slaps her infant with one hand or arm), (e) biting; (f) stepping or sitting on (the mother steps on her infant with one foot or both feet, or sits on her infant), and (g) rough grooming (the mother pulls her infant's hair or otherwise roughly grooms it, causing distress calls). Abuse events did not last more than a few seconds and therefore were recorded only in terms of their frequency.

Behavioral data collection also included mother–infant interactions such as contact, grooming, restraining, and rejection, and interactions between mothers and other individuals such as contact, proximity, grooming, grooming solicitations, aggression, submission, and avoidance (see Maestripieri, 1998, for behavioral definitions). The frequency of maternal scratching, yawning, body shaking, and self-grooming was also recorded. The rate at which mothers scratched themselves (number of episodes per hour) when their infants were out of contact was used as an indicator of maternal anxiety (Maestripieri, 1993a; Maestripieri et al., 1992; see Schino et al., 1996, for a pharmacological validation of this measure of anxiety).

Chi-square tests were used to compare the mother's dominance rank and the sex of their infants. The mother's age was compared with a *t* test for unpaired samples. Behavioral data were square-root transformed and analyzed with parametric statistics. Tests were two-tailed unless specific predictions were made; *p* values less than .05 were considered to be significant.

Results

Subjects and controls did not differ significantly in terms of age (subjects = 9.00 \pm 0.87 years, range = 5–13; controls = 9.67 \pm 1.38, range = 6–16), $t(16) = -0.41$; dominance rank (subjects: high rank = 6, low rank = 3; controls: high rank = 7, low rank = 2), $\chi^2(1, N = 18) = 0.27$; or sex of their infant (subjects: 5 males and 4 females; controls: 3 males and 6 females), $\chi^2(1, N = 18) = 0.90$.

To validate the pooling of data across the 4 weeks of treatment and observation, we conducted a repeated measures analysis of variance (ANOVA) across weeks. No time-dependent effects of naltrexone were found for any behavioral measure. When the data were pooled across the 4 weeks, subjects and controls did not differ significantly in rates of infant abuse or in any measures of mother–infant interactions (see Table 1). No significant differences were found in interactions between infants and other group members or between mothers and other females' infants. Finally, there were no significant differences in measures of contact, proximity, or aggression and submission between mothers and other group members.

As predicted, naltrexone-treated mothers received more grooming from other individuals than controls (*t* test for unpaired samples), $t(16) = 1.78, p < .05$ (one-tailed), whereas the amount of grooming performed was not significantly different, $t(16) = -0.17$ (see Figure 1). There were no significant differences in the frequency of grooming solicitations done or received by subjects and controls.

The rates of three of four displacement activities were significantly lower among subjects than controls: scratching, $t(16) = -4.39, p < .01$; self-grooming, $t(16) = -3.18, p < .01$; yawning, $t(16) = -4.58, p < .01$; body shaking, $t(16) = -1.52, ns$ (see Figure 2). In particular, the rate of maternal scratching when the infant was out of contact was significantly lower for subjects (0.72 \pm 0.25) than for controls (2.40 \pm 1.97), $t(16) = -3.05, p < .01$.

Discussion

The administration of the opioid receptor blocker naltrexone to rhesus macaque mothers who physically abuse their offspring affected their grooming interactions with other group members and their rates of displacement activities, but did not affect abusive behavior or any other interactions with their offspring. Naltrexone-treated mothers received higher amounts of grooming from other individuals than controls, but grooming performed was not affected by the treatment. The effects of naltrexone on grooming behavior, although not strong, were consistent with those reported

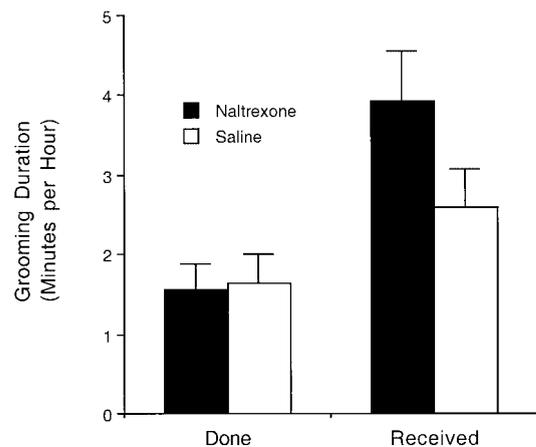


Figure 1. Mean (\pm SEM) amount of grooming done and received by subjects and controls per hour per individual.



Figure 2. Mean (\pm SEM) number of displacement activities exhibited by subjects and controls per hour per individual.

by most previous studies of opioids and adult attachment in monkeys (see the Introduction). Unlike most previous studies, grooming solicitations were not affected by naltrexone. An overall increase in the rate of grooming solicitations, however, is only one way to increase the amount of grooming received. For example, it is possible that naltrexone-treated mothers increased the amount of grooming received simply by sitting next to particular individuals who were most likely to groom them, or by postponing the termination of grooming sessions. Macaque grooming is also often requested and initiated with subtle visual and tactile signals that are not accompanied by obvious changes in body postures (e.g., Mori, 1975). Without detailed information on possible changes in partner preferences or visual and tactile communication, the mechanisms by which naltrexone-treated mothers obtained more grooming from other individuals remain unclear. Furthermore, the possibility that naltrexone altered the attractiveness of abusive mothers as grooming partners, instead of their grooming-seeking behavior, cannot be ruled out.

Taken together, the findings of this and other primate studies are consistent with the hypothesis that endogenous opioids mediate the rewarding properties of receiving grooming. This hypothesis suggests that, although prolonged inhibition of opioid-mediated social reward might eventually lead to the potential extinction of affiliative behavior, in the short run, blockade of the opioid receptors should lead the animals to seek more grooming from other individuals. This hypothesis is consistent with what is known about social grooming in primates. Grooming is considered an altruistic behavior that has costs to the actor and benefits to the recipient (Dunbar, 1991; Maestriperieri, 1993b). One of the main benefits of receiving grooming is reduction of tension and relaxation (Terry, 1970), as manifested in a decrease in heart rate (Boccia, Reite, & Laudenslager, 1989) and in behavioral indicators of anxiety (Schino, Scucchi, Maestriperieri, & Turillazzi, 1988). Thus, it is likely that opioids are involved in mediating aspects of attachment and affiliation that have a strong physical as well as psychological component.

In this study, naltrexone did not affect the frequency of infant abuse. This may be because macaque abusive parenting is not associated with lower maternal attachment, or because maternal

attachment is not affected by manipulations of the opioid system. Both of these hypotheses need to be addressed by future research. Primate studies of opioids and maternal attachment have provided inconsistent results: Kalin et al. (1995) reported that naltrexone increased maternal attachment; Martel et al. (1993) reported that naloxone decreased it; and this study reports no significant effects of naltrexone on any mother–infant interactions. Although some of these inconsistencies may be due to methodological differences among these studies, the role of the opioid system in mediating primate maternal attachment remains unclear.

The strongest behavioral effects of naltrexone in this study occurred with displacement activities such as scratching, self-grooming, and yawning. These effects are unlikely to reflect a general reduction in activity levels because other activities, such as approaching other individuals and aggression, were not affected by naltrexone. However, these effects may be, at least in part, mediated by increased grooming received by naltrexone-treated mothers. Similar reduction of scratching and self-grooming was also reported by previous studies in which similar doses of naltrexone or naloxone produced no side effects on activity levels (Fabre-Nys et al., 1982; Schino & Troisi, 1992). The relation between opioids and anxiety in primates needs to be investigated further. If future studies confirm the anxiolytic effects of opioid receptor blockers reported here, this could represent a further avenue for the investigation of the relation between opioids and attachment in primates. In fact, separation anxiety plays an important role in attachment processes (Bowlby, 1969), and it is possible that the role of opioids in maternal attachment is mediated by their effects on anxiety. Further studies should also investigate the effects of different doses of opiate agonists and antagonists on primate attachment and anxiety, and explore the possibility that different doses of these drugs may have different or opposite effects on these variables.

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