The Role of the Endocrine System in Baboon Maternal Behavior

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Background: *Human mothers display a wide range of parenting skills, and although we have gathered a large body of evidence on a variety of factors affecting maternal behavior, we still know relatively little about the physiologic correlates of variation in parental behavior in primates.*

Methods: *Excreted gonadal and adrenal steroids were measured across parturition in a large sample (*n = *89) of group-living female baboons. Maternal behavior data were collected during the first 2 months of infants' life.*

Results: *We found that changes in the excreted sex steroid hormones and cortisol were associated with baboon mothers' infant-directed behaviors. Mothers who displayed more stress-related behaviors, who were also prone to maintain less contact with their infants, had higher postpartum cortisol levels, higher prepartum pregnanediol-3-glucoronide (PdG) levels, and lower postpartum PdG levels. Mothers with higher prepartum cortisol levels showed higher levels of infant-directed affiliative behaviors.*

Conclusions: *These results point toward the importance of the whole endocrine system as a functional unit in terms of enhancing maternal care in primates. The dramatic physiologic changes occurring across parturition may act, in coordination with the cognitive–experiential system, to help the mother cope with the additional challenges imposed by the newborn.*

Key Words: *Papio hamadryas* sp., maternal behavior, sex steroids, adrenal steroids, urinary metabolites

Maternal care plays a central role in the somatic and psychological development of offspring in both human and nonhuman primates (Hrdy 1999; Pryce et al 1995). The individual's early developmental environment is closely tied to later social and behavioral propensities; indeed, early dysfunctions in mother–infant interactions have been linked to many problems experienced during adulthood, including depression, anxiety, child maltreatment, and psychiatric disorders (Lipman et al 2001; Lupien et al 2000; Rhode 2001; Sanchez et al 2001). Prenatal maternal psychosocial stress also has the potential to influence negatively the development of the central nervous system (Sandman et al 2003; Wadhwa et al 2001). Although researchers have gathered a large body of evidence on a variety of experiential, environmental, and social factors affecting maternal behavior in past decades, we still know relatively little about the physiologic correlates of variation in parental behavior (Leckman and Herman 2002). Despite an increasing number of studies assessing the role of the endocrine system in the shaping of social and infant-directed behaviors during the peripartum period, contradictory evidence still exists on the extent of the effects of endocrine changes on the process that induces maternal responsiveness in primates (Bardi et al 2003a; Fite and French 2000; Fleming et al 1997a; Maestripieri and Megna 2000; Pryce 1996). Because of the many routes of activation of neural mechanisms involved in the priming and regulation of maternal behavior in primates, a number of reasons may have influenced those different outcomes, including whether peripheral hormone levels are reflective of their local action in target tissues (Shoham and Schachter 1996) and the potential disruption of ongoing maternal care via invasive sampling techniques (Whitten et al 1998). Furthermore, the high physiologic and behavioral variability in individuals characterized by a high degree of phenotypic plasticity makes it difficult to generalize results from small sample sizes and across species (Dufty et al 2002; Falk 2000).

Prolactin, oxytocin, and endorphins exercise key roles during pregnancy, coordinating a wide range of physiologic and behavioral modifications; however, available evidence suggests that the balance between estrogen and progesterone is of foremost importance during pregnancy, birth, and lactation (Numan 1994; Pepe and Albrecht 1998). Estrogen regulates the receptor-mediated uptake of low-density lipoprotein-cholesterol, which promotes the production of progesterone, essential for the maintenance of pregnancy (Challis et al 2000).

Sex steroid hormones have been unequivocally associated with maternal behavior in nonprimate mammals (Rosenblatt 2002) and thus are likely candidates for contributing to the onset and maintenance of maternal behavior in primates. Indeed, sex steroid hormones and the adrenal glucocorticoid cortisol have been associated to some degree with maternal behavior in several primate species. In biparental species such as marmosets and tamarins, inexperienced mothers with lower prepartum urinary estradiol (E_2) titers rejected their offspring more often than inexperienced mothers with higher E_2 values, and maternal motivation in experienced mothers was stimulated by the exogenous administration of E_2 and progesterone in nonpregnant females (Pryce et al 1988, 1993). In rhesus macaques, exogenous administration of E_2 increased the rate of interactions with nonrelated infants in ovariectomized rhesus macaques (Maestriepieri and Zehr 1998). In pig-tailed macaques, pregnant females' interest in infants was correlated with changes in their reproductive condition (Maestripieri and Wallen 1995), and some aspects of social behavior recorded during pregnancy changed in association with gender steroid fluctuations (Maestripieri 1999). In Japanese macaques, mothers characterized by a rejecting maternal style showed significantly lower levels of excreted estrone conjugates (E_1C) in late pregnancy (Bardi et al 2001a), changes in social behavior were correlated with E_1C fluctuations during the peripartum period (Bardi et al 2001b), and maternal responsiveness was related to changing levels of estrogen and cortisol during the late prepartum and early postpartum period

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(Bardi et al 2003a). Elevated prolactin and cortisol levels have been related to male parental care (Ziegler et al 2000).

Both the direction and the extent of these associations have generated problematic interpretations, however, because a number of studies have failed to confirm those findings, often within the same species and when conducted by the same research groups. Although Bahr and colleagues originally found an association between progesterone, cortisol, and a maternal competence score in gorillas (Bahr 1995; Bahr et al 1998), later expansion of their studies did not support a relation between hormonal levels and maternal behavior (Bahr et al 2001). Moreover, despite several studies pointing toward a role for ovarian steroid hormones in shaping maternal behavior, Maestripieri and Megna (2000) failed to find a relation between peripheral ovarian steroid hormonal levels during early lactation and individual differences in the maternal style of abusive and controlling mothers. Finally, whereas most studies revealed a positive association between elevated estrogen and maternal behavior, Fite and French (2000) found that estradiol levels were higher in mothers of infants who did not survive.

Contradictory results exist in humans as well. Fleming and colleagues reported that changes in maternal feeling during pregnancy were unrelated to the levels of pregnancy hormones or cortisol (Corter and Fleming 1995) and that cortisol was not associated with attitudinal measures of maternal responsiveness (Fleming et al 1997b). The same research group also found that the pattern of change in the ratio of plasma E_2 to progesterone from early to late pregnancy was related to postpartum attachment feelings (Fleming et al 1997a) and that mothers with higher cortisol levels were more attracted to their own infant's body odor (Fleming et al 1997b).

A large body of human research on changes in hypothalamo-pituitary-adrenal (HPA) and hypothalamic-pituitary-gonadal (HPG) axes functioning during pregnancy and the postpartum period has assessed their relation with mood, anxiety, and stress response, linking these two systems, albeit indirectly, with parenting behavior and infant outcome. Susceptibility to psychosocial stressors during lactation has been found in several studies, pointing toward a central mechanism that influences both reproduction and the hypothalamo-pituitary-adrenal HPA axis for mediating the effects of environmental challenges (Carter et al 2001). Others found that the degree of change in circulating hormones in response to happy and sad emotions was small and possibly not functionally significant (Turner et al 2002). Finally, effects of the postpartum maternal endocrine status have been significantly associated with the child's temperament (Susman et al 2001).

The baboon provides an excellent model for the study of the endocrinology of human pregnancy because the characteristics of the menstrual cycle in baboons are very similar to those of women, and the pattern of estrogens and progesterone secretion are virtually identical (Stevens 1997). In addition, the baboon has a visually identifiable menstrual cycle and pregnancy status. The goal of this study was to assess the relation between the overall endocrine steroid changes during the peripartum period and maternal behavior. Because adrenocortical activity is likewise affected by the changes in physiologic status that occur during the peripartum period, we also evaluated the synergistic functioning of the HPA and HPG axes across parturition for its effect on the quality of maternal care in baboons. In particular, we tested the hypotheses that maternal behavior is positively correlated with high values of the estrogen–progesterone balance, and that physiologic peripartum stress, as measured by cortisol levels, is negatively correlated with later mother–infant levels of interaction. This project was designed to account for multiple sources of variation and for the great physiologic and behavioral individual phenotypic plasticity using a large, extensively monitored subject pool. Because our aim was to compare two sets of variables divided naturally in two groups, the endocrine and the behavioral sets, we used canonical correlation analysis to take into account the complexity of the relations within and between the two sets, thus considering for the first time in any primate species the overall association between hormonal levels and maternal behavior during the late pregnancy–early lactation period.

Methods and Materials

Study Sample

The subjects include 89 pregnant female savannah baboons (*Papio hamadryas* sp.) and their newborn offspring. Females were of known lineage and were between the ages of 5 and 20 years (mean age = 11.4 ± 3.6 SD). All females were housed in similar outdoor enclosures (47 m^2), including a heated sheltered area for the winter, at the Southwest Foundation for Biomedical Research, San Antonio, Texas. The enclosures had perches, swings, and standard toys available at all times. Subjects lived in social groups including one adult male and 8–20 adult females. Subjects were never transferred from a group to another during the course of the study, and they were all born in captivity. The subjects were part of a planned breeding program and were not used for other research during the course of the study. Offspring remained within the home cage until they were weaned at the age of 12–15 months. Animals were fed commercially available diet daily. Grain was scattered in the cage daily, and water was supplied ad libitum.

Dominance matrices were constructed using the prepartum data by considering the directionality of affiliative, submissive, and aggressive behaviors given and received by the subject and with all other adult individuals within the social group. Social rank was further determined by the subject's priority of access to a preferred food source (fruit), which was placed at the front of the cage by the observer who then recorded the order of approaching females. Each individual in each social group was then ranked on a scale of high, medium, and low rank by evaluating the dominance matrices and food access.

Gender distribution among the 89 newborns was homogeneous (43 males, 46 females). Maternal rank and age were also homogeneously distributed in the sample ($\chi^2_{[4]} = 2.1$, *ns*), with no significant interaction between these two factors ($r = .1$, $n = 89$, *ns*). Maternal experience, as represented by the number of previous offspring delivered, was also homogeneously distributed in the sample: the number of previous offspring ranged between 1 and 9 (mean number of offspring = 4.8 ± 2.1 SD). As expected, we found a significant association between age and number of previous offspring ($r = .7$, $n = 89$, $p < .05$).

Data Collection

Each subject was monitored for pregnancy by recording changes in the gender skin size and color. The scoring of the gender skin swelling (on a scale of 1–4 plus menstruation) was used to indicate the menstrual cyclicity (Hendrickx 1965). Pregnancy was then determined starting when the normal cycling was interrupted and choosing the estimated date of parturition as 185 days after the last day of fully swollen gender skin. The average estimated data of parturition was within 5 days of the

Table 1. Definitions of the Seventeen Behavioral Units Used

Behavior	Definition
Ventral Contact	Torso of infant in contact with the ventrum of mother (d)
Mother Break	Mother ceasing contact with infant (f)
Within Arm's Reach	Infant not in contact but close enough to touch (d)
Out of Arm's Reach	Infant not in contact and not within reach (d)
Enlist to Cling	Mother compels infant to cling by holding her hand to infant or crouching to encourage dorsal clinging (d)
Restrain	Mother keeps infant from breaking contact (d)
Retrieve	Mother rescues infant by pulling infant toward her and forces infant to cling (d)
Detach	Mother pulls hands or feet of infant away from her body (d)
Watch	Mother looks intently at infant (d)
Grooming	Mother cleans or manipulates the hair or skin of infant (d)
Manipulate	Mother uses hands or feet to explore infant (d)
Huddle	Mother gathers infant close with both arms (d)
Lipsmack	Rapid, repetitive opening and closing of lips directed to infant, to communicate a positive interaction (f)
Startle	Rapid reflexive jerking motion of the body (f)
Brow Wipe	Rapid movement of hand across the brow (f)
Muzzle Wipe	Rapid movement of hand across the muzzle (f)
Scratch	Use of finger, hand, or foot to rake or pick the skin (f)

d, duration (in sec); f, frequency

actual data of parturition. Urine samples were collected starting 6 weeks before the expected date of parturition and ending 4 weeks after parturition. The subjects were moved from the home enclosure through a transfer chute to a separator area. Urine was collected from a clean pan under the separator cage. Upon urinating, females were rewarded with fruit and returned to their social group. Samples were collected twice per week for each subject, from 7 to 9 AM; 1600 samples were collected. Maternal behavior observations started on the day of the birth of the infant and ended 8 weeks later. Each observation session was 15 min long and was balanced for morning (8 AM–12 NOON) and afternoon (1–5 PM) collection. On average, 60 observations (15 hours) were recorded for each subject, for a total of 1335 hours of data. Definitions of the original maternal behaviors are provided in Table 1. Duration was collected for status behaviors such as contact or grooming, frequency was collected for instantaneous behaviors such as startle and muzzle wipe. Behavioral data were recorded on a laptop computer with the Observer data collection system (Noldus Information Technology, Sterling, Virginia). The subjects were observed by trained individuals with an interobserver reliability greater than 85%. To assess interobserver reliability, trial sessions were performed with two observers focusing at the same time on a single subject. Records were then compared, line by line, and the number of inconsistencies was divided by the total number of entries.

Hormone Assays

Enzyme immunoassays (EIAs) were used to measure levels of excreted gonadal and adrenal steroids, including cortisol, pregnanediol-3-glucoronide (PdG), and various estrogen conjugates (E_1C). Assay validation and details on the procedure have been reported elsewhere (French et al 1996). Briefly, microtiter plates (Nunc-Immuno MaxiSorp F96; Nalge Nunc International, Rochester, New York) were coated with 50 μl of antibody raised against a steroid-bovine albumin antigen in rabbit and diluted to the appropriate concentration in EIA phosphate buffer (.1 mol/L sodium phosphate, containing .087 NaCl and .1% bovine serum albumin [BSA]). Coated plates were sealed, incubated for 1–2 days, and washed before to remove antibody that was not covalently bonded to the plate well. The EIA buffer was added to each well, along with duplicate aliquots of reference standard (Sigma Chemical, St. Louis, Missouri), quality control samples, and urine samples. Steroid-horseradish peroxidase (HRP) conjugate was added to wells, and the plates were incubated for 2 hours. After incubation, the plates were washed to separate unbound from bound hormone. Substrate solution (3-ethylbenzthiazoline-6-sulforic acid [ABTS-H_2O_2]) was added immediately, and absorbance was measured at 410 nm (reference 570 nm) with a Dynatech MR5000 Microtiter Plate Reader (Chantilly, Virginia). A four-parameter sigmoid-fit curve was used to calculate sample concentrations. Aliquots taken from a pool of pregnant baboon urine were assayed on each plate to monitor assay quality control. The intraassay coefficients of variation (CV) were 3.3%, 3.7%, and 9.6% for cortisol, PdG, and E1C, respectively. Interassay CVs were 6.2%, 7.5%, and 17.5% for cortisol, PdG, and E1C, respectively. To control for variation in fluid intake and output by baboons, hormone concentrations were corrected for the creatinine content of each sample using a modified Jaffé end point reaction assay (described in French et al 1996).

Statistical Analysis

We used principal components analysis (PCA) to cluster the original maternal behaviors in four categories. The purpose of this analysis was to take a set of correlated behaviors and to find a linear combination of these to produce indices that are uncorrelated. The lack of correlation is a useful property of the new set of variables, because it indicates that they are measuring different "dimensions" in the data. Moreover, PCA reduces the number of original variables into a smaller set of combined ones, thus enabling us to describe the variation in the data set in a more economic and efficient way (Diekhoff 1992). Given the relatively low power of the PCA in our dataset (overall variance explained = 40%), we used this procedure to explore the data parameters more thoroughly and as a tool to create more meaningful behavior categories.

We then used a canonical correlation analysis to investigate the relation between the four behavioral categories (X set of variables) and the peripartum hormonal levels (Y set of variables). We chose to consider prepartum and postpartum levels separately because of the completely different physiologic condition of females in these two reproductive states. The approach that a canonical correlation analysis takes to answering the question of an association between the behavioral and the endocrine sets during the peripartum period is to search for a linear combination of X and Y, say

$$U = a_1X_1 + a_2X_2 + \ldots + a_pX_p \text{ and}$$

$$V = a_1Y_1 + a_2Y_2 + \ldots + a_pY_p,$$

where these linear combinations are chosen so that the correlation between U and V is as large as possible. Interpretation of these linear combinations, and therefore of the relations between the original set of variables X and Y, can be described in terms of the coefficients a_{ij}, as well as the univariate correlations among

Table 2. Eigenvalues, Contribution Rates, and Matrix of Correlation Between the Seventeen Maternal Behavior Variables and the Four Indices Extracted by Principal Component Analysis

	Behavioral Categories				
Behavioral Unit	Time in Contact	Maternal Affiliative	Maternal Maintenance of Contact	Maternal Stress	Mean Values
Ventral Contact	−.866	.059	.005	.214	46.1 ± 6.1
Mother Break	.728	.210	.200	.313	2.0 ± 1.4
Within Arm's Reach	.876	−.038	−.014	−.092	2.9 ± 1.8
Away Arm's Reach	.679	−.062	−.371	−.219	3.1 ± 2.9
Enlist to Cling	−.078	−.046	.686	−.209	.3 ± .1
Restrain	−.083	−.117	.711	.060	.9 ± .6
Retrieve	.441	.295	.561	.229	.2 ± .1
Detach	−.120	.722	−.148	−.156	.1 ± .1
Watch	.147	.484	.025	−.209	2.0 ± .8
Grooming	−.119	.636	.034	−.107	4.0 ± 3.0
Manipulate	.125	.790	.067	.271	.4 ± .3
Huddle	−.215	.301	−.056	.105	1.0 ± .9
Lipsmack	.082	.099	−.148	.103	.1 ± .1
Startle	−.109	−.037	−.245	.5031	6.4 ± 5.5
Brow Wipe	.060	−.072	−.353	.112	1.1 ± .7
Muzzle Wipe	−.245	.031	.210	.674	1.8 ± 1.1
Scratch	−.100	.019	.186	.750	6.9 ± 4.3
Eigenvalues	3.02	2.14	1.75	1.60	
Variance Explained (%)	17.78	12.57	10.32	9.40	

The coefficients in each column of the matrix of correlation (coefficients of eigenvectors) indicate how much weight is assigned to each index. Mean values are expressed in min/hour.

the original variables (Manly 1994). The percentage of variance explained by new variables gives an idea of how much they reflect the variation expressed in the original data set. Because there is an overlap of variance explained between the right and left set of canonical correlation, redundancy is calculated together with the percentage of the variance explained by the new variables.

Because we used statistics requiring multinormal distributions, original data were transformed by square-root transformation when they were not normally distributed. It has been demonstrated that temperature affects frequency and duration of these behaviors in the colony under study (Brent et al 2003), thus original contact-related behaviors (ventro–ventral contact, other contact, proximity, huddle) were also corrected by regressing them with the daily temperature recorded at the time of observation.

All analyses were two-tailed. Data elaboration was carried out using the Statistica package (Statsoft 1998).

Results

Principal component analysis indicated that four groups of maternal behavior variables were highly correlated (Table 2). The total variance explained by the four components was modest (about 40%), and therefore we decided to include in each component the behavioral units that showed the highest correlation, including not significant and rare behaviors, to avoid losing too much information. The first group was positively correlated with the amount of time spent in contact between mothers and infants and inversely correlated with the number of contacts broken by the mother and the time spent away from her, both within and outside the mothers' arms reach. Therefore, we calculated the percentage of total time spent in contact between mothers and infants and included it as the first behavioral category (termed "time in contact"). The second group was highly correlated with watch, grooming, manipulate, detach, and, in part, with huddle. All these variables indicate affiliative interactions directed from the mothers to the infants, and we therefore calculated a second category including the duration of all these behaviors and called it maternal affiliative. We included lipsmack in this category even though it was not correlated with the other variables because the behavior pattern represents a common affiliative interaction in baboons. The third group showed high correlation with enlist to cling, restrain, and retrieve and was therefore called "maternal maintenance of contact"; we included the duration of these three variables in this category. The final group, maternal stress, was highly correlated with scratch, startle, and muzzle wipe. Brow wipe was also included in this category because of its affinity with the other variables. In most primate species, behaviors such as scratch and other displacement activities, such as brow wipe, muzzle wipe, and self-grooming, have been shown to be linked to anxiety and stress (Brent et al 2002; Maestripieri 1993), therefore those behaviors were selected for the maternal stress category.

After choosing the four behavioral categories, we calculated the association between the behavioral set and the endocrine set, composed from the individual average prepartum and postpartum levels of E_1C, PdG, and cortisol, using canonical correlation analysis. The correlation matrix between the behavioral data set (time in contact, maternal maintenance of contact, maternal affiliative, and maternal stress) and the endocrine data set (prepartum and postpartum E_1C, PdG, and cortisol levels) is shown in Table 3. Univariate significant associations ($p < .05$) were found among maternal stress and prepartum PdG ($r = .24$; Figure 1), postpartum PdG ($r = -.22$; Figure 2), and postpartum cortisol ($r = .30$; Figure 3), and between maternal affiliative behaviors and prepartum cortisol ($r = .25$; Figure 4). Univariate trends for associations ($p < .1$) were found between maternal maintenance of contact and prepartum cortisol ($r = -.17$) and

Table 3. Matrix of Correlation Between the Four Behavioral Categories (Time in Contact, Maternal Affiliative, Maternal Maintenance of Contact, and Maternal Stress) and the Six Individual Average Hormonal Levels

	Endocrine Levels					
Behavior Categories	Prepartum E_1C	Postpartum E_1C	Prepartum PdG	Postpartum PdG	Prepartum Cortisol	Postpartum Cortisol
Maternal Stress	.12	−.13	.24[a]	−.22[a]	.14	.30[a]
Maternal Maintenance of Contact	−.08	−.03	−.07	−.02	−.17[b]	−.12
Maternal Affiliative	−.02	.01	−.01	.03	.25[a]	.04
Time in Contact	.14	.13	.08	.07	.17[b]	.11

E_1C, estrone conjugates; PdG, pregnanediol-3-glucoronide.
[a]Significant correlation ($p < .05$).
[b]Trend of association ($p < .1$).

between time in contact and prepartum cortisol ($r = .16$). Even if significant, these correlations were only able to explain a modest portion of variance, thus confirming that the endocrine system alone is insufficient to prime maternal behavior in baboons.

When a canonical correlation analysis was performed, we found a significant association between the behavioral and the endocrine systems (Canonical $R = .50$, $\Phi^2_{(24)} = 40.1$, $p = .02$). The variance extracted by the behavioral set of canonical roots (left set) was 100% with 10.3% redundancy, and that extracted by the endocrine set (right set) was 68.3% with 8.5% redundancy. Weights for both the left and right canonical roots are shown in Table 4. Canonical scores for each individual were calculated according to the canonical equation and plotted in Figure 5. In the first canonical root (behavioral set), the highest weight is for maternal stress (−.94), with marginal weights for maternal maintenance of contact (.36) and time in contact (−.25). In the second canonical root (endocrine set), the highest weights are for postpartum cortisol (−.64), prepartum PdG (−.45), and postpartum PdG (.47), with a marginal contribution for prepartum E_1C (−.22). We used the combination of the two canonical equations and their weights, as well as the univariate correlation reported in Table 3, to interpret specific relations within the overall association between the endocrine and behavioral systems. This approach revealed that mothers who displayed more stress-related behavior and less time maintaining contact with their infants had higher postpartum cortisol levels, higher prepartum PdG levels, and lower postpartum PdG levels. Moreover, mothers who displayed high durations of affiliative behaviors had higher prepartum cortisol levels.

Discussion

Maternal behavior in mammals is a highly complex and integrated behavioral system that relies on a number of environmental, genetic, and physiologic factors to regulate the neural circuits required for its expression (Keverne 1995; Leckman and Herman 2002; Pryce 1996). Understanding the cascade of events leading from pregnancy to the manifestation of maternal behavior is critical to our appreciation of many forms of psychopathology because it has been persuasively demonstrated that early mother–infant interactions can shape infant neural and behavioral development (Bardi and Huffman 2002; Fairbanks 1989; Meaney 2001).

This study focused on the late pregnancy–early lactation period in baboons to assess overall relations between the dramatic changes occurring in the endocrine system and the onset and maintenance of maternal behavior during this critical phase. Because of the inherent complexity of the process

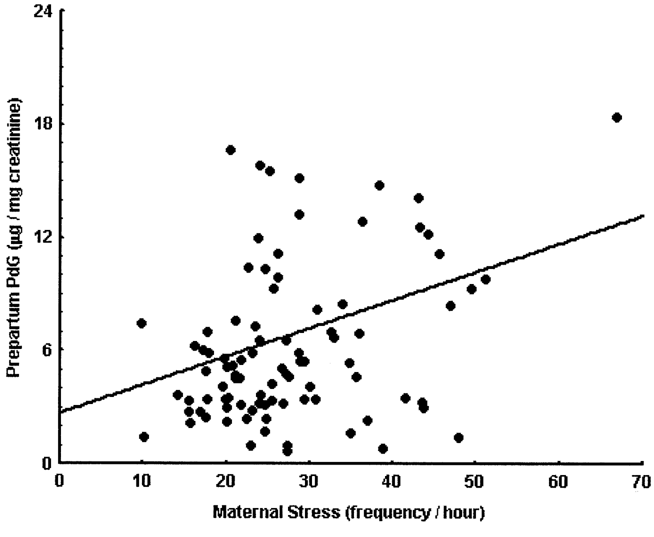

Figure 1. Scatterplot of the univariate significant association between behavioral categories and hormones ($n = 89$). Positive association between prepartum pregnanediol-3-glucoronide (PdG) and maternal stress. Untransformed values were used for the figure.

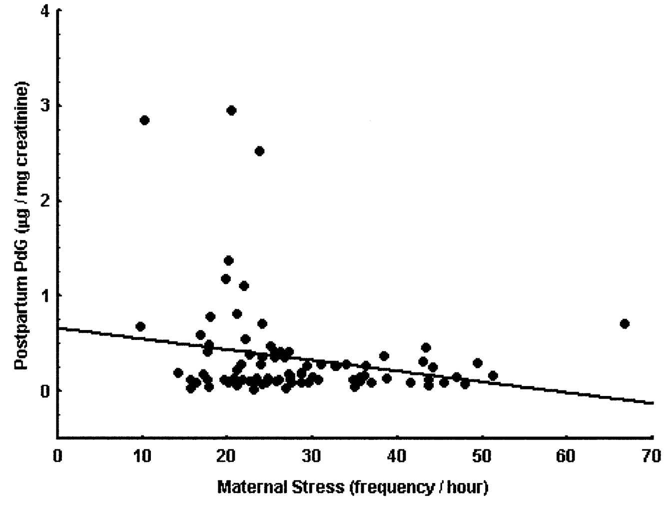

Figure 2. Scatterplot of the univariate significant association between behavioral categories and hormones ($n = 89$). Negative association between postpartum pregnanediol-3-glucoronide (PdG) and maternal stress. Untransformed values were used for the figure.

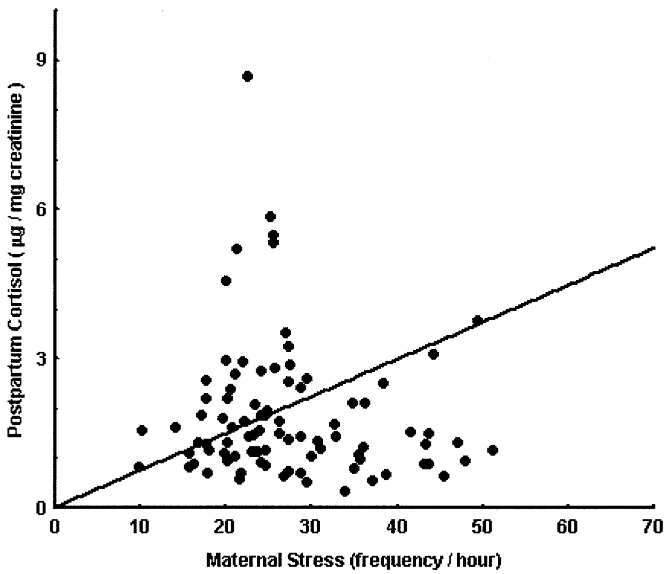

Figure 3. Scatterplot of the univariate significant association between behavioral categories and hormones ($n = 89$). Positive association between postpartum cortisol and maternal stress. Untransformed values were used for the figure.

involved, assessing the association between peripartum hormonal fluctuations and mother–infant interactions has been extremely problematic in the past, both in human and nonhuman primates (Bardi et al 2003c; Fairbanks 1996; McLean and Smith 1999; Numan 1994), thus generating many contradictory results (Maestripieri 2001; Rosenblatt and Snowdon 1996). One of the most important problems is related to the large physiologic and behavioral variability in a group characterized by a high degree of individual phenotypic plasticity (Dufty et al 2002; Falk 2000), and thus we used a large database consisting of nearly 90 subjects and spanning several years of observation. We found for the first time that changes in the sex steroid hormones and cortisol were unequivocally associated with quality and quantity of baboon mothers' infant-directed behaviors. In particular, we found that mothers who displayed more stress-related behaviors, who were also prone to maintain less contact with their infants, had higher postpartum cortisol levels, higher prepartum PdG levels, and lower postpartum PdG levels. At the same time, we found from the univariate correlations (Table 3) that mothers with higher prepartum cortisol levels tended to display higher levels of infant-directed affiliative behaviors. We did not find any direct association between E_1C levels and maternal behavior, except for a trend in positive association between prepartum E_1C and the percentage of time in contact.

Contrasting evidence exists on the relation between adreno-

Table 4. Right (Endocrine Levels) and Left (Behaviors) Sets of Canonical Weights Found by the Canonical Analysis

Set	Canonical Weight
Left Set (Behaviors)	
Time in contact	−.25
Maternal stress	−.94
Maternal maintenance of contact	.36
Maternal affiliative	−.08
Right Set (Endocrine)	
Prepartum	
E_1C	−.22
PdG	−.45
Cortisol	−.06
Postpartum	
E_1C	.15
PdG	.47
Cortisol	−.64

E_1C, estrone conjugates; PdG, pregnanediol-3-glucoronide.

Weights represent the coefficients of the canonical equations derived by the association between endocrine and behavioral variables and give an idea of the relative importance of the original variables on the overall correlation of the two sets.

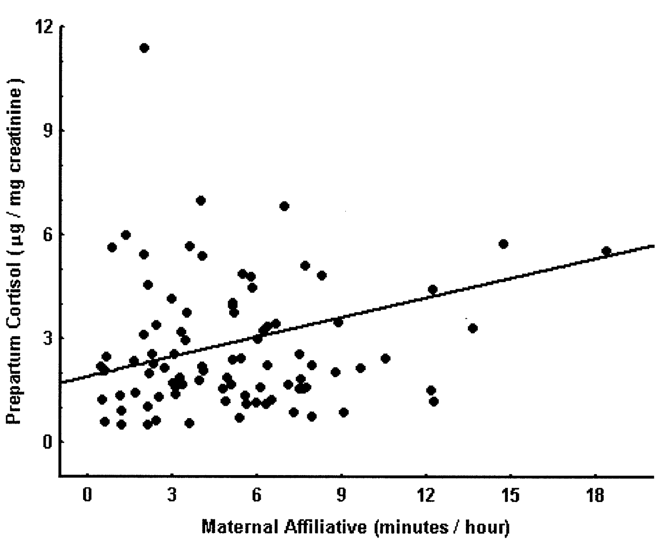

Figure 4. Scatterplot of the univariate significant association between behavioral categories and hormones ($n = 89$). Positive association between prepartum cortisol and maternal affiliative. Untransformed values were used for the figure.

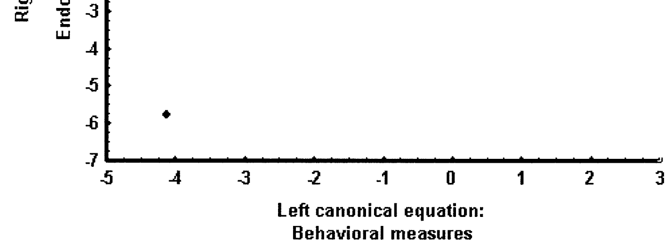

Figure 5. Scatterplot of individual canonical scores as obtained from the canonical equations ($n = 89$). The left canonical equation is a linear combination of the behavioral variables (time in contact, maternal maintenance of contact, maternal affiliative, and maternal stress), and the right canonical equation is a linear combination of the endocrine variables (prepartum and postpartum estrone conjugates, pregnanediol-3-glucoronide, and cortisol levels). The coefficients of each canonical equation are shown in Table 4.

cortical activity and maternal behavior in primates. On one hand, psychogenic stressors that may result in fear or anxiety are associated with elevated adrenocortical production of glucocorticoids (Johnson et al 1996), and high cortisol levels could therefore be expected to have a negative impact on the emotional status of the mothers. Indeed, we found that baboon mothers with higher postpartum cortisol levels displayed more stress-related behaviors and tended to encourage infant contact for shorter amounts of time. On the other hand, others have reported that the prepartum increase in estrogen levels and the association with high levels of glucocorticoids during pregnancy appear to be linked to adaptive behavioral modifications that prepare mothers for interaction with newborns (Bahr et al 1998; Bardi et al 2003a; Fleming et al 1997b). This relation may explain the positive association between prepartum cortisol levels and maternal affiliative behavior directed toward the newborns we found in baboon mothers. The role played by the adrenocortical hormones may follow a dual pathway. During pregnancy, when a state of mild but sustained hypercortisolism is normal for both human and nonhuman primates (McLean and Smith 1999), modifications in the adrenocortical activity may be functional to ensure an increase in attentiveness and arousability toward the newborns. Because this condition has been attributed to an estrogen-stimulated increase in cortisol-binding globulin and placental production of corticotropin-releasing hormone (CRH), estrogens play an indirect but significant role in the process. After parturition, a significant reduction in cortisol levels has been reported as the usual physiologic condition, although hypercortisolism may endure for several days (Bahr et al 1998; Bardi et al 2003a; Fleming et al 1997a; McLean and Smith 1999). Therefore, if hypercorticolism during lactation endures for more than a few days, it may be that psychogenic stressors closely related to fear and anxiety prevail, as is the case for many forms of psychiatric disturbances during the postpartum period (Altshuler et al 1998; Brent et al 2002; Sainfort and Stern 2000).

Self-directed behaviors and other displacement activities have been used as an indicator of stress and anxiety in several primate species, including baboons (Brent et al 2002; Castles and Whiten 1998), and although these behaviors can reflect a variety of responses to stress, their occurrence is often associated with periods of unpredictable changes, such as during crowding, sustained aggression, or cognitive challenge (Aureli and de Waal 1997; Leavens et al 2001). Self-scratching has been reported as an indicator of anxiety in macaque mothers, with rates higher during the birth season than during the mating season (Maestripieri 1993). The prevalence of self-scratching and other displacement activities was also found to be higher after birth of an infant in baboons (Brent et al 2002). Therefore, the positive association we found between self-directed behaviors and high postpartum cortisol levels points toward a pivotal role played by hypercortisolism during the postpartum period. Future research may indicate its potential in screening risk factors in primate neomothers.

Progesterone played a significant role in the positive association found between the endocrine and the maternal behavioral systems in baboon mothers. Higher levels of prepartum progesterone, paralleled by low levels of postpartum progesterone, were associated with the stressed and low contact-seeking phenotypic mothers. These results are consistent with the hypothesis that high values of the estrogen–progesterone ratio during late pregnancy is associated with the processes altering the psychoneurology of mothers, thus eliciting maternal behavior via an increase in attentiveness and arousability toward newborns (Bardi et al 2001a, 2001b; Maestripieri 1999; Maestripieri and Zehr 1998). This mechanism could be mediated by the ability of sex steroid hormones to alter the function of the serotonin neural system (Bethea et al 2002). The ability of progesterone and estrogens to affect the function of the serotonin neural system at both afferent and efferent circuits can explain the impact of sex hormones on mood, cognition, and anxiety, thus modulating maternal motivation and, in the end, maternal behavior. Adrenocortical activity is also directly affected by changes in sex steroid hormones. Therefore, sex steroid hormones may have both a direct and indirect effect on maternal motivation, and this could provide a cellular mechanism by which sex hormones could impact maternal behavior. In this scenario, the intricate relation between the cognitive and experiential system and the endocrine system in primates could be disentangled in terms of their relative importance: steroid hormones could have a great impact on maternal behavior, but only when mothers are lacking experience or other stimuli directed to enhance their mood and reduce their anxiety toward newborns. In this sense, ovarian steroids would act as a secondary, backup system. This framework would help explain infant rejection in primates, an extreme form of poor maternal behavior, which is confined primarily to primiparous mothers in Old World monkeys and apes (Caine and Reite 1983; Maestripieri et al 1997). These results clearly point to the necessity of further studies assessing the direct relation among steroid hormones, serotonin, and maternal behavior in experienced and inexperienced mothers.

The lack of association of estrogen with any specific system was unexpected, considering the number of previous studies that have shown the importance of estrogens in priming maternal behavior in mammals (Numan 1994; Rosenblatt and Snowdon 1996), the central coordinating role of this hormone during pregnancy (Challis et al 2000), and evidence that estrogen is related to several aspects of maternal behavior in primates (Bardi et al 2001a, 2001b, 2003b; Maestripieri 1999; Maestripieri and Zehr 1998). It may be possible that when the overall endocrine activity is considered, the integrative coordinating role of estrogen is more important than any specific direct influence on maternal behavior.

In conclusion, our results in baboons clearly point toward the importance of the whole endocrine system as a functional unit in terms of enhancing maternal care in primates. The dramatic physiologic changes occurring during late pregnancy and early lactation clearly are primarily functional to parturition itself and may act secondarily in coordination with the cognitive–experiential system in helping the mother to cope with the additional problems that the newborn imposes. Further studies and larger samples are needed to assess the single contribution of every factor in a more specific way and to interpret the causative pathways of the relation between the endocrine and the behavioral systems in primate maternal behavior.

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Altshuler LL, Hendrick V, Cohen LS (1998): Course of mood and anxiety disorders during pregnancy and the postpartum period. *J Clin Psychiatry* 59:29–33.

Aureli F, de Waal FBM (1997): Inhibition of social behavior in chimpanzees under high-density conditions. *Am J Primatol* 41:213–228.

Bahr NI (1995): Environmental factors and hormones: Their significance for maternal behavior in captive gorillas. In: Pryce CR, Martin RD, Skuse D, editors. *Motherhood in Human and Nonhuman Primates.* Basel: Karger, 94–105.

Bahr NI, Martin RD, Pryce CR (2001): Peripartum sex steroid profiles and endocrine correlates of postpartum maternal behavior in captive gorillas (*Gorilla gorilla gorilla*). *Horm Behav* 40:533–541.

Bahr NI, Pryce CR, Dobeli M, Martin RD (1998): Evidence from urinary cortisol that maternal behavior is related to stress in gorillas. *Physiol Behav* 64:429–437.

Bardi M, Huffman MA (2002): Effects of maternal style on infant behavior in Japanese macaques (*Macaca fuscata*). *Dev Psychobiol* 41:364–372.

Bardi M, Shimizu K, Barrett GM, Borgognini-Tarli SM, Huffman MA (2003a): Peripartum cortisol levels and mother-infant interactions in Japanese macaques. *Am J Phys Anthropol* 39:239–246.

Bardi M, Shimizu K, Barrett GM, Borgognini-Tarli SM, Huffman MA (2003b): Peripartum sex steroid changes and maternal style in rhesus and Japanese macaques. *Gen Comp Endocrinol* 133:323–331.

Bardi M, Shimizu K, Borgognini-Tarli SM (2003c): Mother–infant relationships and maternal estrogen metabolites changes in macaques (*Macaca fuscata, M. mulatta*). *Primates* 44:91–98.

Bardi M, Shimizu K, Fujita S, Borgognini-Tarli S, Huffman MA (2001a): Hormonal correlates of maternal style in captive macaques (*Macaca fuscata, M. mulatta*). *Int J Primatol* 22:647–662.

Bardi M, Shimizu K, Fujita S, Borgognini-Tarli S, Huffman MA (2001b): Social behavior and hormonal correlates during the perinatal period in Japanese macaques. *Horm Behav* 39:239–246.

Bethea CL, Mirkes SJ, Su A, Michelson D (2002): Effects of oral estrogen, raloxifene and arzoxifene on gene expression in serotonin neurons of macaques. *Psychoneuroendocrinology* 27:431–445.

Brent L, Koban T, Ramirez S (2002): Abnormal, abusive, and stress-related behaviors in baboon mothers. *Biol Psychiatry* 52:1046–1056.

Brent L, Koban T, Stacey E (2003): The influence of temperature on the behavior of captive mother-infant baboons. *Behaviour* 140:209–224.

Caine NG, Reite M (1983): *Child Abuse: The Non-Human Primate Data*. New York: Liss.

Carter CS, Altemus M, Chrousos GP (2001): Neuroendocrine and emotional changes in the post-partum period. *Prog Brain Res* 133:241–249.

Castles DL, Whiten A (1998): Post-conflict behaviour of wild olive baboons. II. Stress and self-directed behaviour. *Ethology* 104:148–160.

Challis JRG, Matthews SG, Gibb W, Lye SJ (2000): Endocrine and paracrine regulation of birth at term and preterm. *Endocr Rev* 21:514–550.

Corter C, Fleming AS (1995): Psychobiology of maternal behavior in human beings. In: Bornstein M, editor. *Handbook of Parenting.* Hillsdale, NJ: Erlbaum, 87–116.

Diekhoff G (1992): *Statistics for the Social and Behavioral Sciences*. Dubuque, IA: Wm. C. Brown.

Dufty AM, Clobert J, Moller AP (2002): Hormones, developmental plasticity and adaptation. *Trends Ecol Evol* 17:190–196.

Fairbanks LA (1989): Early experience and cross-generational continuity of mother–infant contact in vervet monkeys. *Dev Psychobiol* 22:669–681.

Fairbanks LA (1996): Individual differences in maternal style: Causes and consequences for mothers and offspring. In: Rosenblatt JS, Snowdon CT, editors. *Parental Care: Evolution, Mechanisms, and Adaptive Significance,* vol. 25. San Diego, CA: Academic Press, 579–611 .

Falk D (2000): *Primate Diversity*. New York: W. W. Norton.

Fite JE, French JA (2000): Pre- and postpartum sex steroids in female marmosets (*Callithrix kuhlii*): Is there a link with infant survivorship and maternal behavior? *Horm Behav* 38:1–12.

Fleming AS, Ruble D, Krieger H, Wong PY (1997a): Hormonal and experiential correlates of maternal responsiveness during pregnancy and the puerperium in human mothers. *Horm Behav* 31:145–158.

Fleming AS, Steiner M, Corter C (1997b): Cortisol, hedonics, and maternal responsiveness in human mothers. *Horm Behav* 32:85–98.

French JA, Brewer KJ, Shaffner CM, Schalley J, Hightower-Merritt DL, Smith TE, Bell SM (1996): Urinary steroid and gonadotropin excretion across the reproductive cycle in females Wied's black tufted-ear marmosets (*Callithrix kuhili*). *Am J Primatol* 40:231–245.

Hendrickx AG (1965): The menstrual cycle of the baboon as determined by the vaginal smear, vaginal biopsy, and perineal swelling. In: Vagtborg H, editor. *The Baboon in Medical Research,* vol. II. Austin, TX: University of Texas Press, 70–83.

Hrdy SB (1999): *Mother Nature: A History of Mothers, Infants, and Natural Selection*. New York: Ballantine.

Johnson EO, Kamilaris TC, Carter CS, Calogero AE, Gold PW, Chrousos GP (1996): The biobehavioral consequences of psychogenic stress in a small, social primate (*Callithrix jacchus jacchus*). *Biol Psychiatry* 40:317–337.

Keverne EB (1995): Neurochemical changes accompanying the reproductive process: Their significance for maternal care in primates and other mammals. In: Pryce CR, Martin RD, Skuse D, editors. *Motherhood in Human and Nonhuman Primates: Biosocial Determinants.* Basel: Karger, 69–77.

Leavens DA, Aureli F, Hopkins WD, Hyatt CW (2001): Effects of cognitive challenge on self-directed behaviors by chimpanzees (*Pan troglodytes*). *Am J Primatol* 55:1–14.

Leckman JF, Herman AE (2002): Maternal behavior and developmental psychopathology. *Biol Psychiatry* 51:27–53.

Lipman EL, MacMillan HL, Boyle MH (2001): Childhood abuse and psychiatric disorders among single and married mothers. *Am J Psychiatry* 158:73–77.

Lupien SJ, King S, Meaney MJ, McEwen BS (2000): Child's stress hormone levels correlate with mother's socioeconomic status and depressive state. *Biol Psychiatry* 48:976–980.

Maestripieri D (1993): Maternal anxiety in rhesus macaques (*Macaca mulatta*). I. Measurement of anxiety and identification of anxiety-eliciting situations. *Ethology* 95:19–31.

Maestripieri D (1999): Changes in social behavior and their hormonal correlates during pregnancy in pig-tail macaques. *Int J Primatol* 20:707–718.

Maestripieri D (2001): Biological bases of maternal attachment. *Curr Dir Psychol Sci* 10:79–83.

Maestripieri D, Megna NL (2000): Hormones and behavior in rhesus macaque abusive and nonabusive mothers, 2. Mother-infant interactions. *Physiol Behav* 71:43–49.

Maestripieri D, Wallen K (1995): Interest in infants varies with reproductive condition in group-living female pigtail macaques (*Macaca nemestrina*). *Physiol Behav* 57:353–358.

Maestripieri D, Wallen K, Carroll KA (1997): Genealogical and demographic influences on infant abuse and neglect in group-living sooty mangabeys (*Cercocebus atys*). *Dev Psychobiol* 31:175–180.

Maestripieri D, Zehr JL (1998): Maternal responsiveness increases during pregnancy and after estrogen treatment in macaques. *Horm Behav* 34:223–230.

Manly BFJ (1994): *Multivariate Statistical Methods*. London: Chapman and Hall.

McLean M, Smith R (1999): Corticotropin-releasing hormone in human pregnancy and parturition. *Trends Endocrinol Metab* 10:174–178.

Meaney MJ (2001): Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. *Annu Rev Neurosci* 24:1161–1.

Numan M (1994): Maternal behavior. In: Knobil E, Neill JD, editors. *The Physiology of Reproduction,* 2nd ed. New York: Raven Press, 221–302.

Pepe GJ, Albrecht ED (1998): Central integrative role of oestrogen in the regulation of placental steroidogenic maturation and the development of the fetal pituitary-adrenocortical axis in the baboon. *Hum Reprod Update* 4:406–419.

Pryce CR (1996): Socialization, hormones, and the regulation of maternal behavior in nonhuman simian primates. In: Rosenblatt JS, Snowdon CT, editors. *Parental Care: Evolution, Mechanisms, and Adaptive Significance,* vol. 25. San Diego, CA: Academic Press, 423–476.

Pryce CR, Abbott DH, Hodges JH, Martin RD (1988): Maternal behavior is related to prepartum urinary estradiol levels in red-bellied tamarin monkeys. *Physiol Behav* 44:717–726.

Pryce CR, Dobeli M, Martin RD (1993): Effects of sex steroids on maternal motivation in the common marmosets (*Callithrix jacchus*): Development and application of an operant system with maternal reinforcement. *J Comp Psychol* 107:99–115.

Pryce CR, Martin RD, Skuse D (1995): *Motherhood in Human and Nonhuman Primates*. Basel: Karger.

Rhode A (2001): Psychiatric disorders in pregnancy and postpartum. *Gynakologe* 34:315–323.

Rosenblatt JS (2002): Hormonal bases of parenting in mammals. In: Bornstein MH, editor. *Handbook of Parenting, Volume 2. Biology and Ecology of Parenting*. Mahwah, NJ: Erlbaum, 31–60.

Rosenblatt JS, Snowdon CT (1996): *Parental Care: Evolution, Mechanisms and Adaptive Significance,*vol. 25. San Diego, CA: Academic Press.

Sanchez MM, Ladd CO, Plotsky PM (2001): Early adverse experience as a developmental risk factor for later psychopathology: Evidence from rodent and primate models. *Dev Psychopathol* 13:419–449.

Saintfort R, Stern TA (2000): Cross-cultural and neuropsychiatric aspects of a postpartum delusional state. *Harv Rev Psychiatry* 8:141–147.

Sandman CA, Glynn L, Wadhwa PD, Chicz-DeMet A, Porto M, Garite T (2003): Maternal hypothalamic-pituitary-adrenal disregulation during the third trimester influences human fetal responses. *Dev Neurosci* 25:41–49.

Shoham Z, Schachter M (1996): Estrogen biosynthesis—regulation, action, remote effects, and value of monitoring in ovarian stimulation cycles. *Fertil Steril* 65:687–701.

Statsoft. (1998): *STATISTICA for Windows*. (computer program manual) Tulsa, OK: Author.

Stevens VC (1997): Some reproductive studies in the baboon. *Human Reprod Update* 3:533–540.

Susman EJ, Schmeelk KH, Ponirakis A, Gariepy JL (2001): Maternal prenatal, postpartum, and concurrent stressors and temperament in 3-year-olds: A person and variable analysis. *Dev Psychopathol* 13:629–652.

Turner RA, Altemus M, Yip DN, Kupferman E, Fletcher D, Bostrom A, et al (2002): Effects of emotion on oxytocin, prolactin, and ACTH in women. *Stress* 5:269–276.

Wadhwa PD, Sandman CA, Garite TJ (2001): The neurobiology of stress in human pregnancy: Implications for prematurity and development of the fetal central nervous system. *Prog Brain Res* 133:131–142.

Whitten PL, Brockman DK, Stavisky RC (1998): Recent advances in noninvasive techniques to monitor hormone-behavior interactions. *Yearb Phys Anthropol* 41:1–23.

Ziegler TE, Wegner FH, Carlson AA, Lazaro-Perea C, Snowdon CT (2000): Prolactin levels during the periparturitional period in the biparental cotton-top tamarin (*Saguinus oedipus*): Interactions with gender, androgen levels, and parenting. *Horm Behav* 38:111–122.