Immature development in wild Assamese macaques (*Macaca assamensis*)

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Summary

Relationships between adult attributes and lifetime fitness have been previously explored in numerous studies, but although many adult attributes diversify during childhood or even prenatally, and although lifetime fitness is driven by survival until maturation, the pattern of early development and its consequences for lifetime fitness have been studied to a much lesser extent. Consequently there are several fundamental knowledge gaps regarding the ultimate and proximate mechanism behind variation in phenotypes and survival during the developmental period. Play activity, for example, was repeatedly emphasized to be the behavioural hallmark of mammalian development, and early theories about the evolution and function of play date to the 1870s. However, our current knowledge about the costs and benefits and the evolution of play is still marginal, and current theories about the evolution of play are based on the largely untested assumptions that play benefits motor skill acquisition, or that the developmental costs and benefits of play are rather negligible. Similarly, epigenetic prenatal maternal stress effects on offspring phenotype with considerable long-term consequences on adult phenotype have been well known for several decades even in humans, but the debate whether and how these effects may be evolutionary adaptive or maladaptive is still in its infancy, with the most prominent theory basing on largely untested assumptions that may hardly apply to natural conditions. Also, the existence of differentiated male-immature relationships even in some promiscuous mammals was shown a long time ago, but whether and how these relationships may benefit the development of the immature is still not well understood.

This thesis aims to fill some fundamental knowledge gaps on these topics by investigating the causes and consequences of variation in immature development in wild Assamese macaques (*Macaca assamensis*) with particular focus on immature growth. Growth is a central aspect of early development and the entire life history of an organism, and variation in growth rate may have strong consequences for life history and lifetime fitness. Growth is, therefore, assumed to be under strong positive selection and of high ontogenetic priority. Growth rates are highly plastic even within species, which may basically be caused by starvation avoidance in reaction to reduced energy availability, resource allocation to other, size-independent fitness traits and/or time constraints on maturation caused by a predictable increase in adult mortality. This thesis will address all of these possibilities. For this purpose, I measured monthly body sizes of all immatures of the group noninvasively via photogrammetry, collected behavioural data including detailed records of play behaviour on 17 immatures from birth onwards, recorded the first occurrences of 38 gross motor skills for each of these immatures, collected pre- and postnatal maternal faecal samples of all mothers for faecal glucocorticoid metabolite analysis and roughly assessed immature immune function from daily records of visible signs of eye infection during a two

month outbreak of conjunctivitis. Additionally, monthly food availability data which are part of the log-term field project were integrated into the analysis.

First I tested the two most prominent hypotheses about the costs and benefits of play. The “surplus resource”-hypothesis bases on the largely untested assumption that play is never performed at the expense of growth but uses only surplus energy which remains after investment in growth such that the developmental costs of play are negligible. Previous studies have shown positive correlations between play and growth rates, but since these studies failed to control for energy intake, these positive relationships may be entirely mediated by energy intake. The “motor skill”-hypothesis postulates that locomotor play benefits the individual by accelerating motor skill acquisition, but also this assumption was never adequately tested since previous correlational studies did not control for reversed causality, that is, better motor skills may enable higher play rates. My results on Assamese macaque immatures contradict the “surplus resource”-hypothesis and support the “motor skill”-hypothesis. I show first-time evidence that after controlling for food availability, investment in locomotor play is strongly at the expense of growth and probably increases age at maturation. Additionally, locomotor play entails benefits by accelerating motor skill acquisition as revealed by a time-series analysis. Within this pattern, growth rates and the proportion of time spent in locomotor play were also constrained by food availability and influenced by the sex of the offspring. Males invested increasing food availability primarily in play in order to achieve faster motor skill acquisition and females in growth in order to achieve faster maturation, which may correspond to their adult sex roles.

Next I explored the effects of prenatal maternal stress (PreGC, in terms of faecal glucocorticoid metabolite level) on offspring phenotype. Two prominent theories were proposed to explain the long-term effects of PreGC or early adversity on offspring phenotype, which both predict accelerated reproduction and thus growth in reaction to predicted reduced life expectancy (“predictive adaptive responses”, PAR). Both theories differ in the mechanism of how offspring may predict its life expectancy. The “external PAR”-hypothesis assumes PreGC to inform the offspring about adverse prenatal environmental conditions which predict similar conditions during its adult life, but the applicability of this assumption to long-lived species and/or unpredictable environments has been questioned. The “internal PAR”-hypothesis postulates that early life adversity may result in adverse somatic states throughout life, which enables the offspring to predict its life expectancy from its current somatic state without reference to an external environmental forecast. Studies which test between these hypotheses are currently lacking which may be due to the difficulties that emerge from the largely identical predictions. My analyses reveal that in my study population, PreGC is negatively correlated to prenatal food availability and postnatal immune function and positively correlated to offspring growth and body size. The effects on offspring phenotype remained also after controlling for potentially confounding postnatal variables like postnatal maternal physiological stress, maternal caretaking style, food availability and investment in play. Since Assamese macaques are long-lived and evolved and live in a highly unpredictable environment, the PreGC-effects on offspring phenotype are not only in support of a PAR but in particular of the “internal PAR”-hypothesis because external

PARs would be highly dysfunctional and maladaptive under such conditions and can therefore be excluded.

Collectively the current evidence on the relationship between PreGC and offspring growth is highly inconsistent and ranges from positive to negative effects even within the same species which has hampered broader generalizations. Hence in a next step, I developed a novel parsimonious framework that integrates different competing hypotheses and explains the entire range of observed effects. This framework postulates that prenatal maternal exposure to environmental stress results in a) reduced maternal investment and thus reduced extrinsic offspring growth during gestation and lactation (but not after lactation), and b) elevated PreGC-levels which epigenetically increase the intrinsic offspring growth rate. Thus if both processes coincide, they may largely cancel each other out during the period of maternal dependence while the growth rate after lactation is unaffected by maternal investment and may thus reflect the prenatally increased intrinsic growth rate only, ultimately resulting in overall accelerated growth.

I tested these predictions in a large-scale comparative analysis of published data across mammals (88 studies on 11 species ranging from rodents to ungulates and primates) and by analysing data from my field project. The results strongly supported my predictions but also revealed an unpredicted additional effect of gestational timing of maternal stress exposure. In the comparative analysis, early-gestational stress exposure resulted in unaffected offspring growth rates during gestation and lactation and increased growth rates after lactation, which was in accordance with my predictions. Prenatal stress exposure during the second half of gestation, however, leads to reduced offspring growth rates during gestation and lactation and unaffected growth rates after lactation, which resembles my predictions of reduced maternal investment effects and suggests that PreGC-effects on offspring growth are limited to the first half of gestation. Interestingly, all these results were independent of the species. The results of early-gestational maternal stress are also reflected in my results on Assamese macaques. Further analyses suggest that the “unaffected” growth rate during lactation is most likely the result of the combined, counterbalancing effects of increased PreGC and reduced maternal investment.

In my fourth study I investigated the pattern of male-immature relationships in Assamese macaques and whether and how they may benefit the immature. Assamese macaques are highly promiscuous, but it was previously shown that they still form differentiated male-immature bonds which partly reflect paternity. Building on that, I found that male-immature bonds are maintained by the immature and last beyond weaning and thus beyond the period of high infanticide risk. Immatures seek the proximity of their preferred male in particular if their mother is absent and if other unpreferred males are present, suggesting that male-immature bonds provide protection for the immature. The rate of mild harassment the immature received from other group members is not affected by the presence of the preferred male though, but the strength of the male-immature relationship is positively correlated to the agonistic support the immature receives from the male. How this support benefits immature development and/or fitness remains unresolved and is open to future research.

In summary, my results provide first time evidence for several fundamental questions on offspring development. I tested basic assumptions of prominent hypotheses on the evolution of play and confirmed the “motor skill”-hypothesis by showing time-series causality but rejected the basic assumption of the “surplus resource”-hypothesis by showing a resource allocation trade-off between investment in play and investment in growth. These novel findings may bring about a new hypothesis of the evolution of play which may coherently explain both within- and between-species variation in play rates via the relationship between the respective costs and benefits of play. I tested for the first time between competing hypotheses on epigenetic prenatal stress effects and provided results in support of an internal, somatic state-based PAR. I further provided and tested a novel integrative framework for prenatal stress effects on offspring growth which explains the previously highly inconsistent results and provides an entirely new perspective on the adaptive value of PreGC-effects. In particular, it contrasts the current perspective by suggesting that the short-term adaptive PreGC-effect is reflected in *unaffected* offspring growth rates during the period of (reduced) maternal investment whereas negative correlations between PreGC and offspring growth result from the *absence* of PreGC-effects on offspring growth.

Chapter 1:

General introduction

Important predispositions for mammalian adult attributes develop during childhood or even prenatally. Across animals, a key feature of immature development with strong consequences for reproduction and survival is physical growth (Stearns 1992; Kappeler and Pereira 2003; Brown et al. 2004; Dmitriew 2011; Jones 2011; Pontzer et al. 2014; Sibly et al. 2014). Embedded in the life history of an individual, mammalian growth rate may be influenced by resource availability, survival rate or resource allocation trade-offs, which may relate to other childhood characteristics like play for skill acquisition or parental care (Clutton-Brock 1991; Pereira and Fairbanks 2002; Pereira and Leigh 2003; Burghardt 2005; Maestripieri and Mateo 2009; Gubernick 2013). Additionally, early life adversity may affect growth rates either immediately ("developmental constraints") or via long-term recalibration of developmental trajectories to optimize an organism's life history ("predictive adaptive response", PAR; Maestripieri and Klimczuk 2013; Hanson and Gluckman 2014). Prenatal maternal stress in response to prenatal adverse conditions can have strong and long-lasting effects on diverse aspects of offspring development including growth rates (Hanson and Gluckman 2014; Moisiadis and Matthews 2014a, b). Such effects may be linked either to variation in maternal physiological stress (in terms of glucocorticoid levels) or to maternal investment or to both (Maestripieri and Mateo 2009; Maestripieri and Klimczuk 2013; Sheriff and Love 2013). Currently, there are several fundamental gaps in our knowledge of whether and how immature growth may be influenced by these features, because the evidence is inconsistent or lacking. In this study I aim to identify and partly fill some of the most essential gaps by analysing original data on wild immature Assamese macaque (*Macaca assamensis*) and by comparative analysis of published data across mammals.

1.1 A short introduction to life history theory

Life history theory aims to explain

> *"the variation in timing of fertility, growth, developmental rates, and death of living organisms, as well as events directly tied to these parameters" (Hill 1993, p.78)*
> *and*
> *"the strategies that organisms use to allocate their limited time and energy to the various activities that comprise their life cycle"*
> *(Del Giudice and Belsky 2011, p.155).*

Life history theory lies at the heart of evolutionary theory as it explains some of the most pronounced variations in phenotypes (Stearns 1992; Kappeler et al. 2003). Placental mammals share a uniform basic life cycle characterised by placental gestation, viviparity and maternal lactation. At the same time they show enormous variation in life span, adult body size, age at first reproduction and reproductive rate, and this variation is also reflected within the primate order (Kappeler et al. 2003). Mammalian life spans range from about one year in some rodents to up to 100 years in humans, elephants and whales, thus spanning a difference of two magnitudes, and similar ranges are found for body size and reproductive rate (Kappeler et al. 2003; Robeck and Monfort 2006; Sibly and Brown 2007; Keane et al. 2015). Likewise, age at maturation varies from several weeks in some rodents and insectivores to 10 years or more in elephants, and some primates and whales (Millar and Zammuto 1983; Harvey and Zammuto 1985; Wich et al. 2004; Robeck and Monfort 2006; Mumby et al. 2015). Notably, these variations are not limited to between-species comparisons but to some extent also occur within species (Stearns 1992; Dmitriew 2011).

The observed variation in life history traits is not randomly distributed but correlated to each other. As early as 350 BC, Aristotle noted that

> *"The reasons for some animals being long-lived and others short-lived and, in a word, causes of the length and brevity of life call for investigation … As a matter of fact … it is a general rule that the larger live longer than the smaller…".*
> *(Aristotle, "On Longevity and Shortness of Life")*

Although Aristotle's further conclusions proved wrong, this basic size-longevity relationship is nowadays well established across animals and within mammals and forms the backbone of life history theory (Stearns 1992; Kappeler et al. 2003; Healy et al. 2014). Apart from being larger, long-lived mammals also tend to have higher ages at first reproduction and lower reproduction rates, and these relationships remain after controlling for adult body size (Harvey and Zammuto 1985; Stearns 1992; Kappeler et al. 2003; Healy et al. 2014). These associations distribute life histories along a fast-slow continuum, with small adult body sizes, low ages at sexual maturity, short life spans and high reproduction rates at the fast end and vice versa at the slow end (Stearns 1992; Kappeler et al. 2003; Healy et al. 2014; Sibly et al. 2014). This is surprising because body size is positively correlated to fecundity and/or offspring quality as well as mating success and survival (Dmitriew 2011), hence the most adaptive strategy would be to maximise growth, maturation rate, body size, reproduction rate, and life span all at the same time ("Darwinian demon", Law 1979). The observed fast-slow continuum indicates that such a strategy is constrained by trade-offs in resource allocation to either growth and survival or reproduction which fundamentally limits life history options (Stearns 1992). Along the fast-slow continuum, the position of a species is determined by its

evolutionary environment. Reduced life expectancy due to increased mortality risk leads to time constraints on reproduction, resulting in accelerated reproduction and faster optimal paces of life (Stearns 1992; Healy et al. 2014).

Increased mortality risk and reduced life expectancy are associated with increased uncertainty of future reproduction (Clutton-Brock 1984; Stearns 1992). Faster paces of life are therefore also characterized by a resource allocation shift from future to current reproduction (Stearns 1992). This can be viewed as a shift towards a "putting all eggs in one basket" strategy and thus an increase in risk-taking which is also reflected in behavioural, or personality, traits (Stearns 2000; Ghalambor and Martin 2001; Wolf et al. 2007; Réale et al. 2010; Del Giudice and Belsky 2011; Jones 2011; Quinn et al. 2011). In general, an increasing pace of life is associated with increasing activity and risk-taking, and in particular with increasing aggression, boldness and dominance seeking, lower sociability and reduced parental effort (Réale et al. 2007; Wolf et al. 2007; Réale et al. 2010; Del Giudice and Belsky 2011). Variation in physical and also behavioural traits can be driven by variation in levels of, or responsiveness to, hormones like steroids (e.g. androgens and glucocorticoids) and thus by differences in neurophysiology (Stearns 1992; Finch and Rose 1995; Wingfield 2005; Weinstock 2008; Balthazart et al. 2012; Wingfield 2013).

In recent decades, life history theory has strongly benefited from the integration of ecological influences on within-species phenotype variation and the (re-)discovery of adaptive phenotype plasticity (Roux 1881; Bradshaw 1965; Via et al. 1995; Schlichting and Pigliucci 1998; Hanson and Gluckman 2014). This led to the discovery of epigenetic regulation of phenotypes and consequently the development of the eco-evo-devo concept (Reik et al. 2001; Bird 2002; Weaver et al. 2004; Pigliucci 2007; Abouheif et al. 2014; Gilbert et al. 2015). Epigenetic effects explain phenotype variation that is not driven by fixed, genetically encoded information but by altered transcription of this genetic information (e.g. via altered DNA-methylation), and numerous epigenetic pathways were detected which in part can alter phenotypes over multiple generations (Jones and Takai 2001; Bird 2002; Lummaa and Clutton-Brock 2002; Weaver et al. 2004; Tobi et al. 2009; Burton and Metcalfe 2014; Gapp et al. 2014; Hanson et al. 2014; Teh et al. 2014). One of the most studied pathways relates to the maternal stress response, which not only alters maternal behaviour and metabolism (Becker et al. 2002) but also influences offspring phenotype due to the epigenetic effects during gestation that are associated with foetal exposure to maternal glucocorticoids (Gapp et al. 2014; Hanson and Gluckman 2014; Moisiadis and Matthews 2014a, b). The stress response is activated in response to many environmental and social stressors (Becker et al. 2002; Wingfield 2005; Sheriff and Love 2013; Wingfield 2013) but can be socially buffered (Sachser et al. 1998; DeVries et al. 2003; Engh et al. 2006a; Kikusui et al. 2006; Charuvastra and Cloitre 2008; Young et al. 2014; Hennessy et al. 2015). Various effects of prenatal maternal stress on offspring phenotype that last into adulthood or even over multiple generations have been shown, but it is still debated whether these effects reflect an adaptive or maladaptive outcome of the maternal stress response (Maestripieri and Klimczuk 2013; Sheriff and Love 2013; Burton and Metcalfe 2014; Hanson and Gluckman 2014; Veru et al. 2014).

Two central life history traits are age and body size at maturation, which are both linked to growth rate during childhood (Stearns 1992; Kappeler and Pereira 2003; Brown et al. 2004; Dmitriew 2011; Jones 2011; Pontzer et al. 2014; Sibly et al. 2014). Lifetime reproductive success is primarily driven by survival until reproduction which is affected by both mortality rate during childhood and age of maturation, i.e. increasing time periods between birth and first reproduction (Roff 1980; Stearns 1992; Jones 2009; Dmitriew 2011). Thus, independent of the optimal pace of life, growth rates are under strong positive selection to minimize the age at maturation and maximize body size, and should therefore be of high ontogenetic priority (Dmitriew 2011). However, realised mammalian growth rates are rarely the maximal physiological growth rates, and since periods of growth and reproduction are in general temporally decoupled in mammals, this difference cannot be attributed to immediate resource allocation trade-offs between growth and reproduction (Dmitriew 2011). Even more puzzling, the total energy expenditure especially of primates is strongly reduced compared to other mammals which results in particularly reduced growth rates (Jones 2011; Pontzer et al. 2014).

In the following sections I will discuss several aspects which in combination may set optimal growth rates below the physiologically possible maximum and explain variation in mammalian growth rates.

1.2 Causes of variation in general growth rate

General growth rates are influenced by basically three mechanisms, which are starvation avoidance, time constraints, and resource allocation trade-offs (Stearns 1992; Janson and van Schaik 2002; Dmitriew 2011). First, increased growth rates may directly increase immature starvation risk and thus mortality risk in case of insufficient energy intake (Janson and van Schaik 2002; Dmitriew 2011). Increased growth-related (or energy-intake-related) mortality risk, therefore, generally leads to reduced growth rates to avoid starvation and increase survival until reproduction (Janson and van Schaik 2002; Dmitriew 2011). Second, an increase in immature mortality that is not (e.g. predation risk) or negatively (size-dependent mortality) related to growth rate results in time constraints on development and will accelerate growth to reduce length of childhood and increase survival until reproduction (Janson and van Schaik 2002; Dmitriew 2011). If increased mortality is not restricted to childhood, but reduces life expectancy in general, then time constraints will additionally act on lifetime reproduction and thus additionally accelerate growth to accelerate maturation and reproduction (Dmitriew 2011; Nettle et al. 2013; Healy et al. 2014). Third, resource allocation to growth may be traded-off against investment in other, size-independent fitness traits associated with survival, health, sexual signals, or competitive ability (Mangel and Stamps 2001; Dmitriew 2011).

1.2.1 Energy intake and starvation risk

The most obvious cause of growth rate reduction derives from developmental constraints due to reduced energy intake which limits the amount of resources that can be allocated to growth. It was shown for numerous species that growth rates are reduced in reaction to reduced energy intake or food availability, which can be viewed as an immediate adaptive response to avoid starvation (Dunham 1978; Metz et al. 1980; Jones 1986; Wiggins 1990; Lindell 1997; Bergallo and Magnusson 2002; Karakaş et al. 2005; in primates: Garcia et al. 2009; Onyango et al. 2013). Energy intake is strongly related to food availability which varies in the long-term with climate conditions along latitudinal or altitudinal clines and their related ecosystems, and in the short term with seasonal or stochastic environmental changes (Dmitriew 2011; Heesen et al. 2013; Hille and Cooper 2015). In mammals, energy intake of the offspring is also predicted by maternal investment during gestation and lactation which can vary with maternal energy intake and maternal physical condition but also with offspring sex and between species (Roberts et al. 1985; Bowen 2009; Hinde 2009; Hinde et al. 2009; Hinde and Milligan 2011; Hinde 2013; Hanson and Gluckman 2014). Additionally, maternal investment and condition can be reduced in reaction to prenatal maternal exposure to environmental stressors (Laurien-Kehnen and Trillmich 2004; Tygesen et al. 2008; Munoz et al. 2009; Hinde and Milligan 2011; Klaus et al. 2013; Sheriff and Love 2013; Zhu et al. 2013; Hanson and Gluckman 2014). Prenatal food restriction in rats for example leads to reduced postnatal mammary gland size, and heat stress in domestic cows leads to reduced postnatal mammary gland size and milk yield (Tao and Dahl 2013; Wattez et al. 2014).

Energy intake of immatures is also affected by constraints on foraging behaviour. Since foraging increases exposure to predators and reduces vigilance, constrained foraging results primarily from increased predation risk (Abrams 1991; Dmitriew 2011; Carthey and Banks 2015). Predation risk leads to a trade-off between foraging and survival which ultimately results in reduced foraging (particularly in habitats with high predation risk) and increased spatial and temporal predator avoidance e.g. by staying in safer places like burrows or trees or shifting to nocturnality (Anholt and Werner 1995; Cowlishaw 1997; Metcalfe et al. 1999; Heithaus and Dill 2002; Dmitriew 2011; Healy et al. 2014). Alternatively, mammals can directly reduce predation risk by communal vigilance and defence via parental care and gregariousness (van Schaik 1983; Wrangham and Rubenstein 1986; Elgar 1989; van Noordwijk et al. 1993; Nunn and van Schaik 2000; Heithaus and Dill 2002; Caro 2005; Silk 2007; Shultz et al. 2011; Micheletta et al. 2012; Stankowich et al. 2014; Mahr et al. 2015; Josephs et al. 2016).

In addition, individual energy intake is also affected by (contest and/or scramble) competition for food resources which increases with population density or group size and represents a drawback of gregariousness (Clutton-Brock and Harvey 1977; van Schaik 1983; Wrangham and Rubenstein 1986; Chapman and Chapman 2000; Kappeler and Fichtel 2015; Markham et al. 2015). Especially dyadic contest competition encounters are decided by physical strength which is strongly related to body size (Clutton-Brock et al. 1979; Austad

1983; Hand 1986; Preuschoft and van Schaik 2000; Keil and Watson 2010; Mohamad et al. 2010); hence energy intake of immatures in particular can be highly constrained by competition with older conspecifics. It was shown for mammals, however, that third-party interventions in favour of the looser of a conflict can reverse the outcome of the current and even of future purely dyadic encounters with the same opponent (Hand 1986; Preuschoft and van Schaik 2000; Bissonnette et al. 2009; Berghänel et al. 2011b). In mammals, and particularly in primates, such interventions are frequently based on social bonds between the supporting and the supported individual (Feh 1999; Schino 2007; Berghänel et al. 2011a; Ostner and Schülke 2014).

In mammals, strong mother-offspring bonds provide the main source of support for immatures (Smuts et al. 1987; Silk 2003; Altmann and Alberts 2005; Broad et al. 2006; Silk 2007; Garcia et al. 2009; Maestripieri and Mateo 2009). Alternatively support may also derive from father-offspring bonds where the benefits for the inclusive fitness of the male are explicit (Trivers 1972; Smuts and Gubernick 1992; Maestripieri 1998; Alberts and Fitzpatrick 2012). Surprisingly, differentiated male-infant bonds are also found in highly promiscuous mammals like many primates where fatherhood should be largely concealed and unknown (Trivers 1972; Díaz-Muñoz 2011; Alberts and Fitzpatrick 2012). It was shown that despite high levels of promiscuity, male-immature bonds may still reflect some degree of paternity in such species (Moscovice et al. 2009; Díaz-Muñoz 2011; Langos et al. 2013; Ostner et al. 2013) which is eventually mediated by paternal kin discrimination (Pfefferle et al. 2014a; Pfefferle et al. 2014b) or male-female bonds (Palombit et al. 1997; Moscovice et al. 2010; Massen and Sterck 2013; Ostner et al. 2013). Despite some evidence, it still remains largely unknown whether these bonds primarily provide support and competitive benefits for the immatures (Buchan et al. 2003; Charpentier et al. 2008; Moscovice et al. 2009; Huchard et al. 2013; Langos et al. 2015) or whether they serve male interests e.g. by increased access to infants used as tools in social bonding with other adult males (Ogawa 1995; Paul et al. 1996; Henkel et al. 2010) or females (Smith and Whitten 1988; Smuts and Gubernick 1992; Muller and Thompson 2012).

1.2.2 Time constraints on development

Time constraints on development can result from increased mortality during childhood and/or overall reduced life expectancy (Dmitriew 2011; Nettle et al. 2013; Healy et al. 2014). If unavoidable mortality during childhood, e.g. caused by predation, increases, the immature may accelerate growth to reduce length of childhood and increase survival until reproduction (Stearns 1992; Janson and van Schaik 2002; Jones 2009; Dmitriew 2011). Similarly size-dependent mortality, due to e.g. size-dependent predation risk or winter survival, may accelerate growth, with the latter one being additionally time constrained with decreasing time between birth and winter (or other seasonal constraints, Dmitriew 2011; Dantzer et al. 2013). Accelerated growth may also result from reduced total life expectancy which leads to time constraints on reproduction and should therefore cause accelerated growth, maturation and reproduction (Dmitriew 2011; Nettle et al. 2013; Healy et al. 2014).

Reduced life expectancy can result from increased predation risk, but also from adverse somatic states which may result from the long-term effects of developmental constraints and/or adverse adult environments (Maestripieri and Klimczuk 2013; Nettle et al. 2013; Del Giudice 2014a; Hanson and Gluckman 2014; Healy et al. 2014).

The last point is most evident in annual species in seasonal habitats where lifetime expectancy decreases with increasing date of birth and late birth frequently leads to accelerated growth and reproduction (Dmitriew 2011). While this exact example may rarely apply to mammals, they may still follow the same basic principle. Across mammals, growth, maturation and reproduction are particularly slow (controlled for body size effects) in primates, bats and naked mole rats which also face the lowest predation risk due to their lifestyle (Jones 2011; Healy et al. 2014; Pontzer et al. 2014; Grimm 2015). Primates as an Order tend to have an arboreal and gregarious lifestyle (Jones 2011), bats are not only volant but also often form roost groups in burrows or caves (Kunz and Fenton 2003; Healy et al. 2014), and naked mole rats are gregarious and spend most of their time underground (Healy et al. 2014; Williams and Shattuck 2015). Especially in primates, pace of life may be additionally slowed down by highly unpredictable food availability and thus increased immature starvation risk, and this slow pace of life is even reflected in strongly reduced total energy expenditure compared to other mammals (Janson and van Schaik 2002; Jones 2011; Pontzer et al. 2014).

Variation in the predicted life expectancy may influence immature growth rates not only on evolutionary time scales but also within a current population due to phenotypic plasticity (Dmitriew 2011). This raises the question how and under which circumstances the immature may be able to predict its future life expectancy and respond to it with organizational phenotype recalibration (Nettle et al. 2013; Del Giudice 2014a; Del Giudice 2014b; Hanson and Gluckman 2014; Nettle and Bateson 2015). Two different epigenetic hypotheses have been proposed to explain such organizational predictive adaptive responses (PAR). The internal PAR-hypothesis argues that developmental constraints during gestation and childhood may result in adverse somatic states which will transfer into adulthood and inevitably result in reduced life expectancies (Nettle et al. 2013; Nettle and Bateson 2015). The external PAR-hypothesis claims that elevated prenatal maternal glucocorticoid levels inform the offspring about adverse prenatal environmental conditions which predict future environmental conditions particularly during adulthood, thus enabling the offspring to recalibrate its phenotype to optimally match this future environment (Hanson and Gluckman 2014).

Both the internal and the external PAR-hypothesis make largely identical predictions, namely accelerated growth, maturation and reproduction in reaction to reduced life expectancy, which makes it difficult to differentiate between them (Nettle et al. 2013; Nettle and Bateson 2015). However, they differ fundamentally in their preconditions to be functional and thus adaptive. External, but not internal PARs rely strongly on high correlations between prenatal and future environments especially during adulthood and thus high environmental predictabilities (Kuzawa and Quinn 2009; Nettle et al. 2013; Burton and Metcalfe 2014; Del Giudice 2014b; Nettle and Bateson 2015). Therefore the applicability

of the external PAR-hypothesis to long-lived species like many primates was questioned since environmental predictability may strongly decrease with increasing time gaps (Nettle et al. 2013; Nettle and Bateson 2015), and longevity was argued to be particularly related to highly unpredictable environments due to an adaptive risk-spreading strategy in reaction to highly variable immature survival (Janson and van Schaik 2002; Jones 2011; Pontzer et al. 2014).

Numerous studies have explored the effects of prenatal maternal stress or early life adversity on offspring development (Hanson and Gluckman 2014; Moisiadis and Matthews 2014a, b). However, the results of these studies are currently inconclusive since especially the effects on offspring growth rate are highly variable, ranging from strongly positive (Patin et al. 2002; Hauser et al. 2007; Schöpper et al. 2012; Dantzer et al. 2013) to strongly negative effects (Patin et al. 2002; Hauser et al. 2006; de Vries et al. 2007; Emack et al. 2008) even within the same species. Additionally, studies which test these hypotheses on wild populations facing solely natural stressors and environmental predictabilities are rare and completely lacking for long-lived animals (Hauser et al. 2008; Mateo 2009; Dantzer et al. 2013; Maestripieri and Klimczuk 2013; Sheriff and Love 2013; Lehrner et al. 2014; King and Laplante 2015).

1.2.3 Trade-offs between time constraints and starvation risk

It is obvious from the previous arguments that increased mortality risk can lead to both accelerated growth due to time constraints on development and/or decelerated growth to reduce growth-related mortality due to starvation risk, which can result in a trade-off between both (Janson and van Schaik 2002; Dmitriew 2011). Such trade-offs may not only result from different but also from the same source of mortality. Predation risk, for example, may not only directly affect mortality through predation but also indirectly through constrained foraging, with the first resulting in time constraints and the second in increased starvation risk (Anholt and Werner 1995; Metcalfe et al. 1999; Heithaus and Dill 2002). Under such circumstances the optimal growth rate might reflect a compromise between these two forces and may be ultimately unaffected if both effects compensate each other (Dmitriew 2011). More importantly, such a trade-off may also apply to constrained energy intake alone, where starvation avoidance will decelerate growth, but mortality-related time constraints may set the optimal growth rate above the one that is needed to minimalize starvation risk and mortality.

1.2.4 Resource allocation to size-independent fitness traits

Periods of growth and reproduction are largely temporally separated in mammals, hence growth rates cannot be influenced by immediate resource allocation trade-offs between investments in growth and reproduction. Investment in growth may, however, be traded off against resource allocation to maintenance and repair (Stearns 1992; Dmitriew 2011; Pontzer et al. 2014). They may also be traded off against investment into size-independent offspring attributes which may increase fitness by increasing survival and/or

reproductive success (Dmitriew 2011). One such attribute may be sexual signals like sexual ornaments (Ohlsson et al. 2002; Naguib and Nemitz 2007), but it was argued that such signals must be honest and condition-dependent and may thus be rarely independent from body size (Reynolds and Gross 1992; Scheuber et al. 2003; Dmitriew 2011). Another attribute may be immune function which has been shown to be highly energy intensive but may also increase survival (Mangel and Stamps 2001; Brzęk and Konarzewski 2007).

Another size-independent fitness trait is motor skills, which may increase both survival and reproductive success and may be acquired via investment into energy-intensive locomotor play (Bekoff 1988; Byers and Walker 1995) that may be traded off against growth. Motor skills may increase size-independent flight-/fight-competence which is beneficial in sexual or food contest competition as well as during predatory attacks, ultimately increasing reproductive success and survival (Bekoff 1988; Nunes et al. 2004a; Cameron et al. 2008; Fagen and Fagen 2009; Pellegrini 2009; Blumstein et al. 2013). Social locomotor play may also increase social competence which can translate into increased reproductive success via adult social bonding and coalitionary support (Pellegrini 2009; Silk et al. 2009; Graham and Burghardt 2010; Schülke et al. 2010). Despite the fact that play is the hallmark of childhood in many mammals, particularly in primates, it has rarely been studied so far (Graham and Burghardt 2010). It is widely assumed that investment in locomotor play accelerates motor skill acquisition (Bekoff 1988; Byers and Walker 1995), but previous studies hardly found any benefits of play. This led to the conclusion that the benefits of play may be rather minor or negligible (Martin and Caro 1985; Graham and Burghardt 2010), and that play is of lower ontogenetic priority than growth and will never be performed at the expense of growth but will only use surplus energy which remains after investment in growth (Martin 1982; Bekoff and Byers 1992; Burghardt 2005; Graham and Burghardt 2010). Thus, the impact of locomotor play on motor skill acquisition and growth remains largely unexplored, which represents a fundamental gap in our understanding of life history evolution (Martin and Caro 1985; Byers and Walker 1995; Fulton et al. 2001; Graham and Burghardt 2010).

1.3 Causes of variation in growth rate over age

Growth rates may not only vary between individuals and species but may also change with age within an individual. In the simplest case growth rates vary with energy intake, but growth rates can also be systematically increased due to compensatory or accelerated growth (Dmitriew 2011). Compensatory (or catch-up) growth can be found in reaction to periods of constrained growth and ultimately result in unaffected overall growth rates and reduced or eliminated differences in body sizes at maturation (Dmitriew 2011). Accelerated growth, in contrast, is not (necessarily) preceded by periods of constrained growth and aims at increasing overall growth rates and results in increased body sizes at maturation and/or accelerated maturation. A typical example of accelerated growth is adolescent growth spurt, but accelerated growth may also occur in reaction to increased time constraints on development and/or reproduction (Dmitriew 2011). Compensatory as well as accelerated growth has been shown for many vertebrate species including humans and other mammals

(Wilson and Osbourn 1960; Sigg et al. 1982; Boersma and Wit 1997; Roseboom et al. 2000; Hamada and Udono 2002; Ali et al. 2003; Onyango et al. 2013; Sanna et al. 2015).

Models suggest that compensatory or accelerated growth should only occur in case of time constraints on development (Dmitriew 2011). Across mammals, slow maturation and longevity are related to (and enabled by) strongly reduced mortality due to reduced predation risk and thus low time constraints on development (Janson and van Schaik 2002; Jones 2011; Healy et al. 2014; Pontzer et al. 2014). This makes the evidence for compensatory or accelerated growth in long-lived species like humans and many other primates puzzling. Increasing growth rates are also associated with long-term costs due to qualitative attributes, including increased somatic deformations and risk for coronary heart diseases as well as reduced functional efficiency, telomere lengths and life spans (Boersma and Wit 1997; Roseboom et al. 2000; Mangel and Stamps 2001; Metcalfe and Monaghan 2001; Hales and Ozanne 2003; Fisher et al. 2006; Dmitriew 2011; see also Marcil-Ferland et al. 2013), thus it is hard to tell whether some cases of compensatory growth may in fact be internal PARs in reaction to developmental constraints (Nettle et al. 2013; Nettle and Bateson 2015).

1.4 The Assamese macaque: a super-model species

In the previous section I outlined the theoretical background and current evidence on the evolution of different growth rates. I have also highlighted some fundamental knowledge gaps, namely a) the costs and benefits of play, b) the benefits of male-immature bonds for the immature in highly promiscuous species, and c) the inconsistent evidence for PARs and particularly the fundamental lack of studies on wild long-lived mammals in consideration of environmental predictabilities. Wild Assamese macaques provide a good study system for all of these questions since they a) show high rates of immature play and an arboreal lifestyle where increased motor skills may be particularly beneficial, b) are group-living and highly promiscuous but form differentiated male-immature bonds, and c) are long-lived, slow-developing mammals which evolved and live in a highly unpredictable environment, thus providing a critical test case for the PAR-hypotheses.

Assamese macaques are cercopithecine primates native to South and Southeast Asia. They live in multi-male multi-female groups with female philopatry and male dispersal from the natal group between late infancy and adulthood. Female Assamese macaques reach sexual maturity within 5–6 years (Fürtbauer et al. 2010), whereas males show delayed maturation (fully grown ~9–10 years, personal observation). Average gestation length is 164 days and interbirth interval is bimodally distributed around 14 and 23 months (Fürtbauer et al. 2010; Ostner et al. 2013). Assamese macaques are highly arboreal spending about 90% of their activity time off the ground (Schülke et al. 2011). Typical for a primate species, immatures play frequently both solitarily and socially (personal observation).

Assamese macaques evolved and live in a highly unpredictable environment. Environmental conditions have been shown to be highly unpredictable in Southeast Asian forests in general (van Schaik and Pfannes 2005) as well as in in our study area (Heesen et al.

2013) where year-to-year predictabilities were very low (for food abundance: r = 0.08, p = 0.88, over 7 years; for rain fall: r = -0.09, p = 0.86, over 8 years). However, rain fall and consequently (but to a lesser extent) also food availability are seasonal and thus roughly predictable within years (Kumsuk et al. 1999; Grassman et al. 2005; Borries et al. 2011; Heesen et al. 2013). Reproduction is strictly seasonal, and the birth season lasts from April to July (Fürtbauer et al. 2010). Female reproduction is condition dependent, i.e. the probability of conception increases with food availability and female condition, and female condition is particularly reduced in lactating females (Heesen et al. 2013), hence increased maternal investment may directly be traded off against future reproduction.

Assamese macaques are highly promiscuous, but males show differentiated and stable spatial relationships with immatures which are to some degree related to paternity. Male mating and paternity skew are low (Ostner et al. 2011; Sukmak et al. 2014), and females conceal ovulation from males and show high mating synchrony (Fürtbauer et al. 2011a; Fürtbauer et al. 2011b). Despite this high level of promiscuity, males form differentiated spatial relationships with immatures which are related to paternity and spatial male-mother relationships around conception (Ostner et al. 2013). However it remains unknown whether these spatial relationships are maintained by the males or the infants, and whether they provide benefits to the immature.

1.5 Study aims and approaches

The general aim of this study is to advance our understanding of the evolutionary processes that drive variation in growth rates. In the previous sections I highlighted some essential open questions which refer to the evolution of play, male-immature bonds and prenatal maternal stress effects on offspring development, and argued that studying Assamese macaques in their natural habitat, and thus under a valid ecological setting, provide outstanding opportunities to address these questions. To investigate these topics, I collected behavioural data through detailed immature focal protocols, measured monthly body sizes noninvasively via photogrammetry, recorded the timing of the first observation of 38 different motor skills to calculate the age at first occurrence for each motor skill in each individual, collected pre- and postnatal maternal faecal samples of all mothers for faecal glucocorticoid metabolite analysis and recorded visible signs of eye infection on a daily basis during a two month outbreak of conjunctivitis to roughly assess immature immune function. Additionally I included monthly food availability data in my analysis which are part of the long-term field project and provided by Julia Ostner and Oliver Schülke.

In study 1 (**Chapter 2**) I explore the costs and benefits of energy-intensive locomotor play. In particular I investigate whether resource allocation to locomotor play is traded off against resource allocation to growth. Thereby I test the widely accepted but never directly tested “surplus resource”-hypothesis which proposes that investment in play is never performed at the expense of growth and uses surplus resources only because growth takes strong ontogenetic priority over play due to its crucial role in life history. Additionally I test

the also widespread but never adequately investigated hypothesis that investment in locomotor play may be beneficial by accelerating motor skill acquisition.

In study 2 (**Chapter 3**) I investigate the cause and consequences of prenatal maternal physiological stress (in terms of elevated prenatal glucocorticoid levels, PreGC) in wild Assamese macaques, thus providing first-time data on a wild long-lived mammal. I explore the relationship between prenatal food availability and PreGC, and how PreGC affects growth rates, body sizes, motor skill acquisition and immune function of the offspring. Since these offspring attributes as well as PreGC may also be related to postnatal maternal physiological stress levels and/or maternal caretaking style (Maestripieri and Mateo 2009; Del Cerro et al. 2010; Hinde and Milligan 2011; Sachser et al. 2013; Weinstock 2015), I will additionally test whether PreGC-effects on offspring phenotype may be mediated by these postnatal aspects.

In study 3 (**Chapter 4**) I aim at disentangling the highly inconsistent evidence of prenatal maternal stress effects on offspring growth across mammals, which ranges from highly positive to highly negative effects even within the same species. For this purpose I develop a new, integrative framework and test predictions derived from this framework in comparative tests of published data across mammals and by more detailed analysis of PreGC-effects on offspring growth in our study group.

Study 4 (**Chapter 5**) explores the pattern and function of male-immature bonds in our highly promiscuous study species. This study was conducted together with Christin Minge who was a diploma student under my supervision. We examine whether the pattern found in our group reflects male care or is better explained by alternative explanations like the “male mating effort”-hypothesis. We investigate how male-immature association may translate into benefits for the immature, and particularly whether bonded males provide agonistic support to the immature during conflicts.

Chapter 2

Locomotor play drives motor skill acquisition at the expense of growth: a life history trade-off

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Abstract

The developmental costs and benefits of early locomotor play are a puzzling topic in biology, psychology, and health sciences. Evolutionary theory predicts that energy-intensive behaviour like play can evolve only if there are considerable benefits. Prominent theories propose that locomotor play is (i) low-cost, using surplus energy remaining after growth and maintenance and (ii) beneficial as it trains motor skills. However, both theories are largely untested. Studying wild Assamese macaques, we combined behavioural observations of locomotor play and motor skill acquisition with quantitative measures of natural food availability and individual growth rates measured non-invasively via photogrammetry. Our results show that investments in locomotor play were indeed beneficial by accelerating motor skill acquisition but carried sizable costs in terms of reduced growth. Even under moderate natural energy restriction investment in locomotor play accounted for up to 50% of variance in growth, which strongly contradicts the current theory that locomotor play uses only surplus energy remaining after growth and maintenance. Male immatures played more, acquired motor skills faster, and grew less than female immatures, leading to persisting size differences until the age of female maturity. Hence, depending on skill requirements, investment in play can take ontogenetic priority over physical development unconstrained by costs of play with consequences for life history, which strongly highlights the ontogenetic and evolutionary importance of play.

Introduction

Growth is a key life history process in animal development with strong consequences for reproduction and survival (Stearns 1992; Kappeler and Pereira 2003; Brown et al. 2004; Dmitriew 2011; Jones 2011; Pontzer et al. 2014; Sibly et al. 2014). Life history theory proposes that under ecological constraints, resource allocation to growth is traded against concurrent investments in other processes and energy demanding activities (Stearns 1992; Brown et al. 2004; Jones 2011; Pontzer et al. 2014). One such activity characteristic for many immature vertebrates is play (Burghardt 2005; Graham and Burghardt 2010). Play generally is assumed to be of minor ontogenetic importance and thus not considered as a growth rate limiting factor (Brown et al. 2004; Graham and Burghardt 2010; Dmitriew 2011; Jones 2011; Sibly et al. 2014). However, the developmental costs and benefits and its significance in life history are largely unknown (Graham and Burghardt 2010). If play is performed at the expense of growth, it must be of key ontogenetic importance and should evolve only in case of considerable benefits. Here we aim at testing this hypothesis by investigating for the first time the relationship between investments in locomotor play and growth, and identifying the benefits of locomotor play, in an ecologically valid setting.

It is a longstanding assumption in biology and psychology that physical development takes strong ontogenetic and evolutionary priority over competence acquisition via play ("surplus resource hypothesis"; Graham and Burghardt 2010). Locomotor play has been shown to involve energy costs in mammals (Miller and Byers 1991; Pellegrini et al. 1998). However, the developmental costs of play are thought to be naturally buffered because only surplus resources remaining after maintenance and growth are allocated to play (Spencer 1872; Martin 1982; Bekoff and Byers 1992; Graham and Burghardt 2010), and resource allocation to play is developmentally cost-free and negligible for life history trade-offs. This hypothesis is indirectly supported (a) by findings that growth rates (in primates: Garcia et al. 2009; Onyango et al. 2013) and play rates (across mammals: Müller-Schwarze et al. 1982; Martin and Caro 1985; Espinosa et al. 1992; Sharpe et al. 2002; Nunes et al. 2004a; Cameron et al. 2008) increase with increasing food availability and (b) by the phylogenetic distribution of play since play probably originated when animals “had sufficient metabolic resources, and could accumulate [significantly] more energy than required for growth and maintenance” (Graham and Burghardt 2010, p. 404). Although many ontogenetic and evolutionary theories on early development and life history trade-offs build more or less explicitly on the surplus resource hypothesis (Martin 1982; Nunes et al. 2004a; Pellegrini et al. 2007; Pellegrini 2009; Graham and Burghardt 2010; Dmitriew 2011; Jones 2011), it has not been directly explored yet.

The main benefit of locomotor play is thought to be an acceleration of motor skill acquisition depending on the rate and/or intensity of play, which in turn may increase flight/fight competence (“motor training hypothesis”; Groos and Baldwin 1898; Bekoff 1988; Byers and Walker 1995; Maestripieri 1995; Nunes et al. 2004a; Pellegrini 2009; Graham and Burghardt 2010; Pellegrini et al. 2013). This assumption is the basis of health recommendations and development-stimulating measures (UNOSDP 2008; WHO 2011;

UNICEF 2012), but has not been adequately tested (Martin and Caro 1985; Byers and Walker 1995; Fulton et al. 2001; Graham and Burghardt 2010), and current evidence is indirect and inconclusive. Across mammals, it has been shown that sex differences in play correspond to the diverging needs of adults (Pereira and Fairbanks 2002; Maestripieri and Ross 2004; Cameron et al. 2008; Pellegrini 2009; Graham and Burghardt 2010), the peak of play activity matches the sensitive periods of motor brain areas (Byers and Walker 1995; Graham and Burghardt 2010), and early social play may predict later dominance relationships (Blumstein et al. 2013). However, the causality of correlations between locomotor play rate and motor skill level in mammals including humans (Nunes et al. 2004a; Fisher et al. 2005) remains unresolved, because enhanced motor skills may also enable higher play rates (Fulton et al. 2001; Wrotniak et al. 2006).

Our longitudinal study aims to fill these two fundamental gaps by directly investigating whether locomotor play is a) developmentally beneficial by accelerating motor skill acquisition and b) developmentally costly because resource allocation to locomotor play is traded-off against investments in growth. We combine behavioural observations of locomotor play and latencies of motor skill acquisition with quantitative measures of natural food availability and individual growth rates measured non-invasively via photogrammetry. The study was conducted on 17 infants of a wild unprovisioned multi-male - multi-female group of Assamese macaques (*Macaca assamensis*) living in their natural habitat with a diverse predator community at Phu Khieo Wildlife Sanctuary in Thailand. Body size measures were recorded for all group members to evaluate the complete growth trajectories of both sexes from birth until adulthood.

Methods

Study site and subjects

The study was conducted from May 2011 – December 2012 at a long-term study site (established in 2005) at the Phu Khieo Wildlife Sanctuary (157,300 ha, 16°5'–35'N, 101°20'–55'E, 300 to 1300 masl) in north-eastern Thailand (Borries et al. 2002; Schülke et al. 2011; Heesen et al. 2013; Ostner et al. 2013). Female Assamese macaques are philopatric and reach sexual maturity within 5–6 years, whereas males disperse from their natal group between late infancy and adulthood and show delayed maturation (fully grown ~9–10 years). Timing of reproduction is strictly seasonal, and birth season ranges from April to July (Fürtbauer et al. 2010). Across age-sex classes Assamese macaques are strongly arboreal spending about 90% of their activity time off the ground (Schülke et al. 2011), including during locomotor play activity (Fig. S2.1).

Data were collected on a fully habituated social group consisting of 22 adults (9 males, 13 females), 23 juveniles (10 males, 13 females), and 12 infants born in 2011 (6 males, 6 females) and 5 infants born in 2012 (2 males, 3 females). All 17 infants were focal animals. The first 2011 cohort became juvenile after weaning at 12 months of age, but were observed

for another 6 month until the end of the study. Therefore, we use the term immatures whenever these six months are also included in an analysis.

During 30 min focal animal protocols instantaneous activity data were recorded every minute (1385.4 focal hours, mean ± SD: 5.5 ± 0.2h per individual and month, 86,518 records). We recorded whether the infant was resting, feeding, travelling, socially interacting (either affiliative like grooming, or agonistic) or engaged in solitary or social play. Solitary play was divided into solitary object and solitary locomotor play, and social play was always locomotor and divided into rough & tumble play (including elements of chasing and/or wrestling) and other social play (like sexual play or the clumsy interactions at the advent of social play; Fig. S2.2). Social play was differentiated from other social behaviours like sitting in body contact, grooming, or aggression by the use of a play-face and/or regular role-changes. Independent from this general activity, we additionally recorded every minute the height of the individual in the tree in 5m steps and its positional behavior (i.e. whether the individual was lying, sitting, standing, walking, running, jumping, climbing, hanging or brachiating).

Motor skills

We recorded all occurrences of 18 different basic motor skills for all 17 focal animals (N = 5,333 ad libitum records) to assess the individual latencies of acquisition, i.e. the age at first occurrence for each separate motor skill in each individual. The skills were jumping or running (both either on the ground or in a tree), jumping a distance from branch to branch of either more or less than 1m in more versus less than 5m height, and hanging from either all extremities or one or two arms or legs either in a solitary context versus in a unpredictable social play context where the open skill (Poulton 1957) is played out (see Table S2.1 for details).

Growth rate

Size was measured every month via photogrammetry from the length of the lower arms. We took 1,706 pictures of the 17 focal animals (6.4 ± 2.1 pictures per individual and month; mean ± SE) and 1,754 of all 23 juveniles which were one to four years old at the beginning of the study (4.4 ± 1.9 pictures per individual and month). Picture and object distance were simultaneously recorded using a Nikon D5000 camera and a Bosch PLR 50 laser distance measurement tool (accuracy ± 2mm) as described in (Breuer et al. 2007). Number of pixels in the picture was determined using ImageJ 1.44p (National Institutes of Health, USA). Length was then calculated by multiplying the object distance with the number of pixels in the picture (Breuer et al. 2007) and applying a correction (Fig. S2.3). Length measurements were highly reliable between observers (N = 179 picture random blind subset, correlation between values generated by two raters r = 0.950). Outliers (mean ± 2SD) were excluded for each month and individual separately, and monthly individual average size from the remaining pictures was used for analyses. Since linear growth is expected for increase in volume instead of length, we used the cubic value of our length measure (= size index). Growth rate indices were then calculated as slopes of linear regressions of these monthly values over time.

Intensity of locomotor play

In our study, solitary and social (i.e. 83% rough and tumble) locomotor play strongly differed in intensity, challenge level, and age curve. The rate of high intensity locomotion (running, climbing, jumping, hanging and pendulously travelling; Pellegrini et al. 1998; Pellegrini et al. 2013) was much higher during social than during solitary locomotor play. Conversely, the rate of low and medium intensive locomotion (i.e. standing and walking) was higher during solitary than during social locomotor play (Fig. S2.4). Probably due to neuromuscular immaturity infants exhibited low intensity solitary locomotor play first, but soon changed to social locomotor play (Fig. S2.2, S2.5, Table S2.2). Since both the rate and the intensity of play may affect skill acquisition (Bekoff 1988), we used a statistical interaction term of locomotor play time and the proportion of social of all locomotor play as predictor of skill acquisition.

Availability of ecological energy resources

Monthly food availability indices were calculated based on the fruit abundance in 650 trees and the density of these tree species, based on 44 botanical plots within the home range of the study group, covering 20.75 ha of forest (for details and seasonal variation of food availability in the study side see Heesen et al. 2013). The food availability index is correlated to individual energy intake (Heesen et al. 2013). Since differences in lactation may have a strong impact on individual energy intake and behaviour (Leventakou et al. 2013), we additionally placed the infants into two lactation categories, i.e., whether the mother conceived again early in the lactation period (i.e. at 8 and 10 months of offspring age, N = 2) or well after weaning (inter-birth intervals are bimodally distributed in our group since females can conceive in the subsequent mating season or one year after). Since female rank was neither correlated to female energy intake in our group (see also Majolo et al. 2012; Heesen et al. 2013) nor to the energy content or yield of maternal milk in rhesus macaques (*Macaca mulatta,* Hinde 2006), we did not control for mother's rank.

Statistical analyses

All statistical analyses were run with R 3.1.2. All tests were two-tailed with alpha level set to 0.05. Test assumptions were controlled for by computing variance inflation factors (vif for all LMM and GLM; all vif < 2.2) and applying Shapiro-Wilk tests (all $p \geq 0.18$) in addition to visual inspection of scatterplots, histograms and Q-Q plots of residuals to check for normality, linearity and homogeneity of variance.

Growth vs. locomotor play

We ran a partial correlation between individual growth rates and the proportion of time individuals spent in locomotor play and controlled for individual differences in average food availability (the average of the monthly food availability indices an individual was

exposed to from birth to the end of the study period) and lactation category. To avoid strong influences of different life spans (i.e., different proportions of different life history stages), the infants born in 2012 were excluded from the analysis of the growth-play trade-off. Covariance between growth and locomotor play could be mediated by time budget constraints on independent feeding time, i.e., increasing time proportions in locomotor play might be at the expense of independent feeding time and thus energy intake, which in turn could affect growth rate. Therefore we ran additional partial correlations to investigate potential covariance of the time spent feeding or resting with growth rate and/or the time spent in locomotor play.

Growth and locomotor play vs. food availability

We applied LMMs (R 3.1.2, packages car, lme4 and MuMIn; individual as random factors) to explore the relationships between food availability and (a) the proportion of activity time the individuals spent in locomotor play and (b) individual growth rates. For (a), we used monthly values but excluded the first two months of age since low play rates were probably due to physical immaturity at this age (Fig. S2.2, Table S2.2). Test assumptions were met after the response variable was square-root (for LMM on all individuals) or cubic-root transformed (for LMM on females). Monthly values were, however, not applicable for (b). Since growth rate indices were calculated as linear regression slopes of size over time, which is based on one average value per individual and month (see above), meaningful calculations required six-month periods (i.e., linear regressions over six values). Growth rate calculations of consecutive months were based on strongly overlapping periods, and were highly auto-correlated (Fig. S2.6a). No apparent auto-correlation was found if every other month was ignored (Fig. S2.6b), so we treated these data as independent data points.

Growth vs. age

We applied sex-specific continuous piecewise regressions with Davies tests for change in slope (R 3.1.2, packages segmented, sm) to explore long-term patterns and age-dependent changes in growth rate. Average monthly size indices of all 40 immatures were used. Average individual adult body size indices were calculated from all pictures taken occasionally throughout the study period, and all adults with fewer than three data points were excluded (N = 7 of 22). The significance of the difference between male and female growth rates before the growth spurt at four years was tested using a GLM (R 3.1.2) including an interaction between age and sex.

Locomotor play vs. motor skill acquisition

We applied a LMM (R 3.1.2, packages car, lme4, MuMIn and rgl; square-root transformation of the response variable to meet test assumptions) to explore the relationship between the time spent in locomotor play from birth to the acquisition of a motor skill and the latencies of this skill´s acquisition, with separate values for each motor skill and individual (N=184) and the motor skill labels as a random factor. Time spent in

locomotor play was calculated as interaction between the proportion of time in and the average intensity of locomotor play, thus accounting for the two dimensions of locomotor play (see above). To control for reversed causality (i.e. motor skill level predicts amount of locomotor play; Fulton et al. 2001; Wrotniak et al. 2006) and methodological skew (i.e., motor skills may be easier and earlier detectible in more active infants) we also included the time spent in locomotor play after the acquisition of a motor skill (same time span) as a proxy for variation in overall locomotor play times into the model . Sex of the infant was included to control for sex-specific genetic programming. Age at acquisition of the previous motor skill in the acquisition sequence was added as a predictor to control for inter-dependence between the motor skills. The sequence was generated by applying the I&SI-rankorder-method (Matman1.1, de Vries 1998) on a before-after matrix (i.e. how often motor skill A was acquired before or after motor skill B over all individuals; Table S2.1).

We included only cases where play duration values were based on at least 400 instantaneous records per individual to control for sampling effort. Since this precondition was not met for the majority of infants for the two motor skills acquired first during ontogeny, these were excluded from analyses. Also, five individuals which were born more than one week prior to the start of observations were excluded from analysis. We ran a t-test (paired, two-sided) to compare the latencies of the motor skill acquisition (normalized via mean-scaling within each motor skill) to explore overall sex differences.

Results

Controlling for temporal variation in food availability, we found a strong negative correlation between individual growth rates and time spent in locomotor play (Fig. 2.1a, see also Fig. S2.7). The range in locomotor play time (4.6 - 12.2% activity time, mean ± SD: 7.7 ± 2.3%) accounted for a difference in growth rate of about 30% (Fig. 2.1a). This energy trade-off was not caused by time constraints on feeding behaviour since resting time, not feeding time, was traded in for locomotor play time (Fig. 2.1b-e, S2.8). The trade-off between play and growth was also independent of infant sex, and both sexes fit the same regression line (Fig. 2.1a). All infants spent time in locomotor play during periods of low food availability even though low food availability also slowed down growth (Fig. 2.2).

Play also carried benefits. Across motor skills, skill acquisition latency was predicted by the statistical interaction of the proportion of time spent in locomotor play and the intensity of locomotor play: The higher the proportion of (high intensity rough and tumble) social locomotor play of all locomotor play the stronger the effect of play duration on skill acquisition latency (Fig. 2.3, S2.9). This interaction remained the strongest predictor also after controlling for variation in overall levels of locomotor play (measured as play time immediately after the acquisition; Fig. 2.3). Sex of the infant was not significant and thus excluded from the final model. Since the motor skill cannot influence the amount of play before its acquisition, these results suggests that locomotor play may drive motor skill acquisition (Granger 1969).

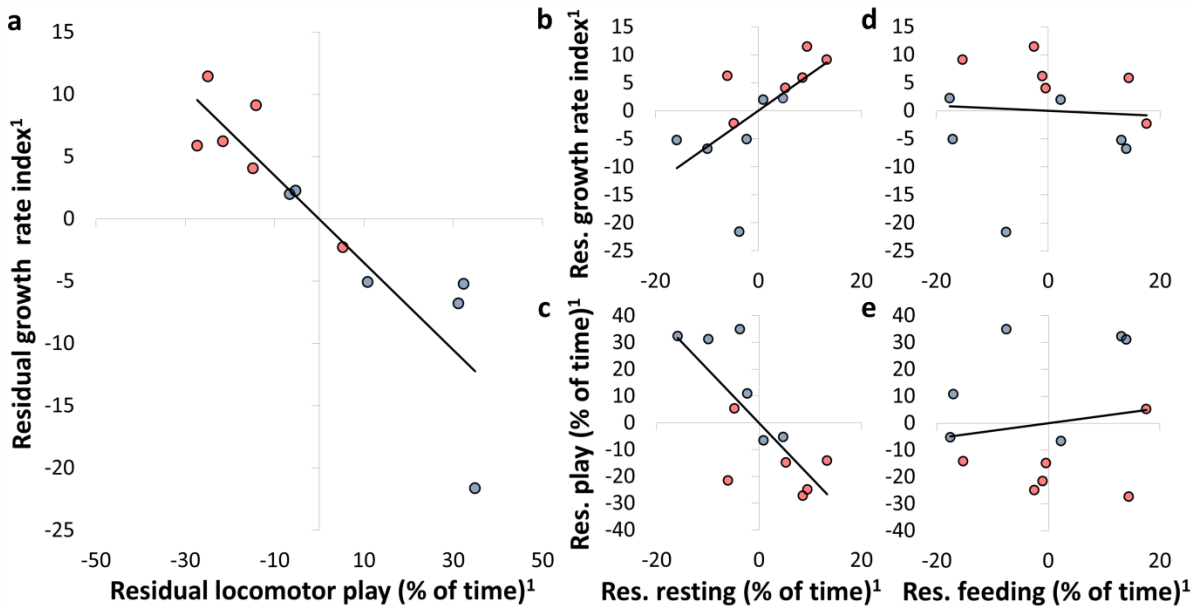


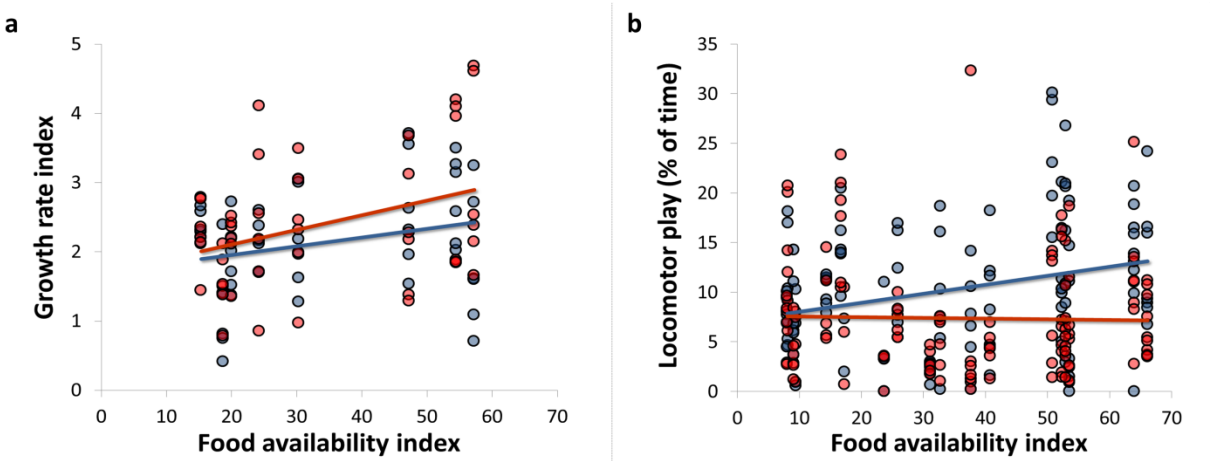
Figure 2.1. Energy trade-off between locomotor play and growth. Red: female, blue: male. Residual plots of the individual values for the whole study period (Pearson partial correlations controlled for average food availability and lactation category). Only the individuals born in the first year are included (N = 12). [1]Residuals are translated into deviations from average in %. **(a)** growth rate over locomotor play (r = - 0.889, p < 0.001); additionally controlled for sex (no figure): r = - 0.785, p = 0.002, additionally controlled for average play intensity (no figure): r = - 0.895, p < 0.001, **(b and c)** growth rate (r = 0.612, p = 0.060) and locomotor play (r = - 0.759, p = 0.011) over resting time, **(d and e)** growth rate (r = - 0.037, p = 0.919) and locomotor play (r = 0.155, p = 0.668) over feeding time.

Although these general patterns were independent of infant sex, we found sex-specific adaptations to the energy trade-off. The more food was available the more female immatures invested in growth and male immatures in locomotor play (Fig. 2.2, Fig. S2.8). Consequently, male immatures grew less (p = 0.017, t = -2.84, N = 12, Fig. 2.1a), participated more in locomotor play (p = 0.028, t = 2.57, N = 12; Fig. 2.1a), and acquired motor skills faster than female immatures (p = 0.006, t = 2.78, N = 184, all two-sided t-tests). In a cross-sectional analysis across all group members and ages both sexes accelerated growth following the cessation of the play period (from birth through four years of age; Fig. 2.4). Throughout their first four years of life, however, males grew slower than females, leading to persisting size differences until the age of female maturity, with females reaching adult female body size about five months earlier than males (Fig. 2.4d).

Discussion

Using behavioural observation, photogrammetric measurements and measurements of food availability under natural conditions, we have shown that resource allocation to locomotor play causes sizable developmental costs. Even under moderate natural energy restriction, investments in locomotor play have strong negative effects on growth, accounting for up to 50% of variance in growth with persisting consequences for life history. These results contradict current theory stating that physical development takes strong

ontogenetic priority over play for skill acquisition (Martin 1982; Müller-Schwarze et al. 1982; Martin and Caro 1985; Bekoff and Byers 1992; Nunes et al. 2004a; Burghardt 2005; Pellegrini 2009; Graham and Burghardt 2010; Kenrick et al. 2010). If developmental costs of play are high, play should be associated with considerable benefits compensating for these costs. In line with this, our results confirm the widespread, but so far unconfirmed, assumption that locomotor play is developmentally beneficial by accelerating motor skill development (Groos and Baldwin 1898; Bekoff 1988; Byers and Walker 1995; Maestripieri 1995; Fulton et al. 2001; Nunes et al. 2004a; Fisher et al. 2005; Pellegrini 2009; Graham and Burghardt 2010). Additionally, we found sex-differential life history strategies with female immatures focusing their investment on growth at the expense of locomotor play and motor skill acquisition and vice versa in males.



Growth rate vs. food availability (males):

Variable	Estimate (Beta)	SD	t-value	p-value
Intercept	2.127	0.108		
Food availability	0.201	0.11	1.84	0.07

Rates of locomotor play vs. food availability (males):

Variable	Estimate (Beta)	SD	t-value	p-value
Intercept	11.69	1.52		
Food availability	1.295	0.564	2.3	0.021

Growth rate vs. food availability (females):

Variable	Estimate (Beta)	SD	t-value	p-value
Intercept	2.439	0.165		
Food availability	0.356	0.118	3.03	0.003

Rates of locomotor play vs. food availability (females):

Variable	Estimate (Beta)	SD	t-value	p-value
Intercept	1.794	0.093		
Food availability	-0.073	0.038	-1.92	0.09

Figure 2.2. Sex-specific investment in growth and locomotor play with increasing food availability. Red: female, blue: male. **(a)** growth rate over food availability: with increasing food availability, female immatures invested in increased growth rates (model significance $p = 0.003$ compared to null model, $R^2 = 0.251$, $N = 52$), whereas male immatures did not (model significance $p = 0.07$, $R^2 = 0.065$, $N = 48$; all: $p < 0.001$, $R^2 = 0.171$), **(b)** locomotor play over food availability: male immatures invested energy from increased food availability in locomotor play (model significance $p = 0.021$, $R^2 = 0.360$, $N = 109$), whereas female immatures did not (model significance $p = 0.084$, $R^2 = 0.321$, $N = 119$; all: $p = 0.95$, $R^2 = 0.032$; all model predictor variables z-transformed)

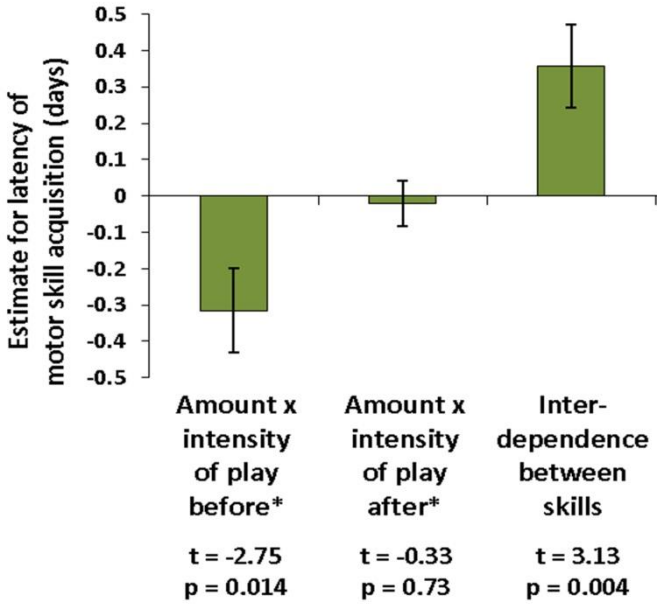


Figure 2.3. Latencies of motor skill acquisition are predicted by the interaction between the amount and the intensity of locomotor play before the acquisition. Estimates ± SD of the z-transformed variables predicting latency of motor skill acquisition of 16 skills (LMM, N = 184). Random factor: motor skill labels, model significance: $p = 0.014$, $R^2 = 0.715$, intercept: estimate 8.2 ± 0.4. *before/after the respective age of motor skill acquisition. Sex of the infant was not significant and thus excluded from the model.

According to the "surplus resource hypothesis" the energy excess after growth is a precondition for the proximate occurrence as well as the evolution of play in animals (Burghardt 2005; Graham and Burghardt 2010). Indeed these links may be rather complex, considering the underlying correlates like prolonged development, parental care and large brains as well as the existence of several structurally and functionally different play types (Burghardt 2005; Graham and Burghardt 2010). However, our results of a trade-off even under moderate activity levels and ecological conditions contradict predictions that enough energy after growth needs to be available for play to occur and that the developmental or even energy costs of physically active play are negligible (Martin 1982; Martin and Caro 1985; Bekoff and Byers 1992; Burghardt 2005; Graham and Burghardt 2010). Instead, they support findings in humans where extreme physical activity during childhood in athletes of competitive sports affects growth and sexual maturation (Malina et al. 2013). The surplus resource hypothesis has been so influential that resource allocation to immature play was not even mentioned in recent reviews summarizing ecological and evolutionary factors limiting growth rates (Dmitriew 2011; Jones 2011). Our results thus strongly contribute to current life history theory by identifying resource allocation to physically active play as one crucial factor in the process.

Our results support the motor training hypothesis which proposes that physically active play accelerates motor skill acquisition (Bekoff 1988; Byers and Walker 1995). Accordingly, play may increase fitness by decreasing immature mortality and increasing future dominance rank across mammals (Nunes et al. 2004a; Cameron et al. 2008; Fagen and Fagen 2009; Blumstein et al. 2013) because motor skills enhance flight/fight competence which can prevent damage of physical integrity caused by predation and fights (Bekoff 1988; Pellegrini 2009). Previous studies provide correlational evidence of a positive association between rates of play and motor skills in mammals including humans (Nunes et al. 2004b; Fisher et al.

2005). Higher levels of motor skills, however, may also enable higher levels and amounts of play (Fulton et al. 2001; Wrotniak et al. 2006), so the causality remained unclear. To our knowledge our study is the first that shows time series causality supporting the "motor training hypothesis".

Sex differences in energy allocation as found in our study are unexpected in the light of sexual selection theory predicting polygynous males to invest in body size and weaponry (Clutton-Brock 1988). In cercopithecine primates, however, female investment in growth and maturation is important, because reproductive lifespan and thus age at first reproduction is a major fitness component for females but not for males (van Schaik 1989; Onyango et al. 2013; Dubuc et al. 2014). Male reproductive success is driven by their dominance rank at prime age (Ostner et al. 2008b; Dubuc et al. 2014) and coalitionary activity (Schülke et al. 2010), both of which are likely to be affected also by fight/flight competence and thus motor skills (Pellegrini 2009). Notably the developmental benefits of play may not be limited to motor skill acquisition but may also enhance social skill development and train behavioural flexibility to deal with unexpected events (Pellegrini 2009; Graham and Burghardt 2010). The sex differences in energy allocation to growth or locomotor play may thus correspond to sex-differential life history strategies.

One of the most puzzling phenomena in life history theory is prolonged juvenility (from weaning until sexual maturation), which can last several years in primates and large mammals with individuals being independent but not yet reproductive (Pereira and Fairbanks 2002; Kappeler and Pereira 2003; Barton and Capellini 2011; Jones 2011; Kuzawa et al. 2014; Pontzer et al. 2014). In addition to the extra energy required for the development of large brains (Janson and van Schaik 2002; Barton and Capellini 2011; Navarrete et al. 2011; Kuzawa et al. 2014), it has been proposed that the acquisition of complex skills may require sufficient time causing prolonged juvenility to be associated with low growth rates (e.g. Poirier and Smith 1974). Janson & van Schaik (2002) argued that this hypothesis lacks causality since it is unclear how skill acquisition may force, or rely on, low growth rates or sexual immaturity. They proposed the alternative (though not mutually exclusive) "juvenile risk aversion"-hypothesis, stating that low growth rates evolved to avoid the high risk of starvation and predation during juvenility (Janson and van Schaik 2002; Jones 2011). Our results provide a potential causal link between skill acquisition via energy demanding locomotor play and low growth rates. We show that growth rates are indeed restricted by resource availability as proposed by the "juvenile risk aversion"-hypothesis, but also that the resources available to growth are limited not only by ecology (i.e. energy intake) but also by the amount of locomotor play for skill acquisition (i.e. individual skill requirements). This indicates that both mechanisms are involved in causing low growth rates and thus extended juvenility.

The strong ontogenetic trade-off between growth and locomotor play for motor skill acquisition suggests that animals may face a health trade-off from birth between unconstrained physical development, their flight/fight competence, and physical integrity challenged by predation and adult fights. This health trade-off may also include disease risk as resource allocation to intense physical activity reduces resource allocation to immune

function and increases infection risk in humans (Romeo et al. 2010). This plasticity may be utilized via pre- and postnatal maternal effects, because under unstable ecological or social conditions, or high predation pressure, mothers could inhibit or encourage infant locomotion and physical activity to accelerate either physical development and health or motor skill acquisition (Maestripieri 1996). We suggest that future research explores the long-term effects of locomotor play on life-history traits like age at sexual maturity, adult body size, rank acquisition, survival and fecundity as well as the impact on the development of social and sexual networks to evaluate the long-term fitness costs.

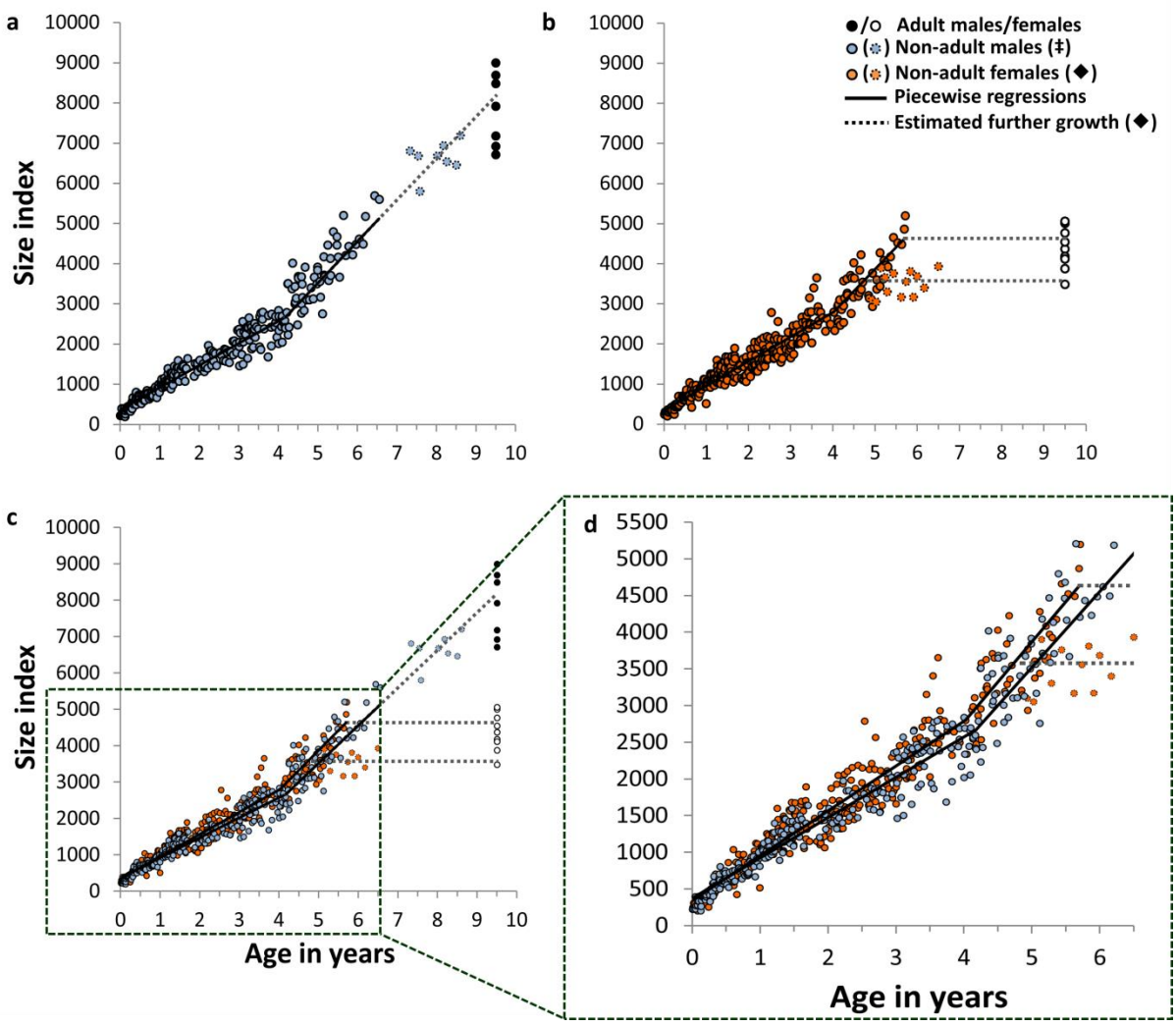


Figure 2.4. Sex differences in growth rate over age. (a) Male body size index over age (break point = 4.2 ± 0.15 years, adjusted R^2 = 0.952, p < 0.0001; slopes different at p < 0.0001; N = 278; ‡ open blue circles: exact birth date unknown, excluded from regression). **(b)** Female body size index over age (break point = 4.0 ± 0.15 years, adjusted R^2 = 0.935, p < 0.0001; slopes different at p < 0.0001; N = 331; ◆ open red circles and lower scattered line: female with low age (5.0 years) at first birth, excluded from regression). **(c and d)** Before growth spurt, female growth rate was 11.1% higher than male growth rate (GLM: interaction Age*Sex p<0.01), resulting in an average body size difference of 13.0% at age 3.6–4.1 years. Black lines: piecewise regressions, grey scattered lines: extrapolated further growth (adult values set to the age of 9.5 years, the estimated full-grown age of males).

When suffering from malnutrition, supplemental food provisioning increases play and motor skill acquisition also in human children (Espinosa et al. 1992; Adu-Afarwuah et al. 2007). Our results show that enhancing physical activity as recommended by the World Health Organization and United Nations (UNOSDP 2008; WHO 2011; UNICEF 2012) is indeed beneficial in terms of accelerated motor skill acquisition but is accompanied by constrained physical development even under moderate malnutrition and activity levels. This may add a new aspect to the currently highly debated concept of the developmental origins of health and (noncommunicable) disease (DOHaD, Hanson and Gluckman 2014), but it also suggests that reduced growth can be adaptive and developmentally beneficial rather than being generally pathological.

Altogether our results show that locomotor play entails high developmental benefits but also costs; hence, differential life history strategies may determine the level of acceptable costs. They also show that play behaviour and physical growth are of high phenotypic plasticity (Kappeler and Pereira 2003; Dmitriew 2011; Hanson and Gluckman 2014). That investments in play can take ontogenetic priority over unconstrained physical development with persisting consequences for life history strongly highlights the ontogenetic and evolutionary importance of play.

Data accessibility: The raw data from the study are available on request.

Competing interests: We have no competing interests.

Author Contributions: A.B. collected and analysed data, A.B., O.S. and J.O. designed the study and wrote the paper. J.O. and O.S. contributed equally. All authors gave final approval for publication.

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Supplementary Material

Supplementary figures

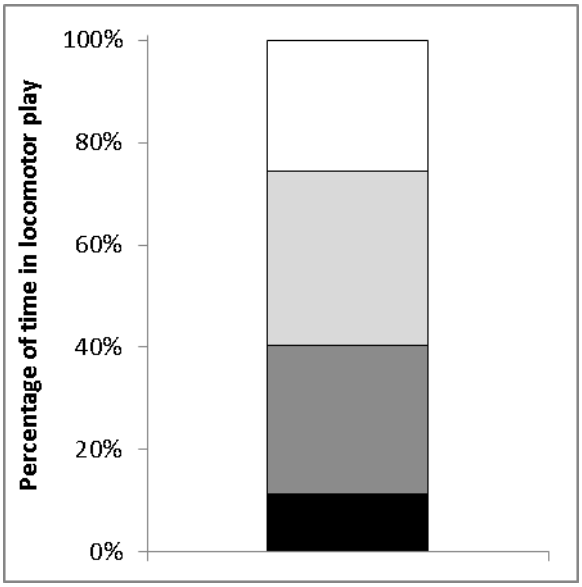

Figure S2.1: Percentage of time in locomotor play at different tree heights. Black: on ground, dark grey: 0-5m, light grey: 5-10m, white: >10m

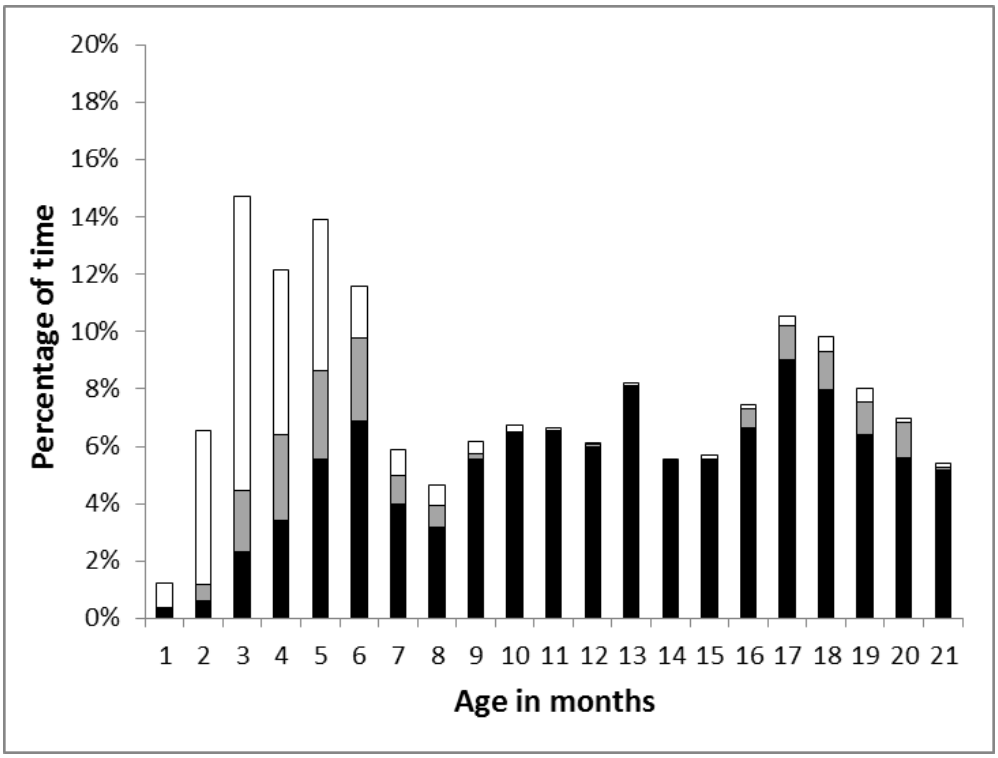

Figure S2.2: Percentage of different play pattern at different ages. Black: rough & tumble social locomotor play (i.e. chasing, wrestling, fighting), grey: other social locomotor play (like sexual play or the clumsy interactions at the advent of social play), white: solitary locomotor play

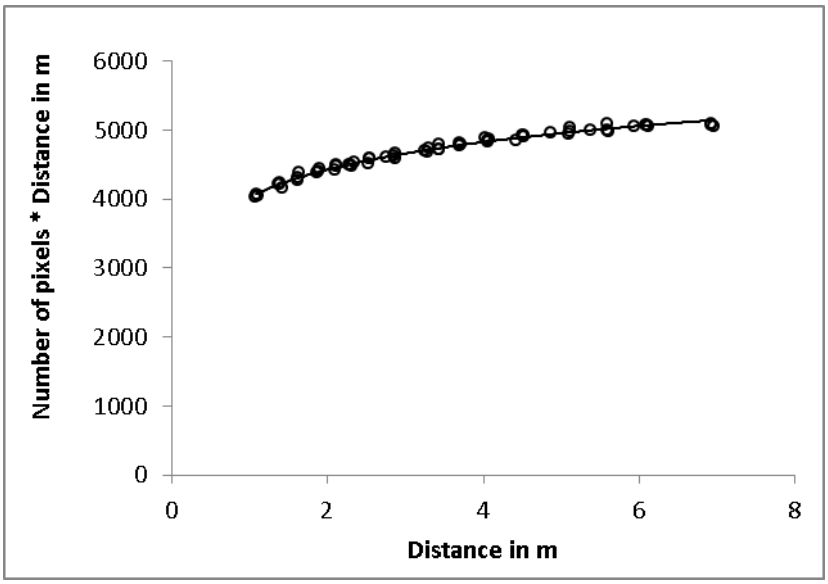

Figure S2.3: Validation of photogrammetric measurement. 59 pictures and distance records of a sharp-edged object of known size (165.0mm) were taken from 1-7m distance. The relationship between distance and the product of the number of pixels in the picture and the distance should be a constant, but we found a systematic logarithmic deviation (see figure, R^2 = 0.987), probably due to changes in relative lens positions caused by autofocus. Correction of the calculated values for this relationship and transformation into relevant measures resulted in a constant value (Mean ± SD: 165.00 ± 1.35mm) and was thus applied to all values in the study.

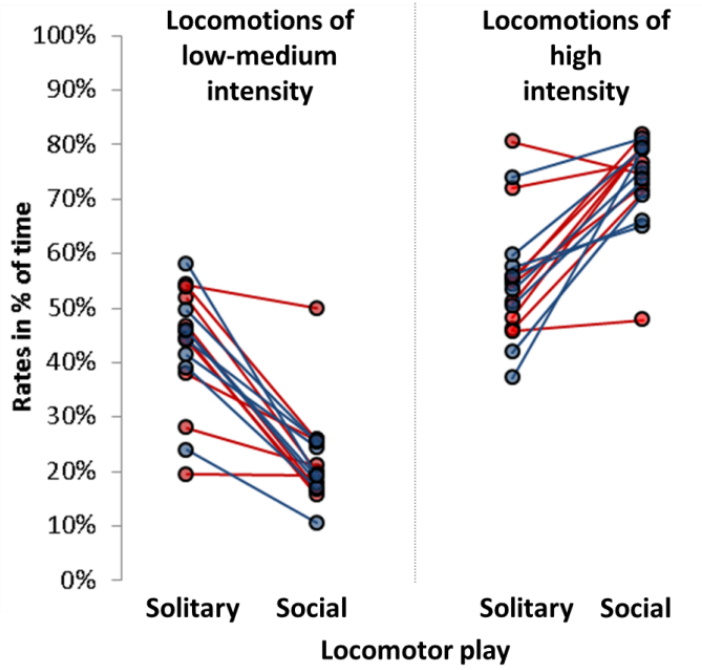

Figure S2.4: Differences between solitary and social locomotor play in locomotion intensity. Rates of locomotions of low and medium intensity (i.e. standing and walking) strongly decreased from solitary to social locomotor play ($t = -8.12$, $p < 0.0001$), while rates of high intensive locomotions (i.e. running, climbing, jumping, hanging and pendulously travelling) strongly increased ($t = 6.13$, $p < 0.0001$, both pairwise two-sided t-tests). Blue: males, red: females.

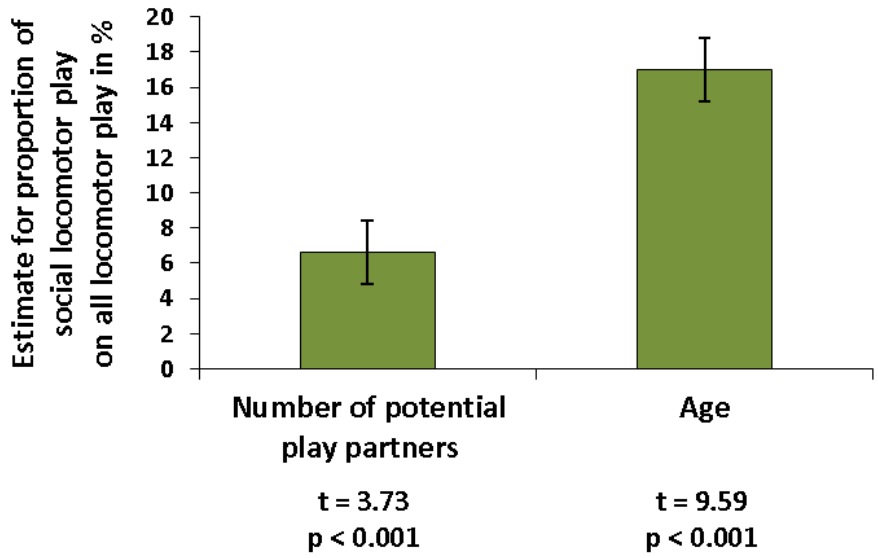

Figure S2.5: The proportion of social on all locomotor play was positively related to age and the number of potential play partners around. In addition to age, the proportion of social on all locomotor play (i.e. intensity of locomotor play) was also predicted by the number of same-aged individuals, and thus potential play partners, in the group (GLMM with values from the first year of life and individuals as random factors; model significance: $p < 0.001$; Intercept: estimate 83.8 ± 1.6)

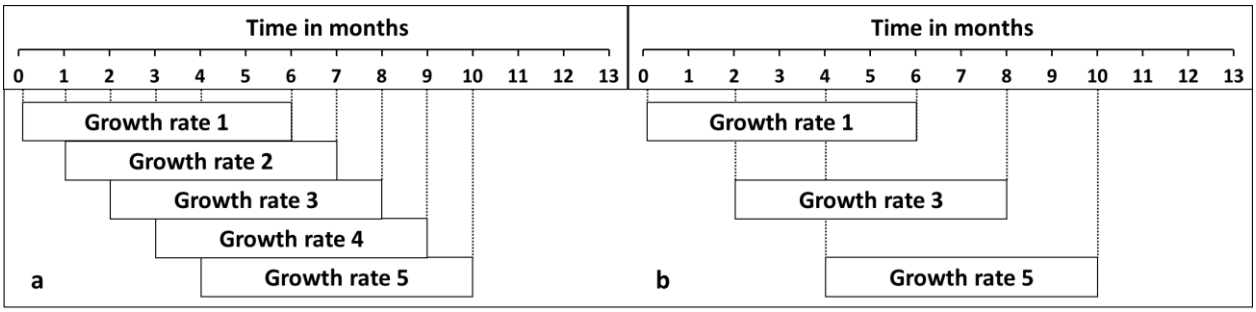

Figure S2.6: Period overlap for monthly growth rate calculation. Growth rate indices were calculated for six-month periods. **(a)** Growth rate indices for consecutive months showed strong temporal overlap and were thus highly correlated to each other ($r = 0.586$, $p < 0.001$). **(b)** Growth rate indices calculated every other month did not show strong auto-correlation anymore ($r = 0.179$, $p = 0.104$) and were used in our analyses.

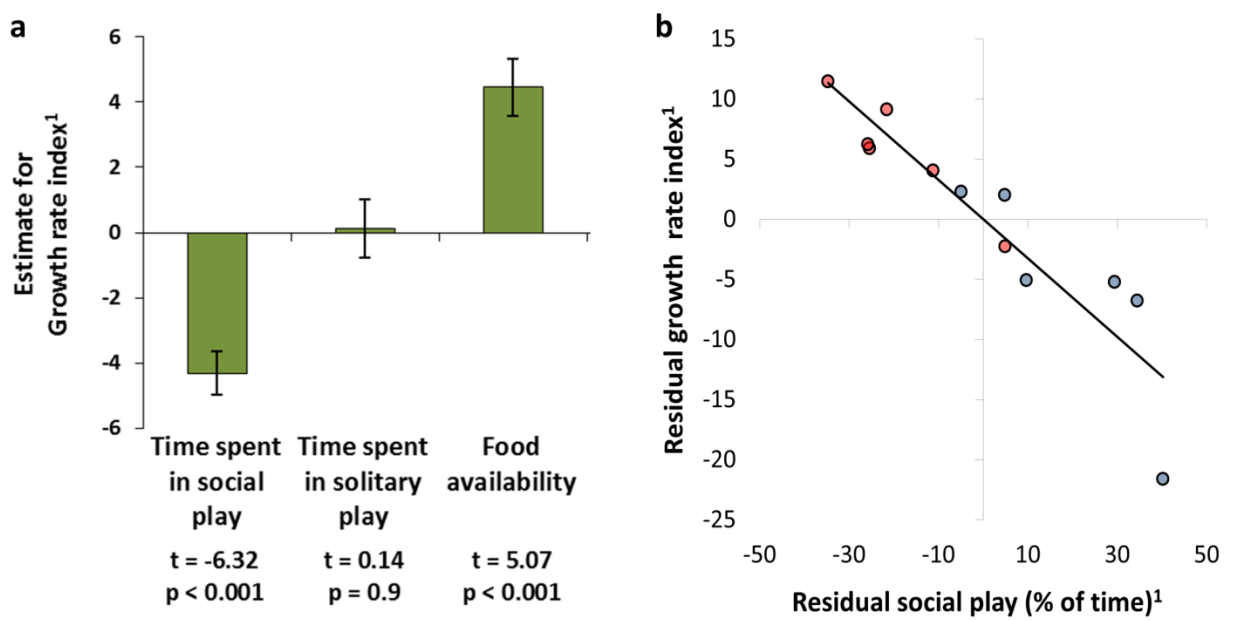

Figure S2.7: Energy trade-off between social locomotor play and growth. Red: female, blue: male. [1]Residuals are translated into deviations from average in %. **(a)** Splitting locomotor play into social and solitary locomotor play, growth was traded-off against social but not solitary locomotor play (GLM, model significance $p < 0.001$ compared to null model, $R^2 = 0.845$, N = 12), **(b)** Growth rate over social locomotor play ($r = -0.916$, $p = 0.001$); additionally controlled for sex (no figure): $r = -0.835$, $p = 0.005$ (Residual plot of the individual values for the whole study period; Pearson partial correlation controlled for average food availability and lactation category; N = 12).

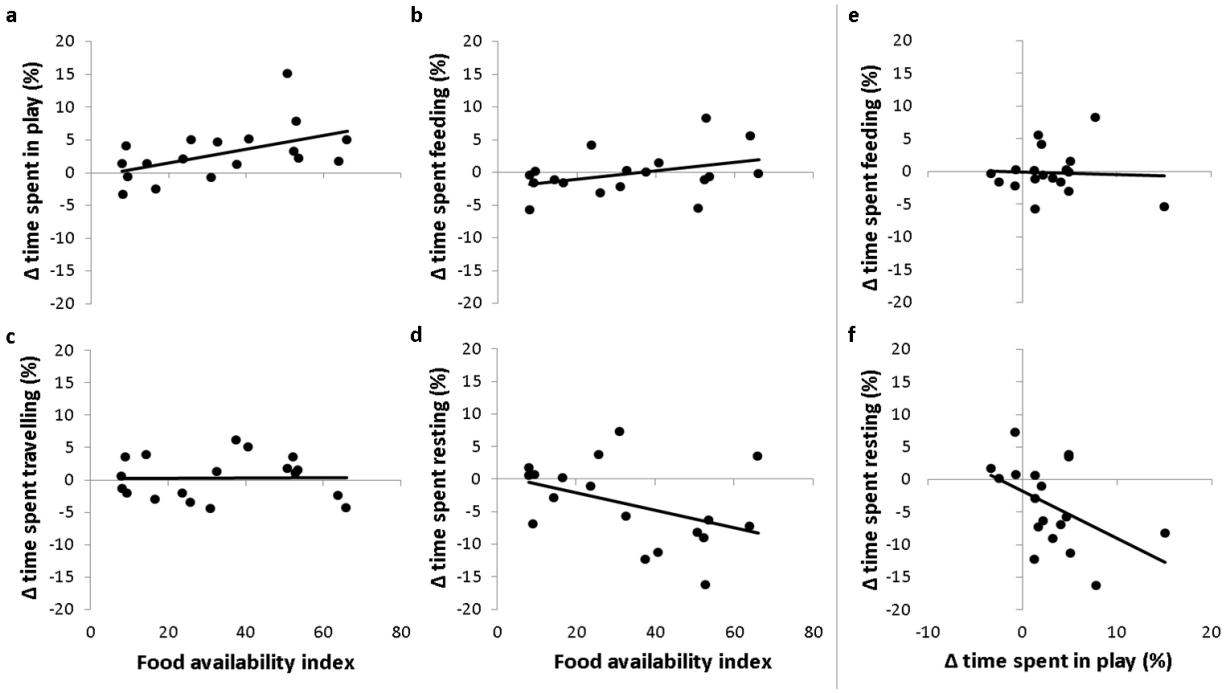

Figure S2.8. Time budget analysis: Sex differences (Δ) in time spent in locomotor play were due to sex differences in resting time, not feeding time. Two-tailed Pearson correlations; Δ = $mean_{males}$ – $mean_{females}$ per month; N = 18. **(a)** Locomotor play over food availability (r = 0.667, p = 0.003), **(b)** feeding over food availability (r = 0.372, p = 0.128), **(c)** travelling over food availability (r = - 0.014, p = 0.957), **(d)** resting over food availability (r = - 0.419, p = 0.083), **(e)** feeding over locomotor play (r = 0.101, p = 0.690), **(f)** resting over locomotor play (r = - 0.753, p < 0.001).

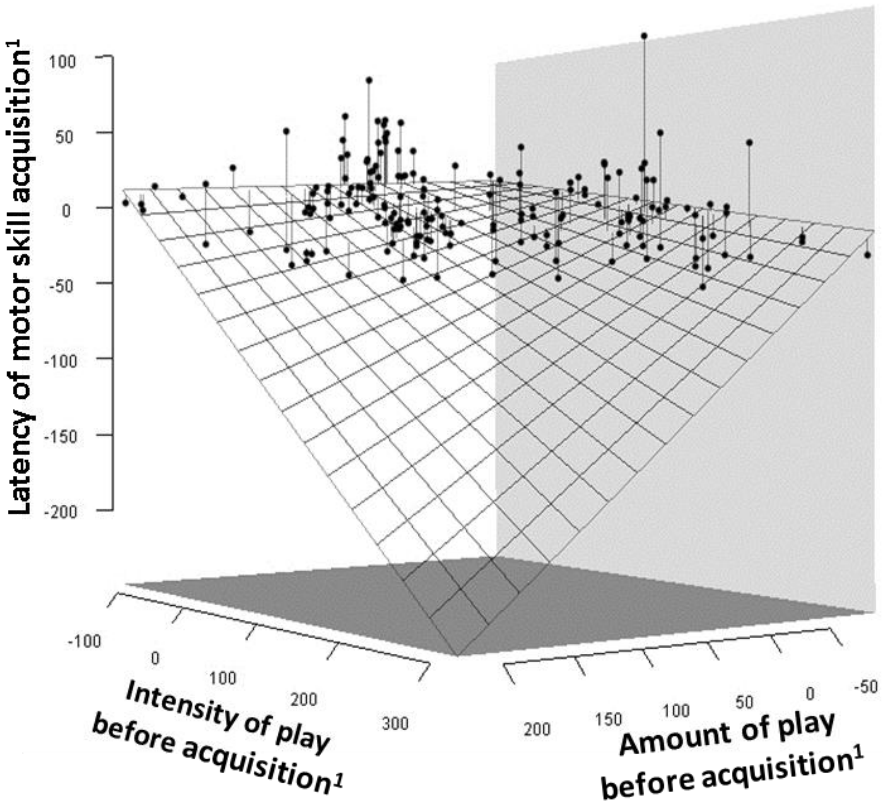

Figure S2.9: Latencies of motor skill acquisition as a function of average intensity and time spent in locomotor play before acquisition. [1]Plotted are deviations from the respective motor skill specific averages in % (N = 184)

Supplementary tables

Table S2.1 provides a list of 18 motor skills scored for their first occurrence in an infant in this study. We calculated a sequence of occurrence by applying a method established for dominance hierarchy analyses (de Vries 1998). After constructing a matrix of all skills over all skills we entered for every combination how often (across infants) skill A was observed before skill B. The sequence of items in the matrix was reshuffled 10,000 times in order to identify the sequence with the highest linearity or maximal transitivity of relations between skills (Corrected Linearity index h' = 0.998 ($p < 0.001$), Directional Consistency Index (DCI) = 0.716). This sequence was used to control our analyses of determinants of skill acquisition latencies for auto-correlation effects between the latencies of sequential skills.

Acknowledging that the nature of a skill relates to the predictability of the interacting environment (Poulton 1957), we treated several motor patterns as two different skills depending on whether they occurred as closed skills (Poulton 1957) in a solitary locomotor play context or as open skills in the much more unpredictable social locomotor play context. Hanging on all extremities, one or two arms or one or two legs when involved in social locomotor play involved play partners that jump on, cling to or pull the subject and was typically performed on moving substrates (branches). These skills all developed in a social context long after they were observed in a solitary context (27.3 ± 2.6 days later (mean ± SE), $t = 10.51$, $p < 0.0001$, pairwise two-sided t-test). * jumping from branch to branch

Table S2.1: List of the 18 motor skills used in this study.

Sequence	Motor skill	Average age of acquisition (Mean±SD)
1	Hanging on all extremities in solitary context	33.8 ± 15
2	Hanging on two arms in solitary context	36.2 ± 14.6
3	Jumping on ground	47.7 ± 15.2
4	Hanging on one arm in solitary context	50.7 ± 20.7
5	Jumping in tree	51.1 ± 15.8
6	Running on ground	54.8 ± 14.5
7	Hanging on two legs in solitary context	59.4 ± 15.3
8	Running in tree	63.9 ± 18.3
9	Hanging on all extremities in social play context	59.8 ± 16.8
10	Jumping a distance of <1m in less than 5m height*	67.6 ± 20.5
11	Hanging on two arms in social play context	62.2 ± 15.7
12	Jumping a distance of <1m in more than 5m height*	67.7 ± 13.3
13	Hanging on one leg in solitary context	71.6 ± 27.3
14	Hanging on two legs in social play context	79.9 ± 19.5
15	Hanging on one arm in social play context	77.8 ± 21.7
16	Jumping a distance of 1-2m in less than 5m height*	105.6 ± 28.7
17	Jumping a distance of 1-2m in more than 5m height*	116.8 ± 27.5
18	Hanging on one leg in social play context	108.4 ± 21.3

Table S2.2: Percentage of time spent in locomotor play (mean ± SD) for each sex and age

Age in months	All locomotor play:		Solitary locomotor play:		Social locomotor play:		Social rough&tumble play:	
	males	females	males	females	males	females	males	females
1	0.5±0.8	0.9±2.1	0.5±0.8	0.9±2.1	0.9±2.3	0.0±0.1	0.0±0.0	0.0±0.0
2	5.3±6.1	4.7±8.3	5.0±5.9	4.7±8.3	1.4±1.9	1.0±1.5	0.2±0.5	0.0±0.0
3	9.5±8.9	12.7±12.1	7.1±6.0	12.2±11.8	6.1±3.4	3.0±2.5	2.5±3.6	0.5±0.9
4	7.5±4.3	9.6±5.7	4.6±2.1	7.0±5.5	6.5±3.8	6.4±4.6	2.9±3.1	2.7±1.9
5	11.3±8.3	8.5±6.0	5.6±3.5	4.5±3.3	9.2±6	7.3±5	5.7±6.6	4.0±3.7
6	11.8±8.5	5.6±3.8	1.7±1.4	2.0±1.9	13.3±7.7	7.3±4.7	10.1±7.7	3.7±2.7
7	3.9±3.3	5.3±4.4	0.6±0.8	2.0±4.3	4.7±3.8	3.9±3.2	3.3±2.8	3.2±2.9
8	1.8±2.3	4.5±3.1	0.2±0.2	1.0±1.0	1.6±2.2	4.6±3.7	1.6±2.2	3.5±2.7
9	5.5±5.2	5.6±6.7	0.2±0.3	1.4±2.0	5.7±5.2	4.6±5.9	5.3±5.3	4.2±5.2
10	8.1±2.3	5.4±2.0	0.4±0.6	0.2±0.5	7.7±2.1	5.2±2.2	7.7±2.1	5.2±2.1
11	9.2±3.0	3.9±2.2	0.1±0.1	0.2±0.2	9.3±3.1	3.8±2.2	9.2±3.1	3.7±2.1
12	5.8±2.6	6.4±3.2	0.0±0.1	0.0±0.1	6.0±2.7	6.4±3.2	5.8±2.6	6.3±3.2
13	11.7±8.1	3.9±1.1	0.1±0.3	0.0±0.0	11.7±7.9	3.9±1.2	11.6±7.9	3.9±1.1
14	8.4±7.6	3.8±2.5	0.0±0.0	0.0±0.1	8.5±7.7	3.8±2.5	8.4±7.6	3.8±2.5
15	8.2±5.5	2.4±3.2	0.3±0.4	0.0±0.0	8.0±5.5	2.6±3.2	7.9±5.5	2.4±3.2
16	9.8±3.6	5.5±3.7	0.0±0.0	0.2±0.2	10.7±4.4	5.7±3.7	9.8±3.6	5.2±3.5
17	11.6±4.3	6.8±2.3	0.3±0.5	0.3±0.4	12.7±5.8	7.2±3.2	11.2±3.9	6.4±2.0
18	12.6±8.5	5.1±3.0	0.6±0.7	0.4±0.5	13.9±8.7	5.3±3.4	12.0±7.9	4.7±2.7
19	7.7±5.3	5.2±3.4	0.3±0.4	0.4±0.5	8.3±5.6	5.7±3.5	7.4±5.2	4.7±3.5
20	10.2±7.9	3.4±1.1	0.1±0.3	0.1±0.2	11.6±9.5	4.1±2	10.0±8.0	3.3±1.1

Chapter 3

Prenatal stress effects in a wild, long-lived primate: predictive adaptive responses in an unpredictable environment

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Abstract

Prenatal maternal stress affects offspring phenotype in numerous species including humans, but it is debated whether these effects are evolutionarily adaptive. Relating stress to adverse conditions, current explanations invoke either short-term developmental constraints on offspring phenotype resulting in decelerated growth to avoid starvation, or long-term predictive adaptive responses (PARs) resulting in accelerated growth and reproduction in response to reduced life expectancies. Two PAR-subtypes were proposed, acting either on predicted internal somatic states or predicted external environmental conditions, but since both affect phenotypes similarly, they are largely indistinguishable. Only external, but not internal PARs though, rely on high environmental stability particularly in long-lived species. We report on a crucial test case in a wild long-lived mammal, the Assamese macaque (*Macaca assamensis*) that evolved and lives in an unpredictable environment where external PARs are probably not advantageous. We quantified food availability, growth, motor skills, maternal caretaking style, and maternal physiological stress from faecal glucocorticoid measures. Prenatal maternal stress was negatively correlated to prenatal food availability and led to accelerated offspring growth accompanied by decelerated motor skill acquisition and reduced immune function. These results support the “internal PAR”-theory which stresses the role of stable adverse internal somatic states rather than stable external environments.

Introduction

The role of prenatal maternal stress in the concept of the developmental origins of health and disease receives a great deal of attention (Laviola and Macrì 2013; Hanson and Gluckman 2014; Moisiadis and Matthews 2014a, b; Weinstock 2015). Numerous animal and human studies have shown elevated prenatal maternal physiological stress (i.e. elevated prenatal maternal glucocorticoid levels; PreGC) in response to a wide range of external adversities like predation, climatic, social, or nutritional stress, and PreGC to cause various effects on offspring phenotype (Coe and Lubach 2008; Laviola and Macrì 2013; Sheriff and Love 2013; Hanson and Gluckman 2014; Moisiadis and Matthews 2014b, a; Veru et al. 2014; Weinstock 2015). It remains unclear whether prenatal maternal stress effects on offspring phenotype are adaptive from an evolutionary point of view (Laviola and Macrì 2013; Sachser et al. 2013; Sheriff and Love 2013; Del Giudice 2014a; Hanson and Gluckman 2014; Belsky et al. 2015). Current adaptive theories propose that under adverse conditions, these effects benefit the offspring either in the short- (developmental constraints) or in the long-term (predictive adaptive responses, PARs). The developmental constraints-hypothesis predicts the offspring to reduce its investment into development, and particularly growth, to reduce starvation risk under adverse conditions. The PAR-hypothesis proposes that PreGC prepares the offspring for its likely long-term future. From life history theory, the PAR-hypothesis predicts that under adverse conditions, the offspring should accelerate its growth, maturation, reproduction and its general pace of life, because adverse conditions are likely to reduce offspring's life expectancy (Metcalfe and Monaghan 2001; Dantzer et al. 2013; Nettle et al. 2013; Hanson and Gluckman 2014; Rickard et al. 2014; Belsky et al. 2015; Nettle and Bateson 2015; Tung et al. 2016). Under limited resources, such an adaptive recalibration may be part of a life-history trade-off and at the expense of more quality-related attributes (like skill acquisition or immune function) the benefits of which accumulate with increasing life span (Metcalfe and Monaghan 2001; Belsky et al. 2015).

The original and most prominent version of the PAR-hypothesis proposes that if PreGC changes with prenatal environmental conditions and if prenatal environmental conditions forecast future environmental conditions, then PreGC may adaptively recalibrate the offspring´s phenotype to match similar environmental conditions during its adulthood, thereby increasing its fitness compared to unaltered, mismatched phenotypes (external PAR, Hanson and Gluckman 2014). It has been argued, however, that external PARs rely on rather unrealistically high environmental stabilities particularly in the case of long time gaps between birth and adulthood and are otherwise not advantageous (Kuzawa and Quinn 2009; Nettle et al. 2013; Burton and Metcalfe 2014; Nettle and Bateson 2015). In a more stochastic environment, altered offspring phenotypes will face stronger and more frequent adult phenotype-environment mismatches than unaltered phenotypes which match the evolutionary average environment (Nettle et al. 2013; Nettle and Bateson 2015). Recently, another subtype of PAR was proposed which leads to similar effects but is independent of environmental (in)stability and only relies on the rather inevitable long-term effect of early life developmental constraints on adult mortality (Nettle et al. 2013; Nettle and Bateson 2015). This internal PAR-hypothesis proposes that offspring facing PreGC-related developmental constraints could utilize its currently impaired

somatic state to predict its rather unavoidably impaired future somatic state and reduced life expectancy and recalibrate its life history pace to optimally cope with these constraints in the long term (Nettle et al. 2013; Nettle and Bateson 2015; Tung et al. 2016).

Previous studies on various taxa found that PreGC is related to decreasing prenatal food intake and reduced pre- and postnatal maternal physical condition and investment and thus resource availability for the offspring (Bowen 2009; Hinde and Milligan 2011; Klaus et al. 2013; Sheriff and Love 2013; Tao and Dahl 2013). Both PreGC and reduced resource availability were shown to constrain offspring development in terms of reduced offspring growth (Patin et al. 2002; Emack et al. 2008; Berghänel et al. 2015), immune function (Coe and Lubach 2008; Palmer 2011; Tao and Dahl 2013; Lavergne et al. 2014; Veru et al. 2014), skill acquisition (Coe and Lubach 2008; Cao et al. 2014; Berghänel et al. 2015; Weinstock 2015), and cognitive or neuro-development (Coe and Lubach 2008; Del Giudice 2014a; Moisiadis and Matthews 2014a; Weinstock 2015). These developmental constraints have long-term consequences since adverse early life conditions lead to disadvantaged adult phenotypes including health deterioration, increased mortality, shortened life spans and reduced reproductive success in long-lived species including humans, roe deer, elephants and baboons (Metcalfe and Monaghan 2001; Hayward et al. 2013; Douhard et al. 2014; Nettle 2014; Jacobs et al. 2015; Lea et al. 2015; Mumby et al. 2015; Tung et al. 2016). Such detrimental short- and long-term effects question the existence of PARs and suggest that PreGC and early adversity merely lead to developmental constraints and silver spoon effects (Hayward et al. 2013; Lea et al. 2015). However, PreGC and early adversity can also lead to increased offspring growth rates or accelerated reproduction even in the same species (Patin et al. 2002; Mueller and Bale 2006; Hauser et al. 2007; Schöpper et al. 2012; Dantzer et al. 2013; Nettle 2014; Rickard et al. 2014; Belsky et al. 2015; Mumby et al. 2015; Rendina et al. 2016) which was claimed to support the existence of PARs (Hanson and Gluckman 2014; Rickard et al. 2014; Belsky et al. 2015).

The ambiguity in these results makes it currently difficult to assess the adaptive value of prenatal maternal effects on offspring phenotype and to differentiate between developmental constraints and PARs (Sheriff and Love 2013). It is also difficult to further distinguish between the internal and external PAR hypotheses, because they differ primarily in whether the mechanism requires high environmental predictability, but make otherwise similar predictions and are mutually compatible (Nettle and Bateson 2015). Most studies were conducted on captive animals and humans exposed to highly artificial and/or extreme stressors (Patin et al. 2002; Hauser et al. 2007; Emack et al. 2008; Hayward et al. 2013; Cao et al. 2014) and to environmental predictabilities that may strongly differ from the natural, evolutionary relevant, conditions. Studies on wild animals facing natural ecological conditions and evolutionary relevant stressors are extremely rare (Mateo 2009; Dantzer et al. 2013; Maestripieri and Klimczuk 2013; Sheriff and Love 2013; Lavergne et al. 2014). In particular, the occurrence of prenatal maternal stress effects in long-lived species has not been investigated under natural conditions yet, although it represents a critical test case for the internal PAR hypothesis (Wells 2007b; Maestripieri and Klimczuk 2013; Nettle et al. 2013; Sheriff and Love 2013; Mumby et al. 2015; Nettle and Bateson 2015).

This study provides such a test case presenting the first data on the causes and consequences of a wider range of pre- and postnatal maternal effects in a wild long-lived mammal, the Assamese macaque (*Macaca assamensis*), under natural ecological conditions. We have previously shown for our study group that immatures experience remarkable postnatal developmental constraints, with decreasing postnatal food availability being associated with reduced rates of growth and play, and consequently also decelerated motor skill acquisition (Berghänel et al. 2015). Here we investigate whether prenatal maternal food availability and PreGC lead to mere developmental constraints or a PAR in our study group. Environmental conditions are exceptionally unpredictable in Southeast Asian forests (van Schaik and Pfannes 2005; Corlett and Primack 2011; Heesen et al. 2013). In our study area year-to-year predictability of food abundance (correlation between successive years $r = 0.05$, $p = 0.92$, over 8 years) and rainfall ($r = -0.09$, $p = 0.86$, over 8 years) are very low. Hence our long-lived study species lives and probably evolved in a highly unpredictable environment (Tosi et al. 2003; Corlett and Primack 2011; Jones 2011) where an external PAR would by definition be unlikely to be advantageous and can therefore be excluded making it a test case of the internal PAR-hypothesis.

We combined observations of offspring behaviour with measures of maternal pre- and postnatal physiological stress (via faecal glucocorticoid measures), quantitative measures of natural food availability, and individual offspring growth rates measured via photogrammetry. To assess whether accelerated growth is accompanied by detrimental effects on more quality-related offspring attributes, we additionally measured offspring motor skill acquisition and used an outbreak of conjunctivitis to non-invasively and roughly assess immune function.

We first predict that prenatal maternal food availability is negatively correlated to PreGC which might be further associated with maternal rank and offspring sex (Schöpper et al. 2012; Sachser et al. 2013; Hanson and Gluckman 2014; Moisiadis and Matthews 2014a, b). In the case of a PAR, we predict that PreGC leads to increased postnatal growth rates accompanied by decelerated motor skill acquisition and reduced immune function. In the case of mere developmental constraints we predict that PreGC leads instead to decreased postnatal growth rates in addition to decelerated motor skill acquisition and reduced immune function. PreGC-effects on offspring phenotype may be mediated by prenatal food availability, sex of the offspring, maternal caretaking style, and postnatal maternal glucocorticoid levels during the lactation period (PostGC)(Patin et al. 2002; Nguyen et al. 2008; Maestripieri and Mateo 2009; Hinde and Milligan 2011; Klaus et al. 2013; Sachser et al. 2013; Sheriff and Love 2013; Moisiadis and Matthews 2014b; Belsky et al. 2015; Weinstock 2015). Hence if applicable, we controlled PreGC-effects on offspring phenotype for these variables as well as potential developmental constraints and trade-offs due to postnatal food availability and investment in (energy demanding physically active) social play (Berghänel et al. 2015). We also consider that increased postnatal growth rates may not be a consequence of accelerated life history but serve to compensate for reduced prenatal growth rate and aim at reducing body size differences at maturation (Metcalfe and Monaghan 2001; Dmitriew 2011). We therefore analyse PreGC-effects on offspring body size at age 16-18 months to distinguish between these two possibilities.

Methods

Study site and subjects

The study was conducted from May 2011 – December 2012 at the Phu Khieo Wildlife Sanctuary in Thailand. Assamese macaques are characterized by female philopatry and male dispersal. Females are fully grown and sexually mature at the age of 5-6yrs, and males are fully grown with 9-10yrs (Fürtbauer et al. 2010; Berghänel et al. 2015). Average gestation length is 164 days and interbirth interval is bimodally distributed around 14 and 23 months (Fürtbauer et al. 2010). Female reproduction is seasonal and condition dependent, i.e. probability of conception increases with food availability and female condition (Heesen et al. 2013). Infant suckling occurs throughout the first 12 months of life (weaning age); however, it occurs at high rates during the first six months only and rates are low during the second six months (Fig. S3.1). Therefore, we defined the lactation period here as the first six months of life (Heesen et al. 2013). We collected data on a fully habituated social group consisting of 24 adults (9 males, 15 females), 4-7 subadult males, 16-19 juveniles (4-8 males, 11-12 females), and 12 infants born in 2011 (6 males, 6 females) and 5 infants born in 2012 (2 males, 3 females). All 17 infants born to 15 mothers were focal animals.

Data collection

Behavioural data

Behavioural data were recorded during 30 min focal animal protocols (1385.4 focal hours, mean ± SD: 5.5 ± 0.2h per individual and month, 86,518 instantaneous records). We recorded instantaneously at 1min intervals whether the infant was resting, feeding, travelling, socially interacting (affiliative or agonistic) or engaged in solitary or social play. Social play was differentiated from other social behaviours like sitting in body contact, grooming, or aggression by the use of a play-face and/or regular role-changes. We additionally recorded every minute whether or not the infant was in nipple contact, suckling, carried by and/or clasped by the mother. We recorded continuously all social interactions of the focal infants. This included approaches and departures into and from 1.5m proximity, instances of body contact, grooming and agonistic interactions, being restrained from leaving the mother and being refused nipple contact for the first time. In addition we recorded all aggressive encounters of all group members ad libitum.

Motor skills

For all 17 focal animals, we recorded all occurrences of 18 different motor skills (N = 5,333 ad libitum records; including closed and open motor skills (Poulton 1957)) to assess individual latencies of skill acquisition, i.e. age at first occurrence for each separate motor skill and individual. All 18 motor skills were acquired by all individuals within the lactation period; (Berghänel et al. 2015), Table S3.1.

Growth rate

Size was measured every month via photogrammetry from the length of the lower arm from birth until the end of the study. We took 1,706 pictures of the 17 focal animals (6.4 ± 2.1 pictures per individual and month; mean ± SE). Picture and object distance were recorded in parallel, and length was calculated by multiplying the object distance with the number of pixels in the picture (Berghänel et al. 2015; Galbany et al. 2016)(electronic supplementary material). Outliers (> mean ± 2SD) were excluded for each month and individual separately, and monthly individual average size and age from the remaining pictures entered the analyses. Since linear growth is expected for increase in volume instead of length, we used the cubic value of our length measure (= size index). The relationship between size index and age was linear with normal distribution of residuals, and data were largely unbounded ((Berghänel et al. 2015), electronic supplementary material). Growth rates were calculated as slopes of linear regressions of these monthly values over time.

Eye infection

During a 2 months-outbreak of conjunctivitis during the lactation period, we recorded on a daily basis whether an infant showed external signs of infection or not (Fig. S3.3; mean ± SD: 22.8 ± 1.6 records per individual). From these data we calculated the percentage of days an individual had been seen with signs of infection as an approximation of immune function.

Availability of ecological energy resources

Monthly food availability indices were calculated based on fruit abundance of 650 trees of the 57 most important food species representing 69% of feeding time for plant matter and the density of these tree species, based on 44 botanical plots within the home range of the study group, covering 20.75 ha of forest. Density was multiplied with phenology scores and summed across tree species to calculate the food abundance index; for details and seasonal variation of food availability in the study site see (Heesen et al. 2013). Individual energy intake is closely correlated to this index, but not to female rank (Heesen et al. 2013).

Collection of faecal samples and GC analyses

Faecal samples were collected from mothers during gestation (N = 309, mean ± SD per female and month: 3.0 ± 1.8; PreGC) and lactation (months 1 - 6, N = 253, 2.5 ± 1.7; PostGC); for details see supplementary material and (Shutt et al. 2012)). Faecal samples were extracted in ethanol and extracts were analysed for immunoreactive 11β-hydroxyetiocholanolone (GC), a major metabolite of cortisol in primate faeces (Heistermann et al. 2006), using enzyme immunoassay. The assay, carried out as described in (Heistermann et al. 2004), has been validated for monitoring adrenocortical activity in numerous primate species (Heistermann et al. 2006) including Assamese macaques (Ostner et al. 2008a; Fürtbauer et al. 2014). Prior to each assay, extracts were diluted 1:200 to 1:2000 (depending on concentration) with assay buffer. Assay sensitivity at 90% binding was

2.0 pg. Intra- and inter-assay coefficients of variation, determined by replicate measurements of high- and low-value quality controls, were 5.2% and 9.7% (high) and 7.7% and 13.6% (low). We ran each sample in duplicate and calculated mass steroid metabolite per mass faecal wet weight in ng/g.

Statistical analyses

If not stated otherwise, all analyses were run with R 3.1.4 (R development core team 2011). Tests were two-tailed with alpha level set to 0.05. We ensured that test assumptions were fulfilled by computing variance inflation factors (vifs), dffits and dfbetas for all general linear models (LM), generalized linear models (GLM) and generalized least squares models (GLS; packages car, nlme and piecewiseSEM, (Fox and Weisberg 2011; Lefcheck 2016; Pinheiro et al. 2016)) and visual inspection of scatterplots, residual plots, histograms, and Q-Q plots of residuals to check for normality, linearity and homogeneity of variance. All p-values were adjusted for multiple testing (function p.adjust with Holm-correction). Only offspring of the first cohort (N = 12) was included in the analyses on body size at 16-18 months and conjunctivitis (occurred in first cohort only). All other analyses included all individuals from both cohorts (N = 17) with year of birth as control variable.

Previous studies have shown that PreGC-effects on offspring phenotype are often specific for certain gestational trimesters (Mueller and Bale 2006; Cao et al. 2014; Moisiadis and Matthews 2014a, b; Veru et al. 2014). Therefore we analysed PreGC-effects on offspring growth not only using the average GC-level throughout gestation, but also using GC-levels of each trimester separately (each gestational trimester = 55 days). Based on birth dates (day 0), early gestation ranged from -165 to -111 days, mid from -110 to -56 days, late from -55 to 0 days and early-to-mid gestation from -165 to -56 days.

Female rank order

The female dominance rank order was calculated via the I&SI-rank order-method (Matman1.1, (de Vries 1998)) on a winner-loser-matrix based on dyadic decided conflicts including unprovoked submissions and decided aggressive encounters without mutual aggression or mutual submission (Ostner et al. 2008a).

Maternal style

We ran a principal component analysis (SPSS 20.0; IBM) to detect whether and how different types of mother-infant-interactions during the lactation period belong to independent maternal style dimensions. We assessed a mother's responsibility for maintaining proximity within 1.5m to her infant, by calculating the respective Hinde-index as the difference between the proportion of approaches by the mother and the proportion of her departures (Hinde and Atkinson 1970a) and included this variable into the analysis. Since we are not aware of principal component analysis that can implement a control variable, all measures were mean-scaled for year of birth before analysis.

Model 1-6: General description

We ran 6 different models. Model 1 tested our prediction that PreGC is related to prenatal food availability, and Model 2 explored relationships between PreGC and postnatal maternal attributes. Model 3 investigated PreGC-effects on postnatal offspring growth rate and whether these effects are due to PreGC during a certain gestational period. Model 4-6 investigated whether the PreGC-effect on offspring growth rate translates into body size differences at 16-18 months and is accompanied by reduced immune function and decelerated motor skill acquisition. Model 3, 4 and 6 included pre- and postnatal food availability, PostGC, maternal caretaking style, sex of the offspring, investment in social play (in proportion of time) and growth rate (only Model 6) as control variables. Model 5 had few cases and was only controlled for prenatal food availability. When using repeated measures (Model 1,3,4,6) we ran a GLS with ID as grouping variable and (continuous) first-order autoregressive covariance structure (CAR1; Model 6: AR1).

If not stated otherwise, postnatal food availability, PostGC and investment in social play were calculated as average between birth and age at measurement, resulting in different time periods and thus separate values for each data point. For food availability, we first estimated daily indices based on linear interpolation between the monthly indices, and then calculated the average of these daily indices for the respective time period. To control for sampling effort, we included only data points in the analyses which are based on at least 3 measurements of PostGC on different days and 400 instantaneous records for time spent in social play.

We calculated covariance matrices and variation inflation factors (vifs). If a predictor of interest had a high vif (>4) and was significant, the null-hypothesis had to be rejected, but the estimated effect of the predictor had to be reassessed in a reduced model (O'brien 2007) with the correlated control variable excluded if $|r| > 0.7$.

PreGC and prenatal food availability (Model 1)

To analyse the effect of prenatal food availability on PreGC, we ran a GLS with mother-ID as grouping variable (N = 296 faecal samples) that controlled for maternal rank, offspring sex, year of birth, day of gestation and day time of sampling. We entered a long- and a short-term measure of prenatal food availability in the model, i.e. average food availability during the three month leading up to the sampling day ("before") or on the day prior to faecal sampling ("present"). Test assumptions were met after log-transformation of the response variable.

PreGC and postnatal maternal attributes (Model 2)

To analyse correlations between average PreGC during gestation and postnatal maternal caretaking style and physiological stress (PostGC), we ran a LM (N = 17) with offspring sex and postnatal food availability (highly correlated to year of birth r = 0.994) as control variables.

PreGC-effects on postnatal offspring growth rate (Model 3)

We provide a GLS with infant-ID as grouping variable (N = 227) which quantifies how offspring body size was predicted by an interaction between average PreGC during gestation

and age at measurement, controlling for interactions between age and the control variables including year of birth. Since many body size measurements were taken after lactation and PostGC-sampling period had ended, we included the average PostGC through lactation instead of time-varying PostGC as control variable.

PreGC-effects on offspring body size at 16-18 months of age (Model 4)

We provide a GLS with infant-ID as grouping variable (N = 34) to investigate the effect of average PreGC during gestation on offspring body size at 16-18 months of age, additionally controlling for age at measurement. The average PostGC through lactation instead of time-varying PostGC was included as control variable.

PreGC-effects on offspring immune function (Model 5)

We investigated the effect of average PreGC during gestation on the proportion of days an individual was seen with signs of pink eye during the outbreak applying a binomial logit-link GLM controlling for prenatal food availability (N = 12).

PreGC-effects on offspring motor skill acquisition (Model 6)

We investigated the effect of average PreGC during gestation on the latencies of skill acquisition with a GLS (N=173) with motor skill labels as categorical control variable and infant-ID as grouping variable. The autoregressive term (AR1) was based on an ordinal motor skill acquisition sequence which was generated by applying the I&SI-rankorder-method (Matman1.1, de Vries 1998) on a before-after matrix (i.e. how often motor skill A was acquired before or after motor skill B over all individuals; see (Berghänel et al. 2015)). The resulting sequence was highly linear (corrected Linearity index h' = 0.998, $p < 0.001$) and the overall consistency of pairwise sequence was 0.716. Five individuals were born more than one week prior to the start of observations and therefore excluded from this analysis.

Table 3.1. Maternal style – Principal component analysis. Cut-off value = 0.4, KMO = 0.716, Bartlett's Test $p < 0.001$.

Principal component analysis:	Component	
	Protectiveness	Rejectiveness
Close proximity (average duration)	0.908	
Body contact (average duration)	0.898	
Body contact (total time)	0.841	
Clasping (% of time)	0.788	
Carrying (% of time)	0.788	
Restrain rate	0.640	
Hinde index mother (proximity)	0.554	
Aggression rate		0.856
Age of refused nipple contact		-0.744

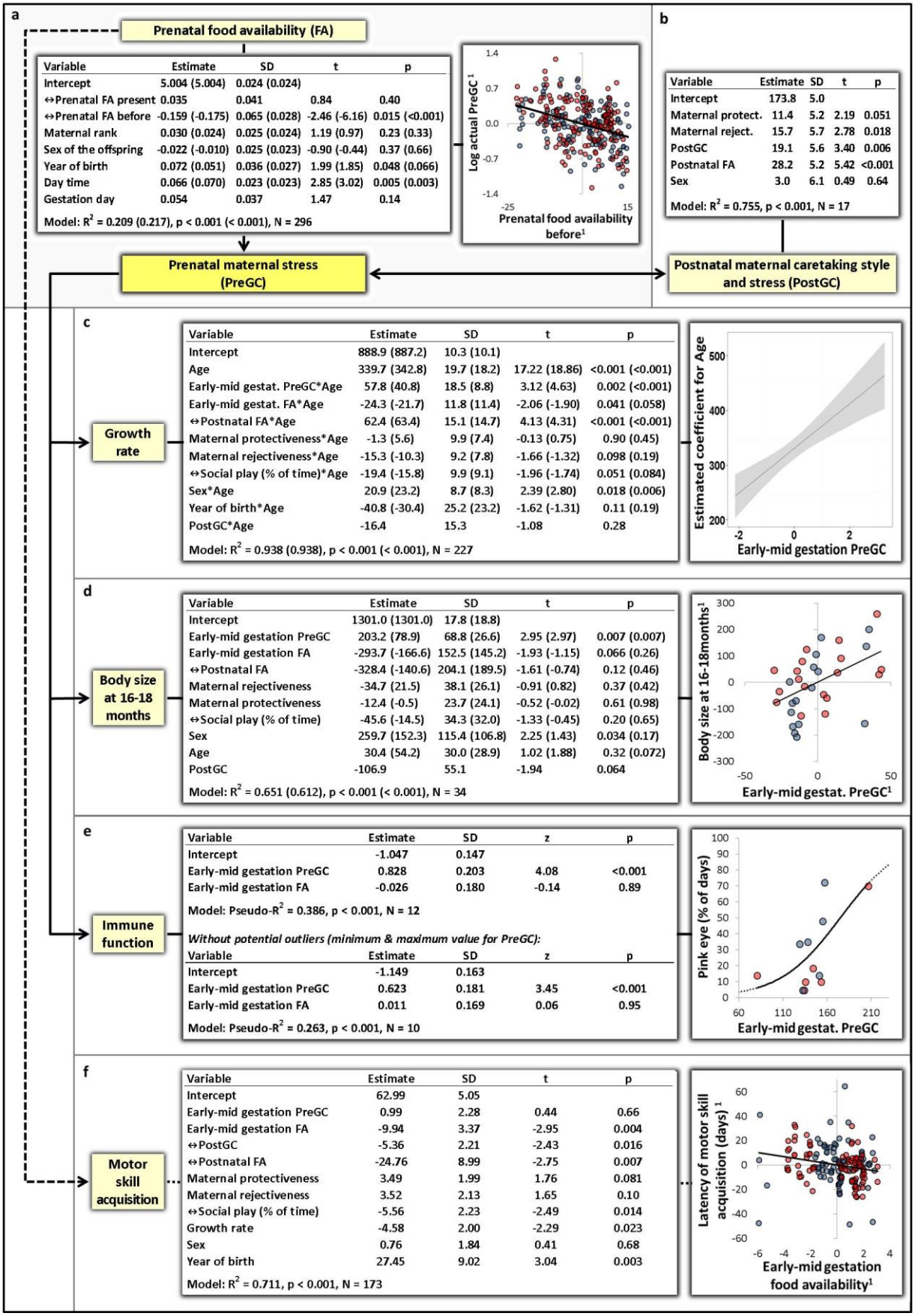

Figure 3.1. (*Caption Overleaf.*)

Figure 3.1. (*Overleaf.*) Causes and consequences of maternal physiological stress. Red: females, blue: males. Values in brackets: reduced model after exclusion of the collinear control variable(s) (see text). Superscript 1 in the artwork denotes model residuals (partial regression plot). All fixed effects were z-transformed. Sex: male/female = 0/1. **(a)** Prenatal food availability predicted gestational maternal GC-level (PreGC). (Model 1, GLS, response variable: PreGC (individual samples, log-transformed), grouping variable: mother-ID; ↔on the day the GC in the faecal sample were produced ('present') or during the three month leading up to the sampling day ('before'). **(b)** Postnatal maternal GC-level (PostGC) and rejectiveness, and by trend also protectiveness, were independently related to PreGC (Model 2, LM, response variable: average PreGC during gestation). **(c)** PreGC during the first and second gestational trimester predicted postnatal growth rates (Model 3, GLS, response variable: monthly body size index, grouping variable: infant-ID; ↔from birth until age of separate measurement). We report the main effect for age only because all other main effects do not inform the research question. Chart: the interaction between age and early-mid-gestation PreGC of the reduced model is plotted, i.e. the influence of PreGC on the estimate of age (shaded: 95% confidence interval; package: interplot [65]). **(d)** Body size at the age of 16–18 months was predicted by early-to-mid-gestational PreGC (Model 4, GLS, response variable: body size indices at 16–18 months of age, grouping variable: infant-ID; ↔from birth until age of separate measurement). **(e)** Proportion of days with signs of conjunctivitis during an outbreak was predicted by early-to-mid-gestational PreGC (Model 5, binomial logit-link GLM, response variable: counts of days with signs/without signs). Scatterplot: original data, logit regression line based on model estimates. **(f)** Latency of motor skill acquisition decreased with increasing pre- and postnatal food availability but not early- to-mid-gestational PreGC (Model 6, GLS, response variable: individual age at first occurrence, grouping variable: infant-ID, with motor skill labels as categorical control variable (not shown); ↔from birth until age of separate measurement).

Results

Environmental conditions, maternal characteristics and maternal physiological stress

Firstly, we analysed potential predictors of current maternal glucocorticoid levels during gestation (PreGC). Controlling for maternal rank, sex of the offspring, year of birth, day of gestation and day time of sampling, we found in the full model that PreGC was negatively correlated to the average longer-term prenatal food availability before sampling but not to the present prenatal food availability at GC sampling (Fig. 3.1a). Hence an accumulating effect of food shortages and thus probably reduced maternal physical condition was associated with increased physiological stress during gestation. Prenatal food availability before sampling was highly correlated to present prenatal food availability and day of gestation in the model (r = -0.767 and 0.731) which affected its estimate but not its significance (Fig. 3.1a; vif in full model = 8.91, without present prenatal food availability and day of gestation: vif = 1.65).

Secondly, we analysed associations between PreGC and postnatal maternal caretaking style and glucocorticoid level during the lactation period (PostGC). The variation in maternal caretaking was characterized by two independent components which we labelled maternal protectiveness and maternal rejectiveness (Table 3.1). Controlling for postnatal food availability and offspring sex, PreGC was positively correlated to maternal rejectiveness and PostGC, whereas the relationship with maternal protectiveness showed a statistical trend (Fig. 3.1b).

Maternal physiological stress and offspring attributes

Next we investigated PreGC-effects on postnatal offspring growth rate and whether these effects are due to PreGC during a certain gestational period. PreGC had significant effects on the offspring´s growth rate and body size also after controlling for pre- and postnatal food availability, PostGC, maternal rejectiveness and protectiveness, parallel investment in social play, and sex of the offspring. Offspring growth rate was positively correlated to PreGC during the first and second trimester (early-to-mid-gestational PreGC; Fig. 3.1c) but not to PreGC during the third trimester (Table S3.2). As a result, early-to-mid-gestational PreGC was a better predictor of offspring growth rate than the average GC levels throughout gestation (Table S3.3). The interactions of age with early-mid gestational PreGC and PostGC were highly correlated in the model (r = -0.865) which affected the effect size by but not the significance of the early-mid gestational PreGC effect (Fig. 3.1c; vif in full model = 9.39, without PostGC: vif = 2.13).

Lastly we investigated whether this effect on offspring growth translates into body size differences at 16-18 months and is accompanied by reduced immune function and decelerated motor skill acquisition. The positive effect of early-to-mid-gestational PreGC on offspring growth rate led to increased offspring body size at the age of 16-18 months (Fig. 3.1d), thus constituting a generally accelerated life history pace instead of a simple catch-up growth. Early-mid gestational PreGC was highly correlated to PostGC in the full model (r = -0.930) which strongly affected its estimate but not its significance (Fig. 3.1d; vif in full model = 14.48, without PostGC: vif = 1.95).

After controlling for prenatal food availability, early-to-mid-gestational PreGC was correlated to the proportion of days with signs of conjunctivitis during an outbreak which lasted for two months (Fig. 3.1e).

Latency of offspring motor skill acquisition was not predicted by early-mid gestation PreGC after controlling for pre- and postnatal food availability, PostGC, maternal rejectiveness and protectiveness, parallel investment in social play, sex of the offspring and growth rate (Fig. 3.1f). Instead, across motor skills the latency of skill acquisition increased with decreasing pre- and postnatal food availability, indicating direct developmental constraints probably due to reduced pre- and postnatal maternal investment.

Discussion

Our results provide the first evidence for strong effects of elevated prenatal maternal physiological stress (PreGC) on offspring development in a wild non-human primate living under natural conditions, thus adding fundamental data to the sparse literature on PreGC-effects in wild animals. We demonstrate that PreGC-effects can result from a PAR also in long-lived, slow-developing mammals living in a rather unpredictable environment and being exposed to moderate, evolutionarily relevant stressors only. Although the effects of prenatal maternal stress on offspring adult fitness are beyond the scope of this study, our results provide evidence for the existence of internal, somatic state-based PARs in a species where external, environment forecast-based PARs can be excluded by definition.

The negative relationship between prenatal maternal stress hormone levels and prior food availability in our study suggest that physiological stress was related to maternal physical condition. This probably leads to reduced energy intake of the offspring and developmental constraints, since prenatal maternal stress has been shown to increase with decreasing maternal energy intake and physical condition and to lead to reduced gestational and lactational investment in many mammals (Bowen 2009; Hinde and Milligan 2011; Klaus et al. 2013; Sheriff and Love 2013; Tao and Dahl 2013). PreGC-effects in terms of developmental constraints due to reduced maternal investment could be reflected in or compensated by postnatal maternal caretaking style (Weinstock 2015). In our study, maternal style during lactation varied along two axes similar to those found in previous studies (Bardi and Huffman 2002). PreGC was related to maternal rejectiveness and by trend also to maternal protectiveness which is in agreement with previous findings (Patin et al. 2002; Nguyen et al. 2008; Klaus et al. 2013; Sheriff and Love 2013). Yet, the relationships between PreGC and offspring phenotype found in our study were neither mediated by postnatal maternal caretaking style nor glucocorticoid level during the lactation period (PostGC).

PreGC was negatively related to a coarse measure of offspring immune function, supporting previous results (Coe and Lubach 2008; Palmer 2011; Tao and Dahl 2013; Lavergne et al. 2014; Veru et al. 2014). We also found decelerating prenatal maternal effects on the offspring´s motor skill acquisition, but these effects were due to prenatal food availability instead of PreGC, and probably directly linked to reduced maternal investment. Previous studies reported PreGC-effects on motor skill acquisition (Coe and Lubach 2008; Cao et al. 2014) but did not control for maternal energy intake and condition.

The negative prenatal effects on offspring phenotype in our study are in line with predictions from the developmental constraints-hypothesis proposing that early adversity constrains offspring development. Developmental constraints lead to disadvantaged adult phenotypes including health deterioration, reduced reproductive success and life expectancy (Hayward et al. 2013; Douhard et al. 2014; Nettle 2014; Jacobs et al. 2015; Lea et al. 2015; Mumby et al. 2015; Tung et al. 2016). The internal PAR-hypothesis proposes accelerated growth and reproduction in reaction to developmental constraints and the resulting reduced life expectancy (Nettle et al. 2013; Rickard et al. 2014). The positive effect of PreGC on offspring growth rate and body size at 16 - 18 months in our study supports this prediction. Previous results on growth were, however, highly inconsistent, with some studies reporting a positive (Patin et al. 2002; Mueller and Bale 2006; Hauser et al. 2007; Schöpper et al. 2012; Dantzer et al. 2013) and others a negative relationship with PreGC (Patin et al. 2002; Hauser et al. 2006; Emack et al. 2008) even in the same species. This inconsistency indicates that PreGC is rather invariably related to developmental constraints but does not always induce a PAR. Induction of a PAR might be caused by a stressor´s timing during gestation due to varying effects of PreGC on placenta morphology or critical developmental periods which constrain plasticity (Hanson and Gluckman 2014; Moisiadis and Matthews 2014a, b). The positive effect of PreGC on growth accompanied by the negative effect on immune function in our study suggests that investments into these processes are traded-off against each

other, and that PreGC rearranges the setting of this trade-off in favour of growth (Metcalfe and Monaghan 2001; Belsky et al. 2015). The dataset of the present study did not allow us to test this hypothesis directly since data on the age of onset of reproduction, longevity or lifetime reproductive success are not available. Still previous results suggest that such a trade-off is inevitable because growth and immune function as well as neurodevelopment all strongly rely on available resources (Metcalfe and Monaghan 2001; Coe and Lubach 2008; Martin et al. 2008; Palmer 2011; Berghänel et al. 2015).

Previous research focusing on PARs in long-lived mammals including humans provided no evidence for a PAR and concluded that early adversity may lead solely to developmental constraints and disadvantaged adult phenotypes in such species (Hayward et al. 2013; Douhard et al. 2014; Jacobs et al. 2015; Lea et al. 2015; Mumby et al. 2015). These studies, however, tested predictions of external but not for internal PARs (Nettle and Bateson 2015). The external PAR-hypothesis assumes that individuals with increased adult phenotype-environment-matching always outperform less or mismatched individuals (Nettle et al. 2013; Hanson and Gluckman 2014; Nettle and Bateson 2015). Consequently the above mentioned studies tested and refuted the resulting critical prediction that under adverse conditions during adulthood, individuals which faced similar (i.e. adverse) early life conditions outperform those which faced different (i.e. optimal) early life conditions. This prediction does not result from the "internal PAR"-hypothesis since early life and adult somatic states are causally linked and adult phenotype mismatches are impossible as long as other confounding variables such as genetic or adult environmental differences are identical (Nettle et al. 2013; Nettle and Bateson 2015). Compared to phenotypes of developmentally unconstrained offspring, the phenotype of developmentally constrained offspring will therefore always be disadvantaged. Hence developmentally constrained adults will hardly outcompete unconstrained ones, but internal PARs will enable them to make the best of a bad job by performing better than without this phenotype recalibration. Results of these previous studies conform to (Hayward et al. 2013; Douhard et al. 2014; Jacobs et al. 2015; Lea et al. 2015) or even support this view (Nettle 2014; Rickard et al. 2014; Mumby et al. 2015).

Our combined with previous results suggest that PARs in long-lived species are internal rather than external, but external PARs may still apply in short-lived species. Environmental predictability is related to seasonal environmental variation in many of these species and thus potentially high (Kuzawa and Quinn 2009). However, correlations within a stressor over lifetime (e.g. seasonal changes in temperature or food availability) and correlations between stressors (e.g. seasonal population density and individual predation risk) may be positive or negative and can change as season proceeds. Under such complex conditions it would be expected that external PARs predicting seasonal variation rely on specific prenatal cues rather than the general and unspecific PreGC or environmental adversity. It was shown that offspring maturation in root voles varies with seasonal changes in prenatal maternal melatonin (day length) and chemical by-products of grass ingestion (Kuzawa and Quinn 2009). The strongest evidence for internal and against PreGC-related external PARs comes from studies on cross-generational effects of early life conditions (Burton and Metcalfe

2014). Effects of PreGC or early life adversity on offspring phenotype in the first generation are passed on to subsequent generations independent from the prenatal environmental conditions of those subsequent generations, in species ranging from short-lived (Drosophila, rats) to long-lived like humans (Metcalfe and Monaghan 2001; Sheriff and Love 2013; Burton and Metcalfe 2014; Hanson and Gluckman 2014). While such effects would usually be maladaptive (and easily avoidable) from the external PAR-perspective (but see (Taborsky 2006)), they conform to internal PARs since mothers facing a disadvantaged adult somatic state due to their own developmental constraints may reduce their maternal investment and thus re-induce developmental constraints in their offspring (Burton and Metcalfe 2014).

Data accessibility: The data used in this article will be available from dryad (doi: 10.5061/dryad.jq68q) after an embargo period.

Authors' contribution: A.B. collected and analysed data, M.H. ran hormone analyses, A.B., O.S. and J.O. designed the study, all authors wrote the paper and J.O. and O.S. contributed equally as last authors.

Competing interests: We declare we have no competing interests.

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Supplementary material

Prenatal stress effects in a wild, long-lived primate: predictive adaptive responses in an unpredictable environment

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Supplementary methods

Growth data

Picture and object distance were recorded parallel using a Nikon D5000 camera and a Bosch PLR 50 laser distance measurement tool (accuracy ± 2mm). Number of pixels in the picture was determined using ImageJ 1.44p (National Institute of Health, USA). We ran a basic LMM with body size index as response variable, age as predictor variable and immature ID as random effect (N = 227). This model was highly linear (R2 = 0.932) and the residuals of this model were normally distributed (Shapiro-Wilcoxon-test: W = 0.991, p = 0.15). The data were largely unbounded at both ends: based on the normal distribution of our data, the probability of a size index ≤ 0 at birth was 0.9% (i.e. the standard distribution of the data were bounded at about -2.4 standard deviations at birth), and the maximal size indices were far from adult body size (Fig. S3.2; Berghänel et al. 2015) with a probability of <0.001% that an immature at the end of the study period has a size index ≥ the minimal adult body size index measured in our study group.

Collection and preparation of faecal samples for GC analyses

Samples uncontaminated with urine or water were collected immediately after defecation, homogenized and approximately 0.5g of faecal material was transferred into a tube containing 4ml of 80% ethanol (Shutt et al. 2012). Upon return to the field site stress hormone metabolites were extracted from the samples using a validated field extraction protocol following (Shutt et al. 2012). 2ml of each sample extract was transferred into a polypropylene tube and stored at ambient temperature until transport to the endocrinology laboratory at the German Primate Center Göttingen where samples were stored at -20°C until analysis.

Supplementary figures

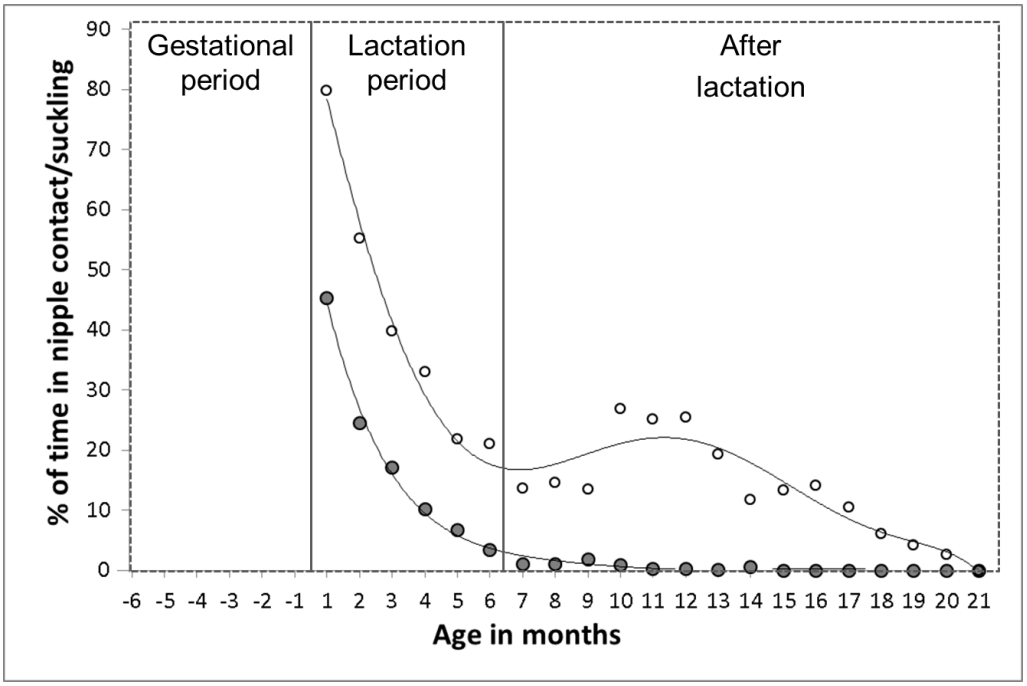

Figure S3.1. Frequencies of time in nipple contact (white) and time suckling (grey) over age.

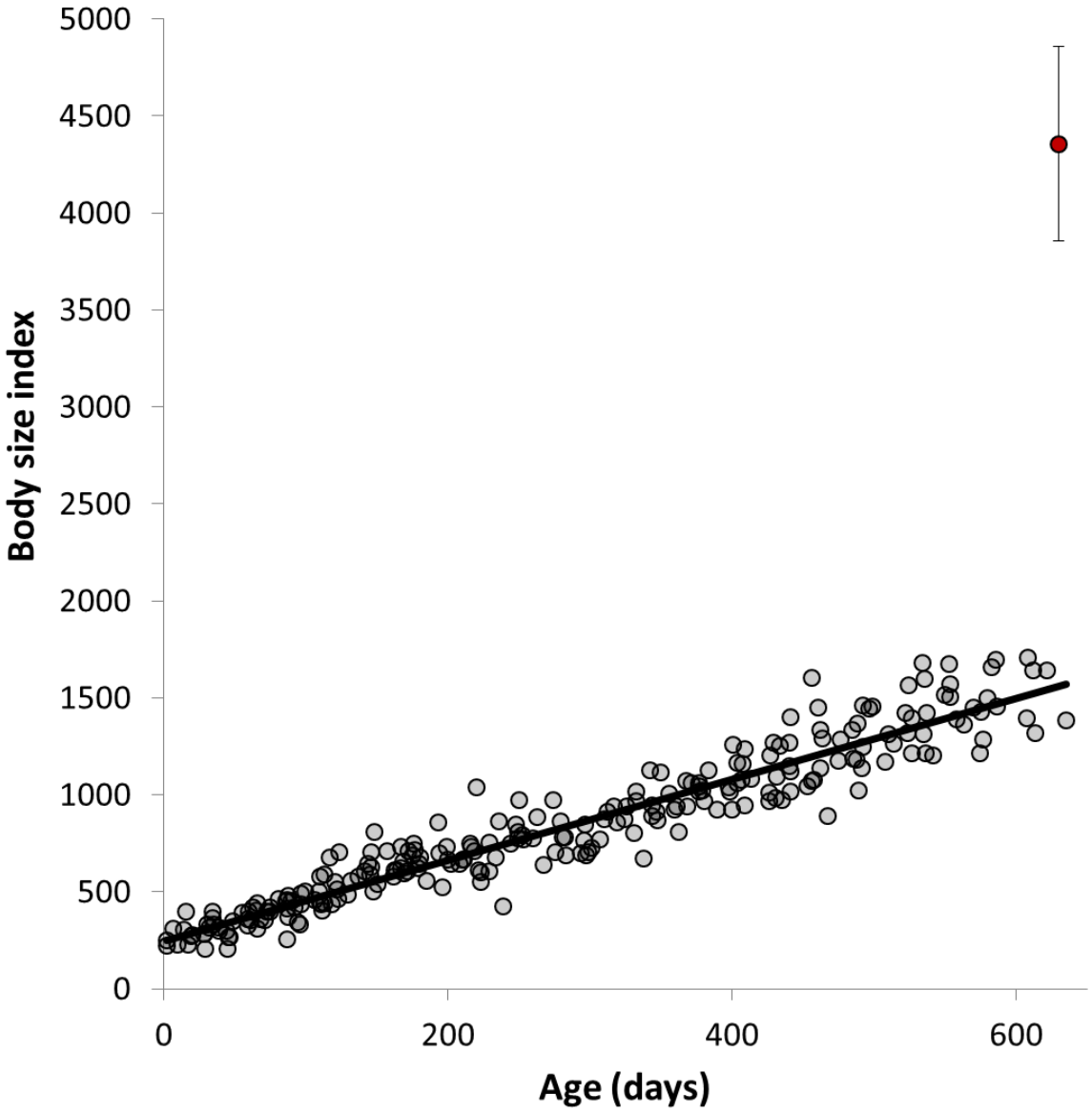

Figure S3.2. Body size index increases linearly with age and was far from reaching adult female body size at the end of the study period. Grey: immatures, red: adult females (mean ± SD).

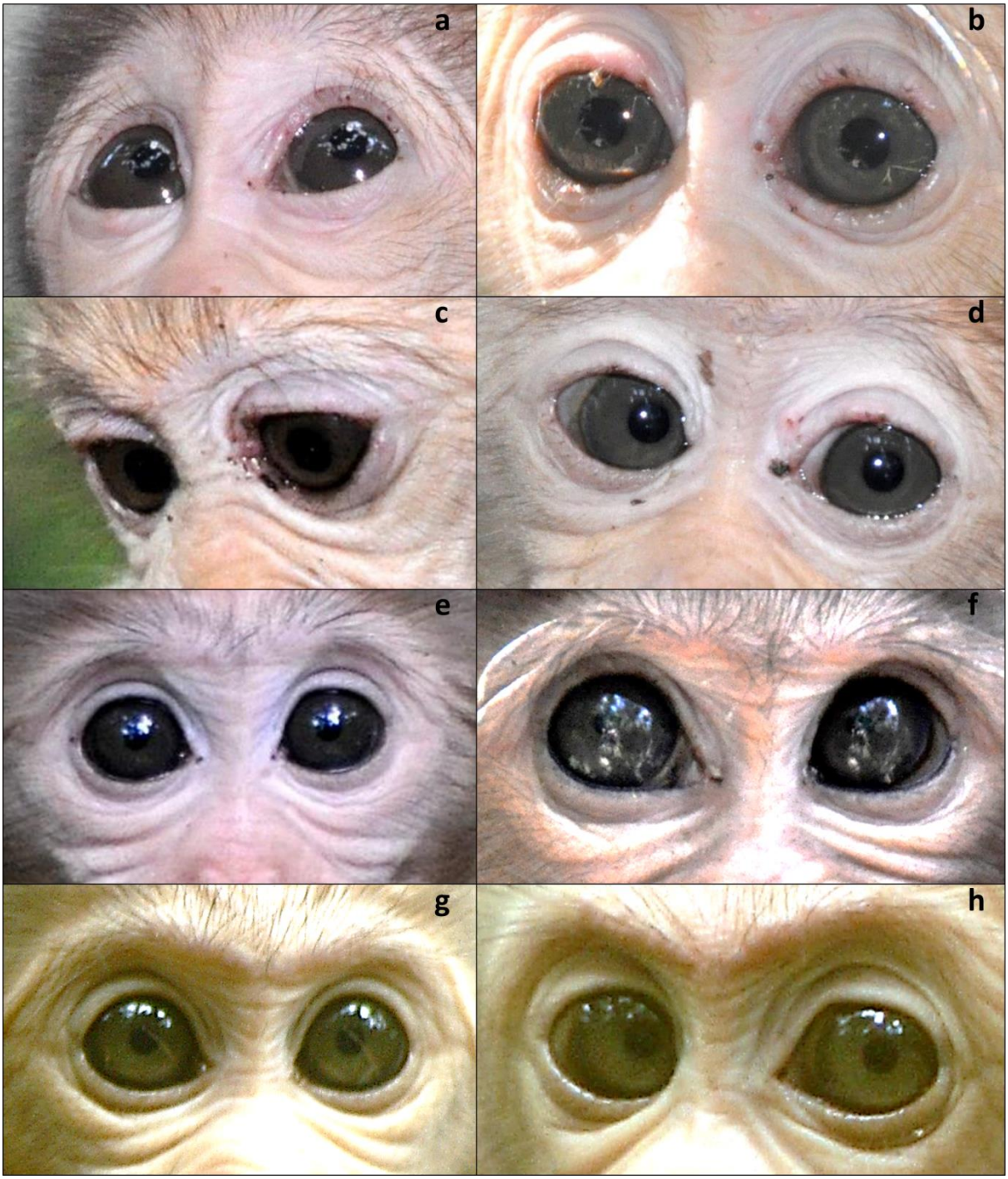

Figure S3.3. Conjunctivitis was diagnosed by swelling, reddening and sometimes suppuration of infant conjunctiva. (a-d) infected infants, (e-h) uninfected infants

Supplementary tables

Table S3.1: List of the 18 motor skills used in this study. * jumping from branch to branch. For more details, see (Berghänel et al. 2015).

Sequence	Motor skill	Average age of acquisition (Mean±SD)
1	Hanging on all extremities in solitary context	33.8 ± 15.0
2	Hanging on two arms in solitary context	36.2 ± 14.6
3	Jumping on ground	47.7 ± 15.2
4	Hanging on one arm in solitary context	50.7 ± 20.7
5	Jumping in tree	51.1 ± 15.8
6	Running on ground	54.8 ± 14.5
7	Hanging on two legs in solitary context	59.4 ± 15.3
8	Running in tree	63.9 ± 18.3
9	Hanging on all extremities in social play context	59.8 ± 16.8
10	Jumping a distance of <1m in less than 5m height*	67.6 ± 20.5
11	Hanging on two arms in social play context	62.2 ± 15.7
12	Jumping a distance of <1m in more than 5m height*	67.7 ± 13.3
13	Hanging on one leg in solitary context	71.6 ± 27.3
14	Hanging on two legs in social play context	79.9 ± 19.5
15	Hanging on one arm in social play context	77.8 ± 21.7
16	Jumping a distance of 1-2m in less than 5m height*	105.6 ± 28.7
17	Jumping a distance of 1-2m in more than 5m height*	116.8 ± 27.5
18	Hanging on one leg in social play context	108.4 ± 21.3

Table S3.2: Offspring growth rate was positively correlated to PreGC during the first and second trimester but not to PreGC during the third trimester. All fixed effects were z-transformed. Sex: male/female = 0/1. Values in brackets: reduced model after exclusion of PostGC. ↔Time-varying measure from birth until age of separate measurement. Values in brackets: reduced model after exclusion of PostGC*Age

Variable	Estimate	SD	t	p
Intercept	**888.5 (886.1)**	**10.1 (9.9)**		
Age	**323.5 (337.7)**	**22.4 (20.3)**	**14.47 (16.60)**	**<0.001 (<0.001)**
Early-gestation PreGC*Age	**47.9 (36.7)**	**13.7 (10.9)**	**3.49 (3.36)**	**<0.001 (<0.001)**
Mid-gestation PreGC*Age	**36.6 (21.1)**	**13.8 (8.9)**	**2.65 (2.38)**	**0.009 (0.018)**
Late-gestation PreGC*Age	**-2.7 (-5.5)**	**9.5 (9.2)**	**-0.28 (-0.60)**	**0.78 (0.55)**
Prenatal food availability*Age	**-23.0 (-20.8)**	**12.2 (12.0)**	**-1.89 (-1.74)**	**0.060 (0.084)**
↔Postnatal food availability*Age	**53.1 (59.8)**	**16.6 (15.8)**	**3.21 (3.78)**	**0.002 (<0.001)**
Maternal protectiveness*Age	**-8.5 (1.2)**	**9.9 (7.6)**	**-0.86 (0.15)**	**0.39 (0.88)**
Maternal rejectiveness*Age	**-22.5 (-15.8)**	**11.0 (10.2)**	**-2.04 (-1.54)**	**0.042 (0.12)**
↔Social play (% of time)*Age	**-17.5 (-13.8)**	**10.5 (9.8)**	**-1.66 (-1.42)**	**0.098 (0.16)**
Sex*Age	**19.6 (21.6)**	**8.7 (8.3)**	**2.24 (2.61)**	**0.026 (0.010)**
Year of birth*Age	**-43.4 (-30.7)**	**24.5 (22.9)**	**-1.77 (-1.34)**	**0.078 (0.18)**
PostGC*Age	**-25.1**	**14.9**	**-1.69**	**0.093**

Model: R^2 = 0.942 (0.941), p < 0.001 (< 0.001), N = 227

Table S3.3: Early-to-mid-gestational PreGC was a better predictor of offspring growth rate than the average GC levels throughout gestation. All fixed effects were z-transformed. Sex: male/female = 0/1. Values in brackets: reduced model after exclusion of PostGC. ↔Time-varying measure from birth until age of separate measurement. Values in brackets: reduced model after exclusion of PostGC*Age

Variable	Estimate	SD	t	p
Intercept	**889.2 (887.3)**	**10.4 (10.2)**		
Age	**336.5 (342.3)**	**20.7 (18.4)**	**16.25 (18.63)**	**<0.001 (<0.001)**
PreGC throughout gestation*Age	**8.6 (5.5)**	**17.6 (16.6)**	**0.49 (0.33)**	**0.63 (0.74)**
Early-mid gestation PreGC*Age	**51.9 (36.4)**	**23.3 (16.1)**	**2.23 (2.27)**	**0.027 (0.025)**
Early-mid gestation food availability*Age	**-23.6 (-21.5)**	**11.9 (11.5)**	**-1.98 (-1.87)**	**0.049 (0.063)**
↔Postnatal food availability*Age	**59.6 (62.2)**	**16.0 (15.1)**	**3.73 (4.12)**	**<0.001 (<0.001)**
Maternal protectiveness*Age	**-1.7 (5.6)**	**10.1 (7.5)**	**-0.17 (0.75)**	**0.87 (0.45)**
Maternal rejectiveness*Age	**-16.9 (-11.2)**	**9.7 (8.3)**	**-1.74 (-1.35)**	**0.083 (0.18)**
↔Social play (% of time)*Age	**-18.1 (-14.7)**	**10.7 (9.9)**	**-1.68 (-1.49)**	**0.094 (0.14)**
Sex*Age	**21.4 (23.5)**	**9.0 (8.5)**	**2.38 (2.77)**	**0.018 (0.006)**
Year of birth*Age	**-39.8 (-29.5)**	**25.5 (23.5)**	**-1.56 (-1.26)**	**0.12 (0.21)**
PostGC*Age	**-17.7**	**15.6**	**-1.14**	**0.26**

Model: R^2 = 0.937 (0.938), p < 0.001 (< 0.001), N = 227

Chapter 4

Prenatal stress accelerates offspring growth to compensate for reduced maternal investment across mammals

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Manuscript in preparation

Abstract

Prenatal maternal stress (PREMS) affects many aspects of offspring development in a variety of mammalian species. Current theories of the pathology and evolution of PREMS are based on opposing assumptions and make contradictory predictions. This is reflected in available data which shows that PREMS can have positive but also strongly negative effects on offspring growth, even within the same species. Here we present a comparative analysis of published data which, together with original data from a wild long-lived primate, support a novel parsimonious framework that explains the full range of PREMS-effects on offspring growth across mammals. We show that PREMS is negatively correlated to maternal energy investment and consequently extrinsic offspring growth. At the same time, PREMS leads to elevated foetal glucocorticoid exposure which triggers increased intrinsic offspring growth rate that compensates for reduced maternal investment. The result is an unaltered growth rate during gestation and lactation and increased growth rate following lactation. This recalibration of intrinsic offspring growth rate requires that PREMS occurs during the first half of gestation, while late-gestational PREMS is correlated to reduced maternal investment only, resulting in reduced offspring growth rates during gestation and lactation and unaltered growth rates after lactation. Thus, PREMS-effects provide short- and long-term benefits to both mother and offspring under adverse conditions. In the short-term, PREMS-effects enable the mother to reduce maternal investment into current offspring along with recalibrating the offspring´s life-history settings to buffer it from the corresponding developmental constraints. In the long-term, PREMS ensures future maternal reproduction and accelerates offspring maturation.

Introduction

The developmental origins of health and disease (DOHaD), and particularly the role of prenatal maternal stress (PREMS), are a matter of current debate (Hanson and Gluckman 2014; Moisiadis and Matthews 2014a, b; Weinstock 2015). Numerous animal and human studies have shown that PREMS affects several aspects of offspring development and adult health, including growth, obesity, immune function, neurodevelopment, behaviour and skill acquisition (Coe and Lubach 2008; Lucassen et al. 2013; Hanson and Gluckman 2014; Moisiadis and Matthews 2014b, a; Weinstock 2015). These effects are usually considered as maladaptive and clinical (Boonstra 2013; Sheriff and Love 2013; Del Giudice 2014a; Hanson and Gluckman 2014). However, this interpretation may result from a health definition that is too narrow, and it is debated whether most PREMS-effects can be interpreted as being adaptive from an evolutionary point of view (Boonstra 2013; Sheriff and Love 2013; Bateson et al. 2014; Del Giudice 2014a; Hanson and Gluckman 2014). Growth is a crucial aspect of life history across mammals and consequently also of adaptive explanations of PREMS-effects on offspring phenotype (Kuzawa and Quinn 2009; Dmitriew 2011; Hanson and Gluckman 2014). However, it is currently difficult to assess the adaptive value of PREMS-effects since evidence for PREMS-effects on offspring growth is ambiguous, ranging from positive to negative effects even within the same species (Patin et al. 2002; Mueller and Bale 2006; de Vries et al. 2007; Hauser et al. 2007; Emack et al. 2008; Schöpper et al. 2012; Dantzer et al. 2013; Berghänel et al. 2015). This ambiguity in the results is reflected in the diversity of adaptive explanations, predicting either reduced (developmental constraints, thrifty phenotypes) or increased (predictive adaptive responses or PAR) growth rates in reaction to PREMS (Wells 2003; Nettle et al. 2013; Hanson and Gluckman 2014). Alternatively, ambiguous effects may result from variation in the timing of stress exposure creating opposing effects on placenta morphology or critical developmental periods (Rutherford 2013; Hanson and Gluckman 2014). Yet a pattern of timing effects across mammals is still missing. In this study we analyse published results in the light of a new, integrative framework and test its predictions with original data on a wild long-living primate facing naturally occurring stressors under natural ecological conditions.

PREMS encompasses nutritional, social, predatory, parasitic, or environmental stresses and causes elevated prenatal maternal physiological stress (PreGC, if measured as glucocorticoid levels) (Sheriff and Love 2013). In mammals, PREMS and PreGC are negatively related to maternal energy intake and physical condition, morphology and transmittance of the placenta, and prenatal and lactational maternal investment (Roberts et al. 1985; Laurien-Kehnen and Trillmich 2004; Bowen 2009; Hinde et al. 2009; Munoz et al. 2009; Hinde and Milligan 2011; Klaus et al. 2013; Sheriff and Love 2013; Tao and Dahl 2013; Zhu et al. 2013; Hanson and Gluckman 2014). Prenatal food restriction in rats leads to reduced postnatal mammary gland size, and heat stress in domestic cows leads to reduced postnatal mammary gland size and milk yield (Tao and Dahl 2013; Wattez et al. 2014). Reduced prenatal and lactational investment, but also elevated PREMS and PreGC are associated with reduced pre- and postnatal offspring growth (Roberts et al. 1985; Bowen 2009; Hinde et al. 2009; Hinde and

Milligan 2011; Stehulova et al. 2013; Hanson and Gluckman 2014). These results have been interpreted as support for the “thrifty phenotype”-hypothesis which proposes that prenatal growth restriction via reduced energy intake or PreGC-exposure is adaptive by adjusting offspring phenotype to the predicted adverse pre- and postnatal conditions and reducing its starvation risk (Wells 2003; Maestripieri and Klimczuk 2013; Sheriff and Love 2013).

The “thrifty phenotype”-hypothesis was questioned on theoretical and empirical grounds (Wells 2003; Maestripieri and Klimczuk 2013; Hanson and Gluckman 2014). It was shown that across species, growth rates are highly plastic and are immediately reduced in reaction to reduced energy intake to avoid starvation (Metz et al. 1980; Bergallo and Magnusson 2002; Karakaş et al. 2005; Garcia et al. 2009; Onyango et al. 2013), which may sufficiently explain the observed associations (“developmental constraints”). Thrifty phenotypes may be adaptive for the mother but rather maladaptive for the offspring because they constrain its future phenotypic plasticity and particularly its ability to adaptively utilize increased future energy availability (Wells 2003). Growth rates are under strong positive selection since they are positively related to offspring survival, speed of sexual maturation and adult body size, hence growth rate reduction may lead to reduced starvation and cumulative mortality risk but should always be kept to a minimum (Dmitriew 2011). The “thrifty phenotype”-hypothesis of prenatal offspring programming is contradicted by cross-fostering studies (Desai et al. 1996; Hauser et al. 2006; Wattez et al. 2014) showing reductions in postnatal offspring growth rate to result from PREMS of the nursing mother rather than the offspring´s prenatal environment (see also Brabham et al. 2000; Dancause et al. 2012; Hanson and Gluckman 2014; Weinstock 2015), which supports the “developmental constraints”-hypothesis.

However, both the “thrifty phenotype”- and the “developmental constraints”-hypothesis are challenged by other studies which reported positive instead of negative relationships between PREMS and/or PreGC and offspring growth rate (Emgard et al. 2007; Ford et al. 2007; Schöpper et al. 2012; Dantzer et al. 2013; von Engelhardt et al. 2015). These results support the PAR-hypotheses which take the entire life history of an individual into account and postulate that early adverse conditions lead to reduced life expectancies and consequently increased offspring growth rates and accelerated reproduction. The “internal PAR”-hypothesis proposes that developmental constraints due to PREMS result in disadvantaged early somatic states which will inevitably lead to disadvantaged somatic states during adulthood and reduced life expectancies (Nettle et al. 2013; Nettle and Bateson 2015). In this scenario the offspring can use its actual adverse somatic state to predict its future adverse somatic state and recalibrate its life history setting to accelerate growth and reproduction even if this comes at other phenotypic costs. The “external PAR”-hypothesis proposes that PreGC relates to adverse prenatal environmental conditions which forecast future adverse environmental conditions across the lifespan (Hanson and Gluckman 2014). Offspring can use this prenatal cue to recalibrate its phenotype to optimally match the forecasted adverse adult environment, which again would be reflected in accelerated growth and reproduction. Hence to be functional and adaptive, external but not internal PARs rely on high environmental predictability which may rarely apply to most long-lived

species (Nettle et al. 2013; Nettle and Bateson 2015). Conversely, internal but not external PARs rely on developmental constraints on early somatic state, and evidence for PREMS-effects on adult phenotype without detectable developmental constraints on offspring body size during early life have been seen as supporting the "external PAR"-hypothesis (Hanson and Gluckman 2014).

None of the current hypotheses explain the entire range of observed PREMS-effects on offspring growth. Deviations from predictions of the respective hypothesis are usually attributed to variation caused by the duration and intensity of exposure to stress or the timing of a stressor during gestation (Hanson and Gluckman 2014; Moisiadis and Matthews 2014a). In general, foetal plasticity decreases with age and may be particularly high during early gestation (Kuzawa and Quinn 2009). In humans, the hypothalamic-pituitary-testicular axis which affects growth in multiple ways shows a critical period of high plasticity during early gestation (Kuzawa and Quinn 2009; Castaneda Cortes et al. 2014), and PREMS-effects on placenta morphology also strongly differ between early and late gestation (Rutherford 2013). In contrast, reduced pre- and postnatal offspring growth rates are typically associated with late- rather than early-gestational PREMS (Roseboom et al. 2000; Patin et al. 2002; Bailey et al. 2004). This temporal variation in phenotypic plasticity cannot easily be reconciled with current hypotheses.

In this study, we propose and test a new, integrative framework which proposes an alternative interpretation of current evidence concerning PREMS-effects on offspring growth across mammals (Fig. 4.1). This framework is based on several arguments. First it is important to note that developmental constraints, internal PAR and external PAR are not mutually exclusive hypotheses (Nettle et al. 2013; Hanson and Gluckman 2014). Second, PREMS-effects on offspring growth would be most adaptive if they provide both short- and long-term benefits for both the mother and the offspring (Wells 2003; Sheriff and Love 2013). Third, the main driver of lifetime reproductive success is offspring survival until reproduction; hence reduced extrinsic growth rates in immediate reaction to reduced maternal investment (developmental constraints) may adaptively reduce starvation risk but also entail high costs (see above) which should optimally be selected against (Dmitriew 2011). Fourth, elevated PreGC is strongly related to reduced maternal investment in mammals (see above) and thus a reliable predictor of particularly early life adversity which facilitates short-term PARs (Kuzawa and Quinn 2009).

Based on these arguments and current evidence, we propose that PREMS affects offspring growth in two opposing ways (Fig. 4.1): (i) through reduced maternal investment (extrinsic growth reduction, Fig. 4.1 red path) and (ii) through phenotype recalibration mediated by PreGC-exposure (intrinsic growth acceleration, Fig. 4.1 blue path). We propose that intrinsic growth proliferation via PreGC is not only beneficial in the long-term by accelerating reproduction as proposed by classical PAR-hypotheses but also in the short-term by compensating for the detrimental effects of reduced maternal investment on offspring growth. In detail, we predict that PREMS (i) is associated with decreased maternal energy intake, physical condition and investment and consequently a reduced extrinsic offspring growth rate during gestation and lactation (Fig. 4.1a,b), and (ii) results in an

increased intrinsic offspring growth rate regulated via PreGC (Fig. 4.1a,c). Importantly, (i) is restricted to the gestation and lactation period, while this is not the case for (ii)(Fig. 4.1a-c). Thus if both processes coincide, then intrinsic and extrinsic effects on offspring growth rate will largely cancel each other out during gestation and lactation while offspring growth rate after lactation is not affected by (i) and should largely reflect the prenatally increased intrinsic growth rate only (ii)(Fig. 4.1d).

From the new framework we predict that PreGC-exposure increases offspring growth rate during gestation and lactation as well as after lactation (ii)(Fig. 4.1c), but that this effect is cancelled out during gestation and lactation by the opposing PREMS-effect on offspring energy intake due to reduced maternal investment (i)(Fig. 4.1d). In contrast to the current view our framework entails a reversed interpretation of PreGC-effects on offspring growth in which PreGC-effects are reflected in rather unaltered offspring growth while negative associations between PreGC and offspring growth are mediated by reduced maternal investment and reflect insufficient or lacking PreGC-effects. We tested our predictions in comparative analyses of published data and investigating the consequences of prenatal food availability and maternal physiological stress levels (PreGC) on offspring growth in a long-lived primate in an ecologically valid setting. The field study was conducted on a wild un-provisioned group of Assamese macaques (*Macaca assamensis*) living in their natural habitat at Phu Khieo Wildlife Sanctuary in Thailand. We combined behavioural observations with faecal glucocorticoid measurements, quantitative measures of natural food availability, and individual offspring growth rates measured non-invasively via photogrammetry.

Methods

Comparative analysis

We searched the literature for studies on prenatal maternal effects on offspring phenotype and explicit information on offspring growth rates during and/or after the lactation period. Only studies where the offspring was nursed by the birth mother were taken into account. Relative growth rate was defined as the difference between the offspring growth rate after PREMS-exposure and the offspring growth rate under the control (i.e. no treatment) condition. We extracted information on the existence and directionality of PREMS-effects scoring whether the offspring of PREMS-mothers showed higher (1), equal (0) or lower (-1) growth rates than the offspring of control (i.e. untreated) mothers, with different sex effects resulting in intermediate scores (i.e. 0.5 and -0.5, respectively). These effect scores were used in all statistical analyses. Spearman correlations and generalised linear models were calculated with R 3.1.2. All Wilcoxon tests were done with R 3.1.2 (package exactRankTests) and thus corrected for the number of ties, and all partial correlations were done with R 3.1.2 (package ppcor). All statistical tests were two-sided with alpha level set to 0.05.

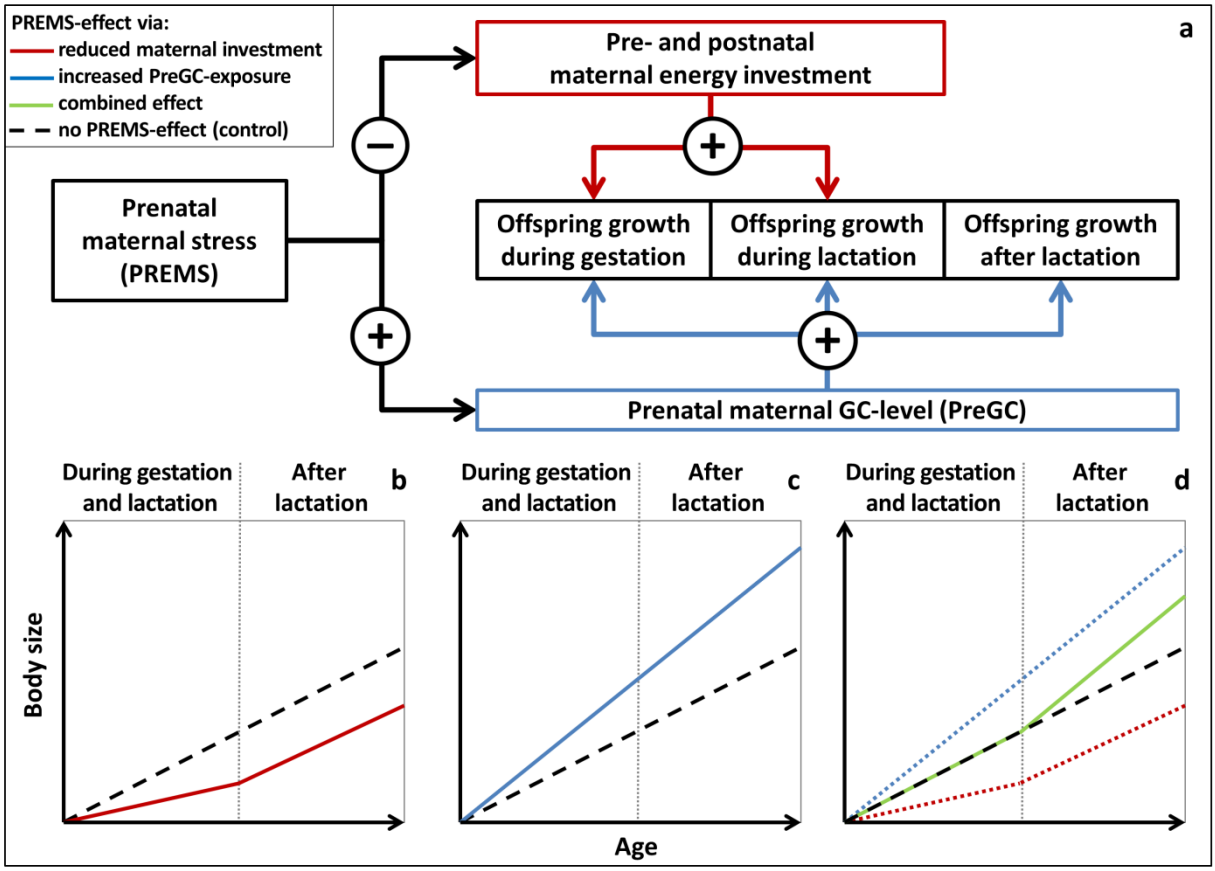


Figure 4.1: Schematic illustration of the predicted PREMS-effects on offspring growth via reduced maternal investment (extrinsic reduction) and via PreGC-exposure (intrinsic proliferation). a) PREMS worsens maternal physical condition resulting in reduced maternal investment and increased PreGC-levels. **b)** Reduced maternal investment reduces extrinsic offspring growth rates during gestation and lactation but not after lactation whereas **c)** increased PreGC increases the general intrinsic growth rate during gestation and lactation as well as after lactation. **d)** If both processes coincide, effects will be largely cancelled out during gestation and lactation resulting in a realised growth rate that, in the strongest case, is indifferent from an unaltered growth rate. However, growth rates after lactation are not affected by maternal investment and therefore reflect the PreGC-related intrinsically increased growth rates only.

Study site and subjects

Data were collected at the Phu Khieo Wildlife Sanctuary in North-Eastern Thailand on a fully habituated social group from May 2011 – December 2012. Assamese macaques are slow-developing, slow-reproducing mammals with strong signs of a capital breeding strategy, and food availability in our study area has previously been shown to be rather unpredictable (Fürtbauer et al. 2010; Heesen et al. 2013; Berghänel et al. 2015). They are characterized by female philopatry and male dispersal. Females are fully grown and sexually mature at the age of 5-6yrs, and males are fully grown with 9-10yrs (Fürtbauer et al. 2010; Berghänel et al. 2015). Gestation length is 164 days and interbirth interval ~22 months (bimodal distribution; range 12.6–24.7 months) (Fürtbauer et al. 2010). Offspring is fully

weaned at ~12 months, but lactation is substantial during the first six months only and marginal after this age (Berghänel et al. 2016). Therefore we defined the lactation period as the first six months of life (Heesen et al. 2013). Our study group consisted of 24 adult individuals (9 males, 15 females), 4-7 subadult males, 16-19 juveniles (4-8 males, 11-12 females), and 12 infants born in 2011 (6 males, 6 females) and 5 infants born in 2012 (2 males, 3 females). All 17 infants were focal animals.

Behavioural data

During 30 min focal animal protocols instantaneous activity data were recorded every minute (86,518 records, 1385.4 focal hours, mean ± SD: 5.5 ± 0.2h per individual and month; Altmann 1974). We recorded instantaneously whether the infant was travelling, feeding, resting, socially interacting or solitarily or socially playing. Play-face expression and/or regular role-changes were used to differentiate between social play and other social interactions like sitting in body contact, grooming, or aggression (for more details, see (Berghänel et al. 2015)). Proportion of time spent in social play was calculated as the percentage of time spent in social play. In parallel we recorded continuous data on mother-infant-aggression and infant distress calling. For each of the first 20 distress calls of an infant (separated by at least 1 min.) we recorded the separate ages of the infant in days, and defined the age at first distress calls as the average of these age values. All aggressive encounters of all group members were recorded ad libitum.

Growth rate

For all 17 focal animals we measured size monthly via photogrammetry from the length of the lower arms (1,706 pictures; mean ± SE: 6.4 ± 2.1 pictures per individual and month). We recorded the picture and the object distance in parallel using a Nikon D5000 camera and a Bosch PLR 50 laser distance measurement tool (accuracy ± 2mm) and analysed pictures with ImageJ 1.44p (National Institutes of Health, USA) as described in (Breuer et al. 2007; Berghänel et al. 2015). We excluded outliers (mean ± 2SD) separately for each month and individual and used the remaining values to calculate individual average sizes per month. These values were cubed to approximate linear volume growth (size index), and the linear regression slopes of these monthly values over time were used as growth rate indices (for more details, see (Berghänel et al. 2015)).

Collection of faecal samples and GC analyses

We collected faecal samples of mothers during the gestation (N = 309, mean ± SD per female and month: 3.0 ± 1.8; PreGC) and the lactation period (months 1 - 6, N = 253, 2.5 ± 1.7 per female and month; PostGC). Following homogenization, an aliquot of approximately 0.5g of faecal material was transferred into a tube containing 4ml of 80% watery ethanol (Shutt et al. 2012). Stress hormone metabolites were extracted from the samples using a validated field extraction protocol following (Shutt et al. 2012) and transported to the endocrinology laboratory at the German Primate Center Göttingen for analysis.

Faecal extracts were analysed for immunoreactive 11β-hydroxyetiocholanolone (GC), a major metabolite of cortisol in the faeces of primates (Heistermann et al. 2006), including the Assamese macaque (Ostner et al. 2008a) by using enzyme immunoassay (Ganswindt et al. 2003). The assay has been successfully applied previously to monitor stress hormone output in male and female Assamese macaques (Ostner et al. 2008a; Fürtbauer et al. 2014). Sensitivity of the assay at 90% binding was 1.0 pg. Intra- and inter-assay coefficients of variation, determined by replicate measurements of high- and low-value quality controls, were 5.2% and 9.7% (high) and 7.7% and 13.6% (low), respectively. We ran each sample in duplicate and calculated mass steroid metabolite per mass faecal dried weight in ng/g.

Availability of ecological energy resources

We calculated food availability indices for each month. Based on 44 botanical plots within the home range of the study group (covering 20.75 ha of forest) the monthly fruit abundance in 650 trees and the density of these tree species in the home range were used to calculate the indices (for details see Heesen et al. 2013). It was previously shown that the food availability index is closely correlated to individual energy intake (Heesen et al. 2013).

Analysis

All analyses were run with R 3.1.2. All tests were two-tailed with alpha level set to 0.05. Log-likelihood values were based on AIC-comparisons. Due to a female rank change during the lactation period of the 5 infants born in 2012 which was later followed by a group split, we mean-scaled data for year of birth prior to all analyses that included postnatal data of the infants born in 2012.

We have previously shown that proportion of time spent in locomotor play and growth rate are both positively correlated to food availability, and that growth rate and proportion of time spent in vigorous social play are negatively correlated to each other when controlled for food availability (Berghänel et al. 2015). Within this trade-off, we found sex-specific strategies, with males playing more and growing less than females. Therefore all analyses which involved late growth rates (i.e. growth rates after the lactation period) were controlled for sex of the offspring or, for more detailed (i.e. continuous) controlling, for late rates of social play and late food availability. In addition, we have previously shown that general offspring growth rates were correlated not only to PreGC but particularly to maternal PreGC levels during the first two gestational trimesters (early-mid gestation PreGC), thus we always used this measure in our analyses (Berghänel et al. 2016).

Early energy availability of the offspring during the lactation period

As mentioned above, we have previously shown that growth rate and proportion of time spent in play are positively correlated to food availability and that individual growth rate is strongly negatively correlated to proportion of time spent in social play when controlled for average food availability ($r = -0.916$) due to a strong energy trade-off between the two (Berghänel et al. 2015). In other words, we found that

Growth rate × Proportion of time spent in social play ≈ constant for each given food availability, or

Growth rate × Proportion of time spent in social play ≈ a × food availability + b (a, b = constant).

Indeed, 'Growth rate × Proportion of time spent in social play' was positively correlated to food availability ($r=0.777$, $p=0.002$, $N=12$, Fig. S4.1). Building on that, we estimated the individual early energy availability of the offspring (i.e. during lactation period) as

Early energy availability = Growth rate × Proportion of time spent in social play

based on the individual growth rate and proportion of time spent in social play during the lactation period.

Results

Comparative analyses provided strong support for our predictions (Table 4.1, Fig. 4.2). The mammal data set was compiled from 68 publications reporting 88 studies on 11 species ranging from rodents to ungulates and primates. Effects of prenatal maternal stress (PREMS) on pre- and postnatal offspring growth were highly variable, ranging from positive to negative effects even within the same species (Table 4.1). This variance was largely due to different PREMS-effects on offspring growth depending on the developmental period as well as the timing of the onset of PREMS during gestation whereas duration of stress exposure had marginal effects only (Fig. 4.2).

In line with our predictions, we found that relative growth rates (i.e. growth rates of the offspring of PREMS-mothers compared to growth rates of the offspring of control mothers) were significantly higher after lactation than during gestation and lactation with no difference between the gestation and the lactation period (Table 4.1, Fig. 4.2). This increase right at the onset of nutritional independence from the mother suggests that offspring growth rates following PREMS-exposure were particularly constrained during the gestation and lactation period perhaps resulting from reduced maternal investment (Fig. 4.1).

Remarkably, we found that during all developmental periods and regardless of the species, relative growth rates following late-gestational PREMS were consistently lower than those following early-gestational PREMS (Fig. 4.2). PREMS starting during the first half of gestation led to unaffected offspring growth rates during gestation and lactation and increased growth rates after lactation (Fig. 4.2), which is consistent with our predictions if both the extrinsic (maternal investment-related) and the intrinsic (PreGC-related) PREMS-effects work in concert (Fig. 4.1d). In contrast, PREMS starting only in the second half of gestation led to reduced offspring growth rates during gestation and lactation and unaffected growth rates after lactation (Fig. 4.2) which is in line with our predictions of a mere extrinsic maternal investment-related PREMS-effect (Fig. 4.1b). Hence late gestation PREMS reduces maternal condition and therefore her investment in the offspring and consequently reduces offspring growth during gestation and lactation (Fig. 4.1a, b) but this reduced growth rate is not compensated for by

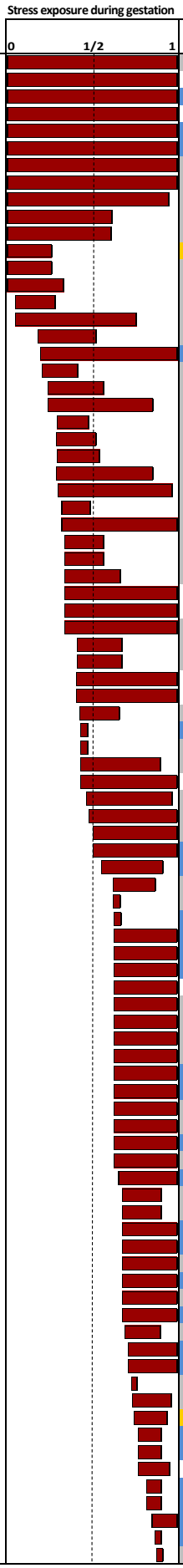
increased intrinsic growth rates via PreGC (Fig. 4.1a,c,d). All patterns also held if we took into account only those studies which provide data about elevated PreGC-levels (or increase PreGC-levels directly via injections, Fig. S4.3), or which did not apply litter culling (Fig. S4.4) or which found any PREMS-effects on offspring growth at all (Fig. S4.5).

Case study on wild Assamese macaques

We have previously shown for our study individuals that prenatal food availability predicts PreGC which is related to postnatal developmental constraints (in terms of delayed motor skill acquisition) and reduced pre- and postnatal maternal condition which in turn predicts future maternal reproduction (Heesen et al. 2013; Berghänel et al. 2016). Overall postnatal offspring growth rate is positively correlated to prenatal maternal physiological stress during the first and second trimester of gestation (early-mid gestation PreGC).

Based on this and in line with our predictions, early-mid gestation PreGC was positively correlated to late (i.e. after lactation) offspring growth rate but not to early offspring growth rate (i.e. during lactation; Fig. 4.3a-c), and early and late growth rates were not correlated ($r = -0.152$, $p = 0.64$). Early-mid gestation PreGC was a significantly stronger predictor of late offspring growth than PreGC during the first half of gestation (Fig. S4.6; but all results of this study remained also for PreGC during the first half of gestation, Fig. S4.7). The relationship between early-mid gestation PreGC and late offspring growth remained after controlling for perinatal food availability (Fig. 4.3c), hence a simple compensatory growth reaction following low perinatal maternal food availability leading to low early energy availability of the offspring can be excluded. Early-mid gestation PreGC predicted late growth rates also after controlling for other potential factors (i.e. amount of late social play and late food availability or PostGC, Fig. S4.6).

The difference between early and late growth rate was not driven by the PreGC-related intrinsic increase of late growth but by an extrinsic decrease of early growth due to reduced perinatal food availability (i.e. during gestation and lactation, Fig. 4.3e,f; for separate effects of pre- and postnatal food availability see Fig. S4.8). The lower the perinatal maternal food availability, the lower the realized early growth rate was compared to the late (i.e. intrinsic) growth rate. This relationship remained after controlling for other potential factors (i.e. early-mid gestation PreGC and sex of the offspring, Fig. 4.3f). Perinatal food availability was positively correlated to the early energy expenditure of the offspring (controlled for year of birth: $r = 0.596$, $p = 0.015$, $N = 17$; Fig. 4.3d; for separate effects of pre- and postnatal food availability see Fig. S4.9), suggesting that perinatal food availability triggered maternal lactational investment and offspring energy intake. This is further supported by the negative correlation between perinatal food availability and age of first distress calls of the offspring (controlled for maternal offspring-directed aggression and year of birth: $r = 0.569$, $p = 0.027$, $N = 17$). The intrinsic (late) growth rate was negatively correlated, and thus compensatory, to perinatal food availability ($r = -0.688$, $p = 0.019$, controlled for sex of the offspring; Fig. S4.10). Hence the prenatally-caused increase in intrinsic growth rate that was evident after the lactation period was extrinsically counterbalanced during lactation by reduced energy intake that resulted from reduced lactational investment by prenatally stressed mothers, leading to widely compensating effects of the intrinsic and extrinsic offspring growth modulations during lactation.



Species	Relative growth rate* during gestation	during lactation	after lactation	Stressor	Study
Guinea pig	=	=	=	social stress[2]	Sachser et al. 1996
Guinea pig	?	?	=	social stress[2]	Kemme et al. 2007
Lab rat	↘	=	↗	food restriction[2,5]	Li et al. 2015
Lab rat	?	?	=	electric shock[2,5]	Estanislau et al. 2005
Lab rat	↘	↘	=	dexamethasone treatment[5]	Welberg et al. 2001
Lab rat	↘	?	↗	food restriction[2,5]	Desai et al. 1996
Lab rat	=	=	↗	food restriction[2,5]	Alheiros-Lira et al. 2015
Lab rat	=	=	=	transport, injection[5]	Peters 1986
Lab rat	=	=	?	electric shock[2]	Takahashi et al. 1988
Guinea pig	=	♀↗ | ♂=	♀↗ | ♂=	strobe light	Schöpper et al. 2012
Domestic sheep	=	=	?	food restriction[1]	Rooke et al. 2010
Domestic sheep	↗	=	?	food restriction[2]	Munoz et al. 2008
Domestic sheep	=	=	?	food restriction[2]	Munoz et al. 2009
Lab rat	=	=	↗	diverse stressors[5]	Mueller et al. 2006
Lab rat	=	=	?	physical restraint[2,5]	Sanchez et al. 1993
Lab rat	=	=	?	physical restraint[2,5]	Sanchez et al. 1993
Domestic sheep	=	↗	=	food restriction[1]	Ford et al. 2007
Lab rat	↘	↘	?	cold water[2]	Drago et al. 1999
Domestic pig	=	=	?	social stress[2,4]	Couret et al. 2009
Comm. Marmoset	=	=	↗	dexamethasone treatment[5,6]	Hauser et al. 2007
Mouse	=	=	?	physical restraint[2,5]	Torrente et al. 2002
Domestic pig	=	=	♀= | ♂↗	HCA treatment[4,8]	Mack et al. 2014
Lab rat	=	=	?	physical restraint[2,5]	Sanchez et al. 1993
Rhesus macaque	=	=	?	acoustic startle	Bailey et al. 2004
Lab rat	=	=	?	various stressors[2,5]	Secoli et al. 1998
Guinea pig	=	♀↗ | ♂=	♀↗ | ♂=	social stress[2]	von Engelhardt et al. 2015
Domestic pig	=	?	=	ACTH treatment and snaring[4,8]	Haussmann et al. 2000
Domestic cattle	=	=	?	heat stress[2]	Shell et al. 1995
Domestic pig	=	=	?	social stress[4]	Jarvis et al. 2006
Domestic pig	=	=	?	social stress[2,4]	Ringgenberg et al. 2012
Lab rat	=	=	♀= | ♂↗	diverse stressors[5]	Mueller et al. 2006
Lab rat	?	?	↗	betamethasone treatment[5]	Emgard et al. 2007
Lab rat	?	?	↗	dexamethasone treatment[5]	Emgard et al. 2007
Mouse	=	=	?	physical restraint[2,5]	Maeyama et al. 2015
Domestic pig	=	=	?	ACTH treatment[4,8]	Lay etal 2008
Domestic pig	=	=	?	rough handling[4]	Lay etal 2008
Red squirrel	?	↗	?	cortisol treatment	Dantzer et al. 2013
Red squirrel	?	↗	?	population density	Dantzer et al. 2013
Domestic pig	=	=	?	ACTH treatment[4,8]	Otten et al. 2007
Lab rat	↘	↗	?	predator exposure	Patin et al. 2002
Lab rat	=	=	=	predator exposure[2,7]	Lordi et al. 2000
Lab rat	=	=	♀↘ | ♂=	physical restraint[2,5]	Baker et al. 2008
Lab rat	?	?	↗	physical restraint[2]	Morley-Fletcher et al. 2003
Guinea pig	=	♀= | ♂↘	?	diverse alternating stressors[3]	Emack et al. 2008
Lab rat	=	=	=	predator odor[5]	St-Cyr et al. 2015
Vervet monkey	=	↘	?	dexamethasone treatment	de Vries et al. 2007
Root vole	↘	↘	♀= | ♂↘	predator exposure[2]	Bian et al. 2005
Lab rat	↘	↘	?	predator exposure[7]	Korgan et al. 2014
Rhesus macaque	=	↘	?	acoustic startle[7]	Bailey et al. 2004
Comm. Marmoset	=	=	=	dexamethasone treatment[5]	Hauser et al. 2007
Lab rat	↘	↘	?	predator exposure[7]	Patin et al. 2002
Lab rat	↘	↘	?	physical restraint[2,5]	Herrenkohl et al. 1976
Lab rat	↘	↘	=	food restriction[2,5]	Wattez et al. 2014
Lab rat	↘	=	=	physical restraint[2]	Van den Hove et al. 2005
Lab rat	?	?	=	physical restraint[2,5]	Bowman et al. 2004
Lab rat	=	=	=	physical restraint[2,5]	Berger et al. 2002
Lab rat	=	=	?	heat and physical restraint [1]	Klein et al. 1995
Lab rat	=	↘	=	heat and physical restraint [2,5]	Zimmerberg et al. 1998
Lab rat	=	♀= | ♂↘	?	noice,light,heat[2,5]	Meek et al. 2000
Lab rat	↘	?	=	food restriction[2,5]	do Nascimento et al. 2014
Lab rat	↘	=	=	dexamethasone treatment[5,7]	O´Regan et al. 2004
Lab rat	=	=	=	ACTH treatment[5]	Holson et al. 1995
Lab rat	=	↘	=	corticosterone treatment[5]	Holson et al. 1995
Lab rat	↘	↘	=	dexamethasone treatment[5]	Holson et al. 1995
Lab rat	=	=	=	heat and physical restraint [5]	Holson et al. 1995
Guinea pig	↘	↘	=	food restriction[2,7]	Laurien-Kehnen et al. 2004
Mouse	=	↘	=	electric shock[2,5]	Fonseca et al. 2002
Domestic pig	=	↘	?	social stress[4]	Jarvis et al. 2006
Lab rat	↘	↘	=	dexamethasone[6]	Brabham et al. 2000
Lab rat	↘	↘	=	dexamethasone[5,6]	Hauser et al. 2006
Lab rat	=	=	?	electric shock[2,5]	Sobrian et al. 1992
Lab rat	↘	↘	=	dexamethasone[5,7]	Franko et al. 2010
Lab rat	=	=	♀= | ♂↗	diverse stressors[5]	Mueller et al. 2006
Lab rat	↘	=	=	dexamethasone treatment[5]	Welberg et al. 2001
Domestic pig	=	=	?	social stress[2,4]	Couret et al. 2009
Domestic sheep	↘	↘	=	food restriction[2]	Husted et al. 2007
Domestic sheep	↘	↘	=	food restriction[2]	Tygesen et al. 2008
Guinea pig	=	=	♀= | ♂↘	strobe light	Kapoor et al. 2005, 2008
Domestic pig	=	=	?	ACTH treatment[4,8]	Kanitz et al. 2003
Domestic pig	↗	=	?	ACTH treatment[4,8]	Otten et al. 2007
Lab rat	↘	↘	=	dexamethasone treatment[7]	Slotkin et al. 1996
Lab rat	↘	=	?	dexamethasone treatment[5]	Muneoka et al. 1997
Lab rat	?	=	↗	electric shock[2]	Ehrlich et al. 2015
Lab rat	↘	=	=	corticosterone treatment[7]	Oliveira et al. 2006
Lab rat	↘	↘	↘	dexamethasone treatment[7]	Oliveira et al. 2006
Domestic cattle	↘	↘	=	heat stress[1]	Tao et al. 2012
Lab rat	↘	↘	=	predator exposure[2,7]	Lordi et al. 2000
Guinea pig	=	=	♀= | ♂↘	strobe light	Kapoor et al. 2005, 2008

Table 4.1 (preceding page): Literature review on the relationship between the gestation period of stress exposure and PREMS-effects on offspring growth rate during gestation, during lactation and after lactation across mammals (for references see table, only first author mentioned). PREMS-effects on growth rate did not differ from the gestation to the lactation period ($p = 0.88$, $N = 74$, paired Wilcoxon tests), and both were correlated to each other (Spearman´s $Rho = 0.518$, $p < 0.001$; $N = 74$). Relative growth rates* after the lactation period were higher than those during the gestation ($p < 0.001$, $N = 44$) and the lactation period ($p < 0.001$, $N = 42$; both paired Wilcoxon tests), indicating that offspring growth rates following PREMS were particularly reduced during the gestation and lactation period due to reduced maternal investment.
[1] no effect on cortisol levels detected
[2] physiological stress/glucocorticoids not tested
[3] alternating exposure to strobe light, social stress, forced foraging and food restriction
[4] extremely shortened lactation period
[5] pup sizes equalized by culling
[6] no effect on knee-heel-length
[7] estimated from growth trajectories
[8] HCA…Hydrocortisone acetate, ACTH…Adrenocorticotropic hormone (Corticotropin)
* growth rates of the offspring from PREMS-mothers compared to control offspring (ordinal rank ascription for analysis: higher/equal/lower = 1/0/-1, higher/lower in one sex only = 0.5/-0.5)

Discussion

Our results on a wild non-human primate, combined with our comparative analyses of published data, supports a novel, integrative framework explaining the observed range of prenatal stress effects on offspring growth across mammals. We show that prenatal maternal stress is associated with a) decreased maternal energy investment into gestation and lactation and consequently decreased extrinsic offspring growth rate, and b) increased PreGC-level which results in increased intrinsic offspring growth rates mediated by PreGC-exposure during a critical period during the first half of gestation. This accelerated intrinsic growth ultimately buffers the offspring´s phenotype from the adverse early conditions as far as possible and accelerates long-term growth and potentially also reproduction. Thus, the results provide evidence for both a short-term PAR in anticipation of developmental constraints and a long-term PAR based on the same mechanism, making PreGC-effects on offspring development a highly adaptive strategy.

Our interpretation is in agreement with previous results. Detrimental effects of PREMS on placenta size and function were extensively discussed in previous reviews (Rutherford 2013; Hanson and Gluckman 2014). In cross-fostering studies with late-gestational PREMS (Hauser et al. 2006; Wattez et al. 2014) reductions in postnatal offspring growth rate resulted from the prenatal treatment of the nursing mother rather than the offspring´s prenatal environment. Early-gestational maternal food restriction leads to shorter and less frequent maternal facilitation of infant suckling as well as shorter and less frequent infant suckling, but does not affect offspring growth during lactation (Munoz et al. 2009). Late-gestational maternal food restriction is related to decreased offspring growth rates during lactation but not to offspring growth rates after weaning, and the offspring growth variation

during lactation is directly related to differences in milk intake (Tygesen et al. 2008). Conversely, late-gestational stress does not affect offspring growth during lactation if goat kids are fed a standardized milk replacer from birth on (Roussel et al. 2005). These together with our results support our interpretation that negative effects of late-gestational PREMS on offspring growth are caused by reduced gestational and lactational investment of the mother, and that this effect is compensated by increased intrinsic offspring growth if PREMS occurred during early gestation.

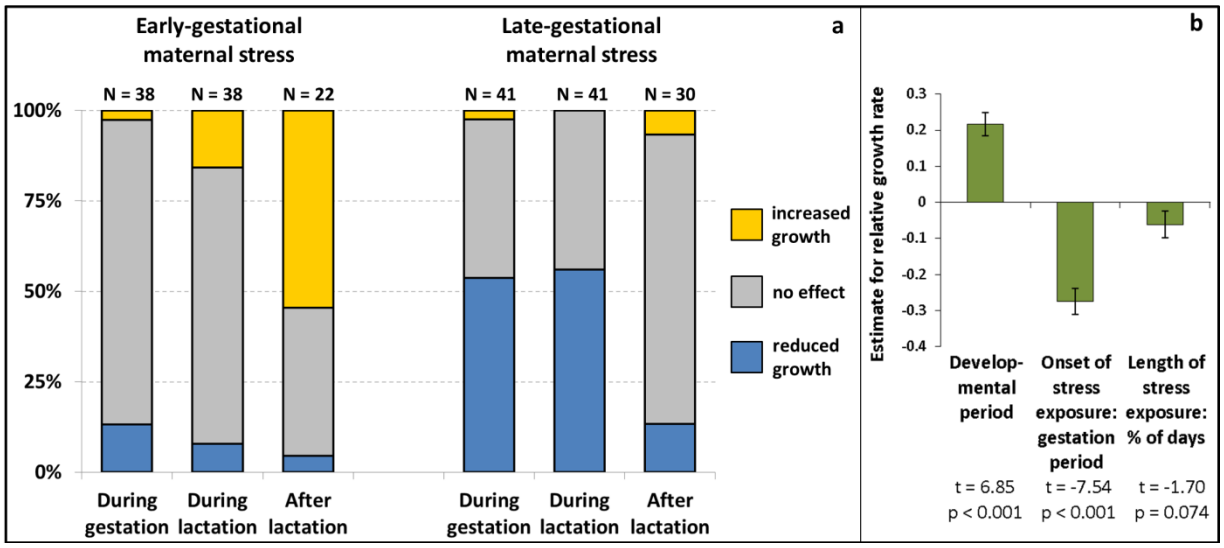


Figure 4.2: Effects of early- vs. late-gestational maternal stress on offspring growth rates during gestation, during lactation and after lactation across mammals. a) Early-/Late-gestational: first/second half of gestation. Percentage of previous studies (Table 4.1) reporting a higher (white), equal (grey) or lower (black) growth rate in offspring from PREMS-mothers compared to control mothers (relative growth rate; ordinal rank ascription for analysis: higher/equal/lower = 1/0/-1, higher/lower in one sex only = 0.5/-0.5). For each developmental period, relative growth rates following PREMS during the first half of gestation were higher than those following PREMS during the second half of gestation (during gestation: $p < 0.001$, N = 77; during lactation: $p < 0.001$, N = 77; after lactation: $p < 0.001$, N = 51; all unpaired Wilcoxon tests). Relative growth rates following PREMS during the first half of gestation were indifferent from 0 during gestation and lactation (during gestation: $p = 0.10$, median = 0; during lactation: $p = 0.36$, median = 0) but higher after lactation ($p = 0.002$, median = 1; all paired Wilcoxon tests). Growth rates following PREMS during the second half of gestation were significantly lower than control during gestation and lactation (during gestation: $p < 0.001$, median = -1; during lactation: $p < 0.001$, median = -1) but indifferent from control after lactation ($p = 0.59$, median = 0; all paired Wilcoxon tests). **b)** In a GLMM (random factor: species), relative growth rates were independently predicted by developmental period (during gestation and lactation = 1, after lactation = 2), gestation period of onset of stress exposure (first half of gestation = 0, second half of gestation = 1) and by trend also by length of stress exposure (in percentage of gestation days) but not by a continuous measure of onset of stress exposure (ranging from 0 to 1, $p = 0.49$, excluded from the final model; for full model and for length of stress exposure in number of days see Fig. S4.2a,b). Generalised LMM (random factor: species): Model significance: $p < 0.001$, $R^2 = 0.340$, N = 210, intercept: estimate -0.16 ± 0.04 (Estimates ± SD of the z-transformed variables are plotted).

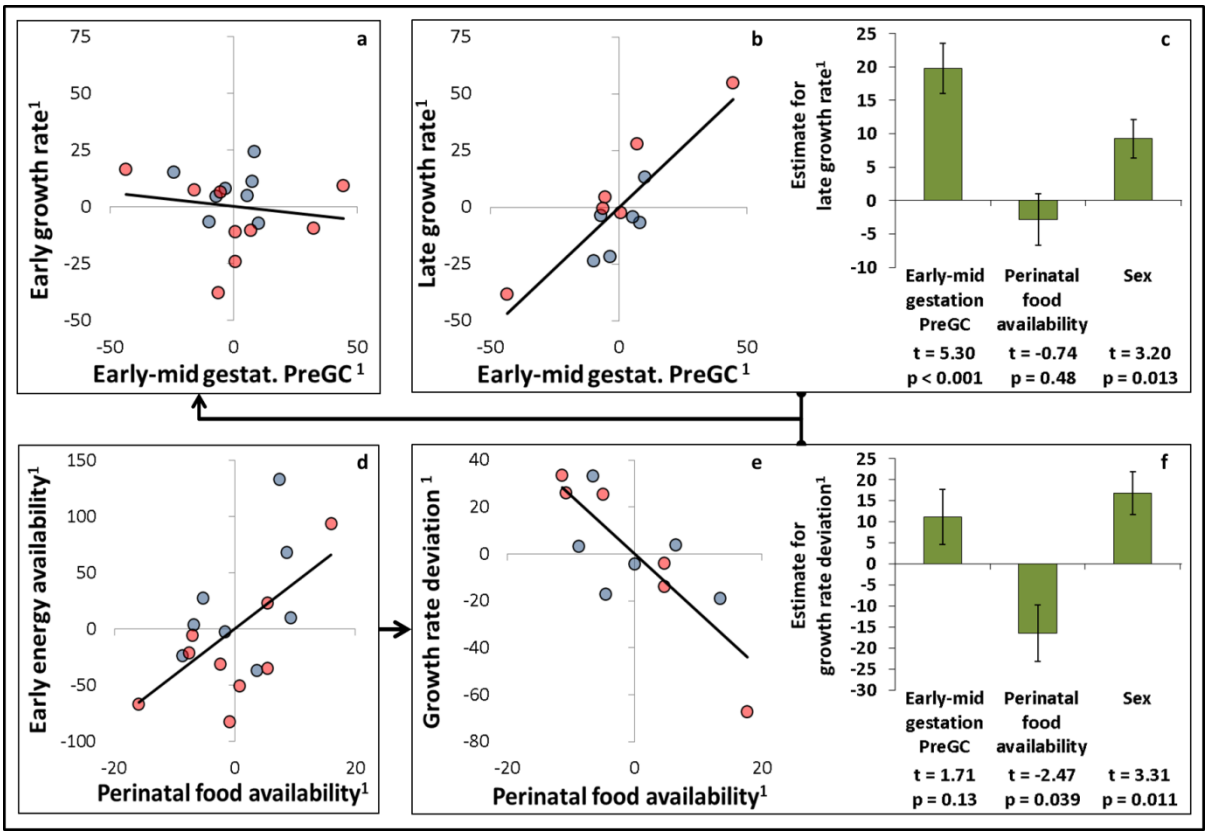


Figure 4.3: Early-mid gestation PreGC predicted growth rates after lactation but not during lactation, and the difference between these two growth rates was due to perinatal food availability which was related to the energy availability of the offspring during lactation. Perinatal: during gestation and lactation, early: during lactation, late: after lactation, early-mid gestation: first and second gestational trimester. [1]Residuals are translated into deviations from average in %. **a,b)** Early-mid gestation PreGC accelerated offspring growth rates after lactation ($r = 0.873$, $p < 0.001$, $N = 12$; controlled for perinatal food availability and offspring sex: $r = 0.882$, $p < 0.001$; without the two potential outliers: $r = 0.564$, $p = 0.089$), but not during the lactation period ($r = -0.150$, $p = 0.57$, $N = 17$; controlled for year of birth; within the offspring of the first year only ($N = 12$): $r = -0.009$, $p = 0.98$). **c)** The relationship between early-mid gestation PreGC and late offspring growth rates remained after controlling for perinatal food availability (GLM: Model significance: $p < 0.001$, $R^2 = 0.857$, intercept: estimate 0.0 ± 2.7; Estimates ± SD of the z-transformed variables are plotted). **d)** Perinatal maternal food availability was positively correlated to the energy availability and thus probably energy intake of the offspring during lactation ($r = 0.596$, $p = 0.015$, $N = 17$; controlled for year of birth). **e, f)** The lower the perinatal maternal food availability, the more reduced was the realised early compared to the intrinsic (i.e. late) offspring growth rate. Thus differences in perinatal food availability were responsible for the balancing of early growth rates (deviation was calculated as late minus early growth rate, growth rate deviation in % of late growth rate). **e)** Perinatal food availability predicts deviation of the realised early from the intrinsic growth rate (controlled for offspring sex: $r = -0.825$, $p = 0.002$). **f)** This relationship remained also after controlling for the increasing effect of early-mid gestation PreGC on the intrinsic (late) growth rate **(**controlled for offspring sex and early-mid gestation PreGC: $r = -0.657$, $p = 0.039$, GLM: Model significance: $p = 0.003$, $R^2 = 0.732$, intercept: estimate -0.19 ± 4.68; Estimates ± SD of the z-transformed variables are plotted).

PreGC during the first half of gestation led to increased offspring growth rates after lactation in our comparative analysis and our field study, and we have previously shown for the same study group that this results in an increased overall growth rate and increased body size at the age of 16-18 months, and similar results were shown across mammals (Schöpper et al. 2012; Mack et al. 2014; Li et al. 2015; Berghänel et al. 2016). These results support the PAR-hypothesis which predicts accelerated offspring growth and reproduction in face of adverse conditions and reduced life expectancy. We have shown for our study species that this effect must be due to an internal PAR because Assamese macaques evolved and live in a highly unpredictable environment. Thus, prenatal conditions cannot be forecasts of the environment during adulthood and adjustment to prenatal conditions would necessarily decrease rather than increase adult phenotype-environment matching and would therefore be dysfunctional and maladaptive (Nettle et al. 2013; Nettle and Bateson 2015; Berghänel et al. 2016). We have further argued that current evidence suggests that internal PARs may also better explain results from other, also short-lived mammals (Kuzawa and Quinn 2009; Burton and Metcalfe 2014; Berghänel et al. 2016).

Proponents of the "external PAR"-hypothesis have argued that internal PARs rely on developmental constraints and can therefore not explain the numerous cases were PREMS-effects on adult phenotype are evident without detectable developmental constraints on offspring growth during early life (Hanson and Gluckman 2014). In contrast to this interpretation, we suggest that it is precisely this absence of detectable short-term PREMS-effects on early offspring growth which represents the primary adaptive PreGC-effect, because PREMS is almost always related to reduced maternal investment and developmental constraints. Despite the fact that early-gestational PreGC balances the realised growth rate during gestation and lactation, it causes strong developmental constraints on other, more quality-related offspring attributes like immune function and motor skill acquisition. This was observed in our study group (Berghänel et al. 2016) and in many other studies across mammals (Hanson and Gluckman 2014; Moisiadis and Matthews 2014a), hence the observed lack of PREMS-effects on offspring growth does not imply an absence of developmental constraints.

To program the foetus to a compensatory growth rate and faster life history, it seems necessary that prenatal stress exposure occurs early enough during gestation before the respective critical period has passed by: later exposure fails to cause compensatory offspring growth but still reduces maternal energy investment, resulting in decreased offspring growth rates during gestation and lactation and unaffected growth rates after lactation. However, findings from experimental studies may strongly underestimate the adaptive power of PreGC-effects. Under ecological conditions it might rarely be the case that a considerable stressor occurs during late gestation without any influence during early gestation because natural stressors usually change slowly and continuously (Boonstra 2013). Thus our results underscore the need for more studies on wild populations facing ecological conditions and naturally occurring stressors.

Our results suggest that across mammals, PreGC-effects on offspring growth are limited to a critical period which generally lies around the first half of gestation. This pattern

is puzzling considering the strong differences in gestation length and developmental states of the foetus at mid-gestation across mammals. However, late-gestational stress may have a much stronger effect on maternal condition and gestational and lactational investment then early-gestational stress and this effect perhaps cannot be compensated by further increased intrinsic growth rate of the offspring. Such a theory would be in line with the observed effects on offspring growth during gestation and lactation but fails to explain the observed deviation of the offspring growth rates after lactation. Furthermore the effects of early gestational stress were not affected by the additional occurrence of late-gestational stress in our analyses, which strongly contradicts this hypothesis. Alternatively it was shown that PREMS-effects on placenta morphology strongly differ between the first (period of rapid placenta growth) and the second half of gestation (Rutherford 2013). However, these effects are contrary to our results because PREMS decreases the ability of the placenta to support foetal growth during the first half but increases it during the second half of gestation (Rutherford 2013), which indicates that PREMS-effects on placenta morphology compensate for, rather than cause, the temporal pattern of PREMS-effects on offspring growth. The most convincing explanation may therefore be the generally negative relationship between foetal plasticity and age. PreGC-effects on relatively small numbers of (highly plastic stem-) cells might lead to more homogenous effects on offspring phenotype than PreGC-effects on large and differentiated tissues (Rutherford 2013), hence recalibration of resource allocation during this period may entail less frictional loss and higher efficiency. In support of this view, the hypothalamic-pituitary-testicular axis which affects growth in multiple ways shows a critical period of high plasticity during early gestation in humans (Kuzawa and Quinn 2009; Castaneda Cortes et al. 2014).

In summary our results strongly contradict the “thrifty phenotype”-hypothesis and show that PREMS-effects on offspring growth include both developmental constraints due to reduced maternal investment and, within these constraints, predictive adaptive responses due to PreGC-effects during early gestation. In particular we show that PREMS reduces maternal investment into gestation and lactation and that the corresponding PreGC re-adjusts the developmental trajectory and thus life history setting of the offspring to prevent the adverse effects of the reduced maternal investment on growth and body size-related survival and to accelerate growth and maturation in the long-term to adapt to reduced life expectancy. However, it was repeatedly shown that this recalibration comes at strong costs in terms of increased disease risk, altered neurodevelopment and reduced skill acquisition, which shows that this recalibration is subject to strong developmental trade-offs and constraints. Adverse early conditions may consequently lead to reduced fitness for both the mother and the offspring if compared to optimal conditions, but maximize it for both under suboptimal conditions (Sheriff and Love 2013). Our results emphasise the importance to differentiate between PREMS-effects (namely reduced maternal investment and increased PreGC) and PreGC-effects which accelerate offspring growth during a limited critical period. In contrast to the prevailing view, our results suggest that PreGC-effects on offspring growth are reflected in rather unaltered growth rates during gestation and lactation and are only detectable after lactation, while negative PREMS-effects on offspring growth are rather due

to an absence of PreGC-effects on offspring growth but may result in spurious negative correlations between PreGC-level and offspring growth.

Our results disentangle a central aspect of one of the most studied epigenetic effect on offspring phenotype and life history. An important next step would be to investigate the long-term effects of early- and late-gestational maternal stress on offspring maturation, reproduction and fitness. Currently, the most elucidating results come from human studies of the Dutch famine cohort. Consistent with our results, maternal exposure to the famine during late but not during early gestation led to reduced offspring birth weight (Roseboom et al. 2000). Notably, the offspring of prenatally exposed mothers gave birth to smaller infants with reduced perinatal survival compared to the offspring of prenatally unexposed mothers, but the offspring of mothers exposed during early gestation gave birth to infants with lower birthweight but also higher perinatal survival than the offspring of mothers exposed during late gestation (Lummaa and Clutton-Brock 2002). Hence in keeping with our results, PREMS reduces the reproductive performance and fitness of the offspring but early-gestational PreGC-effects may buffer this effect to some degree. More importantly, these results suggest that our results also apply to humans and further our understanding of the evolution of human life history and the developmental origins of health and disease (DOHaD, Hanson and Gluckman 2014).

Data and materials availability: The raw data from the study are available on request.
Competing interests: We have no competing interests.
Author contributions: A.B. collected and analysed data, A.B., O.S. and J.O. designed the study and wrote the paper, M.H. supervised the hormone analyses. J.O. and O.S. contributed equally. All authors reviewed the manuscript.
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Supplementary Material

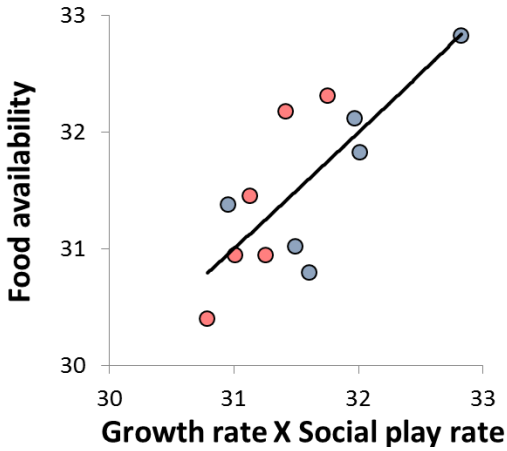

Figure S4.1: The product of growth rate X proportion of time spent in social play (´Growth rate X Social play rate´) was positively correlated to concurrent food availability.

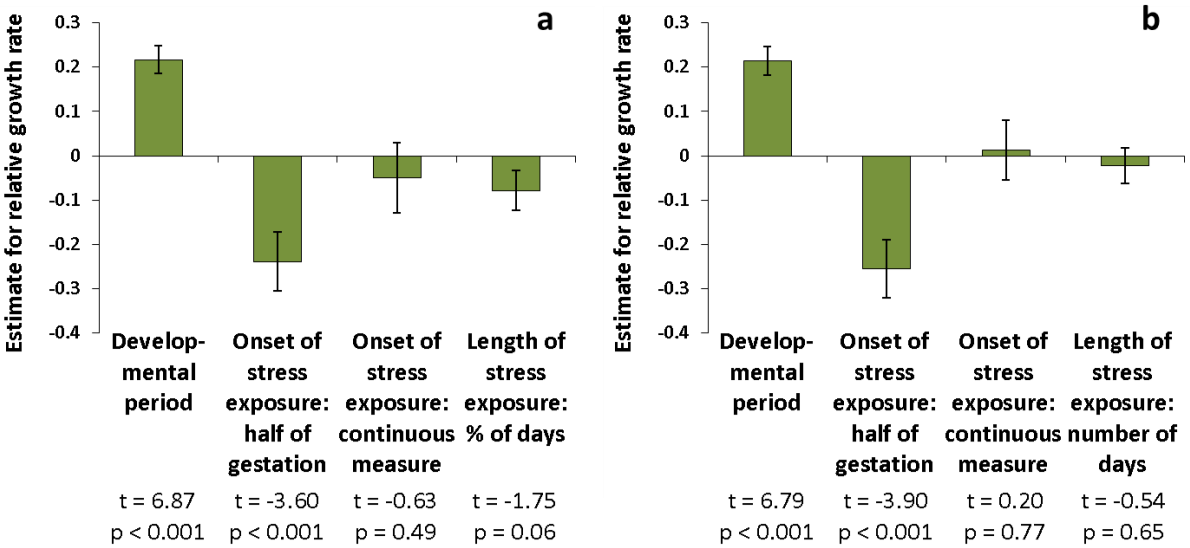

Figure S4.2: Relative growth rates were independently predicted by developmental period, gestation period of onset of stress exposure and by trend also by length of stress exposure (in percentage of gestation days) but not by a continuous measure of onset of stress exposure. Estimates ± SD of the z-transformed variables are plotted. Developmental period: gestation/lactation = 1, after lactation = 2; gestation period of onset of stress exposure: first half of gestation = 0, second half of gestation = 1; continuous measure of onset of stress exposure: ranging from 0 to 1, see Table 4.1. **a)** Full model with length of stress exposure in percentage of gestation days. Generalised LMM (random factor: species): Model significance: $p < 0.001$, $R^2 = 0.341$, intercept: estimate -0.16 ± 0.04. **b)** Full model with length of stress exposure in days. Generalised LMM (random factor: species): Model significance: $p < 0.001$, $R^2 = 0.351$, intercept: estimate -0.13 ± 0.06.

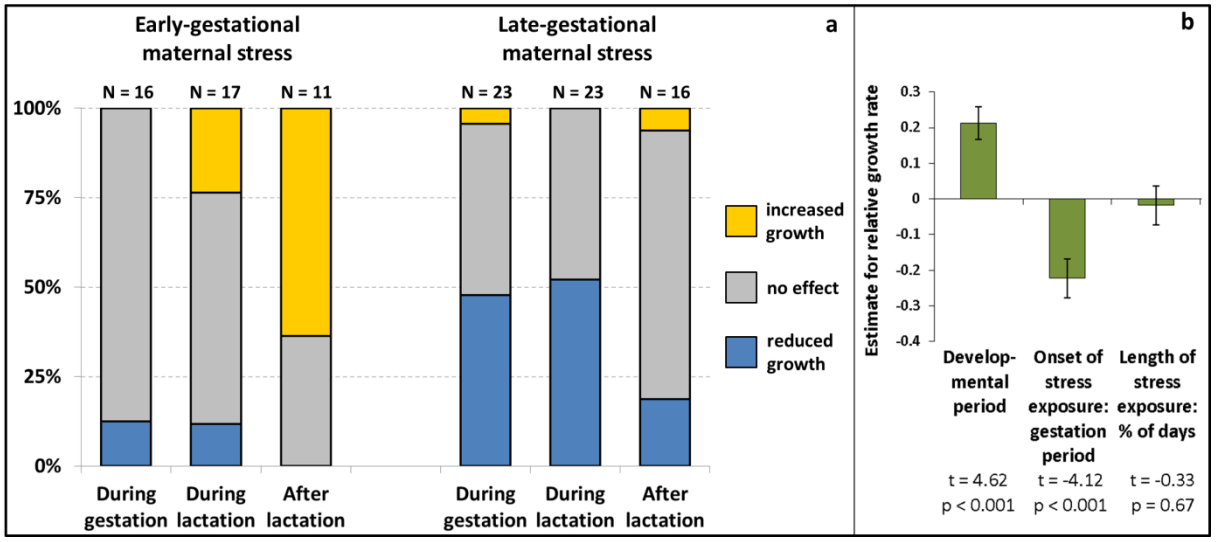

Figure S4.3: The pattern found in the literature review also holds if only the subset of studies which provide data about elevated PreGC-levels (or increase PreGC-levels directly via injections) is taken into account. Early-/Late-gestational: first/second half of gestation. Percentage of previous studies (see Table 4.1) reporting a higher (white), equal (grey) or lower (black) growth rate in offspring from PREMS-mothers compared to control mothers. b) Generalised LMM (random factor: species): Model significance: $p < 0.001$, $R^2 = 0.378$, N = 106, intercept: estimate -0.05 ± 0.10 (Estimates ± SD of the z-transformed variables are plotted).

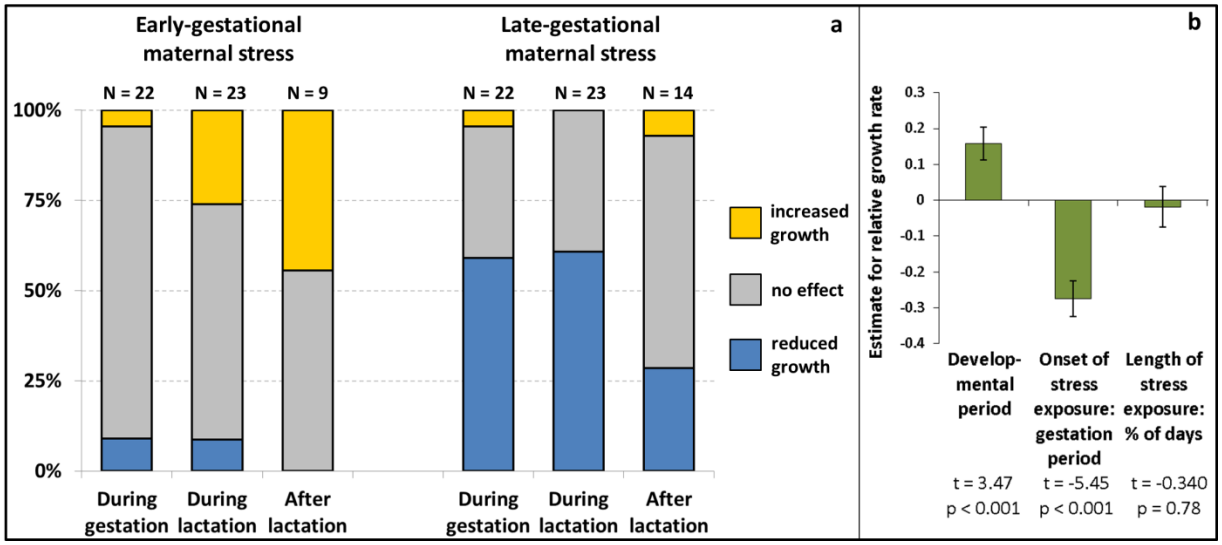

Figure S4.4: The pattern found in the literature review also holds if only the subset of studies without litter culling is taken into account. Early-/Late-gestational: first/second half of gestation. Percentage of previous studies (see Table 4.1) reporting a higher (white), equal (grey) or lower (black) growth rate in offspring from PREMS-mothers compared to control mothers. b) Generalised LMM (random factor: species): Model significance: $p < 0.001$, $R^2 = 0.322$, N = 113, intercept: estimate -0.18 ± 0.07 (Estimates ± SD of the z-transformed variables are plotted).

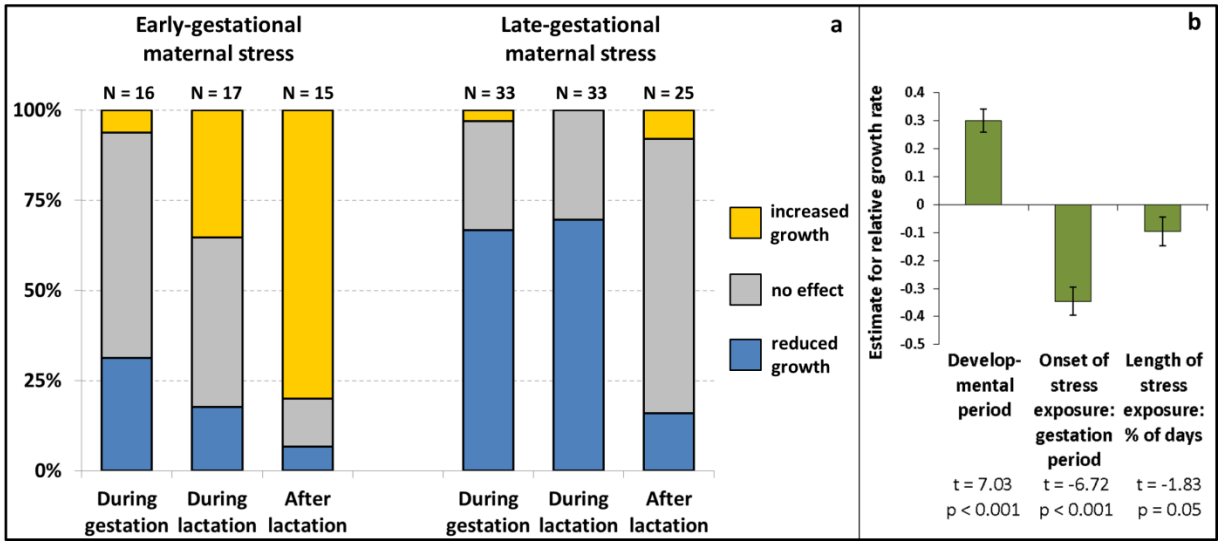

Figure S4.5: The pattern found in the literature review also holds if only the subset of studies which found any effects is taken into account. Early-/Late-gestational: first/second half of gestation. Percentage of previous studies (see Table 4.1) reporting a higher (white), equal (grey) or lower (black) growth rate in offspring from PREMS-mothers compared to control mothers. b) Generalised LMM (random factor: species): Model significance: $p < 0.001$, $R^2 = 0.443$, N = 139, intercept: estimate -0.22 ± 0.06 (Estimates ± SD of the z-transformed variables are plotted).

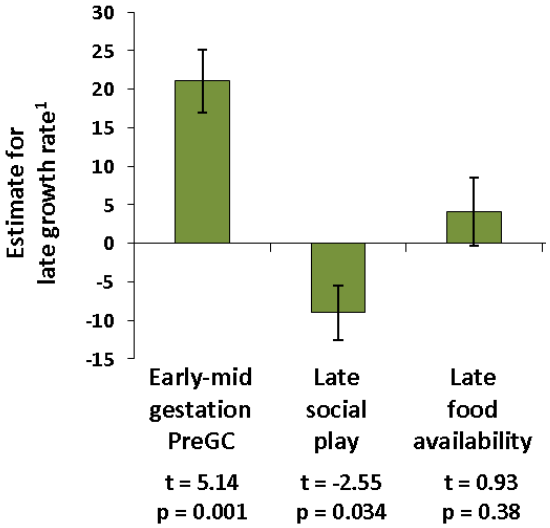

Figure S4.6: Early-mid gestation PreGC predicted late growth rates (i.e. after lactation) also after controlling for late proportion of time spent in social play and late food availability (N = 12). Estimates ± SD of the z-transformed variables are plotted. GLM: Model significance: $p < 0.001$, $R^2 = 0.820$, intercept: estimate 0.0 ± 3.0. The same model with PostGC instead of early-mid gestation PreGC ($p = 0.016$): log-likelihood = 0.008. The same model with PreGC during the first half of gestation instead of early-mid gestation PreGC ($p = 0.018$): log-likelihood = 0.007.

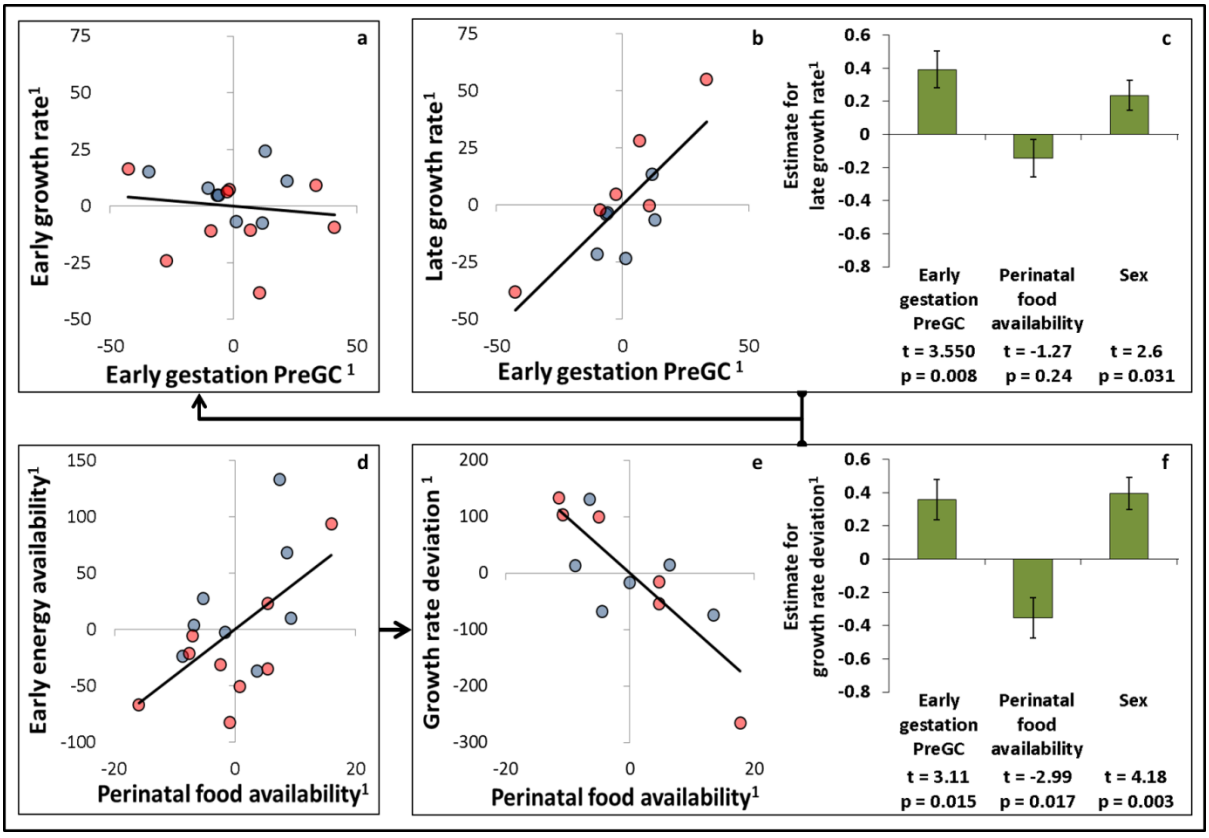

Figure S4.7: Also early gestational PreGC predicted growth rates after lactation but not during lactation, and the difference between these two growth rates was due to perinatal food availability which was related to the energy availability of the offspring during lactation. Perinatal: during gestation and lactation, early: during lactation, late: after lactation, early gestation: first half of gestation. [1]Residuals are translated into deviations from average in %. **a-c)** PreGC during the first half of gestation accelerated offspring growth rates after lactation (r = 0.809, p = 0.001, N = 12; controlled for perinatal food availability and offspring sex: r = 0.782, p = 0.008; GLM: Model significance: p = 0.002, R^2 = 0.750, intercept: estimate 2.38 ± 0.08; without the two potential outliers: r = 0.425), but not during the lactation period (r = -0.103, p = 0.71, N = 17; controlled for year of birth; within the offspring of the first year only (N = 12): r = -0.220, p = 0.49). **d)** Perinatal maternal food availability was positively correlated to the energy availability and thus probably energy intake of the offspring during lactation (r = 0.596, p = 0.015, N = 17; controlled for year of birth). **e, f)** The lower the perinatal maternal food availability, the more reduced was the realised early compared to the intrinsic (i.e. late) offspring growth rate. Thus differences in perinatal food availability were responsible for the balancing of early growth rates (deviation was calculated as late minus early growth rate). **e)** Perinatal food availability predicts deviation of the realised early from the intrinsic growth rate (controlled for offspring sex: r = -0.825, p = 0.002). **f)** This relationship remained also after controlling for the increasing effect of early PreGC on the intrinsic (late) growth rate **(**controlled for offspring sex and early gestational PreGC: r = -0.726, p = 0.017, GLM: Model significance: p < 0.001, R^2 = 0.834, intercept: estimate 0.00 ± 0.09).

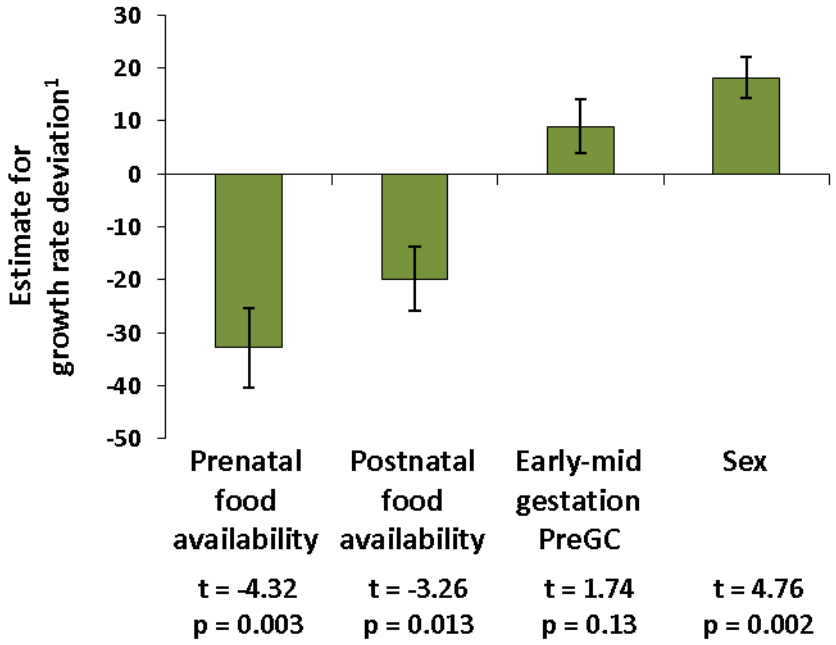

Figure S4.8: The difference between early and late growth rate was not driven by the PreGC-related intrinsic increase of late growth but by an extrinsic decrease of early growth due to reduced pre- and postnatal food availability. GLM: Model significance: p = 0.001, R^2 = 0.853, intercept: estimate -0.19 ± 3.46.

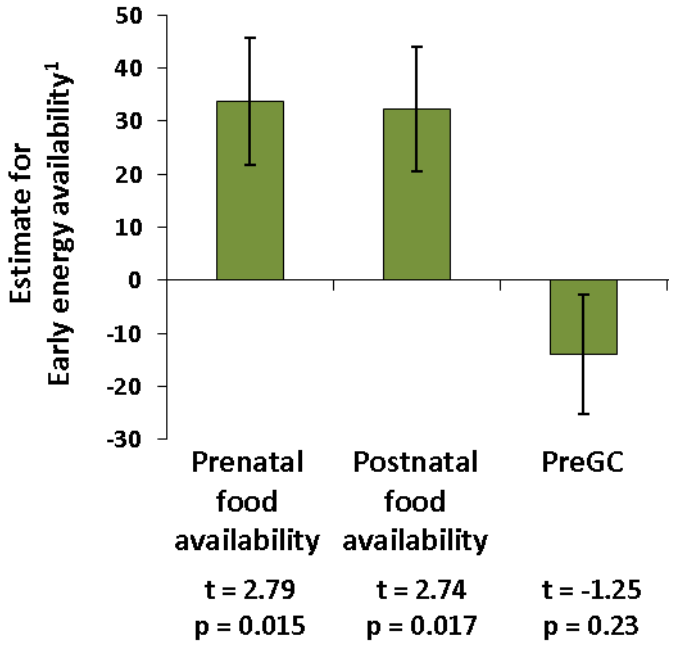

Figure S4.9: GLM predicting early energy availability of the offspring (N = 17). Model significance: p = 0.023, R^2 = 0.396, intercept: estimate 0.0 ± 9.7. (Estimates ± SD of the z-transformed variables are plotted).

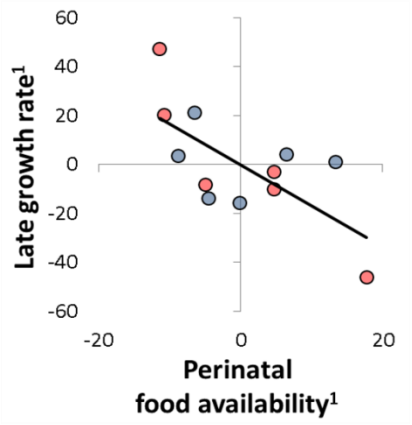

Figure S4.10: The intrinsic (late) growth rate was negatively, and thus compensatory, correlated to perinatal food availability (r = -0.688, p = 0.019, controlled for sex of the offspring).

Chapter 5

Patterns and consequences of male-infant relationships in wild Assamese macaques

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Abstract

Male care for offspring is unexpected in polygynandrous mammals. Evidence from non-human primates, however, indicates not only the existence of stable male-immature associations in multimale-multifemale groups, but also male care in form of protection from infanticidal attacks and conspecific harassment. Here, we investigate the relationship characteristics, dynamics and consequences of male-immature associations in wild Assamese macaques, *Macaca assamensis*, at Phu Khieo Wildlife Sanctuary, Thailand, to inform hypotheses of their evolutionary origins. Female Assamese macaques reproduce seasonally and do not signal ovulation resulting in low mating and paternity skew. However, male-immature associations are predicted by paternity and male behaviour potentially reflects paternal effort. We present focal animal data on 12 immatures followed from birth beyond weaning into their juvenile life (1,188 focal hours). The distribution of composite sociality indices suggests that male-immature relationships were highly differentiated. Association patterns and the degree of differentiation remained stable from six months well into the juvenile phase suggesting that male protection extends beyond the phase of high infanticide risk. Based on Hinde indices immatures were responsible for maintaining the relationships. The likelihood that an infant was associated with its preferred male increased if the mother was absent and if other males were present in proximity, suggesting that immatures sought protection. The presence of the preferred male did not decrease the rate of mild aggression immatures received from group members, but the stronger the relationship between an immature and a male, the more often it received agonistic support from him. Future studies will have to assess whether this agonistic support translates into improved fitness and represents true paternal care.

Introduction

Most mammalian males do not provide care for infants and - if present at all after conception - associate and interact with immatures only rarely (van Schaik and Kappeler 1997). The rarity of male care for offspring has been explained by the high costs of missed mating opportunities and by a high degree of paternity uncertainty in polygynandrous mating systems (Trivers 1972; Clutton-Brock and Parker 1992). Yet, in primates, especially in species of the cercopithecine subfamily where males and females are associated year-round and typically live in polygynandrous multimale-multifemale groups (Cords 2012), males and immatures are frequently found in close spatial association and affiliative or supportive interaction (Maestripieri 1998). Variation within and between cercopithecine species in the degree of immature-male association and its consequences has not been fully explored yet.

When investigating evolutionary explanations for male-immature associations it has proven useful to separate male reproductive investments into mating effort and paternal effort (Muller and Emery Thompson 2012). The paternal care hypothesis proposes that associations reflect care provided by the male for his current offspring thereby increasing the offspring's chances of survival and consequently the provider's fitness (Trivers 1972). Instead of directly caring for infants, e.g. carrying and food sharing, males may protect their offspring from conspecific threats to the physical integrity and survival of offspring (van Schaik and Paul 1996; Buchan et al. 2003). Conspecific threats may become manifest in increased injury risk from harassment by other group members (Altmann 1980; Smuts 1985; Shopland and Altmann 1987; van Noordwijk and van Schaik 1988; de Ruiter et al. 1994; Kleindorfer and Wasser 2004) as well as infanticide. Like other mammals in which time spent lactating exceeds the time spent gestating, primate infants face a high risk of infanticide by males (van Noordwijk and van Schaik 2000; van Schaik 2000b). High skew in mating and paternity success further increases the risk of infanticide (Palombit 2000; Henzi and Barrett 2003; Palombit 2003; Ostner et al. 2013).

Studies of primates living in multimale-multifemale groups provide mixed evidence for the paternal care hypothesis. For true paternal care to evolve males need to accurately distinguish their offspring from other infants (Alberts and Fitzpatrick 2012). In polygynandrous species males may assess paternity probability based on their own mating behaviour, association history with the infant's mother, and possibly phenotype matching (Busse and Hamilton 1981; Palombit et al. 1997; Borries et al. 1999; van Schaik 2000a; Buchan et al. 2003; Widdig 2007; Charpentier et al. 2008; Lemasson et al. 2008; Moscovice et al. 2009; Moscovice et al. 2010; Ostner et al. 2013). Playback experiments with chacma baboons (*Papio ursinus*) suggest that males respond more strongly to playbacks of a mother's distress calls if they are in a close affiliative relationship with the female (Palombit et al. 1997). Together with the fact that chacma baboon females form close affiliative relationships or "friendships" with sires and likely sires of current offspring (Moscovice et al. 2009) and that these relationships and the associated support by the male friend end abruptly upon the death of the offspring (Palombit et al. 1997), these experiments suggest that male behaviour evolved as paternal protection against conspecific threat.

Chacma baboon males preferentially support both related and those unrelated juveniles with whose mother they previously had formed a close affiliative relationship (Moscovice et al. 2009) and provide enhanced access to food and undisturbed feeding (Huchard et al. 2013). Yellow baboon males (*P. cynocephalus*) also preferentially support their genetic offspring in agonistic conflicts during the juvenile phase (Buchan et al. 2003) and the presence of the father accelerates offspring maturation (Charpentier et al. 2008) which may result from accelerated socialisation or reduced social stress (Fairbanks 1993). In rhesus (*M. mulatta*) and Assamese

macaques (*M. assamensis*) fathers associate more with their dependent genetic offspring than with other infants (Langos et al. 2013; Ostner et al. 2013), but rhesus macaque fathers fail to support their genetic offspring in conflicts against other group members (Kulik et al. 2012). Male-immature associations are not predicted by paternity in Barbary macaques, *M. sylvanus* (Paul et al. 1996; Ménard et al. 2001) and mountain gorillas, *Gorilla beringei* (Rosenbaum et al. 2015).

The mating effort hypothesis for the evolution of male care proposes that male-immature associations evolved as a form of male mating effort (Seyfarth 1978) rather than paternal effort, with the male endearing himself to the female to enhance his future mating success with her. Accordingly, the hypothesis predicts that male-infant associations and male care will evolve independently of paternity as a mere by-product of male mating effort (Smuts 1985; van Schaik and Paul 1996; Ménard et al. 2001; Ostner et al. 2013). The mating effort hypothesis is supported by long-term studies of wild Assamese macaques, free-ranging and captive rhesus macaques, and wild chimpanzees (*Pan troglodytes*) where male-infant or male-mother association predicted male mating success (Smuts 1985; Kulik et al. 2012; Massen et al. 2012; Langos et al. 2013; Massen and Sterck 2013; Ostner et al. 2013). In all of these species it has recently been shown that male-female relationships are stable well beyond one female reproductive cycle (Langergraber et al. 2013; Massen and Sterck 2013; Ostner et al. 2013; Haunhorst et al. 2016). A close heterosexual relationship may be formed at some point, increase current and/or future mating success, remain stable through the gestation period and on into early infancy of the subsequent offspring which often but not always is fathered by the male friend (Ostner et al. 2013). Thus male-female association in these species could potentially reflect both mating effort and paternal effort. To date, most studies of male care focussed either only on the first few weeks or months of an infant's life (Lemasson et al. 2008; Nguyen et al. 2009; Huchard et al. 2013) or on the juvenile life phase alone (Buchan et al. 2003; Charpentier et al. 2008; Moscovice et al. 2009; Huchard et al. 2013) and many studies lack details on the nature of male-immature social relationships.

In Assamese macaques patterns of male-female and male-immature spatial association are consistent with the paternal care hypothesis as well as a modified version of the mating effort hypothesis, the friends-with-benefits hypothesis, which proposes that male-female relationships evolve for male mating benefits with the female friend without assuming that the relationship necessarily has to form prior to the mating season (Ostner et al. 2013). The different evolutionary routes to male-immature association produce different relationship characteristics, i.e. differences concerning the responsibility for relationship maintenance and relationship stability. In Assamese macaques we currently lack an understanding of the quality of male-immature relationships beyond spatial patterns as well as the possible benefits accruing for infants from selectively associating with adult males.

Reproduction in Assamese macaques is seasonal and females either exhibit approximately one year or two year interbirth-intervals (Fürtbauer et al. 2011a; Ostner et al. 2013). Male mating skew and paternity skew are low (Ostner et al. 2011; Sukmak et al. 2014). Infanticide has been directly observed (Kalbitz, Ostner, Schülke, unpubl. data) and could be adaptive because male tenures are long (Ostner et al. 2013) and the chance for a female to conceive in the same year increases from 38% if the infant survives to 75% if the infant is lost before weaning (Schülke & Ostner, unpubl. data). The risk of infanticide from within the group is reduced though, because ovulation is concealed from males (Fürtbauer et al. 2011a), females exhibit high mating synchrony (Fürtbauer et al. 2011b) and mate with all males in the group leaving each of them with a non-zero chance of paternity for every infant. Although the timing of ovulation is concealed from males, males seem to infer some paternity certainty based on past mating history with the infant's mother (Ostner et al. 2013).

Table 5.1. Summary of hypotheses and predictions

Hypothesis	Prediction	Supported?
Mating effort	1) Males are mainly responsible for maintaining close proximity (≤1.5 m) to infant.	No
	2) The male–immature relationship ends with the mother's conception.	No
Paternal effort	The degree of preference for preferred offspring relative to other infants remains constant.	Yes
Against infanticide	1) Differentiation in male–immature relationships is stronger during preweaning compared to postweaning period and peaks during first 6 mo of life.	Yes / no
	2) Total time spent in proximity with the PM is highest during the first 6 mo of life and decreases with increasing age.	No
	3) The presence of the PM in proximity in the preweaning period is negatively associated with the presence of the mother and positively with the presence of nonpreferred males.	Yes
Against harrassment	1) Total time spent in proximity to the PM is constant and association strength remains high across the entire study period.	Yes
	2) The presence of the PM in proximity in the pre- and postweaning period is predicted negatively by the presence of the mother and positively by the presence of nonpreferred males.	Yes
	3) The presence of the PM in proximity decreases immatures' rate of aggression received from and submission given to group members.	No
	4) PMs support immatures in conflicts more often than nonpreferred males do.	Yes

See text for further explanation. PM = preferred male.

In this study we analyse immature focal animal data collected over the first 21 months of an immature's life and determine the distribution of the strength of male-immature affiliative relationships (see Table 5.1 for a summary of hypotheses and predictions). Based on our previous finding of selective male-immature associations (Ostner et al. 2013) we expect affiliative relationships to be differentiated, i.e. stronger and more consistent relationships in a few male-immature dyads. If *male care evolved as mating effort* alone, we predict that (1) males are mainly responsible for maintaining close proximity (less than 1.5m) to the infant and (2) males should terminate their relationship with the infant as soon as the infant's mother conceives again. If *male care evolved as paternal effort* alone the time spent in association may vary with the risks the offspring faces, but the degree of preference for their preferred offspring relative to other infants should remain constant. Specifically, if *male care serves an anti-infanticide function* we predict (1) that differentiation in male-immature social relationships is stronger during the pre-weaning (month 1-12)

compared to the post-weaning period (13-21 months) and peaks during the first six months of life when the risk of infanticide is highest, (2) that the total time spent in proximity (≤5m) to the preferred male is highest during the first six months of life and decreases with increasing age/decreasing infanticide risk and (3) that the presence of the preferred male in proximity of ≤5m in the pre-weaning period (month 1-12) is negatively associated with the presence of the mother and positively with the presence of non-preferred males, because infanticide risk is higher in the absence of the mother and around non-preferred males. If *male care serves an anti-harassment function*, we predict (1) that the total time spent in proximity to the preferred male remains constant and association strength remains high across the entire study period, as immatures, due to their slow development, are still vulnerable to threats from aggressive conspecifics even after reaching independence, (2) that the presence of the preferred male in proximity of ≤5m in both the pre- and the post-weaning period is predicted negatively by the presence of the mother and positively by the presence of non-preferred males, because the risk of harassment by aggressive conspecifics increases in the absence of the mother and the presence of an non-preferred male. Most importantly, we predict (3) that the presence of the preferred males in proximity (≤5m) decreases immatures' rate of aggression received from and submission given to group members and (4) that preferred males support immatures' in conflicts more often than non-preferred males.

Material and methods

Study site and study group

The study was conducted at Phu Khieo Wildlife Sanctuary (PKWS, 16°05-35'N and 101°20-55'E) in North-Eastern Thailand, an area of maximal protection status that is part of the contiguous ca. 6500 km^2 protected Western Isaan Forest Complex (Koenig et al. 2004). The forest at the study site Huai Mai Sot Yai (16°27'N, 101°38'E, 600–800 m a.s.l.) comprises mainly hill and evergreen forest with dry dipterocarp patches and bamboo stands (Borries et al. 2002), its vegetation is dense and the terrain hilly (Schülke et al. 2011). Large populations of large herbivores like elephants and gaurs as well as a diverse community of predators suggest the habitat is relatively intact (Kumsuk et al. 1999). Assamese macaques feed mainly on fruit from a large number of tree species and spend around 60% of their active time in the middle and upper strata of the forest (Schülke et al. 2011; Heesen et al. 2013).

We collected observational data on twelve immatures (all born in 2011; see Table 5.2) from May 2011 through December 2012 from a fully habituated group of wild Assamese macaques that comprised 60 individuals in the 2011 birth season (9 adult males, 15 adult females, 1 subadult male, 23 juveniles, 12 infants) and 65 individuals (10 adult males, 15 adult females, 40 immatures) in 2012 (Berghänel et al. 2015). We classified immatures as infants until 12 month of age, and as juveniles from 13 months onwards. Infants included here were born during the study (eight cases) or 1-2 months prior (4 cases). Date of birth was known from demographic monitoring of the group (10 cases exact day, 2 cases estimated as the midpoint of a 4-9 day period; Table 5.2). The study group split in late August 2012 when 11 individuals (3 adult males, 4 adult females with their offspring born 2011) emigrating from the main group (Table 5.2). This study was undertaken completely non-invasively and with permission from the Department of National Parks, Wildlife and Plant Conservation (DNP) and the National Research Council of Thailand (NRCT) (permit: 2008/045).

Table 5.2. Twelve focal infants, birth dates, focal time, and group residency of Assamese macaques at Phu Khieo Wildlife Sanctuary

Sex	Exact date of birth	Focal hours	Left group August 2012
Female	March 23, 2011	95.8	N
Male	April 10, 2011	101.5	Y
Female	April 20, 2011	92.1	Y
Female	April 20, 2011	103.5	N
Male	April 25, 2011	103.3	Y
Male	May 12, 2011[a]	106.8	N
Female	May 15, 2011[b]	100.6	N
Male	May 29, 2011	95.9	Y
Male	June 9, 2011	101.5	N
Female	June 11, 2011	93.1	N
Female	June 16, 2011	98.5	N
Male	July 2, 2011	95.8	N

[a] Midpoint between May 9 and May 16. [b] Midpoint between May 14 and May 17.

Behavioural data collection

Throughout the 20 month study period we collected behavioural data almost daily using 30min focal animal sampling (Altmann 1974). We followed all twelve immatures born in 2011 during all-day follows of the group from sleeping tree to sleeping tree (range: 92.1 – 106.8 hours focal animal sampling per individual, total = 1,188h). We continuously recorded all social behaviours (agonistic and affiliative) to measure frequencies and durations. At 10min intervals we recorded the identities of all group members within 5m of the focal animal, i.e. 5m proximity. For the analysis of differentiation and relationship maintenance (Composite Sociality and Hinde Indices, see below) we only included social interactions that derived from individual approaches/departures (within 1.5m, i.e. close proximity) of the immatures themselves to/from males and vice versa in our analysis, i.e. we excluded interactions wherein immatures were carried by conspecifics into proximity or into interactions with others in order to restrict our analysis to purely infant-related interactions. Sample size for the analyses varied depending on availability of the respective type of data.

Differentiation of immature-male relationships

We calculated the Composite Sociality Index (CSI) (Silk et al. 2006) for each adult male-immature dyad based on continuous focal sampling records from the entire study period to determine the strength of the association between each male and immature. Because the study group split in August 2012 we corrected male-immature dyadic focal time for the time the dyad co-resided in the same group. Our CSI describes the relative strength of an affiliative relationship based on the frequency (f) and duration (d) of close spatial proximity of ≤1.5m (P) and body contact (B) for each male-immature dyad relative to the mean across all dyads ($CSI = (Pd_{ij}/Pd_{mean} + Pf_{ij}/Pf_{mean} + Bd_{ij}/Bd_{mean} + Bf_{ij}/Bf_{mean})/4$). Grooming was too rare to be included, i.e. the mean number of grooming interactions per dyad was

close to 1, yielding an unduly high influence of a single observed event on the resulting CSI value. All components included in the CSI were correlated in row-wise matrix correlations with 10.000 permutations using Kendall-Tau correlations (mean $rho_{rw,ave}$ = 0.63 ± 0.18; range $rho_{rw,ave}$ = 0.49 – 0.87). All values were corrected for observation time and we subtracted approaches followed by body contact from the first and second term. Dyads with values >1 had a stronger relationship than the average male-immature dyad in the group (Fig. 5.1). The male with the highest CSI-score, i.e. the top partner, was classified as an immature's preferred male partner. For eleven of the twelve infants the preferred male partner had an above-average relationship with the infant, i.e. a CSI above 1 (see results).

Responsibility for maintaining immature-male relationship

For every immature-male dyad with more than 20 tolerated approaches, i.e. approaches not leading to an agonistic interaction (Palombit et al. 1997; Moscovice et al. 2009) we calculated the Hinde-Index (Hinde and Atkinson 1970b) to determine which partner was responsible for the maintenance of close spatial association (≤1.5m). Our Hinde index is based on the number of approaches (A) by the immature (i) or the male (m) as well as the number of departures (D) by either individual (Hinde Index = $(A_i/(A_i+A_m) – (D_i/(D_i+D_m))*100$). Values of the Hinde Index range from –100 to +100. Positive values (above +10) indicate responsibility of the immature and high negative values (below – 10) responsibility of the male (Hill 1987). The number of dyads with more than 20 tolerated approaches was 40 across the entire study period. We also compared mean Hinde-Indices of the respective preferred male-immature dyads with the mean across all other possible male-immature dyads in the group.

Temporal stability of differentiation and partner choice in immature-male associations

In order to assess the temporal stability of immatures' choice of preferred partners we calculated the Consistency-Index (modified from Silk et al. (2010) as follows: C = (Y-U)/(Y-1) with Y = number of months that the immature was present and U = the number of different males that were an immatures' preferred male across different months of life. The values of C range from 0 (different partners in each month) to 1 (same partner across all months of life).

In order to assess the temporal stability of the differentiation in immature-male associations we split the data into month of life blocks and calculated an Association Index for each immature that expressed how often and how long it spent time in close proximity to its preferred male relative to the averages across other males in that month of an immature's life. Specifically, for each month and immature we divided the frequency of time spent within 1.5m of the preferred male (controlled for focal observation time) by the average frequency of time spent within 1.5m of any other male. The same was done for duration of time spent within 1.5m; the two terms were then summed and divided by 2 ($AI = (Pd_{ij}/Pd_{mean} + Pf_{ij}/Pf_{mean})/2$). The Association Index could not be calculated for some months for some immatures, because the average frequency of association was close to 1 rendering the measure inaccurate. In our comparison of relationship differentiation across month of life we included months with values for at least 7 immatures, i.e. excluded months 1, 2, 20 and 21 from this analysis (mean number of immatures per month ± SD: 10.52 ± 1.42). Thus, we report mean Association-Indices with preferred males for the periods from 3 - 6 months (highest infanticide risk), 7 - 12 months (moderate infanticide risk), and 13 - 19 months of immature age (period after weaning).

Influence of preferred male's presence on immature aggression received (and submission given)

To investigate whether the presence of the preferred male affected the rate of aggression immatures received, we created a data set of 887 pairs of observations around proximity scans that differed only by the presence/absence of the preferred male and were otherwise matched for the age-sex composition of all individuals within 5m of the immature focal animal, i.e. the pairs of observations were matched for the number of adult males, adult females, juveniles and infants as well as mother present/absent. We then tested whether (a) an immature received aggression or in a second model (b) gave submission in an observation depending on whether or not the preferred male was around at this point in time.

Male agonistic support of immatures

We investigated the relationship between the strength of male-immature relationships based on the CSI and the frequency of support (counts) the infant received from the male in conflicts with other group members.

Statistical analysis

All statistical analyses were performed using R.2.1.4 software (R development core team 2011). We used Generalized Linear Mixed Models (GLMM; Baayen 2008) to investigate whether the presence of a second male (potential aggressor) and the mother (potential protector) in proximity (≤ 5m) predicted the presence/absence of the preferred male in the proximity of the immature, with the presence of a second male as well as the mother (binomial) as fixed effects. Immature focal identity (to account for non-independence of repeated observations within individuals), immature sex and age-sex composition of group of other individuals within 5m proximity of the focal immature were set as random factors. We ran the GLMM three times for different time periods of an immature's life (entire study period: 1-21 months; pre-weaning: 1-12 months; post-weaning: 13-21 months).

To analyse whether the presence of the preferred male predicted the occurrence of aggression received or the rate of submission given by the immature (inclusive and exclusive of the aggression given by/submission given towards the preferred male), we ran GLMMs with the presence of the preferred male (binomial) as the fixed effect and immature identity, immature sex and age-sex composition of group of other individuals within 5m proximity of the focal immature as random factors. GLMMs were run using the function 'lmer' from the R package 'lme4' (Bates et al. 2011). GLMMs were fitted with binomial error structure and logit link function. Using a likelihood test (R function 'anova', package 'stats'), we determined the statistical significance of the full model by comparing its fit with that of a null model including only the intercept and the random effects. Additional analyses revealed no strong correlation among predictors (Pearson correlation) and no violation of model assumption due to overdispersion, and influential cases using functions dfbeta and dffits.

Finally, we ran a GLMM with the number of times a male supported an immature in agonistic conflicts as the response, immature identity and male identity as random factors and the z-transformed CSI value of the immature-male dyad as a fixed effect. We followed the same procedures as mentioned above but fitted a Poisson model. For all comparisons between different life phases we used two-sided Wilcoxon's signed rank tests. Due to small sample sizes we used exact tests as recommended by (Mundry and Fischer 1998).

Results

Characterization of male-immature relationships

Across the 108 male-immature dyads relationships were clearly differentiated as indicated by a strongly skewed distribution of CSI scores, with a median of 0.2, well below the mean of 1 and 10% of the dyads featuring scores above 3 (Fig. 5.1). Across infants the mean CSI of the top partner, the single preferred male, was 3.5, more than 2 standard deviations from the mean of 1. The CSI scores for one immature were all smaller than 1 and we chose the male with the highest CSI (CSI = 0.8) as preferred male. For six infants the CSI scores with the top two males differed by less than 0.5. For our analyses we defined the male with the higher CSI as the single preferred male, however we run all analyses again with these runner-up males, i.e. the second top males (separated by less than 0.5 in CSI score from top preferred), which did not significantly change our results or conclusions. For the other six immatures the CSI values for the preferred and the second closest male differed by 1.7 ± 1.2 (mean ± SD).

Infants spent 43% of their time with their mother, 11% with their preferred male and 7% with any other male (time spent within 5m proximity). Every focal hour they spent a mean of 2:05 min in close proximity (within 1.5m) or body contact with their preferred male (1.28 times/focal hour) compared to a mean of 27 sec/focal hour or 0.27 times /focal hour with other males.

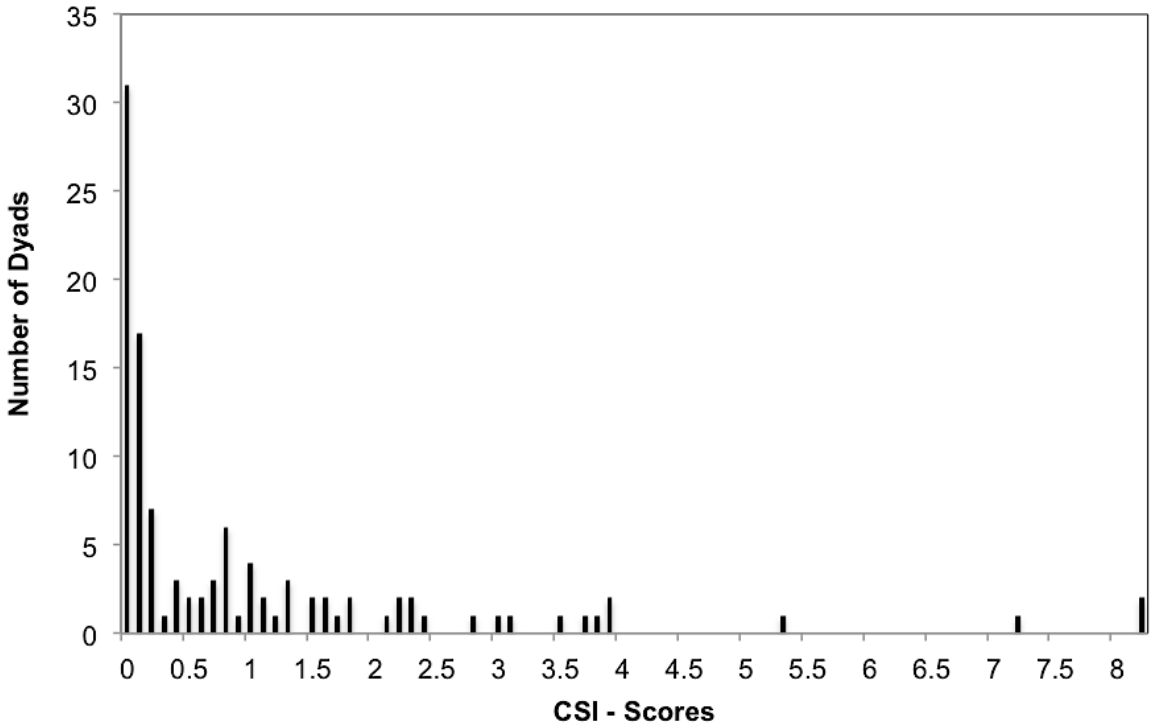

Figure 5.1: Differentiation of immature-male social relationships in a histogram of CSI scores of all immature-male dyads (N = 108) of one group of Assamese macaques at Phu Khieo Wildlife Sanctuary as a measure of the strength of an affiliative relationship (data from May 2011 to December 2012). The median is 0.2, 10% of scores exceeded 3.0, and the mean is by definition 1.

Testing predictions of the mating effort hypothesis

The Hinde-Indices of male-immature dyads were positive in 98% of cases (N = 40 male-immature dyads with more than 20 tolerated approaches) with a mean score ± SD of 20 ± 13, implying that immatures were responsible for maintaining close proximity to males much more than vice versa which is in contrast to our prediction based on the mating effort hypothesis (Fig. 5.2). If split into the pre- (1 - 12 months of age) and post- (13 -21 months of age) weaning period, 93% (N = 30 male-immature dyads with more than 20 tolerated approaches) of Hinde-Indices were positive with a mean score ± SD of 22 ± 14 before and 93% (N = 14 male-immature dyads with more than 20 tolerated approaches) positive indices post-weaning with a mean ± SD of 22 ± 15 (Fig. 5.2). Immatures sought the proximity of their preferred male more than that of other males. The mean Hinde-Index of all preferred male-immature dyads (mean ± SD = 29 ± 10) was 35% higher than the mean Hinde-Index of all other male-immature dyads (mean ± SD = 14 ± 12, Wilcoxon signed rank test: V = 2, Z = -2.91, N = 12 (all focal infants), p = 0.001).

Immatures' choice of the preferred male partner was stable. Across the entire study period and averaged across immatures, immatures chose the same preferred male partner from month to month in 80% of cases (Consistency-Index mean ± SD = 0.79 ± 0.16, range: 0.38 - 0.94). All of the seven offspring of mothers that conceived again during the study period maintained their strong relationship with their preferred male partner upon conception of their sibling, which again is in contrast with our prediction based on the mating effort hypothesis.

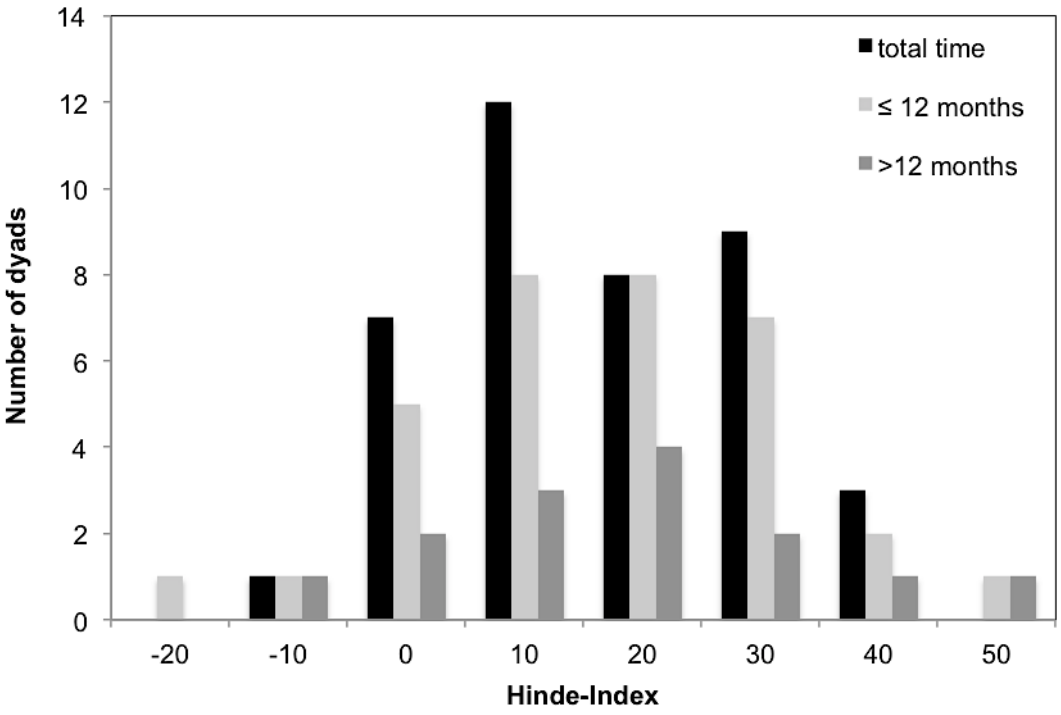

Figure 5.2: Histogram of Hinde-Indices as a measure of partners' responsibility for maintaining immature-male association in a group of Assamese macaques at Phu Khieo Wildlife Sanctuary. Black: entire study period, light grey, before weaning (1-12 months), dark grey: after weaning (13 - 21 months). Positive values above 10 indicate that immatures are responsible for initiating and maintaining close spatial proximity within 1.5m (see methods for details).

Testing predictions of the paternal care hypothesis - Temporal stability of differentiation of male-immature associations across the first 21 months of life

Based on the Association Index the relative strength of the association with the preferred male exceeded the mean across males in 82% of immatures for every single month of life (mean ± SD = 10.5 ± 1.42 immatures per month, Fig. 5.3). This degree of preference or the strength of male-immature associations differed significantly for pre- (median= 4.31; interquartile range = 3.66 – 5.11) and post-weaning periods (median = 3.43; interquartile range = 2.39 – 4.15; Wilcoxon signed rank test: V = 8, Z = -2.43, N = 12 (all focal infants), p = 0.01), a finding consistent with predictions based on the anti-infanticide hypothesis, but not between early (3 – 6 months; median = 4.30; interquartile range = 3.52 -5.67) and late infancy (7 – 12 months; median = 3.92; interquartile range = 3.52 – 5.03; Wilcoxon signed rank test: V = 18; Z = -1.33, N = 11 (one infant excluded due to insufficient data during this period), p = 0.21).

In contrast to predictions from the anti-infanticide hypothesis and consistent with predictions from anti-harassment hypothesis, the absolute time that immatures spent in proximity to their preferred male did not differ between the pre- and post-weaning phase (two-sided Wilcoxon signed rank test, V = 28, Z = -0.86, N = 12 (all focal infants), p = 0.42, Fig. 5.4). Time spent close to mothers significantly declined after weaning (two-sided Wilcoxon signed rank test, V = 0, Z = -3.06, N = 12 (all focal infants), p < 0.001). Time spent with other group members than preferred males or mothers doubled from the pre- to the post-weaning phase (Fig. 5.4).

Comparing associations on smaller timescales revealed that until 3 months of age mothers always were in sight, when immatures spent time in proximity to the preferred male (7%) and nearly always until 6 months of age (9% with the preferred male and of these 6% with mother as well, Fig. 5.4). Once infants were 7 months old they spent twice as much time in proximity to their preferred male (18% month 7-12 vs. 9% month 1-6, two-sided Wilcoxon signed rank test V = 12, Z = -2.12, N = 12 (all focal infants), p = 0.03). This change was associated with a significant decrease in time immatures spent with their mothers (Wilcoxon signed rank test, V = 0, Z = -3.06, N = 12, p = 0.001, Fig. 5.4). There was no difference in time spent in proximity to preferred males between late infancy (7-12 months) and the post weaning phase (13-21 months, two-sided Wilcoxon signed rank test, V= 18, Z = -1.65, N = 12, p = 0.11, Fig. 5.5).

The preferred male was more likely to be in proximity (≤ 5m) in the presence of a second male (i.e. a potential aggressor) before weaning (R^2 full model = 0.21, full vs. null-model Chi^2 = 39.35, p < 0.001), after weaning (R^2 full model = 0.26, full vs. null-model Chi^2 = 26.73, p < 0.001) and across the entire study period (R^2 full model = 0.18, full vs. null-model Chi^2 = 41.15, p < 0.001; Table 5.3). Mother's presence (potential protector) had a significant negative effect on the likelihood that the preferred male was in proximity across the study period. This effect was pronounced in the pre-weaning period compared to the post-weaning period (Table 5.3). When mothers were absent (Fig. 5.4), immatures were associated with their preferred male for 24% of their time (10% with other males) during the first 12 months of life compared to 11% (10% with other males) after weaning. Taken together these results support predictions derived from the anti-harassment and from the anti-infanticide hypothesis.

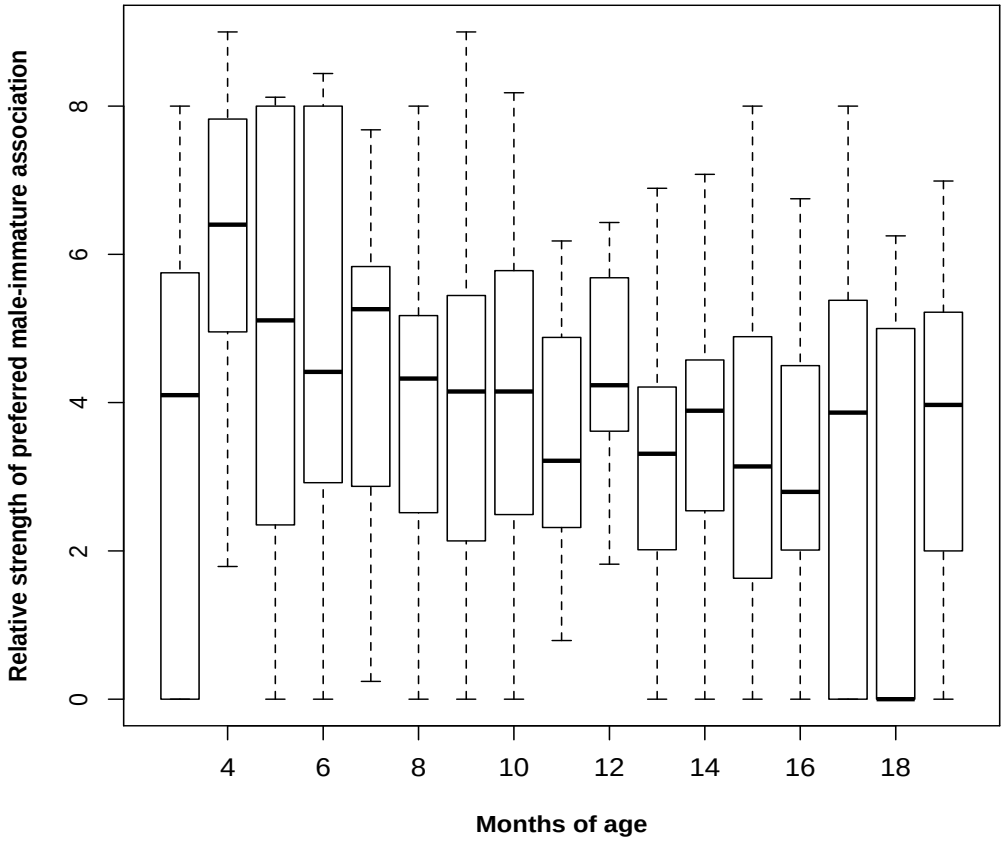

Figure 5.3: Temporal stability of the differentiation in immature-male associations from 3 – 19 months of age in Assamese macaques at Phu Khieo Wildlife Sanctuary. Depicted are medians and 25%-75% percentiles across immatures of their Association Indices with preferred males. Association Indices are frequency and duration of close association within 1.5m with the preferred male relative to the mean across males for a given immature.

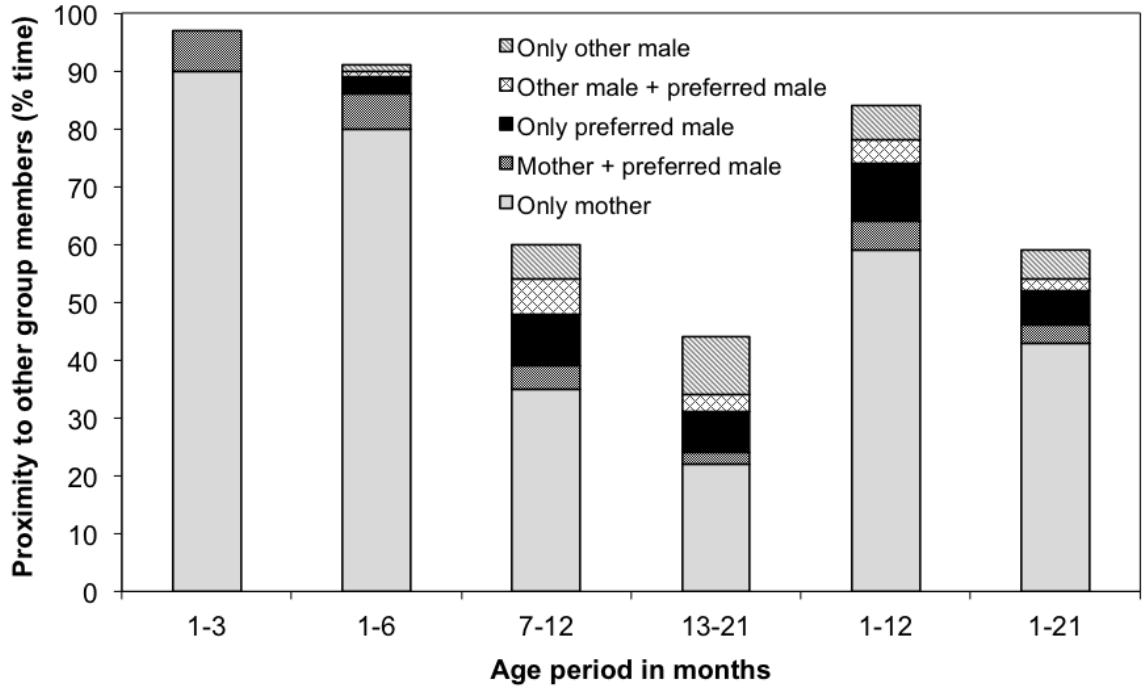

Figure 5.4: Time immature Assamese macaques from Phu Khieo Wildlife Sanctuary spent in proximity (≤5m) to different group members for different immature age intervals expressed as proportion of active time.

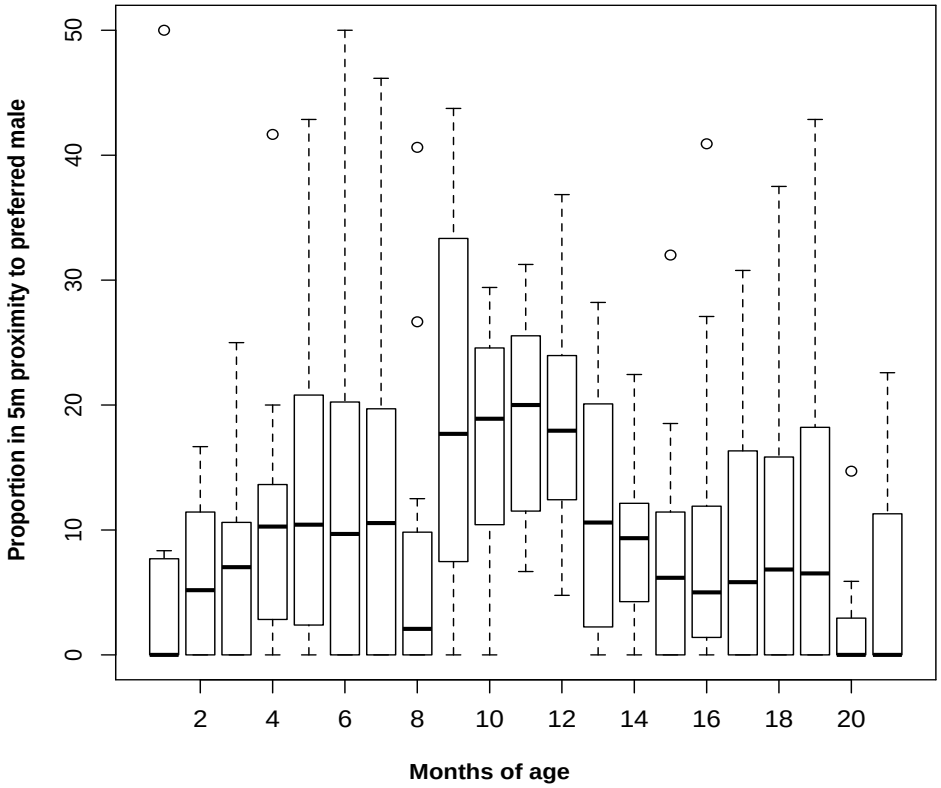

Figure 5.5: Time immature Assamese macaques from Phu Khieo Wildlife Sanctuary spent in proximity to preferred male across months of life expressed as proportion of active time. Depicted are medians and 25%-75% percentiles across immatures.

Table 5.3. Predictors of preferred male presence in proximity (≤ 5 m) of an immature Assamese macaque at Phu Khieo Wildlife Sanctuary

Age period	Fixed factors	Estimate ± SE	z-value	P
1-21 months	Mother in sight (yes)[a]	-0.53 ± 0.14	-3.75	<0.001
	Other adult male in sight (yes)[a]	0.87 ± 0.14	6.03	<0.001
1-12 months	Mother in sight (yes)[a]	-0.94 ± 0.18	-5.35	<0.001
	Other adult male in sight (yes)[a]	0.83 ± 0.19	4.45	<0.001
13-21 months	Mother in sight (yes)[a]	-0.51 ± 0.20	-2.57	<0.01
	Other adult male in sight (yes)[a]	0.96 ± 0.19	5.00	<0.001

Results of three GLMMs controlling for immature identity and group composition with number of observations: 1 – 21 mo, N = 5526; 1 – 12 mo, N = 3240; 13 – 21 mo, N = 2286 proximity scans.
[a] Reference category: no.

Table 5.4. Influence of preferred male (PM) presence on the likelihood of immatures receiving aggression (including aggression received by PM) and giving submission (including submission given to PM) in Assamese macaques at Phu Khieo Wildlife Sanctuary.

Response variable	Fixed factors	Estimate ± SE	z-value	p
Received aggression (incl. PM)	Pref. males in sight (yes)[a]	0.57±0.25	2.27	0.023
Given submission (incl. PM)	Pref. male in sight (yes)[a]	0.48±0.20	2.37	0.018

GLMMs controlling for immature identity (N = 12) and immature sex and local group composition (N = 167). Number of observations: 1774. SE: standard error
[a] Reference category: no.

Influence of the preferred male on the rate of aggression received/submission given by immatures

Overall immatures received a mean ± SD of 0.75 ± 0.24 bouts of aggression per hour. Aggressors were either other immatures up to age 5 (60%) or adults (40%). The average rates of aggression received were significantly higher after weaning than before (Wilcoxon signed rank test, V = 1, Z = -2.98, N = 12 (all focal infants), $p < 0.001$) mainly driven by increased aggression received from other immatures. Aggression against mothers carrying immatures was not included in this calculation, which may partly explain the lower pre-weaning rates.

Although full models were different from null models, the presence of the preferred male in proximity (≤ 5m) did not reduce the rate of aggression immatures received from conspecifics (R^2 full model = 0.20, full vs. null-model Chi^2 = 5.32, p = 0.02) or reduce the rate of submission given to conspecifics across the study period (R^2 full model = 0.16, full vs. null-model Chi^2 = 5.68, p = 0.017, Table 5.4). The rate of aggression received and submission given, in fact, significantly increased in the presence of the preferred male. This was probably due to the mild aggression given by preferred males which spent more time with the infant in proximity which is not controlled for in this analysis. After excluding the mild aggression given by preferred males to immatures the resulting full model of aggression received did not differ from the null model with only the random factors and the intercept (Full vs. null-model Chi^2 = 0.02, p = 0.89). Likewise, after excluding the submission given by immatures to their preferred male the presence of the preferred male did not predict the rate of given submissions towards group members anymore (Full vs. null-model Chi^2 = 0.21, p = 0.65). These results do not support our predictions based on the anti-harassment hypothesis.

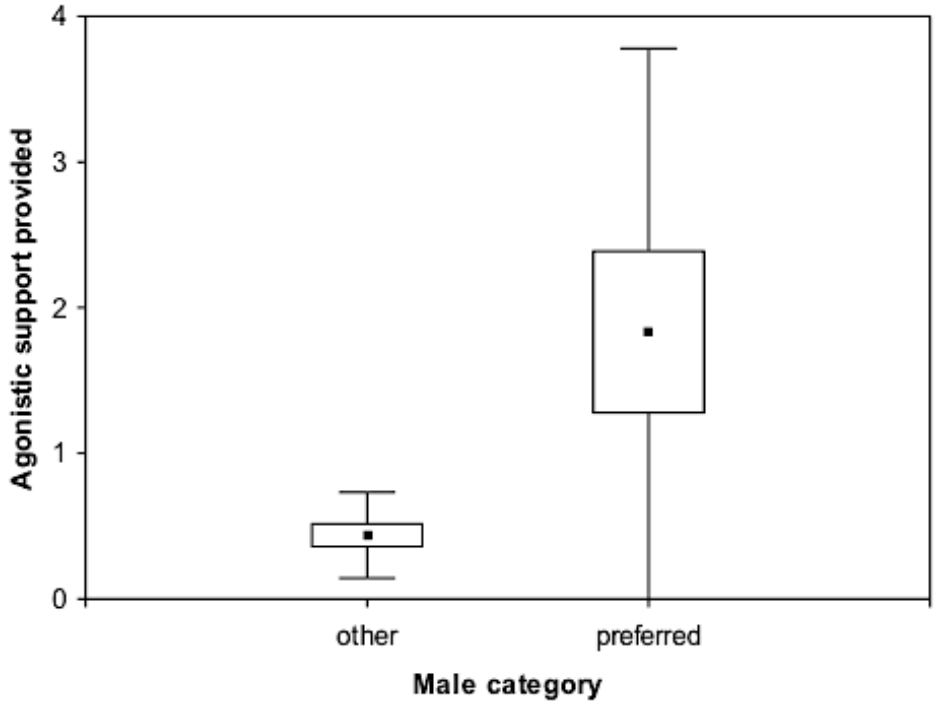

Figure 5.6: Agonistic support provided by preferred and the average other male to infant Assamese macaques at Phu Khieo Wildlife Sanctuary during the study period May 2011 to December 2012. Values are averages across immatures (mid-point), standard error (boxes) and standard deviation (whiskers).

Agonistic support for immatures

In line with the anti-harassment hypothesis adult males intervened on behalf of immatures in 50% of adult interventions. For 75% of immatures the preferred male provided more support than any other male. Immatures received support more than four times as often from their preferred male (mean ± SD = 1.8 ± 1.9) than from the average non-preferred male (mean ± SD = 0.4 ± 0.3; Wilcoxon signed rank test: V = 10.5; Z = -2.24, N = 12 (all focal infants), p = 0.02), a difference that is exacerbated if support by close runner-ups to the preferred male are included for six immatures (preferred and runner-ups: mean ± SD = 1.7 ± 1.4 vs. non-preferred males: mean ± SD = 0.3 ± 0.2, Fig. 5.6). Treating immature preference as a continuous variable, the rate of agonistic support received from a male was significantly predicted by the strength of the affiliative relationships between the immature and the male; the higher the CSI between the immature and the male the more often he supported the immature (R^2 full model = 0.35, full vs. null-model Chi^2 = 28.58, $p < 0.001$, estimate zCSI = 0.58 ± 0.002, $p < 0.001$).

Discussion

Based on our relatively small sample of immatures from a single group from birth through their infancy into their early juvenile period we conclude that Assamese macaque immatures and males form highly differentiated affiliative relationships. All but one immature had one or two relationships that was stronger than the average male-immature relationship in the group and was clearly set apart in strength and immature responsibility from relationships an immature had with other males. In the following we discuss whether such non-random patterns of affiliative relationships would evolve as male mating effort or male parental effort and which form of parental care may be provided to the immature.

Our predictions derived from the mating effort hypothesis about immature-male relationships were not met. Immatures, not males, were responsible for maintaining close spatial proximity. That immatures approach males more often than vice versa seems to contrast Assamese macaques from rhesus macaques where social interactions are initiated more often by males than immatures (Langos et al. 2013). The infant's greater initiative in relationship maintenance compared to the male may be mediated by the mother as a means to foster male-infant association (Widdig 2007). Both the strength of the relationship and partner choice for the preferred male were stable through the pre- and well into the post-weaning period. Following the rationale of the mating effort hypothesis, if males affiliated with immatures only to endear themselves to the mothers in the expectation of mating privileges, males should abandon immatures upon the conception of the subsequent offspring, as mating privileges will not lead to increased reproductive success from this point on. Even if males are unaware of the timing of conception as in Assamese macaques, they seem to be aware of whether females will conceive during a given mating season (Fürtbauer et al. 2011a). Relationships of immatures with their preferred partners were not affected by their mother conceiving again. Thus, the classical mating effort hypothesis alone cannot explain why immatures establish special relationships with certain males.

We have previously shown for the same group using spatial non-directional data that the time a male spends in proximity to an immature is predicted both by paternity and by the time the male spent with the mother around the time the immature was sired (Ostner et al. 2013). The results of the present study indicate that the male-immature association is established and maintained by the immature and its mother rather than the male. The main

association partners of immature Assamese macaques are often their fathers or males with high estimates of paternity certainty as in chacma baboons and rhesus macaques (Moscovice et al. 2009; Huchard et al. 2010; Moscovice et al. 2010; Langos et al. 2013) but not in yellow baboons (Nguyen et al. 2009). Therefore, any help given by males to immatures may be interpreted as paternal care (but see Alberts and Fitzpatrick 2012).

This study did not provide clear evidence in support of the anti-infanticide hypothesis of paternal care. The degree of differentiation in immature-male relationships did not follow gradual changes in the risk of infanticide with immature age but decreased when infanticide risk ceased following weaning. The absolute time the preferred male spent around the immature increased instead of decreased after six months of age, i.e. after the period of maximum infanticide risk, and then remained stable until the end of our study period. Paternity confusion may be so effective in Assamese macaques (Fürtbauer et al. 2011a) that infanticide from within the group is rare and possibly maladaptive. In this study the risk of infanticide by recent immigrants was zero because no adult males immigrated during the study period or the preceding six months. In rhesus macaques only genetic fathers, but not non-sires, affiliate more with immatures during infancy, i.e. when vulnerability is high, compared to later juvenility (Langos et al. 2013). Within the baboon clade chacma baboons are characterized by a higher incidence of infanticide compared to olive and yellow baboons (Palombit 2003) and consequently, male-mother-immature associations in olive and yellow baboons may provide females with protection against non-lethal aggression or promote future male-juvenile bonding rather than being explained by infanticide avoidance (Lemasson et al. 2008; Nguyen et al. 2009). Apart from variation in infanticide risk variation may exist in the effectiveness of protection by the mother. It has been argued that females may be effective protectors against male infanticide in species with smaller sexual dimorphism in body size and weaponry (Palombit 2003) which may apply to Assamese macaques. Thus, male protection from male infanticide either is so effective that it is rarely observed (van Schaik 2000b) or male protection is irrelevant either because immigration rates are low and paternity certainty within groups is distributed or because females are effective protectors.

Predictions derived from the anti-harassment hypothesis of paternal care were partly met. The time immatures spent in proximity to preferred males was relatively constant throughout the observation period and did not drop after weaning. The presence of the preferred male in proximity of an immature, however, did not reduce the probability of receiving aggression from any group member, because the preferred males themselves sometimes acted aggressively against the immatures. Even after excluding interactions between the immature and its preferred male we did not find support for reduced aggression received, submission given, or aggression given by immatures, which is in contrast to chimpanzee males that are less aggressive towards their genetic offspring compared to unrelated immatures (Lehmann et al. 2006). The benefit may come in form of protection against others: Yellow baboon infants in association with those males that spent most time with their mother receive less harassment from other females and generally utter fewer distress calls (Nguyen et al. 2009), but these males are often not their sires or likely sires. In our detailed situational analyses preferred males were present more often when the mother as alternative protector was absent and when other males as potential aggressors were present. The latter results mimic findings for chacma baboons (Huchard et al. 2013). Most crucially, in the present study preferred males acted as protectors, because they supported the immature four to five times more often than the average male as described for chacma and yellow baboons (Moscovice et al. 2009).

Follow-up work to our study should focus on the opportunity to support to conclusively test whether males preferentially support their own over others' immature offspring (Buchan et al. 2003) and long-term data to test whether the presence of fathers affect offspring fitness (Charpentier et al. 2008). It has been hypothesized that this true paternal care is more common in species exhibiting exaggerated sexual swellings as reliable indicators of ovulation probability where males have high paternity certainty selecting for differential investment in genetic offspring (Alberts and Fitzpatrick 2012). Like all macaques of the sinica group clade (Maestripieri 1998), Assamese macaques show frequent male-immature association and affiliation but lack reliable indicators of ovulation (Fürtbauer et al. 2010). Yet, in our study population genetic paternity is predictive of male-immature association also after weaning when mother-immature association is reduced (Ostner et al. 2013) and results of the present study indicate that this association is maintained by the immature, is risk sensitive, and benefits the immature in terms of enhanced agonistic support. Thus, true paternal care may evolve in the absence of good ovulation indicators. Barbary and rhesus macaque females provide better cues to ovulation than Assamese macaques but less precise than yellow and chacma baboons (Brauch et al. 2007; Dubuc et al. 2009; Pfefferle et al. 2011; Young et al. 2013): In rhesus macaques male-immature associations, nevertheless, are predicted by paternity (Langos et al. 2013) and are associated with faster growth (Langos et al. 2015). Unlike in yellow baboons, co-residence with the father did not affect the offspring's life time reproductive success in rhesus macaques though (Langos et al. 2015). In Barbary macaques male-immature association is not predicted by paternity (van Schaik and Paul 1996; Ménard et al. 2001) and may be selected for the benefits it confers to males in agonistic buffering and male bonding (Paul et al. 1996; Berghänel et al. 2011a) whereas short-term and long-term benefits for immatures remain unknown. The crucial data for comparative test of the hypothesis that true paternal care evolved together with precise indicators of ovulation are not yet available. We hope this study stimulates further research, as the results suggest a complex picture.

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Chapter 6:
General discussion

The aim of this study was to advance our understanding of the evolutionary processes that drive variation in development by addressing some fundamental unanswered questions regarding the evolution of play, male-immature bonds and prenatal maternal stress effects on offspring development. In this final chapter, I will discuss some further implications of my results that result from taking a broader perspective. In the first section I will suggest a novel life-history framework for the evolution of play which arises from the resource allocation trade-off between growth and play for motor skill acquisition (**Chapter 2**) and which may explain both within- and between-species variation in play rates. In the second section I will discuss some new perspectives on current evidence which results from my findings in **Chapters 3-5**. I will first discuss how different stressors and reproductive strategies may integrate into one generalized predictive adaptive response (PAR). Secondly I will discuss the moderating role of social bonds, and particularly male-immature bonds, within such a framework. Third I will suggest a new, integrative PAR which is based on a short-term external and a long-term internal PAR and which may provide a more convincing framework that can resolve several discrepancies in the theories and empirical evidence on PARs. Fourth I will discuss a new crucial question that emerges from the results in **Chapter 4**, namely how a PreGC-driven immediate compensatory growth during a period of reduced energy availability can be adaptive despite the widely acknowledged and empirically proven prediction that such conditions must result in adaptively reduced growth rates to reduce starvation risk (see also **Chapter 2**). Fifth I will investigate how prenatal stress effects on offspring behaviour relate to the results from **Chapters 3 and 4**.

6.1 On the evolution of play

Play is the hallmark of childhood in many species. Play is common in mammals and particularly primates and also occurs in other vertebrates like birds (Diamond et al. 2006) and some reptiles and fishes (Burghardt 2005), but it is largely absent in invertebrates with the octopus being a remarkable exception (Burghardt 2005; Kuba et al. 2006). This phylogenetic distribution led to the widely accepted hypothesis that play evolved only in “higher” species that can accumulate sufficient surplus resources ("surplus resource hypothesis", Spencer 1872; Burghardt 2005; Graham and Burghardt 2010; Auerbach et al. 2015). This hypothesis bases on the assumption that play can only use surplus resources after maintenance and growth due to the high ontogenetic priority of growth. This is, however, strongly contradicted by the results from **Chapter 2** which were recently confirmed in a study on mountain goats (Théoret-Gosselin et al. 2015).

Play rates can also differ within species due to strong sex differences, which is commonly referred to different adult sex roles since play seems to partially reflect adult behaviour in many species (Martin and Caro 1985; Byers and Walker 1995; Graham and Burghardt 2010). Sex-differences in play rates which correspond to adult sex roles and

competitive needs were shown for many species (Olioff and Stewart 1978; Sachs and Harris 1978; Biben 1986; Brown 1988; Lovejoy and Wallen 1988; Fairbanks 1993; Nash 1993; van Noordwijk et al. 1993; Watts and Pusey 1993; Maestripieri and Ross 2004; Förster and Cords 2005; McCormack et al. 2006; Paukner and Suomi 2008), and although skill acquisition was rarely quantified (Nunes et al. 2004b; Fisher et al. 2005), such patterns were commonly interpreted as strong support for the "motor skill"-hypothesis (Byers and Walker 1995; Paukner and Suomi 2008). In **Chapter 2**, I found strong sex differences in how wild Assamese macaques allocate available resources to growth or locomotor play for motor skill acquisition. Male immatures focused their investment on play and female immatures on growth, resulting in higher play rates, faster motor skill acquisition and lower growth rates in males compared to females. Following the common line of argument, I argued that these differences may correspond to adult reproductive strategies, with females gaining more from prolonged reproductive lifespans and males gaining more from increased flight/fight competence during their prime age.

Other authors have argued that increased motor skills through play may primarily benefit the individual in the short-term by increasing immature survival until reproduction (Martin and Caro 1985; Byers and Walker 1995; Fagen and Fagen 2004; Graham and Burghardt 2010). This view is supported by results on horses (*Equus caballus*), brown bears (*Ursus arctos*) and mountain goats (*Oreamnos americanus*) where immature survival was positively correlated to play rates even after controlling for body size effects (Fagen and Fagen 2004; Cameron et al. 2008; Fagen and Fagen 2009; Théoret-Gosselin et al. 2015). In mountain goats, the positive effect of play on survival was particularly strong during summer when mortality is primarily driven by predation, indicating that this effect was due to enhanced motor skills and escape performance (Théoret-Gosselin et al. 2015). However, the question of how such short-term benefits may relate to sex differences in play has been largely neglected so far. Based on the trade-off between growth and play presented in **Chapter 2** and confirmed by the recent study on mountain goats (Théoret-Gosselin et al. 2015), I will discuss and shortly test a life history-based model which could explain the observed sex differences in play rates from the perspective of such short-term benefits on immature survival. Subsequently, I will discuss whether and how this framework may be generalizable to other, and also long-term, benefits of play and whether and how it may also apply to differences between species, thus providing a general model for the evolution of play both between and within species.

Survival until first reproduction decreases with increasing age at sexual maturation (Roff 1980; Stearns 1992; Jones 2009; Dmitriew 2011). Survival until first reproduction therefore increases with faster maturation due to faster growth or lower adult body size, or with decreased predation risk due to enhanced motor skills acquired via play. The ideal strategy would therefore be to increase both growth rates and motor skills. However, I have shown in **Chapter 2** that increased play rates for motor skill acquisition are traded off against growth rates and age at sexual maturation, hence decreased predation risk through accelerated motor skill acquisition will inevitably increase age at first maturation. Additionally, the relationship between play rate and pace of motor skill acquisition in

Chapter 2 was linear only after square-root transformation of the response variable (age at skill acquisition), hence the effect of play on the age of motor skill acquisition decreases as play rate increases and may asymptotically fade out for very high rates of play (Rodrigue et al. 2005).

Following this, investments in play affect survival until reproduction in two coupled and opposing ways (Fig. 6.1). On the one hand, increasing rates of play enhance motor skills in the described asymptotic way, and a certain decrease in predation rate via motor skill enhancement may accumulate with increasing age at maturation. On the other hand, a certain increase in play rate results in a fixed increase in age at maturation and thus a decrease in survival until reproduction. The benefits of play may therefore increase with increasing age at maturation but fade asymptotically out as play rates increase and may therefore be overcompensated from a certain play rate onwards by the continuously increasing costs of play in terms of increased age at maturation. Sex differences in resource allocation to play may thus reflect different optimal settings of this trade-off depending on the age at maturation (Fig. 6.1).

In mathematical terms, survival until maturation (**S**, ranging from 0-1) is a function of predation rate (**p**, in proportion per year) and age at maturation (**m**, in years) following

$$\textbf{(1)}\ \boldsymbol{S = (1 - p)^{m}},$$

and the costs of play arise from

$$\textbf{(2)}\ \boldsymbol{m = m_b + m_r * r}$$

with **r** being play rate in proportion of time, $\mathbf{m_b}$ being age at maturation without play and $\mathbf{m_r}$ being the increase in age at maturation per proportion of play. The benefits of play on survival until maturation result from an altered predation rate **p** by

$$\textbf{(3)}\ \boldsymbol{\Delta p = ln(r) * i * p}$$

with **ln(r)** being motor skill level as a function of **r** and **i** being the influence of **ln(r)** on predation rate **p**. Integrating **(2)** and **(3)** into **(1)** results in

$$\textbf{(4)}\ \boldsymbol{S = (1 - p + \ln(r) * i * p)^{(m_b + m_r * r)}}$$

This rather simple model provides some interesting results (Fig. 6.2). First, there is an optimal play rate (r_{opt}) for each age at maturation (m), with r_{opt} = 0 for low m and increasing r_{opt} as m increases. Second, the impact of m on r_{opt} increases with increasing impact of motor skill level on predation rate (i). Consequently, the minimal m for which r_{opt} is higher than zero increases with decreasing i. Third, r_{opt} is largely independent of the predation rate (Fig. 6.2g-m). However, predation rates limit the maximal m since high m are highly maladaptive under high predation rates (Fig. 6.2a-f). Notably, the predictions of the model do not exactly

match the sex differences in play rates and age at maturation found in **Chapter 2** because each setting that would correctly predict female play rates results in an optimal male play rate that is higher than the observed. Play time in **Chapter 2** was measured as proportion of activity time while play rate in the model reflects the total amount of play over time which can also be driven by the length of the play period, which in theory could reduce the comparability of the measures. However, both male and female Assamese macaques seem to cease play around the age of 4 years (personal observation) hence this problem may not arise in this case, but further investigation would be needed. Additionally, as I will discuss in more detail below, male but not female play rates increased with increasing food availability in **Chapter 2**, suggesting that realized play rates are constrained by energy intake in males but not in females.

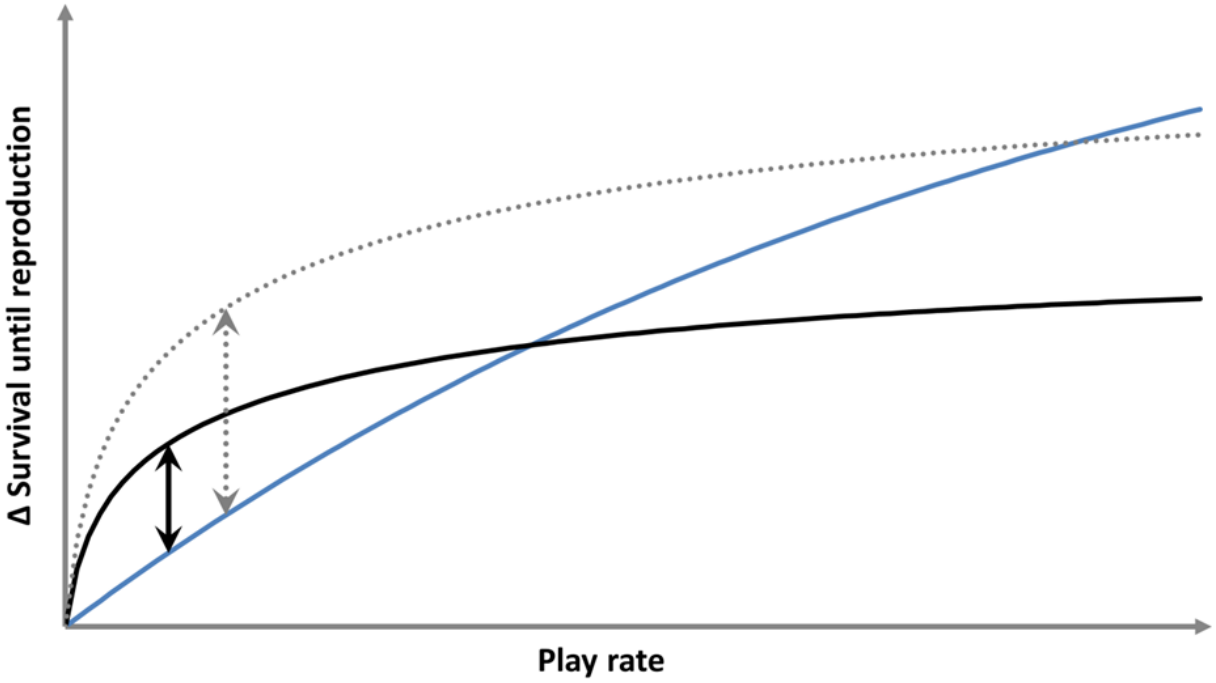

Figure 6.1: Schematic illustration of the model, with optimal play rates resulting from the costs (blue) and the benefits (black and grey) of play on survival until reproduction. The model bases on the results from **Chapter 2** which show that increasing play rates linearly reduce growth and increase age at maturation and non-linearly accelerate motor skill acquisition, and on the assumptions that the negative effect of a constant predation rate on survival until reproduction accumulates with increasing age at maturation (equation 1) and that increasing motor skill levels reduce predation rate. Hence on the one hand, the costs of predation on survival until reproduction increase linearly with increasing play rates due to their effect on age at maturation (blue line). On the other hand, the benefits of play on survival until reproduction increase asymptotically with increasing play rates (black line) and accumulate and thus increase linearly with age at maturation (dotted grey line). This will result in an optimal play rate with a maximal net benefit (black arrow) which increases with increasing age at maturation (dotted grey arrow).

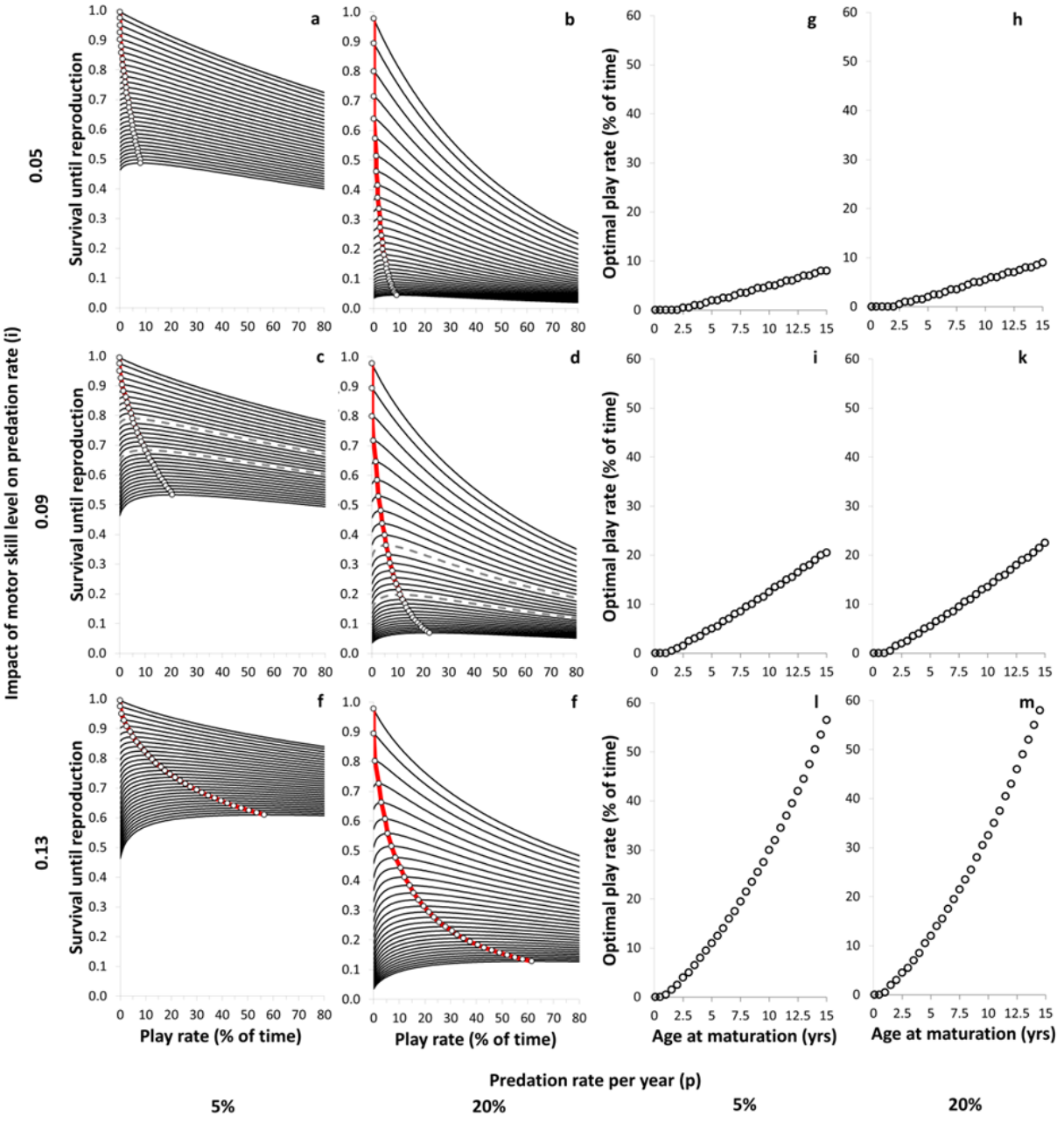

Figure 6.2: Results of the model. Shown are the relationships between play rates, survival until reproduction and age at maturation under different values for predation rate and impact of motor skill level on predation rate. The impact of play rate on age at maturation is assumed to be constant. **(a-f)** Black lines represent different ages at maturation, increasing from 0 (top line) to 15 years (bottom line) in 0.5-year-intervalls. Points and red lines represent the respective optimal play rates. Optimal play rates increase with increasing age at maturation, and the slope of this relationship increases with increasing impact of motor skill level on predation rate while predation rate per se has no influence. The grey, dashed lines reflect the results in **Chapter 2** (top line: females, bottom line: males). **(g-m)** Bivariate plots of the relationship between age at maturation and optimal play rate which emphasize the marginal impact of predation rate on this relationship and the threshold in age at maturation below which the optimal play rate is zero. This threshold decreases as the impact of motor skill level on predation rate increases.

This basic model supports the hypothesis that sex differences in play can be simply explained by short-term effects on survival until reproduction. It shows that within a species, the optimal play rate is determined by the trade-off between the costs (in terms of growth reduction) and benefits (in terms of motor skill acquisition) and only depends on the age at maturation. Remarkably, the optimal play rate in this model is largely independent from the predation rate and thus also independent from potential size-, age- or play-dependent variation in predation rate (Childs 1986; Claessen et al. 2002; Bowen 2009; Graham and Burghardt 2010). A first look at empirical evidence seems to support the results of the model. Rates of play are higher in the sex with larger adult body size in sexually dimorphic species (Olioff and Stewart 1978; Sachs and Harris 1978; Biben 1986; Brown 1988; Lovejoy and Wallen 1988; Fairbanks 1993; Nash 1993; van Noordwijk et al. 1993; Watts and Pusey 1993; Maestripieri and Ross 2004; Nunes et al. 2004b; Förster and Cords 2005; McCormack et al. 2006; Paukner and Suomi 2008) while there are no sex differences in species with no or negligible adult sexual dimorphism (de Oliveira et al. 2003; Cameron et al. 2008). In support of my hypothesis, female spotted hyenas (*Crocuta crocuta*) play more, are larger and also attain sexual maturation later than males (Frank 1986; Pedersen et al. 1990; Frank et al. 1995; Swanson et al. 2013). The only exception seems to be the Gelada baboon (*Theropithecus gelada*) which shows pronounced sexual dimorphism but no sex differences in play rates (Mancini and Palagi 2009).

Different adult body sizes can however also be achieved by different growth rates, and particularly sex-specific growth spurts, hence large adult body size dimorphism may not necessarily be reflected in large differences in age at maturity (e.g. Sanna et al. 2015). Unfortunately there is only a handful of species where both sex-specific play rates and growth pattern are reported, hence further investigation is needed. Most of these relationships between play rate and adult sexual dimorphism are also consistent with long-term benefits of play since sexual dimorphism reflects adult sex differences in the amount of intrasexual competition and thus adult sex roles. However, my model also applies to long-term benefits since both the equations for the costs and benefits of play would primarily change in terminology but only marginally in structure. The main modification would be that differences in the benefits of play do not relate to different ages at maturation but different needs as adults. Both sexes may strongly differ in how much a certain increase in skill level benefits adult fitness, e.g. due to differences in need for hunting skills or levels of intrasexual competition. Hence despite this model showing that short-term benefits would be sufficient to explain sex-specific play rates, the effects of long-term benefits would be in the same direction and can be easily integrated into the model. This may generalize the shown pattern and thus stabilize its evolution, in particular if both short- and long-term benefits coincide. However, if e.g. females mature earlier but also benefit more from motor skills during adulthood than males (e.g. via hunting skills), then short-and long-term effects will work in opposite directions and may result in equal optimal play rates for both sexes. Hence a model that integrates both short- and long-term benefits may lead to more complex and more realistic results.

In a next step, I will discuss whether the ratio between short-term costs and benefits of play and its relation to age at maturity as outlined in the model also explains differences in play rates between species, and particularly the general phylogenetic distribution of the occurrence and absence of play. Compared to intraspecific variation, interspecific variation of age at maturation is primarily driven by mortality, and particularly predation, rate (Harvey and Zammuto 1985; Harvey and Purvis 1999; Ghalambor and Martin 2001; Dmitriew 2011; Jones 2011; Healy et al. 2014; Grimm 2015; Walsh et al. 2015). This difference does not, however, affect the applicability of the model to interspecific variation because predation, or mortality, rate only marginally affects optimal play rates. Indeed, the model makes clear predictions on which species should or should not play based on the interaction between age at maturation and the potential influence of enhanced motor skills on predation rate (Fig. 6.2). First, it predicts that large animals with a high age at maturation should play more than small animals, and very small animals below a threshold age at maturation should not play at all. This threshold in age at maturation is largely determined by the influence of enhanced motor skills on predation rate: in the model, this threshold is about a half year in the case of a high impact and 2 years in the case of a low impact (Fig. 6.2) but can also increase up to 12 years or more if the impact is very low ($i < 0.01$) and drop to 0 if the impact is very high ($i > 0.21$).

Empirical evidence seems to support our prediction. Across animals, play occurs primarily in mammals and birds and occasionally in other vertebrates but is largely absent in invertebrates which are commonly also characterized by low life expectancies (Burghardt 2005; Graham and Burghardt 2010). Within mammals, play behaviour is common in large, long-lived animals like primates, cetaceans, carnivores, elephants and ungulates and absent in small, short-lived animals like shrews (Guinet 1991; Burghardt 2005; Graham and Burghardt 2010). However, play is also frequent in rodents, ranging from small, short-lived species like voles, rats or mice to medium-sized, longer-lived species like squirrels (Pellis and Iwaniuk 2000; Iwaniuk et al. 2001; Nunes et al. 2004a; Thorington and Ferrell 2006; Graham and Burghardt 2010). It could be argued that the impact of motor skills on predation rate may be particularly high in these species, which is supported by their morphological (e.g. gerbils, hopping mouse) and lifestyle characteristics (e.g. living and staying close to burrows and preparing and scenting escape paths) which strongly focus on flight response. This argument may be supported by the typical non-playing mammals like hedgehogs, pangolins and moles which are characterized by rather motor skill-independent predation avoidance due to armour or strict burrow-living (Graham and Burghardt 2010). Despite sparse information, current evidence suggests that play may also be frequent in bats, which are of low body size but relatively long-lived (Graham and Burghardt 2010).

From a more general perspective, rates and complexity of play are rather independent of phylogenetic associations, social complexity or relative brain and neocortex size but positively related to age at first reproduction in rodents, primates and marsupials even after controlling for body size (Pellis and Iwaniuk 1999, 2000; Iwaniuk et al. 2001; Graham and Burghardt 2010). A similar effect of age at first reproduction was also found across birds (Diamond and Bond 2003; Graham and Burghardt 2010), and reports of play behaviour in reptiles are restricted to long-lived species like turtles, crocodiles and monitor lizards (Graham and Burghardt 2010).

These results are in line with my predictions and the results of the model, suggesting that the trade-off between the play-driven and costly increase in age at maturation and the play-driven increase in fitness due to skill acquisition (**Chapter 2**) explains much of the variance in the occurrence and rate of play both within and between species.

One puzzling feature of the model is that if the benefits of play are sufficiently high, it allows for very high optimal play rates which were rarely observed in reality. This indicates that play rates are constrained by additional factors. Trivially, play rates may be constrained by time allocation to other activities like feeding and resting. More importantly, as was shown in **Chapter 2** and several other studies, play rates are also constrained by food availability (Müller-Schwarze et al. 1982; Martin and Caro 1985; Espinosa et al. 1992; Sharpe et al. 2002; Nunes et al. 2004a; Cameron et al. 2008). In **Chapter 2**, the proportion of time spent in locomotor play was positively correlated to food availability in males but unaffected by food availability in females, with males and females playing on average the same amount at low food availability. This may suggest that females achieve their optimal play rates even under low food availability while males require optimal food availability to achieve their optimum. Interestingly, males seem to play at very high rates during periods of high food availability. Thus male immatures may aim to catch up their optimal play rates on average by compensating for the constrained play rates during periods of low food availability.

In **Chapter 3**, I show that prenatal maternal stress results in accelerated offspring growth and probably faster maturation. From the perspective of the model, such accelerated maturation should be accompanied by reduced optimal play rates. Additionally, prenatal maternal stress has a negative impact on motor skill acquisition (**Chapter 3**), which ultimately reduces the benefits of play and should lead to an additional decrease in the optimal play rate. Yet I found no correlation between the proportion of time spent in vigorous social play and prenatal maternal stress (**Chapter 3**). If males did not achieve their optimal growth rates under natural conditions, then a reduced optimal play rate in reaction to prenatal maternal stress would not translate into reduced realized male play rates. Indeed, within females only, the proportion of time spent in vigorous social play is negatively correlated to PreGC ($r = -0.735$, $p = 0.024$, $N = 9$). In further support of the model, prenatal maternal stress reduces play rates also in rats (Ward and Stehm 1991; Takahashi et al. 1992; Morley-Fletcher et al. 2003).

In summary, the trade-off between growth and play for skill acquisition and its consequences for life history (**Chapter 2**) may provide a new perspective on the evolution of play rates both within and between species. Despite the model being developed to explain sex-specific play rates from the short-term benefits of play-related motor skill acquisition, it is also applicable to long-term benefits of play and also to other potentially play-related skills like social skills. Indeed, the model should apply to any kind of size-independent fitness trait as long as investment in this trait is at the expense of growth and the relationship between investment and fitness benefits is asymptotic (e.g. Naguib and Nemitz 2007). The model may also explain the widespread decrease in play rates over age, and particularly the rare occurrence of adult play (Fagen 1977; Graham and Burghardt 2010). More sophisticated analyses are needed to draw conclusion since age-dependent patterns of play can be highly

complex (Sachs and Harris 1978) and the prevalence of play during early childhood may also be driven by increased neural plasticity during this age period (Byers and Walker 1995; Khazipov et al. 2004; Graham and Burghardt 2010; McKenzie et al. 2014). Future models should integrate the trade-off between time allocation to play and other activities which will probably reduce optimal play rates. In the case of Assamese macaques I have shown in **Chapter 2** that only resting time but not feeding time was traded in for play time, hence the costs that result from time allocation to play may be rather small even within this range of relatively high play rates. Most importantly, a more sophisticated model must integrate the constraints on the optimal play rate that result from food availability and thus starvation risk.

6.2 On the evolution and mechanism of prenatal maternal stress effects

In **Chapter 3 and 4**, I explored the causes and consequences of prenatal maternal stress. I showed that in my study population, the prenatal maternal faecal glucocorticoid metabolite level (PreGC) was elevated in reaction to reduced prenatal food availability and related to alterations in several postnatal phenotype aspects of the offspring. PreGC was associated with reduced immune function but also accelerated growth and increased body size at 16-18 months of age in the offspring. I have argued that this effect on offspring growth must be due to an internal, somatic state-based predictive adaptive response (PAR) because Assamese macaques evolved and live in a highly unpredictable environment where external, environmental forecast-based PARs would be maladaptive. I further proposed a novel framework which explains the entire range of prenatal maternal stress effects on offspring growth and provided evidence from my study population and across mammals which supports this framework. In detail, my results suggest that prenatal maternal stress is associated with both reduced maternal investment and elevated PreGC-level. Consequently, the extrinsic offspring growth rate was reduced during gestation and lactation but the intrinsic offspring growth rate was accelerated by early-gestational PreGC, resulting in indifferent growth rates during gestation and lactation and accelerated growth after lactation. Late-gestational PreGC did not, however, affect the intrinsic offspring growth rates, which resulted in reduced growth rates during gestation and lactation due to reduced maternal investment, and indifferent growth rates after lactation. In the next sections I will discuss some further implications of these results.

6.2.1 The integration of various stressors into one adaptive response

Physiological stress was correlated to decreased food availability in my study population (**Chapter 3**) and other studies (Chapman et al. 2007; Behie et al. 2010; Foerster and Monfort 2010), but in general it is a rather unselective response which can also be caused by other stressors like population density, social stress, parasite load, weather conditions or predation risk (Chapman et al. 2007; Behie et al. 2010; Boonstra 2013; Dantzer et al. 2013; Sheriff and Love 2013; Del Giudice 2014a; Young et al. 2014). This variety may

complicate interpretations of prenatal maternal stress effects. If prenatal stress is related to reduced maternal and consequently offspring energy intake as shown in **Chapter 3 and 4**, a short-term adaptive response will be reflected in reduced growth rates to avoid starvation (Dmitriew 2011), hence an accelerated growth as found in **Chapter 3** must be due to a long-term (predictive) adaptive response. However, other stressors would lead to an opposing prediction. If prenatal stress is related to increased predation risk, a short-term adaptive response will be reflected in a rather accelerated growth to speed up maturation (Dmitriew 2011). Since prenatal glucocorticoids inform the offspring about the stress level but not about the kind of stressor (but see Dias and Ressler 2014), such contradictory stressor-dependent adaptive responses would make prenatal stress effects rather maladaptive.

Thus to be adaptive, PreGC-effects must be general and adaptive to whatever the actual stressors might have been. Under natural conditions, one common feature of all potential stressors is reduced energy intake (including reduced ranging and foraging behaviour) and/or increased energy expenditure and thus potentially reduced maternal physical condition (Maniam and Morris 2012). Reduced prenatal maternal energy intake and consequently perinatal maternal physical condition were frequently associated with elevated PreGC and various prenatal stressors (Kinsley and Svare 1986a; Ward and Wainwright 1988; Brabham et al. 2000; Laurien-Kehnen and Trillmich 2004; Weingrill et al. 2004; Wingfield 2005; Ford et al. 2007; Baker et al. 2008; Rooke et al. 2010; Maniam and Morris 2012; Tao et al. 2012; Mack et al. 2014; Wattez et al. 2014). Following this, PreGC may always relate to reduced maternal investment and developmental constraints, and particularly internal PARs may always be adaptive, no matter what the actual stressor might be.

However, this line of argument may be limited to species where prenatal stress effects reflect a reproductive strategy where females reduce their actual maternal investment in favour of future reproduction under adverse conditions. Other species may rather shift their resource allocation from future to current reproduction, in particular if future reproduction is rather uncertain (Stearns 1992). In extreme cases, females will invest their entire reproductive effort into one single reproductive event (semelparity). Yet another species may follow an intermediate strategy. Such intermediate species are not, or to a lesser extent, expected to reduce their current maternal investment in reaction to adverse conditions and thus also not to induce PreGC-effects in their offspring, and may thus provide interesting insight into the evolution of prenatal stress effects. Elk (*Cervus canadensis*) reduce foraging and birth rates in reaction to increased wolf density, indicating that they do not (or less) reduce investment in current offspring in favour of future reproduction (Boonstra 2013). Following the line of argument in **Chapter 4**, it would be maladaptive to induce prenatal stress effects in the offspring under such circumstances (i.e. unaffected maternal investment). Indeed, neither predation risk nor birth rate correlates to faecal glucocorticoid metabolite levels in elks, suggesting that elk mothers conceal the actual environmental stress as well as their physical condition from the foetus (Boonstra 2013; Clinchy et al. 2013). Similar effects were also shown in birds like gray-headed juncos (*Junco hyemalis dorsalis*)(Clinchy et al. 2013).

A particularly revealing patterns was found in tropical stonechats (*Saxicola torquata axillaris*) and song sparrows (*Melospiza melodia*)(Clinchy et al. 2013). In both species, predation risk is negatively correlated to birth rate, but glucocorticoid levels are only elevated in parental males but not in parental females (Clinchy et al. 2013). Notably, in song sparrows, this effect is not caused by differences in glucocorticoid secretion but by elevated levels of corticosteroid-binding globulin in females which effectively reduces the level of free glucocorticoids (Clinchy et al. 2011; Clinchy et al. 2013). Interestingly, such pattern can also be found within individuals. Snowshoe hares (*Lepus americanus*), which have a strongly limited breeding and growth season, invest much less in the first compared to the second litter within a year, both pre- and postnatal (Sheriff et al. 2009). In line with my results in **Chapter 4**, they also have much higher prenatal faecal glucocorticoid metabolite concentrations during the first compared to the second gestation which may adaptively recalibrate offspring development (Sheriff et al. 2009). Importantly, concealing the presence of an actual environmental stressor from the offspring would be rather maladaptive if PreGC aims to inform the offspring about the precise maternal environment in order to prepare it for such an environment in the future. Consequently, such a strategy is only adaptive if PreGC relates to resource availability and maternal investment strategies. However, song sparrow hatching success was reduced under increased predation risk independent from actual nest predation, which indicates that mothers may still reduce maternal investment to some degree.

In summary these results suggest that PreGC-effects do not aim to inform the offspring about the actual maternal physical condition, or even the current external environment, but about the anticipated maternal investment to generate an adaptive response in the offspring, which supports my interpretation of the results in **Chapter 4**. Whether reduced maternal nutrition and condition results in reduced maternal investment in the current offspring or not may depend on other aspects like the general or current reproductive strategy of the mother, and mothers seem to be able to actively adjust their PreGC-levels to their maternal investment. However, I have shown that in my study population, PreGC relates to prenatal food availability (**Chapter 3**) while postnatal reduction in the extrinsic offspring growth rate during the lactation period is driven by pre- but also postnatal food availability (**Chapter 4**). Thus PreGC does only partially and thus approximately predict maternal investment based on the available prenatal information.

6.2.2 The moderating role of social bonds

Social bonds may provide further intriguing insight into the potential of maternal adjustment of investment and PreGC. Differentiated and stable social bonds were shown for several gregarious mammals and birds (Wilkinson 1985; Connor et al. 2001; de Villiers et al. 2003; Wasilewski 2003; Emery et al. 2007; Cameron et al. 2009; Mitani 2009; Berghänel et al. 2011a; Kappeler and Fichtel 2015). It was shown that individual glucocorticoid levels decrease with the strength and stability of social bonds (Sachser et al. 1998; Engh et al. 2006a; Charuvastra and Cloitre 2008; Young et al. 2014) and that this effect is particularly strong in

pregnant and cycling females (Crockford et al. 2008). Prima facie, this pattern seems to be rather maladaptive in the context of prenatal stress effects because it may blur the informational value of glucocorticoids about the current maternal condition or anticipated investment. However, differentiated and stable social bonds increase female birth rate, reproductive success and longevity and offspring survival (Silk et al. 2003; Silk 2007; Cameron et al. 2009; Palombit 2009; Frère et al. 2010; Silk et al. 2010; Micheletta et al. 2012; Huchard et al. 2013; Archie et al. 2014; Lehmann et al. 2015; Nuñez et al. 2015; for similar effects in rodents see Bauer et al. 2015) and may thus increase the benefits of maternal investment in current reproduction and reduce the costs of current investment in terms of reduced future reproduction. Notably, it was shown that social bonds do not per se reduce glucocorticoid levels but lessen the effects of other social and environmental stressors and have no effect in the absence of such immediately impacting stressors (Wittig et al. 2008; Young et al. 2014) which is in line with the "social buffering"-hypothesis (Kikusui et al. 2006; Hennessy et al. 2015). Consequently, the lack of stable social bonds cannot be viewed as a stressor in itself but stable social bonds may attenuate the effects of other stressors on the degree of current maternal investment (Lycett et al. 1998; Hill et al. 2000; Johnson 2003; Engh et al. 2006a, b; Leigh and Bernstein 2006; Silk et al. 2006; Wittig et al. 2008).

Previous results on my study group suggest that PreGC-levels are particularly reduced by mother-male bonds (Fürtbauer et al. 2014) which predict future male-offspring bonds (Ostner et al. 2013) that last far beyond infancy (**Chapter 5**), suggesting that such male-immature bonds provide benefits to the offspring that are taken into account by the mother. I have shown in **Chapter 5** that these differentiated male-immature relationships provide male support to the offspring in agonistic encounters and may particularly compensate for temporary non-availability of the mother in dicey situations. Previous studies suggest that such male support increases food access and energy intake of the offspring and thus offspring growth and pace of maturation (Huchard et al. 2013; Langos et al. 2015). However, I could not detect any relationship between offspring growth rate and male support or the strength of male-immature bond, even after controlling for the confounding variables found in **Chapter 2-4** (i.e. general food availability, rates of locomotor play and PreGC). It might be that immatures try to be close to their preferred males if they are otherwise excluded from feeding, which may balance differences in food access and consequently differences in growth rates, but my dataset did not allow testing for that.

Additionally it was shown that third-party interventions in favour of the looser of a conflict can reverse the outcome of future purely dyadic encounters (Berghänel et al. 2011b) hence the influence of male support may transcend far beyond the actual support situation. Indeed agonistic support may also prevent maladaptive, size-based winner-loser effects in the offspring (Hsu and Wolf 1999; Dugatkin and Earley 2003; Dugatkin and Druen 2004; Dugatkin and Earley 2004; Hemelrijk et al. 2008; Hsu et al. 2009). Male-immature bonds may also increase offspring survival by reduced infanticide and predation risk (Fernandez-Duque et al. 2009; Palombit 2009). Hence mothers may benefit from increased investment in current offspring if they can rely on male care for their offspring, even if this may not translate in increased offspring growth, and should adjust their PreGC-level accordingly.

In summary, stable female-female and female-male bonds play a special role in moderating PreGC-effects due to their predictive long-term benefits, and their supposed effects on current maternal investment may be viewed as a maternal PAR. However, whether and how stable social bonds will indeed affect maternal investment is open to future research. Alternatively, our results suggest that PreGC-effects do not primarily aim to reduce the effects of decreased maternal investment but ultimately aim to reduce the effect of the associated adverse somatic state and reduced life expectancy of the offspring on its lifetime reproductive success (Nettle et al. 2013; Sheriff and Love 2013; Hanson and Gluckman 2014; Nettle and Bateson 2015). Hence if strong and stable social bonds benefit the survival and somatic state of the offspring and thus its life expectancy by all means, then a reduced PreGC-level in reaction to such bonds may be adaptive even if maternal investment is not altered by social bonds.

6.2.3 Fortune-telling and evolution: How to bring PARs down to earth

External PARs base on the assumption that PreGC-exposure informs the foetus about his adult environment and enables him to adaptively recalibrate his adult phenotype (Hanson and Gluckman 2014). External PARs were therefore criticized for their rather "crystal ball gazing" character particularly in long-lived species and/or stochastic environments where prenatal and adult environments are probably highly uncorrelated (Wells 2007b; Kuzawa and Quinn 2009; Nettle et al. 2013; Del Giudice 2014b; Nettle et al. 2014).

I have shown in **Chapter 3 and 4** that prenatal maternal stress effects on offspring growth suggest a strong PAR in wild Assamese macaques despite them being a long-lived species that evolved and live in a highly unpredictable environment. I have argued that these circumstances exclude an external PAR and support the alternative, internal PAR-hypothesis. Internal PARs rely on the rather inevitable long-term mortality costs of developmental constraints (Nettle et al. 2013), and it was argued that they are in turn not predictive but rather immediate adaptive responses (Hanson and Gluckman 2014). Indeed, proponents of the internal PAR-hypothesis have also argued that "*it is not particularly useful to conceptualize [developmental constraints] as being a cue or providing information*" and that the relationship of developmental constraints to future somatic states "*is that of cause to consequence, and it would be an unusual usage of the term information to describe events as conveying information about their consequences*" (Nettle and Bateson 2015). More importantly, internal PARs rely on the occurrence of developmental constraints in the first place, which is not only rather maladaptive but also does not explain the occurrence of long-term consequences of early adversity on adult phenotype without detectable developmental constraints on immature growth.

Irrespective of this debate, my results do not only exclude an external PAR but are also not entirely consistent with an internal PAR. PreGC was related to prenatal maternal food availability and maternal pre- and postnatal condition, but postnatal offspring development was consistently triggered by PreGC instead of pre- or postnatal food

availability or PostGC (**Chapter 3 and 4**). Hence growth acceleration was not driven by developmental constraints as proposed by the internal PAR-hypothesis but by elevated PreGC-levels as proposed by the external PAR-hypothesis. In the following I will argue that this pattern may indicate a rather integrative PAR which consists of both a short-term external and a long-term internal PAR.

In **Chapter 4** I demonstrated a strong relationship between PreGC and maternal condition and investment during both gestation and lactation which also confirms previous results (Patin et al. 2002; Tygesen et al. 2008; Sheriff and Love 2013; Tao and Dahl 2013; Wattez et al. 2014; St-Cyr and McGowan 2015). This makes PreGC a good predictor of the early, maternally provided environment of the offspring, thus opening a door for short-term external PARs even in highly unpredictable environments and long-lived species (Kuzawa and Quinn 2009; Hayward et al. 2013). The reliability of such a PreGC-cue could be very high since mothers would be principally able to increase the match by readjustment of PreGC or maternal investment (but see above), and would be under strong positive natural selection since increased reliability would increase both the mother´s and offspring´s fitness. Indeed, section 6.2.1 lists several cases in birds and mammals which strongly suggest that mothers actively adjust their glucocorticoid levels or the impact of their glucocorticoid levels to their expected maternal investment e.g. via increased corticosteroid-binding globulin secretion.

Such a short-term external PAR seems to be more adaptive than a purely internal, somatic-state based mechanism as it enables forecast-derived adaptive recalibration of the offspring´s developmental settings before it suffers unnecessarily damaging somatic states or even stunted growth from the developmental constraints. Additionally it enables the offspring to recalibrate its developmental trajectory during earliest life and thus during a period when such recalibration may be most efficient and less costly (see below). However, such a short-term external PAR is not sufficient to explain the results from **Chapter 3 and 4**. Short-term PAR could merely aim at buffered (i.e. unaffected) growth rates to avoid the detrimental effects of reduced growth and to enhance short-term survival. Accelerated growth and reproduction in expectation of reduced energy intake are only adaptive in anticipation of long-term reduced life expectancy, which in our study must be related to long-term somatic state damage due to an internal PAR since external PARs can be excluded (**Chapter 3**). The most adaptive strategy seems therefore to be a concert of short-term external and long-term internal PAR, which retains the advantages but at the same time avoids the disadvantages of both. Elevated PreGC could be used as a highly reliable cue to predict adverse early “environmental” conditions (due to reduced pre- and postnatal maternal investment, **Chapter 4**) which will foreseeably result in developmental constraints, adverse short- and long-term somatic state and reduced life expectancy. PreGC then recalibrates offspring phenotype and development due to an anticipated internal PAR before the (uncalibrated) detrimental effects on offspring somatic state take place (**Chapter 3, 4**).

6.2.4 PARs as a deus ex machina: How to bring mystery back to PAR

"That no god intervenes, unless a knot shows
up that is worthy of such an untangler"
(Horace 19BC, Ars poetica)

My results on prenatal maternal stress effects (**Chapter 3 and 4**) may provide some solutions for some crucial questions but also raise a new question: Which resource pool enables foetuses and infants to react to reduced energy intake with immediate compensatory growth? Sequential compensatory growth in reaction to periods of constrained growth was shown for many species but is usually reflected in above-average growth rates during a period of high energy intake that follows a period of food and consequently growth restriction (Wilson and Osbourn 1960; Boersma and Wit 1997; Roseboom et al. 2000; Ali et al. 2003; Dmitriew 2011). Consonant with that, I have shown in **Chapter 2** that Assamese macaques reduce their growth rate in immediate reaction to reduced food availability. In contrast, I have shown in **Chapter 4** that reduced maternal investment due to increased prenatal maternal stress analogously results in reduced extrinsic offspring growth rate but that this effect is immediately compensated by a PreGC-driven increase in intrinsic growth rate as long as PreGC applies during the first half of gestation. Reduced offspring growth rate can be extremely costly since lifetime reproductive success is primarily predicted by the survival until reproductive age (Jones 2009; Kuzawa and Quinn 2009), which in turn strongly depends on offspring body size at weaning (Thompson et al. 2011). Hence an immediate compensatory growth may be highly beneficial but is usually not realized in direct reaction to acute food restriction (Dmitriew 2011; **Chapter 2**). This indicates that PreGC-effects rely on a mechanism that is restricted to early gestation and not functional or feasible during later life, which may represent the ultimate adaptive benefit of predictive PreGC-effects (Hanson and Gluckman 2014).

Growth rates are immediately reduced in reaction to reduced energy intake across species (Dmitriew 2011) including wild Assamese macaques (**Chapter 2**). While this strategy adaptively reduces starvation risk, it may come at the costs of increased age at maturation and thus reduced survival until reproduction as well as delayed onset of reproduction (Dmitriew 2011). Hence if both of these fitness attributes are under time constraints due to increased immature mortality or decreased overall life expectancy, such periods of growth restriction may be compensated by periods of accelerated growth during subsequent periods of ample food availability even if this comes with time allocation costs on the quality of tissue growth (Metcalfe and Monaghan 2001; Dmitriew 2011).

At a first glance, an immediate compensatory growth during periods of energy restriction as found in **Chapter 4** may thus result in a rather maladaptive increase of starvation risk. It may be argued that PreGC-driven internal PAR take the entire life history of the individual into account (Nettle et al. 2013; Del Giudice 2014a; Del Giudice 2014b; Nettle and Bateson 2015), thus cancelling out the growth-decelerating effects of increased

starvation risk by the growth-accelerating effects of increased time constraints on reproduction due to an overall reduced life expectancy (Dmitriew 2011). However, this raises the question of why such a mechanism does not apply to immediate reactions to developmental constraints (Nettle et al. 2013; Nettle and Bateson 2015). Hence the only coherent explanation that does not rely on a "deus ex machina" may be that PreGC-driven intrinsic growth acceleration does not substantially increase starvation risk but bases on an adaptive mobilization of alternative recourses that may be only feasible during (early) gestation. Two possible, not mutually exclusive mechanisms are conceivable: an increase in metabolic efficiency and total energy expenditure, and/or a shift in resource allocation from other ontogenetic processes, or even maintenance, towards growth.

Increased metabolic efficiency can be driven by changes in hormonal systems (Mehls et al. 1993; Khani and Tayek 2001; MacLean et al. 2004; Voutilainen and Tenhola 2012; Montanholi et al. 2013). Indeed, the PAR-hypotheses originate from human studies which have shown that prenatal maternal stress and low birth weight are associated with metabolic syndrome later in life, including obesity, diabetes and cardiometabolic disease risk, which in turn are associated with increased insulin resistance which may promote increased metabolic "efficiency" and accelerated growth (Soto et al. 2003; Wells 2007a; Hanson and Gluckman 2014; Bouret et al. 2015). Insulin resistance increases glucose levels in the blood which enables a higher total energy expenditure but may also increase risk for diabetes in later life, and insulin resistance is associated with compensatory growth (Soto et al. 2003; Wells 2003, 2007a). In line with our results in **Chapter 4**, risk for diabetes, and thus maybe insulin resistance, is most prevalent in children within the normal range of birthweight compared to those with reduced birthweight (McCance et al. 1994). Additionally, early-mid gestational food restriction in sheep (*Ovis aries*) results in unaffected birthweight and increased postnatal growth rates, and these effects are associated with altered glucose metabolism and insulin levels (Ford et al. 2007).

Prenatal maternal stress throughout gestation also alters the hypothalamic-pituitary-adrenal (HPA) axis and thus the pattern of offspring cortisol secretion, which in turn affects offspring metabolism (Haussmann et al. 2000; Bloomfield et al. 2004; Kapoor and Matthews 2008; Weinstock 2008; Glover et al. 2010; Beijers et al. 2014; Hanson and Gluckman 2014; Moisiadis and Matthews 2014b; Mustoe et al. 2014; Weinstock 2015). In general, these effects are positive and lead to increased offspring cortisol levels and thus increased energy availability throughout life, but the interactions between PreGC and the HPA-axis are manifold and in part contradictory and sex-dependent and still subject to research (Beijers et al. 2014; Hanson and Gluckman 2014; Moisiadis and Matthews 2014b). Moreover, glucocorticoids are frequently associated with increased metabolic efficiency but also decreasing growth rates (Mehls et al. 1993; Khani and Tayek 2001; Voutilainen and Tenhola 2012; Montanholi et al. 2013). Intriguingly, even periconceptual food restriction in sheep accelerates late gestational maturation of the HPA-axis but this effect is not correlated to maternal glucocorticoid levels (Bloomfield et al. 2004), indicating that alterations of the HPA-axis may be rather due to reduced maternal investment and developmental constraints. Indeed, alterations of the HPA-axis can similarly be caused by postnatal immature stress

(Núñez et al. 1996; Liu et al. 1997; Meerlo et al. 1999; Liu et al. 2000; Weaver et al. 2004; Macrì and Würbel 2006; Spencer et al. 2009), which supports this interpretation.

These results may suggest that prenatal maternal stress makes available energy resources easier accessible to the offspring, but they do not necessary indicate an increased metabolic efficiency or increased total energy expenditure. Indeed, my results in **Chapter 4** rather contradict such a hypothesis. My rough measure of energy expenditure during lactation was positively related to pre- and postnatal food availability and thus maternal investment, but there was no effect of PreGC, hence the PreGC-driven intrinsic growth acceleration was probably not due to increased energy expenditure.

Additionally, it was consistently shown that prenatal maternal stress impairs various other phenotypic attributes like cognitive and neurodevelopment (Weller et al. 1988; Bergman et al. 2010; Pryce et al. 2011; Sandman et al. 2012; Del Giudice 2014a; Kingston and Tough 2014; Moisiadis and Matthews 2014a), skill acquisition (Schneider et al. 1999; Buitelaar et al. 2003; Coe and Lubach 2008; Hauser et al. 2008; Cao et al. 2014; Weinstock 2015), immune function (Coe and Lubach 2008; Merlot et al. 2008; Couret et al. 2009; Beijers et al. 2010; Palmer 2011; Merlot et al. 2013; Lavergne et al. 2014; Veru et al. 2014) and stress resistance (Hanson and Gluckman 2014; Lehrner et al. 2014; Moisiadis and Matthews 2014a), and these findings are supported by my results in **Chapter 3**. This further contradicts the hypothesis of increased metabolic efficiency and rather refers to a shifting of resource allocation from several ontogenetic processes towards growth (Petry et al. 1997; Wells 2003, 2007a). This may be supported by my results in **Chapter 3** which indicate that a certain increase in growth rate is much less at the expense of motor skill acquisition if it is driven by PreGC rather than by an decrease in the rate of energy-intensive play, suggesting that PreGC mobilizes resources from a wider range of developmental processes in a more balanced way.

Such resource allocation shifting towards growth can be driven by changes in growth hormones. Indeed, it was shown that PreGC affects several neural circuits which are interconnected and related to growth hormones, like the hypothalamic-pituitary-adrenal, -thyroid, and -gonadal axes (Haussmann et al. 2000; Viau 2002; Kemme et al. 2007; Popma et al. 2007; Kapoor and Matthews 2008; Weinstock 2008; Glover et al. 2010; Kapoor and Matthews 2011; Beijers et al. 2014; Castaneda Cortes et al. 2014; Hanson and Gluckman 2014; Moisiadis and Matthews 2014b; Mustoe et al. 2014; Weinstock 2015). Early-mid gestational maternal food restriction in sheep was related to increased postnatal infant plasma concentrations of thyroidal growth hormone T3 (triiodothyronine), leading to unaffected body weights at weaning (Rooke et al. 2010), and relationships between PreGC and different growth hormones including insulin-like growth factors were also shown in other studies (Gallaher et al. 1998; Munoz et al. 2008; Sheriff and Love 2013; Hanson and Gluckman 2014; Lavergne et al. 2014; Moisiadis and Matthews 2014a, b; Li et al. 2015).

Altogether, it seems that the immediate compensatory growth in reaction to reduced maternal investment as shown in **Chapter 4** are enabled by a shift of resource allocation from several systems towards growth, rather than by increased metabolic efficiency and total energy expenditure. This in turn raises the question of why such an adaptive

mechanism is restricted to early-gestational PreGC-effects and unfeasible during later development. It was argued that such a complex phenotype recalibration may be more efficient and entails lower phenotype quality costs if it applies during early development (Rutherford 2013). Indeed such a hormonal recalibration may lead to more homogeneous results and phenotypes and less frictional loss if it is applied to a low number of highly plastic (stem) cells than on already well-developed tissues (Metcalfe and Monaghan 2001; Rutherford 2013). This is reflected in the early-gestational critical periods of PreGC-effects on offspring growth (**Chapter 4**) and other related systems like the hypothalamic-pituitary-gonadal axis (Kuzawa and Quinn 2009; Castaneda Cortes et al. 2014). Within the gestation period, this critical period may be additionally constrained by a process that largely blurs the information value of maternal PreGC, that is, the onset of foetal glucocorticoid secretion during later gestation (Hennessy et al. 1982; Sliwowska et al. 2006).

In summary the effects of early-gestational PreGC on offspring growth may be primarily driven by a recalibration of growth hormone secretion which consequently shifts resource allocation from several ontogenetic processes to growth. Current evidence seems to rather contradict the hypothesis that PreGC-exposure increases metabolic efficiency and total energy expenditure, and the frequently observed alteration in the HPA-axis and its consequences for offspring cortisol secretion seem to be a reaction to the developmental constraints associated with prenatal maternal stress rather than a PreGC-effect. Reduced immune function and cognitive abilities and thus shifted resource allocation could, however, also be a consequence of increased cortisol levels (Wingfield 2005), but this would fail to explain the restriction of the effects to early gestation. In any case much more work is needed to derive final conclusions, and particularly a comprehensive review of current evidence in the light of my suggested novel framework (**Chapter 4**) would be highly advantageous.

6.2.5 Prenatal stress effects on behaviour and the role of sex-specific reproductive strategies

Prenatal stress effects on physical offspring phenotype seem to generally support my predictions from **Chapter 4**. However, sex-specific prenatal stress effects on offspring behaviour may seem to contradict my predictions (see below). It has been argued that maternal effects on offspring behaviour represent an external PAR in reaction to the current social environment which prepares the offspring for a similar social environment during its adulthood but which can also be readjusted during later stages of life if the social environment changes (Sachser et al. 2011; Sachser et al. 2013). In this section, I will discuss these behavioural effects from the perspective of an internal PAR, and particularly from the perspective of my integrative framework provided in **Chapter 4**. I will argue that these sex-specific prenatal stress effects on offspring behaviour conform to predictions of the internal PAR-hypothesis and my framework and lead to new predictions allowing further testing of the framework.

Prenatal stress effects on offspring behaviour were shown in many studies. In general, prenatal maternal stress results in higher HPA-activity and cortisol levels and consequently in a higher and faster stress response in the offspring, leading to higher anxiety and avoidance

behaviour even in adult offspring (Drago et al. 1999; Estanislau and Morato 2005; Emack et al. 2008; Weinstock 2008; Laloux et al. 2012; Sheriff and Love 2013; Hanson and Gluckman 2014; St-Cyr and McGowan 2015). These effects are generally sex-dependent and more pronounced in male compared to female offspring. In guinea pigs (*Cavia aperea f. porcellus*), prenatal stress results in female behavioural masculinization and male behavioural demasculinization accompanied by reduced testosterone levels in males (Sachser and Kaiser 1996; Kaiser and Sachser 2005; Kapoor and Matthews 2005; Kemme et al. 2007; Kapoor and Matthews 2011; Sachser et al. 2011; Sachser et al. 2013). Similar effects are also found in wild cavies (*Cavia aperea*) and in other species (Kaiser and Sachser 2005; Emack et al. 2008; Siegeler et al. 2011). Prenatal stress feminizes juvenile play pattern of male rats (Ward and Stehm 1991), reduces social behaviour of adult male rats (Lee et al. 2007; Ehrlich and Rainnie 2015), reduces intermale aggression in mice (Kinsley and Svare 1986b) and increases offspring-directed aggressiveness and restlessness in female pigs (*Sus scrofa domestica*)(Jarvis et al. 2006).

It was argued that these sex-specific prenatal stress effects on offspring behaviour may be adaptive due to an (postnatally re-adjustable) external PAR (Sachser et al. 2011; Sachser et al. 2013; Kappeler and Fichtel 2015). If prenatal social stress predicts future social stress e.g. due to high population densities, then female masculinization may result in higher dominance positions and increased access to food and thus higher reproductive success (Sachser et al. 2011). This argument can be broadened to general environmental stress because females would benefit from the same behavioural adjustment if prenatal food restriction caused by various stressors predicts adult food restriction (Kappeler and Fichtel 2015). The adaptive value of male demasculinization, however, is thought to be restricted to social stress, with agonistic encounter avoidance due to a queuing strategy for dominance acquisition being an adaptive reproductive strategy under high population densities in species with high reproductive skew (Sachser et al. 2011).

Here I will suggest an alternative explanation for these sex-specific prenatal stress effects which does not rely on a forecast-based external PAR but conforms with an internal PAR and PreGC-driven accelerated reproduction in anticipation of reduced life expectancy (Nettle et al. 2013). It is well established that behavioural, or personality, traits are correlated to different life histories, and particularly different paces of life history (Réale et al. 2007; Wolf et al. 2007; Réale et al. 2010). In general, an increasing pace of life is associated with lower life expectancy, faster growth, earlier reproduction, and higher aggressiveness, boldness, risk-taking and activity level (Wolf et al. 2007; Réale et al. 2010). From this perspective the prenatal stress effects on female offspring behaviour strongly match the predictions of accelerated reproduction under reduced life expectancy (Sachser et al. 2013). However, prenatal stress effects on male offspring behaviour seem to contradict these predictions and suggest that males rather aim at reducing their mortality risk and thus increasing their life expectancy. In guinea pigs, this assumption is further supported by other specific prenatal stress effects: prenatal maternal stress during the first two or last two gestational trimesters leads to accelerated postnatal growth in females but not in males, and

this was associated with a lower age at first reproduction in females (Schöpper et al. 2012; von Engelhardt et al. 2015).

These results for guinea pigs may seem to contradict the predictions of an internal PAR and my framework from **Chapter 4**. However, this may be due to sex-specific reproductive strategies which are currently not implemented in my framework. In most species female reproductive skew is much lower than male reproductive skew. Hence lifetime reproductive success of females primarily depends on the length of reproductive lifespan while lifetime reproductive success of males is much less driven by reproductive lifespan but primarily depends on female monopolization potential which in turn strongly depends on their comparative intra-sexual competitive power (van Schaik 1989; Johnson 2003; Ostner et al. 2008b; Onyango et al. 2013; Dubuc et al. 2014). This sex difference may have strong implications for life history and may explain large sex differences in how available resources are allocated e.g. to growth or play (**Chapter 2**). From an internal PAR-perspective, this sex difference should lead to sex-specific prenatal stress effects due to different time constraints on maturation and reproduction in consequence of reduced life expectancy (Johnson 2003). Since accelerated growth is accompanied by several phenotypic costs, males should rather avoid these costs due to the lower benefits of accelerated maturation and primarily maximize their adult life span to maximize the chance to enter a period of high female monopolization potential. Such a male strategy matches well the assumed fitness benefits of demasculinized male behaviour as suggested by Sachser et al. (2011) but circumvents the problematic aspects of an stressor-specific external PAR and explains it from a general internal PAR-perspective. In consequence, sex-specific prenatal stress effects on offspring behaviour provide new and more detailed predictions of my framework provided in **Chapter 4** and may thus allow to further test it.

6.3 Conclusions and outlook

In this thesis, I investigated some crucial gaps in our knowledge of the evolution of variance in growth. Specifically I focussed on the costs and benefits of play, the inconsistent results of epigenetic prenatal stress effects on offspring growth and the benefits of male-immature relationships to the immature. I collected data on wild Assamese macaques where pattern of food availability, mortality, spatial and social play options, social relationships and the strength of stressors likely match those during the evolution of play, prenatal stress effects and male-immature relationships. I tested and falsified a long-standing assumption of the most prominent theory for the evolution of play and ran time-series analyses that provide the first evidence for the causality in the link between play and motor skill development. Conducting the first tests that explicitly differentiate between two competing evolutionary explanations for the occurrence of epigenetic prenatal maternal stress effects on offspring development in a critical test case, I provided evidence against the prominent external PAR-hypothesis and support for the recently developed internal PAR-hypothesis. I integrated previous theories of prenatal stress effects into a novel coherent framework reconciling the highly inconsistent maternal stress effects on offspring growth. Analysing

data on wild Assamese macaques and running a comparative analysis on 88 studies including 11 mammalian species ranging from rodent to primates and ungulates, I found strong support for this new framework.

From a life history perspective, I show that despite mammalian growth rates being under strong positive selection and thus of high ontogenetic priority, they still show considerable phenotypic plasticity that relates to starvation avoidance, time constraints on development, and resource allocation to size-independent fitness traits. Confirming previous results from several species, Assamese macaques reduce their growth rates in reaction to reduced resource availability to avoid starvation. Most obviously, reduced resource availability can result from reduced energy intake due to reduced food availability and maternal investment, which has been shown for many species and also applies to Assamese macaques. Immature resource availability may further be restricted by feeding competition which could be counter-balanced by agonistic support from closely bonded adult males. I found Assamese macaques forming differentiated and long-lasting male immature bonds which provide agonistic support to the immature. Resource allocation to growth also can be traded off against investment into size-independent fitness traits, and particularly into locomotor play for motor skill acquisition which may increase offspring survival and adult fitness but also increases age at maturation in Assamese macaques. In anticipation of reduced maternal investment and the resulting time constraint on development, intrinsic growth rates are accelerated by epigenetic phenotype recalibration during early gestation via an integrative predictive adaptive response (PAR) in Assamese macaques and across mammals. These partly novel findings start to close some of the fundamental knowledge gaps but also raise new questions.

Assamese macaques invest in social locomotor play despite these investments being at the expense of growth and probably age at maturation. This is in clear contradiction to the basic assumption of current theory about the evolution of play (“surplus resource hypothesis”) and suggests that social locomotor play entails high fitness benefits. Indeed, social locomotor play accelerates motor skill acquisition in Assamese macaques which may entail short- and/or long-term benefits. The sex differences in play rate in Assamese macaques and many other species correspond to adult sex-roles, suggesting that play provides primarily long-term benefits. However, play is also associated with short-term survival benefits in some species, and I have shown that such short-term survival benefits may sufficiently explain within- and between species variation in play rates. It remains to be shown whether motor skill level translates into fight/flight competence. Social play may also train social skills and help to form social bonds which may provide further short- or long-term benefits, but neither of these relationships has been comprehensively tested so far. An important next step will be to investigate the detailed and collective short- and long-term fitness benefits of play. I have argued that the trade-off between play and growth may explain the phylogenetic occurrence of play based on variance in age at maturation and the fitness benefits of play, and a first preliminary review of published data seems to support this hypothesis. The surplus resource hypothesis also makes predictions about the phylogenetic distribution of play based on the accumulation of sufficient surplus resources.

Comparative studies considering ability to accumulate sufficient resources, age at maturation, and (potential) fitness benefits of play will allow competitive tests of the two hypotheses and further our understanding of the evolution of play.

My results suggest that across mammals, prenatal maternal stress reduces maternal investment and increases maternal PreGC-level which accelerates intrinsic offspring growth to compensate for the negative effect of reduced maternal investment and may accelerate development and, consequently, reproduction. The positive effect of PreGC on offspring growth resulting in increased offspring body size at the age of 16-18 months in Assamese macaques suggests that the effect is lasting and may accelerate maturation and thus goes well beyond simple growth compensation. Future research will have to confirm these long-term effects of PreGC. Furthermore, the sex-specific impact of the length of reproductive lifespan on lifetime reproductive success and thus potential sex differences in time constraints on maturation caused by lower life expectancy provide testable predictions for this framework. The physiological mechanism that enables immediate growth rate compensation during the period of reduced maternal investment and accelerated growth in the longer term also requires future investigation. Since numerous studies explored the physiology underlying prenatal stress effects, a promising avenue for future research is a comprehensive comparative review which considers the different effects of early- and late-gestational maternal stress to disentangle the various possible pathways and relate them to PreGC-effects (e.g. effects on growth hormones) or developmental constraints effects due to reduced maternal investment (e.g. most effects on offspring HPA axis and cortisol levels).

The results on prenatal stress effects in Assamese macaques exclude both an external, environmental forecast-based PAR and a pure internal, somatic state-based PAR. Instead, the results suggest that prenatal stress effects result from an integrative PAR based on a short-term external and a long-term internal PAR. I have argued that such a mechanism may also apply to other, also short-lived species for several reasons. However, to my knowledge this is the first study that tries to differentiate between external and internal PARs, hence further more sophisticated studies particularly in wild short-lived species are needed. I have argued that social bonds may play an important moderating role in prenatal stress effects due to positive effects on the mother and/or offspring. It remains to be investigated whether strong and stable social bonds increase current maternal investment e.g. by increasing offspring survival and/or reducing the costs of current on future reproduction, or whether they primarily provide benefits to the offspring that compensate for reduced maternal investment, or both. Of particular interest in this context are the ultimate benefits of male-female and male-immature bonds for the mother and the offspring beyond agonistic support.

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I hereby declare that I have written this thesis independently and with no other aids or sources than quoted.

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