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Title: Brain size, life histories and maternal investment in eutherian mammals

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Abstract

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 both 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 post-natal 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 trade-offs between brain and body growth, or between brain growth and litter size. Once 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.

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Brain size varies extensively between 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, 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 between brain size, survival and lifespan[6-7]. Developmental costs hypotheses on the other hand, assume that brain growth has to be 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 whether 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 length, but these were conducted either 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

85 correlates with BMR[8,13], evidence that this reflects maternal metabolic constraints
86 on either pre- or postnatal brain growth is lacking[16].

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

104 Here we use phylogenetic comparative methods to examine the
105 developmental mechanisms underlying mammalian brain size evolution, and
106 comprehensively test predictions 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 trade-offs 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. To these ends, we use phylogenetic generalized linear models (PGLM) 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 (see Methods).

Results

Pre- and post-natal contributions to adult brain size. Adult and neonate brain size are positively correlated, controlling for both adult and neonate body mass (Figure 1 and Table 1). Additionally controlling for gestation length 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

129 growth and the amount of time *in utero*); when this is done, adult brain size is
130 significantly positively correlated with neonate brain size (t_{117}=5.54, p<0.001).
131 Neonate body mass was not associated with adult brain size independently of
132 neonate brain size: adding neonate mass to the predictors did not improve the
133 model fit (model 1 versus model 2 in Table 1; LR_1=1.8, p>0.05), and neonate body
134 mass correlates with adult brain size only when neonate brain size is excluded from
135 the model (t_{118}=3.71, n=122, p<0.001). The addition of post-natal brain growth,
136 however, significantly improves the fit of the initial model (model 1 versus model 3
137 in Table 1; LR_1=269.9, p<0.001, increase in R^2 from 0.92 to 0.99). The effect sizes (as
138 estimated by t-values in model 3) suggest that postnatal brain growth may be a
139 stronger predictor of adult brain size, and running the initial model with postnatal
140 brain growth instead of neonate brain size yields a higher R^2 (0.97). Nevertheless,
141 the likelihood ratio test comparing model 3 to the same model but without neonate
142 brain size is highly significant (LR_1=70.89, p<0.001). Hence, variation in brain size at
143 birth and in the amount of brain growth postnatally have independent influences on
144 adult brain size.

145 Neonate brain size and postnatal brain growth are uncorrelated, controlling
146 for neonate body mass and maternal mass (t_{119}=1.30, p>0.1), further emphasizing
147 the independent contributions of fetal and postnatal growth to adult brain size.
148 There was also no significant interaction between the effects on adult brain size of
149 neonatal brain size and postnatal brain growth when this interaction term was
150 added to model 1 (t_{118}=-0.84, p>0.1). These results therefore suggest that there is no

151 trade-off between pre- and postnatal brain growth, and that their effects on adult
152 brain size are additive rather than multiplicative.

153

154 **Correlates of neonate brain size.** Accounting for allometric effects (neonate body
155 mass and maternal body mass), neonate brain size is positively associated with
156 gestation length (Table 2, model 1). Adding litter size to the predictors in model 1
157 did not improve the model fit (LR_1=1.18, p>0.1) and litter size was not significantly
158 associated with neonate brain size (Table 2, model 2). To check that the apparent
159 effect of gestation length is not simply a side-effect of some more general growth or
160 early life-history correlate of brain size, lactation length was added as a predictor to
161 model 1 (reducing sample size to 111): neonate brain size remained significantly
162 associated with gestation length (t_{105}=6.14, p<0.001) but was unrelated to lactation
163 length (t_{105}=0.77, p>0.1), and the likelihood ratio test for models with and without
164 lactation was non-significant (LR_1=0.6, p>0.5). Because the relationship between
165 brain growth and litter size may interact with developmental state (i.e. a trade-off
166 occurs in altricial but not in precocial species[5]), we ran a model with developmental
167 state and the interaction between developmental state and litter size added as
168 predictors. The effects of neonate mass, maternal mass and gestation length
169 remained significant (neonate mass, t_{102}=5.34, p<0.001; maternal mass, t_{102}= 3.64,
170 p<0.001; gestation length, t_{102}=4.91, p<0.001), and in addition there was a
171 significant effect of developmental state (precociality is associated with larger brain
172 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 these analyses, neonate brain size increases with neonate body size, hence showing no signs of a trade-off 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 length. Gestation length 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 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 using masses of individuals from which the BMR data were obtained instead of species average female body mass (t_{40}=3.27, p<0.01). With litter size and developmental state, and their interaction, added as predictors in the model, neonate brain size was still significantly positively related to gestation length (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 length 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 length[22].

Correlates of postnatal brain growth. The relative amount of postnatal brain growth (controlling for effects of postnatal body growth) is associated with lactation duration (Table 3). Litter size was not significantly related to postnatal brain growth (model 2, table 3). Mirroring the analyses of neonatal brain size, gestation length was added to the predictors to check that the apparent effect is specific to lactation length. Postnatal brain growth remained significantly associated with lactation and was unrelated to gestation length (model 3, Table 3). Similarly, the effect of lactation length remains significant when either age at first reproduction or juvenile period 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. The test comparing model 4 (including juvenile period) to model 1 is non-significant (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 length and not with litter size, developmental state, or juvenile period. As was the case for prenatal development, in all these analyses brain growth is

positively associated with body growth, hence showing no signs of a trade-off between neural and somatic growth.

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 is further reinforced when a similar model is run for the post-lactation juvenile period, as the latter variable remains non-significant 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; note that the effect of lactation remained significant in this smaller sample). In a smaller subset of the data (n=23) for which daily milk energy intake per offspring was available, there was also no significant association between this variable and postnatal brain growth (controlling for lactation and body growth, t=-0.28, p>0.5). We tried running models with different combinations of milk composition and intake variables, but obtained no significant results (see Table S1 in supplementary information).

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 standard deviations 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 masses 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 masses (t_{41}=-0.08, p>0.5), ruling out an indirect relationship between BMR and postnatal brain growth mediated by length 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+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 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 (the interval between

261 weaning and sexual maturity) is not significantly associated with brain size either
262 with or without maternal investment in the model (with, t_{79}=1.30, p>0.1; without,
263 t_{80}=1.85, p>0.05), and again the model including maternal investment provides a
264 better fit than that without (LR_1=11.52, p<0.001; increase in R^2 from 0.89 to 0.91).
265 Finally, controlling for body size, adult lifespan is positively correlated with brain
266 size (t_{80}=2.96, p<0.01, n=85), but inclusion of the duration of maternal investment in
267 the model provides a significantly better fit (LR_1=12.1 , p<0.001, increase in R^2 from
268 0.89 to 0.91), and in this improved model, maternal investment is significantly
269 correlated with brain size (t_{79}=3.52, p<0.001) but adult lifespan is not (t_{79}=1.32,
270 p=0.19).

271

272 **Discussion**

273 Our results suggest that larger brains take longer to grow both pre- and
274 postnatally, resulting in prolonged maternal investment. Whilst not ruling out the
275 idea that large brains facilitate enhanced survival and slower, longer lives through a
276 generalized "cognitive buffer" effect, the specificity of the correlations between
277 brain growth and associated phases of maternal investment, together with the fact
278 that postnatal life histories are uncorrelated with adult brain size after taking
279 maternal investment into account, strongly support the argument that life history
280 correlates reflect the developmental costs of large brains[9]. Our results provide
281 support for both the maternal energy hypothesis[11,12] and the broader "expensive
282 brain" hypothesis[5], although, as predicted by Charnov & Berrigan[9], some of the

283 trade-offs reported previously[5] appear to be secondary consequences of the
284 fundamental variable of the rate at which mothers can convert energy into offspring.
285 In particular, neither litter size nor its interaction with developmental state added
286 any explanatory power to the statistical models once gestation, lactation and
287 allometry were accounted for. We conclude that brain growth is primarily related to
288 the duration and rate of maternal investment, with the apparent trade-off with litter
289 size, and differences in correlates between altricial and precocial species, being
290 secondary consequences of variability in gestation and lactation. We did however
291 find that precocial species give birth to larger-brained offspring even after
292 controlling for body size and gestation length. This indicates that the rate, as well as
293 the duration, of fetal brain growth is increased in precocial compared to altricial
294 species, and suggests that the state of the offspring at birth is not entirely
295 determined by the length of gestation.

296 We found no evidence of trade-offs between brain growth and body growth
297 either pre- or postnatally, nor between the amount of brain growth pre- versus
298 postnatally. Indeed, relative amounts of pre- and postnatal brain growth are
299 uncorrelated, consistent with independent genetic control of these two phases of
300 brain growth[19] and suggesting that they have additive rather than either
301 multiplicative or mutually compensating effects on adult brain size. These findings
302 raise the important questions for future research of what structural and functional
303 implications follow from evolutionary changes in pre- versus postnatal brain
304 growth, and whether changes in the two different phases are associated with
305 different selection pressures.

306 Models of life history evolution have tended to assume that organisms vary
307 along a single "slow-fast" continuum, implying that different components of life
308 history such as growth, reproductive rate and lifespan, are tightly interlinked, and
309 thus that ratios between them are invariant across taxa[23-24]. This view has recently
310 been challenged on both theoretical and empirical grounds[25-26]. Empirically,
311 dissection of mammalian life history variation using phylogenetic factor analyses
312 identified two distinct dimensions[25]. The first loads heavily on gestation length,
313 neonate size and – though less consistently - on litter size. The second factor loads
314 heavily on inter-birth interval, age at weaning and age at sexual maturity. Our
315 results suggest that brain size may be a key consideration in understanding how
316 such life history traits evolved, and we note that the two factors identified[25]
317 correspond broadly to pre- and postnatal influences on brain growth respectively.
318 We predict that neonatal brain size would load heavily on the first factor and
319 postnatal brain growth on the second. Although explanations of life history
320 evolution have focused on body size and environmental factors such as mortality,
321 brain size may represent an intrinsic factor whose role has so far been under
322 appreciated[4].

323 Our results clarify the long-disputed relationship between brain size and
324 metabolic rates. The maternal energy hypothesis[11,12] suggests that basal metabolic
325 rates constrain maternal investment in brain growth, but direct evidence linking
326 BMR to neonate brain size has been lacking, with the only analysis of those variables
327 finding no relationship[16]. Our analysis shows that neonate brain size correlates
328 positively with BMR after taking phylogeny, allometry and gestation length into

account. Since the correlation is evident when controlling for gestation length, it supports the hypothesis that the metabolic rate of the mother constrains the rate of brain growth in the foetus[12]. The finding is also consistent with the hypothesis that the correlation between brain size and BMR is a placental (but not marsupial) trait "related to the intimate physiological contact between mother and offspring during gestation" [8]. The hypothesis that metabolic rate influences prenatal brain growth through an effect on gestation length[22] was however, not supported; there was no significant correlation between BMR and gestation length after controlling for other factors. The restriction of an effect of BMR to the prenatal period together with the significant effects of other maternal investment variables operating at least partly independently of one another 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]. 'Labyrinthine' placentas, in which maternal and fetal tissues are highly interdigitated, are associated with shorter gestations but no difference in neonate brain or body size, suggesting that fetal growth rates are faster in species with labyrinthine placentas[28]. However, there was no difference in the relative brain size of neonates, indicating that higher growth rates are not targeted specifically at the brain[28]. How higher metabolic rates are translated into additional physiological support for fetal brain growth is thus an important and so far unanswered question.

One possibility is that energy turnover constrains the ability of the mother to supply the fetus with specific nutrients, such as long-chain fatty acids[26].

Similarly, although relative rates of postnatal brain growth are likely to vary, we were unable to find any relationship between brain growth and milk composition, milk energy value or daily milk energy intake at peak lactation. This finding agrees 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]. However, sample sizes were relatively small in our analyses of milk composition in relation to postnatal brain development, and re-analysis with larger data sets when these become available would be interesting, as would analysis of specific nutrients that may play a role in postnatal brain development.

The issue of evolutionary changes in rate versus duration of brain growth is important for understanding the developmental basis of human brain evolution. Most discussions of this subject assume that large relative brain size in humans was developmentally achieved via an exceptional prolongation of postnatal brain growth, creating enhanced opportunities for environmental input to the developing brain[31-33]. A re-analysis by Vinicuis[34] however shows 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: a moderate extension of postnatal brain growth, a derived developmental allometry and 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. Vinicius' 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 note above, the physiological mechanisms that co-vary with brain growth rates remain unknown. Finally, Vinicius' third mechanism[34] implies a trade-off 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. Whilst large brains undoubtedly confer benefits, we found no support for hypotheses predicated on specific associations between brain size and either juvenile period[35] or adult lifespan[6-7]. It is still possible that large brains operate as "cognitive buffers", since 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

396 domain-general cognitive benefits[6]. Given that brain size evolution in mammals is
397 associated with a variety of specific neural systems and structures[36-38,] domain-
398 specific mechanisms should be given equal consideration in attempts to establish
399 the cognitive benefits that offset the developmental costs of large brains.

400

401 **Methods**

402 **Data.** We extracted data from the literature on 128 eutherian mammal species as follows.
403 (i) Brain and body masses: neonate brain and body mass, adult brain and body mass,
404 maternal (adult female) body mass (all in grams). Postnatal growth (brain or body) was
405 calculated as the difference between adult size and neonate size. (ii) Developmental,
406 maternal investment and life history variables: litter size (number of offspring per litter),
407 developmental state at birth (altricial if eyes closed at birth, versus precocial if eyes open at
408 birth), duration of gestation (days), duration of lactation (days), milk composition (as % of
409 fats, proteins and sugars) and milk energetic value (as sum of the energy provided by its
410 components, given milk composition; in KJ) both at peak lactation, daily milk energy intake
411 (milk energetic value multiplied by daily milk intake in ml/day at peak lactation; in KJ/day),
412 age at first reproduction (days), lifespan (days). (iii) Basal metabolic rate (BMR, ml
413 O_2/hour) together with body masses for the animals from which the BMR data were taken
414 (Body $mass_{BMR,}$ in g). We used only estimates of BMR that fulfilled the requirements of the
415 protocol described in McNab[39] (measurement in thermoneutral environment, on adult non-
416 reproducing individuals, quietly resting and post-absorptive). Further details of data and
417 sources and the full data set are provided in supplementary information (Text_S1 and
418 Dataset_S1).

Statistical analysis. We investigated the correlated evolution of brain size, body size, maternal investment and life history variables using phylogenetic generalized linear models (PGLM)[40], which allowed us to incorporate phylogeny into statistical models[40-42]. 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 (where the data have no phylogenetic structure) and 1 (where the best fit to the data is provided by a 'Brownian Motion' model of trait evolution[43], with variation at the tips proportional to the duration of common evolution[42,44] We report λ values tests for significant departure from either 0 or 1 for each analysis. 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 ANCOVA. In the PGLM framework, more complex models can be 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-squared values and log-likelihood scores. Alternative nested models are compared using the likelihood ratio (LR) test (where LR=-2[log-likelihood(better fitting model)-log-likelihood(worse fitting model)], the best fitting model having the highest log-likelihood score) whose 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[40,44]. All statistical tests were 2-tailed with α-level of significance set at 0.05. These analyses were carried out using the CAIC R package (R v.2.11.1, The R Foundation for Statistical Computing, http://ww.R-project.org), available from http://r-forge.r-project.org/projects/caic. The phylogeny

444 (including branch lengths) for the species in our dataset was extracted from a published
445 supertree of mammals[45-46]

446 Continuous variables were $\log_{10}$-transformed to improve normality, with the
447 exception of milk composition (%) data which were square-rooted and then arcsine-
448 transformed[47]. Because, brain mass can be a substantial proportion of overall body mass in
449 neonates analyses of these variables could potentially be influenced by autocorrelation and
450 consequent issues of collinearity. Likewise, age at first reproduction includes the period of
451 lactation and lifespan includes the period up to age at first reproduction. We therefore ran
452 analyses based on non-overlapping measures [neonate body mass with brain mass
453 subtracted, age at first reproduction with lactation subtracted (=juvenile period), and
454 lifespan with age at first reproduction subtracted (=adult lifespan]. We do include some
455 analyses in which age at first reproduction and lactation appear as predictors in the same
456 model for comparability with other studies that use this variable, whilst noting the issue of
457 autocorrelation. Bivariate plots and residuals were examined to check for violation of
458 homogeneity of variance. We checked for the effects of outliers by re-running analyses after
459 deleting data points generating large residuals (greater than the mean by three standard
460 deviations or more). However, removing outliers qualitatively affected conclusions in only
461 one case. This outlier was caused by a data point for humans. Because humans are
462 particularly large brained they potentially exert high leverage on regressions; hence we re-
463 ran analyses with and without humans, but the outcome was affected in just the one case
464 mentioned above, so we report results including humans unless otherwise stated.

465

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Figure legends

Figure 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 (either neonate or adult). See Table 1 for results of statistical analysis.

Table legends

Table 1. PGLM analysis of pre- and postnatal contributions to adult brain size, controlling for body size. Variables not included in a particular model are indicated by blank entries in the Table. Significant predictors of adult brain size indicated in bold type. Lh=maximized log-likelihood, λ=estimated ML value of lambda (phylogenetic signal) which is included as a parameter in the models, with p-values for tests of statistical difference from a model with no phylogenetic signal ($p(\lambda=0)$ and a model with $\lambda=1$ ($p(\lambda=1)$).

Table 2. PGLM analysis of neonate brain size. Significant predictors of neonate brain size indicated in bold type. Other details as for Table 1.

Table 3. PGLM analysis of postnatal brain growth. Significant predictors of postnatal brain growth indicated in bold type. Other details as for Table 1.

592 Table 4. PGLM analysis of postnatal brain growth, lactation and milk composition.

593 Significant predictors of postnatal brain growth indicated in bold type. Other details

594 as for Table 1.

Table 1.

Model (n=122)	Model 1	Model 2	Model 3
Parameter	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(λ=0)	<0.001	<0.001	<0.001
p(λ=1)	<0.001	<0.01	<0.001
Model summary			
Lh	55.39	56.29	190.35
Adjusted R^2	0.917	0.923	0.991

Table 2.

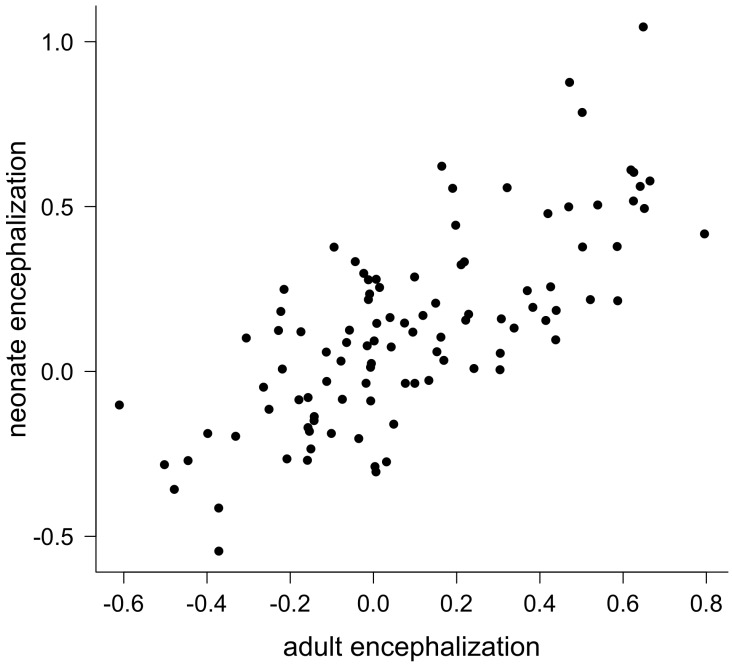
Model (n=128)	Model 1	Model 2
Parameter	t, p-value	t, p-value
Intercept	-2.60, <0.001	-2.49, <0.001
Neonatal body mass	**6.05, <0.001**	**6.00, <0.001**
Maternal body size	**3.13, <0.01**	**3.25, <0.01**
Gestation length	**7.20, <0.01**	**6.38, <0.001**
Litter size	-	-1.14, >0.1
λ	0.90	0.90
p(λ=0)	<0.001	<0.001
p(λ=1)	<0.01	<0.01
Model summary		
Lh	58.06	58.65
Adjusted R^2	0.92	0.92

Table 3.

Model (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, p>0.5	-	-
Age at first reproduction	-	-	-	1.69, >0.1	-
Juvenile period	-	-	-	-	1.82, >0.05
λ	0.67	0.67	0.67	0.60	0.57
p(λ=0)	<0.01	<0.01	<0.01	>0.05	>0.1
p(λ=1)	<0.001	<0.001	<0.001	<0.001	<0.001
Model summary					
Lh	1.01	1.03	1.01	2.38	2.52
Adjusted R^2	0.85	0.85	0.85	0.86	0.87

Table 4.

Model (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(λ=0)	>0.5	>0.5	>0.1	>0.1	>0.5
p(λ=1)	<0.001	<0.001	<0.001	<0.001	<0.001
Model summary					
Lh	0.55	0.52	0.33	0.30	0.51
Adjusted R^2	0.92	0.92	0.90	0.91	0.91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