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RESEARCH ARTICLE

Maternal Effects and the Endocrine Regulation of Mandrill Growth

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Maternal effects can influence offspring growth and development, and thus fitness. However, the physiological factors mediating these effects in nonhuman primates are not well understood. We investigated the impact of maternal effects on variation in three important components of the endocrine regulation of growth in male and female mandrills (*Mandrillus sphinx*), from birth to 9 years of age. Using a mixed longitudinal set ($N = 252$) of plasma samples, we measured concentrations of insulin-like growth factor-I (IGF-I), growth hormone binding protein (GHBP), and free testosterone (free T). We evaluated the relationship of ontogenetic patterns of changes in hormone concentration to patterns of growth in body mass and body length, and determined that these endocrine factors play a significant role in growth of both young (infant and juvenile) and adolescent male mandrills, but only in growth of young female mandrills. We also use mixed models analysis to determine the relative contribution of the effects of maternal rank, parity, and age on variation in hormone and binding protein concentrations. Our results suggest that all of these maternal effects account for significant variation in hormone and binding protein concentrations in all male age groups. Of the maternal effects measured, maternal rank was the most frequently identified significant maternal effect on variation in hormone and binding protein concentrations. We suggest that these endocrine factors provide mechanisms that contribute to the maternal effects on offspring growth previously noted in this population. Am. J. Primatol. 74:890–900, 2012.

Key words: mandrills; hormones; body size; maternal effects; growth

INTRODUCTION

Parental effects can improve offspring fitness through influences on developmental plasticity, conferred via mechanistic pathways with origins in parental physiology [Mousseau & Fox, 1998]. Both maternal and paternal effects can act in an adaptive manner by responding to specific ecological or social cues, and exert strong influence on offspring development, through both gestation and postnatal life. Several studies of captive and free-ranging nonhuman primates have demonstrated strong and pervasive maternal effects on offspring development. For example, in captive and wild baboons, male and female development is affected by paternal presence and dominance rank [Charpentier et al., 2008], and maternal dominance rank such that offspring of higher ranking mothers grow faster, and reach reproductive maturation earlier Altmann & Alberts, 2005; Garcia et al., 2009; [Johnson, 2003]. Male and female mandrills (*Mandrillus sphinx*) also show effects of maternal rank on somatic growth and development, with offspring of higher ranking mothers showing higher size-for-age, and a subsequent positive influence on reproductive success [Setchell et al., 2002, 2006].

Hormones as Mechanisms for Transmission of Maternal Effects

All maternal effects are mediated at some level by physiological factors, although these are not

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well understood. Endocrine communication between mother and offspring plays a particularly important role in shaping behavioral and somatic development, both pre- and postnatally. Evidence from developmental programming studies suggests that maternal nutrition, among other factors, directly affects offspring metabolism, size, and longevity, through components of the somatotropic axis, including insulin-like growth factor-I (IGF-I) and growth hormone (GH) [e.g., Dunn & Bale, 2009]. These components of the somatotropic axis regulate fetal and infant growth patterns in relation to manipulated maternal diet and environmental factors, such as protein supply [Muaku et al., 1995], nutrient restriction [McDonald et al., 2007], cold exposure [Hyatt et al., 2008], and immobilization [Gao et al., 2011]. Effects of altered hormone levels seem to be the greatest during the latter part of gestation, since they result in changed size of offspring at birth, which sets up a cascade of effects for postnatal life [Rehfeldt et al., 2004]. In baboons, for example, moderate maternal nutrient restriction downregulated most aspects of the IGF system in fetal livers, including expression of both IGF I and II and their receptors [Li et al., 2009]. While GH is a key component of the somatotropic axis, accurate measurement of this hormone requires frequent sampling. However, measurement of growth hormone binding protein (GHBP) can serve as a proxy for GH that has activated its receptor; GHBP has been identified as the product of either alternative splicing or proteolysis of the growth hormone receptor (GHR) [Dastot et al., 1996].

Sex steroids mediate maternal effects on offspring growth and development both independently and by their impact on the GH-IGF-I axis [Chowen et al., 1996]. Spotted hyena (*Crocuta crocuta*) females exhibit increasing androgen levels during gestation, which have been argued to organize behavioral profiles (e.g., aggression, mounting) in offspring according to maternal rank [Dloniak et al., 2006]. Ring-tailed lemurs (*Lemur catta*), in which females are socially dominant, seem to follow a similar pathway to spotted hyenas: androgen levels increase during gestation and female offspring possess masculinized external genitalia [Drea, 2010]. In marmosets (*Callithrix geoffroyi*), increased androgen levels in early gestation (first trimester) are associated with decreased in utero growth and lower birth weight, but might also be implicated in facilitating "catch-up growth" during the juvenile period [Smith et al., 2010].

Evidence for Maternal Effects in Mandrills

Mandrills have the highest levels of sexual size dimorphism of any extant primate [Setchell et al., 2001]. There is a high degree of individual variation along the developmental trajectory leading to maximal adult expression of secondary sexual traits in male mandrills [Setchell et al., 2006; Setchell & Dixson, 2002]. Maternal age and rank exert significant effects on male and female infant mandrill growth, with sons and daughters of older and higher ranking mothers having higher mass-for-age residual scores [Setchell et al., 2001]. Postweaning growth in female mandrills is not similarly affected by maternal age or rank, but it appears that these maternal effects play an important role in mediating not only male offspring survival, but also rate of development—sons of older and higher ranking mothers undergo more rapid development during adolescence [Setchell et al., 2006]. In addition, individual rank and group demographic factors relate to rate of maturation—dominant males and those with fewer peers develop faster than other males [Setchell et al., 2006]. Although the postweaning growth patterns in females seem to escape significant influence from maternal factors, it is likely that the earlier effects help to shape growth trajectories that influence reproductive success since females that reach heavier weights earlier in development experience earlier ages at first birth [Setchell et al., 2001].

Aims and Predictions

In order to examine how maternal influences on offspring growth in mandrills are effected through hormonal mechanisms, we measured levels of IGF-I, GHBP, and free testosterone (free T—males only) in mixed longitudinal plasma samples from the semi-free ranging population at the Centre International de Recherches Médicales, Franceville (CIRMF), Gabon. Previous analyses with total testosterone (from plasma) and testosterone metabolites (from feces) suggest that testosterone plays an important role in male mandrill growth and development of ornamentation [Setchell et al., 2008; Setchell & Dixson, 2001; Wickings & Dixson, 1992]. This study measures free T or the testosterone in circulation that is not bound to carrier proteins (e.g., sex hormone binding globulin, albumin, cortisol-binding globulin). Measuring free T offers an index of the biologically active portion of this important androgen [Malisch & Breuner, 2010]. Although a small percentage (1–2%, on average) of the total amount of circulating testosterone is in this unbound state, this may fluctuate throughout ontogeny.

This study aims to determine whether IGF-I, GHBP, and free T are important for growth in male and female mandrills, and whether maternal effects influence concentrations of these hormones. If these bioactive molecules are important for growth in mandrills, and if maternal factors contribute to variation in concentrations throughout ontogeny, then they may provide important mechanistic pathways through which mandrill mothers modify offspring developmental trajectories, and, as has previously been argued, offspring fitness. We first describe

age-related patterns of the hormones and binding protein measured in male and female mandrills, and assess their contribution to growth in mass and length. We then evaluate variation in concentrations in relation to (1) maternal age; (2) maternal parity; and (3) maternal rank. We test the following three predictions: (1) IGF-I and GHBP are significant predictors of early growth in male and female mandrills, and free T is a significant predictor of growth in adolescent male mandrills; (2) maternal factors are more related to variation in hormone levels in younger animals than in older ones, since effects conveyed via placental or lactational effects on offspring hormones might diminish with age; (3) since earlier studies suggest maternal rank is the most important maternal effect on offspring development, this will also be the most influential maternal factor for explaining variation in IGF-I, GHBP, and free T.

METHODS

This research complied with protocols approved by the CIRMF ethics committee, the Ethical Committee of Ile de France for animal experimentation, and the Gabonese ethics committee, and adhered to the legal requirements of the country in which the research was conducted (Gabon). This research also adhered to the American Society of Primatologists principles for the ethical treatment of primates.

Study Population

The CIRMF mandrill colony was established in 1983–1984, when 15 animals (seven males, eight females) originating from the wild were released into a 6.5 ha naturally rain-forested enclosure. All further additions to the group have been due to reproduction of the founder animals while some animals have been removed. A second semi-free-ranging group was established in 1994 (3.5 ha) by transferring 17 mandrills (including four adult males and six adult females) from the first enclosure. The animals forage freely in the enclosure, and receive daily supplements of monkey chow and seasonal fruits. Water is available ad libitum. Group sizes during the study period ranged from 15 in 1983–1984 to a maximum of 104 animals in 2002, corresponding to smaller groups observed in the wild [Rogers et al., 1996].

We analyzed 252 plasma samples from animals aged 0–9 years (Table I), collected between 1986 and 2005. These samples span the range of somatic growth for male and female mandrills [Setchell et al., 2001]. We divided female growth into two periods: birth to 5 years (infant and juvenile), and 5–9 years (adolescence and early adulthood), since average age at first birth in this colony occurs at 4.7 years [Setchell et al., 2002]. We also divided male growth into two periods: birth to 4 years (infant/juvenile period) and 4–9 years (adolescence and period of completion of somatic growth for both sexes) [Setchell et al., 2006]. We collected mass and length measurements during veterinary exams and obtained information on maternal age, rank (categorized as "high" (upper quartile), "middle" (25–75% of females dominated), or "low" (lower quartile), after [Setchell et al., 2001]), and parity from long-term colony records.

TABLE I. Composition of Sample

	No. of individuals	No. of samples	Age range (years)
Females			
	9	1	0.73–3.15
	8	2	1.60–8.22
	13	3	1.11–8.14
	3	4	1.17–8.30
	5	5	0.11–8.89
	5	6	0.19–8.31
Total female samples	43	131	0.11–8.89
Males			
	8	1	1.30–5.70
	3	2	0.30–8.00
	5	3	0.40–4.30
	11	4	1.20–8.40
	7	5	1.30–8.50
	1	6	0.30–9.00
	1	7	4.40–8.30
Total male samples	36	121	0.30–9.00

Capture, Anesthesia, and Blood Sampling

The mandrills are captured annually for veterinary examination, and additional captures occurred for research purposes in some years. Animals are captured by closing the door to the feeding pen at approximately 10 am (morning feeding time), and anesthetized by blowpipe intramuscular injections of ketamine (Imalgène 1000, Merial, Lyon, France; 10 mg/kg body weight). Once anesthetized, animals are transported to the primate center for veterinary examination and blood sampling. They are then replaced in the covered feeding pen to recover from anesthesia, and released into the enclosure when fully awake.

Blood samples are taken via venipuncture approximately 20 min after anesthesia. Seven milliliters of blood are collected from the femoral vein into vacutainer tubes containing ethylenediaminetetraacetic acid. Samples were spun to separate plasma and stored at −80°C at CIRMF. After obtaining CITES permits for export and import of the samples, they were shipped to The George Washington University, and stored at −80°C until analysis.

Hormone Assay

We measured hormones using commercially available enzyme immunoassay kits (IGF-I and free

T: ALPCO Diagnostics, Salem, NH, 22-IGFHU-E01, and 11-FTSHU-E01; GHBP: DSL, Webster, TX, DSL-10–4800), validated by standard parallelism and recovery tests [Bernstein, 2004]. Assay sensitivities were IGF-I 0.09 ng/ml; GHBP1.69 pmol/l; free T 0.17 pg/ml. Intraassay coefficients of variation (CVs) ranged 4.1–6.2% and interassay CVs ranged 4.8–7.6%. We diluted samples 1:50 for IGF-I analysis [Bernstein et al., 2007], and any other samples subsequently exceeding the highest value of the curve were diluted further and reanalyzed. We incorporated the dilution factor into the final calculation of results. We read plates on a Dynex MRX absorbance reader (Dynex Technologies, Chantilly, VA).

Data Treatment

The mixed longitudinal sample varied in age range and number of samples per individual (Table I). We examined the relationship of hormones to growth in two ways. First, we used nonparametric lowess regression to describe ontogenetic variation in hormones across the ages sampled. Lowess estimates locally weighted regression lines by successively analyzing small segments or "windows" of bivariate data scatters [Efron & Tibshirani, 1991]. We set the lowess tension to 0.5 in all cases, meaning that half of the data points were included in each running window; this prevents the lowess from following local irregularities in raw data too closely, yet captures enough of the variation in the data scatter to accurately represent trends for groups.

Individual "hormone residuals" were calculated from lowess regressions—we used a method that calculates size-for-age [Moses et al., 1992]—and fit these values through IGF-I and GHBP data for males and females. Mann–Whitney U tests were then used to evaluate whether sex differences in lowess-described patterns were significant. We $\log_{10}$ transformed data for subsequent analysis to obtain an approximately normal distribution. We used ordinary least-squares (OLS) regression to assess the relationship between hormones and growth by specifying models that included mass or length as dependent variables, and all hormones measured as independent predictor variables, separately for each sex.

To examine the overall relationship between hormones, maternal factors, and covariates, we employed variance component mixed models (VCMM). Mixed models contain both fixed and random effects, and are particularly useful for repeated measures analysis because they have the capacity to estimate a number of different covariance structures and adjust for the correlation between repeated measures of the same subject. We used VCMM to explore the variation in hormone levels attributable to maternal effects (fixed effects: maternal rank—high, middle, low; maternal parity—primiparous, multiparous; maternal age-–young <5 years, old >5 years) and individual rank (fixed effect: rank, for male free T analysis only). We included individual identity and weight-for-age, calculated from a lowess-smoothed trend through the data set, as random effects. We performed post-hoc tests of significant difference among fixed effect categories using the Bonferroni correction for multiple comparisons.

We considered a P value of less than 0.05 as significant. We performed all analyses using SYSTAT, version 13 (SYSTAT Software, Inc., Chicago, IL).

RESULTS

Hormone Patterns

Both sexes show a consistent increase in IGF-I concentrations from the youngest samples until 4 years, when concentrations plateau throughout adulthood (Fig. 1). In the first year of life, there is no significant sex difference in IGF-I (Mann–Whitney U: TS = 54.00, $P = 0.57$, $N = 4$ males, 6 females). There is a great deal of variation in IGF-I concentrations, especially from 2 years onward. Male IGF-I concentrations are significantly higher than those of females after 1 year of age, despite some overlap at all ages sampled (Mann–Whitney U: TS = 3.33, $P = 0.01$, $N = 98$ males, 104 females). The vertical displacement of the lowess regression in males relative to females is likely due to a higher proportion of male samples having very high concentrations between 3 and 9 years of age (e.g., around 2000 ng/ml).

GHBP concentrations show a less curvilinear trajectory up to 9 years of age in both sexes

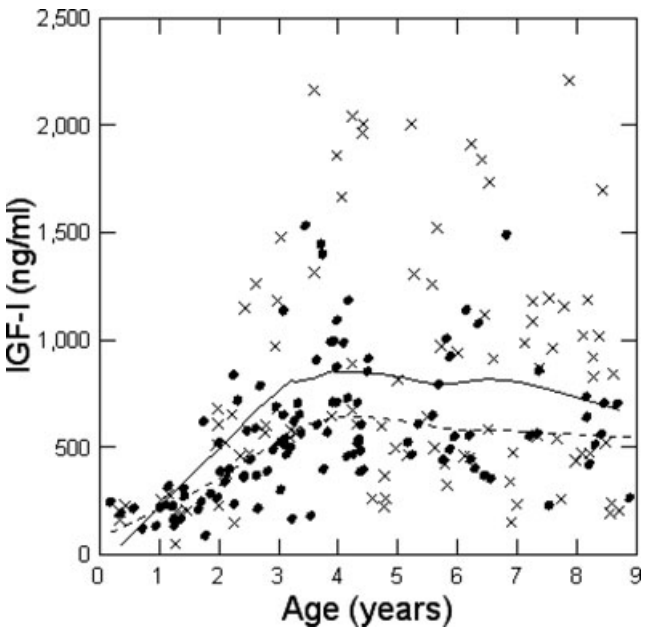

Fig. 1. Female (solid circle, dashed line) and male (crosses, solid line) IGF-I concentrations from 0 to 9 years of age. IGF-I, insulin-like growth factor-I; ng/ml, nanograms/milliliter.

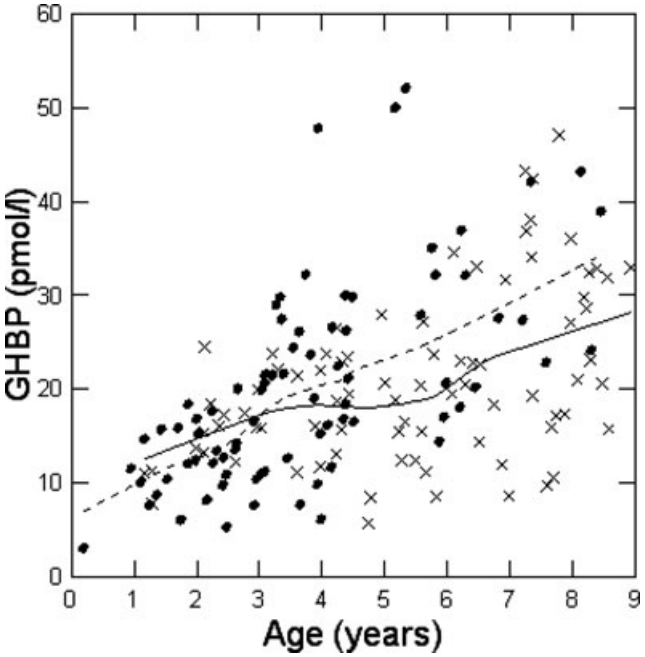

Fig. 2. Female (solid circle, dashed line) and male (crosses, solid line) GHBP concentrations from 0 to 9 years of age. GHBP, growth hormone binding protein; pmol/l, picomoles/liter.

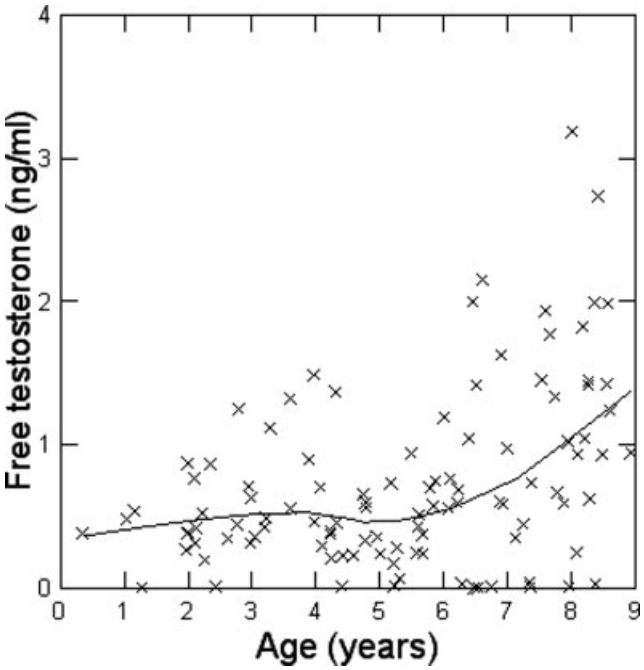

Fig. 3. Male free testosterone concentrations from 0 to 9 years of age. ng/ml, nanograms/milliliter.

(Fig. 2). Males appear to have higher levels than females from birth to 3 years of age; however, this difference is not significant (Mann–Whitney U: TS = 509.00, $P = 0.62$, $N = 15$ males, 29 females). After 3 years, females show higher levels than males (Mann–Whitney U: TS = 1,199.00, $P < 0.01$, $N = 66$ males, 51 females), although both sexes show consistent increases in levels with age. Unlike IGF-I, GHBP concentrations do not seem to plateau in the oldest individuals.

Free T concentrations remain low through the first 6 years in male mandrills, and then increase steadily (Fig. 3). However, free T begins to increase at younger ages in some individuals while concentrations remain low even at 7 or 8 years of age in others.

Hormones, Mass, and Length

For both female and male mandrills, IGF-I and body mass show similar trajectories up to the point of plateau in IGF-I at around 4 years, after which body mass continues to increase (Fig. 4). The relationship of GHBP to body mass differs from that seen for IGF-I, with both sexes (Fig. 5). GHBP continues to increase throughout the ages sampled, and parallels the mass growth curves more closely.

The early part of the female body length growth curve (1–4 years) approximates the rise in IGF-I levels (Fig. 6A), as does the male length/IGF-I curve (Fig. 6B). However, the male body length growth curve continues rising after this point, while females experience another period of increase to 6 years, then plateau. The continually increasing GHBP curves are a closer match to body length growth curves than IGF-1 for both sexes (Fig. 7). In males, the free T curve matches that of body mass more closely than that of body length (Fig. 8), although the upswing of the free T curve at the oldest ages suggests that it would continue its increase at older ages, and perhaps continue to parallel the body mass and body length curves.

In younger females, IGF-I and GHBP predict mass with considerable strength, but only IGF-I was as a significant predictor of body length, and not a very strong one (Table II). Neither IGF-I nor GHBP emerges as a significant predictor of body mass or length in older females. IGF-I and GHBP, but not free T, return significant predictions of mass in younger males. Only IGF-I emerges as a significant predictor of length, while GHBP and free T do not contribute significantly to predictions of this measure. However, analysis of older males returns GHBP and free T as significant predictors of body mass and length, while IGF-I does not contribute to predictions of mass and length.

Maternal Effects on Hormones

For young females, maternal traits did not carry significant effects on offspring hormone concentrations. We did not examine the influence of maternal effects on hormones in older females, since hormones were not significant predictors of growth for this age–sex class.

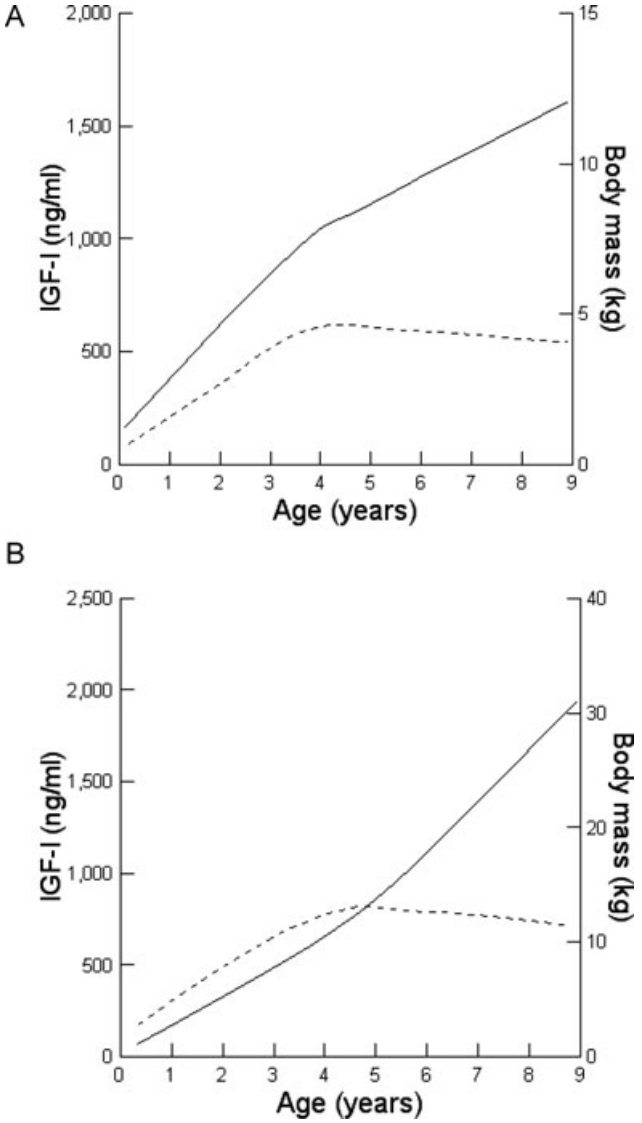

Fig. 4. Body mass growth curve (solid line) and IGF-I pattern (dashed line) in female (A) and male (B) mandrills. IGF-I, insulin-like growth factor-I; ng/ml, nanograms/milliliter; kg, kilograms.

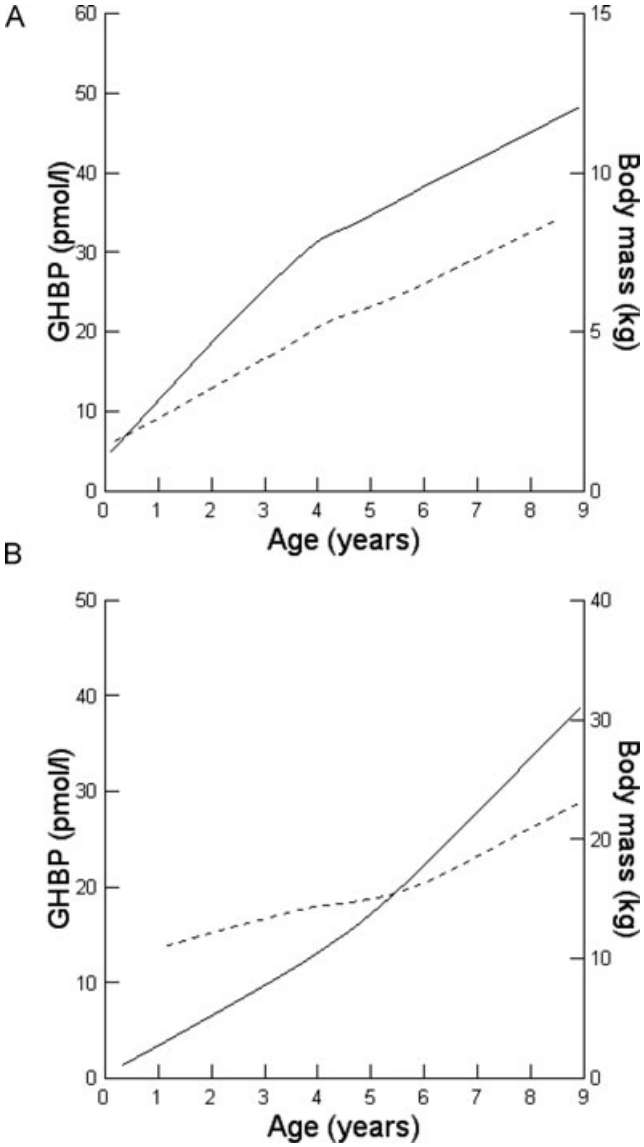

Fig. 5. Body mass growth curve (solid line) and GHBP pattern (dashed line) in female (A) and male (B) mandrills. GHBP, growth hormone binding protein; pmol/l, picomoles/liter; kg, kilograms.

In young males, maternal rank also demonstrated a significant effect on IGF-I and GHBP concentrations, although the direction of these relationships was not consistent (Table III). Young male offspring's IGF-I concentrations were higher in those individuals with high- vs. mid-ranking mothers, but young males born to mothers of low rank had higher GHBP concentrations than those born to high-ranking mothers. Multiparous mothers also conferred higher GHBP concentrations on young sons compared to primiparous mothers.

In older males, only GHBP and free T concentrations showed effects of maternal factors. GHBP concentrations were significantly affected by maternal rank, in an opposite direction from that seen for younger males. Specifically, offspring of high- and mid-ranking mothers had higher GHBP concentrations than offspring of low-ranking mothers. Free T was the only hormone that was significantly influenced by maternal age; offspring of older mothers had higher free T concentrations than offspring of younger mothers. Free T concentrations were not significantly affected by individual male rank.

DISCUSSION

Our results support our first prediction that IGF-I and GHBP are important for early growth in mass and length in male and female mandrills, and that

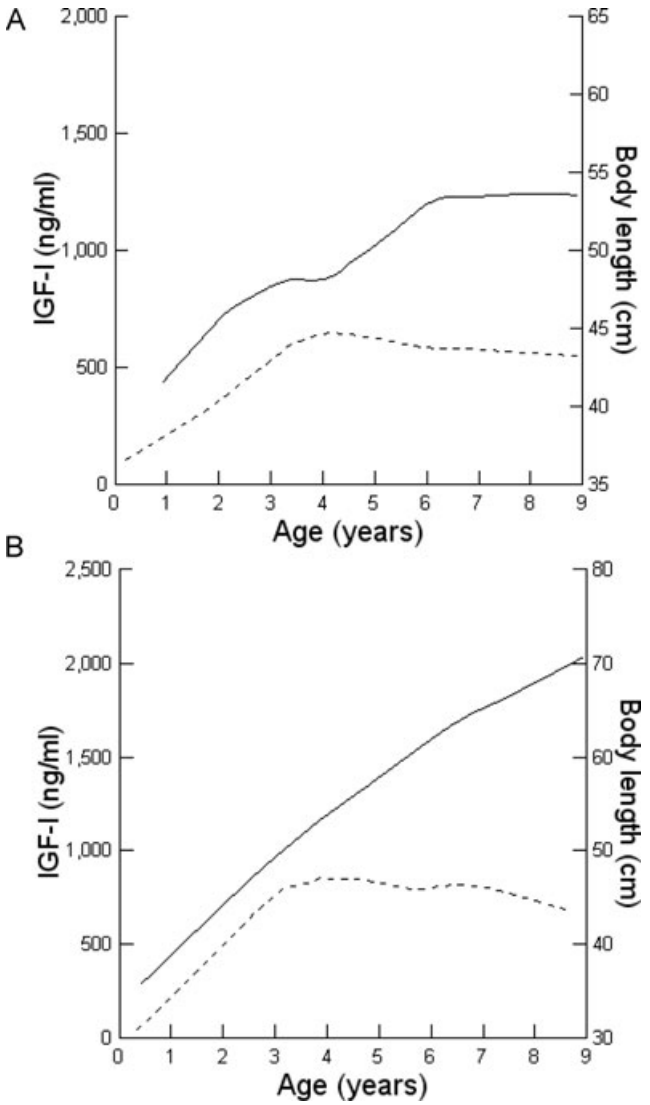

Fig. 6. Body length growth curve (solid line) and IGF-I pattern (dashed line) in female (A) and male (B) mandrills. IGF-I, insulin-like growth factor-I; ng/ml, nanograms/milliliter; cm, centimeters.

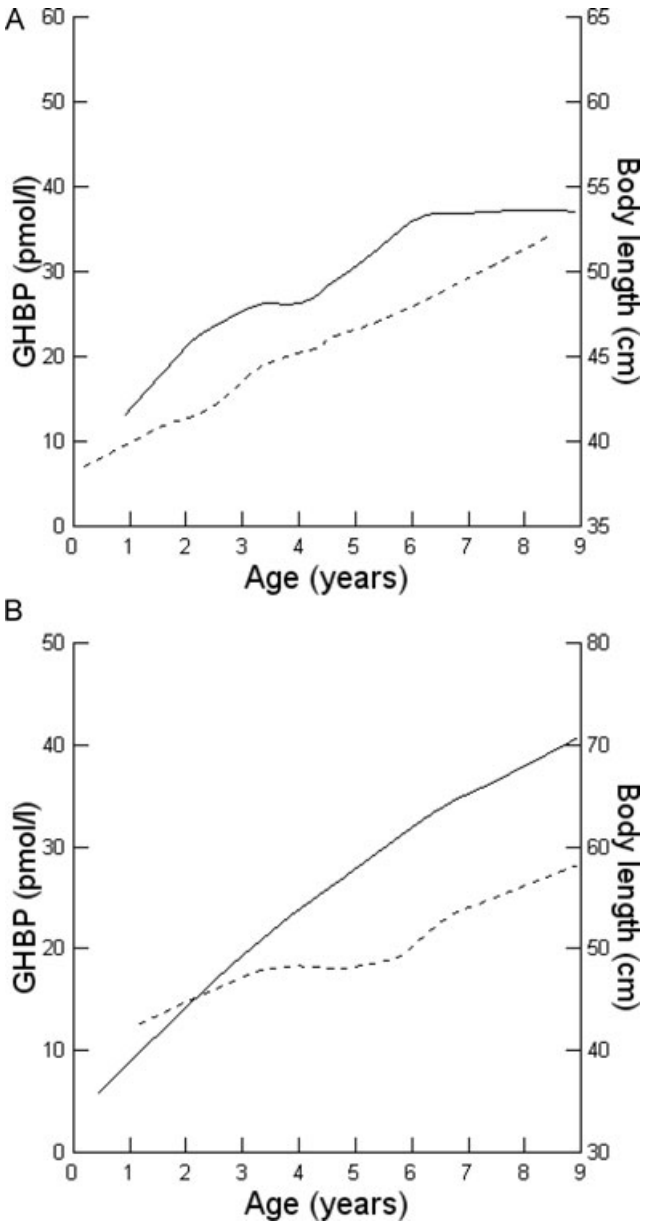

Fig. 7. Body length growth curve (solid line) and GHBP pattern (dashed line) in female (A) and male (B) mandrills. GHBP, growth hormone binding protein; pmol/l, picomoles/liter; cm, centimeters.

free T is also important for adolescent growth in male mandrills. Our analyses of the influence of maternal effects on hormone levels in young males show some support for the prediction that maternal factors are most important at younger ages. Specifically, maternal rank and parity, but not maternal age, influenced all bioactive factors measured in male mandrills. We also found some support for our third prediction that maternal rank will be the most influential maternal factor for explaining hormone variation. Overall, maternal rank influenced all hormones measured except for free T in adolescent males. Maternal parity influenced GHBP in the young male group, and maternal age influenced only free T in the adolescent male group.

The positive relationship of IGF-I to rank in young individuals of both sexes suggests that this hormone may be one mechanism mediating the previously noted effect of higher mass-for-age in offspring of dominant females in this population [Setchell et al., 2001]. The higher GHBP in offspring of low-ranking mothers might represent a mechanism by which compensatory growth occurs in light-for-age male mandrills born to low-ranking mothers; by maintaining high circulating levels of GH, its anabolic properties are enhanced and more energetic

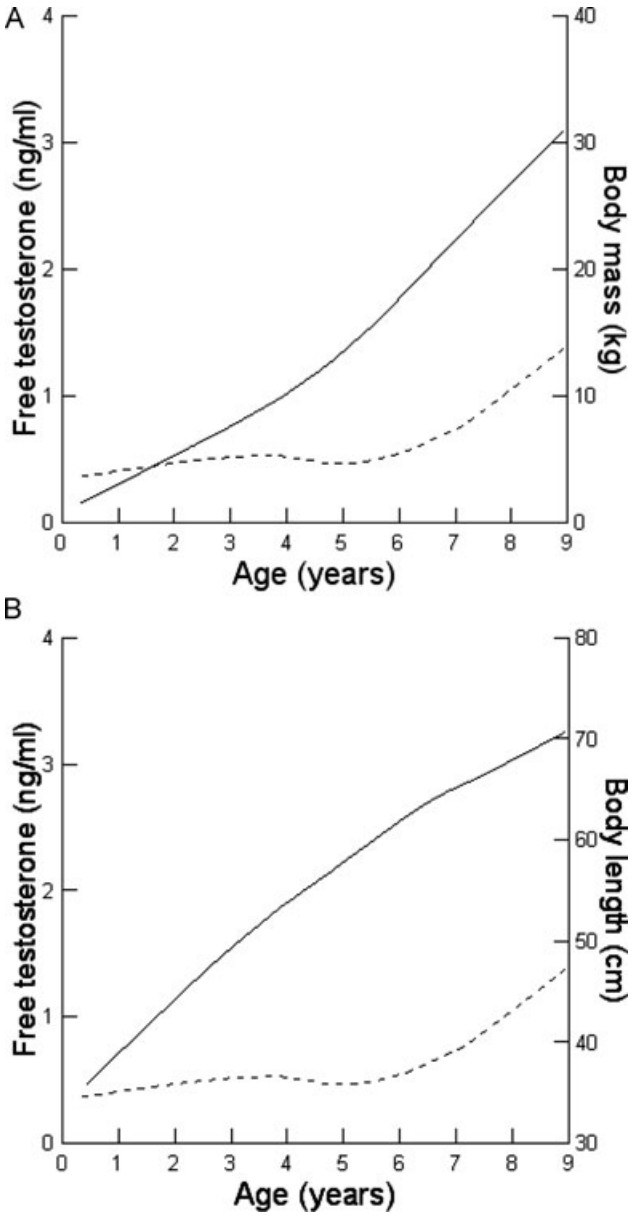

Fig. 8. Body mass (A) and body length (B) growth curves (solid lines), and free testosterone pattern (dashed line) in male mandrills. ng/ml, nanograms/milliliter; kg, kilograms; cm, centimeters.

intake can be directed toward growth processes [e.g., Hornick et al., 2000].

The fact that maternal age did not significantly influence GHBP levels in offspring, but parity did, suggests a mechanism through which maternal investment in offspring growth might be organized differently in first-time vs. multiparous mothers. Parity has been demonstrated in some nonhuman primate species to influence birth weight [e.g., Fessler et al., 2005; Hopper et al., 2008]. Experimental evidence in sheep suggests that expression of components of the somatotropic axis, including receptors, is organized differently in offspring of primiparous mothers compared to multiparous mothers [Hyatt et al., 2007]. Primiparous mothers, likely still undergoing more growth than multiparous mothers, may experience alterations in nutrient partitioning due to their own growth, and subsequent modifications to IGF-I levels during pregnancy [e.g., Jones et al., 2010]. Primiparous mothers may also be more susceptible to short-term nutritional stress, which can affect offspring insulin and IGF sensitivity in postnatal life [Shen et al., 2005].

Adolescent males born to older mothers had higher testosterone than males born to younger mothers. This may be linked to changes in body composition associated with increased age in older mothers. In older humans, multiparous mothers have more centralized fat depots [Lassek & Gaulin, 1996]. Human waist circumference may also predict birth sex ratio and there is a positive correlation between maternal testosterone levels and thicker middles [Manning et al., 1996]. However, studies in Old World monkeys suggest that in general, body mass and fat deposits decline as a function of age [Glassman & Coelho, 1987], so the relationship between older age and fat distribution in female mandrills is not easily predictable.

In an investigation of the relationship between maternal rank and foraging condition (e.g., food enhanced, not food enhanced), Altmann and Alberts [2005] found that maternal rank and parity were significantly positively predictive of juvenile offspring size and that in turn, large juvenile size predicted an earlier age at sexual maturation. Therefore, even when controlling for environmental factors that might be expected to strongly influence offspring condition (e.g., foraging condition), maternal factors consistently and clearly showed effects on offspring development that are likely to translate into fitness effects. Previous studies have demonstrated a strong link between maternal factors and patterns of offspring development in mandrills, even though these semi-free ranging animals also receive some food supplementation [Setchell et al., 2001]. In mandrills, trajectories of maturation leading to sexual maturation and the acquisition of alpha rank (for males) influence individual timelines of reproduction and fitness, since these can clearly influence lifetime reproductive output [Setchell et al., 2006]. Altmann and Alberts [2005] suggested that these benefits visited upon offspring might occur via positive effects on nutritional intake and lowered energy expenditure. The results of the present study suggest that modification of hormone and binding profiles, influenced by maternal diet and nutritional status [e.g., Altmann & Alberts, 2005], is one way that these benefits might be mediated.

That maternal rank might influence offspring hormone concentrations in a meaningful way, or even in a way that illustrates some sort of

TABLE II. Results of Least Squares Regression Analysis

Sex/age	Dependent	Effect	Std coefficient	t	P	Adjusted multiple R^2	P-value for R^2	Std error of estimate
Females 0–5 years	Mass	IGF-I	0.59	6.23	<0.01	0.54	<0.01	0.11
		GHBP	0.35	3.69	<0.01			
	CRL	IGF-I	0.36	2.57	0.01	0.11	0.03	0.04
		GHBP	0.08	0.60	0.55			
Males 0–4 years	Mass	IGF-I	0.67	7.46	<0.01	0.78	<0.01	0.06
		GHBP	0.84	2.15	0.05			
		Free T	0.24	0.90	0.39			
	CRL	IGF-I	0.73	4.93	<0.01	0.61	<0.01	0.03
		GHBP	0.30	2.03	0.06			
		Free T	0.10	0.65	0.53			
Females 5–9 years	Mass	IGF-I	–0.03	–0.10	0.92	0.01	0.88	0.11
		GHBP	0.13	0.48	0.64			
	CRL	IGF-I	0.24	0.73	0.49	0.02	0.72	0.04
		GHBP	0.16	0.43	0.64			
Males 4–9 years	Mass	IGF-I	–0.10	–0.77	0.45	0.47	<0.01	0.11
		GHBP	0.54	4.77	<0.01			
		Free T	0.37	2.23	0.01			
	CRL	IGF-I	–0.06	–0.41	0.69	0.37	<0.01	0.03
		GHBP	0.49	3.49	<0.01			
		Free T	0.34	2.16	0.04			

IGF-I, insulin-like growth factor-I; GHBP, growth hormone binding protein; Free T, free testosterone; CRL, crown-rump length.

TABLE III. Results of Mixed Models Analysis for Each Sex and Age Range

Sex/ age	Hormone	Explanatory variable	F-ratio	df	P	Nature of pairwise comparisons
Males 0–4 years	IGF-I	Maternal rank	3.631	2, 29	0.04	High > mid
	GHBP	Maternal rank	7.967	2, 18	<0.01	Low > high
		Maternal parity	9.466	1, 18	0.01	Parous > primiparous
Males 4–9 years	GHBP	Maternal rank	3.464	2, 50	0.04	High > low; mid > low
	Free T	Maternal age	4.470	1, 75	0.04	Old > young

All post hoc pairwise comparisons ($P < 0.05$) include Bonferroni correction for multiple pairwise comparisons
IGF-I, insulin-like growth factor-I; GHBP, growth hormone binding protein; Free T, free testosterone.

programming influence, is not unexpected. Whereas the effect of maternal stress-related hormones in the lifelong programming of offspring phenotypes has been reported in nonprimate mammals [e.g., Sheriff et al., 2010], similar findings from wild primate populations have been harder to document. Recent research documents fecal glucocorticoid concentrations in subadult male yellow baboons that are inversely related to maternal dominance rank, suggesting organizational maternal effects on the hypothalamic–pituitary–adrenal axis in these primates ([Onyango et al., 2008]; but see Gesquiere and colleagues [2005] for a discussion of individual endocrine variability). Moreover, parity is also linked to variation in hormone concentrations during gestation in baboons (primiparous mothers have higher fecal estrogen concentrations [Altmann et al., 2004]). Our findings are in line with the findings of these studies in baboons, even though the hormones assayed for the present study are part of different hormone axes. Overall, this suggests that several different aspects of endocrine physiology in cercopithecine primates are influenced by maternal factors, and that in turn, these effects are felt as influences on offspring growth, maturation, and fitness.

In sum, we have demonstrated that variation in important growth-related endocrine factors is linked to maternal effects in male mandrills. These findings: (1) provide mechanistic pathways through which factors such as maternal rank, parity, and age might influence offspring growth in mandrills and other nonhuman primates; (2) support previous studies in this population which suggested that maternal effects conferred during the period of lactation persist after weaning [Setchell et al., 2001]; and (3) add to other recent studies that demonstrate that maternal effects influence hormone levels of offspring at older ages [Onyango et al., 2008]. While measures of circulating hormone concentrations provide a partial picture of the pathways through which the maternal environment affects offspring development, information about specific tissue-level

effects are needed to round out an understanding of this issue [Bernstein, 2010]. Measuring concentrations of GHBP, itself a product of activated receptors, offers some insight into this issue. Future investigations will include examination of intergenerational hormone patterns and concentrations in order to provide further perspective on the relationship of maternal effects on hormones and growth in mandrills.

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REFERENCES

Altmann J, Alberts SC. 2005. Growth rates in a wild primate population: ecological influences and maternal effects. Behav Ecol Sociobiol 57:490–501.

Altmann J, Lynch JW, Nguyen N, Alberts SC, Gesquiere LR. 2004. Life-history correlates of steroid concentrations in wild peripartum baboons. Am J Primatol 64:95–106.

Bernstein RM. 2004. Hormones and body size evolution in Old World monkeys [dissertation]. Urbana, IL: University of Illinois at Urbana-Champaign. 402 p. Available from: University Microfilms, Ann Arbor, MI; 3153247.

Bernstein RM. 2010. The big and small of it: how body size evolves. Yearb Phys Anthropol 143:46–62.

Bernstein RM, Leigh SR, Donovan SM, Monaco MH. 2007. Hormones and body size evolution in papionin primates. Am J Phys Anthropol 132:247–260.

Charpentier MJE, Van Horn RC, Altmann J, Alberts SC. 2008. Paternal effects on offspring fitness in a multimale primate society. Proc Natl Acad Sci USA 105:1988–1992.

Chowen JA, Garcia-Segura LM, Gonzalez-Parra S, Argente J.1996. Sex steroid effects on the development and functioning of the growth hormone axis. Cell Mol Neurobiol 16:297–310.

Dastot F, Sobrier M, Duquesony P, Duriez B, Goosens M, Amselem S. 1996. Alternatively spliced forms in the cytoplasmic domain of the human growth hormone (GH) receptor regulate its ability to generate a soluble GH-binding protein. Proc Natl Acad Sci USA 93:10723–10728.

Dloniak SM, French JA, Holekamp KE. 2006. Rank-related maternal effects of androgens on behaviour in wild spotted hyaenas. Nature 439:1190–1193.

Drea CM. 2010. Endocrine correlates of pregnancy in the ring-tailed lemur (*Lemur catta*): implications for the masculinization of daughters. Horm Behav 59:417–427.

Dunn GA, Bale TL. 2009. Maternal high-fat diet promotes body length increases and insulin insensitivity in second-generation mice. Endocrinology 150:4999–5009.

Efron B, Tibshirani R. 1991. Statistical data analysis in the computer age. Science 253:390–395.

Fessler DM, Navarrete CD, Hopkins W, Izard MK. 2005. Examining the terminal investment hypothesis in humans and chimpanzees: associations among maternal age, parity, and birth weight. Am J Phys Anthropol 127:95–104.

Gao P, Ishige A, Murakami Y, Nakata H, Oka J, Munakata K, Yamamoto M, Nishimura K, Watanabe K. 2011. Maternal stress affects postnatal growth and the pituitary expression of prolactin in mouse offspring. J Neurosci Res 89:329–340.

Garcia C, Lee PC, Rosetta L. 2009. Growth in colony living anubis baboon infants and its relationship with maternal activity budgets and reproductive status. Am J Phys Anthropol 138:123–135.

Gesquiere LR, Altmann J, Khan MZ, Couret J, Yu JC, Endres CS, Lynch JW, Ogola P, Fox EA, Alberts SC, Wango EO. 2005. Coming of age: steroid hormones of wild immature baboons (*Papio cynocephalus*). Am J Primatol 67:83–100.

Glassman DM, Coelho AM Jr. 1987. Principal components analysis of physical growth in savannah baboons. Am J Phys Anthropol 72:59–66.

Hadley ME. 2000. Endocrinology 5th ed. Upper Saddle River, NJ: Prentice Hall. 585 p.

Hopper KJ, Capozzi DK, Newsome JT. 2008. Effects of maternal and infant characteristics on birth weight and gestation length in a colony of rhesus macaques (*Macaca mulatta*). Comp Med 58:597–603.

Hornick JL, Van Eenaeme C, Gerard O, Dufrasne I, Istasse L. 2000. Mechanisms of reduced and compensatory growth. Domes Anim Endocrinol 19:121–132.

Hyatt MA, Budge H, Walker D, Stephenson T, Symonds ME. 2007. Effects of maternal parity and late gestational nutrition on mRNA abundance for growth factors in the liver of postnatal sheep. Am J Physiol 292:R1934–R1942.

Hyatt MA, Butt EA, Budge H, Stephenson T, Symonds ME. 2008. Effects of maternal cold exposure and nutrient restriction on the ghrelin receptor, the GH-IGF axis, and metabolic regulation in the postnatal ovine liver. Reproduction 135:723–732.

Johnson SE. 2003. Life history and the competitive environment: trajectories of growth, maturation, and reproductive output among chacma baboons. Am J Phys Anthropol 120:83–98.

Jones RL, Cederberg HM, Wheeler SJ, Poston L, Hutchinson CJ, Seed PT, Oliver RL, Baker PN. 2010. Relationship between maternal growth, infant birth weight and nutrient partitioning in teenage pregnancies. BJOG 117:200–211.

Lassek WD, Gaulin SJC. 1996. Changes in body fat distribution in relation to parity in American women: a covert form of maternal depletion. Am J Phys Anthropol 131:295–302.

Li C, Schlabritz-Loutsevitch NE, Hubbard GB, Han V, Nygard K, Cox LA, McDonald TJ, Nathanielsz PW. 2009. Effects of maternal global nutrient restriction on fetal baboon hepatic insulin-like growth factor system genes and gene products. Endocrinology 150:4634–4642.

Malisch JL, Breuner CW. 2010. Steroid-binding proteins and free steroids in birds. Mol Cell Endocrinol 316:42–52.

Manning JT, Anderton R, Washington SM. 1996. Women's waists and the sex ratio of their progeny: evolutionary aspects of the ideal female body shape. J Hum Evol 31:41–47.

McDonald TJ, Nijland MJ, Nathanielsz PW. 2007. The insulin-like growth factor system and the fetal brain: effects of poor nutrition. Rev Endocr Metab Disord 8:71–84.

Moses LE, Gale LC, Altmann J. 1992. Methods for analysis of unbalanced, longitudinal, growth data. Am J Primatol 28:49–59.

Mousseau TA, Fox CW. 1998. The adaptive significance of maternal effects. Trends Ecol Evol 13:403–407.

Muaku SM, Underwood LE, Selvais PL, Ketelslegers JM, Matier D. 1995. Maternal protein restriction early or late in rat pregnancy has differential effects on fetal growth, plasma insulin-like growth-factor I (IGF-I) and liver IGF-I gene expression. Growth Regul 5:125–132.

Onyango PO, Gesquiere LR, Wango EO, Alberts SC, Altmann J, 2008. Persistence of maternal effects in baboons: mother's

dominance rank at son's conception predicts stress hormone levels in subadult males. Horm Behav 54:319–324.
Rehfeldt C, Nissen PM, Kuhn G, Vestergaard M, Ender K, Oksbjerg N. 2004. Effects of maternal nutrition and porcine growth hormone (pGH) treatment during gestation on endocrine and metabolic factors in sows, fetuses, and pigs, skeletal muscle development, and postnatal growth. Domest Anim Endocrinol 27:267–285.
Rogers ME, Abernathy KA, Fontaine B, Wickings EG, White LJT, Tutin CEG. 1996. Ten days in the life of a mandrill horde in the Lope Reserve, Gabon. Am J Primatol 40:297–313.
Setchell JM, Dixson AF. 2001. Circannual changes in the secondary sexual adornments of semifree-ranging male and female mandrills (*Mandrillus sphinx*). Am J Primatol 53:109–121.
Setchell JM, Dixson AF. 2002. Developmental variables and dominance rank in adolescent male mandrills (*Mandrillus sphinx*). Am J Primatol 56:9–25.
Setchell JM, Lee PC, Wickings EJ, Dixson AF. 2001. Growth and ontogeny of sexual size dimorphism in the mandrill (*Mandrillus sphinx*). Am J Phys Anthropol 115:349–360.
Setchell JM, Lee PC, Wickings EJ, Dixson AF. 2002. Reproductive parameters and maternal investment in mandrills (*Mandrillus sphinx*). Int J Primatol 23:51–68.
Setchell JM, Smith T, Wickings EJ, Knapp LA. 2008. Social correlates of testosterone and ornamentation in male mandrills. Horm Behav 54:365–372.
Setchell JM, Wickings EJ, Knapp LA. 2006. Life history in male mandrills (*Mandrillus sphinx*): physical development, dominance rank, and group association. Am J Phys Anthropol 131:498–510.
Shen WH, Wisniowski P, Denne SC, Boyle DW, Liechty EA. 2005. Anabolic effects of insulin and IGF-I in the ovine fetus are reduced by prolonged maternal fasting. Am J Physiol 288:E907–E913.
Sheriff MJ, Krebs CJ, Boonstra R. 2010. The ghosts of predators past: population cycles and the role of maternal programming under fluctuating predation risk. Ecology 91:2983–2994.
Smith AS, Birnie AK, French JA. 2010. Maternal androgen levels during pregnancy are associated with early-life growth in Geoffroy's marmosets, *Callithrix geoffroyi*. Gen Comp Endocrinol 166:307–313.
Wickings EJ, Dixson AF. 1992. Testicular function, secondary sexual development, and social status in male mandrills (*Mandrillus sphinx*). Physiol Behav 52:909–916.