Maternal investment, life histories, and the costs of brain growth in mammals

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Brain size variation in mammals correlates with life histories: larger-brained species have longer gestations, mature later, and have increased lifespans. These patterns have been explained in terms of developmental costs (larger brains take longer to grow) and cognitive benefits (large brains enhance survival and increase lifespan). In support of the developmental cost hypothesis, we show that evolutionary changes in pre- and postnatal brain growth correlate specifically with duration of the relevant phases of maternal investment (gestation and lactation, respectively). We also find support for the hypothesis that the rate of fetal brain growth is related to the energy turnover of the mother. In contrast, we find no support for hypotheses proposing that costs are accommodated through direct tradeoffs between brain and body growth, or between brain growth and litter size. When the duration of maternal investment is taken into account, adult brain size is uncorrelated with other life history traits such as lifespan. Hence, the general pattern of slower life histories in large-brained species appears to be a direct consequence of developmental costs.

phylogenetic | neonate | cognition | maturation | altricial

Brain size varies extensively among species. Many comparative studies have been aimed at understanding how and why such variation evolved, and have identified a range of factors associated with the evolution of large brains. One general factor robustly correlated with brain size is life history; larger-brained species, such as humans, develop slowly and have extended periods of juvenility and long lifespans, effects that remain after accounting for differences in body size (1–8). These associations have been interpreted in two different ways. First, life history correlates could reflect the benefits of large brains in providing a "cognitive buffer" against environmental unpredictability, improving survival and permitting long lives (2, 6, 7). Second, selection on brain size might have secondary consequences for life history because larger brains impose a developmental cost in terms of a need for extended growth and maturation (3–5, 8).

Because large brains must have both benefits and costs, the two types of explanation for the association between brain size and life history are not necessarily incompatible (3–7). They do, however, make different predictions. The cognitive buffer hypothesis predicts correlations among brain size, survival, and lifespan (6, 7). Developmental costs hypotheses, on the other hand, assume that brain growth is traded off against aspects of production, including growth, maturation time, and reproductive rates, causing larger-brained species to grow and mature more slowly and to have lower fertility (4, 5, 8–10). This idea overlaps with the "maternal energy hypothesis," which suggests that maternal investment and energy availability constrain the development of large brains, predicting that brain size correlates with the duration of maternal investment and with maternal basal metabolic rate (BMR) (11, 12). Recent comparative evidence is consistent with both cognitive buffer and developmental cost ideas; brain size variation in adult mammals is positively correlated with lifespan (6, 7) as well as with the durations of gestation, lactation, and the juvenile period (4, 5, 8, 13, 14).

Little attempt has so far been made to distinguish between the effects of these different developmental and life history traits, making individual correlations with brain size difficult to interpret. In particular, it is unknown whether maternal investment and lifespan are both independently associated with brain size or life history correlations are driven primarily by one of these factors. Furthermore, most studies focus on correlates of adult brain size, which can provide only indirect evidence for developmental costs. A critical and more direct test is whether brain growth during specific phases of development correlates with the relevant aspects of maternal investment and maturation time. Evidence on this question is limited. Some studies have demonstrated a positive correlation between neonate brain size and gestation duration, but these were conducted before the advent of powerful phylogenetic comparative methods (5–16) or on small samples of primate species (10, 17). Studies of postnatal brain growth have also been limited to small samples of primates, and do not support the critical prediction of an association between postnatal brain growth and lactation (10, 17), a finding in tension with the result that adult brain size correlates with lactation duration in a wider range of mammals (5). Similarly, although recent studies find that adult brain size correlates with BMR (8, 13), evidence that this reflects maternal metabolic constraints on pre- or postnatal brain growth is lacking (16).

Indeed, it is not even clear how variability in pre- and postnatal brain growth combine to influence variation in adult brain size. The relative amounts of pre- and postnatal brain growth differ significantly among species (17), and analysis of the genetic correlates of brain size evolution suggests that the two phases of brain growth are genetically dissociable (18). Hence, they could in principle make independent contributions to species differences in adult brain size. However, it has been suggested that the relative brain sizes of neonates and adults are uncorrelated in mammals (8, 10, 19), implying that pre- and postnatal brain growth are traded off. If true, this would suggest that differences in prenatal maternal investment have no impact on adult brain size. To the contrary, recent evidence suggests that neonate and adult brain size are positively correlated in precocial species, but not in altricial species (5, 20). Thus, the question of what developmental mechanisms underpin the evolution of differences in brain size requires further investigation. Given that different neurodevelopmental processes are concentrated in different phases (21), and that opportunities for environmental input occur principally after birth, determining the developmental mechanisms of brain size evolution is likely to be important for understanding its neuroanatomical and functional consequences.

Here we examine the developmental mechanisms underlying mammalian brain size evolution, and comprehensively test pre-

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dictions of the developmental costs hypothesis. Specifically, we examine the contributions of both pre- and postnatal growth to variation in adult brain size, and test the prediction that these phases correlate specifically with gestation and lactation duration, respectively, even after controlling for other reproductive and life history variables. We also test whether costs are accommodated through tradeoffs between brain and body growth, or between brain size and litter size, and we evaluate at which stage, if any, maternal metabolic rate is related to brain growth. We evaluate the relative statistical power of developmental costs and cognitive buffer hypotheses as explanations for correlations between brain size and life history, by testing whether brain size is independently associated with maternal investment and other life history variables, such as lifespan. We use phylogenetic generalized linear models (PGLMs) to test for correlated evolution among traits. We explore the effects of specific variables on the explanatory power of the models by statistically comparing models with versus without the variables in question using the log-likelihood ratio (LR) test (*Methods*).

Results

Pre- and Postnatal Contributions to Adult Brain Size. Adult and neonate brain size are positively correlated, controlling for both adult and neonate body mass (Fig. 1 and Table 1). Additionally controlling for gestation duration effectively turns neonate brain size into a rate of relative brain growth (i.e., tests whether adult brain size increases with the amount of prenatal brain growth relative to prenatal body growth and the amount of time in utero); when this is done, adult brain size is significantly positively correlated with neonate brain size ($t_{117} = 5.54$, $P < 0.001$). Neonate body mass was not associated with adult brain size independently of neonate brain size: adding neonate mass to the predictors did not improve the model fit (model 1 versus model 2 in Table 1; $LR_1 = 1.8$, $P > 0.05$), and neonate body mass correlates with adult brain size only when neonate brain size is excluded from the model ($t_{118} = 3.71$, $P < 0.001$). The addition of postnatal brain growth to model 1 significantly improves the fit of the initial model (model 1 vs. model 3 in Table 1; $LR_1 = 269.9$, $P < 0.001$, increase in R^2 from 0.92 to 0.99), and both neonate brain size and postnatal brain growth are significant predictors. Hence, variation in brain size at birth and in the amount of brain growth postnatally have independent influences on adult brain size.

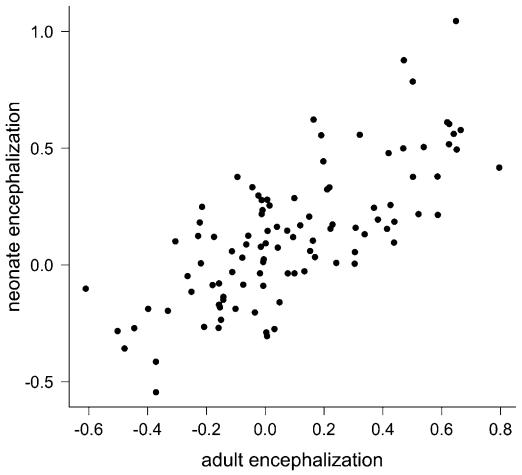

Fig. 1. Association between relative brain size of neonate and adult mammals. Encephalization scores are the residuals from phylogenetic generalized linear models for brain size on the appropriate body size (neonate or adult). Table 1 provides results of statistical analysis.

Emphasizing the independent contributions of fetal and postnatal growth to adult brain size, neonate brain size and postnatal brain growth are uncorrelated, controlling for neonate body mass and maternal mass ($t_{119} = 1.30$, $P > 0.1$). There was also no significant interaction between the effects of neonatal brain size and postnatal brain growth on adult brain size when this interaction term was added to model 1 ($t_{118} = -0.84$, $P > 0.1$). These results therefore suggest that there is no tradeoff between pre- and postnatal brain growth, and that their effects on adult brain size are additive rather than multiplicative.

Correlates of Neonate Brain Size. Accounting for allometric effects (neonate body mass and maternal body mass), neonate brain size is positively associated with gestation duration (Table 2, model 1). Adding litter size to the predictors in model 1 did not improve the model fit ($LR_1 = 1.18$, $P > 0.1$), and litter size was not significantly associated with neonate brain size (Table 2, model 2). To check that the apparent effect of gestation duration is not simply a side effect of some more general growth or early life history correlate of brain size, lactation duration was added as a predictor to model 1: neonate brain size remained significantly associated with gestation duration ($t_{105} = 6.14$, $P < 0.001$) but was unrelated to lactation duration ($t_{105} = 0.77$, $P > 0.1$), and the likelihood ratio test for models with and without lactation was nonsignificant ($LR_1 = 0.6$, $P > 0.5$). Because the relationship between brain growth and litter size may interact with developmental state [i.e., a tradeoff occurs in altricial but not in precocial species (5)], we ran a model with developmental state and the interaction between developmental state and litter size added as predictors. The effects of neonate mass, maternal mass, and gestation duration remained significant (neonate mass, $t_{102} = 5.34$, $P < 0.001$; maternal mass, $t_{102} = 3.64$, $P < 0.001$; gestation duration, $t_{102} = 4.91$, $P < 0.001$), and in addition there was a significant effect of developmental state (precociality is associated with larger brain size: $t_{102} = 2.49$, $P < 0.05$). However, there was still no main effect of litter size ($t_{102} = 0.11$, $P > 0.5$), nor a significant interaction between developmental state and litter size ($t_{102} = -1.81$, $P > 0.05$). Note that maternal size was positively associated with neonate brain size in these analyses, even after controlling for other variables, suggesting that larger females produce more encephalized offspring, reiterating the importance of maternal investment. Note also that, in all analyses, neonate brain size increases with neonate body size, showing no signs of a tradeoff between neural and somatic growth.

We tested for a possible association of BMR with neonatal brain size, controlling for neonate body mass, maternal body mass, and gestation duration. Gestation duration remained a significant predictor of neonate brain size ($t_{40} = 6.41$, $P < 0.001$), and BMR was also positively correlated with neonate brain size ($t_{40} = 3.07$, $P < 0.01$). The model including BMR provided a significantly better fit than the one omitting it ($LR_1 = 7.50$, $P < 0.01$, increase in R^2 from 0.93 to 0.96). BMR remained positively correlated with neonate brain size when controlling for body size by using mass of individuals from which the BMR data were obtained ($t_{40} = 3.27$, $P < 0.01$). With litter size, developmental state, and their interaction, added as predictors in the model, neonate brain size was still significantly positively related to gestation duration ($t_{38} = 2.94$, $P < 0.01$) and BMR ($t_{39} = 2.21$, $P < 0.05$), but unrelated to litter size ($t_{38} = -1.03$, $P > 0.1$), developmental state ($t_{38} = -0.61$, $P > 0.5$), and their interaction ($t_{38} = -0.67$, $P > 0.5$). Gestation duration and BMR were uncorrelated after controlling for female body mass ($t_{42} = -1.67$, $P > 0.1$). Hence, these results are consistent with the hypothesis that BMR constrains neonate brain size directly via effects on fetal brain growth rate rather than indirectly through effects on gestation duration (22).

Table 1. PGLM analysis of pre- and postnatal contributions to adult brain size, controlling for body size

	Model 1	Model 2	Model 3
Parameter (n = 122)	t (P value)	t (P value)	t (P value)
Intercept	−3.1 (<0.01)	−2.88 (<0.01)	4.75 (<0.001)
Neonatal brain size	6.82 (<0.001*)	6.07 (<0.001*)	17.12 (<0.001*)
Adult body size	9.61 (<0.001*)	8.77 (<0.001*)	3.95 (<0.001*)
Neonatal body mass	—	−1.54 (0.13)	—
Postnatal brain growth	—	—	31.2 (<0.001*)
λ	0.79	0.74	0.70
P value (λ = 0)	<0.001	<0.001	<0.001
P value (λ = 1)	<0.001	<0.01	<0.001
Model summary			
Maximized log-likelihood	55.39	56.29	190.35
Adjusted R^2	0.917	0.923	0.991

Variables not included in a particular model are indicated by dashes. λ is the estimated ML value of the phylogenetic signal, included as a parameter in the models, with P values for tests of statistical difference from a model with no phylogenetic signal (λ = 0) and a model with a λ of 1.
*Significant predictors of adult brain size.

Correlates of Postnatal Brain Growth. Relative postnatal brain growth (controlling for postnatal body growth) is positively associated with lactation duration but not litter size (Table 3). Mirroring the analyses of neonatal brain size, gestation duration was added to the predictors to check that the apparent effect is specific to lactation duration. Postnatal brain growth remained significantly associated with lactation and was unrelated to gestation duration (model 3, Table 3). Similarly, the effect of lactation duration remained significant when age at first reproduction or juvenile period (the interval between weaning and sexual maturity) is added as a predictor (models 3 and 4, Table 3), indicating that it is specifically prolongation of lactation, rather than a general slowing of postnatal maturation, that is associated with increased postnatal brain growth. Results of the test comparing model 4 (including juvenile period) with model 1 are nonsignificant (LR_1 = 3.02, $P > 0.05$), reinforcing the lack of an independent effect of juvenile period. The addition of developmental state at birth, litter size, and their interaction to the predictors in model 1 (Table 3) revealed no main effects (developmental state, $t_{89} = -0.30$, $P > 0.5$; litter size, −0.12, $P > 0.5$) or interaction ($t_{89} = -0.09$, $P > 0.5$). Hence, controlling for allometry, postnatal brain growth is robustly associated with lactation duration but not with litter size, developmental state, or juvenile period. As for prenatal development, in all these analyses, brain growth is positively associated with body growth, suggesting no tradeoff between neural and somatic growth.

Table 2. PGLM analysis of neonate brain size. n = 128

	Model 1	Model 2
Parameter	t (P value)	t (P value)
Intercept	−2.60 (<0.001)	−2.49 (<0.001)
Neonatal body mass	6.05 (<0.001*)	6.00 (<0.001*)
Maternal body size	3.13 (<0.01*)	3.25 (<0.01*)
Gestation	7.20 (<0.01*)	6.38 (<0.001*)
Litter size	—	−1.14 (>0.1)
λ	0.90	0.90
P value (λ = 0)	<0.001	<0.001
P value (λ = 1)	<0.01	<0.01
Model summary		
Maximized log-likelihood	58.06	58.65
Adjusted R^2	0.92	0.92

Details are the same as in Table 1.
*Significant predictors of neonate brain size.

Although age at first reproduction was unrelated to postnatal brain growth when lactation was in the model, if lactation was removed from the predictors, age at first reproduction became significant (t_{92} = 2.70, $P < 0.01$). This is consistent with the prediction of developmental costs hypotheses that the correlation between large brains and later age at first reproduction is a consequence of prolonged maternal investment. The specific association between brain growth and lactation was further reinforced when a similar model was run for the postlactation juvenile period, as the latter variable remains nonsignificant even without lactation in the model (t_{92} = 1.80, $P > 0.05$).

There were no significant associations between postnatal brain growth and milk composition (Table 4) or daily milk energy intake per offspring (controlling for lactation and body growth, $t_{20} = -0.28$, $P > 0.5$). We tried running models with different combinations of milk composition and intake variables, but obtained no significant results (Table S1).

Adding BMR to the predictors, postnatal brain growth is significantly positively related to both lactation (t_{39} = 4.14, $P < 0.001$), and BMR (t_{39} = 2.84, $P < 0.05$). However, the association with BMR appears to be driven by *Homo sapiens*, which is a large outlier in the regression of postnatal brain growth on body size and lactation (residual approximately three SDs larger than the mean). When humans were excluded from the analysis, there was no significant relationship between postnatal brain growth and BMR (controlling for size with female body mass, $t_{38} = 1.45$, $P > 0.05$; controlling for size using BMR sample body mass estimates, $t_{38} = 1.10$, $P > 0.05$). In addition, even if humans were included, there was no significant association between postnatal brain growth and BMR when BMR sample body mass instead of mean female body mass was used to control for size ($t_{39} = 0.92$, $P > 0.1$). Postnatal brain growth remained positively associated with lactation in all models. Finally, BMR was not associated with lactation, controlling for either maternal body mass ($t_{41} = -0.75$, $P > 0.5$), or BMR sample body mass ($t_{41} = -0.08$, $P > 0.5$), ruling out an indirect relationship between BMR and postnatal brain growth mediated by duration of lactation.

Is the Association Between Brain Size and Life History Independent of Maternal Investment? Controlling for adult body size, adult brain size is significantly positively associated with age at first reproduction (t_{80} = 3.02, $P < 0.01$). However, inclusion of the duration of maternal investment (gestation plus lactation) in the model provides a significantly better fit (LR_1 = 11.52, $P < 0.001$, increase in R^2 from 0.89 to 0.91). Furthermore, in this improved model, maternal investment is significantly associated with brain

Table 3. PGLM analysis of postnatal brain growth (n = 96)

	Model 1	Model 2	Model 3	Model 4	Model 5
Parameter	t (*P* value)	t (*P* value)	t (*P* value)	t (*P* value)	t (*P* value)
Intercept	−8.41 (<0.001)	−8.13 (<0.001)	−5.56 (<0.001)	−8.54 (<0.001)	−9.64 (<0.001)
Postnatal body growth	17.60 (<0.001*)	17.47 (<0.001*)	13.89 (<0.001*)	14.13 (<0.001*)	14.67 (<0.001*)
Lactation	3.83 (<0.001*)	3.78 (<0.001*)	3.75 (<0.001*)	3.06 (<0.01*)	3.80 (<0.001*)
Litter size	—	0.18 (>0.5)	—	—	—
Gestation	—	—	−0.05 (>0.5)	—	—
AFR	—	—	—	1.69 (>0.1)	—
Juvenile period	—	—	—	—	1.82 (>0.05)
λ	0.67	0.67	0.67	0.60	0.57
P value (λ = 0)	<0.01	<0.01	<0.01	>0.05	>0.1
P value (λ = 1)	<0.001	<0.001	<0.001	<0.001	<0.001
Model summary					
Maximized log-likelihood	1.01	1.03	1.01	2.38	2.52
Adjusted R^2	0.85	0.85	0.85	0.86	0.87

Details are the same as in Table 1. AFR, age at first reproduction.
*Significant predictors of postnatal brain growth.

size (t_{79} = 3.53, $P < 0.001$), but age at first reproduction is not (age at first reproduction, t_{79} = 1.58, P = 0.12). Juvenile period is not significantly associated with brain size with or without maternal investment in the model (with, t_{79} = 1.30, $P > 0.1$; without, t_{80} = 1.85, $P > 0.05$), and again the model including maternal investment provides a better fit than that without (LR_1 = 11.52, $P < 0.001$; increase in R^2 from 0.89 to 0.91). Finally, controlling for body size, adult lifespan is positively correlated with brain size (t_{80} = 2.96, $P < 0.01$), but inclusion of the duration of maternal investment in the model provides a significantly better fit (LR_1 = 12.1, $P < 0.001$, increase in R^2 from 0.89 to 0.91), and in this improved model, maternal investment is significantly correlated with brain size (t_{79} = 3.52, $P < 0.001$), but adult lifespan is not (t_{79} = 1.32, P = 0.19).

Discussion

Our results suggest that larger brains take longer to grow pre- and postnatally, resulting in prolonged maternal investment. Whilst not ruling out the idea that large brains facilitate enhanced survival and slower, longer lives through a generalized cognitive buffer effect, the specificity of the correlations between brain growth and associated phases of maternal investment, together with the fact that postnatal life histories are uncorrelated with adult brain size after taking maternal investment into account, strongly support the argument that life history correlates reflect the developmental costs of large brains (9). Our results provide support for both the maternal energy hypothesis (11, 12) and the broader "expensive brain" hypothesis (5), although, as predicted by Charnov and Berrigan (9), some of the tradeoffs reported previously (5) appear to be secondary consequences of the fundamental variable of the rate at which mothers can convert energy into offspring. In particular, neither litter size nor its interaction with developmental state added any explanatory power to the statistical models after gestation, lactation, and allometry were accounted for. We conclude that brain growth is primarily related to the duration and rate of maternal investment, with the apparent tradeoff with litter size, and differences in correlates between altricial and precocial species, being secondary consequences of variability in gestation and lactation. We found that precocial species give birth to larger-brained offspring even after controlling for body size and gestation length. This indicates that the rate, as well as the duration, of fetal brain growth is increased in precocial compared with altricial species, and that the state of the offspring at birth is not entirely determined by the duration of gestation.

We found no evidence of tradeoffs between brain growth and body growth pre- or postnatally, nor between the amount of brain growth pre- versus postnatally. Indeed, relative amounts of

Table 4. PGLM analysis of postnatal brain growth, lactation and milk composition (n = 48)

	Model 1	Model 2	Model 3	Model 4	Model 5
Parameter	t (*P* value)	t (*P* value)	t (*P* value)	t (*P* value)	t (*P* value)
Intercept	−6.94 (<0.001)	−8.28 (<0.001)	−6.25 (<0.001)	−7.28 (<0.001)	−7.42 (<0.001)
Postnatal body growth	13.87 (<0.001*)	13.65 (<0.001*)	15.02 (<0.001*)	14.09 (<0.001*)	14.56 (<0.001*)
Lactation	4.20 (<0.001*)	4.19 (<0.001*)	4.19 (<0.001*)	4.17 (<0.001*)	4.31 (<0.001*)
Dry matter, %	0.81 (>0.1)	—	—	—	—
Fat, %	—	0.71 (>0.1)	—	—	—
Protein, %	—	—	−0.24 (>0.5)	—	—
Sugar, %	—	—	—	−0.04 (>0.5)	—
Milk energy	—	—	—	—	0.66 (>0.5)
λ	0.10	0.14	0.25	0.23	0.16
P value (λ = 0)	>0.5	>0.5	>0.1	>0.1	>0.5
P value (λ = 1)	<0.001	<0.001	<0.001	<0.001	<0.001
Summary					
Maximized log-likelihood	0.55	0.52	0.33	0.30	0.51
Adjusted R^2	0.92	0.92	0.90	0.91	0.91

Details are the same as in Table 1.
*Significant predictors of adult brain.

pre- and postnatal brain growth were uncorrelated, consistent with independent genetic control of these two phases of brain growth (19), and suggesting that they have additive rather than multiplicative or mutually compensating effects on adult brain size. These findings raise the important question for future research of what structural and functional implications follow from evolutionary changes in pre- versus postnatal brain growth, and whether changes in the two different phases are associated with different selection pressures.

Models of life history evolution tend to assume that organisms vary along a single "slow–fast" continuum, implying that different components of life history, such as growth, reproductive rate, and lifespan, are tightly interlinked, and thus that ratios between them are invariant across taxa (23, 24). This assumption has recently been challenged (25, 26). Phylogenetic factor analyses reveal that there are at least two distinct dimensions (25). The first loads heavily on gestation duration and neonate size and less consistently on litter size. The second factor loads heavily on interbirth interval, age at weaning, and age at sexual maturity. Interestingly, these two factors correspond broadly to the pre- and postnatal influences on brain growth identified here. We suggest that brain size may be a key consideration in understanding how life history traits evolved. Although explanations of life history evolution have focused on body size and environmental factors such as mortality, brain size may represent an intrinsic factor, the role of which has so far been underappreciated (4).

Our results clarify the long-disputed relationship between brain size and metabolic rates. The maternal energy hypothesis (11, 12) suggests that BMRs constrain maternal investment in brain growth, but direct evidence linking BMR to neonate brain size has been lacking, with the only analysis of those variables finding no relationship (16). We have shown that neonate brain size correlates positively with BMR after taking body size and gestation length into account, supporting the hypothesis that the metabolic rate of the mother constrains the rate of brain growth in the fetus (12). However, the hypothesis that metabolic rate influences prenatal brain growth through an effect on gestation duration (22) was not supported, as there was no significant correlation between BMR and gestation duration. The restriction of an effect of BMR to the prenatal period, together with the significant effects of other maternal investment variables, also clarifies why the positive association between BMR and adult brain size is relatively weak (13).

Although it has been suggested that the structure of the placenta might influence nutrient transfer and hence prenatal brain growth (15, 27), recent comparative studies find no evidence for a specific relationship between placental structure and brain growth (28, 29). Capellini et al. found that variation among mammals in placental structure correlated with fetal growth rates and gestation duration, but not with neonate brain size (28). How higher metabolic rates are translated into additional physiological support for fetal brain growth is thus an important and yet-unanswered question.

We were unable to find any relationship between brain growth and milk composition, milk energy value, or daily milk energy intake at peak lactation. Although sample sizes were relatively small in the analyses of milk composition, the lack of an association with brain growth accords with the observation that convergent evolution of large brain size and extended postnatal brain growth in humans and capuchin monkeys (*Cebus apella*) has not resulted in convergence in milk composition (30).

The developmental basis of the evolution of large brain size in humans has often been considered to be an exceptional prolongation of postnatal brain growth, creating enhanced opportunities for environmental input to the developing brain (31–33). However, Vinicius (34) showed that the ways in which human brain and body growth patterns depart from those of other primates are more complex than this, including at least three distinct mechanisms: (*i*) a moderate extension of postnatal brain growth, (*ii*) a derived developmental allometry, and (*iii*) a retardation of postnatal body growth. The first mechanism fits the general link between lactation and postnatal brain growth reported here, and suggests that brain size may be a better predictor of the "natural" weaning age for humans than is body size. The second mechanism (34) suggests a difference in the rate of brain growth between humans and other anthropoids, congruent with our finding that variation in brain growth rates, as well as durations, contribute to adult brain size. As we noted earlier, the physiological mechanisms of differences in brain growth rates remain unknown. Finally, the third mechanism (34) implies a tradeoff between postnatal brain and body growth; we found no evidence for this as a general pattern among eutherian mammals, so its occurrence in humans must be presumed to be evolutionarily unusual.

In conclusion, our results emphasize the energetic costs of brain development as a driver of associations between brain size and life history in mammals. Although large brains undoubtedly confer benefits, we found no support for hypotheses predicated on specific associations between brain size and juvenile period (35) or adult lifespan (6, 7). It is still possible that large brains operate as cognitive buffers, as the selective advantage of slower-growing, larger brains may be reduced mortality mediated by cognitive capacities (4, 7). However, the cognitive buffer hypothesis as formulated assumes that such cognitive capacities are "domain-general," facilitating survival and long lifespans through increased behavioral flexibility (6). The lack of a significant association between brain size and adult lifespan after controlling for maternal investment suggests that it is not specifically lifespan and an associated need for flexibility that drives the patterns, undermining the link made between life history correlations of brain size and domain-general cognitive benefits (6). Given that brain size evolution in mammals is associated with a variety of specific neural systems and structures (36–38), domain-specific mechanisms should be given equal consideration in attempts to establish the cognitive benefits that offset the developmental costs of large brains.

Methods

Data. We extracted data from the literature for 128 eutherian mammal species on the following variables: (*i*) neonate and adult brain and body masses, with postnatal growth calculated as the difference between neonate and adult values; (*ii*) developmental, maternal investment, and life history variables of litter size, developmental state at birth (altricial if eyes closed at birth vs. precocial if eyes open at birth), duration of gestation (in d), duration of lactation (in d), milk composition (as percentages of fats, proteins, and sugars), and milk energetic value, daily milk energy intake, age at first reproduction (in d), and lifespan (in d); and (*iii*) BMR (mL O_2/h) and body masses for the animals from which the BMR data were taken (body $mass_{BMR}$, in g). Further details of data and sources and the full data set are provided in *SI Methods* and Dataset S1.

Statistical Analysis. We investigated the correlated evolution of brain size, body size, maternal investment, and life history variables by using PGLMs, which allowed us to incorporate phylogeny into statistical models (39–41). In PGLM analysis, regression parameters are found by maximum likelihood (ML) and "weighted" by the variance–covariance matrix that represents the phylogenetic relationships among the species. In each regression, the phylogenetic signal is estimated as the value of λ of the residuals, varying between 0 (at which data have no phylogenetic structure) and 1 [at which the best fit to the data is provided by a Brownian motion model of trait evolution (42)], with variation at the tips proportional to the duration of common evolution (41–43). We report tests for significant departure of λ from 0 or 1. The estimated ML value of λ is incorporated as a parameter in the model, thus controlling for phylogenetic dependence in the data. Incorporating a discrete binary trait, such as developmental state, as a predictor in regression models amounts to a phylogenetic analysis of covariance. More complex models are compared to simpler models to investigate whether incorporating additional variables of interest provides a better fit to the data. Our tables of results indicate which variables were

included in each model, significance tests for these variables, and overall model parameters: values of λ, R^2 values, and LR scores. Alternative nested models are compared by using the likelihood ratio (LR) test (where LR=-2*[(log-likelihood of better fitting model)-(log-likelihood of worse fitting model)], the best fitting model having the highest log-likelihood score). Significance is evaluated against a χ^2 distribution with degrees of freedom corresponding to the difference in the number of parameters between the two competing models (39, 43). All statistical tests were two-tailed, with α level of significance set at 0.05. These analyses were carried out using the CAIC R package (R, version 2.11.1). The phylogeny (including branch lengths) for the species in our dataset was extracted from a published supertree of mammals (44).

Continuous variables were $\log_{10}$-transformed to improve normality, with the exception of milk composition (percentage) data, which were square-rooted and then arcsine-transformed (45). Bivariate plots and residuals were examined to check for violation of homogeneity of variance. We checked for the effects of outliers by rerunning analyses after deleting data points generating large residuals (greater than the mean by three SDs or more). However, removing outliers qualitatively affected conclusions in only one case. This outlier was caused by a data point for humans. Because humans are particularly large-brained, they potentially exert high leverage on regressions; hence, we reran analyses with and without humans, but the outcome was affected in just the one case mentioned in *Results*, so we report results including humans unless otherwise stated.

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