LETTER

doi:10.1038/nature10629

Energetics and the evolution of human brain size

Ana Navarrete[1], Carel P. van Schaik[1] & Karin Isler[1]

The human brain stands out among mammals by being unusually large. The expensive-tissue hypothesis[1] explains its evolution by proposing a trade-off between the size of the brain and that of the digestive tract, which is smaller than expected for a primate of our body size. Although this hypothesis is widely accepted, empirical support so far has been equivocal. Here we test it in a sample of 100 mammalian species, including 23 primates, by analysing brain size and organ mass data. We found that, controlling for fat-free body mass, brain size is not negatively correlated with the mass of the digestive tract or any other expensive organ, thus refuting the expensive-tissue hypothesis. Nonetheless, consistent with the existence of energy trade-offs with brain size, we find that the size of brains and adipose depots are negatively correlated in mammals, indicating that encephalization and fat storage are compensatory strategies to buffer against starvation. However, these two strategies can be combined if fat storage does not unduly hamper locomotor efficiency. We propose that human encephalization was made possible by a combination of stabilization of energy inputs and a redirection of energy from locomotion, growth and reproduction.

Brains are energetically expensive[2]. The human brain is about three times larger than that of our closest living relative, the chimpanzee, and thus requires much more energy. However, relative whole-body energy consumption rates of individuals at rest are about equal in the two species[3], which raises the question of how humans manage to cover the energetic requirements of their much enlarged brains. One of the best-known attempts to solve this central riddle of human evolution is the expensive-tissue hypothesis, proposed by Aiello and Wheeler in 1995[1]. It postulates an evolutionary trade-off (although obviously not an immediate physiological one) between the size of the brain and that of the digestive tract in anthropoid primates. Thus, if other processes have reduced a species' energetic needs of digestion, it should be able to evolve a relatively larger brain. It has therefore been suggested that early hominins evolved larger brains as a dietary shift towards more meat[1], cooked food and underground tubers[4] gradually allowed for a smaller digestive tract.

The proposed trade-off would gain plausibility as a general principle if it were confirmed in other mammals. As stressed by Aiello *et al.*[5], empirical support for a negative correlation across anthropoid primate species was weak from the beginning (see Supplementary Information, section 1 for a re-analysis), and subsequent comparative studies in other taxa remained ambiguous, with positive support in fish[6], but not in bats or birds[7,8]. Yet, this highly intuitive idea has found broad acceptance in palaeoanthropology[9] and many other fields[10–12], and is fuelling public discussions about the optimal human diet. Thus, a proper empirical test of the expensive-tissue hypothesis across a broad array of taxa is urgently needed, but has not been conducted—until now—owing to a lack of morphological data, nor has there been an examination of the broader trade-offs among other expensive organs predicted by an extension of this hypothesis[7].

Here we examine the presence of correlated evolution between the size of various visceral organs (heart, lungs, stomach, intestines, kidneys, spleen and liver) and that of the brain in a new sample of 100 mammalian species, including 23 primate species (see Supplementary Data). In this analysis, it is crucial to control for body size, but the usual measure taken for this, body mass, is highly affected by variation in the size of adipose depots. This variation may confound or even reverse the direction of correlations among organs (Supplementary Fig. 2 and Supplementary Table 4b). Here, we therefore used fat-free body mass as the best proxy for body size.

Contrary to the predictions of the expensive-tissue hypothesis, we found no negative correlations between the relative size of the brain and the digestive tract, other expensive organs or their combined sum among mammals or within non-human primates, controlling for fat-free body mass, even though statistical power was sufficient to detect these negative correlations if they existed (see Table 1). We also did not find any trade-offs among other expensive organs (Fig. 1). These results therefore refute the expensive-tissue hypothesis as a general principle to explain the interspecific variation of relative brain size in mammals. In our view, this finding reduces the plausibility of the argument that human encephalization was made possible by a reduction of the digestive tract[1,5].

Energy trade-offs with other tissues that are less expensive but very abundant[7] may nonetheless explain part of brain size variation. For instance, adipose depots make up an appreciable proportion of body mass in some mammals[13]. Although not metabolically expensive, adipose tissue has an energetic cost because it has to be carried around and may increase predation-induced mortality (see Supplementary Information 3.7). Fat stores enable animals to cope with periods of reduced food intake and thus act as a physiological buffer against starvation. On the other hand, relatively large brains have also been proposed to act as cognitive buffers against starvation[14,15]. It is therefore possible that encephalization and fat storage are complementary strategies to buffer against starvation. In our sample of mammals, there is indeed a negative correlation between brain size and the size of fat stores, controlling for fat-free body mass (Table 1 and Supplementary Information 3.1), with the exception of primates (but see Supplementary Information 3.6). This negative relationship becomes stronger if potential error variation is removed, for instance by analysing only wild-caught females (Fig. 2 and Supplementary Information 3.4). The strongest trade-off between fat storage and brain size evolution is expected in taxa that exhibit a high cost of transport for increased whole body mass, such as climbing or flying mammals

Table 1 | Regressions of brain volume on other organ masses

	Mammals ($N = 100$)		Primates ($N = 23$)	
Organ	β	P value	β	P value
Heart	0.15	0.13	0.65	0.007
Lungs	−0.03	0.73	0.44	0.07
Kidneys	0.01	0.92	0.34	0.08
Liver	−0.02	0.84	0.20	0.30
Digestive tract	0.16	0.06	0.48	0.005
Stomach	0.15	0.042	0.17	0.19
Intestines	0.11	0.15	0.41	0.008
Spleen	−0.02	0.60	0.15	0.13
Visceral organs	0.05	0.64	0.50	0.029
Adipose depots	−0.07	0.017	−0.01	0.92

Data were controlled for fat-free body mass. Statistical details and the results of the $N = 45$ species subsample are listed in Supplementary Information 3.1.

[1]Anthropological Institute and Museum, University of Zurich, Winterthurerstrasse 190, 8057 Zurich, Switzerland.

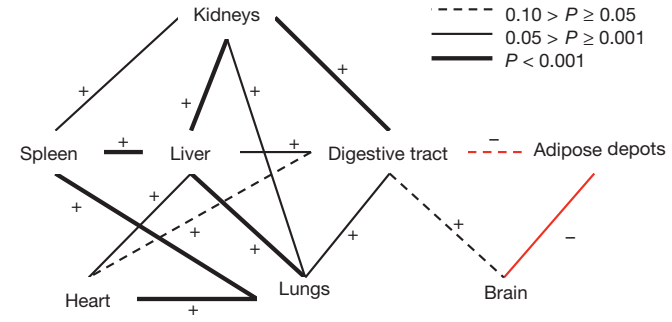

Figure 1 | Correlations between the masses of visceral organs, brains and adipose depots in mammals. The analysis is based on a sample of 100 mammalian species and controls for phylogenetic relationships and fat-free body mass. Statistical details are listed in the Supplementary Information 3.1.

and birds. The only animals that can easily combine both strategies of fat storage and brain enlargement may be those that do not face an increased cost of transport for increased whole body mass, for example, aquatic mammals or large bipeds[16]. However, more detailed studies of seasonal variation in body mass are needed to investigate which conditions or lifestyles favour one or the other, or a combination of both strategies.

Refuting the expensive-tissue hypothesis raises questions about the determinants of the evolution of the greatly enlarged human brain. Although there are various cognitive benefits to increased brain size[17], empirical evidence shows that a focus on the energy costs of growing and maintaining brain tissue helps to explain the interspecific variation in brain size[18]. This approach has recently been synthesized in a general energy-based framework[19], which incorporates earlier ideas on energetic aspects of brain size evolution[1,5,18]. Figure 3 depicts the two possible pathways enabling increased encephalization from a given ancestral state: additional or stabilized energy inputs, and redirection of energy from other functions. Here we apply this framework to develop hypotheses for the remarkable increase of brain size during the evolution of the genus *Homo*.

Larger brains are sometimes paid for by a permanent increase in net energy intake of an organism, as indexed by its basal metabolic rate (BMR); this is shown by the positive correlation between BMR and brain size in a large sample of placental[20] and marsupial mammals[21]. This was confirmed in the present data set, in which we could control

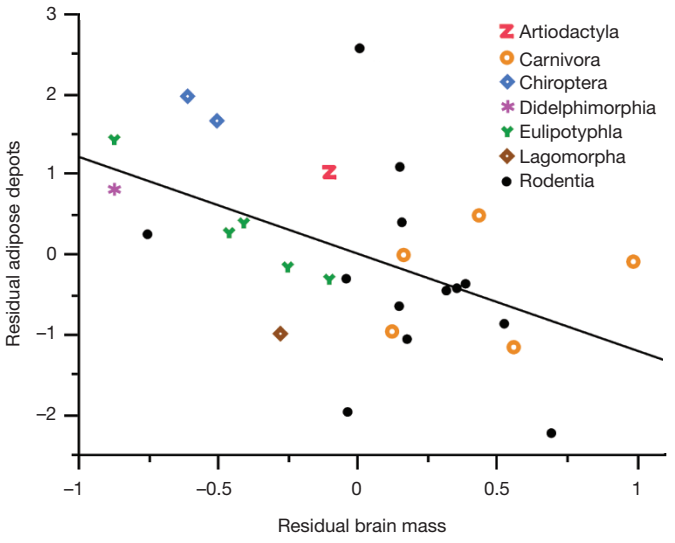

Figure 2 | Correlation between residual brain mass and residual adipose depots mass in wild-caught female mammals, controlling for fat-free body mass. Species-level values: $N = 28$ species, $r^2 = 0.258$, $P = 0.006$. PGLS: $\lambda = 1.00$, $\beta = -0.12$, t value $= -3.42$, $P = 0.002$.

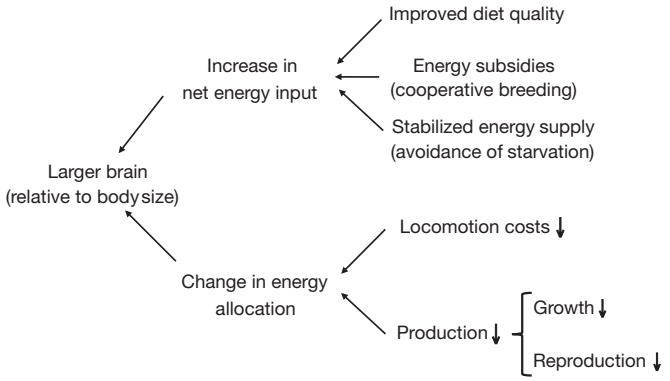

Figure 3 | The expensive-brain framework[19] proposes complementary pathways for an adaptive increase in relative brain size. First, brains can get larger when energy inputs are stabilized on a higher level (higher total metabolic turnover[20]) through an increase in mean dietary quality (for example, more animal fat and protein in early *Homo*[4,22,24]), energy subsidies from other individuals (for example, cooperative breeding, allomaternal care[19,21]) or by reducing fluctuations in energy inputs (for example, cognitive solutions[15], including culture). Second, at constant total energy intake, energy allocation to other functions may be reduced, such as locomotion (for example, efficient bipedalism[27,28]) or production (for example, slower life history pace[30]).

for fat-free body mass ($N = 64$, PGLS, brain size as response, fat-free body mass and body mass associated with BMR measurements as covariates, effect of BMR: $\lambda = 0.96$, $P = 0.026$, $\beta = 0.24$). We humans exhibit the BMR expected for a mammal or primate of our body mass, but because we have much larger adipose depots (about 14–26% in healthy adults[22]) than chimpanzees and bonobos (about 3–10% (ref. 23)), human BMR relative to fat-free body mass is appreciably higher than theirs[24]. Therefore, if extant apes are representative of the last common ancestor, brain enlargement during human evolution was partially paid for through a permanent increase in net energy intake.

Starting with Early Pleistocene *Homo*, this increase could have come from any of the three sources listed in Fig. 3. First, they improved diet quality as indicated by increased consumption of meat and bone marrow[1] and by tool-assisted food processing, at one point including cooking[4]. Second, despite having moved into highly seasonal habitats[9] they reduced temporal fluctuations in energy budgets by cognitive buffering[25], which is also known for other primates[15] and birds[14]. Third, provisioning and food sharing probably arose with the adoption of cooperative breeding and substantial meat acquisition among the earlier representatives of the genus *Homo*[4,26]. Comparative research suggests that such energy subsidies for reproducing females and dependent offspring can support increased brain size[19,21].

The second pathway to brain enlargement is increased energy allocation to the brain by savings on other expensive functions, although the expensive-tissue hypothesis for organs is no longer supported. One likely trade-off could be found between brain size and the costs of locomotion. The efficient form of bipedal locomotion that arose with the transition from australopithecines to early *Homo*[27] could have led to major reductions in energy expenditure in two ways. On one hand, its low costs in comparison with the climbing and quadrupedal locomotion of nonhuman apes[28] should have lowered daily energy expenditure on locomotion[7], and on the other hand, bipedalism may reduce the effect of increased weight due to adipose depots on the energy costs of locomotion (Supplementary Information 3.7). A second potential trade-off would be the one between brain size and production, comprising both growth and reproductive effort, which has been demonstrated for mammals[19,29]. Beginning with early *Homo* our lineage has increased brain size and reduced the pace of life history[30], but nonetheless increased birth rates due to cooperative breeding.

In sum, we do not claim unique processes operating exclusively in human evolution. All these processes are known to operate among mammals in general. We propose that during human evolution improved diet quality, allomaternal subsidies, cognitive buffering, reduced locomotion costs and reduced allocation to production all operated simultaneously, thus enabling the extraordinary brain enlargement in our lineage.

METHODS SUMMARY

Following a strict protocol (Supplementary Information 2), A.N. dissected a large number of mammalian specimens obtained from various sources. Visceral organs (kidneys, spleen, liver, stomach, intestines, heart and lungs) were separated, cleaned, emptied, and immediately weighed. As skulls had to be preserved intact, cranial capacity was determined and converted into an estimate of brain mass. We excluded individuals that were immature, emaciated, pregnant, or exhibited visible organ pathologies from analysis. Hence, our final sample included 191 specimens from 100 species, with a bias towards carnivores and primates (Supplementary Data and Supplementary Information 3.2). The sample size of 100 species yields a power of 0.8 for these analyses, which was determined a priori using a published data set of 39 mammal species.

Traditionally, whole body mass has been used for controlling for body size effects in comparative analyses. However, this measure is highly affected by variation in the size of adipose depots. Even if two species have a similar fat-free body mass and body composition, large adipose depots in one species result in organs that seem relatively small in comparison to those of a species with smaller adipose depots. Therefore, correlations between organs are expected to be mostly positive if we controlled for whole body mass (Supplementary Fig. 2). To avoid this bias, we used fat-free body mass to control for body size effects. For 45 species in our sample, fat-free body mass was known because adipose depots of whole body were measured directly. For the other 55 species, a proxy was calculated from the measurement of abdominal adipose depots (Supplementary Information 3.1 and 3.3).

All analyses took phylogenetic relatedness into account (Supplementary Fig. 3). Additionally, we tested sex-specific and wild/captive subsamples separately (Supplementary Information 3.4), and investigated potential autocorrelation effects (Supplementary Information 3.5).

Full Methods and any associated references are available in the online version of the paper at www.nature.com/nature.

Received 23 May; accepted 12 October 2011.
Published online 9 November 2011.

1. Aiello, L. C. & Wheeler, P. The expensive-tissue hypothesis—the brain and the digestive system in human and primate evolution. *Curr. Anthropol.* **36,** 199–221 (1995).
2. Mink, J. W., Blumenschine, R. J. & Adams, D. B. Ratio of central nervous system to body metabolism in vertebrates—its constancy and functional basis. *Am. J. Physiol.* **241,** R203–R212 (1981).
3. Bruhn, J. M. & Benedict, F. G. The respiratory metabolism of the chimpanzee. *Proc. Am. Acad. Arts Sci.* **71,** 259–326 (1936).
4. Wrangham, R. *Catching Fire: How Cooking Made Us Human* (Basic Books, 2009).
5. Aiello, L. C., Bates, N. & Joffe, T. in *Evolutionary Anatomy of the Primate Cerebral Cortex* (eds Dean, F. & Gibson, K.) 57–78 (Cambridge Univ. Press, 2001).
6. Kaufman, J. A., Hladik, C. M. & Pasquet, P. On the expensive-tissue hypothesis: independent support from highly encephalized fish. *Curr. Anthropol.* **44,** 705–707 (2003).
7. Isler, K. & van Schaik, C. P. Costs of encephalisation: the energy trade-off hypothesis tested on birds. *J. Hum. Evol.* **51,** 228–243 (2006).
8. Jones, K. E. & MacLarnon, A. M. Affording larger brains: testing hypotheses of mammalian brain evolution on bats. *Am. Nat.* **164,** E20–E31 (2004).
9. Potts, R. Environmental hypotheses of hominin evolution. *Yearb. Phys. Anthropol.* **107,** 93–136 (1998).
10. Mau, M., Südekum, K.-H. & Kaiser, T. M. Why cattle feed much and humans think much—new approach to confirm the expensive tissue hypothesis by molecular data. *Biosci. Hypotheses* **2,** 205–208 (2009).
11. Pfefferle, A. D. *et al.* Comparative expression analysis of the phosphocreatine circuit in extant primates: implications for human brain evolution. *J. Hum. Evol.* **60,** 205–212 (2011).
12. Santoro, S. *et al.* Preliminary results from digestive adaptation: a new surgical proposal for treating obesity, based on physiology and evolution. *Sao Paulo Med. J.* **124,** 192–197 (2006).
13. Pond, C. M. *The Fats of Life* (Cambridge Univ. Press, 1998).
14. Sol, D. Revisiting the cognitive buffer hypothesis for the evolution of large brains. *Biol. Lett.* **5,** 130–133 (2009).
15. van Woerden, J. T., van Schaik, C. P. & Isler, K. Effects of seasonality on brain size evolution: evidence from strepsirrhine primates. *Am. Nat.* **176,** 758–767 (2010).
16. Garland, T. Scaling the ecological cost of transport to body mass in terrestrial mammals. *Am. Nat.* **121,** 571–587 (1983).
17. Reader, S. M., Hager, Y. & Laland, K. N. The evolution of primate general and cultural intelligence. *Philos. Trans. R. Soc. B* **366,** 1017–1027 (2011).
18. Martin, R. D. Relative brain size and basal metabolic rate in terrestrial vertebrates. *Nature* **293,** 57–60 (1981).
19. Isler, K. & van Schaik, C. P. The expensive brain: a framework for explaining evolutionary changes in brain size. *J. Hum. Evol.* **57,** 392–400 (2009).
20. Isler, K. & van Schaik, C. P. Metabolic costs of brain size evolution. *Biol. Lett.* **2,** 557–560 (2006).
21. Isler, K. Energetic trade-offs between brain size and offspring production: marsupials confirm a general mammalian pattern. *Bioessays* **33,** 173–179 (2011).
22. Wells, J. C. K. *The Evolutionary Biology of Human Body Fatness* (Cambridge Univ. Press, 2009).
23. Zihlman, A. L. in *The Pygmy Chimpanzee* (ed. Susman, R. L.) 179–200 (Plenum Press, 1984).
24. Aiello, L. C. & Wells, J. C. K. Energetics and the evolution of the genus *Homo*. *Annu. Rev. Anthropol.* **31,** 323–338 (2002).
25. Kaplan, H., Hill, K., Lancaster, J. & Hurtado, A. M. A theory of human life history evolution: diet, intelligence, and longevity. *Evol. Anthropol.* **9,** 156–185 (2000).
26. Burkart, J. M., Hrdy, S. B. & van Schaik, C. P. Cooperative breeding and human cognitive evolution. *Evol. Anthropol.* **18,** 175–186 (2009).
27. Pontzer, H. *et al.* Locomotor anatomy and biomechanics of the Dmanisi hominins. *J. Hum. Evol.* **58,** 492–504 (2010).
28. Pontzer, H., Raichlen, D. A. & Sockol, M. D. The metabolic cost of walking in humans, chimpanzees, and early hominins. *J. Hum. Evol.* **56,** 43–54 (2009).
29. Isler, K. & van Schaik, C. P. Why are there so few smart mammals (but so many smart birds)? *Biol. Lett.* **5,** 125–129 (2009).
30. Dean, C. *et al.* Growth processes in teeth distinguish modern humans from *Homo erectus* and earlier hominins. *Nature* **414,** 628–631 (2001).

Supplementary Information is linked to the online version of the paper at www.nature.com/nature.

Acknowledgements We thank R. D. Martin and J. Wermuth for sharing the Chivers data set, J. van Woerden for sharing her endocranial volume data, and M. Genoud for sharing his revised compilation of mammalian BMR values. Specimens were provided by numerous institutions, museums and colleagues (Supplementary Information 2). We acknowledge valuable comments by L. Aiello and R. D. Martin. Financial support was provided by the Swiss National Science Foundation (grant number 3100A0-117789), the A.H. Schultz-Stiftung and the European Integrated Activities grant SYNTHESYS (grant application number HU-TAF-4916).

Author Contributions K.I. and C.P.v.S. designed the project. A.N. performed the pilot study and collected the data. A.N. and K.I. performed the analyses and all three authors wrote the manuscript.

Author Information Reprints and permissions information is available at www.nature.com/reprints. The authors declare no competing financial interests. Readers are welcome to comment on the online version of this article at www.nature.com/nature. Correspondence and requests for materials should be addressed to A.N. (a.navarrete@aim.uzh.ch) or K.I. (kisler@aim.uzh.ch).

METHODS

Power analysis. To estimate the sample size needed to detect a correlation between brain size and digestive tract mass in mammals, controlling for fat-free body mass, we used an independent data set of 39 mammalian species[31]. In a multiple regression, digestive tract mass has a standard error of the residual error, σ, of 0.343, and a raw effect size δ of 0.096. Therefore, for a level of significance of $\alpha = 0.05$, the sample size required to achieve a power of 0.8 is 103 species. We thus aimed at collecting data from more than 100 mammal species.

Specimens. Four hundred and fifty four specimens of 133 mammal species were obtained from various sources and dissected following a strict protocol (Supplementary Information 2) by A.N. Visceral organs (kidneys, spleen, liver, stomach, intestines, heart and lungs) were separated, cleaned, emptied, and immediately weighed. As skulls had to be preserved intact, cranial capacity was determined using the seed filling method[32], and converted into an estimate of brain mass by multiplying it by 1.036 (ref. 33). Specimens were excluded from analyses if they were juvenile or subadult, emaciated, pregnant, previously stored in formalin or alcohol, had visible pathologies of the organs (such as tumours or internal parasites), a broken neurocranium, unknown body mass before dissection, or if the organ measurements were incomplete. Our final sample included 191 specimens from 100 species, with a bias towards larger orders and especially carnivores and primates (see Supplementary Information 3.2 for species and family coverage and an additional analysis on subfamily level). Species values were obtained by calculating the average of male and female specimens (see Supplementary Information 3.4 for an analysis of sex-specific and wild/captive subsamples). Intestine mass was defined as the sum of ileum, caecum and colon mass, and digestive tract mass as the sum of stomach and intestines mass. BMR data of the species of our sample or of closely related taxa were taken from the literature. Data and sources are listed in Supplementary Data.

Adipose depots. For 45 species in our sample, adipose depots of the whole body were measured directly. For the other 55 species, only abdominal adipose depots were measured, from which we calculated a proxy of total adipose depots by scaling the abdominal depots mass with a factor 3.419. This scaling factor was derived from a comparison of the two measurements for 292 individuals for which body mass and one of the two adipose depots measurements was available (Supplementary Fig. 1). Alternatively, the total mass of adipose depots was calculated from abdominal mass using a prediction equation derived from nine specimens for which both measurements were available (results shown in Supplementary Information 3.3). Fat-free body mass was calculated as whole body mass minus total adipose depots mass.

Statistical analyses. All variables were log-transformed and phylogenetic regressions were run using pglmEstLambda in the CAIC[34] package in R[35]. This function uses the PGLS method, estimating λ as an index of the amount of phylogenetic autocorrelation in the data. If λ is 0, species values are phylogenetically independent and the analysis is equivalent to a species means least-squares regression. If λ is close to 1, the phylogenetic signal implies that trait evolution follows Brownian motion, and the analysis is equivalent to the classic method of calculating independent contrasts. If analyses yielded unstable estimates of λ due to the small sample size within orders (λ not significantly different from both 0 and 1), we additionally ran the analyses with λ set to 0 or 1. The models included brain mass as response, body size as covariate and organ mass as effect.

Visceral organs, the brain and adipose depots are part of the same body, and therefore autocorrelation effects could be suspected to influence our results. Two methods to remove these effects are reported in the Supplementary Information 3.5, and the results corroborate our findings. Analyses were done both using the total sample of 100 species and the subsample with total adipose depot mass of 45 species.

Whole body mass versus fat-free body mass. Traditionally, whole body mass has been used for controlling for body size effects in comparative analyses. However, this measure is highly affected by variation in the size of adipose depots and using it to control for body size may have an effect on the correlation between organs. Even if two species have a similar fat-free body mass and body composition, large adipose depots in one species result in organs that seem relatively small in comparison to those of a species with smaller adipose depots. Therefore, correlations between organs are mostly positive if we control for whole body mass. This bias is expected to disappear if fat-free body mass is used to control for body size effects (Supplementary Fig. 2).

These relationships were confirmed by our analyses. Brain–organ correlations were mostly positive, if whole body mass was included in the model (Supplementary Tables 4 and 5). Controlling for fat-free body mass instead of whole body mass reduced or eliminated this bias in most groups, with the notable exception of primates, in which positive correlations between organs persist, and brain size is not negatively related to adipose depots mass. We argue (Supplementary Information 3.6) that these discrepancies are due to a combination of error and peculiar captivity effects in foregut fermenting primates, and that primates would follow the general mammal trend if more complete data were available.

31. Pitts, G. & Bullard, T. in *Body Composition in Animals and Man* (ed. Reit, J. T.) 45–70 (National Academy of Science Pub No. 1598, 1968).
32. Isler, K. *et al.* Endocranial volumes of primate species: scaling analyses using a comprehensive and reliable data set. *J. Hum. Evol.* **55,** 967–978 (2008).
33. Rehkämper, G., Frahm, H. D. & Zilles, K. Quantitative development of brain and brain structures in birds (Galliformes and Passeriformes) compared to that in mammals (Insectivores and Primates). *Brain Behav. Evol.* **37,** 125–143 (1991).
34. Orme, D., Freckleton, R. P., Thomas, G., Petzoldt, T. & Fritz, S. *CAIC: Comparative Analyses Using Independent Contrasts* ⟨http://r-forge.r-project.org/projects/caic⟩ (2009).
35. R Development Core Team. R: a language and environment for statistical computing (R Foundation for Statistical Computing, 2010).