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Age at Reproductive Debut: Developmental Predictors and Consequences for Lactation, Infant Mass, and Subsequent Reproduction in Rhesus Macaques (*Macaca mulatta*)

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Abstract

Objectives—The age at which females initiate their reproductive career is a critical life-history parameter with potential consequences on their residual reproductive value and lifetime fitness. The age at reproductive debut may be intimately tied to the somatic capacity of the mother to rear her young, but relatively little is known about the influence of age of first birth on milk synthesis within a broader framework of reproductive scheduling, infant outcomes, and other life-history tradeoffs.

Material and Methods—Our study investigated the predictors of age at first reproduction among 108 captive rhesus macaque (*Macaca mulatta*) females, and associations with their milk synthesis at peak lactation, infant mass and ability to subsequently conceive and reproduce.

Results—The majority of females reproduced in their fourth year (typical breeders); far fewer initiated their reproductive career one year earlier or one year later (respectively early and late breeders). Early breeders (3-year-old) benefited from highly favorable early life development (better juvenile growth, high dominance rank) to accelerate reproduction, but were impaired in milk synthesis due to lower somatic resources and their own continued growth. Comparatively, late breeders suffered from poor developmental conditions, only partially compensated by their delayed reproduction, and evinced compromised milk synthesis. Typical breeders not only produced higher available milk energy but also had best reproductive performance during the breeding and birth seasons following primiparity.

Discussion—Here we refine and extend our understanding of how life-history tradeoffs manifest in the magnitude, sources, and consequences of variation in age of reproductive debut. These findings provide insight into primate reproductive flexibility in light of constraints and opportunities.

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Keywords

Milk; Life-History Tradeoffs; Inter-Birth Interval; Infant Development; Maternal Condition

Age of first reproduction is a critical life-history parameter because the timing of reproductive debut, and embedded tradeoffs, potentially impact an organism's residual reproductive value and lifetime success (Bercovitch and Berard 1993; Blomquist, 2013; Williams 1966; Altmann 1986). Life history theory provides a framework for understanding the tradeoffs within the context of maternal behavioral biology and the allocation of resources among maternal condition, current reproduction, and transitions to future reproduction (Clutton-Brock, 1984; Pianka and Parker, 1975; Stearns 1989; Emery Thompson 2016; McNamara and Houston, 1996). As mammalian females typically provide the behavioral care and physiological investment that shape offspring development, the age of “reproductive debut” (Wallin et al., 1983; Engstrom 1978; Vigil and Geary 2006) is intimately tied to the somatic capacity of the mother to rear her young (Altmann 1986). Typically younger and smaller than their multiparous counterparts, primiparous mothers have fewer embodied resources to allocate to more biological imperatives—maintenance, development, and reproduction— while rearing proportionately larger offspring (Hinde, 2009; Nuñez et al., 2015; Lu et al., 2016). Reproductive debut during somatic growth, termed adolescent pregnancy, brings these tradeoffs into particularly stark contrast, as mothers apportion investment between their own continued development and toward supporting the development of their offspring (Nuñez et al. 2015; Altmann 1986). Given these constraints, primiparity has been associated with higher mortality, greater morbidity, and slower growth for the offspring (see Nowak et al., 2000; guinea pig, *Cavia porcellus*: Künkele 2000; bighorn ewe, *Ovis canadensis* Festa-Bianchet et al., 1995; mountain gorillas, *Gorilla beringei*: Robbins et al. 2006; baboon, *Papio spp.* Smuts and Nicolson, 1989; rhesus macaque, *Macaca mulatta*: Mas Rivera & Bercovitch 2008; but see Nuñez et al., 2015). Poorer offspring outcomes of primiparous mothers can be due to the lack of maternal behavioral experience or reduced efficiency (rhesus macaque: Bercovitch et al., 2000; sheep, *Ovis aries*: Dwyer, 2008; rat, *Rattus norvegicus*: Künkele and Kenagy, 1997; mouse, *Mus musculus*: Lopatina et al., 2011) and/or limited somatic reserves and physiological ability to sustain gestation and lactation (African elephant, *Loxodonta africana*, Moss, 2001; human, *Homo sapiens*: Fraser et al., 1995; Friede et al., 1987). Offspring of immature mothers are more likely to experience intrauterine growth restriction, low birth mass, and pre-term birth resulting in lower birth mass (humans: United States and Canada: Kramer et al., 2000; United States: Akinbami et al., 2000; Utah: Fraser et al., 1995; Gambia: Allal et al., 2004; Pumé: Kramer, 2008 and see King, 2003; Scholl et al., 1994), a primary cause for neonatal mortality (humans, Pumé, Kramer, 2008; sheep, Dwyer, 2008).

Females may be accelerated or delayed in their reproductive debut relative to other females within their population (e.g. chimpanzee, *Pan troglodytes*, Emery Thompson et al., 2016; humans: Nettle et al., 2011). Early reproductive debut may increase lifetime reproductive success by lengthening females' reproductive career (Descamps et al., 2006; Kaar et al., 1996) but may also compromise their own development, condition, and long-term survival (Blomquist, 2013). Widely among mammals, young primiparity is associated with reduced

long-term survival (orangutan, *Pongo spp.*: Cocks, 2007; rhesus macaque, Blomquist, 2013; horseshoe bat, *Rhinolophus ferrumequinum*: Ransome, 1995; red deer, *Cervus elaphus*: Clutton-Brock et al., 1983; Antarctic fur seal, *Arctocephalus gazella*: Lunn et al., 1994; northern elephant seal, *Mirounga angustirostris*: Reiter and Boeuf, 1991). However, early reproductive onset had no reported influence on lifespan in other species within many of these same orders (bighorn ewe: Festa-Bianchet et al., 1995; Columbian ground squirrels, *Spermophilus columianus*: Neuhaus et al., 2004; southern elephant seals, *Mirounga leonina*: Pistorius et al., 2004). Among humans, adolescent motherhood has been identified as a critical global health concern because of the higher risks of complications during pregnancy and parturition, higher maternal and infant mortality and small neonatal size (Conde-Agudelo et al., 2005; Fullerton et al., 1997; World Health Organization, 2011). Young primiparity also negatively influenced subsequent reproduction through reduced fertility on the season following first birth and/or longer inter-birth interval in bison (*Bison bison*: Green and Rothstein, 1991), rhesus macaque (Wilson et al., 1983) and bonnet macaque (*Macaca radiata*: Small and Rodman, 1980). Although young primiparity did not extend inter-birth interval in mountain gorillas (*Gorilla beringei*: Robbins et al., 2006). Notably, our understanding of delayed reproductive debut is substantially obscured within the literature as nearly all empirical investigations evaluate the causes and consequences of early debut, binning typical and late debut together.

Several environmental and individual factors influence the timing of reproductive debut. Faster mass gain during early development is associated with earlier sexual maturation (rhesus macaque: Zehr et al., 2005; baboon: Altmann and Alberts, 2004; human, UK: Ong et al., 2009; pig, *Sus scrofa*: Tummaruk et al., 2009; elephant, Lee et al., 2013) and faster onset of reproduction (rhesus macaque: Bercovitch et al., 1998; bison: Green and Rothstein, 1991; bighorn ewe: Jorgenson et al., 1993). Greater resource availability also accelerates reproductive debut (Japanese macaque, *Macaca fuscata*: Kurita et al., 2008; baboon: Strum and Western, 1982). Higher social rank is also associated with younger age of reproductive maturity, likely through improved access to resources and buffering from socially-induced endocrine perturbation (rhesus macaque: Bercovitch and Berard, 1993; Wilson et al., 1983; Zehr et al., 2005; baboon: Bercovitch and Strum, 1993; Charpentier et al., 2008; Barbary macaque, *Macaca sylvanus*: Kuester and Paul, 1988; Paul and Thommen, 1984; long-tailed macaque, *Macaca fascicularis*: van Noordwijk and van Schaik, 2007, 1999; mandrill, *Mandrillus sphinx*: Setchell et al., 2002; Setchell and Wickings, 2004). The importance of somatic condition and access to resources is further substantiated by the positive correlation between population density and age of reproductive debut (rhesus macaque: Bercovitch and Berard, 1993; long-tailed macaque: van Noordwijk and van Schaik, 1999; Japanese macaque: Watanabe et al., 1992; and see Gaillard et al., 1998).

Reproductive timing is also particularly important in the context of seasonal reproduction because “missed” breeding opportunities one season substantially delay reproduction until the subsequent breeding season. Unlike species characterized by continuous receptivity (e.g. baboon: Beehner et al., 2006; Wasser, 1996) and/or giving birth to multiple offspring (e.g. marmosets, Callitrichidae: Rutherford and Tardif, 2009; Tardif et al., 2001), species with annual breeding seasons of singleton offspring can not flexibly compensate for suboptimal conditions by manipulating birth timing or litter size. For long-lived species with seasonal

reproduction, and therefore time-limited birth season, the timing of a females' own birth within the season can potentially influence the timing of her own reproductive debut years later. The extension of the period of growth, by several months, afforded by an early birth helps females attain conceptive thresholds one season earlier than females born late during the birth season (Neuhaus et al., 2004). Parturition timing within the season is additionally related to age of reproductive debut: young primiparous mothers who conceive later during the breeding season benefit from several additional months of growth critical for their ability to sustain pregnancy and lactation (Antarctic fur seal: Lunn et al., 1994; bonnet macaque: Silk, 1989; rhesus macaque: Wilson et al., 1983). In turn, birth timing within the season is likely to influence infant survival in relation to resources available for weaning transitions and social competition (lion-tailed macaque, *Macaca silenus*: Clarke et al., 1992; gray mouse lemur, *Microcebus murinus*: Radespiel and Zimmermann, 2001; bonnet macaque: Silk, 1989; red-bellied lemur, *Eulemur rubriventer*: Tecot, 2010; or see Nuñez et al., 2015). Among captive rhesus macaques, Small and Smith (1986) reported no influence of birth timing on survival but found that late birth is associated with both a larger infant and slower growth. Finally, birth timing also has consequences on females' reproductive success during the following season. Females who deliver late in the season may be handicapped in their ability to conceive due to the short horizon to the subsequent breeding season coinciding with peak lactation (Drickamer, 1974).

Lactation, in part, underlies the above relationships among maternal condition, infant outcomes, and transitions to subsequent reproduction. Among mammals, the physiological synthesis of milk is the most energetically costly maternal activity (Clutton-Brock et al., 1989; Gerhart et al., 1997; Gittleman and Thompson, 1988). Females mobilize somatic resources to support offspring growth and biobehavioral development for extended periods among primates (Hinde and Capitanio, 2010; Hinde et al. 2015). Body condition (human: Dewey et al., 1994; Quinn et al., 2016; rhesus macaque: Hinde, 2007a; baboon: Roberts et al., 1985; marmoset: Tardif et al., 2001), parasite load (rhesus macaque: Hinde, 2007a), and nutritional intake (baboon: Roberts et al., 1985) have all been implicated in the capacity to synthesize milk in terms of quantity (volume/yield), quality (energetic density), or both (Hinde and Milligan 2011). Primiparous mothers produce lower yields of milk than do multiparous mothers (Doreau et al., 1991; Miller et al., 2006), even controlling for body size (Hinde et al., 2009). Additionally, composition of milk produced by primiparous mothers can differ nutritional content (Doreau et al., 1991) and hormonal concentrations (human: Breakey, 2015; rhesus macaque: Hinde et al., 2015; Bernstein and Hinde 2016), but not always (dairy cow, *Bos taurus*: Fukasawa et al., 2008; rhesus macaque: Hinde et al., 2015, 2013, 2009). The effects of parturition timing on milk synthesis are less understood and have been evaluated pooling primiparous and multiparous mothers. Among Iberian red deer, dams produced less milk the later they calved during the birth season (Landete-Castillejos et al., 2001), but among rhesus macaques, parturition timing within the birth season was not associated with milk synthesis (Hinde et al., 2009).

Milk is instrumental for infants to survive and thrive, influencing health and growth (e.g. rat: Prado et al., 1997; red deer: Landete-Castillejos et al., 2001; rhesus macaque: Hinde et al., 2009; reviewed in Hinde, 2013), and neurobehavioral development (rat: Catalani et al., 2011; Liu et al., 2014; rhesus macaque: Dettmer et al., 2017; reviewed in Dettmer, et al.

2014). To date, how the age of reproductive debut influences lactational performance remains largely unexplored. Among dairy cows, experimental manipulations for early reproduction compromised milk yield and composition and reduced health (Ettema and Santos, 2004). Adolescent girls (15-17.5 years old) produce less milk than do adults (Motil et al. 1997), but that study included both primiparous and multiparous mothers. Somatic reserves are likely to vary as a function of age at first birth, because primiparous females support the substantial costs of pregnancy and lactation mostly through the reserves accumulated during juvenility. Consequently, females initiating reproduction when older may benefit from a protracted period of growth and greater accumulation of somatic resources (Allal et al., 2004). Primate females may have been shaped by natural selection to initiate reproduction upon attaining a threshold condition to sustain pregnancy and lactation such that milk production is fairly standardized among primiparous females, independently of age. Similarly, morphological and functional development of the mammary gland, contingent on the hormonal milieu from earlier life stages and pregnancy may precipitate similar milk production among primiparous mothers. Alternatively, the different tradeoffs at different ages, conditions, and timings of reproductive debut may influence substantial variation in milk yield or composition even among females typically grouped collectively. To date, the influence of age at first birth on milk production and composition has not been investigated from an evolutionary perspective. As such, lactation appears to be a critical missing piece to fully understand flexibility of reproductive tactics and associated consequences among mammals.

The present retrospective study investigated parameters implicated in the age at successful reproductive debut (Vigil and Geary 2006, Engstrom 1978), and the impact on maternal investment, infant outcomes, and subsequent reproduction among captive rhesus macaques. Investigations of primate behavioral ecology, physiology, and reproduction are relevant for life-history insights and biomedical translation (e.g. Amato, 2016; Kinnally, 2014; Hopper et al., 2008), by identifying reproductive mechanisms which are, otherwise, particularly difficult to isolate from socioeconomic and cultural factors in human studies (Phillips et al., 2014; Strier, 1994; Emery Thompson, 2013). Rhesus macaques live in multi-male, multi-female social groups and are typical Old World cercopithecines characterized by male dispersal, female philopatry, and matrilineal dominance hierarchies (Beisner and Isbell, 2011; de Waal and Luttrell, 1985). Dominance interactions among rhesus macaques are highly asymmetrical, leading to relatively frequent despotic, nepotistic, and aggressive social interactions (Beisner and Isbell, 2011; Thierry, 2004; Silk 2002). Rhesus macaques are distributed widely in temperate to subtropical zones through much of South Asia (Timmins et al. 2008). Wild-living, provisioned, and captive rhesus macaques have a 3 month periodicity of breeding annually (Mehlman et al., 1997; Altmann 1962) and females typically produce a single infant during a birth season, after 165 days of gestation (Silk et al., 1995; Conaway and Koford, 1965; Vandenbergh and Vessey, 1968). Lactation lasts ~9-12 months (Austin et al. 2013) with a peak lactation occurring typically from 3-4 months of infant age (Oftedal 1984, Hinde et al., 2009, Bernstein and Hinde, 2016). Females either reproduce routinely on the subsequent year or have a two-year inter-birth interval (Gomendio, 1990). Among captive and provisioned free-ranging rhesus populations, females

typically produce their first offspring during the birth seasons of their 3rd to 5th years of age (Bercovitch and Berard, 1993; Wilson et al., 1983).

Based on published reports, we expected the proportional representation of females successfully giving birth to their first infant at 3, 4 and 5 years old to be ~10%, ~80% and ~10% of the population, referred to as early, typical, and late breeders respectively (Wilson et al., 1983). These subjects provide the opportunity to investigate hypotheses and predictions about the flexibility of reproductive tactics in relation to developmental and contemporary constraints (Table 1). We predicted that better circumstances and conditions during development—born early, higher rank, and better growth—would afford females the opportunity for earlier reproductive debut. In contrast, females experiencing substantial constraint during early life—born late, lower rank, and slower growth would have later age of reproductive debut. Since early breeders are expected to be more energetically constrained due to lower bodily resources and likely face greater tradeoffs between development and reproduction, we predicted that milk composition and/or yield would be lower than milk synthesized by typical breeders and late breeders. Alternatively, if there are no differences in milk synthesis among age groups, we can infer that functional development of the mammary gland on the first reproductive effort is constrained independently of maternal somatic resources. Given the influence of maternal somatic condition and milk energetics on infant development, we predicted that infants of early breeders would have lower mass at peak lactation compared to the infants of typical and late breeders. We further predicted typical breeders and late breeders to be more likely to reproduce the subsequent year compared to early breeders (Table 1).

Methods

Subjects

To investigate causes and consequences of age at successful reproductive debut, we studied $N=108$ primiparous mothers and their infants at the California National Primate Research Center (CNPRC). In this retrospective study, data from primiparous females were analyzed whose milk had been collected at peak lactation during systematic sampling in the Comparative Lactation Lab at the CNPRC from 2005-2012 (2005: $N=21$; 2006: $N=12$; 2007: $N=7$; 2010: $N=32$; 2011: $N=8$; 2012: $N=28$). Given the aims of the larger lactation study, the subjects included here had successfully carried to term and supported their infant through the neonatal period. Subjects lived in the long-term, outdoor, conventional breeding colony at the CNPRC. Mother-infant dyads were members of large social groups containing multiple adult females, adult males, juveniles, and infants, constituted of ~50 to ~150 animals with different degrees of kinship from closely related to non-kin in a social structure similar to that found among wild-living rhesus groups (Beisner and Isbell, 2008; Weinstein and Capitano, 2008). Each outdoor corral (0.2ha) included multiple climbing structures and food distribution stations. Subjects were fed a commercial diet of Purina Monkey Chow twice daily and supplemented bi-weekly with fresh fruits and vegetables.

Maternal and Infant Characteristics

Archival animal records maintained by the CNPRC provided key demographic and morphometric information for all subjects. From early life, animals were weighed every 3-4 months during routine physical exams. Longitudinal measures of body mass (kg) during infancy and juvenility were obtained from archival records at ~120 days, ~1year, and ~2 years for all mothers in the study. Female reproductive information included pregnancy information derived from manual palpation of the uterus and conception age estimated by Primate Medicine staff. Reproductive histories indicated none of the females had previously conceived, and therefore were both primiparous and primigravid, but some early, unrecognized pregnancy loss may have occurred. Of the 108 subjects, N=80 remained in the breeding colony for evaluation of subsequent reproduction in the breeding season and birth season immediately following their debut parity. Twenty-eight animals were relocated due to colony management or experimental assignment. The social rank of these females were determined by the behavioral management team at the CNPRC using standardized observation of social interactions and linear hierarchy analyses described elsewhere (McCowan et al., 2008). Females' individual ranks were tertile binned into “high”, “middle,” or “low” as a function of number of adolescent and adult females within the social group, unless this tertile split separated a female from the majority of her matriline. In such an event, a female was binned with the majority of her matriline (Hinde et al., 2009).

Milk Collection and Analysis

Milk Collection—Milk samples were collected following standard methods for non-human primates (Hinde et al., 2009; Hinde and Capitanio, 2010). When infants were 3-4 months of age (mean \pm SD = 111.1 \pm 9.6 days), mothers and infants were temporarily removed from the social group for maternal and infant morphometrics and milk collection. These procedures were conducted in conjunction with biobehavioral assessment (Hinde and Capitanio, 2010) during the period of peak lactation (Ofstedal, 1984; Riek, 2008). Mother and infant were captured in their home corral between 0745 and 0900 and relocated to temporary indoor housing for milk collection procedures. Following mother-infant separation, milk accumulated for 3.5-4 hours (mean \pm SD = 221.8 \pm 11.7 min). Midday after the milk accumulation period, mothers were sedated with ketamine hydrochloride (5 – 10 mg/kg, IM), chest & nipple areas were swabbed with alcohol-soaked gauze, and chest hair was trimmed. Once positioned sitting up, mothers were administered exogenous oxytocin (2 IU/Kg, 0.1 mL/kg, IM) to physiologically elicit myoepithelial cell contraction and milk let down within 30 seconds. Full evacuation of milk from the mammary was accomplished by gentle hand stripping of the nipple directing the milk stream into the collection container (15 ml tube). To prevent sampling biases, the full evacuation of mammary was systematically determined through the transition from streaming milk to solitary droplets during hand collection for all animals to ensure consistent methods. Following collection, ~10 minutes per animal, milk sample tubes were placed directly into wet ice and transported to laboratory facilities, samples were vortexed on low for 5 seconds, aliquoted into cryovials and frozen at -80°C. Mothers and infants were reunited following biobehavioral assessment and returned to their social group. All procedures were conducted in compliance with protocols approved by the UC Davis Institutional Animal Care and Use Committee Approval.

Milk Composition, Yield, and Available Milk Energy—Proximate assays and a commercial milk analyzer were used to measure gross milk composition (Hinde and Milligan, 2011; Miller et al., 2013). For the 2005, 2006 and 2007 seasons (N = 40), milk composition analyses were conducted in the Nutrition Laboratory at the Smithsonian National Zoological Park (SNZP) in Washington, DC using standard methods (Hinde, 2007b; Hinde et al., 2009; Milligan et al., 2008; Oftedal and Iverson, 1995; Power et al., 2008). Fat concentration was measured via a modified Rose-Gottlieb method: total lipids were assayed by sequential extractions with ethanol diethyl ether and petroleum ether. Sugar was assayed by the phenol-sulfuric acid method (DuBois et al., 1956; Marier and Boulet, 1959). Protein concentration was calculated based on nitrogen content (determined using a CHN elemental gas analyzer, Model 2400, PerkinElmer, Norwalk, CT) and estimated as 6.38**nitrogen*. Methods for proximal composition analysis are described with more details elsewhere (Hinde et al., 2009; Hood et al., 2009). Samples from the 2010, 2011 and 2012 seasons (N = 68) were analyzed at the Comparative Lactation Laboratory, Harvard University using a MIRIS milk analyzer calibrated for macaque milk samples (Miller et al., 2013) using the same samples previously assayed at the Nutrition Lab at the SNZP. The MIRIS analyzer uses an infrared transmission spectroscopy to measure the macronutrients. Samples were assayed in duplicate. Pooled bovine whole milk samples were used as controls at the initiation and completion of each assay. Based on these bovine samples, the inter-assay CV (calculated as the standard deviation divided by the mean value of all replicates) for fat was 2.52%, for protein was 1.64%, and for sugar was 4.11%. The intra-assay CV (calculated as the average of the individual CVs generated by dividing the standard deviation by the mean value of each days internal standard duplicates) for fat was 1.34%, for protein was 1.05%, and for sugar was 1.86%. Milk yield was measured gravimetrically as total sample (g) obtained by full evacuation of milk from both mammary glands after a standard period of milk accumulation (3.5–4 hr). This method of estimating relative differences in milk production among individuals has been used for other primates (Ôta et al., 1991), validated with doubly labeled water (Tardif et al., 2001), and has been associated with infant mass and growth in the CNPRC population (Hinde, 2007b; Hinde et al., 2009). Gross Energy was calculated based on the following energetic values as per Oftedal (1984): 9.11 kcal/g for fat, 3.95 kcal/g for sugars and 5.86 kcal/g for proteins and allowed for an estimate of the total energy density of milk (kcal/g). Available milk energy (AME) was calculated by multiplying milk energy density (kcal/g) by milk yield (g) (Hinde, 2009; Hinde and Capitanio, 2010).

Statistical Analyses

Raw data were transformed in preparation for statistical analyses. Because of reproductive seasonality, distribution of age at first birth could not reach normality and was thus binned into discrete categories of reproductive debut of 3, 4, or 5 years of age. Birth timing within the season, whether a female's own birth or the parturition during her reproductive debut (her first infant's birth), was calculated as number of days after February 1st of the respective year. Subject mass (kg) at 4 months, 1 year, and 2 years were used to calculate daily growth by dividing mass differences (in grams) by the number of days between measurements closest to these target ages. Growth during infancy was calculated from ~120 days to ~1 year, and growth during juvenility was calculated from ~1 year to ~2 years of age. The

infants of study females were weighed at peak lactation in conjunction with the milk collection procedure between 90-124 post-natal days. Because infant mass was not measured at the exact same age for all subjects, the age of animals was always included in models accounting for mass or studying predictors of mass. Milk characteristics (energetic density, yield and AME) were not normally distributed according to goodness of fit evaluation and were thus log transformed for statistical analysis. Milk fat and protein concentrations were log transformed and sugar concentration was squared transformed for the same reasons. Following transformation, these variables presented a good fit through Shapiro-Wilk evaluation ($P > 0.1$).

Causes and consequences of the age at first reproduction were analyzed using multiple regression models. Analyses first consisted of an exploration of overall differences in causes and consequences of age at first reproduction, using ANOVAs or multiple regression estimates. When the studied variable was influenced by a factor varying independently from age at first reproduction, the analysis was developed controlling for this co-factor (milk characteristics and infant mass were corrected for infant sex and age). Then more complex multiple regression models (ordinal logistic regression models when the outcome variable was ordinal) were developed incorporating factors that covary with age at first reproduction and likely to mediate its effects on studied outcomes. The assay method was included as a covariate when milk characteristics were explored because of slight, previously-described differences in milk macronutrients results obtained between laboratory specific proximate assays and near-infrared spectroscopy (Miller et al., 2013). Standardized experimental protocol for milk collection restricted variation in milk accumulation (mins) with no significant influence of this parameter on any of the milk parameters. Milk accumulation time was consequently not included as a predictor for milk parameters in statistical models.

For the identification of predictors of age at first reproduction, a multinomial ordinal logistic model investigated the contribution of dominance rank, female's own birth timing within her birth season, pre-partum absolute mass and growths in the determination of age at first reproduction, set as the outcome. The analysis of the consequences of age at first reproduction included infant birth timing within the season, maternal post-partum mass, milk characteristics, infant growth and ability of the mother to reproduce on the following season. Maternal characteristics including age at first birth were used as co-variables to identify their influence on maternal mass at peak lactation and infant birth timing using regression models. Then, age at first birth as well as mother and infant characteristics were tested as predictors for milk characteristics (energetic density, macronutrients yield, and AME). Infant mass at peak lactation was set as the outcome in models evaluating the contribution of age at first birth, maternal and infant variables and milk characteristics. Finally, the influence of age at first birth on females' conception (yes/no) and pregnancy outcome (viable/not viable) the following season was analyzed with maternal, infant and milk characteristics as additional predictors in binomial logistic regression models. Final models were selected following comparisons using Akaike's Information Criteria (AICc) to measure goodness of fit after forward and backward stepwise inclusion of predictors (Akaike, 1974; Aho et al., 2014). Analyses were performed using JMP 12 (SAS Institute, Inc.) and statistical significance was accepted at $P = 0.05$ (Barber and Ogle, 2014).

Results

In our sample, age at first viable infant birth ranged from 2.92 to 5.10 years with a mean \pm SEM of 4.02 ± 0.04 years. Among the 108 studied females, 81% (87/108) delivered their first infant at ~ 4 years old (3.99 ± 0.01 , range: 3.69-4.27 years); 8% (9/108, 3.08 ± 0.03 , range: 2.92-3.22 years) initiated reproduction as soon as 3 years old and 11% (12/108, 4.95 ± 0.03 , range: 4.7-5.1 years) produced their first infant at 5 years of age. Hereafter we refer to these primiparous age groups as early, typical, and late breeders.

Predictors of Age at Successful Reproductive Debut

Initiation of reproduction at 3, 4 and 5 years varied as a function of the primipara's own birth timing within the season, growth trajectory, and dominance rank. Early breeders were born earlier within their own birth season than were typical and late breeders (early breeders: March 26th ± 11.4 days, typical breeders: April 20th ± 3.7 days, late breeders: April 22th ± 9.9 days, $F_{2,106} = 4.4$, $P = 0.04$, $N = 108$). Early, typical, and late breeders did not differ in their absolute mass during their own infancy as assessed at ~ 120 days ($F_{2,106} = 0.6$, $P = 0.5$, $N = 108$), or at one year old ($F_{2,106} = 0.7$, $P = 0.5$, $N = 108$) but late breeders were lighter at 2 years old than were early and typical breeders (early breeders: 3.52 ± 0.12 , typical breeders: 3.37 ± 0.04 , late breeders: 3.15 ± 0.11 kg; $F_{2,106} = 4.0$, $P = 0.05$, $N = 108$). Early, typical and late breeders did not differ in their daily growth as infants ($F_{2,106} < 0.01$, $P = 0.99$, $N = 108$) but late breeders had lower daily mass gain during juvenility (early breeders: 3.55 ± 0.27 , typical breeders: 3.40 ± 0.09 , late breeders: 2.86 ± 0.23 g/day; $F_{2,106} = 5.1$, $P = 0.03$, $N = 108$). Early breeders were characterized by a high proportion of high-ranking females and a low proportion of mid- and low-ranking females. Mid-ranking females were proportionately more represented among typical breeders while late breeders were characterized by a high proportion of low-ranking females and a very low proportion of high-ranking females ($\chi^2 = 10$, $P = 0.04$, $N = 108$; Fig. 1).

Combining these predictors of age at successful reproductive debut for AICc model selection generated a multiple regression model (model: $\chi^2 = 13.65$, $R^2 = 0.14$, $P = 0.003$, $N = 108$) in which high dominance rank ($\beta \pm SE = 0.9 \pm 0.4$, $P = 0.02$), juvenile growth ($\beta \pm SE = 0.5 \pm 0.3$, $P = 0.18$) and having been born early in the female's own birth season ($\beta \pm SE = 0.01 \pm 0.009$, $P = 0.06$) predicted early reproductive debut. Absolute mass (kg) at 4 months, 1 year and 2 years, as well as growth during infancy were not retained in the model. The retention of both rank and juvenile growth in the model indicates that the influence of rank on the age at first birth is not solely due to a faster growth of high ranked females. Indeed, for our study mothers, rank was not associated with growth during either infancy ($F_{2,106} = 0.3$, $P = 0.7$, $N = 108$) or juvenility ($F_{2,106} = 0.6$, $P = 0.5$, $N = 108$).

Age at Reproductive Debut and Parturition-Timing within the Season

The younger a female initiated reproduction, the later she delivered her infant within her debut birth season (early breeders: April 28th ± 7 days, typical breeders: April 16th ± 2 days, late breeders: April 4th ± 6 days; $F_{2,106} = 3.5$, $P = 0.03$, $N = 108$; Fig. 2). AICc model construction identified that high-ranking females delivered earlier during the birth season compared with mid- and low-ranking females ($\beta \pm SE = -4.3 \pm 2.0$, $P = 0.04$). When

controlling for rank, age at reproductive debut remained negatively associated with parturition-timing (early & typical – late: $\beta \pm SE = 10.6 \pm 3.5$, $P = 0.003$; early - typical: $\beta \pm SE = 6.6 \pm 3.6$, $P = 0.07$; model: $F_{3,105} = 3.81$, $adjR^2 = 0.07$, $P = 0.01$, $N = 108$; Fig. 2).

Reproductive Debut and Female Mass across Time

Predictably, younger primiparae were lower mass at peak lactation than were older primiparae (early = 6.10 ± 0.4 , typical = 7.10 ± 0.1 , late = 7.55 ± 0.3 Kg; $F_{2,105} = 3.8$, $P = 0.02$, $N = 108$). The influence of age at first birth on maternal mass at peak lactation, (3-4 months after debut parturition), was not exclusively due to differences in juvenile growth. After stepwise inclusion of juvenile mass at 2 years old ($\beta \pm SE = 2.3 \pm 0.2$, $P < 0.0001$), typical and late breeders were still heavier than early breeders ($\beta \pm SE = 1.3 \pm 0.3$, $P < 0.0001$) and late breeders were heavier than typical breeders ($\beta \pm SE = 1.0 \pm 0.2$, $P < 0.0001$) reflecting the additional years of adolescent growth (full model: $F_{4,104} = 46.9$, $adjR^2 = 0.63$, $P < 0.0001$, $N = 108$).

In their 4th year, typical breeders had the highest mean mass. In non-pregnant states, typical breeders weighed significantly more than did the late breeders who would go on to conceive in the fall breeding season (typical: 7.03 ± 0.13 kg vs, late: 6.16 ± 0.37 kg, $P = 0.03$). Early breeders were intermediate weighing 6.44 (kg) ± 0.54 kg at 4 years of age (in a non-pregnant state) and not significantly different from typical or late breeders (Full Model: $F_{2,103} = 0.25$, $P = 0.0021$, $adjR^2 = 0.11$, $N = 104$). Several early breeders ($N=4$) were removed from the breeding colony by 4 years of age for project reassignment and could not be included in the analysis.

Milk Synthesis

Age at reproductive debut was associated with milk composition, energy density, yield, and available milk energy. Milk fat and protein concentrations were lower for late breeders than for typical and early breeders controlling for infant age and sex (fat: $\beta \pm SE = 0.23 \pm 0.09$, $P = 0.01$; protein: $\beta \pm SE = 0.16 \pm 0.06$, $P = 0.01$; Table 2). Standard least square means $\pm SE$ for early, typical and late breeders were, respectively, for the proportion of fat: 6.59 ± 0.68 , 7.12 ± 0.22 and $5.40 \pm 0.63\%$ and for the proportion of protein: $2.16 \pm 0.16\%$, $2.27 \pm 0.05\%$ and $1.91 \pm 0.14\%$. Additionally, mothers synthesized lower fat content for daughters ($\beta \pm SE = 0.1 \pm 0.003$, $P = 0.0002$, Table 2). Milk was collected during peak lactation between 3 and 4 months post-partum; the closer to 4 months, the higher the fat and protein concentrations in milk (fat: $\beta \pm SE = 0.007 \pm 0.003$, $P = 0.01$; protein: $\beta \pm SE = 0.003 \pm 0.002$, $P = 0.1$; Table 2). Age at first reproduction did not influence the lactose concentration ($P = 0.4$). Lactose concentration standard least square means $\pm SE$, after controlling for the influence of sex and age of the infant, were for early, typical, and late breeders respectively: 7.34 ± 0.13 , 7.20 ± 0.04 , $7.35 \pm 0.12\%$. Maternal mass, maternal rank, and infant birth timing were not retained as predictors of milk macronutrients by AICc model selection.

Given that late breeders produced lower fat and protein concentrations in milk (Hinde, 2009), late breeders necessarily produced milk of lower energetic density than did typical breeders and early breeders ($\beta \pm SE = 0.16 \pm 0.06$, $P = 0.006$) controlling infant age and sex. Standard least squares means $\pm SE$ for early, typical, and late breeders were 1.02 ± 0.06 ,

1.07 ± 0.02, 0.90 ± 0.06 kcal/g, respectively. Milk energy density increased with infant age ($\beta \pm SE = 0.005 \pm 0.002$, $P = 0.02$) and was higher for mothers of sons than mothers of daughters ($\beta \pm SE = 0.07 \pm 0.02$, $P = 0.0004$) (Full model: $F_{4,104} = 9.75$, $adjR^2 = 0.25$, $P < 0.0001$, $N = 108$). Milk energetic density was not influenced by maternal mass, rank or infant birth timing among these primiparous mothers and these parameters were not retained during AICc model selection (Table 3).

Age at reproductive debut was also associated with the amount of milk synthesized by females. Early breeders produced ~25% less milk than did typical or late breeders, controlling for infant sex and age (standard least square mean ± SE were: early breeders: 9.47 ± 2.10, typical breeders: 12.81 ± 0.68, late breeders: 13.63 ± 1.83g, Figure 3b). Milk yield was higher when mothers were heavier at peak lactation ($\beta \pm SE = 0.14 \pm 0.03$, $P < 0.0001$, Table 2) and infants were born later in the birth season ($\beta \pm SE = 0.004 \pm 0.002$, $P = 0.07$, Table 2), but was slightly lower for high-ranking females ($\beta \pm SE = 0.07 \pm 0.04$, $P = 0.08$, Table 2). Controlling for all these retained predictors, maternal age at reproductive debut was not retained as a predictor of milk yield, (standard least square means for early, typical, and late breeders respectively was 10.39 ± 2.10, 12.83 ± 0.64, and 12.94 ± 1.83g).

Age at reproductive debut was associated with available milk energy (AME, the product of milk energetic density and yield). AME was lower for early breeders than for typical and late breeders ($\beta \pm SE = 0.15 \pm 0.08$, $P = 0.06$, Figure 3c) controlling for infant age only (infant sex was not retained as a predictor of AME). Standard least square means ± SE for early typical and late breeders were, respectively: 9.53 ± 2.12, 13.30 ± 0.69, 11.84 ± 1.96 kcal. When including co-variables of age at reproductive debut in the model, maternal mass, social rank and infant birth timing were retained as predictors for AME production. AME was positively associated with maternal mass at peak lactation ($\beta \pm SE = 0.14 \pm 0.03$, $P < 0.0001$, Table 2), was lower for high-ranking females ($\beta \pm SE = 0.08 \pm 0.04$, $P = 0.04$, Table 2), and was higher when the infant was born late during the season ($\beta \pm SE = 0.004 \pm 0.002$, $P = 0.02$, Table 2). Accounting for these factors, early and late breeders did not differ in the AME they produced. Instead, both early and late reproduction were associated with a lower AME compared with that produced by typical breeders ($\beta \pm SE = 0.20 \pm 0.10$, $P = 0.04$, Table 2). As such, the difference of AME between early and late breeders is mostly due to differences in their mass, parturition timing, and social rank. Accounting for these factors, AME standard least square means were respectively for early, typical and late breeders: 10.82 ± 2.15, 13.26 ± 0.65 and 10.53 ± 2.00 kcal. Taken together these findings show that, per unit maternal mass, typical breeders produced higher available milk energy than did early and late breeders.

Infant Mass

Infants of early breeders were 9% lighter than infants of typical and late breeders ($\beta \pm SE = 0.09 \pm 0.05$, $P = 0.06$, $N = 108$), controlling for infant age and sex. Early, typical and late breeders' infant mass at peak lactation were respectively 0.90kg ± 0.04, 0.99kg ± 0.015 and 0.98kg ± 0.04 (standard least squares means ± SEM). To identify covariates likely to mediate the influence of age at reproductive debut on infant mass, we added maternal parameters as well as milk characteristics (energetic density, yield and AME) during AICc

model selection. Infant mass at peak lactation was still influenced by infant age and sex but was also positively related to maternal mass at peak lactation ($\beta = 0.03 \pm 0.01$, $P = 0.01$) and milk energetic density ($\beta \pm SE = 0.12 \pm 0.07$, $P = 0.1$, model: $F_{5,103} = 7.58$, $adjR^2 = 0.24$, $P < 0.0001$, $N = 108$). Maternal dominance rank, infant birth timing within the birth season, milk yield and available milk energy were not retained as predictors for infant mass at peak lactation. Importantly, when including maternal mass and milk energetic density, age at reproductive debut was no longer retained as a predictor of infant mass; the influence of age at first reproduction on infant mass at peak lactation was mostly mediated by maternal mass and capacity to synthesize milk. A final model was developed that replaced energetic density (kcal/g) with the concentration of fat, protein, and carbohydrate. The model retained milk protein concentration as the most important predictor for infant mass among these primiparae ($\beta \pm SE = 0.13$, $P = 0.06$, model: $F_{5,103} = 8.0$, $adjR^2 = 0.25$, $P < 0.0001$, $N = 108$, Table 4).

Subsequent Reproduction

The probability of conception and successful reproduction during the subsequent breeding season immediately following primiparity was influenced by the age of reproductive debut. From the original $N=108$, $N=80$ remained assigned by colony management in the breeding colony to assess subsequent reproduction. Fewer early and late breeders, compared with typical breeders, became pregnant during the fall breeding season immediately after their first birth (early: 60% (3/5), typical: 86% (56/65), late: 60% (6/10), $\chi^2 = 5.47$, $P = 0.06$, $N = 80$, Fig. 4.a). Including parturition timing within the season of the first birth and social rank improved the amount of variance explained by the model in AICc model selection (Full AICc selected model: $\chi^2 = 46.3$, $R^2 = 0.40$, $P < 0.0001$, $N = 80$). As primiparae, giving birth later within the season reduced likelihood of conception during the subsequent breeding season (birth timing: $\beta \pm SE = -0.09 \pm 0.03$, $P = 0.003$). Mid ranked females were less able to conceive on the season following their primiparous experience compared to high and low ranking females (mid rank: $\beta \pm SE = -2.54 \pm 0.95$, $P = 0.007$; high ranked females = 27/29, 93.1%; middle ranked = 17/25 = 68.0% and low-ranked = 21/26, 80.8%, respectively). When controlling for first infant birth timing and social rank, the age of reproductive debut influenced the probability of conception the subsequent breeding season, with a higher proportion of pregnancy for females who gave birth for the first time at 4 years old ($\beta \pm SE = 1.47 \pm 0.48$, $P = 0.002$, $N = 80$). Milk and infant parameters were not significantly related to ability of females to get pregnant during the season following their first birth. Inclusion of these variables increased AICc value and were thus excluded from the model.

Only 60% (3/5) of early and 40% (4/10) of late breeders were able to give birth to a viable infant on the season following their first birth compared to 75% (49/65) of the 4-year-old mothers (Fig. 4.b). Successful pregnancy on the next season was positively related to first infant's mass at peak lactation ($\beta \pm SE = 4.03 \pm 2.32$, $P = 0.08$) and milk energetic density ($\beta \pm SE = 2.8 \pm 1.6$, $P = 0.08$) and later birth during the first birth season reduced likelihood of producing a viable infant on the subsequent season ($\beta \pm SE = -0.05 \pm 0.02$, $P = 0.003$). Including these covariates revealed that late breeders have a 30% reduction in probability of giving birth to a viable infant on the next season (early & typical – late: $\beta \pm SE = 1.3 \pm 0.5$, $P = 0.006$; $\chi^2 = 22.8$, $R^2 = 0.24$, $P = 0.0004$, $N = 80$).

Discussion

Our study investigated successful reproductive debut, addressing both the aspects of early life that predicted age of first viable birth as well as milk synthesis, infant mass, and subsequent reproduction as a function of age during primiparity (Table 5). In our sample from this captive, outdoor breeding population, 80% successfully reproduced in their fourth year; far fewer initiated their reproductive career one year earlier or one year later, consistent with other populations (Yerkes: Wilson et al., 1983; Cayo Santiago: Bercovitch and Berard, 1993). The precocity of reproduction was mainly predicted by higher dominance rank and better growth during juvenility, but not growth during infancy, the period of maternal dependence. Early and late primiparae, 3- and 5-years old respectively, were compromised in their milk synthesis compared to the more typical 4-year old primiparae. Late breeders produced milk with a lower energetic density, due to low fat and protein concentrations, whereas early breeders produced less milk. As a result, both early and late breeders produced lower available milk energy. Females initiating reproduction in their 3rd year—early breeders—delivered later in the birth season but produced infants that were only slightly smaller than the infants of typical and late breeders. Compared with both early and late breeders, typical breeders were more successful at conceiving during the subsequent fall breeding season and producing a viable, full-term infant on the subsequent birth season a year after producing their first infant. These findings substantiate complex inter-dependencies among life-history tradeoffs across development and reproductive debut.

The age at which a female attained reproductive maturity was determined by her velocity of growth as well as how duration of growth aligned with breeding windows. Daily growth during juvenility, but not infancy, was a predictor of age at first birth. Growth during infancy depends on mother's milk and, as such, reflects maternal physiological investment (Price et al., 1999, Blomquist, 2013). Comparatively, during juvenility, offspring may compensate for deficits in maternal endowment under certain ecological conditions through increased foraging and improved growth after the period of maternal dependence (Nuñez et al. 2015). Growth during juvenility may be a more relevant internal indicator of females' future somatic resources to support reproduction. Particularly slow juvenile growth characterized the females who would evince delayed reproductive debut compared to early and typical breeders. Early breeders particularly benefitted from being born early during their own season. Females born earlier in the birth season and/or who conceived later in their adolescent breeding season were afforded a protracted period of growth that facilitated somatic development to support reproduction. Similarly, in the Columbian ground squirrel being born earlier in the annual birth season is associated with acceleration of reproductive debut (Neuhaus et al., 2004). The slightly faster growth of early breeders, associated with their earlier birth, seemingly permitted these rhesus females to reach a reproductive threshold as soon as their third year, provided they used the extra developmental period by conceiving late in the breeding season and thus delivering late in the birth season. The proximal cause for this delayed parturition timing could be later sexual maturation during the reproductive season (Wilson et al., 1983). Typical breeders delivered during the peak of the birth season. Late breeders, having missed the opportunity to reproduce in their fourth

year, conceived early in the next fall breeding season, delivering their infant relatively early within the birth season of their 5th year.

Rhesus macaques can accelerate reproduction at relatively younger age as function of rank (Wilson et al., 1983, Bercovitch and Berard 1993) as do other socially complex mammalian taxa (Barbary macaques: Paul and Thommen 1984, long-tailed macaques: van Noordwijk and van Schaik, 1999, mandrills: Setchell et al., 2002; baboon: Johnson, 2003; spotted hyena, *Crocuta crocuta*: Holekamp et al., 1996). Higher dominance rank potentially affords greater access to energetic resources (Chancellor and Isbell, 2008; Pusey et al., 1997), reduces psychosocial stress that alters hypothalamic-pituitary-ovarian axis (see Sapolsky, 2005), and facilitates access to mating partners (Wallen and Zehr, 2004). Either isolated or synergistically, these factors accelerate reproductive debut (Fukuda, 1988; Sugiyama and Ohsawa, 1982; Watanabe et al., 1992; Bercovitch & Strum 1993, Williams et al., 2007). Longitudinal results from rhesus on Cayo Santiago island identified population density as an additional critical factor for the age at reproductive debut (Bercovitch and Berard, 1993), suggesting that dominance rank may exert greater influence on timing of reproductive debut when population density or resource availability increases competition and intensity of agonistic interactions. We speculate that social rank mediates the results presented here through the endocrine system via disruption of endocrine pathways underlying ovulation and milk synthesis, rather than in access to resources under these captive conditions, because rank was not correlated with female mass or growth during development in the present study.

Age at successful reproductive debut also influenced maternal mass at peak lactation. Typical breeders were 16% heavier, about one kilogram, than were early breeders, confirming that early breeders sustain lactation with fewer somatic resources. Reproductive debut at 4 years old, compared to accelerating reproductive debut, seemingly affords females the opportunity to gain mass to reduce tradeoffs between maternal condition and current reproduction, reducing maternal depletion, and improving subsequent reproduction (Stearns 1992, Clutton-Brock 1991, McNamara and Houston, 1996). Delaying reproduction until 5 years old, however, has a more marginal gain in mass, only about 6% heavier, less than half a kilogram, than were 4 year-olds at peak lactation. This was likely a consequence of the decelerating growth rate as late breeders approached maturity and adult stature (Cerroni et al., 2000, Lu et al., 2016). Females that were delayed in reproductive debut, however, had lower mass than did typical breeders at 4 years of age. These late breeders seemingly needed additional time to attain somatic reproductive thresholds. Finally, and contrary to our expectations, we found that females starting their reproduction early did not necessarily pay a long-term cost in their growth since they attained similar mass to typical and late breeders at 4 years of age.

Consistent with our predictions, age at reproductive debut influenced milk characteristics including energetic density, yield and available energy. Females delaying their first reproduction to the age of 5 presented the lowest fat and protein concentrations resulting in lower energetic density compared with both early and typical breeders. Considering the higher mass of late breeders, these results highlight some degree of independence between somatic reserves and milk energy density. Maternal mass instead predicted the milk yield,

consistent with previous results in rhesus macaques (Hinde et al., 2009) and other taxa (dairy cattle: Ettema and Santos, 2004; Lin et al., 1988; human: Motil et al., 1997). Consequently, accelerating reproductive debut was associated with a reduced ability to synthesize milk yield, due to the constrained body mass of early breeders. Early breeders produced milk of the lowest available energy, illustrating the constraints of truncated development on physiological investment at reproductive debut (Allal et al., 2004; Ettema and Santos, 2004). Indeed, typical breeders produced more available milk energy per unit maternal mass than did either early or late breeders.

Early breeders may be limited in their energetic investment because of somatic constraints as well as substantial tradeoffs with their own growth (Nuñez et al. 2015). Late breeders may be characterized by more inter-related physiological constraints, likely endocrine, that collectively account for their slower growth during juvenility, delayed conception, and poor milk synthesis. Our findings suggest 4 years old to be an optimal age for reproductive debut as suggested by the high proportion of typical breeders in the present and previous studies (Bercovitch and Berard, 1993; Wilson et al., 1983). Females starting reproduction at the age of 4 synthesize the highest AME due to both high energy density and greater yield of milk. In addition to high milk quality and quantity, these characteristics might offer much more flexibility to typical breeders to respond to environmental variation likely to affect milk energetic density or yield. Environmental influences such as parasite exposure, (Hinde, 2007a) or limited water availability (Adams and Hayes, 2008) can have strong influences on lactation ability and may exert greater effects for early and late breeders whose capacity to synthesize milk was reduced compared to typical breeders.

Age at reproductive debut influenced infant mass mostly through maternal mass and milk energetic density. Infants of early breeders, however, were only slightly lighter than infants of typical and late breeders, suggesting that early reproducers are producing relatively more infant per unit of maternal mass. These findings extend earlier research in this population that revealed that primiparous mothers produced higher infant to mother mass ratios than do multiparous mothers (Hinde, 2007b). In contrast to previous studies emphasizing the role of milk yield (Hinde, 2007b; Hinde et al., 2009), the reduced amount of milk produced by primiparous mothers in the present study demonstrates that when milk yield is low, energetic density becomes the primary contributor for infant growth and mass. More precisely, protein concentration was the main predictor of infant mass consistent with previous research (red deer: Landete-Castillejos et al., 2004; human: Polberger et al., 1989;) and a pattern found more broadly among primates (Hinde and Milligan, 2011; Power et al., 2002). Milk protein concentration directly affects the concentration of growth factors such as IGF-I, critical for early growth and for the metabolism of other milk constituents such as fat (Socha et al., 2011). Taken collectively, these results suggest that late breeders' infants may be handicapped in their growth due to the particularly low protein and fat concentration of their mother's milk, resulting in mass at peak lactation similar to the infants of typical breeders despite their mothers being on average heavier.

The ability of females to conceive and to successfully deliver a viable infant on the season following their first reproductive effort was also associated with age at reproductive debut. The lower success of early breeders may be due to their substantially higher maternal effort

during the breeding season and the timing of their delivery (Wilson et al., 1983). Early breeders gave birth later in the season, and the following breeding season consequently occurs soon after their peak lactation, when their infants are younger compared with typical and late breeders, and require more investment (e.g. infant carrying: Altmann and Samuels, 1992, nursing: Stewart, 1988). The reduced success during the subsequent breeding season for late breeders, however, contrasted with previous description of a faster postpartum recuperation with increasing age in rhesus primiparae (Mas-Rivera and Bercovitch, 2008). Comparatively, late breeders' lower rank can increase behavioral care and maternal vigilance (Mas-Rivera and Bercovitch, 2008) and extend the weaning process (Holekamp et al., 1996). Intensity of maternal behavior (Altmann et al., 1978), particularly nursing dynamics, had long been considered responsible for the duration of lactational amenorrhea in primates (Human, Indonesia: Jones, 1989; !Kung: Konner and Worthman, 1980; McNeilly, 1993, 2001; gorillas, *Gorilla gorilla*: Stewart, 1988; rhesus macaques: Gomendio, 1989; marmosets, *Saguinus oedipus*: Ziegler et al., 1990). More recent studies revealed that sustained positive energy balance influences resumption of estrous (baboon: Rosetta et al., 2011; chimpanzee: Emery Thompson et al., 2012; human: Vallengia and Ellison, 2009). The better ability of typical breeders to provide higher AME likely supported faster infant growth (Hinde et al., 2009) and earlier attainment of weaning thresholds (Lee et al., 1991; Lee, 1996; Reitsem et al. 2015). These factors, combined with the peak timing of parturition, afforded typical breeders the capacity for somatic recovery to conceive during the subsequent breeding season. The poor reproductive performance of the late breeders especially, suggests that these animals have persistent and possibly global constraints in their reproductive function. Our results, in which early and late breeders had compromised subsequent conception compared to typical breeders is consistent with experimental manipulation in dairy cows (Ettma and Santos, 2004).

Importantly when we compare the average reproductive output across groups, we find that at 4 years of age, early breeders, typical breeders, and late breeders had 1.6, 1.0, and 0 offspring respectively. Early breeders seemingly prioritized investment in their own sustained growth at the expense of capacity to synthesize milk, invest in infant mass, and conceive during the subsequent breeding season. Indeed, early breeders were able to attain the same non-pregnant body mass as typical breeders and late breeders at 5 years of age and some were still able to achieve a one year inter-birth interval. Among wild-living chimpanzees, mothers tradeoff offspring growth with reproductive rate (Emery Thompson et al. 2016). Experimental studies of adolescent pregnancy and nutrient partitioning among domesticated sheep indicate that over-nourished, young primiparae prioritize their own development at the expense of offspring growth (Wallace et al., 2001). Such an affect may be particularly exaggerated among young primiparae. Early initiation of reproduction, however, seemingly exerts long-term costs on maternal survival in rhesus macaques (Blomquist, 2009; Blomquist 2013). Importantly, some of the costs of early reproduction might have been obscured by the nutritional ecology of captivity, permitting infant and maternal survival in contrast to other ecological contexts interacting with birth timing and maternal condition (Drickamer, 1974; van Schaik and van Noordwijk, 1985; Altmann 1986). Notably, by restricting the study to females whose reproductive debut was characterized by successful conception, viable birth, and infant survival to peak lactation, we were unable to

evaluate other potential life-history tradeoffs that resulted in reproductive failure among primigravidae.

Our findings in macaques are likely to be of translational importance for maternal and child health in the context of adolescent pregnancy (Phillips et al., 2014). Rhesus macaques share many aspects of growth, development, and reproduction with humans (Cline 2007; Leigh, 2009; Machado, 2013), but on an accelerated time scale (Valerio et al. 1969). As such, early reproductive debut in rhesus macaques corresponds to young adolescent pregnancy <16 years of age in humans (Vogel et al., 2015). Worldwide, just over 10% of all births annually are to girls 10-19 years of age, approximately 16 million, 95% of whom live in the Global South or elsewhere in the developing world (WHO 2011; Vogel et al., 2015). Information on the youngest adolescent mothers 10-15 years old is limited (Vogel et al., 2015), but ~2.5 million births occur to girls aged 12-15 years old in low resource countries (Neal et al., 2012) and in the United States 0.2 per 1000 births were to girls 10-14 in 2015 (Martin et al., 2017). Reported risks associated with young motherhood among humans mostly address gestation (Allal et al., 2004; Fraser et al., 1995; King, 2003; Kramer, 2008; Ganchimeg et al. 2014), parturition complications (Torvie et al., 2015), or postnatal behavioral care (Riva Crugnola et al., 2014; Umaña-Taylor et al., 2013) but not milk synthesis. For exceptionally young girls, the ability to conceive reflects underlying physiological flexibility but functional capacity of the mammary gland is handicapped (Motil et al., 1997) or sustaining lactation is more challenging (Geervani and Jayashree, 1988). Females initiating reproduction within 2 years of menarche or before the age of 16 may confront significant life-history tradeoffs or constraints (King, 2003; Kramer and Lancaster, 2010; Motil et al. 1997) with expected consequences for milk production as found in the youngest macaques in the present study. Importantly, adolescent human mothers (14-18 years old) are less likely to breastfeed than are adult mothers (Wambach and Cohen, 2009) which elevates risk for shorter inter-birth intervals and compounding detrimental effects on both the mother and the infant (DeFranco et al., 2007; King, 2003). We found reduced lactational performance among young primiparae that likely reflects a continuation of constrained investment across gestation into lactation (the first 1000 days in humans). For human infants of very young adolescent mothers, over-feeding during formula provisioning, as supplement or replacement, may represent a stark mismatch between early metabolic organization and post-natal energy availability. Such a mismatch is implicated in poor health outcomes including obesity, metabolic syndrome, and cardiac conditions when offspring have calibrated to maternal resources that can be supplemented or replaced by evolutionarily novel alternatives (Wells, 2014, Wells, 2010).

Conclusions

The findings presented here refine and extend our understanding of accelerated vs. delayed reproduction among mammals. Our results highlight that multiple physiological and social predictors of reproductive debut and capacity have great coherence, substantiating that coordination across physiological systems underlies reproductive flexibility. Taken collectively, these results suggest that early breeding represents a malleable life-history tactic in an Old World primate to accelerate reproduction under the most favorable conditions. In contrast, late breeders manifest reduced capacity for physiological investment

in reproduction and poorer reproductive rate than did typical breeders. While late breeders may represent poor reproductive capacity, possibly shaped by early life, the slow life history of late breeders, if not beneficial during these first reproductive years, might present long-term benefits on fitness through extending lifespan (Blomquist, 2013; see Promislow and Harvey, 1990). Fitness outcomes of age at reproductive debut can also occur trans-generationally on infant development and reproductive success (McNamara and Houston, 1996). Milk characteristics influence infant behavioral development (Dettmer et al. 2017), mostly through the amount of energy available to support experience of physical and social environment (Fairbanks and Hinde, 2013; Hinde, 2013). Infants of females producing higher AME show higher activity levels and better confidence in challenging situations (Hinde and Capitanio, 2010). In cases of restricted available milk energy, to ensure survival, growth is expected to be prioritized over behavioral activity (Allen-Blevins et al. 2015; Hinde et al. 2015) suggesting that infants of young primiparae might be impaired in their early development with potential consequences on their later social competence or reproductive success (Nuñez et al. 2015). Future research on reproductive debut among mammals should carefully disentangle early, typical, and late breeders from one another when considering life-history tradeoffs as well as prioritization between somatic and behavioral development of infants. A better understanding of reproductive debut, in the context of life-history tradeoffs, presents new opportunities to integrate ultimate perspectives with proximate phenomena that present implications for medicine and public health.

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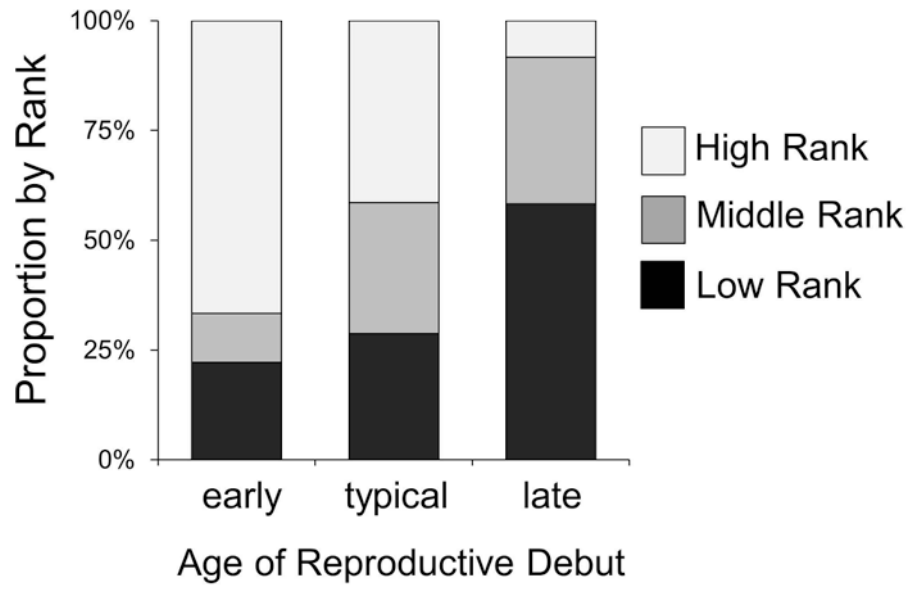


Figure 1. Proportion of high, middle and low ranked females according to age at first reproduction. Higher rank is associated with earlier reproductive debut ($\chi^2 = 10$, $P = 0.04$, $N = 108$).

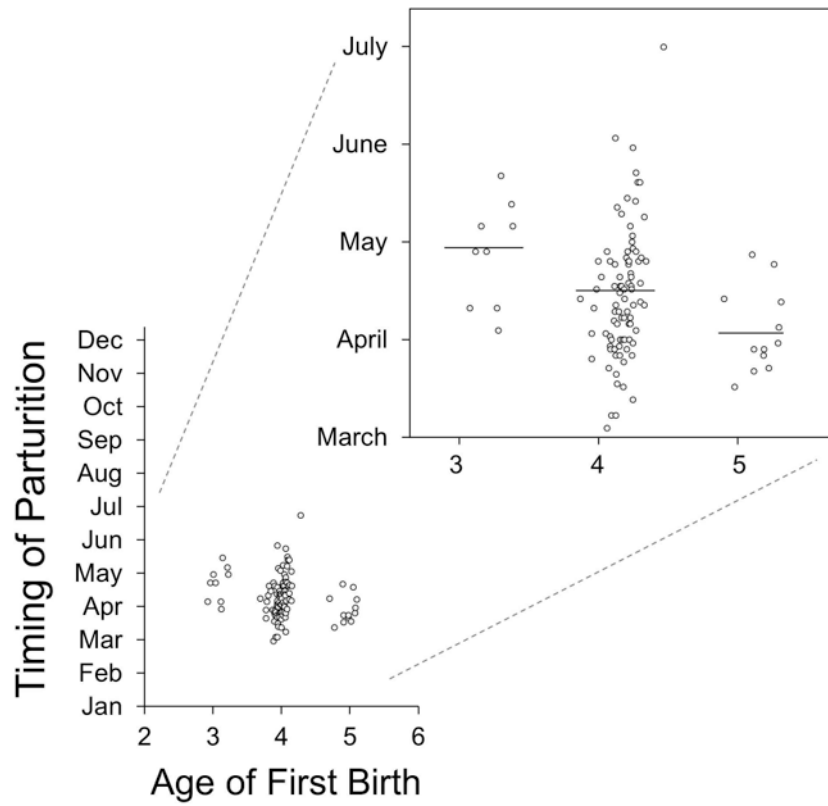


Figure 2. Infant birth timing according to maternal age category at reproductive debut. Younger primiparae deliver later in the birth season than do typical and older primiparae ($F_{2,106} = 3.5$, $P = 0.03$, $N = 108$). Dash lines represent means for each age category.

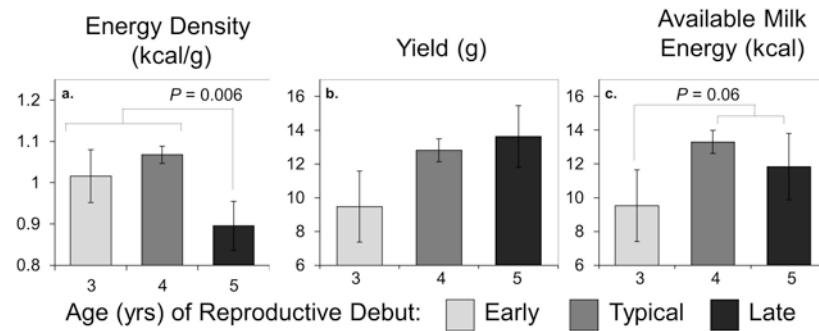


Figure 3.

Adjusted mean \pm SE milk energy density (a), yield (b) and available energy (c) according to age at first reproduction. Accounting for infant age and sex, females initiating reproduction at 5 years old (late breeders) synthesize lower energetic density and females starting reproduction at 3 years old (early breeders) synthesize lower available milk energy compared to females starting reproduction at 4 years old (typical breeders). Least square means differences evaluated through multiple regression models, $N = 108$. Energy density and available milk energy data is corrected for assaying method.

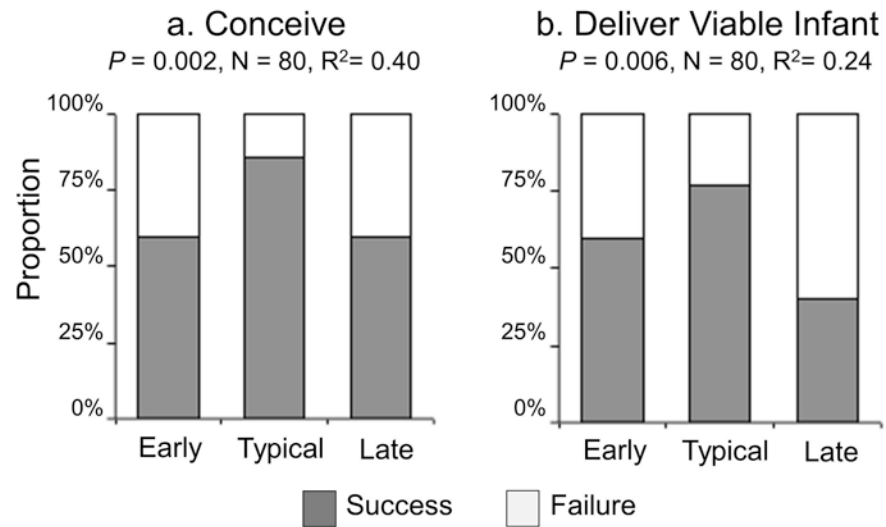


Figure 4. Proportion of females who were able to subsequently conceive (a.) and deliver a viable infant (b.) in the breeding and birth seasons following their reproductive debut. Fewer early and late breeders, compared with typical breeders, became pregnant and gave birth to a viable infant during the year following their first birth ($N = 80$).

Table 1

Hypotheses and predictions for predictors and consequences of age of reproductive debut.

	Parameter	Hypotheses	Predictions
Predictors of Age at Reproductive Debut	Birth Timing	Among seasonally breeding species, when a female is born during her birth season- early, typical, or late- influences the duration of development in relation to the timing of breeding seasons during adolescence.	Females born early within their birth season are more likely to attain threshold conceptive condition in time to conceive during an earlier birthing season, and therefore at a younger age, than females not born early within the birth season.
	Growth Trajectory	Females have to attain somatic thresholds before reproductive debut.	Females characterized by better growth during development are expected to have an earlier age of reproductive debut. Females characterized by slower growth during development are expected to have a later age of reproductive debut
	Social Rank	Social rank within the female dominance hierarchy mediates age at reproductive debut (likely via access to resources and exposure to social aggression that influences hormonal regulation).	High-ranking females have earlier age of reproductive debut than lower-ranking females. Low-ranking females have later age of reproductive debut than higher-ranking females.
Outcomes Associated with Age at Reproductive Debut	Maternal Mass at Peak Lactation	Among seasonally breeding species, age at reproductive debut is associated with female mass.	Typical breeders are expected to be heavier during lactation than are Early Breeders because they have ~1 additional year of growth before reproductive debut. Late breeders are expected to be heavier than early breeders and typical breeders as they have ~2 or ~1 additional years of growth, respectively, before reproductive debut.
	Timing of Parturition	Timing of conception during the breeding season and consequent timing of parturition during the birth season varies as a function of age at reproductive debut.	Early breeders attain conceptive thresholds toward the end of their first adolescent breeding season and subsequently give birth later during the season than other primiparae
	Milk synthesis	Capacity to synthesize milk reflects: A) with somatic reserves established during development. B) functional development of mammary gland during pregnancy.	Longer durations of development or better growth during development improve capacity to synthesize milk energy or volume. Younger, smaller primiparae will be particularly handicapped in their synthesis of milk. Older, larger primipara will produce the greatest available milk energy. As the first reproductive effort for all primiparae, milk synthesis will be similar across ages of reproductive debut.
	Infant mass	Infant somatic development depends on maternal somatic condition and milk synthesis.	Infants will be heavier if their mothers are older, heavier, and synthesizing higher available milk energy.
	Subsequent reproduction	Maternal condition is associated with probability of conception during the breeding season following primiparity and pregnancy outcome on the subsequent birth season. Parturition-timing in the birth season during reproductive debut influences duration of maternal recovery prior to and during the subsequent breeding season.	Typical and late breeders, because they have had a longer period of growth, more somatic resources, and less likely to deplete resources during lactation will be more likely to conceive and successfully produce a viable infant in the next breeding and birth season. Early breeders are more likely to be delayed in their subsequent reproduction. Females who deliver earlier in the birth season are more likely to conceive and successfully reproduce during the next breeding and birth season. Females who deliver later in the birth season are less likely.

Table 2
Multiple regression results for milk energy density, yield and available energy (AME) at peak lactation (N = 108)

	Energy density			Yield			AME		
	β	SE	P	β	SE	P	β	SE	P
Intercept	-0.61	0.2	0.0003	1.09	0.31	0.0006	1.38	0.33	0.0002
Age Reproductive Debut									
Late breeders	-0.16	0.06	0.006	-	-	-	-	-	-
Typical breeders	-	-	-	-	-	-	0.2	0.1	0.04
Dam									
Mass (kg)	-	-	-	0.15	0.03	<0.0001	0.14	0.03	<0.0001
Rank (High)	-	-	-	-0.07	0.04	0.08	-0.08	0.04	0.04
Infant									
Birth time (days)	-	-	-	0.004	0.002	0.07	0.004	0.002	0.02
Sex (female)	-0.06	0.02	0.0003	0.07	0.04	0.09	-	-	-
Age (days)	0.004	0.002	0.01	-	-	-	-	-	-
Assay method (MIRIS)	0.06	0.02	0.0006				0.07	0.04	0.08
			$F_{4,104} = 9.75, P < 0.0001$			$F_{5,103} = 7.00, P < 0.0001$			
			$adjR^2 = 0.25$			$adjR^2 = 0.19$			
						$adjR^2 = 0.22$			

Estimated effects are presented for energy density in Kcal per grams, for yield in grams and for AME in Kcal. Milk characteristics were log transformed to meet normality assumption. For rank, estimated effects are presented for high-ranking individuals, for infant sex, estimated effects are presented for females and for the assaying method, estimated effects are for MIRIS technique.

Multiple regression models reporting influence of age at first birth, maternal and infant characteristics and assaying method on milk fat, sugar and protein concentrations ($N = 108$).

Table 3

	Fat			Lactose			Protein		
	β	SE	P	β	SE	P	β	SE	P
Intercept	0.84	0.32	0.01	66.23	6.29	<0.0001	0.29	0.23	0.2
Age Reproductive Debut									
Late Breeders	0.23	0.09	0.01	-	-	-	0.16	0.06	0.01
Dam									
Mass (kg)	-	-	-	-	-	-	-	-	-
Rank (High)	-	-	-	-	-	-	-	-	-
Infant									
Birth time (days)	-	-	-	-	-	-	-	-	-
Sex (female)	-0.1	0.03	0.0002	1.8	0.5	0.001	-	-	-
Age (days)	0.007	0.003	0.01	-0.12	0.06	0.03	0.003	0.002	0.1
Assay method (MIRIS)	0.12	0.03	<0.0001	-2	0.6	0.0004	-	-	-
	$F_{4,104} = 11.0, P < 0.0001$			$F_{3,108} = 9.9, P < 0.0001$			$F_{2,106} = 5.0, P = 0.009$		
	$adjR^2 = 0.27$			$adjR^2 = 0.20$			$adjR^2 = 0.07$		

Estimated effects are presented for the proportion of fat, lactose and protein in the milk (percentage). Milk fat and protein concentration were log transformed and lactose concentration was square transformed to meet normality assumption. For infant sex, estimated effects are presented for females and for the assaying method, estimated effects are for MIRIS technique.

Table 4

Multiple regression model reporting influence of age at first birth and maternal and infant characteristics on infant growth ($N=108$).

	Infant mass		
	β	SE	P
Intercept	0.22	0.17	0.19
Age Reproductive Debut	-	-	-
Dam			
Mass (kg)	0.03	0.01	0.006
Rank (High)	-	-	-
Milk			
Fat	-	-	-
Sugar	-	-	-
Protein	0.13	0.06	0.04
Infant			
Birth time (days)	-	-	-
Sex (female)	-0.05	0.01	0.0004
Age (days)	0.004	0.001	0.005
Assay method (MIRIS)	0.06	0.01	0.7
	$F_{4,104} = 9.75, P < 0.0001$		
	$adjR^2 = 0.25$		

Estimated effects are presented for the infant mass at peak lactation in kilograms. For infant sex, estimated effects are presented for females and for the assaying method, estimated effects are for MIRIS technique.

Table 5

Summary pattern of results from the present study. Main predictors of the age at first reproduction and consequences on milk synthesis, infant outcomes and females' ability to reproduce on the season following their first birth.

	Early Breeders	Typical breeders	Late breeders
	▼	▼	▼
Mother's Developmental Conditions	Favorable	Average	Challenging
Birth Timing	Early	Mid-season	Mid-season
Growth as Juvenile	Fast	Average	Slow
Dominance Rank	High	Middle	Low
Available Milk Energy	Low	High	Low
Energetic Density	High	High	Low
Yield	Low	High	High
Infant's Developmental Conditions	Challenging	Favorable	Combination
Infant Birth Timing	Late season	Mid-season	Early season
Infant Mass at Peak Lactation	Low	Average	Average
Maternal Dominance Rank	High	Middle	Low
Reproduction Subsequent Season	Reduced	High	Reduced



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