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The neuroendocrinology of primate maternal behavior

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ABSTRACT

In nonhuman primates and humans, similar to other mammals, hormones are not strictly necessary for the expression of maternal behavior, but nevertheless influence variation in maternal responsiveness and parental behavior both within and between individuals. A growing number of correlational and experimental studies have indicated that high circulating estrogen concentrations during pregnancy increase maternal motivation and responsiveness to infant stimuli, while effects of prepartum or postpartum estrogens and progestogens on maternal behavior are less clear. Prolactin is thought to play a role in promoting paternal and alloparental care in primates, but little is known about the relationship between this hormone and maternal behavior. High circulating cortisol levels appear to enhance arousal and responsiveness to infant stimuli in young, relatively inexperienced female primates, but interfere with the expression of maternal behavior in older and more experienced mothers. Among neuropeptides and neurotransmitters, preliminary evidence indicates that oxytocin and endogenous opioids affect maternal attachment to infants, including maintenance of contact, grooming, and responses to separation. Brain serotonin affects anxiety and impulsivity, which in turn may affect maternal behaviors such as infant retrieval or rejection of infants' attempts to make contact with the mother. Although our understanding of the neuroendocrine correlates of primate maternal behavior has grown substantially in the last two decades, very little is known about the mechanisms underlying these effects, e.g., the extent to which these mechanisms may involve changes in perception, emotion, or cognition.

1. Introduction

The laboratory rat has traditionally been the animal model of choice for research on the neuroendocrinology of maternal behavior, as maternal behavior in this species is predictably elicited and easily quantified, and modern invasive techniques for the manipulation and measurement of neuroendocrine variables can be used in this species (e.g., Bridges, 1990). For similar reasons, and with the additional advantage of having a large brain, the sheep has also been a favorite animal model for research in this area (e.g., Keverne and Kendrick, 1994). Studies of the neural and endocrine regulation of maternal behavior in rats and sheep have produced largely converging findings, leading to generalizations concerning the regulation of maternal behavior in mammals (Pryce, 1992; Numan and Insel, 2003).

Until the mid- to late 1980s, virtually no research was conducted on the neuroendocrinology of maternal behavior in primates. In part, this absence of research reflected the belief that maternal behavior in nonhuman primates and humans is learned early in life and later reinforced by experience acquired through reproduction (e.g., Keverne, 1996). Experiments with rhesus monkeys (*Macaca mulatta*) conducted in the 1950s and 1960s showed that socially deprived females displayed neglectful or abusive parenting with their first offspring, suggesting that opportunities to observe maternal behavior exhibited by other individuals and direct experience with one's own mother were necessary for the acquisition and expression of competent maternal care (Harlow and Seay, 1966; Ruppenthal et al., 1976). The abnormal behavior of socially deprived monkeys, however, was more likely the result of brain alterations induced by traumatic early experience and highly artificial laboratory housing conditions than of learning deficits (Maestripieri and Carroll, 1998a). Since the notion that maternal behavior is learned was consistent with the behaviorist paradigm, which dominated research in psychology for many decades, the "learning" interpretation of social-deprivation experiments went unchallenged for many years. The complementary assumption that maternal behavior in nonhuman primates and humans was largely emancipated from hormonal and other biological influences also went unchallenged for a long time (e.g., Coe, 1990; Keverne, 1996).

Studies of monkeys and humans in the late 1980s and 1990s, however, began to provide evidence that although hormones are not necessary for the expression of primate maternal behavior, they

Abbreviations: 5-HIAA, 5-hydroxyindoleacetic acid; ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; CSF, cerebrospinal fluid; E_1C, estrone conjugates; HPA, hypothalamic-pituitary-adrenal; ICV, intracerebroventricular; PdG, pregnanediol-glucuronide; PVN, paraventricular nucleus of the hypothalamus; SON, supraoptic nucleus.

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nevertheless may influence it (Pryce et al., 1988, 1993; Maestripieri and Wallen, 1995; Maestripieri and Zehr, 1998). This is similar to what occurs in rodents, in which virgin females can be induced to express maternal motivation and behavior simply through gradual and repeated exposure to pups, a process known as sensitization (Numan and Insel, 2003). Studies with nonhuman primates and humans conducted in the past two decades have shown that hormones can influence the motivation to interact with infants and the quality of parental behavior, not only in females, but in males as well.

Because primates are generally characterized by long lifespans, slow life histories, and long periods of immature development, experience with infants gathered during the juvenile period can play a more significant role in the acquisition of primate parenting skills than in animals with short lifespans such as many rodents (e.g., Pryce, 1996). Female primates typically produce one infant at a time, and rarely twins, and invest heavily in each offspring, compared to other animals. Maternal investment in primates involves not only nutritional investment but also transport, protection, and transfer of social skills that are crucial for survival and success in a complex social environment. The importance of maternal investment in primates and the high cost of replacing a lost infant are other evolutionary reasons why experience is expected to play an important role in the acquisition and refinement of mothering skills. The same reasons, however, may also explain why parental motivation and behavior are not fully emancipated from hormonal influences: it would be too risky to do so. For example, a female primate who, for some reason, missed the opportunity to acquire experience with infants during the juvenile period and, as a result, lacked the motivation or the skills to take care of her own offspring, would pay a very high price. Hormones (including prenatal hormonal exposure) and neuropeptides increase the likelihood that females are motivated to interact with infants, thus gaining opportunities for learning, and also to maintain close contact with newborn offspring and meet their basic needs. Hormone and neuropeptide differences between individuals, and hormone and neuropeptide changes across ages and reproductive conditions, also ensure that levels of maternal motivation and maternal behavior are tailored to stable individual characteristics and are expressed at appropriate times in one's lifespan.

In this review article, we first address some of the considerations and caveats that should be kept in mind when interpreting findings on the neuroendocrinology of primate maternal behavior. Next, we briefly describe general patterns of maternal behavior in primates, highlighting major similarities and differences among taxa. We then review and examine the evidence that each of the major hormones, neuropeptides, and neutrotransmitters that have been implicated in the regulation of maternal behavior in nonprimate mammals – gonadal steroids, lactogenic hormones, oxytocin, hypothalamic-pituitary-adrenal (HPA) axis hormones, endogenous opioids, and serotonin – influences maternal behavior in nonhuman primates and humans. We conclude with a brief summary and a discussion of future research directions.

2. Considerations and caveats

The growing number of studies on the neuroendocrinology of parental behavior in primates, including humans, has increased our understanding both of normative parenting within species and of variation among species and among individuals. Most studies to date, however, have been correlational and have been conducted with relatively non-invasive measures of endocrine function. Experimental studies manipulating hormonal or neuropeptide signaling or investigating the effects of hormones, neuropeptides, or neurotransmitters in the central nervous system are still rare in primates. In addition, most of the available data come from a few species or taxonomic families within the primate order (e.g., humans, great apes, macaques, baboons, marmosets and tamarins), while virtually no data are available for prosimians, tarsiers, many cercopithecine, colobine, and cebid monkeys, gibbons and siamangs. Therefore, caution is necessary in generalizing the findings of these studies to all primates. Furthermore, most studies to date have involved captive primate populations, and very few have been conducted in the field. Because the ecological and social environment can modulate the influence of hormones on behavior, more studies of wild primates are necessary to ensure that research findings and conclusions have broad ecological validity.

Another important consideration in interpreting findings on neuroendocrine influences on maternal behavior is the endocrine methodology used. Studies of endocrine and neuroendocrine function in primates have traditionally utilized measures of circulating (plasma or serum) hormone concentrations. More recently, however, methods for characterizing excreted (urinary or fecal) hormone levels have been applied to a wide variety of species, while central concentrations of hormones, neuropeptides, monoamine neurotransmitters or their metabolites have occasionally been determined, either in cerebrospinal fluid (CSF) or in brain tissue. Each of these approaches has both advantages and drawbacks (see Harper and Austad, 2000; Bardi et al., 2003a). For example, measures of hormone levels in the peripheral circulation can provide an accurate indication of the hormone concentrations to which tissues are exposed at a precise point in time, but, for many hormones, are highly sensitive to acute perturbation. Thus, capture and sampling procedures can alter hormone levels, as well as behavioral and reproductive outcomes. In addition, circulating levels of many hormones undergo pronounced circadian and ultradian rhythms, potentially introducing substantial variability into hormone measures.

Fecal and urinary hormone levels, in contrast, provide non-invasive, time-integrated measures of hormone concentrations present in the body over a period of hours. Therefore, these measures are often useful for assessing differences in baseline hormone levels among individuals or within individuals across different conditions, but generally do not provide a useful measure of acute changes in hormone levels. Moreover, species may differ in their metabolic pathways and excretion patterns for specific hormones (e.g., which metabolites are excreted, relative rates of excretion in urine vs. feces, time course of excretion). Thus, proper use and interpretation of urinary or fecal hormone measures requires extensive biochemical and physiological validation, to ensure that the hormone or metabolite being assayed and the medium in which it is measured are biologically relevant (e.g., Ziegler et al., 1996a; Harper and Austad, 2000; Touma et al., 2003). Finally, some hormones, neuropeptides, and neurotransmitters, such as oxytocin, corticotropin-releasing hormone, and serotonin, are released both peripherally and within the brain, and do not readily cross the blood–brain barrier. Consequently, circulating or excreted concentrations of these substances may not accurately reflect central levels and may bear little relevance to the regulation of behavior. In these cases, characterization of hormone, neuropeptide, or neurotransmitter concentrations within the brain or CSF may be necessary; however, such approaches require relatively invasive or even terminal procedures, precluding their use in many primate studies.

Several additional caveats should be kept in mind when interpreting data on hormone–behavior interactions (Pfaff et al., 2004; Nelson, 2005). First, the biological effects of a hormone (or neuropeptide/neurotransmitter) are determined not only by concentrations of the hormone itself, but also by numbers and affinities of hormone receptors, and, for steroid hormones, by circulating concentrations of carrier proteins and availability of nuclear co-activator or co-repressor proteins. However, these variables are rarely evaluated in studies of primates. Second, many hormone–behavior relationships are not manifest as linear correlations. Instead, the relationship is often curvilinear so that, for example, hormones may have clear effects on behavior at low concentrations, but not at high