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RESEARCH ARTICLE

Relations Among Birth Condition, Maternal Condition, and Postnatal Growth in Captive Common Marmoset Monkeys (*Callithrix jacchus*)

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The present study characterizes the relations among maternal condition, litter size, birth condition, and growth in body weight for a population of common marmosets. The subjects of the study were marmosets born into a single colony between 1994 and 2001. Three sets of analyses were conducted to answer the following questions: 1) Is there a relationship between litter size, maternal condition, and birth condition? In the study population, maternal body weight, maternal age, litter size, and birth condition were related in a complex fashion. Birth weight and prenatal long-bone growth, as reflected in knee–heel length, were both related to maternal age, with older mothers supporting higher prenatal growth. Age and maternal condition appeared to interact as determinants of long-bone growth, as the combination of older and larger mothers resulted in significantly longer knee–heel lengths in their offspring. 2) Is there a relationship between birth condition or maternal condition and subsequent growth or final adult size? The early growth rate in this population was similar to early growth rates reported for three different marmoset colonies, suggesting that early growth may be relatively inflexible in this species. However, within this population, the variation that did occur in early growth rate was related to birth weight and maternal weight. Later growth and adult weight were related to birth weight and litter size: small twin infants displayed slower later growth rates and were smaller as adults than twins that began life at a higher birth weight, while the birth weight of triplets was not related to adult size. In these marmosets, small infants that were the result of increased litter size differed from small infants whose small birth size resulted from other factors. This reinforces the proposal that the causes of low birth weight will be relevant to the development of the marmoset as a model of prenatal environmental effects. Am. J. Primatol. 62:83–94, 2004.

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INTRODUCTION

Models that use spontaneous differences in the perinatal environment stemming from different litter sizes (e.g., rodents [Kennedy, 1957; Aubert et al., 1980; Faust et al., 1980; Oscai, 1982; Bunag et al., 1990; Young, 2002]) or different positions in utero (e.g., rabbits [Flake et al., 1987; Buchmiller-Crair et al., 2001]) are valuable tools for determining the effects of the perinatal environment on growth, metabolism, cardiovascular function, and nervous system function. The marmoset monkey could be used in a similar fashion to examine the pre- and postnatal effects of litter size on growth, health, and lifespan in a primate, given that marmosets have a variable litter size. The development of such a model would benefit from a thorough understanding of the relations among litter size, maternal condition, birth condition, and subsequent growth and adult size.

In captivity, marmosets routinely produce litters ranging from one to three infants, and occasionally produce litters of four or five. As in other litter-bearing mammals, litter size in marmosets has a consistent effect on birth weight, and the average individual birth weight tends to decrease as litter size increases [Tardif & Smucny, 2003]. Many captive common marmoset colonies exhibit two secular trends: both adult body weight and the average litter size increase over time [Poole & Evans, 1982; Hearn, 1983; Box & Hubrecht, 1987; Rothe et al., 1987]. The relation between higher maternal weight and higher ovulation number/litter size in marmosets has been documented [Tardif & Jaquish, 1994; Tardif and Jaquish, 1997]. Captive marmosets show significant variation in size, in terms of adult body weight. The average weight of adult marmosets in the wild is around 350 g [Araujo et al., 2000]. The reported average adult weight in captive populations varies by 60%, from 283 g [Peters & Guerra, 1998] to 300 g [Abbott & Hearn, 1978] to 350 g [Tardif et al., 2001] to 530 g [Poole & Evans, 1982]. It is unknown whether the adult size attained is related to an animal's litter size or birth condition.

The present study characterizes the relations among litter size (twin vs. triplet), birth condition, maternal condition, and growth in body weight for a population of common marmosets.

MATERIALS AND METHODS

The subjects of the study were 89 common marmosets born into a single colony between 1994 and 2001. All of the subjects were born and reared in family groups consisting of a mated pair and up to six older siblings. They were reared in litters of one or two, since at least one infant in each triplet litter died by day 7, a typical outcome for these large marmoset litters [e.g., Hearn, 1987; Tardif & Smucny, 2003]. Initial analyses revealed no relation between the rearing litter size and any of the growth variables, so this variable was not considered further. The housing and maintenance conditions for this colony were previously described by Tardif et al. [1998].

The animals were weighed on the day following birth. Birth condition, weight change over time, and adult size were measured in subsets of the 89 subjects. We measured birth biparietal diameter and birth knee–heel length by averaging repeated measures taken with a caliper, as described in Power et al. [2001].

TABLE I. Description of Independent and Dependent Variables in GLM Analyses

Analysis	Dependent variable	Independent variables	Sample size	Significant at $P <$
1a. Relation of maternal factors and litter size to birth condition	Birth weight	Litter size Maternal age Maternal weight	89	0.017
1b. Relation of maternal factors and litter size to birth condition	Birth knee-heel length	Litter size Maternal age Maternal weight	59	0.017
1c. Relation of maternal factors and litter size to birth condition	Birth biparietal diameter	Litter size Maternal age Maternal weight	86	0.017
2a. Relation of birth condition and maternal condition to growth rate	Early growth rate	Litter size Birth weight Maternal age Maternal weight	68	0.0125
2b. Relation of birth condition and maternal condition to growth rate	Later growth rate	Litter size Birth weight Maternal age Maternal weight	68	0.0125
3a. Relation of birth condition and maternal condition to adult size	Adult weight	Litter size Birth weight Maternal age Maternal weight	77	0.0125
3b. Relation of birth condition and maternal condition to adult size	Adult knee-heel length	Litter size Birth weight Maternal age Maternal weight	44	0.0125

Measurements were taken on the morning following the day of birth, around 36 hr after birth. We assessed weight change over time by weighing the subjects in their home cages, placing a scale in the cage, and recording and averaging at least 10 weights over a 10–15-min period [Jaquish et al., 1997]. Weights were taken at least once a week until the animals were approximately 6 months old, and once every 1–4 weeks thereafter. Infants under approximately 1.5 months of age were removed from the group for weighing. After that age, all animals were weighed between 0900 and 1030 hr in their home cages. Adult weight and knee–heel length were taken between 17–22 months of age, in a fashion identical to that used for the birth measures. Dams were weighed at least once a week. Their average weight during the month following delivery was used as their maternal weight. Table I provides the sample size for each of the size or growth measurements used in subsequent analyses.

A Lowess regression (an iterative, locally weighted least-squares method) was used to determine the relation between weight and age for each subject that lived to at least 17 months of age, and for which weights were available throughout the

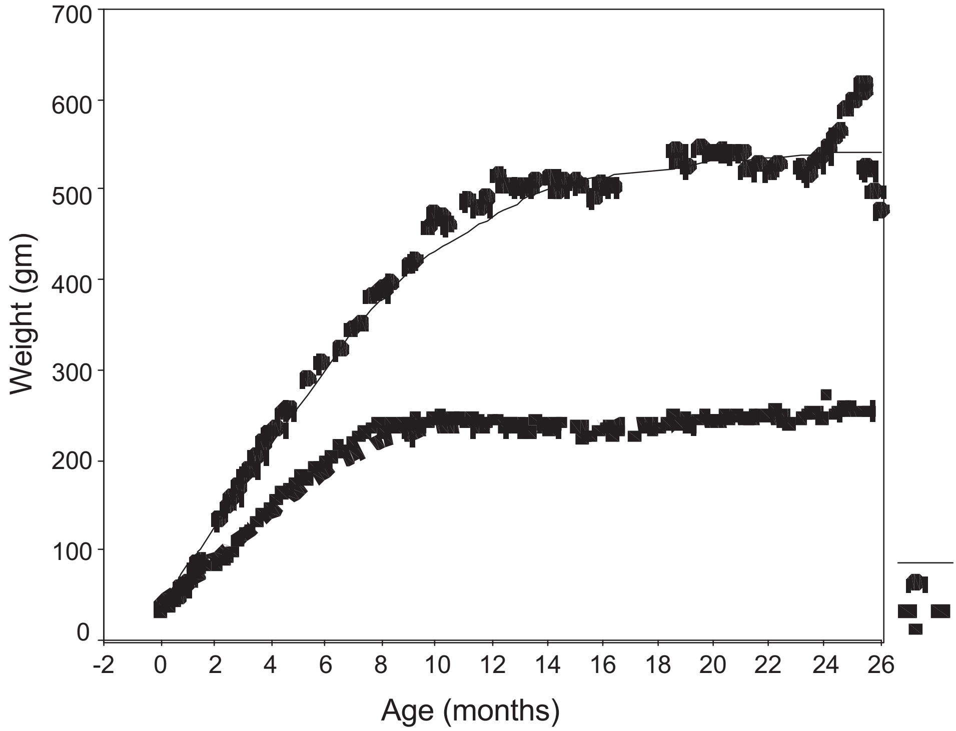

Fig. 1. Relation of body weight to age (0–26 months) for two common marmosets. One animal continues to increase in body weight throughout the period, at a decreasing rate, while the other's weight plateaus at a relatively early age. Both of these animals lived into adulthood.

period from birth to 17 months. The age of 17 months was chosen because previous reports have indicated that marmosets attain their adult weight by 17–18 months of age [Abbott & Hearn, 1978]. Following this method, all individuals displayed an initial period of relatively rapid growth with a linear slope. This period was followed by another, less rapid growth period. After the second growth period, 58% of individuals continued to gain weight up to 17 months of age. This pattern of growth was a simple, decelerating exponential curve, which Kirkwood [1985] previously described as the common growth pattern for marmosets. However, 42% had reached a weight plateau by the end of the second growth period (examples in Fig. 1). We then used the Lowess regression curve lines to calculate a first (early) growth rate, and a second (later) growth rate by visually determining the first two points at which the regression line deviated from the linear direction, and calculating growth in grams per day.

Three sets of analyses were conducted to address the following questions:

1. Is there a relationship between litter size or maternal condition and birth condition?
2. Is there a relationship between birth condition or maternal condition and subsequent growth?
3. Is there a relationship between birth condition or maternal condition and final adult size attained?

Table I provides a description of the variables in each set of analyses. All analyses were conducted using generalized linear models, and maternal identity was included as a random factor in order to avoid the pseudoreplication effects inherent in having more than one offspring from each dam. All analyses were conducted using SPSS (version 10). Due to the repeated use of data in multiple analyses, the probability designated as significant was adjusted as 0.05 divided by the number of independent variables in the analysis [Kleinbaum et al., 1988] (see Table I).

RESULTS

1. Is there a relationship between litter size or maternal age/weight and birth condition? In this study population, maternal body weight, maternal age, litter size, and birth condition were related in a complex fashion. Previous studies revealed the positive relation between maternal weight and litter size in this species [Tardif & Jaquish, 1994, 1997]. Logistic analyses of the relation between maternal weight and litter size in this population revealed the same relationship ($F = 3.99$, $dF = 45$; $P < 0.05$).

Table II provides descriptive statistics on birth condition variables for this population, relative to litter size. Singletons are included in these descriptive statistics but were eliminated from the analyses because of the small sample size ($n = 5$). Birth condition measures were, as expected, all highly correlated ($r = 0.573$–0.730, $P < 0.0001$).

Birth weight was related to maternal age ($F = 13.782$, $dF = 1{,}57$, $P < 0.0001$), but not to maternal weight, and birth weights were lower for the offspring of younger mothers (illustrated in Fig. 2). Birth knee–heel length was related to maternal age ($F = 35.384$, $dF = 1{,}31$, $P < 0.0001$) and maternal weight ($F = 16.775$, $dF = 1{,}31$, $P < 0.0001$). Figure 3 illustrates the relations among these three variables, indicating that knee–heel length was significantly higher for the offspring of older mothers, but only if the mothers were of medium-to-high weight. Birth biparietal diameter was not significantly related to any of the independent variables.

2. Is there a relationship between birth condition or maternal condition and subsequent growth? Table III provides descriptive statistics on the growth variables. Again, data on the small group of singletons are presented, but were not used in the analyses. On average, the growth rate remained linear until 5.3 months of age (range = 3.2–9.0), at which point it declined.

The early growth rate averaged 1.15 g/day. It was related to birth weight ($F = 9.258$, $dF = 1{,}46$, $P = 0.004$) and tended to be related to maternal weight

TABLE II. Birth Condition Relative to Litter Size

Litter size		Weight (g)	BPD (mm)	KHL (cm)
1	Mean ± S.D.	34.70 ± 3.81	20.34 ± 0.47	2.47 ± 0.21
	n	5	3	3
2	Mean	30.24 ± 3.33	19.72 ± 0.62	2.34 ± 0.10
	n	59	55	33
3	Mean	27.73 ± 2.03	19.11 ± 0.73	2.23 ± 0.07
	n	30	31	26
Total	Mean	29.68 ± 3.41	19.53 ± 0.73	2.30 ± 0.11
	n	94	89	62

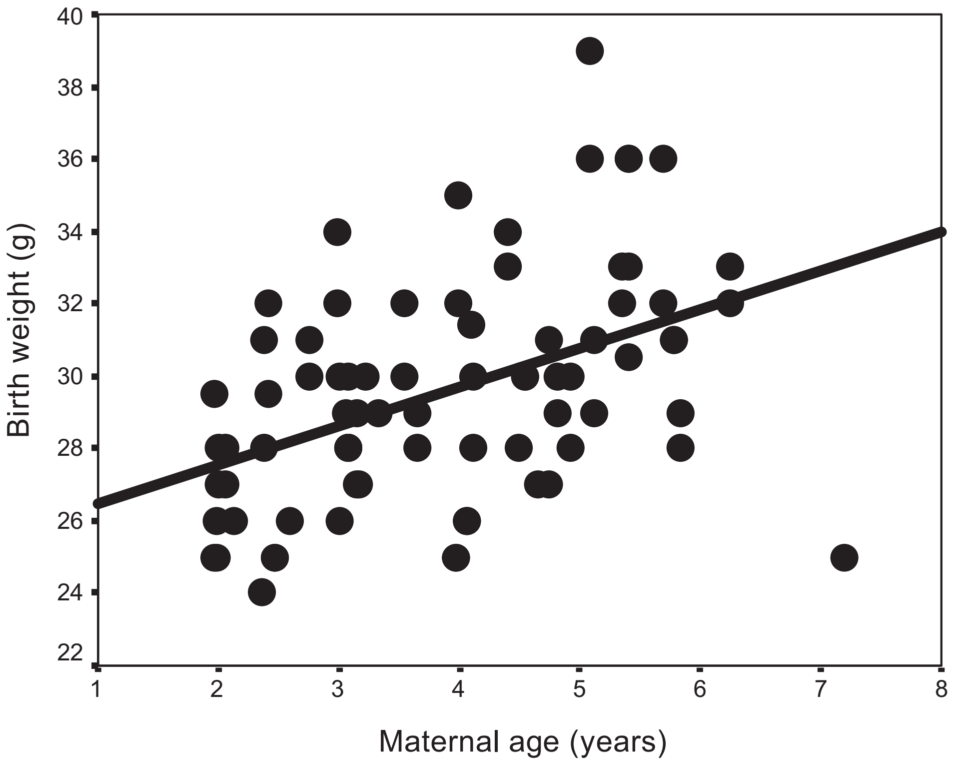

Fig. 2. Relation of birth weight to maternal age.

(F = 5.883, dF = 1,46, $P = 0.019$). Low-birth-weight infants had significantly lower initial weight gain (Fig. 4), but the effect was less marked if the mother's weight was low.

The later growth rate averaged 0.83 g/day and was more variable than the early rate (coefficient of variation for early and late growth rates = 0.041 and 0.153, respectively). The later growth rate was related to birth weight (F = 10.44, dF = 1,46, $P = 0.002$) and litter size (F = 48.93, dF = 1,3.02, $P = 0.006$), but not to maternal weight or maternal age. Figure 5 illustrates the later growth rate relative to birth weight and litter size. Lower birth weight was related to slower growth rates in twins, but not triplets, such that, for small-to-medium birth weights, triplets had higher later growth rates compared to twins. For large-birth-weight infants, there was no difference.

3. Is there a relationship between birth condition or maternal condition and final adult size attained? The relation of adult weight to birth weight and litter size was similar to that of the later growth rate, as illustrated in Fig. 6. Adult weight was related to birth weight (F = 18.11, dF = 1,53, $P < 0.0001$), but not to maternal weight or age.

Adult knee–heel length was related to maternal weight only (F = 11.075, dF = 1,25, $P = 0.003$). The offspring of large mothers had longer adult knee–heel lengths (average length = 6.88 cm) compared to the offspring of small mothers (average length = 6.63 cm) or medium-weight mothers (average length = 6.64 cm).

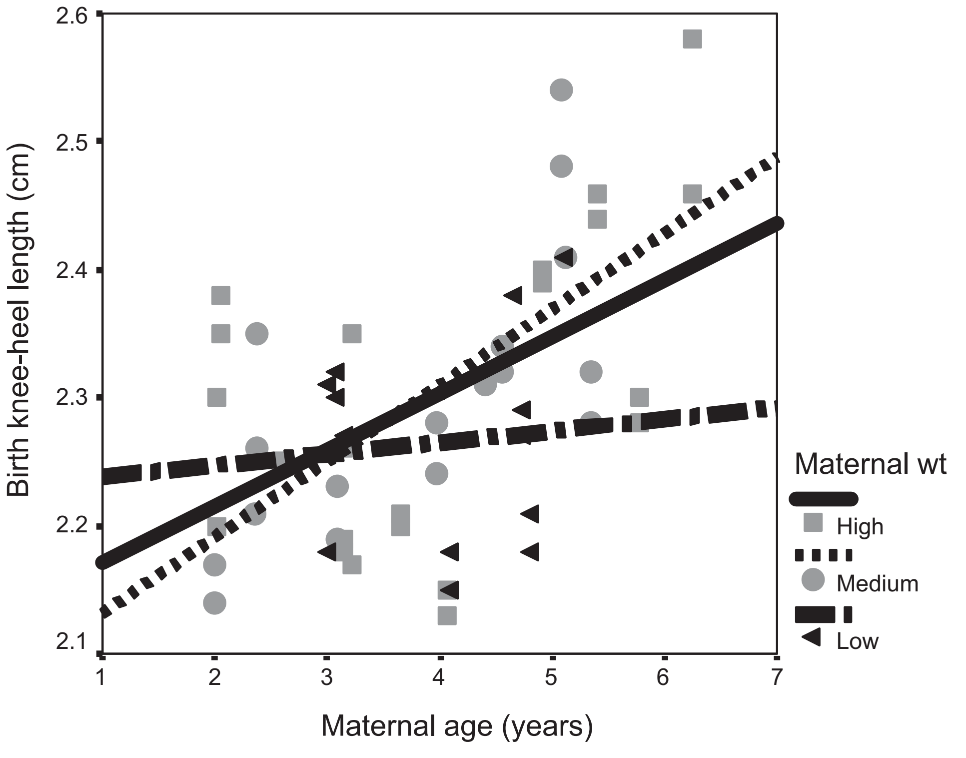

Fig. 3. Relation of birth knee–heel length to maternal age, coded by maternal weight (categorized as low, medium, or high).

TABLE III. Growth Variables Relative to Litter Size

Litter size		Early rate (g/day)	Later rate (g/day)
1	Mean ± SD	1.11 ± 0.13	0.75 ± 0.39
	n	4	5
2	Mean ± SD	1.15 ± 0.22	0.74 ± 0.36
	n	45	47
3	Mean ± SD	1.15 ± 0.20	0.95 ± 0.32
	n	25	26
Total	Mean ± SD	1.15 ± 0.21	0.81 ± 0.36
	n	74	78

DISCUSSION

These results suggest that litter size, maternal condition, birth condition, and growth have a complex interrelationship in marmosets. Figure 7 summarizes these relations. Previous analyses have revealed that ovulation number and litter size are related to maternal weight, with larger mothers having larger litters [Tardif & Jaquish, 1994, 1997]. The population examined in this study shows the same relation. Birth weight and prenatal long-bone growth, as reflected in knee–heel length, were both related to maternal age, with older mothers supporting greater prenatal growth. Age and maternal condition appear to interact as

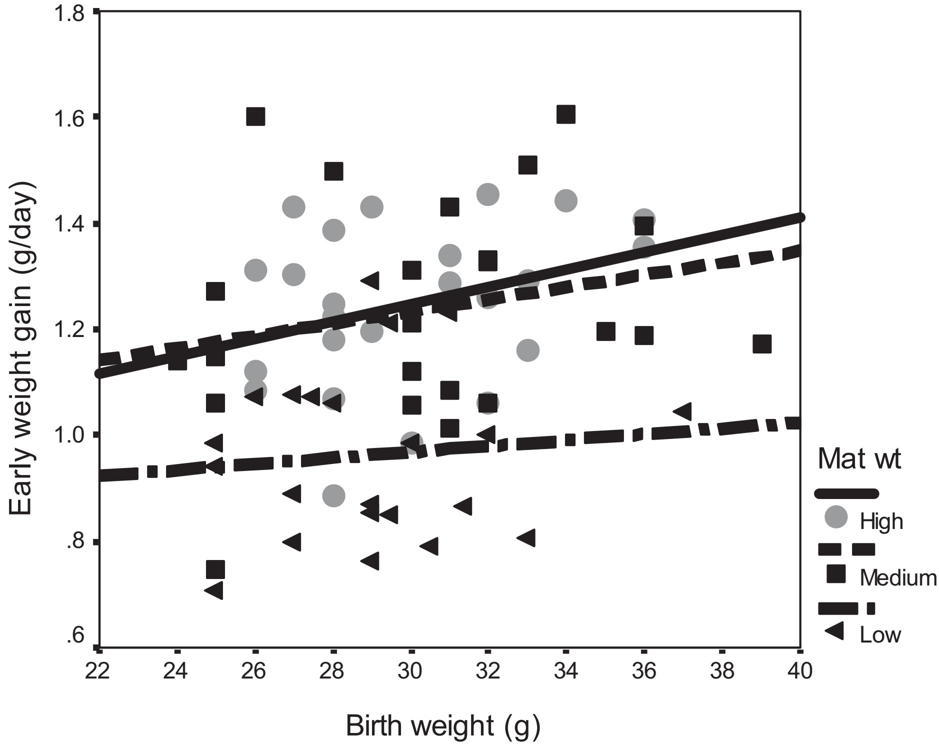

Fig. 4. Relation of early weight gain (gain prior to the first growth rate decline) to maternal weight, coded by birth weight (categorized as low, medium, or high).

determinants of long-bone growth, as the combination of older and larger mothers resulted in significantly longer knee–heel lengths in their offspring. Maternal age was an important variable in relation to the birth condition of offspring, but was not directly associated with any measures of postnatal growth or final adult size of those offspring. In this population, there was a close association between maternal age and parity, in that there were no old, low-parity females. Therefore, we cannot separate the effects of age and parity in this population.

The early growth rate in this population averaged 1.15 g/day, which is similar to early growth rates (1.0, 1.1, and 1.4 g/day) reported by Kirkwood [1985] for three different marmoset colonies. This suggests that early growth may be relatively inflexible in this species. However, within this population, the variation that did occur in early growth rate appeared to be related to birth weight and maternal size. The earliest growth rate encompassed the period of lactation (to approximately day 65–90). Previously, in a subset of this population, we found that in mothers rearing twins, the smaller mothers had less milk fat and lower milk output (as measured by milk weight $\times$ composition), and supported less preweaning growth [Tardif et al., 2001]. This finding further supports the contention that the mother's condition and her lactation ability play a role in the early growth period in marmosets.

In the current study, later growth was related to birth weight for twins, but not for triplets: small twin infants displayed slower later growth rates and were smaller as adults than twins that began life at a higher birth weight. The birth

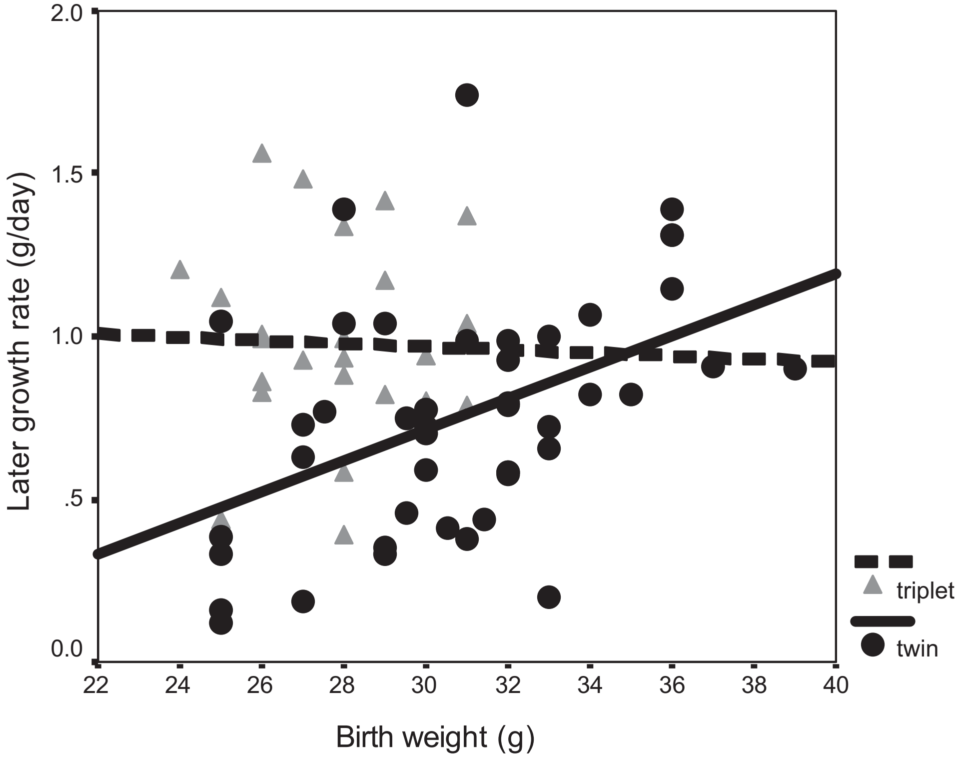

Fig. 5. Relation of later weight gain (gain following the first growth rate decline, but preceding the second growth rate decline) to birth weight, coded by litter size.

weight of an infant born in a triplet litter is likely a reflection of intrauterine competition for resources accessed through the shared, bidiscoid placenta [Hearn, 1983], and maternal resources (as reflected by maternal size) apparently cannot compensate for this higher demand, given that maternal size is not related to birth weight among triplets. Perhaps a genetic predisposition to be small or large is constrained in large (triplet) litters by the increased intrauterine competition for limited resources. If this were the primary factor, one might expect to find a relatively close association between maternal weight and adult weight of offspring in both litter sizes; however, in this population, that is not the case. Alternately, the condition of the mother, as reflected in her body size, may affect the growth trajectory of the fetus. Mothers that are small are more likely to produce twins than triplets, and its possible that at the lower limits of size, maternal size constrains infant birth weights. Therefore, the in utero processes that produce a small twin may be different from those that produce a small triplet, such that there is a carry-over effect on postnatal growth in twins but not in triplets.

It is unknown to what extent these differences in weight (at birth or in adulthood) reflect different body compositions, or whether larger animals are proportionally similar to smaller ones. The only published report on body composition in common marmosets [Power et al., 2001] found that both fat and lean weight were proportionally larger in larger animals; however, the population in which body composition was measured was, in general, relatively small and lean.

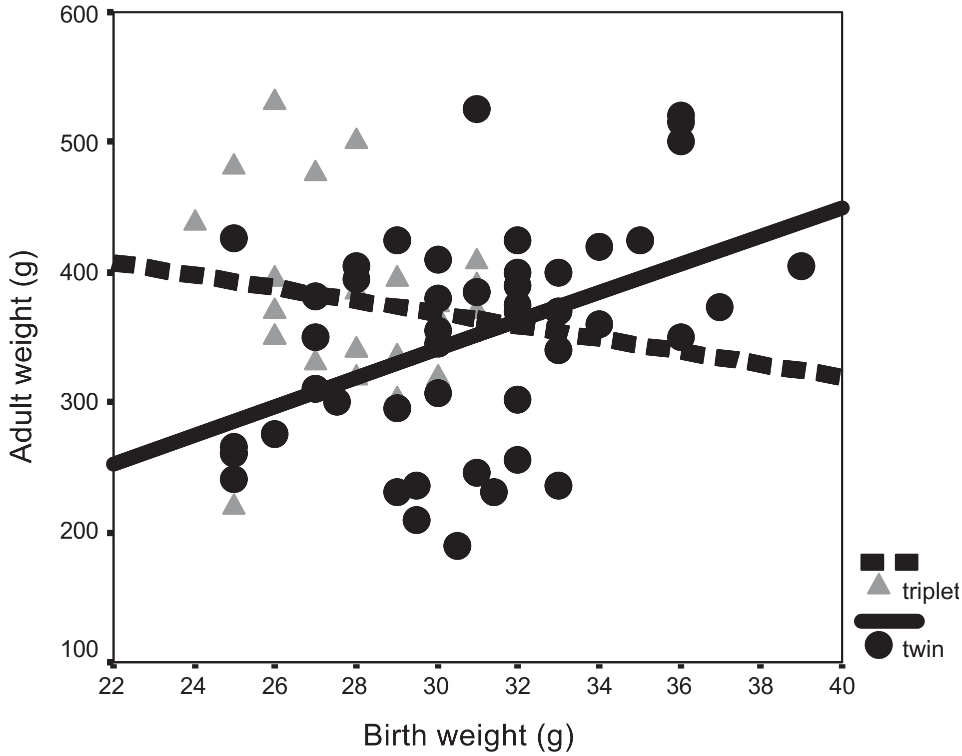

Fig. 6. Relation of adult weight (taken at 17–22 months of age) to birth weight, coded by litter size.

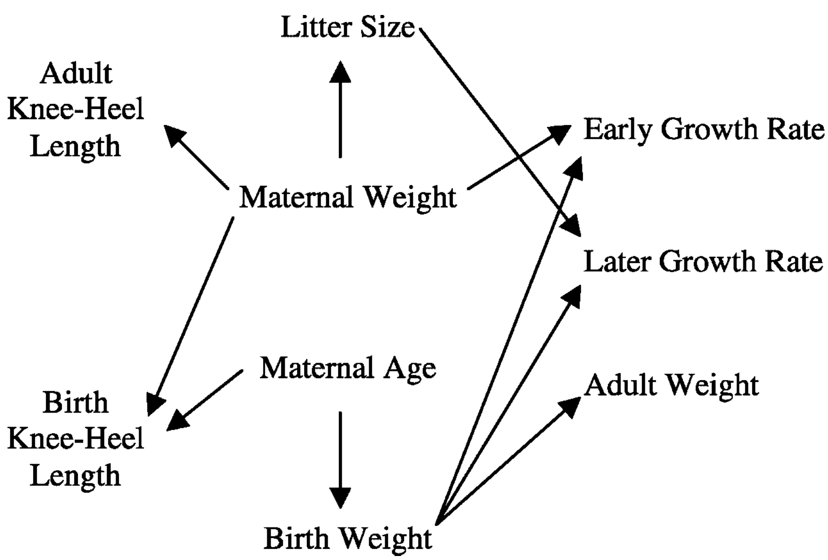

Fig. 7. Summary of relations among maternal condition, birth condition, and growth variables, based upon this and previous studies [Tardif & Jaquish, 1994, 1997].

The combined relations among maternal age, birth weight, growth rate, and litter size suggest an hypothesis for the mechanism underlying the secular trend of increasing average litter size as colonies get older, which has been observed in many marmoset colonies. If a colony has a higher percentage of older mothers because it has been in existence for a longer period of time, this would lead to the birth of more infants with higher birth weights. Since higher birth weights, particularly in twins, are associated with higher later growth rates and adult size, and higher adult weights are in turn associated with increasing litter size, it may be that aging of the breeding population may indirectly lead to increasing litter size through the increased birth size of infants of older mothers.

The relationship between prenatal growth and risk of cardiovascular and renal disease in adulthood, as suggested by human epidemiological studies, has heightened interest in the development of animal models in which prenatal environmental effects can be manipulated or are naturally variable. Models that use spontaneous differences in the perinatal environment stemming from different litter sizes (e.g., rodents [Kennedy, 1957; Aubert et al., 1980; Faust et al., 1980; Oscai, 1982; Bunag et al., 1990; Young, 2002]) or different positions in utero (e.g., rabbits [Flake et al., 1987; Buchmiller-Crair et al., 2001]) are valuable tools for determining the effects of the perinatal environment on growth, metabolism, cardiovascular function, and nervous system function. The marmoset monkey could be used in a similar fashion to examine the pre- and postnatal effects of litter size on growth, health, and lifespan in primates, given that marmosets have a variable litter size and a relatively short lifespan.

One area of interest in developing such a model is determining the importance (or lack of importance) of the mechanism resulting in variation in birth condition, as that condition relates to both subsequent growth and markers of adult health, such as blood pressure. For example, low-birth-weight human infants may differ dramatically in growth patterns and adult weight [e.g., Cianfarani et al., 2001; Ong et al., 2002], and some studies suggest that an interaction between birth condition and subsequent growth is a determinant of adult weight, cardiovascular function, and survival [Huxley et al., 2000; Eriksson & Forsen, 2002]. The present study suggests that small marmoset infants that are the result of increased litter size differ in terms of subsequent growth and adult size from small infants whose small birth size results from other factors. This reinforces the proposal that the causes of low birth weight will be relevant to the development of this species as a model of prenatal effects on adult health.

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