# CHAPTER 19

## Neurobiology of Social Behavior

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The Primate Order comprises over 300 species and a wide range of different social systems (Smuts et al., 1987). Very few species have a fully solitary lifestyle. Most of the others are characterized by permanent associations between two or more adults and their young. Pair living is relatively rare, being characteristic of only 3% to 4% of primate species. Some of these socially monogamous species (e.g., tamarins and marmosets) have a flexible social organization, in which one additional adult male or female may be temporarily associated with the breeding pair. Stable groups with one adult male and several reproductively active females (i.e., harems) are shown by approximately 35% of primate species. The most common type of social organization in nonhuman primates consists of social groups with multiple adult males and females and their young. These multimale/multifemale social groups represent the stable form of organization of about 45% primate species, with an additional 15% of species showing fluctuations between such groups and groups with a harem structure. Variation in social organization among primate species has been explained on the basis of variation in ecological variables such as diet, food-related competition and cooperation (e.g., Wrangham, 1980), and need for protection from predators (e.g., van Schaik) or infanticide (e.g. Dunbar, 1988). Phylogenetic history, however, also accounts for variation in social organization, as groups of closely related species and genera tend to have similar social systems (Rendall & Di Fiore, 1995). Finally, within-species variation in social organization may result from variation in local ecological and demographic conditions.

Regardless of the variation in social systems, it is clear that nonhuman primates are generally highly social organisms, in which successful survival and reproduction depend on complex social interactions with other conspecifics. Accordingly, most primate species exhibit complex behavioral adaptations for communication, affiliation, aggression, mating, and parenting. Group-living monkeys and apes often use vocalizations to alert others of the presence of food and predators, and also to keep in contact with other group members during travel. Facial expressions and body postures play an important role in close-range affiliative, agonistic, and sexual interactions, particularly among Old World monkeys and the great apes. Olfactory and tactile signals are also used in these and other contexts, although olfactory communication is relatively underdeveloped in most primate species relative to other mammals. Social bonds between family and group members are established and maintained through contact, proximity, and grooming. Grooming is an altruistic behavior that can be exchanged for tolerance, sex, or coalitionary support during fights. Aggression and submission, often expressed with facial expressions and body postures, result in the establishment of dominance relationships and hierarchies. In many species, conflict outcomes and dominance ranks are determined not by the individuals' body size and strength but by coalitionary support received from other individuals. Fights between



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two individuals often extend to other group members, whose intervention may reflect attempts to protect a family member or political strategies involving complex cost/benefit analyses. Both affiliative and dominance relationships depend on individuals' memory of their past interactions and their outcome, as well as expectations about future interactions. High dominance rank may confer survival and reproductive benefits such as greater access to food and safe sites or access to more and higher-quality mating partners. Sexual monogamy is rare in primates, or may be nonexistent since extrapair copulations have been reported in socially monogamous primates. Polyandrous systems, in which one female mates with multiple males, are also rare. Polygynous harem systems are more common among species living in small groups, while those living in large multimale/multifemale groups typically have promiscuous mating systems. Successful mating, especially in promiscuous species, depends not only on features that advertise fertility, health, or strength but also on complex social strategies to increase one's attractiveness and deal with competition. Successful reproduction, at least for females, also depends on parental investment in the offspring. Male care is rare among primates, while female care involves not only lactating but also carrying and protecting offspring from predators and conspecifics. Maternal care in many primate species may extend well beyond the period of offspring nutritional dependence. For example, in species with female philopatry and male dispersal such as most cercopithecine monkeys, bonds between female relatives may last throughout the lifespan.

The behavioral adaptations for social life that characterize many primate species must be supported by underlying neurobiological mechanisms so that a relation is expected between complexity of social behavior and complexity of the brain. Consistent with this expectation, studies have shown that there is, across primate species, a linear relation between the average size of the social groups and the ratio between the size of the neocortex and the rest of the brain (although it should be noted that various brain size measures are also correlated with ecological variables; see Clutton-Brock & Harvey, 1977; Milton, 1980; etc., and see Chapter 4). Species that live in larger social groups tend to have a larger neocortex ratio, suggesting that complex social life in large groups is associated with increased cognitive capacity (Dunbar, 1992). Brain size, however, is a crude measure of brain function, just as group size is a crude measure of social complexity. To understand the relation between brain evolution and the evolution of sociality in primates, one needs to have a much deeper knowledge of how specific social behaviors are produced or regulated by specific brain structures or neurochemical systems. Unfortunately, our knowledge of brain-behavior relationships in nonhuman primates is very preliminary. Although in recent years there have been major advances in our understanding of the neural mechanisms underlying social behavior in other mammalian species, particularly rodents (e.g., Young, 2002), research on the neurobiology of social behavior in nonhuman primates has lagged far behind. With the availability of new research techniques such as brain imaging, however, the investigation of the neurobiological substrates of primate social behavior will be a promising area of research in the next few decades.

In this chapter, I review and discuss our current knowledge of the neurobiological regulation of affiliative, aggressive, sexual, and parental behavior in nonhuman primates. Communication is clearly an important component of primate social behavior, but this topic is addressed elsewhere in this volume (see Chapters 1 and 25). Similarly, although the perception and processing of social stimuli is clearly a prerequisite for social behavior, brain mechanisms underlying social cognition are addressed in other chapters (see Chapter 26). This chapter, instead, focuses on social behavior expressed in the context of interactions between two or more individuals.

Different components of social behavior such as affiliation, aggression, mating, and parenting may or may not share some of the same neural substrates, but they probably share common neurochemical controls. For example,

endogenous opioids and oxytocin have been implicated in the regulation of most, if not all, social behaviors in rodents (see later). Similarly, the activity of neurotransmitter systems involving the monoamines dopamine, norepinephrine, and serotonin has been shown to affect the expression or inhibition of a wide range of social activities in many mammals and other vertebrates (see later). The study of neurochemical control of social behavior in primates has been mainly pursued with correlational approaches, in which measures of peptides or monoamines or their metabolites in blood or cerebrospinal fluid (CSF) are analyzed in relation to social behavior, and to a lesser extent, with pharmacological manipulations of neurochemical systems. Attempts to identify specific areas of the brain involved in the regulation of social behavior have mostly been made with lesion studies. Other approaches involving, for example, the electrical stimulation of specific areas of the brain or the imaging of brain activation with positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) have been used less frequently in the context of social behavior studies (but see Rilling et al., 2001, 2004a; Snowdon et al., 2006). Single neuron recording has often been used to address issues of social perception (e.g., to study the processing and recognition of faces and facial expressions) but rarely for social behavior. In this chapter, first I review research on the neurochemical control of primate social behavior, particularly studies of endogenous opioids, oxytocin and vasopressin, and the brain monoamine systems. Then, I review the results of brain lesion studies investigating the neural substrates of primate social behavior. I conclude the chapter by summarizing the main trends emerging from this literature review and discussing future research directions.

## NEUROCHEMICAL CONTROL OF SOCIAL BEHAVIOR

Research conducted with other mammalian species, mostly rodents, has suggested that neuropeptides such as endogenous opioids, oxytocin, and vasopressin are good neurochemical candidates for regulating complex social behaviors. These neuropeptides can influence behavior in conjunction with monoaminergic neurotransmitter systems. For example, in a recent model of the neurobiological regulation of affiliation in mammals, Depue and Morrone-Strupinksy (2005) have argued that dopamine plays an important role in incentive-reward motivation processes (see Chapter 17) associated with the appetitive phase of affiliation, endogenous opioids provide the neurochemical basis for the reward processes associated with the consummatory phase of affiliation, and oxytocin and vasopressin enhance the perception and memory of affiliative stimuli. In this section of the chapter, I review our knowledge of the neurochemical control of primate social behavior, first focusing on neuropeptides, and then on the monoamine systems.

### Endogenous Opioids

Almost 30 years ago, Panksepp and colleagues proposed that brain endogenous opioids play a crucial role in regulating the establishment, maintenance, and disruption of social bonds in mammals and birds (Panksepp et al., 1980). This hypothesis was developed from the observation that the emotional states accompanying the formation of social attachments, the weaning of social bonds, and the distress arising from social separation appear to share similarities with the characteristics of opiate addiction—that is, the development of dependence, tolerance, and withdrawal (Panksepp et al., 1980, 1999). The hypothesized relationship between endogenous opioids and social attachments was framed within the general theory that the emotional substrates of attachments are an evolutionary outgrowth of more primitive brainstem and limbic circuits in the mammalian brain that originally subserved basic physiological needs such as energy balance, thermoregulation, or pain perception.

According to Panksepp and collaborators, a release of endogenous opioids following the exchange, and especially the receipt, of affiliative behavior generates the feeling of pleasure and gratification that arise from the interaction,

whereas a reduction in endogenous opioids results in emotional distress and promotes the need to seek and maintain proximity with a social partner. Although some studies of birds and mammals, including nonhuman primates (e.g., Barr et al., 2008; Kalin et al., 1988; Kraemer, 1992), have provided evidence for the involvement of the opioid system in distress separation responses, there is growing consensus that the neurobiological systems regulating separation distress responses are different from those mediating social rewards (e.g., Insel, 1992; Panskepp et al., 1999). Therefore, more recent theories about opioids and social behavior view endogenous opioids as playing a crucial role in the consummatory phase of affiliative interactions, and therefore in the strengthening of social bonds, but less so in the motivation to establish these bonds or in the response to their disruption or termination (Depue & Morrone-Strupinksy, 2005).

The most systematic attempt to investigate the role of endogenous opioids in the regulation of primate social behavior has been made by Keverne and collaborators with a series of studies in talapoin monkeys and rhesus macaques. They argued that of the different endogenous opioids in the brain, β-endorphin may be the best candidate for the regulation of social behavior, and given the difficulties of measuring this peptide directly in the brain of live primates, they measured its concentration in the CSF (Martensz et al., 1986). β-Endorphin does not gain access to CSF from the blood when CSF and the cerebral extracellular fluid are in equilibrium; therefore, CSF levels of β-endorphin provide a measure of its presence in the extracellular fluid of the brain, a reasonable marker of the level of activity in intracerebral β-endorphin–containing systems (Martensz et al., 1986).

Consistent with Panksepp's hypothesized relationship between endogenous opioids and affiliation, Keverne and colleagues (1989) provided evidence for an association between grooming behavior and opioid release in talapoin monkeys. Specifically, they reported that moving adult talapoin monkeys from isolation housing to pair housing, and therefore providing the monkeys with an opportunity to exchange grooming behavior, was accompanied by a significant increase in CSF concentrations of β-endorphin. There were no significant correlations, however, between the amount of grooming given or received and the concentrations of β-endorphin or their increases following pair housing. Nevertheless, Keverne and colleagues (1989) suggested that the opioid release may have been caused by the tactile stimulation associated with grooming in newly formed pairs, and that this effect may be similar to the stimulation of endogenous opioid release by acupuncture in humans. That endogenous opioids are sensitive to social variables had also been suggested by a previous study, in which CSF concentrations of β-endorphin were found to be highest in male talapoin monkeys of low rank and lowest in those of high rank (Martensz et al., 1986).

A relatively large number of primate studies has attempted to test the following two predictions of Panksepp's hypothesis: (1) the administration of an exogenous opioid such as morphine should create a feeling of social comfort and reduce the motivation to seek social contact or decrease the expression of affiliative behavior, and (2) the blockade of endogenous opioid receptors should increase the need for social attachment and therefore the solicitation of affiliative behavior from social partners. Research by Keverne and colleagues showed that acute treatment of adult talapoin monkeys with the opioid receptor blockers naloxone or naltrexone increased their grooming solicitations and resulted in more grooming received from other individuals (Fabre-Nys et al., 1982; Keverne et al., 1989; Meller et al., 1980). These effects were observed in both pair-housed and in group-living individuals, were dose dependent and stronger for females than for males, and were specific for allogrooming behavior: Self-grooming, aggressive behavior, and locomotor activity were not affected (but in one study male sexual behavior was decreased; Meller et al., 1980). Naltrexone administration was also associated with an increase in testosterone, cortisol, and prolactin, suggesting that some of the effects of opiate receptor blockade on social behavior may have been hormonally

mediated (Meller et al., 1980). An increase in the number of grooming solicitations and in the amount of grooming received from other individuals following naloxone or naltrexone treatment was also reported by two studies of group-living rhesus macaque adult females (Graves et al., 2002; Martel et al., 1995). Keverne and colleagues (1989) found that acute treatment of pair-housed monkeys with nonsedative doses of morphine resulted in a significant decrease in the number of grooming solicitations as well as a decrease in grooming performed. A study of common marmosets, however, reported that morphine administration increased the frequency and duration of social play but had no effects on social contact or grooming (Guard et al., 2002). Since grooming behavior in Old World monkeys may have different functions and be regulated by different mechanisms than grooming behavior in New World primates, the findings of the studies reviewed previously are generally 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 et al., 1988, 1995; Martel et al., 1995; Schino & Troisi, 1992). In a study of group-living long-tailed macaques, juveniles receiving an acute administration of naloxone increased their proximity-seeking behavior toward their mothers, displayed more grooming solicitations to both their mothers and other group members, and received more grooming from them (Schino & Troisi, 1992). Grooming done by the juveniles was not affected by naloxone, while self-grooming decreased. An increase in contact seeking with the mother was also observed in infant and juvenile rhesus macaques treated with naloxone (Martel et al., 1995). Miczek and colleagues (1981) reported that the acute administration of nonsedative doses of morphine in squirrel monkeys decreased the rate of affiliative behavior shown by juveniles toward their mothers. Taken together, these results are consistent with the hypothesis that infant attachment and adult attachment share a common neurochemical substrate (Nelson & Panksepp, 1998).

The role of the opioid system in mediating maternal attachment has been investigated in three primate studies producing 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 minutes 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 et al., 1993). In this study, however, the effects of naloxone on affiliative interactions between mothers and other adults 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. Finally, in another study of rhesus macaques, naltrexone had no significant effects on any aspects of maternal behavior, including abusive parenting (Graves et al., 2002). Although some of these inconsistencies may be due to methodological differences between studies, further research is needed before any firm conclusions can be drawn regarding the relationship between opioids and maternal attachment.

Researchers investigating endogenous opioid release following affiliative interactions made the assumption that the CSF concentrations of β-endorphin mainly reflect the production of this peptide by neurons that originate from the arcuate nucleus of the hypothalamus (e.g., Keverne et al., 1989; Martensz et al., 1986). These neurons project to brain regions that are rich in opiate receptors such as the brainstem, basal ganglia, and areas of the hypothalamus, amygdala, cerebellum, and raphe nuclei. Of the different families of opiate receptors, many of which have multiple subtypes, the μ-opiate receptor family seems to be the most directly implicated in the regulation of social behavior, and β-endorphin has high affinity for these receptors. In brain areas rich

in μ-receptors, β-endorphin neurons interact with dopaminergic and serotonergic neurons, as well as with neurons using oxytocin and vasopressin (at least in rodents). It has been suggested that interactions between μ-opiates and dopamine neurons in the ventral tegmental area (VTA) of the hypothalamus produce the experience of reward associated with the appetitive and consummatory phases of affiliative interactions, while serotonergic input to the hypothalamus via the raphe nuclei may result in reduced arousal and facilitation of opioid-mediated feelings of gratification following affiliation (Depue & Morrone-Strupinksy, 2005). Finally, studies of rats have suggested that oxytocin and vasopressin may facilitate the rewarding effects of endogenous opiates, as oxytocin neurons in the paraventricular nucleus of the hypothalamus project to the β-endorphin neurons in the arcuate nucleus and increase their release of opioids (Csiffary et al., 1992). Oxytocin, vasopressin, and the monoamines, however, can affect affiliation and other forms of social behavior also through mechanisms that are not dependent on endogenous opiates.

### Oxytocin and Vasopressin

Oxytocin and vasopressin are 9-amino acid peptides synthesized in the supraoptic and paraventricular nuclei of the hypothalamus and released into systemic circulation from neurons in the posterior pituitary gland. Hypothalamic neurons synthesizing oxytocin and vasopressin also project to various areas of the brain, and receptors for these peptides have been found in the limbic system of some mammalian species, particularly rodents (Gimpl & Fahrenholz, 2001). Until recently, oxytocin receptors could not be easily identified in the primate brain (Toloczko et al., 1997; Winslow, 2005), but the presence of such receptors has recently been inferred in the hypothalamus, amygdala, septum, orbitofrontal cortex, and hippocampus (Boccia et al., 2001, 2007).

A large body of research conducted mostly with rodents and sheep, but more recently also with humans, has suggested that central oxytocin and vasopressin play an important role in the formation and maintenance of social bonds between adults (e.g., between mating partners) and between parents and offspring (e.g., Young, 2002). In rodents, these peptides have also been implicated in the regulation of sexual and aggressive behavior as well as in stress responses. Little is known, however, about the relation between oxytocin or vasopressin and social behavior in nonhuman primates. An early study by Winslow and Insel (1991) examined the effects of intracerebroventricular administration of two doses of oxytocin and vasopressin, as well as of an oxytocin receptor antagonist (OTA), on aggressive, sexual, and affiliative behavior of pair-housed male squirrel monkeys during an interaction with a familiar adult female. Oxytocin increased aggressive and sexual behavior in a dose-dependent manner in dominants but not in subordinates, while it increased the frequency of approaches and huddles mostly in subordinates. These effects were blocked by OTA. Vasopressin decreased aggressive and affiliative behaviors in both dominants and subordinates. Differences in the effects of oxytocin in dominants and subordinates were tentatively explained in terms of different oxytocin receptor density associated with differences in testosterone between dominants and subordinates.

Research on oxytocin and social behavior in nonhuman primates has been motivated by the interest in developing a primate model for autism. When rhesus monkey infants are separated from their mothers at birth and peer-reared in a small cage, they develop a wide range of behavioral abnormalities, which according to some researchers share some similarities with autism. Winslow and colleagues (2003) measured CSF and plasma oxytocin levels in mother-reared and peer-reared infants to assess whether the behavioral characteristics of peer-reared infants (e.g., low affiliation, high aggression, and high self-directed repetitive behavior) were associated with alterations in oxytocin. In this study, individual differences in CSF oxytocin levels at 18, 24, and 36 months of age did not correlate with differences in plasma oxytocin levels. The peer-reared infants had lower levels of CSF oxytocin than the

mother-reared ones, but there were no differences in CSF vasopressin or plasma oxytocin. CSF oxytocin levels were correlated with time spent engaged in affiliative social behaviors such as allogrooming and male-male mounting independent of rearing condition, while vasopressin levels were negatively correlated with the frequency of fear grimaces at 18 months of age. Taken together, the results of this study provide evidence for an association between CSF oxytocin and affiliative behavior and also suggest that both can be affected by a traumatic early experience such as maternal deprivation. Similar to the Winslow et al. study (2003), Schwandt and colleagues (2007) found no significant correlation between CSF and plasma concentrations of oxytocin and vasopressin in free-ranging female rhesus macaques. Oxytocin was not correlated with any social behavior, although females with low levels of oxytocin were classified as more fearful by human observers. Vasopressin was correlated only with leaping behavior, with females with high vasopressin exhibiting higher frequencies of this behavior.

A possible relationship between CSF oxytocin and affiliation was also inferred from a comparison of closely related primate species. Rosenblum and colleagues (2002) reported that laboratory-born pigtail macaques had lower CSF concentrations of oxytocin than bonnet macaques. The authors of this study described bonnet macaques as very gregarious, affiliative, and affectively stable, while pigtail macaques were described as temperamentally volatile and socially distant. Therefore, the results were interpreted as being supportive of the hypothesis that baseline CSF oxytocin concentrations are related to species-typical social/affective behavior patterns. Bonnet macaques, however, have been described by other researchers as highly competitive and aggressive, while pigtail macaques have been described as peaceful, gregarious, and affiliative (Thierry et al., 2004). Therefore, the significance of the difference in oxytocin levels between these two species remains unclear.

The role of oxytocin in the regulation of parental responsiveness in primates is only beginning to be investigated. In a pilot experiment conducted with two nulliparous rhesus macaque females, Holman and Goy (1995) examined whether an intracerebroventricular injection of oxytocin affected responsiveness to infants. The two females were exposed to an unfamiliar infant in a cage 10 minutes after the injection of oxytocin or saline. The females sat near the infant, and watched, touched, and lip-smacked to the infant more frequently following oxytocin compared to saline administration. In no case, however, was more intense caregiving behavior observed, perhaps because of the environment in which the animals were tested. In another study, CSF levels of oxytocin measured in 10 multiparous rhesus females before parturition, immediately after parturition, and 7 days postpartum were not correlated with mother-infant behaviors such as contact or grooming (Cooke et al., 1997). Finally, Boccia and colleagues (2007) reported that the administration of a human uterine oxytocin receptor blocker reduced the frequency of lip-smacking, approaching, and touching a stimulus infant in one 4-year-old nulliparous rhesus macaque female (in a separate experiment, the same treatment also reduced female sexual behavior, and in both experiments locomotor activity was also significantly reduced). This oxytocin receptor blocker had previously been shown to cross the blood-brain barrier and to accumulate in the hypothalamus, orbitofrontal cortex, amygdala, hippocampus, and septum, suggesting that these are brain areas rich in oxytocin receptors (Boccia et al., 2007). Although the effects of oxytocin receptor blockade on infant-directed behavior in one subject were suggestive of a relation between oxytocin and parental responsiveness, the authors of this study acknowledged that other explanations for their results were also possible.

In a study investigating the possible neurobiological and neurochemical substrates of paternal responsiveness in marmoset monkeys, first-time and experienced fathers who had spent a considerable amount of time carrying infants had a greater number of vasopressin V1a receptors in the prefrontal cortex than adult male nonfathers living in similar social conditions (Kozorovitskiy et al., 2006). There were no

differences in the abundance of vasopressin V1b receptors or oxytocin receptors in the prefrontal cortex, nor in the abundance of V1a receptors in the occipital cortex. Interestingly, fatherhood was also associated with an increased proportion of dendritic spines in the prefrontal cortex, which were immunoreactive for V1a receptor, as well as increased overall density of dendritic spines on pyramidal neurons in the prefrontal cortex. The functional implications of this fatherhood-associated structural reorganization in the prefrontal cortex and the increased abundance of vasopressin V1a receptors remain unclear. Interestingly, Hammock and Young (2005) have suggested that a repetitive polymorphic microsatellite in a regulatory region of the vasopressin 1a receptor gene (AVPR1a) may be responsible for both intraspecific and interspecific variation in social behavior in primates, as in rodents. They found that this polymorphism is present in humans and in bonobos but absent in chimpanzees, and hypothesized that it may be responsible for some of the differences in affiliation and bonding between the latter two species.

Oxytocin and vasopressin have been hypothesized to promote social bonds by facilitating the perception, processing, and memorization of affiliative stimuli (Depue & Morrone-Strupinksy, 2005). It has also been suggested that oxytocin can reduce tension and anxiety associated with social interactions. For example, human studies have suggested that oxytocin released during affiliative social interactions reduces the hypothalamus-pituitary-adrenal (HPA) axis response to stressful events (Uvnas-Moberg, 1998). In an attempt to test this hypothesis with primate data, Parker and colleagues (2005) showed that chronic intranasal administration of oxytocin prior to acute social isolation attenuates the adrenocorticotropic hormone (ACTH) response (but not the cortisol response) to stress in squirrel monkeys (see also Heinrichs et al., 2003, in humans). Since cortisol was not affected and because intranasal oxytocin can penetrate the central nervous system (CNS), this suggests that oxytocin exerts its antistress effects prior to adrenal activation, either in the brain or at the pituitary level.

### Dopamine

Dopaminergic neurons and their projection sites (e.g., the ventral striatum, nucleus accumbens, amygdala, anterior cingulate cortex, and orbitofrontal cortex) constitute what is known as the brain reward system (see Chapter 17). This system regulates a wide range of incentive-motivated behaviors, and these may also include social activities such as affiliation, aggression, mating, and parenting. With regard to affiliation, it has been argued that dopamine plays a crucial role in incentive-reward motivation processes associated with the appetitive phase of affiliation (Depue & Morrone-Strupinksy, 2005). The appetitive phase involves, at the behavioral level, a search and approach system whose function is to bring an individual in contact with affiliative stimuli. Research with rodents has shown that the incentive motivation and experience of reward that underlie the search for and approach to affiliative stimuli depend on the functional properties of dopaminergic neurons in the VTA and nucleus accumbens (NAS) (Depue & Morrone-Strupinksy, 2005). Given the lack of relevant data, whether the same relation between dopamine and the appetitive phase of affiliation holds true also in nonhuman primates remains unclear. There is some evidence, however, that dopamine plays a greater role in the appetitive aspects of primate sexual behavior than in its consummatory components. For example, a dopamine agonist, apomorphine, which acts on dopamine D1 and D2 receptors, enhances male sexual arousal in response to female sexual stimuli in rhesus monkeys (Pomerantz, 1990) but does not appear to affect male copulatory behavior (Chambers & Phoenix, 1989). Quinelorane, another D2 agonist, also stimulates male sexual arousal (Pomerantz, 1991). Whether these effects also occur in females is unclear, since there have been no studies investigating dopaminergic function and sexual behavior in female primates (Dixson, 1998).

In nonhuman primates, brain dopaminergic function has also been investigated in relation to personality traits such novelty seeking, which are expected to influence behaviors such as

exploration, assertiveness, aggressiveness, and dominance. In humans, genetic polymorphisms in the coding region of the dopamine D4 receptor gene (DRD4) have been linked with a number of personality and behavioral disorders both in adults and in children (e.g., Sheese et al., 2007). A study of captive vervet monkeys showed that the DRD4 genetic polymorphism accounts for a significant fraction of interindividual variation in novelty-seeking behavior (e.g., latency to approach novel objects) (Bailey et al., 2007). Correlations between CSF concentrations of the dopamine metabolite homovanillic acid (HVA) and measures of sexual, assertive, and aggressive behavior have been reported by some studies of macaques and vervet monkeys (e.g., Fairbanks et al., 2004; Kaplan et al., 2002; Mehlman et al., 1994, 1997), but these correlations must be interpreted with caution. This is because individual differences in CSF concentrations of HVA are highly positively correlated with those of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) and the norepinephrine metabolite 3-hydroxy-4-methoxyphenylglycol (MHPG) (see later). The CSF concentrations of the three monoamine metabolites also share similarities in their heritability (Freimer et al., 2007; Higley et al., 1993; Rogers et al., 2004), the extent to which they are affected by early stressful experience (Higley et al., 1991; Maestripieri et al., 2006a,b), and age-related changes across the primate lifespan (Higley et al., 1992a). In some cases, correlations between CSF HVA and social behavior may be a by-product of correlations between CSF 5-HIAA or MHPG levels and behavior. For example, the association between low CSF HVA and high dominance status in male vervet monkeys was almost entirely due to the correlation between low 5-HIAA and high dominance and to the correlation between HVA and 5-HIAA (Fairbanks et al., 2004). Kaplan and colleagues (2002), however, reported a strong association between CSF levels of HVA and dominance, which was independent of the other CSF monoamine metabolite concentrations. This association was in the opposite direction to that reported by Fairbanks and colleagues (2004). In unisexual groups of captive long-tailed macaques, adult males and females that became dominant within their groups had significantly higher CSF HVA concentrations than those that became subordinate (Kaplan et al., 2002). Greater dopaminergic activity in dominant females was also suggested by another study in the same species, in which prolactin responses to a challenge with the dopamine antagonist haloperidol were greater in dominants than in subordinates (Shively, 1998). In another study, however, dominant females showed greater striatal dopamine D2 receptor binding than subordinates, suggesting lower dopaminergic activity in dominants (Grant et al., 1998). Given these discrepancies between the results of different studies, and the fact that other studies have failed to report significant correlations between CSF HVA levels and any measures of social behavior (e.g., Cleveland et al., 2004; Maestripieri et al., 2006b), the relation between dopaminergic activity and aggression and dominance in primates remains unclear.

### Norepinephrine

The brain noradrenergic system has been implicated in the regulation of arousal and an individual's aggressive or fearful responses to novel or threatening stimuli. Aggressive and fearful behaviors are associated with increased central and peripheral noradrenergic activity in primates as in other mammals, but this association is not specific to agonistic interactions. Rather, elevated norepinephrine is observed in all situations with high arousal and is an important component of an individual's response to stress. Central norepinephrine may also mediate sexual arousal, but there are no relevant primate data on this topic (Dixson, 1998). Some primate studies have reported correlations between CSF concentrations of norepinephrine or the norepinephrine metabolite MHPG and aggressive behavior, but these correlations have been mixed. For example, Higley and colleagues (1992b) reported that highly aggressive rhesus monkey males had higher CSF levels of norepinephrine than less aggressive monkeys, whereas among females low CSF norepinephrine was associated with high rates of severe aggression

(Higley et al., 1996a). No correlation between CSF MHPG and aggression was found in several other studies of free-ranging rhesus monkeys (Higley et al., 1992b, 1996a; Howell et al., 2007). In long-tailed macaques, CSF MHPG was higher in dominants than in subordinates among males, but not among females (Kaplan et al., 2002), whereas in male vervet monkeys there was no significant correlation between CSF MHPG levels and dominance rank (Fairbanks et al., 2004). Elevated CSF MHPG levels have been reported in rhesus monkey infants rejected and abused by their mothers (Maestripieri et al., 2006a) or in peer-reared infants (Higley et al., 1991). As juveniles, individuals with low CSF MHPG exhibit high avoidance of other individuals (Maestripieri, 2006b), while among adult females, individuals with high CSF MHPG are avoided more by other individuals. In wild vervet monkeys, however, low CSF MHPG levels were associated with higher impulsivity (Fairbanks et al., 1999).

Given the discrepancies in these research findings, it is premature to draw any conclusions about the relation between norepinephrine and social behavior in nonhuman primates. Whether norepinephrine-dependent arousal results in aggressiveness or avoidance might depend on the complex relationship between arousal and anxiety, fear, and impulsivity. Since different types of aggression may have different emotional substrates, the relation between norepinephrine and aggression could be different for different types of aggressive behavior. Furthermore, similar to HVA, the relation between CSF MHPG and aggression may be confounded by the relation between 5-HIAA and aggression and the positive correlation between 5-HIAA and MHPG. Although noradrenergic mechanisms can potentially affect aggression and dominance independently of serotonin, the relation between aggression and serotonin seems to be stronger and more specific (see later) than that between aggression and dopamine or norepinephrine. For example, studies of rodents have shown that the basal activity of the noradrenergic system, unlike that of the serotonergic system, does not consistently differentiate between more and less aggressive individuals (Miczek & Fish, 2006).

### Serotonin

Serotonin is one of the most ancient neurotransmitters in mammals and has been implicated in the regulation of social behavior in a number of other taxa as well (Insel & Winslow, 1998). In humans and other primates, brain neurons that use serotonin as their primary neurotransmitter originate in the raphe nuclei of the brainstem and project to the cerebral cortex as well as to subcortical structures such as the amygdala, septum, hypothalamus, hippocampus, thalamus, and basal ganglia. Studies of serotonin and social behavior in primates have used indirect measures of CNS serotonergic function such as the measurement of 5-HIAA in the CSF or pharmacological and neuroendocrine challenges. The use of CSF 5-HIAA concentration as an indicator of brain serotonin activity has been validated by various methods including postmortem brain studies showing that the CSF content of 5-HIAA reflects the content of this metabolite in the brain (e.g., Banki & Molnar, 1981; Wester et al., 1990). Low concentrations of CSF 5-HIAA are generally interpreted as representative of lower CNS serotonergic function. The relationship between CSF 5-HIAA and specific serotonergic neural pathways in the brain, however, remains unclear (Insel & Winslow, 1998). Administration of the serotonin agonist fenfluramine, which stimulates the release of serotonin from neurons and inhibits its reuptake, has also been used as an indirect method of assessing CNS serotonergic function. Since stimulation of serotonin receptors in the hypothalamus results in increased release of prolactin from the pituitary, plasma concentrations of prolactin following fenfluramine administration can be used as indicators of responsivity of the brain serotonergic system. Finally, the serotonergic system can be challenged by manipulating the availability of tryptophan, the amino acid necessary for the synthesis of this monoamine, or by using other pharmacological serotonin reuptake inhibitors.

Using the previously described techniques, a number of human studies have shown that low CNS serotonin function is related to impaired impulse control and to unrestrained

aggressiveness and violence, particularly in adult males (see Manuck et al., 2006, for a recent review). Similarly, studies of rhesus macaque adult males and females have shown that low levels of CSF 5-HIAA are associated with high impulsivity, risk-taking behavior, and propensity to engage in severe forms of aggression (Higley et al., 1996a,b,c; Howell et al., 2007; Mehlman et al., 1994; Westergaard et al., 1999, 2003; see Higley, 2003, and Manuck et al., 2006, for reviews). In vervet monkeys, individuals fed diets high in tryptophan exhibit lower aggression, whereas individuals placed on diets low in tryptophan become more aggressive, with the increase in aggressiveness being greater for males than for females (Chamberlain et al., 1987; Raleigh et al., 1985, 1986, 1991). Decreased aggression has also been observed following short-term administration of serotonin reuptake inhibitors (Chamberlain et al., 1987; Raleigh et al., 1980, 1985, 1986, 1991), while administration of the serotonin synthesis inhibitor p-chlorophenylalanine (PCPA) results in increased aggression (Kyes et al., 1995; Raleigh & McGuire, 1986; Raleigh et al., 1980, 1983, 1986). In long-tail macaques, individuals showing low responsivity to the fenfluramine challenge were more aggressive toward other individuals and to faces with threatening expressions than individuals exhibiting prolactin responses of greater magnitude (Botchin et al., 1993; Kyes et al., 1995).

A relation between aggressiveness and CSF 5-HIAA concentrations has also been found in comparisons between different genetic strains of rhesus macaques and between closely related species. For example, the more aggressive Chinese-derived rhesus strain has lower CSF 5-HIAA concentrations than the less aggressive Indian-derived strain (Champoux et al., 1997). Furthermore, rhesus macaques have lower CSF 5-HIAA levels than pigtail macaques, a species believed to be generally less aggressive than rhesus macaques (Westergaard et al., 1999). Finally, Kaplan and colleagues (1999) reported that anubis baboons, who are characterized by relatively high levels of intermale aggression, have lower CSF 5-HIAA concentrations than the less aggressive anubis-hamadryas baboon hybrids.

Although it is possible that there is a direct causal relation between brain serotonergic function and aggressive behavior, it is more likely that such a relationship is indirect and mediated by impulse control. In this view, reduced or dysregulated serotonergic function would impair an individual's ability to restrain impulses, and this would be manifested in risky, aggressive, depressed, or addictive behavior depending on the environmental circumstances and the individual's motivational state. The hypothesis that impulse control is an important intervening variable is supported by evidence that, in rhesus macaques, low CSF 5-HIAA is correlated only with aggression involving physical contact and chases, a type of aggression that is more likely to result in serious injuries, and not with milder agonistic behavior involving threats and avoidance, which is commonly associated with the maintenance of dominance relationships (Botchin et al., 1993; Higley et al., 1992b, 1996a,b; Mehlman et al., 1994). Indeed, the relationship between CSF 5-HIAA levels and dominance is not clear, as some studies have reported that CSF 5-HIAA is higher in dominants and lower in subordinates (e.g., Fairbanks et al., 2004; Westergaard et al., 1999) while other studies have reported the opposite pattern or no relation at all (Kaplan et al., 2002; Raleigh et al., 1991; Shively, 1998; Shively et al., 1995; Yodyingyuad et al., 1985). Monkeys with low CSF 5-HIAA concentrations are more likely to exhibit behaviors suggestive of impaired impulse control such as long leaps at high heights and repeated jumping into baited traps in which they are captured (Fairbanks et al., 1999; Higley et al., 1996c; Mehlman et al., 1994). In the laboratory, rhesus macaques with low CSF 5-HIAA concentrations have a lower latency to approach a novel object than do monkeys with high CSF 5-HIAA concentrations (Bennett et al., 2002). In vervet monkeys, individuals with low CSF 5-HIAA concentrations approached a strange and potentially dangerous adult male more quickly and were more likely to act aggressively toward him than monkeys with high CSF 5-HIAA (Fairbanks et al., 2001; see also Manuck et al., 2003). Individuals treated with the selective

serotonin reuptake inhibitor fluoxetine became less impulsive in this strange male test than control individuals (Fairbanks et al., 2001).

Increased tendencies to exhibit risky behaviors and to engage in severe forms of aggression are not the only behavioral manifestations of low CSF 5-HIAA in monkeys. Individuals with low CSF 5-HIAA also show reduced propensities for prosocial behaviors and affiliation. In a study of free-ranging adolescent rhesus macaque males, individuals with low CSF 5-HIAA concentrations exhibited reduced amounts of time spent in proximity and grooming other group members, and a lower number of social partners with whom they interacted (Mehlman et al., 1995; see also Kaplan et al., 1995). Young rhesus males with low CSF 5-HIAA concentrations have also been reported to emigrate from their natal group at an earlier age than males with higher CSF 5-HIAA concentrations (Howell et al., 2007; Kaplan et al., 1995; Mehlman et al., 1995, 1997). In the laboratory, low CSF 5-HIAA concentrations were associated with low rates of affiliative interactions among rhesus juveniles of both sexes (Higley et al., 1996a). Adult females with low CSF 5-HIAA also appear to be less socially oriented, spending more time alone, grooming less, and having fewer conspecifics in close proximity (Cleveland et al., 2004). Adult rhesus males with low CSF 5-HIAA form fewer consorts with estrous females during the mating season, and during these consorts, they groom and mount the females less frequently than males with higher CSF 5-HIAA (Mehlman et al., 1997). In long-tail macaques, individuals with low responses to fenfluramine spent less time in affiliative interactions with other individuals and more time alone (Botchin et al., 1993). In vervet monkeys, Raleigh and colleagues found that enhancing serotonin function by administering tryptophan, the reuptake inhibitor fluoxetine, or the serotonin agonist quipazine increased affiliative behaviors such as approaching and grooming other monkeys (Raleigh et al., 1980, 1983, 1985). In contrast, reducing serotonin function by administering the tryptophan hydroxylase enzyme inhibitor PCPA resulted in social withdrawal and in avoidance of affiliative interactions (Raleigh & McGuire 1990; Raleigh et al., 1980, 1985). These data from vervet monkeys thus suggest that enhancing serotonergic function facilitates the expression of affiliative behavior, whereas reducing serotonergic function inhibits affiliation.

There is some evidence that serotonergic function is related not only to aggressive and affiliative behavior but also to sexual and maternal behavior. Consistent with the results of studies of rodents, serotonin has been shown to exert inhibitory effects on male and female sexual behavior in primates as well (e.g., Gradwell et al., 1975; Pomerantz et al., 1991). Early studies of serotonin and maternal behavior in primates reported that monkey mothers with low CSF 5-HIAA were more protective and restrictive, and that their infants spent more time in contact with them, than mothers with high CSF 5-HIAA (Fairbanks et al., 1998; Lindell et al., 1997). Cleveland and colleagues (2004) found no relationship between CSF 5-HIAA and maternal behavior in the first few postpartum days, but on postpartum days 15 and 20, females with low CSF 5-HIAA broke contact and left their infants less frequently than females with high CSF 5-HIAA. A preliminary study in our laboratory reported a positive correlation between CSF 5-HIAA concentrations measured during pregnancy and maternal rejection behaviors in the first postpartum month in multiparous females (Maestripieri et al., 2005). Our more recent work involving multiple measurements of CSF 5-HIAA during development, however, reported a negative correlation between CSF 5-HIAA and maternal rejection among first-time mothers (Maestripieri et al., 2007).

Serotonin may affect maternal motivation through its actions on oxytocin or prolactin release, or through its effects on emotional expression (Insel & Winslow, 1998; Numan & Insel, 2003). Emotions can be powerful elicitors of maternal behavior in nonhuman primates and humans (Dix, 1991; Maestripieri, 1999; Pryce, 1992). For example, there are marked individual differences in anxiety among rhesus mothers, and such differences translate into differences in maternal style (Maestripieri, 1993a,b). Maternal anxiety has also been implicated in the etiology of infant abuse in macaques (Maestripieri, 1994; Troisi & D'Amato, 1991).

Although the role of impulse control in primate maternal behavior is still poorly understood, it is possible that impulsivity affects how primate mothers interact with their infants, and that high impulsivity is expressed as high rejection rates, thus explaining the association between low CSF 5-HIAA and high rejection rates found in first-time rhesus macaque mothers (Maestripieri et al., 2007).

The occurrence of individual differences in CSF concentrations of 5-HIAA and their association with differences in aggressive, affiliative, and maternal behavior has sparked interest in the origin of this variation. Studies of genotyped primate populations and studies of cross-fostered individuals have provided evidence for moderate to strong heritability of CSF concentrations of 5-HIAA and other monoamine metabolites (Higley et al., 1993; Rogers et al., 2004). Heritability of variation in serotonergic function could arise from any genes whose products participate in serotonin's synthesis, release, reuptake, or metabolism, or in genes that encode serotonin receptors (Manuck et al., 2006). A well-known case of genetic variation in serotonergic function involves the polymorphism in the serotonin transporter (5-HTT or SERT) gene. In humans, rhesus macaques, and other primates as well, the promoter region of this gene (5-HTTLPR) exists in two allelic variants, which differ in length. The short allele confers lower transcriptional efficiency to the serotonin transporter gene (Bennett et al., 2002) and is associated with reduced serotonin reuptake into the presynaptic neuron and reduced serotonergic responsivity to neuroendocrine challenges (Manuck et al., 2006). Human studies have shown that individuals with one or two copies of the short allele have greater amygdala neuronal activation in response to faces with threatening expressions (Skuse, 2006). These individuals also had reduced gray matter in the perigenual cingulate cortex (pACC) and in the amygdala. The pACC has the greatest density of serotonin terminals within the human cortex and it is a major target for projections from the amygdala. fMRI studies have shown that people with at least one short allele had weaker functional interactions between ventromedial prefrontal cortex, pACC, and amygdala, suggesting that the presence of short allele is associated with hyperreactivity of the amygdala in response to threats (Skuse, 2006).

In rhesus macaques, the SERT polymorphism is generally unrelated to CSF concentrations of 5-HIAA, with the exception of individuals who are separated from their mothers at birth and reared with peers (Bennett et al., 2002; Maestripieri et al., 2006a). Nevertheless, individuals who carry the short allele for SERT appear to share some behavioral traits with individuals with low CSF 5-HIAA, including higher aggressiveness and earlier age of male emigration from the group (Trefilov et al., 2000). Rhesus macaque mothers who abuse their infants are more likely to carry the short allele of the serotonin transporter gene than nonabusive mothers (McCormack et., 2009). Furthermore, infants with the short allele who are separated from their mothers at birth or physically abused by them are more likely to show anxiety and fear in response to novelty and dysregulated HPA axis responses to stress and challenges than individuals with the same early experience who are homozygous for the long allele (Barr et al., 2004; Bennett et al., 2002; Lesch et al., 1996; McCormack et al., 2009).

Comparative studies of functional variability of the serotonin transporter gene in seven different species of macaques have shown that species that are believed to more socially tolerant and less despotic and nepotistic such as Barbary macaques, Tibetan macaques, and stumptail macaques are monomorphic for the SERT gene. In contrast, species believed to be more intolerant and aggressive such as rhesus, long-tailed, and pigtail macaques are polymorphic for the SERT gene, with rhesus macaques having the highest degree of polymorphism (Wendland et al., 2005). Tonkean macaques, which are believed to be relatively docile and egalitarian, are polymorphic as well. Although these findings suggest that genetic variation in serotonergic function may play an important role in determining species differences in aggressiveness among macaques, caution is needed in interpreting these results for several reasons. First, species differences in aggressiveness among

macaques are not well established. Second, the species that are polymorphic for the SERT gene are all closely related to each other, and more distantly related from the species that are monomorphic. Although Tonkean macaques would be expected to be monomorphic on the basis of their presumed behavioral characteristics, they are polymorphic like pigtail macaques, a closely related species from which they evolved.

At the individual level, early experience can be an important source of variation in serotonergic function in adulthood. Long-term effects of early maternal deprivation on the development of the brain serotonergic system have been reported in laboratory-reared rhesus macaques (Higley et al., 1991; Kraemer et al., 1989; Shannon et al., 2005). In group-living rhesus macaques, individuals exposed to high rates of maternal rejection in infancy had significantly lower CSF concentrations of 5-HIAA across their first 3 years of life than the individuals exposed to low rates of maternal rejection (Maestripieri et al., 2006a). This difference was found both in individuals reared by their biological mothers and in cross-fostered juveniles, suggesting that it did not reflect genetic similarities between mothers and offspring. Among these juveniles, there was a significant negative correlation between CSF 5-HIAA and rates of scratching (Maestripieri et al., 2006b), suggesting that individuals with low CSF 5-HIAA were more anxious than those with high 5-HIAA (see Maestripieri et al., 1992, and Schino et al., 1991, for the relation between scratching and anxiety). When females who were reared by high-rejection mothers gave birth for the first time, their low 5-HIAA was associated with high rates of maternal rejection toward their own infants (Maestripieri et al., 2007). The maternal rejection rates of daughters closely resembled those of their mothers and the resemblance was particularly strong for the cross-fostered females and their foster mothers (Maestripieri et al., 2007).

The serotonin system may also be involved in the intergenerational transmission of infant abuse. We reported that about half of the females who were abused by their mothers early in life, whether cross-fostered or non–cross-fostered, exhibited abusive parenting toward their first-born offspring, whereas none of the females reared by nonabusive mothers did (including those born to abusive mothers; Maestripieri, 2005). Moreover, the abused females, both cross-fostered and non–cross-fostered, who became abusive mothers had lower CSF 5-HIAA concentrations than the abused females who did not become abusive mothers (Maestripieri et al., 2006a). Since abuse tends to co-occur with high rates of maternal rejection, our findings suggest that experience-induced long-term alterations in serotonergic function in females reared by highly rejecting and abusive mothers contribute to the manifestation of maternal rejection and abusive parenting in adulthood. It is possible that experience-induced reduction in serotonergic function results in elevated anxiety and impaired impulse control, and that high anxiety and impulsivity increase the probability of occurrence of maternal rejection and abusive parenting with one's own offspring later in life, perhaps in conjunction with social learning resulting from direct experience with one's own mother or from observation of maternal interactions with siblings (Maestripieri, 2008).

## THE NEURAL SUBSTRATES OF SOCIAL BEHAVIOR: BRAIN LESION STUDIES

Studies employing brain lesions to investigate the role of different neural structures in the regulation of social behavior have focused mostly on the amygdala, and to a lesser extent on the hypothalamus, the hippocampus, temporal lobes, and orbital frontal cortex. These structures play an important role in the processing of environmental stimuli and the production of emotional responses that regulate survival-related behaviors. These brain regions are also rich in receptors for neuropeptides and monoamines as well as for other hormones and neurotransmitters that have been shown to affect social behavior in primates and other animals (e.g., Way et al., 2007). In highly social organisms such as primates, limbic and cortical responses to social stimuli can play a

fundamental role in an individual's ability to achieve successful survival and reproduction. For example, since the amygdala is necessary for the interpretation of social stimuli and the production of emotional responses that regulate avoidance and aggressive behavior, this structure can potentially play an important role in the regulation of primate social behavior. The hypothalamus plays an important role in regulating the motivational aspects of sexual and maternal behavior, and the hippocampus may be relevant to social behavior regulation insofar as it plays a role in processing the spatial and contextual interrelations of social stimuli. The orbital frontal cortex is strongly connected with brain regions that process all sensory stimuli, while temporal lobes have been implicated in the processing of facial expressions and body movements. Therefore, these structures are likely implicated in the neural control of social cognition, and in the acquisition and processing of information that motivates and controls social interactions.

Studies of brain lesions and social behavior in primates have generally taken two different approaches. Some of them have investigated the effects of lesions on the expression of social behavior in adults, while others have investigated the effects of lesions on the development of social behavior in infants. In general, the results of studies in which temporal lobes, orbital frontal cortex, and hippocampus were lesioned in adults have been consistent with those of studies in which these brain areas were lesioned in infants. In the case of amygdala lesions, however, the results of studies involving adults and infants have produced somewhat inconsistent results (see later).

Young and adult monkeys with lesions of the temporal lobes are generally socially withdrawn or inactive and hyporeactive to fear-inducing stimuli, and in the case of adults, they also show inappropriate sexual behavior such as mounting inanimate objects (Bachevalier et al., 2001; Brown & Schaefer, 1888; Kluver & Bucy, 1937, 1939). Individuals with these lesions appear to have impaired ability to discriminate between conspecifics and objects, and therefore to respond properly to socially relevant stimuli. Lesions of the orbital frontal cortex appear to result in avoidance of social interactions and alterations in aggressiveness and dominance (Butter & Snyder, 1972; Raleigh & Steklis, 1981). Individuals with these lesions also show impairments in their social attachments, such as a weaker preference for their primary caregiver (Goursaud & Bachevalier, 2007).

An early study by Rosvold and colleagues (1954) reported that male rhesus monkeys who had achieved high dominance rank in artificially created social groups fell to the bottom of the hierarchy and behaved submissively following bilateral amygdalectomy and reintroduction to the group. Similarly, in a series of studies conducted with rhesus macaques, stumptail macaques and vervet monkeys, Kling and colleagues reported that individuals with bilateral lesions of the amygdala who were reintroduced into their social groups failed to re-establish functional social relationships with other individuals and were either attacked or ignored by others (Dicks et al., 1969; Kling & Cornell, 1971; Kling & Steklis, 1976; Kling et al., 1970). Changes in maternal and sexual behavior in amygdala-lesioned animals were reported as well (e.g., Kling & Brothers 1992). Spies and colleagues (1976) reported that female rhesus monkeys with bilateral lesions of the amygdala showed impaired sexual proceptive behavior but normal receptivity and copulatory behavior when paired with a male in a cage (similar results have also been obtained with lesions of the hypothalamus; see later).

Early studies involving amygdala lesions in monkeys have been criticized by Amaral (2002; see also Amaral et al., 2003) because these lesions were not selective enough and the behavioral observations were not accurate enough to warrant strong conclusions regarding the relation between amygdala and social behavior. Amaral and colleagues conducted a series of studies involving amygdala lesions in rhesus monkeys, in which the specificity of such lesions was greatly enhanced by the use of ibotenic acid, a neurotoxin that is injected stereotaxically into the brain and selectively destroys the amygdala without affecting adjacent areas. One set of studies examined the effects of amygdala lesions on

the behavior of adult males in a variety of laboratory testing conditions. In dyadic social interactions in which the amygdala-lesioned males and their unoperated controls were tested with the same stimulus individuals, the lesioned males showed reduced latency to engage in social interactions with their partners and greater affiliation, particularly during the early encounters, suggesting that they had lower social anxiety and more social disinhibition than controls (Emery et al., 2001). The lesioned animals also exhibited lower elevations in plasma cortisol levels in response to the social encounters than the controls did, suggesting that the amygdala lesion reduced the extent to which the individuals interpreted the interaction with an unfamiliar individual as stressful (Amaral, 2002). Perhaps as a result of the behavior of the lesioned individuals, the stimulus partners directed more affiliative behavior toward them than toward the controls (Emery et al., 2001). The amygdala-lesioned adult males showed reduced behavioral inhibition also in response to people and novel objects. For example, they had a lower latency to retrieve a grape and to approach and handle a rubber snake than controls (Mason et al., 2006). Thus, adult males with bilateral lesions of the amygdala show behavioral characteristics similar to those of individuals who experienced much larger lesions of the temporal lobes (Kluver & Bucy, 1937, 1939).

Amaral and collaborators also investigated the long-term effects of brain lesions on infant behavioral development. Bilateral lesions of the amygdala or the hippocampus were performed in 2-week-old infants, who were returned to their mothers and reared by them in small cages with or without other mother-infant pairs. Mother-infant behavioral interactions were not significantly altered by amygdala or hippocampus lesions, with the exception of increased mother-infant contact in the amygdala-lesioned group (Bauman et al., 2004). When infants were permanently separated from their mothers at 6 months of age, the amygdala-lesioned infants did not preferentially seek proximity to their mother in a social preference test in which they could choose between their mother and another familiar adult female (Bauman et al., 2004). This finding was interpreted as indicative of an impairment in the perception of potential danger rather than as a specific deficit in the bond with the mother. The amygdala-lesioned infants, however, did not differ significantly from controls in their plasma cortisol response to separation from their mothers or in their cortisol responses to dexamethasone suppression and ACTH challenge (Goursaud et al., 2005). At 6 to 12 AQ5 months of age, the amygdala-lesioned infants showed reduced fear of novel objects such as rubber snakes but more fearful behavior than both hippocampus-lesioned and sham-operated controls during dyadic encounters with both familiar and unfamiliar conspecifics (Bauman et al., 2004; Prather et al., 2001). The behavior of both amygdala- and hippocampus-lesioned infants in both dyadic and group interactions, however, was generally normal and age appropriate. If anything, the amygdala-lesioned infants showed more affiliative and submissive behavior than the infants in the other groups (Bauman et al., 2004). At approximately 18 months of age, dominance tests were conducted in which the juveniles were given the opportunity to retrieve preferred food items in a competitive situation involving other individuals (Bauman et al., 2006). In these tests, the amygdala-lesioned individuals showed longer latencies to retrieve the food, reduced aggressive behaviors, and more frequent fear and submissive behaviors than hippocampus-lesioned individuals and sham-lesioned controls. The behavioral effects of amygdala lesions conducted in infancy, therefore, appeared to be opposite to those of similar lesions performed in adult males. Finally, Goursaud and Bachevalier (2007) reported that rhesus monkeys receiving bilateral ibotenic acid lesions of amygdala and hippocampus at 1 to 2 weeks of age and who were subsequently reared by human caregivers did not differ from controls in their preference for their primary caregiver versus another familiar human when tested in a social preference task at 11 months of age.

Taken together, the results of these studies suggest that an intact amygdala is not necessary for the expression of normal social behavior in

adult macaques or for normal social development in infants (Amaral et al., 2003). Although evidence from single neuron studies suggests that neurons in the amygdala fire at different rates following exposure to different facial expressions of emotion (Gothard et al., 2007), Amaral and colleagues (2003) have recently questioned the hypothesis that the amygdala plays an important role in social cognition (see Brothers, 1996). Rather, their view is that amygdala serves the function of a protection device: It allows an individual to evaluate the extent to which novel objects in the environment or social situations pose a threat or danger and helps the individual to produce an appropriate response, through projections to other areas of the brain such as the cortex and the hippocampus. Without an intact amygdala, monkeys fail to properly evaluate and recognize the riskiness of a particular stimulus. As a result, amygdala-lesioned monkeys show a lack of fear responses to threatening objects and appear to be uninhibited in potentially dangerous social situations.

Primate brain lesion studies investigating hypothalamic influences on social behavior have mostly focused on sexual behavior. Research conducted by Dixson and colleagues showed that lesions of the anterior and medial hypothalamus in female marmosets impair female active initiation of sexual activity (proceptivity) but not responses to male sexual advances (receptivity) (Dixson, 1990; Dixson & Hastings, 1992; Kendrick & Dixson, 1986). Consistent with these results, studies of macaques have shown that electrical stimulation of the ventromedial or preoptic area of the hypothalamus enhances female proceptive behavior toward males (Koyama et al., 1988). Moreover, neurons in the ventromedial hypothalamus increase their firing rate while female macaques are engaged in proceptive behavior or copulation, while those of the preoptic area decrease their firing rate during these activities (Aou et al., 1988). Taken together, the results of these studies' results uggest that the hypothalamic mechanisms regulating sexual behavior in primates may differ from nonprimate mammals in some important ways (Dixson, 1998). Different areas of the hypothalamus may control different components of sexual behavior in female primates, and since female primates are unique in their ability to engage in sexual behavior outside of the fertile phase of their cycle (Wallen, 1990), it is possible that the neural control of sexual behavior in primates overlaps with the neural control of affiliation and bonding to a larger extent than in other mammals. Although the hypothalamus plays an important role in regulating maternal motivation in rodents and other mammals, there have been no studies investigating the effects of hypothalamic lesions on parental motivation and behavior in nonhuman primates.

## CONCLUSIONS

Studies of the neural substrates or neurochemical mechanisms underlying social behavior in nonhuman primates are clearly limited when compared to those conducted with other animals, particularly laboratory rodents. Moreover, since most research on the neurobiology of primate social behavior has been conducted with the few primate species that are readily available in captivity, such as rhesus macaques, marmosets, or squirrel monkeys, the conclusions of these studies may not be generalizable to other primates, let alone to other animals. Nevertheless, the research findings reviewed in this chapter have made a significant contribution to our understanding of the neurobiological regulation of primate social behavior.

Research on social cognition aside, most of the work investigating the neural and neurochemical control of social behavior has focused on the limbic system and its relation to emotional and motivational substrates of behavior. The best experimental evidence linking specific brain regions or neurochemical systems to emotional substrates of social behavior has been obtained for ''negative'' emotions such as anxiety, fear, and impulsivity and for agonistic behaviors such as aggression and avoidance. With the exception of work on endogenous opioids and affiliation, ''positive'' emotions and their relations to affiliation and social bonding have proven more difficult to study.

Research in this area has been driven by findings obtained with rodents, but whether conceptualizations of affiliation and social bonding in rodents can be directly extrapolated to primates remains unclear. Similarly, although there is a wealth of evidence linking social bonding to oxytocin and vasopressin in rodents (e.g., Carter, 1998; Young, 2002), empirical evidence that these peptides affect social bonding in primates is very preliminary or equivocal. Studies of complex affiliative behavior, and to some extent also of aggressive, sexual, and parental behavior, in primates will need greater conceptual and experimental sophistication than studies conducted with laboratory rodents.

Because of ethical and logistical constraints in the study of brain-behavior relationships in nonhuman primates, most studies to date have attempted to measure, often very indirectly, the activity of brain regions or neurochemical systems and then to correlate these measures with aspects of behavior. Although the neuropharmacological manipulation of behavior in complex social settings could be an effective approach for testing neuroethological hypotheses, this approach has generally been underutilized in primate research. The effects of various psychotropic drugs on the social behavior of nonhuman primates have been investigated in a number of studies (see Smith & Byrd, 1983). In many of these studies, however, the relation between drugs and behavior was investigated without a clear understanding of the drug's mechanisms of action in the brain, and without attempting to test specific hypotheses concerning the neurobiological regulation of behavior. Since the physiological and molecular mechanisms of action of many neuropharmacological agents are now well understood, hypothesis-driven neuropharmacological manipulations of social behavior could play an important role in primate neuroethological research.

Brain lesions have proven useful in investigating the role of particular brain regions in the expression of primate social behavior. Brain lesion studies, however, have limitations in that lesions are not always specific and cause permanent and irreversible brain damage. Brain imaging techniques are far less invasive than lesions and hold great promise for future research in primate social neuroethology. One constraint of brain imaging studies of nonhuman primates is that they must be conducted under controlled laboratory conditions. A similar constraint exists also for human studies, but despite this constraint, thousands of brain imaging studies with humans have been conducted in the past few decades, many of which focused on social cognition and social behavior (e.g., Rilling et al., 2004b). Brain imaging—both AQ6
structural and functional—is arguably also the experimental technique with the greatest potential for answering evolutionary questions about brain-behavior relationships in primates (e.g., Rilling & Insel, 1999). By systematically documenting similarities and differences in the structure of different brain regions across primate species and in how these regions are activated during complex social interactions, we could potentially acquire a great deal of new information about the evolution of social and cognitive complexity in the Primate Order and the brain mechanisms that support it.

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Chapter 19

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| AQ1 | 358 | Please add Wrangham to references. |
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