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RESEARCH ARTICLE

Maternal Effects on Offspring Stress Physiology in Wild Chimpanzees

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Early life experiences are known to influence hypothalamic-pituitary-adrenal (HPA) axis development, which can impact health outcomes through the individual's ability to mount appropriate physiological reactions to stressors. In primates, these early experiences are most often mediated through the mother and can include the physiological environment experienced during gestation. Here, we investigate stress physiology of dependent offspring in wild chimpanzees for the first time and examine whether differences in maternal stress physiology are related to differences in offspring stress physiology. Specifically, we explore the relationship between maternal rank and maternal fecal glucocorticoid metabolite (FGM) concentration during pregnancy and early lactation (first 6 months post-partum) and examine whether differences based on maternal rank are associated with dependent offspring FGM concentrations. We found that low-ranking females exhibited significantly higher FGM concentrations during pregnancy than during the first 6 months of lactation. Furthermore, during pregnancy, low-ranking females experienced significantly higher FGM concentrations than high-ranking females. As for dependent offspring, we found that male offspring of low-ranking mothers experienced stronger decreases in FGM concentrations as they aged compared to males with high-ranking mothers or their dependent female counterparts. Together, these results suggest that maternal rank and FGM concentrations experienced during gestation are related to offspring stress physiology and that this relationship is particularly pronounced in males compared to females. Importantly, this study provides the first evidence for maternal effects on the development of offspring HPA function in wild chimpanzees, which likely relates to subsequent health and fitness outcomes. Am. J. Primatol. 80: e22525, 2018.

Key words: offspring stress; maternal effects; gestational programming; chimpanzees

INTRODUCTION

Numerous studies have investigated the relationship between stress physiology and health [reviewed in Sapolsky, 2005]. Stressors are unpredictable or unpleasant stimuli that elicit a complex response across various physiological systems [Romero et al., 2009], including the hypothalamic-pituitary-adrenal (HPA) axis. Seconds after a stressor activates the HPA axis, a class of steroid hormones known as glucocorticoids (GCs) are released. Briefly, GCs function by diverting energy towards behavioral or physiological coping mechanisms that facilitate a return to homeostasis and enhance immediate survival [Romero, 2004; Sapolsky, 1993; Sapolsky et al., 2000]. Thus, acute increases in GC levels are considered a healthy adaptation to unpredictable environmental stimuli; however, chronic exposure to stressors and the associated elevated GCs can have adverse psychological and physiological consequences, such as decreased cognitive abilities, decreased immune

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system function and cardiovascular health, and muscle wasting [Sapolsky, 2005; Tasker, 2006; Tamashiro et al., 2005]. Evidence suggests that HPA axis function and associated reactivity to stressors are programmed early in life [Meaney et al., 2007]. Given the relationship between GCs and health, it is important to understand what factors are associated with the development of the HPA axis.

Mothers can have a profound influence on the development of HPA axis function through behavioral as well as physiological investment [reviewed in Love et al., 2013]. Gestational programming is of particular interest since effects are mediated through maternal physiology, and numerous studies have demonstrated that in utero stress exposure can have profound and long-lasting consequences for offspring stress physiology. The effects of prenatal stress on HPA axis function are variable and depend upon the severity, timing during gestation, and sex of the offspring [reviewed in Glover et al., 2010; Meyer & Hamel, 2014]; however, most studies that have found a positive relationship between prenatal stress and offspring stress physiology report higher baselines GC levels and/or magnified or prolonged responses to acute stressors [e.g., Lesage et al., 2004; Weinstock 2001]. For example, rat pups born to mothers that were subjected to a prenatal restraint test had increased responsiveness of the HPA axis function to stress [Henry et al., 1994; Morley-Fletcher et al., 2003]. Notably, these studies in rats also suggest that the effects of in uterine GC exposure may vary by sex with males often being more affected and often exhibiting a "dysmasculinized" phenotype with behavior, physiology, and gene-expression that is more similar to females [reviewed in Bale, 2015; reviewed in Maccari, 2008]. Maternal stress levels have also been shown to affect offspring stress physiology in primates. Using rhesus macaques, Coe et al. [2003] exposed pregnant females to noise stress during early and late gestation. Both periods of exposure had similar effects, as offspring of exposed mothers were less exploratory and had elevated baseline plasma cortisol levels as well as greater physiological and behavioral reactivity to stressors.

In this study, we examine maternal effects on dependent offspring fecal glucocorticoid metabolite (FGM) concentrations in wild chimpanzees for the first time. Chimpanzees (*Pan troglodytes*) exhibit female-biased dispersal and live in societies with high fission–fusion dynamics [Aureli et al., 2008]. Subgroups (known as 'parties') frequently change in size and composition over the course of the day [Goodall, 1986; Nishida, 1968]. Adult social behavior varies dramatically by sex in the East African subspecies (*P.t. schweinfurthii*). Males are more gregarious then females, as they cooperate during hunts, territorial defense, and form coalitions against other males [Mitani, 2005]. Males also compete intensely for dominant positions in a linear dominance hierarchy where high rank correlates with mating success [Newton-Fisher et al., 2010; Wroblewski et al., 2009].

Compared to males, females are generally less aggressive and gregarious. Variation exists among East African populations [Langergraber et al., 2009; Wakefield, 2013], but females can spend up to 40–70% of their time alone with their dependent offspring [Murray et al., 2007; Gombe: Wrangham & Smuts, 1980; Williams et al., 2002]. Chimpanzee infants are born after an average gestational period of 226 days [Boehm & Pusey, 2013]. While it has been well documented that GC concentrations increase over pregnancy in the great apes [e.g., humans: Mastorakos & Ilias, 2003; chimpanzees and gorillas: Smith et al., 1999] and spike at parturition [bonobos: Behringer et al., 2009; chimpanzees: Murray et al., 2013], little is known about how pregnancy levels vary based on maternal characteristics. After birth, infants are in almost constant contact with their mothers for the first 4–6 months of life [Goodall, 1986; Lonsdorf et al., 2014a], which also corresponds to the period with the highest energetic burden [Emery et al., 2012]. Most offspring are weaned between 4 and 5 years of age [Clark, 1977; van Plooij & Plooij, 1987], but remain with their mother for several years thereafter, spending the majority of time in her company until adolescence begins around 8 years of age [Pusey, 1983].

Given the length of dependency in chimpanzees, there is considerable potential for maternal influence, both directly through nutrition during infancy and indirectly through continued association after weaning. Female dominance rank represents a likely correlate of maternal effects on offspring physiology and behavior. Previous work has demonstrated that rank is positively related to reproductive success [Jones et al., 2010; Pusey et al., 1997], which is generally attributed to better nutrition [Emery et al., 2007; Kahlenberg et al., 2008; Murray et al., 2006]; however, physiological stress levels may also be a critical correlate of the observed differences.

Studies on wild female chimpanzee physiological stress levels have demonstrated several socio-ecological correlates. In the most robust study to date, Emery et al. [2010] found that female urinary cortisol concentrations in the Kanyawara community (Kibale National Park, Uganda) were higher in recent immigrants and low ranking, lactating females. Additionally, the authors demonstrated a negative correlation between food abundance and urinary cortisol concentrations, and a positive correlation between community-wide female–female aggression rates and GC concentrations. It is interesting to note that these patterns are not consistent across chimpanzee populations. Markham et al. [2014] did not find any relationship between diet quality and GC concentrations among

lactating females at Gombe National Park (Tanzania), but did find a relationship involving party size, suggesting that female GC levels in that population are driven primarily by social stressors. Compared to high-ranking females, low-ranking females experienced higher GCs in larger groups and in groups containing more males. These two studies highlight important variation among study sites, but they also demonstrate a persistent theme that female chimpanzee stress physiology varies by dominance rank. It is important to note here that neither of those studies included pregnant females in their analyses.

Relatively little is known about stress physiology in dependent individuals in wild chimpanzees beyond patterns by age [captive: Anestis et al., 2006; wild: Seraphin et al., 2008]. In the captive setting, a series of studies has investigated the relationships between cortisol concentrations, dominance rank, and personality in non-adult chimpanzees [Anestis, 2005; Anestis et al., 2006]. No correlation between cortisol levels and dominance was found, but individuals that scored high on the 'smart' component had significantly higher cortisol levels than those who scored lower [Anestis, 2005]. While personality and temperament are intriguing correlates of GC levels, it is also important to consider maternal effects when possible given that the mother's physiology and behavior may alter the neuroendocrine axis and ultimately temperament [Hinde, 2013].

In this paper, we investigate maternal effects on offspring stress physiology among the Gombe chimpanzees, as measured by fecal glucocorticoid metabolites (FGM). While previous work in this population did not find a main rank effect on FGM concentrations among lactating females [Markham et al., 2014], differences may exist during pregnancy and the first 6 months of life for females in poorer body condition. Low-ranking adult females have smaller body masses, even when controlling for age, and some may have the additional burden of continued investment in their own somatic growth [Pusey et al., 2005]. We therefore predict that low-ranking mothers will have higher FGM concentrations during pregnancy and/or the first 6 months of lactation. We further predict that offspring of low-ranking mothers will differ in their GC physiology; we expect offspring of low-ranking mothers to have higher baseline FGM concentrations that could reflect prenatal or early life GC exposure, or post-natal differences in dietary quality since offspring likely have access to the same resource quality as mothers.

METHODS

Study Site

For this study, we collected data from wild chimpanzees in the Kasekela community at Gombe National Park, Tanzania. This community has been under continuous study since 1960 and all members of the community are well habituated with known maternal relationships. Our mixed cross-sectional/longitudinal study focused on a 4-year period (2009–2013) when we intensively collected physiological samples from all dependent offspring (those offspring that are still nutritionally and/or behaviorally dependent upon the mother, i.e., infants and juveniles). During this period, the study community contained between 58 and 65 individuals with 15–20 dependent offspring and 43–47 adolescents and adults (adolescents aged 8–12 years old; adults aged $\geq$12 years old).

Physiological Samples

We quantified physiological stress levels through non-invasively collected fecal samples. Samples were collected opportunistically as a part of a long-term project on maternal behavior and stress physiology. These data focus on family groups that include the mother, infant, and next oldest sibling. During the study period, researchers followed the same focal family two days in a row in order to pair behavioral data (see below for details) collected on day 1 with FGM concentrations from fecal samples collected on day 2 since previous work demonstrated that raised glucocorticoid metabolites manifest in feces 12–24 hr later [Murray et al., 2013]. Our goal was to follow each family once per month and collect at least one fecal sample from each family member each observation day. Thus, some samples were paired with behavioral data; however many additional female and offspring samples were collected opportunistically and do not correspond to behavioral data. After transport to the on-site laboratory (between 2 and 6 hr on average) we stored samples in a freezer until extraction. Our field extraction method circumvented many of the challenges of delaying extraction, difficulty exporting and shipping fecal samples, and inadvertently extracting hormones into a storage solution. Briefly, we weighed 0.50 g ($\pm$0.02 g) of wet feces and added 5.0 ml of 90% ethanol into 16 $\times$ 1000 mm test tubes. We hand-shook these tubes for 30 s, rotated them for 2 hr, and centrifuged them for 20 min at 1500 rpm. Two 1-ml aliquots of the supernatant were transferred to labeled 12 $\times$ 75 mm test tubes. Both were allowed to air-dry in a sealed Pelican case with desiccant. Once dry, the samples were capped and shipped to the Davee Center for Epidemiology and Endocrinology (Lincoln Park Zoo, Chicago, IL) for FGM analysis via a cortisol enzyme immunoassay, which has been previously validated for this species [Murray et al., 2013].

The cortisol enzyme immunoassay (EIA) method was previously described [Young et al., 2004]. C. Munro (University of California-Davis, CA) provided horseradish peroxidase (HRP) ligands and

polyclonal antiserum (R4866). Cortisol antiserum and HRP were used at dilutions of 1:8500 and 1:20000, respectively [Loeding et al., 2011]. Cross-reactivities of cortisol R4866 antibody are reported as: cortisol 100%, prednisone 6.3%, corticosterone 0.7%, 21- deoxycorticosterone 0.5%, progesterone 0.2%, pregnenolone 0.1%, androstenedione 0.1%, dehydroisoandrosterone-3-sulfate 0.1%, estradiol-17β 0.1%, estriol 0.1%, cholesterol 0.1%, prednisolone 9.9%, cortisone 5.0%, deoxycorticosterone 0.3%, 11- desoxycortisol 0.2%, 17α-hydroxyprogesterone 0.2%, 17α-hydroxypregnenolone 0.1%, testosterone 0.1%, dehydroepiandrosterone 0.1%, aldosterone 0.1%, estrone 0.1%, and spironolactone 0.1% [Young et al., 2004]. The EIA was biochemically validated for chimpanzees by demonstrating 1) parallelism between the binding inhibition curves of fecal extract dilutions and the cortisol standard ($R^2 = 0.969$), and 2) significant recovery (>90%) of exogenous cortisol added to fecal extracts ($y = 0.82x + 3.54$, $R^2 = 0.998$) [Murray et al., 2013]. All samples were run in duplicate. Assay sensitivity was 1.95 pg/well and intra- and inter-assay coefficients of variation were less than 10%.

Behavioral Data

During focal family follows, researchers recorded the activity (e.g., feeding, socializing, resting, traveling) of each focal subject (mother, infant, and next oldest sibling) at 1-min instantaneous point samples. Researchers also recorded behavioral events such as vocalizations *ad libitum* throughout the follow and conducted party composition scans at 5-min intervals until 2011 and 15-min intervals thereafter. The length of focal follows varied due to search times and losing sight of the focal individuals. We set a minimum threshold of 5 hr of day 1 behavioral data for inclusion in any analyses.

Predictors of FGM Concentrations

Female dominance ranks were calculated in collaboration with The Jane Goodall Institute Research Center at Duke University. We calculated adult female dominance ranks from pant grunts, which are submissive vocalizations that function as formal indicators of subordination [Bygott, 1979]. These pant grunts were consolidated in 2-year periods (2008–2009, 2010–2011, 2012–2013), and we calculated continuous dominance ranks based on the Modified David's Score (MDS) [de Vries et al., 2006]. Since only one study has reported that female hierarchies were significant linear [Tai National Forest: Boesch 2003], we followed Markham et al. [2014] to delineate categorical rank. High-ranking females were those that were half standard deviation above the mean MDS; other females were classified as low ranking. A binary rank distinction has been used in related publications [Jones et al., 2010; O'Malley et al., 2016]. Importantly, these rank categories predicted maternal FGM levels by party size and sex ratio in lactating females [Markham et al., 2014].

We determined the average adult party size and percent of fruit in diet for each dependent offspring in each day 1 follow paired with a day 2 fecal sample. Average adult party size was calculated as the average number of adult (≥12 years of age) individuals present in each party composition scan that was recorded over the course of the follow. Following the precedent of other studies [e.g., Wrangham, 2008; Markham et al., 2014] we measured diet quality as the percentage of fruit in the diet. Percentage of fruit in diet was calculated as the number of 1–min scans when the focal was eating fruit divided by the total number of minutes the focal was observed eating during the follow multiplied by 100.

Analyses

Unless otherwise specified, in all generalized linear mixed models (GLMMs) described below we controlled for known seasonal variation in FGM concentrations [Stanton et al., 2015] by transforming day of year into radians and including a set of two sine-plus-cosine functions with annual and semiannual periodicities as additional fixed effects [Stoffer, 2011]. Also, to control for possible diurnal variation in FGM concentrations, only samples collected before 12:00 hr (AM samples) were included in analyses with daily FGM concentration as the response variable. If two samples were collected on the same individual on the same morning those values were averaged. Individual ID was included as a random factor in all models to control for repeated and uneven sampling and mother ID was included in dependent offspring models to control for mothers contributing more than one offspring to the dataset. In all GLMMs the response variable, FGM concentrations, was log 10 transformed for normality and model assumptions were visually assessed using diagnostic residuals plots. All analyses were conducted in R (version 3.0.3, R Core Development Team 2014) using the lme4 [Bates et al., 2015] and lmerTest [Kuznetsova et al., 2015] packages for GLMMs.

To investigate how maternal FGM concentrations vary by reproductive status (pregnancy versus the first 6 months of lactation) and maternal rank, we first classified each maternal sample as having been collected during pregnancy or first 6 months of lactation. All females for whom samples were collected in both reproductive statuses were included in analyses ($N_{\text{females}} = 14$; $N_{\text{samples}} = 158$; Table I). Conception dates for each pregnancy were estimated by subtracting 226 days [Pusey, 2013] from the birth date of an infant and samples collected between

TABLE I. Number of Samples and Mean (SD) FGM Concentrations (ng/g Wet Feces) for Each Female by Reproductive State

Female ID	Reproductive state	Number of samples	Mean (SD)
BAH	Pregnancy	13	34.83 (36.18)
	First 6 mo lactation	9	24.25 (8.990)
DL	Pregnancy	5	62.16 (40.89)
	First 6 mo lactation	8	18.49 (4.801)
FN	Pregnancy	18	26.82 (18.82)
	First 6 mo lactation	14	12.78 (12.78)
GLD	Pregnancy	12	44.16 (38.48)
	First 6 mo lactation	17	21.17 (9.918)
GLI	Pregnancy	18	36.05 (28.87)
	First 6 mo lactation	18	23.80 (14.44)
GM	Pregnancy	7	17.24 (4.584)
	First 6 mo lactation	14	20.02 (9.777)
NUR	Pregnancy	2	13.35 (5.239)
	First 6 mo lactation	3	35.79 (10.76)
Totals	**Pregnancy**	**75**	**33.51 (16.62)**
	First 6 mo Lactation	**83**	**24.21 (5.726)**

conception and parturition were categorized as pregnant. We analyzed the first 6 months of lactation since during this period infants are most nutritionally dependent on mothers and mothers are still investing heavily in milk production [Emery et al., 2012]. Samples were further classified based on the mother's rank category on the day of collection. Samples were evenly distributed across high and low rank and first and second halves of pregnancy ($\chi_1^2 = 0.08, P = 0.773$). Few pregnant females FGM values had paired behavior so we could not test the behavioral correlates of their FGM concentrations in this study. Reproductive status, maternal rank, and the interaction of reproductive status and maternal rank were included as fixed effects in a GLMM with log 10 transformed daily maternal FGM concentration as the response variable.

To test predictors of dependent offspring FGM concentrations, we first used all daily FGM concentrations from dependent offspring regardless of whether there were paired behavioral data available ($N_{\text{offspring}} = 21$; $N_{\text{samples}} = 482$; Table II). In order to examine at what point during development (if any) maternal rank predicts offspring FGM concentrations, we fit two separate GLMMs that differed only in when maternal rank was assessed. Both models included offspring age, offspring sex, maternal rank, and the three-way interaction between offspring age, sex, and maternal rank as fixed effects. Maternal age on the day of collection, whether the dependent offspring was a firstborn (yes/no) were also included as fixed main effects. However, in the first model maternal rank was assigned based on the mother's rank category on the offspring's birth date, whereas in the second model maternal rank was assigned based on the mother's rank category on the day the fecal sample was collected ($N = 96$ samples for which the maternal rank at birth and maternal rank at collection were different). Maternal rank at time of collection may be different than that at birth of the offspring, as up to 8 years could have passed between birth and sampling. The two models, one including maternal rank at birth and one including maternal rank on date of collection, were compared using Akaike's Information Criterion adjusted for small sample size (AICc) [Anderson, 2002].

Using the subset of FGM concentrations for which paired day 1 behavioral data were available ($N_{\text{offspring}} = 13$; $N_{\text{samples}} = 120$; Table II), we investigated the relationship between two additional predictors that have been previously associated with cortisol concentrations in female chimpanzees: adult party size [Kasekela: Markham et al., 2014] and percent fruit in diet [Kanyawara: Emery et al., 2010]. To avoid overfitting the model, rather than fit a three-way interaction, we investigated predictors with this reduced dataset by fitting two separate GLMMs, one for males and one for females. Both models included log 10 transformed offspring daily FGM concentration as the response variable and daily average adult party size, percent of fruit in diet, and the interaction between offspring age and mother's rank at birth as fixed effects. Because density of sampling was much lower for paired samples than opportunistic samples above, in these models we controlled for seasonality by including a single sine-plus-cosine function set with annual periodicity.

Ethical Note

All data collection was non-invasive and observational in nature. Permission to conduct the research was granted by the appropriate governing authorities in Tanzania: The Tanzania Commission

TABLE II. Number of Samples, Age Range, and Mean (SD) Fgm Concentrations (ng/g Wet Feces) for Each Subadult Offspring

Subadult ID	Mother ID	Subadult sex	Firstborn	Mother's rank at birth	Number of samples	Number of paired samples	Age range (yr)	Mean (SD) FGM
BAS	BAH	F	N	Low	6	–	1.97–2.93	32.32 (27.64)
BRZ	BAH	M	Y	Low	10	–	3.65–4.91	29.12 (18.21)
DIA	DL	F	N	Low	27	6	4.10–7.81	23.74 (12.77)
DUK	DL	M	N	Low	3	–	1.29–2.38	44.88 (40.85)
ERI	EZA	M	Y	Low	32	10	1.96–5.90	31.48 (31.44)
FAD	FN	F	N	High	62	20	1.58–6.01	22.65 (12.18)
FAM	FN	F	N	High	51	2	5.11–7.96	23.63 (13.58)
FFT	FN	M	N	High	10	4	1.39–3.04	25.94 (10.27)
GGL	GA	M	N	Low	33	14	1.37–4.36	30.26 (22.10)
GIM	GM	M	N	High	29	4	5.48–7.92	47.43 (46.10)
GIZ	GM	M	N	High	31	11	0.87–4.25	31.42 (22.69)
GLA	GLD	F	Y	Low	9	–	0.69–2.09	43.95 (21.97)
GOS	GLI	F	N	Low	2	–	0.98–1.13	50.80 (42.02)
IPO	IMA	M	N	Low	6	2	2.64–4.50	30.40 (34.97)
KEA	KP	F	N	Low	3	–	4.67–7.54	27.04 (9.74)
MAM	MAK	F	Y	Low	16	–	5.82–7.67	21.59 (14.28)
NYO	NUR	M	Y	High	14	3	0.93–2.94	34.86 (26.75)
SAF	SA	F	N	Low	10	3	1.34–3.92	30.87 (15.21)
SIR	SI	M	N	Low	50	19	2.64–6.80	25.08 (21.35)
TAB	TG	F	N	Low	57	19	2.81–7.15	18.54 (12.02)
ZIN	TZ	M	N	High	21	3	3.80–6.28	29.41 (21.96)
Totals					**482**	**120**	**0.69–7.96**	**31.21 (8.782)**

of Science and Technology, The Tanzania Wildlife Research Institute, and Tanzania National Parks. This research also adheres to the Ethical Treatment of Nonhuman Primates policy of the American Society of Primatologists and the Lincoln Park Zoo's research guidelines.

RESULTS

Maternal FGM Levels by Reproductive Status and Rank

We found that maternal FGM concentrations were a function of both rank and reproductive status ($F_{1,493} = 5.611$, $P = 0.015$, Table III). Specifically, we found that low-ranking females had significantly higher mean FGM concentrations during pregnancy compared to their first 6 months of lactation and that low-ranking pregnant females had higher mean FGM concentrations than high-ranking pregnant females (Fig. 1).

Maternal Effects on Dependent Offspring FGM Levels

The model including maternal rank at offspring birth was a better fit than the model including maternal rank on day of sample collection (Table IV). Here we present the results for the model including maternal rank at birth and include the results for maternal rank on day of sample collection as supporting information (Table S1).

Most interestingly, we found that dependent FGM concentrations were significantly predicted by the three-way interaction between maternal rank at

TABLE III. Results of GLMM Examining Predictors of Maternal FGM Concentrations

Fixed effect	Estimate	se	Numerator df	Denominator df	*F*	*P*
Reproductive status[a]	−0.012	0.077	1	150	4.005	
Rank[b]	0.195	0.058	1	150	5.665	
Sine (annual)	−0.015	0.038	1	150	0.154	0.695
Cosine (annual)	0.058	0.031	1	150	3.604	0.059
Sine (semiannual)	0.086	0.028	1	150	9.256	0.003
Cosine (semiannual)	−0.006	0.028	1	150	0.052	0.820
Reproductive status* rank	−0.201	0.081	1	150	6.111	0.015

[a]First 6 mo lactation is the reference category.
[b]High is the reference category.

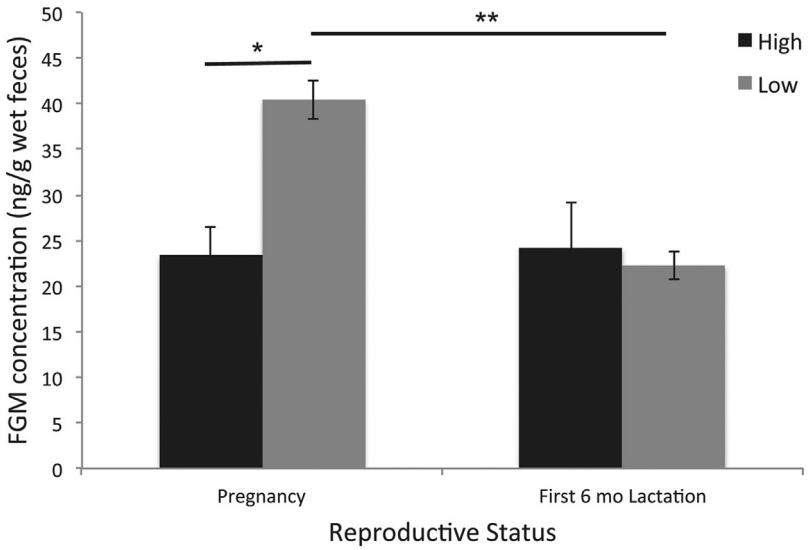

Fig. 1. Mean ± SE maternal fecal glucocorticoid metabolite (FGM) concentrations by reproductive status and rank ($N_{\text{low-ranking females}} = 8$; $N_{\text{high-ranking females}} = 6$). Significant differences are indicated based on Tukey post hoc tests. $^{*}P < 0.05$; $^{**}P < 0.005$.

birth, offspring age, and offspring sex ($F_{1,32.81} = 9.28$, $P = 0.005$) (Table V; Fig. 2). That is, for male offspring of low ranking females, FGM concentrations decreased with age, while FGM concentrations of female offspring were relatively stable. For male offspring of high-ranking females, FGM concentrations of males decreased slightly with age, while those of their female peers remained relative stable (Fig. 2). Additionally, there was a tendency for firstborn offspring to have higher FGM concentrations than laterborn offspring ($F_{1,21.04} = 4.03$, $P = 0.058$), while maternal age was not a significant predictor of offspring FGM concentrations ($F_{1,13.54} = 2.26$, $P = 0.155$).

TABLE IV. Comparison of GLMMs Including Maternal Rank at Birth of Offspring Versus Maternal Rank on Day of Sample Collection

Model	Log likelihood	AICc	Δ AICc	AICc weight
Maternal rank birth	10.70	13.9	0.00	0.999
Maternal eank sample day	3.752	27.8	13.89	0.001

TABLE V. Results of GLMM on Full Physiological Dataset Examining Predictors of Dependent Offspring FGM Concentrations Including Mother's Rank at Birth

Fixed effect	Estimate	se	Numerator df	Denominator df	*F*	*P*
Maternal rank birth[a]	0.113	0.098	1	40.88	10.82	
Offspring age	−0.018	0.014	1	31.85	24.69	
Sex[b]	−0.036	0.096	1	25.59	2.04	
Firstborn[c]	0.010	0.048	1	21.04	4.03	0.058
Mother age	0.005	0.003	1	13.54	2.26	0.155
Sine (annual)	0.075	0.016	1	479.22	22.88	<0.001
Cosine (annual)	0.051	0.016	1	474.02	10.36	0.001
Sine (semiannual)	0.040	0.015	1	472.34	6.76	0.010
Cosine (semiannual)	−0.042	0.016	1	477.42	7.12	0.008
Maternal rank birth* offspring age	−0.022	0.018	1	49.76	20.84	
Maternal rank birth* sex	0.263	0.134	1	23.96	3.88	
Offspring age sex*	0.024	0.018	1	43.81	1.63	
Maternal rank birth*Offspring age* sex	−0.084	0.028	1	32.81	9.28	0.005

[a]High rank is the reference category.
[b]Female is the reference category.
[c]Laterborn is the reference category.

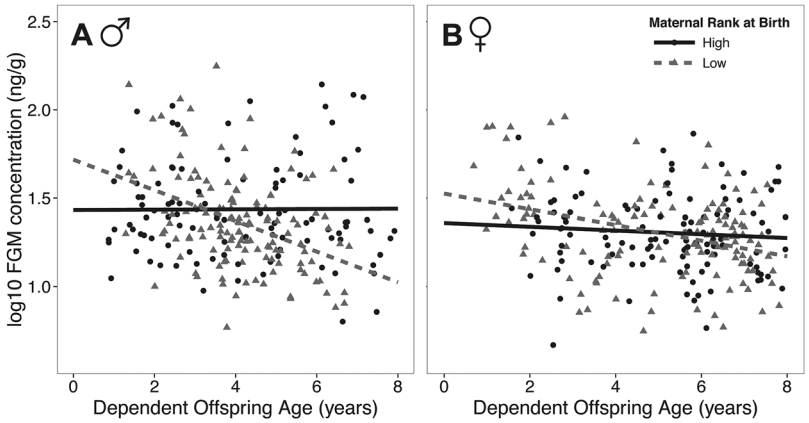

Fig. 2. Relationship between dependent offspring age and log 10 transformed fecal glucocorticoid metabolite (FGM) concentrations by maternal rank at birth for **A**) male dependents ($N_{\text{high-ranking}} = 5$; $N_{\text{low-ranking}} = 6$) and **B**) female dependents ($N_{\text{high-ranking}} = 2$; $N_{\text{low-ranking}} = 8$).

As expected based on the results of analyses on the full dependent offspring dataset, when we analyzed the subset of paired samples we found a significant interaction between maternal rank at birth and offspring age for males ($F_{1,70} = 4.733$, $P = 0.033$), but not for females ($F_{1,49} = 1.228$, $P = 0.273$), with FGM concentrations of low ranking male offspring decreasing with increasing offspring age (Table VI). Maternal age was also not a significant predictor of offspring FGM concentrations for either sex (male: $F_{1,70} = 0.92$, $P = 0.763$; female: $F_{1,49} = 3.591$, $P = 0.064$). Additionally, percentage of fruit in diet was not a significant predictor of either male or female offspring FGM concentrations (male: $F_{1,70} = 0.311$, $P = 0.579$; female: $F_{1,49} = 1.800$, $P = 0.186$). Finally, average daily adult party size was a significant predictor of male ($F_{1,70} = 6.227$, $P = 0.015$; Fig. 3), but not female ($F_{1,49} = 0.608$, $P = 0.439$; Fig. 3) offspring FGM concentrations, with male FGM concentrations increasing with increasing average daily adult party size.

DISCUSSION

In this study, we found that low-ranking females experienced significantly higher FGM concentrations during pregnancy than they did during the first 6 months of lactation. Pregnant low-ranking

TABLE VI. Results of GLMM Examining Predictors of Dependent FGM Concentrations Using Subset of Samples Paired With Behavioral Data

Fixed effect	Estimate	se	Numerator df	Denominator df	*F*	*P*
Males						
Maternal rank birth[a]	0.410	0.215	1	70	3.630	
Offspring age	−0.015	0.031	1	70	7.579	
Average party size	0.015	0.006	1	70	6.227	0.015
Percent fruit	0.080	0.144	1	70	0.311	0.579
Firstborn[b]	0.047	0.098	1	70	0.227	0.635
Mother age	0.002	0.005	1	70	0.092	0.763
Sine (annual)	0.101	0.042	1	70	5.716	0.020
Cosine (annual)	−0.103	0.055	1	70	3.470	0.067
Maternal rank birth* offspring age	−0.111	0.049	1	70	4.733	0.033
Females[c]						
Maternal rank birth a	0.753	0.424	1	49	3.158	0.082
Offspring age	−0.083	0.037	1	49	9.815	0.003
Average party size	0.004	0.005	1	49	0.608	0.439
Percent fruit	0.218	0.163	1	49	1.800	0.186
Mother age	0.063	0.033	1	49	3.591	0.064
Sine (annual)	0.067	0.041	1	49	2.629	<0.001
Cosine (annual)	−0.044	0.057	1	49	0.583	0.449
Maternal rank birth* offspring age	−0.049	0.044	1	49	1.228	0.273

[a]High rank is the reference category.
[b]Laterborn is the reference category.
[c]No female firstborns had paired samples.

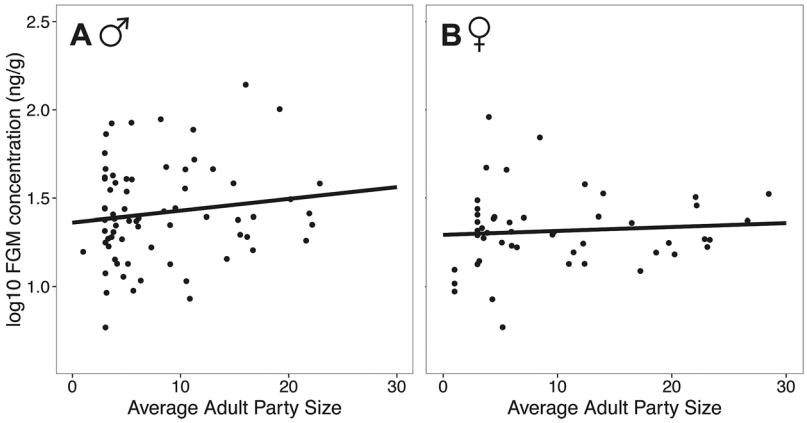

Fig. 3. Relationship between average adult party size and log 10 transformed fecal glucocorticoid metabolite (FGM) concentrations for **A**) male dependents ($N = 9$) and **B**) female dependents ($N = 5$).

females also experienced significantly higher FGM concentrations than their pregnant high-ranking counterparts. Subsequently, male offspring born to low-ranking mothers experienced stronger decreases in FGM concentrations as they aged than either males born to high-ranking mothers or female offspring. Taken together, these results suggest that maternal rank and prenatal GC levels differentially influence male and female offspring stress physiology, and opens up new avenues for research that relate GC profiles to health and fitness outcomes directly.

Generally, FGM concentrations among lactating females in Gombe do not seem to be driven by diet quality [this study; Markham et al., 2014]. However, this relationship may be different for low-ranking females in a more marginal body condition during pregnancy, given their lower diet quality and that many are still investing in somatic growth. Previous studies have indeed demonstrated dietary shifts during pregnancy that suggest pregnant females are more nutritionally-limited than in other reproductive states. For example, Murray et al. [2009] found that the percentage of fruit in the diet increases during pregnancy. Interestingly, O'Malley et al. [2016] also found that low-ranking pregnant females increase meat consumption. This shift may reflect greater nutritional needs for low-ranking females during gestation. An alternate hypothesis for the observed FGM concentrations is that low-ranking pregnant females are more gregarious during their pregnancy for other reasons (e.g., the need to reinforce community membership given infanticide risks) and therefore experience more social stress. Given the evidence for the lasting influence on offspring stress physiology, future studies should explicitly investigate what factors drive the elevated FGM concentrations in low-ranking pregnant females.

Interestingly, FGM concentrations of male offspring of low-ranking mothers decreased more with age than any other rank by sex combination. This relationship may be a result of the down-regulation of the HPA axis for male offspring of low-ranking mothers; the observed sex bias is consistent with numerous other studies reporting that males are more susceptible to prenatal stress effects on HPA axis programming [reviewed in Bale, 2015]. It is important to note here that we observed the same patterns in two different analyses; one analysis did not control for potential confounds (diet quality and party size) to maximize our sample size, but a second analysis on a subset of samples for which paired behavioral data was available did include these covariates. These controls ensured that our results reflected baseline GC differences, independent of likely socio-ecological drivers.

Our results reveal interesting sex differences between subadult FGM concentrations and party size; FGM concentrations for subadult males increases with party size, whereas there is no such relationship for subadult females. We suggest that male offspring may experience increased interaction-related stressors than female offspring given that they interact more with conspecifics and particularly adult males [Lonsdorf et al., 2014b; Murray et al., 2014]. The lack of relationship in subadult females also stands in juxtaposition to that observed in low-ranking lactating females at Gombe, who show a positive relationship between party size and FGM concentrations [Markham et al., 2014]. That study suggested that the risk of aggression is an important driver of female psychosocial stress, a result that was echoed by a positive correlation between female–female aggression rates and the average monthly urinary cortisol concentrations at Kanyawara [Emery et al., 2010; Markham et al., 2014]. Female subadults are much less likely to be aggressed upon than adult females and are also less likely to engage in peer aggression than males [Markham et al., 2015], so this particular form of psychosocial stressor may not be relevant until adulthood.

The unexpected direction of the relationship between maternal rank and basal GC levels for male offspring raises interesting questions. We suggest that prenatal programming may mirror the complex relationship found for early life exposure to stressors [as reviewed in Maestripieri, 2011]. Extreme stressors, such as abuse, neglect, and parental loss, are associated with deleterious outcomes that include decreased cognitive function, enhanced anxiety, and alterations to the HPA axis both in terms of higher baseline levels and greater reactivity [non-human primates: Heim et al., 2008; Lupien et al., 2009; Maestripieri et al., 2005; humans: Repetti et al., 2002; Suomi, 1997; Sanchez et al., 1998]. However, evidence is mounting for a non-linear (*U*-shaped) relationship between exposure to early life stressors and offspring stress physiology, which highlights potential benefits associated with repeated exposure to mild stressors early in life and supports for the stress inoculation hypothesis [e.g, Brockhurst et al., 2015; Edge et al., 2009; Hamel, 2014; Parker et al., 2005, 2006; Seery, 2011].

Although our results suggest that prenatal GC exposure is related to subsequent offspring stress physiology, possibly through the down-regulation of the HPA axis for male offspring, it is possible that post-natal differences in maternal behavior may also influence the offspring's developing HPA axis. Work in rodent models has demonstrated that perinatal maternal behavior can have long-lasting consequences; a series of studies in rats found that maternal licking-grooming behavior affects HPA-associated gene expression by the sixth day of life [Francis et al 1999; Liu et al 1997; Weaver et al., 2004]. Our data lacks the resolution to test such a relationship but it is possible that low-ranking mothers behave differently with their newborn sons in a manner that could influence HPA programming.

This study contributes to a growing body of literature on how maternal stress physiology impacts the development of HPA axis function in offspring. While carefully controlled research in captive or sanctuary settings has begun to unravel maternal effects on offspring stress physiology in primates [e.g., Coe et al., 2003; McCormack et al., 2009], much less is known about this process in wild populations or among chimpanzees. Future work will examine how the observed decrease in basal GC concentrations in offspring of low-ranking females relates to male social behavior, health, and fitness.

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