

Metabolic acceleration and the evolution of human brain size and life history

Herman Pontzer^{1,2}, Mary H. Brown³, David A. Raichlen⁴, Holly Dunsworth⁵, Brian Hare⁶, Kara Walker⁶, Amy Luke⁷, Lara R. Dugas⁷, Ramon Durazo-Arvizu⁷, Dale Schoeller⁸, Jacob Plange-Rhule⁹, Pascal Bovet^{10,11}, Terrence E. Forrester¹², Estelle V. Lambert¹³, Melissa Emery Thompson¹⁴, Robert W. Shumaker^{15,16,17} & Stephen R. Ross³

Humans are distinguished from the other living apes in having larger brains and an unusual life history that combines high reproductive output with slow childhood growth and exceptional longevity¹. This suite of derived traits suggests major changes in energy expenditure and allocation in the human lineage, but direct measures of human and ape metabolism are needed to compare evolved energy strategies among hominoids. Here we used doubly labelled water measurements of total energy expenditure (TEE; kcal day⁻¹) in humans, chimpanzees, bonobos, gorillas and orangutans to test the hypothesis that the human lineage has experienced an acceleration in metabolic rate, providing energy for larger brains and faster reproduction without sacrificing maintenance and longevity. In multivariate regressions including body size and physical activity, human TEE exceeded that of chimpanzees and bonobos, gorillas and orangutans by approximately 400, 635 and 820 kcal day⁻¹, respectively, readily accommodating the cost of humans' greater brain size and reproductive output. Much of the increase in TEE is attributable to humans' greater basal metabolic rate (kcal day⁻¹), indicating increased organ metabolic activity. Humans also had the greatest body fat percentage. An increased metabolic rate, along with changes in energy allocation, was crucial in the evolution of human brain size and life history.

Variation in life history reflects evolved differences in energy expenditure. Each organism must allocate its available metabolic energy, which is largely a function of body size, to the competing needs of growth, reproduction and maintenance, resulting in fundamental trade-offs among these vital tasks^{2–5}. For example, species that reproduce faster than expected for their body mass generally have shorter maximum lifespans, as energy is directed towards reproductive output and away from maintenance^{2–5}. Among primates, this trade-off framework has been expanded to consider the energy needed to grow and maintain large brains^{6,7}.

In this light, humans present an energetic paradox. Humans in natural fertility populations reproduce more often, and produce larger neonates, than any other living hominoid, yet humans also have the longest lifespans and the largest, most metabolically costly brains¹ (Extended Data Fig. 1). This uniquely human suite of derived, metabolically costly traits suggests a lifting of energetic constraints in the hominin lineage, but the critical underlying mechanisms remain largely unknown. Some have hypothesized that a reduced gut⁸ or increased locomotor efficiency⁹ provided the extra energy needed for brain expansion.

However, phylogenetically informed analyses suggest that gut reduction is insufficient to explain increased human brain size¹, and, although human walking is more economical¹⁰, traditional hunter-gatherers travel so much farther per day¹¹ that their daily ranging costs are no lower than wild chimpanzees' (Supplementary Discussion and Supplementary Table 1). Similarly, provisioning of young offspring and their mothers helps to shorten human inter-birth intervals and increase the pace of reproduction¹, but reproduction remains relatively costly for human mothers (Supplementary Discussion, Supplementary Fig. 1 and Supplementary Table 2). Furthermore, it is unclear whether food sharing or other dietary changes are sufficient to fuel larger brains, larger neonates and longer lifespans without an acceleration in metabolic rate to harness increased energy acquisition.

Here, we test the hypothesis that humans have evolved an accelerated metabolic rate and larger energy budget, accommodating larger brains, greater reproductive output and longer lifespans without the expected energetic trade-offs. Increased TEE (kcal day⁻¹) has previously been discounted as an explanation for the human energetic paradox^{1,8}, in part because human basal metabolic rate (BMR; kcal day⁻¹) is broadly similar to that of other primates^{8,11}. However, variation in TEE and BMR among humans and the great apes, our closest evolutionary relatives, is largely unstudied. Lacking sufficient data on TEE and BMR in apes, previous analyses have been unable to compare metabolic rates across the entire hominoid clade and test for metabolic acceleration in humans.

We used the doubly labelled water method¹² to measure TEE in mixed-sex samples of adult chimpanzees (*Pan troglodytes*; $n = 27$), bonobos (*Pan paniscus*; $n = 8$), Western lowland gorillas (*Gorilla gorilla*; $n = 10$) and orangutans (*Pongo* spp.; $n = 11$), and compared these data to similar measures of TEE in a large, adult human sample¹³ (*Homo sapiens*; $n = 141$); this method also provides a measure of body composition (Methods and Table 1). TEE was measured over 7–10 days while individuals followed their normal daily routine. We also compared published measurements of BMR in humans, chimpanzees and orangutans, and we estimated daily locomotor energy expenditure and BMR for adults in our TEE sample to assess their contribution to variation in TEE. Comparisons were performed at the genus level, both to avoid the issue of close phylogenetic relatedness for chimpanzees and bonobos, and because no metabolic differences were apparent between these two species.

Humans exhibited greater TEE than other hominoids, with larger daily energy budgets than all apes except adult male gorillas

¹Department of Anthropology, Hunter College, 695 Park Avenue, New York, New York 10065, USA. ²New York Consortium for Evolutionary Primatology, New York, New York 10065, USA. ³Lester E. Fisher Center for the Study and Conservation of Apes, Lincoln Park Zoo, Chicago, Illinois 60614, USA. ⁴School of Anthropology, University of Arizona, 1099 E South Campus Drive, Tucson, Arizona 85716, USA. ⁵Department of Sociology & Anthropology, University of Rhode Island, 45 Upper College Rd, Kingston, Rhode Island 02881, USA. ⁶Department of Evolutionary Anthropology, Duke University, Durham, North Carolina 27708, USA. ⁷Public Health Sciences, Stritch School of Medicine, Loyola University Chicago, 2160 South First Avenue, Maywood, Illinois 60153, USA. ⁸Nutritional Sciences, Biotechnology Center, University of Wisconsin–Madison, 425 Henry Mall, Madison, Wisconsin 53705, USA. ⁹Kwame Nkrumah University of Science and Technology, Kumasi, Ghana. ¹⁰Institute of Social & Preventive Medicine, Lausanne University Hospital, Rue de la Corniche 10, 1010 Lausanne, Switzerland. ¹¹Ministry of Health, PO Box 52, Victoria, Mahé, Seychelles. ¹²UWI Solutions for Developing Countries, The University of the West Indies, 25 West Road, UWI Mona Campus, Kingston 7, Jamaica. ¹³Research Unit for Exercise Science and Sports Medicine, University of Cape Town, PO Box 115, Newlands 7725, Cape Town, South Africa. ¹⁴Department of Anthropology, University of New Mexico, Albuquerque, New Mexico 87131, USA. ¹⁵Indianapolis Zoo, 1200 W Washington Street, Indianapolis, Indiana 46222, USA. ¹⁶Department of Anthropology and Center for Integrated Study of Animal Behavior, Indiana University, 701 E Kirkwood Avenue, Bloomington, Indiana 47405, USA. ¹⁷Krasnow Institute for Advanced Study, George Mason University, 4400 University Dr., Fairfax, Virginia 22030, USA.

Table 1 | Age, body size and composition, and TEE

Genus	Sex	n	Age (years) (s.d.)	Mass (kg) (s.d.)	FFM (kg) (s.d.)	Body fat* (%) (s.d.)	TEE [†] (kcal day ⁻¹) (s.d.)	BMR [‡]	Walk and climb [‡]
<i>Homo</i>	Female	76	33.5 (6.0)	80.1 (19.8)	46.1 (7.4)	41.1 (7.1)	2,190 (381)	1,474	183
	Male	65	32.6 (5.4)	73.8 (15.2)	56.1 (7.9)	22.9 (7.6)	2,721 (569)	1,640	226
<i>Pan</i>	Female	17	25.8 (11.3)	46.4 (8.1)	43.3 (7.8)	9.0 (5.5)	1,722 (363)	1,214	102
	Male	18	22.3 (10.7)	57.9 (13.4)	53.8 (11.7)	8.4 (4.9)	2,145 (546)	1,401	120
<i>Gorilla</i>	Female	6	19.7 (4.1)	73.7 (7.3)	63.3 (7.0)	13.9 (6.4)	2,030 (527)	-	110
	Male	4	24.5 (11.7)	166.4 (42.5)	148.3 (27.0)	15.2 (4.6)	3,630 (839)	-	253
<i>Pongo</i>	Female	5	27.6 (5.3)	58.2 (4.0)	44.3 (2.5)	23.4 (8.8)	1,476 (268)	984	88
	Male	6	20.0 (10.8)	76.7 (34.1)	62.4 (23.3)	16.4 (8.6)	1,617 (289)	1,090	163

s.d., standard deviation.

*Excludes $n = 6$ *Pan* subjects with negative calculated body fats (Methods).[†]Calculated for *Pan*, *Gorilla*, and *Pongo* using equation 7.17 in ref. 12.[‡]Estimated BMR and locomotion costs were calculated from body mass and daily activity (Methods).

(Table 1). Fat-free mass (FFM) explained 34% of the variance in TEE ($t(195) = 10.18$, $r^2 = 0.34$, $P < 0.001$; Fig. 1 and Supplementary Table 3). Differences among genera accounted for an additional 27% of the variance in TEE, with humans having the highest TEE, followed in order by *Pan*, *Gorilla* and *Pongo* ($P \leq 0.001$ for all comparisons; Fig. 1 and Supplementary Table 3). For comparison, mean FFM was similar for *Homo*, *Pan* and *Pongo* cohorts, yet mean human TEE was $\sim 27\%$ greater than *Pan* and $\sim 58\%$ greater than *Pongo*. Body fat was weakly, negatively correlated with TEE ($\beta = -0.04 \pm 0.02$, $P = 0.02$); age ($P = 0.70$) and sex ($P = 0.26$) were not significant covariates in TEE models including FFM, fat mass and genus (Supplementary Table 3). Results were robust across different models for calculating TEE from isotope enrichment (Supplementary Table 3).

Together, BMR and daily locomotor expenditure accounted for much of the variation in TEE among genera. The mean estimated daily energy cost of walking and climbing among apes in our sample was similar across genera and ~ 100 kcal day⁻¹ below estimated daily walking cost in our human sample (Table 1). Our analyses of published measurements^{14–16} indicate that BMR is lower in *Pan* than in comparably aged humans, in analyses controlling for sex, age and body mass ($P < 0.001$; Methods and Extended Data Fig. 2). The few measurements of *Pongo* BMR^{16,17} appear to be lower still (Extended Data Fig. 2); no data for the *Gorilla* BMR are available. For cohorts in the TEE data set, estimated BMR for *Homo* was ~ 200 kcal day⁻¹ greater than *Pan* and ~ 500 kcal day⁻¹ greater than *Pongo* (Table 1). Estimated physical activity levels (PALs: TEE/estimated BMR; see Table 1), were similar across genera (*Homo*: female 1.5, male 1.7; *Pan*: female 1.4, male 1.5; *Pongo*: female 1.5, male 1.5), indicating that organ activity contributed more than physical activity to variations in TEE.

Body fat percentage, measured from isotope dilution¹², was markedly higher in humans than other hominoids in our TEE sample, and only humans exhibited a significant sex difference (Table 1). Body fat percentage was remarkably low for *Pan*, consistent with measures from dissection¹⁸, and somewhat higher for *Gorilla* and *Pongo*. Indeed, body fat percentages for captive apes were comparable to, or even below, average body fat percentages for humans in physically active, traditional hunter-gatherer populations¹⁹.

Together, these results indicate substantial metabolic evolution across the hominoid clade and a previously uncharacterized diversity in TEE, BMR and body fat percentage (Fig. 2). For a given FFM, humans have greater TEE, BMR and fat mass than other hominoids. Chimpanzees and bonobos have the next largest energy budgets but carry the least amount of body fat. Gorillas have lower TEE and greater body fat than *Pan*. Orangutans have exceptionally low TEE and BMR, and fat percentages similar to gorillas (Table 1).

Comparisons of BMR and TEE indicate that hominin brain and life history evolution were fuelled in large part by increased mass-specific organ metabolic rates (kcal g⁻¹ h⁻¹), and not solely through anatomical or physiological trade-offs. BMR reflects the summed metabolic activity of the organs at rest and is largely shaped by organs with high mass-specific metabolic rates such as the brain, liver and gastrointestinal tract²⁰. If, as assumed in previous studies, organ-mass-specific metabolic rates were similar across hominoids, then humans and apes with

the same FFM should have similar BMRs — the cost of humans' larger brain offset by a reduced gastrointestinal tract⁸. Instead, BMR and TEE are substantially greater for humans, controlling for FFM (Table 1, Figs 1, 2 and Extended Data Fig. 2), indicating an evolutionary increase in the metabolic activity of at least some organ systems. Humans' greater BMR and TEE could readily accommodate the marginal cost of increased reproductive output, estimated at ~ 130 kcal day⁻¹ over the course of a woman's reproductive career in natural fertility populations (Supplementary Discussion, Supplementary Table 2 and Supplementary Fig. 3). Greater metabolic activity could also support humans' derived brain metabolism²¹ and increased somatic maintenance and longevity¹, but more comparative analyses are needed to identify specific mechanisms and associated metabolic costs.

Analysing relatively sedentary human and ape populations allowed us to compare cohorts with similar FFMs, PALs and locomotor expenditures (Table 1), but the pattern of TEE, BMR and body composition variation among genera is expected to hold across more physically active populations. When controlling for body size, TEE is remarkably consistent across populations within a species, regardless of activity level²²: traditional hunter-gatherers have similar size-corrected TEEs to people living in cities¹⁹, and zoo-housed populations of primates and other mammals are similar to their counterparts in the wild^{22–24}. Humans in traditional foraging and farming populations and apes in the wild will generally have lower body fat percentages¹⁹ than the cohorts in the TEE sample (Table 1), but again the pattern of differences seen here is expected to persist: even in captivity,

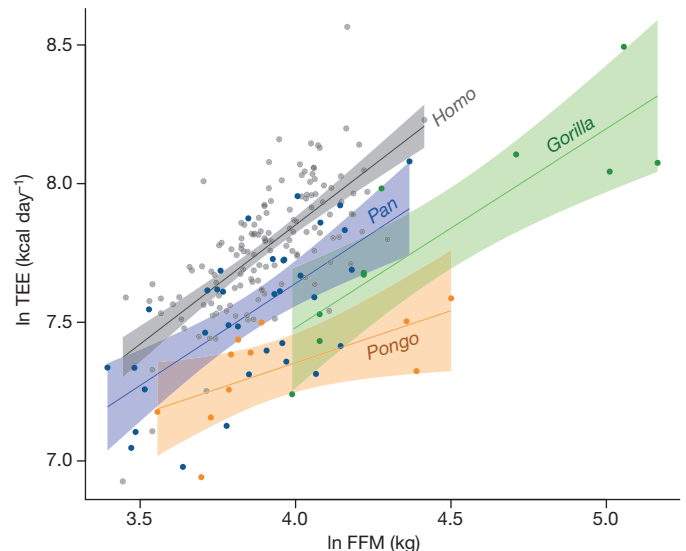


Figure 1 | TTE and FFM for hominoids. Humans (*Homo*, grey, $n = 141$), chimpanzees and bonobos (*Pan*, blue, $n = 35$), gorillas (*Gorilla*, green, $n = 10$), and orangutans (*Pongo*, orange, $n = 11$). Lines and shaded regions indicate least squares regressions and 95% confidence intervals for each genus. TEE for *Homo* exceeds other genera in a general linear model accounting for FFM, fat mass and other variables ($P < 0.001$; Table 1 and Supplementary Table 3).

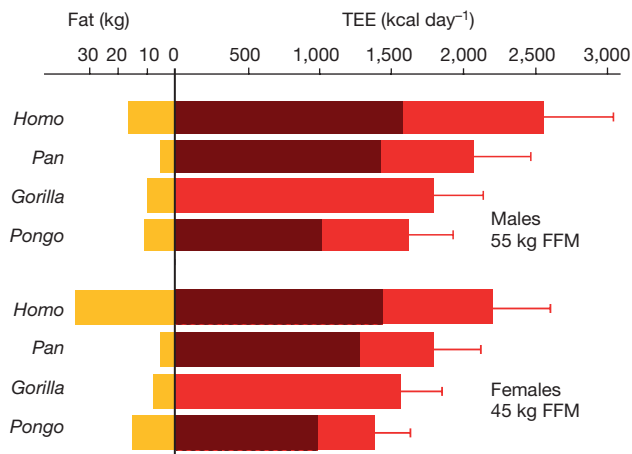


Figure 2 | Predicted TEE, BMR and fat mass for adult hominoids. Values are estimated for males (55 kg FFM) and females (45 kg FFM), using the same FFM across genera. TEE (red bars) is estimated from FFM, fat mass and genus using model C in Supplementary Table 3; error bars represent model standard error. BMR (darker red regions) is estimated from body mass (Methods and Extended Data Fig. 2); no BMR data are available for *Gorilla*. Fat mass (yellow bars) is calculated from FFM using body fat percentages in Table 1.

body fat percentage in *Pan* is remarkably low and fat percentages for *Pongo* and *Gorilla* fall near the very lowest ranges for healthy, physically active human populations¹⁹.

Expansion of the hominin energy budget challenges current models of life history and brain evolution predicated on metabolic stasis and constraint^{1,2,5-9}. Evolved increases in BMR and TEE do not diminish the importance of gut reduction, efficient walking, dietary change and maternal provisioning in the hominin lineage, but rather place these critical adaptations within a different energetic framework. Increased TEE exposes individuals to a greater likelihood of energy shortfalls, providing strong selection for behavioural and anatomical adaptations to mitigate this risk. Gut reduction⁸ allows for greater energy allocation to reproduction and maintenance (including larger brains) while limiting the increase in BMR and TEE. Improved walking efficiency¹⁰, a dietary shift to more energy-dense foods (for example, meat, tubers), and the adoption of cooking²⁵ all effectively increase the net energy gained from foraging, and may have had an essential role in the evolutionary expansion of the hominin energy budget. Food sharing¹ provides an additional source of food energy, and along with increased body fat⁹, provides an important buffer against energy shortfalls, particularly for children and for females shouldering the added energetic burdens of reproduction. We hypothesize that food sharing and increased body fat coevolved with greater TEE to mitigate the inherent risk of increased energy demands.

Metabolic measurements of living hominoids resolve the human energetic paradox and may also point towards strategies for combating obesity and metabolic disease. Humans exhibit an evolved predisposition to deposit fat whereas other hominoids remain relatively lean, even in captivity where activity levels are modest. Untangling the evolutionary pressures and physiological mechanisms shaping the diversity of metabolic strategies among living hominoids may aid efforts to promote and repair metabolic health for humans in industrialized populations and apes in captivity.

Online Content Methods, along with any additional Extended Data display items and Source Data, are available in the online version of the paper; references unique to these sections appear only in the online paper.

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- Isler, K. & van Schaik, C. P. How our ancestors broke through the gray ceiling. *Curr. Anthropol.* **53**, S453–S465 (2012).
- Charnov, E. L. *Life History Invariants* (Oxford Univ. Press, 1993).
- Brown, J. H., Gillooly, J. F., Allen, A. P., Savage, V. M. & West, B. G. Toward a metabolic theory of ecology. *Ecology* **85**, 1771–1789 (2004).
- Stearns, S. C. *The Evolution of Life Histories* (Oxford Univ. Press, 1992).
- Charnov, E. L. The optimal balance between growth rate and survival in mammals. *Evol. Ecol. Res.* **6**, 307–313 (2004).
- Charnov, E. L. & Berrigan, D. Why do primates have such long life spans and so few babies? *Evol. Anthropol.* **1**, 191–194 (1993).
- 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).
- Aiello, L. C. & Wheeler, P. The expensive tissue hypothesis. *Curr. Anthropol.* **36**, 199–221 (1995).
- Navarrete, A., van Schaik, C. P. & Isler, K. Energetics and the evolution of human brain size. *Nature* **480**, 91–93 (2011).
- Pontzer, H., Raichlen, D. A. & Rodman, P. S. Bipedal and quadrupedal locomotion in chimpanzees. *J. Hum. Evol.* **66**, 64–82 (2014).
- Leonard, W. R. & Robertson, M. L. Comparative primate energetics and hominid evolution. *Am. J. Phys. Anthropol.* **102**, 265–281 (1997).
- Speakman, J. R. *Doubly Labelled Water: Theory & Practice* (Chapman & Hall, 1997).
- Pontzer, H. *et al.* Constrained total energy expenditure and metabolic adaptation to physical activity in adult humans. *Curr. Biol.* **26**, 410–417 (2016).
- Butte, N. F. Fat intake of children in relation to energy requirements. *Am. J. Clin. Nutr.* **72** (suppl.), 1246S–1252S (2000).
- Bruhn, J. M. & Benedict, F. G. The respiratory metabolism of the chimpanzee. *Proc. Am. Acad. Arts Sci.* **71**, 259–326 (1936).
- Bruhn, J. M. The respiratory metabolism of infrahuman primates. *Am. J. Physiol.* **110**, 477–484 (1934).
- Pontzer, H., Raichlen, D. A., Shumaker, R. W., Ocozbek, C. & Wich, S. A. Metabolic adaptation for low energy throughput in orangutans. *Proc. Natl Acad. Sci. USA* **107**, 14048–14052 (2010).
- Zihlman, A. L. & Bolter, D. R. Body composition in *Pan paniscus* compared with *Homo sapiens* has implications for changes during human evolution. *Proc. Natl Acad. Sci. USA* **112**, 7466–7471 (2015).
- Pontzer, H. *et al.* Hunter-gatherer energetics and human obesity. *PLoS ONE* **7**, e40503 (2012).
- Wang, Z., Bosy-Westphal, A., Schautz, B. & Müller, M. Mechanistic model of mass-specific basal metabolic rate: evaluation in healthy young adults. *Int. J. Body Compos. Res.* **9**, 147 (2011).
- Bauernfeind, A. L. *et al.* Evolutionary divergence of gene and protein expression in the brains of humans and chimpanzees. *Genome Biol. Evol.* **7**, 2276–2288 (2015).
- Pontzer, H. Constrained total energy expenditure and the evolutionary biology of energy balance. *Exerc. Sport Sci. Rev.* **43**, 110–116 (2015).
- Pontzer, H. *et al.* Primate energy expenditure and life history. *Proc. Natl Acad. Sci. USA* **111**, 1433–1437 (2014).
- Nie, Y. *et al.* Exceptionally low daily energy expenditure in the bamboo-eating giant panda. *Science* **349**, 171–174 (2015).
- Cardomy, R. N., Weintraub, G. S. & Wrangham, R. W. Energetic consequences of thermal and nonthermal food processing. *Proc. Natl Acad. Sci. USA* **108**, 19199–19203 (2011).

Supplementary Information is available in the online version of the paper.

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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 the paper. Correspondence and requests for materials should be addressed to H.P. (hpontzer@hunter.cuny.edu).

METHODS

Sample. Adult apes (age ≥ 10 years) were housed in Association of Zoos and Aquariums accredited zoos in the United States, or in sanctuaries in the Democratic Republic of Congo, with large enclosures. No statistical methods were used to pre-determine sample size. Institutional approvals were obtained from Hunter College and participating facilities before data collection. Human data were drawn from a recent large global study¹³ (United States, Ghana, South Africa, Seychelles, Jamaica; institutional approvals from local governments and Loyola University, and each subject's informed consent, were obtained before data collection). Men and women employed in manual labour were excluded from analyses to better match activity levels across species. Apes were excluded from analyses if they had a dilution space ratio less than 1.00, or had a calculated body fat percentage below -10% , either of which could signal an error in dosing or sample processing. Owing to normal measurement error, the isotope dilution method for calculating body composition can produce marginally negative body fat estimates in subjects with fat percentages near 0. This occurred in $n = 6$ *Pan* subjects (range: -1 to -6% body fat), which is unsurprising given the low body fat percentage in *Pan*¹⁸ (Table 1). These subjects were included in analyses unless otherwise noted; they were excluded from analyses including fat mass (Supplementary Table 3), because negative values cannot be log-transformed. Pregnant and lactating mothers ($n = 2$ bonobo and 2 gorillas) were retained in the sample because 'pregnant/lactating' did not emerge as a significant factor for TEE in multiple regression with FFM and genus ($t(191) = -0.48$, $P = 0.68$). The experiments were not randomized. The investigators were not blinded to allocation during experiments and outcome assessment.

Dosing and sampling. Dosing, sampling and analytical protocols for humans were as described previously¹³. Ape protocols were as described previously²³, and apes from that study ($n = 14$ *Pan*, $n = 3$ *Pongo*, $n = 5$ *Gorilla*) are included in this analysis. Apes drank a sufficient dose of DLW (6% $^2\text{H}_2\text{O}$, 10% H_2^{18}O ; Sigma-Aldrich) to achieve targeted enrichment for their body mass¹², which was measured using a digital scale before the study. Urine or saliva samples were collected once before dosing and then 3–5 times post-dose, over the course of 7–10 days. Isotopic enrichment (^2H and ^{18}O) was measured using isotope ratio mass spectrometry or cavity ring down mass spectrometry. Analysis of residuals indicates results were similar across laboratories and methods (Supplementary Fig. 2).

Calculating TEE. Isotope depletion rates and dilution spaces were calculated via the slope-intercept method¹². Three to five post-dose urine samples were analysed for each subject, enabling us to identify and remove contaminated samples from analysis. Isotope depletion rates were used to calculate ape TEE (kcal day^{-1}) using equation 7.17 in ref. 12, using a food quotient of 0.95 (ref. 23) and a dilution

space ratio of 1.04 following observed ratios in all ape species (1.04 ± 0.02 , $n = 56$ subjects; no effect of genus: $F(53) = 0.55$, $P = 0.58$ ANOVA). We also calculated TEE using equation 17.15 in ref. 12, which is tailored to human subjects and assumes human-like fractionation and insensible water loss. Ape TEE values using the human-tailored equation are $11 \pm 3\%$ greater, but the pattern of TEE differences among hominoids is robust to the choice of equation (Supplementary Table 3). We prefer the more generalized mammalian equation for apes, since apes differ from humans in sweating capability and nasal morphology and are therefore likely to be more like other mammals (rather than humans) in fractionation and insensible water loss.

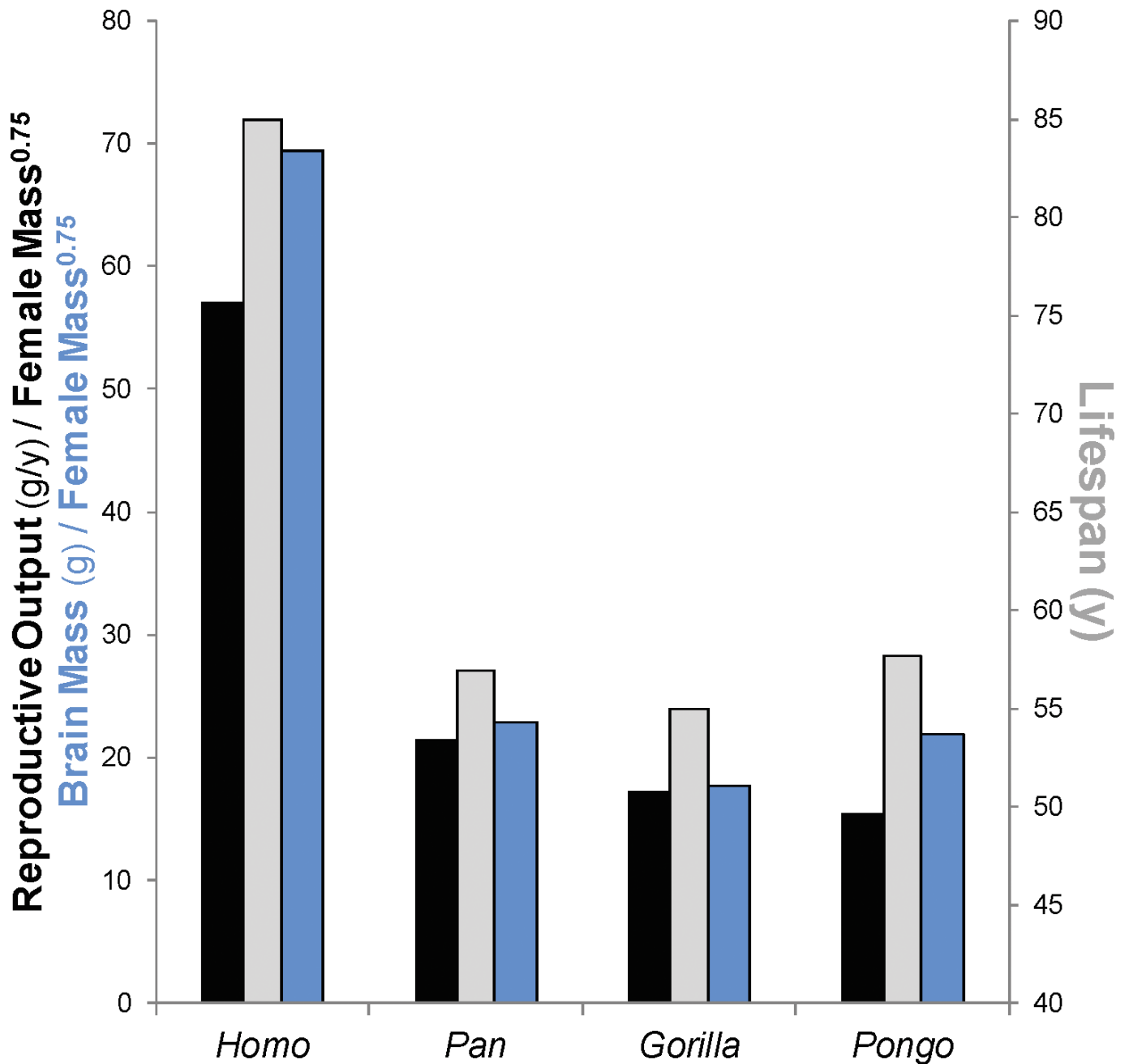
TEE analysis. Variation in TEE was examined via multiple regression²⁶ using ln-transformed values for TEE, FFM and fat mass to reduce heteroscedasticity of residuals. Comparisons were made at the genus level due to the close phylogenetic relatedness of bonobos and chimpanzees. Bonobos and chimpanzees did not differ ($F(32) = 0.007$, $P = 0.80$ ANCOVA) in TEE in analyses controlling for FFM.

Locomotor costs. Humans were fitted with triaxial accelerometers (Actical, Phillips Respironics) and counts per minute were logged for 7 days, corresponding with the DLW measurement period¹⁵. Accelerometry was not feasible for apes. Instead, physical activity was recorded using direct observation for a minimum of 20 h over the DLW measurement period. Distances walked and climbed were recorded every 15 min, using measurements of the enclosures to calibrate distance estimates. Rates of walking and climbing (metres h^{-1}) were calculated and multiplied by 12 to give the estimated distance walked and climbed during the daytime. Night-time activity was not observable in apes and was therefore excluded from analyses for all species.

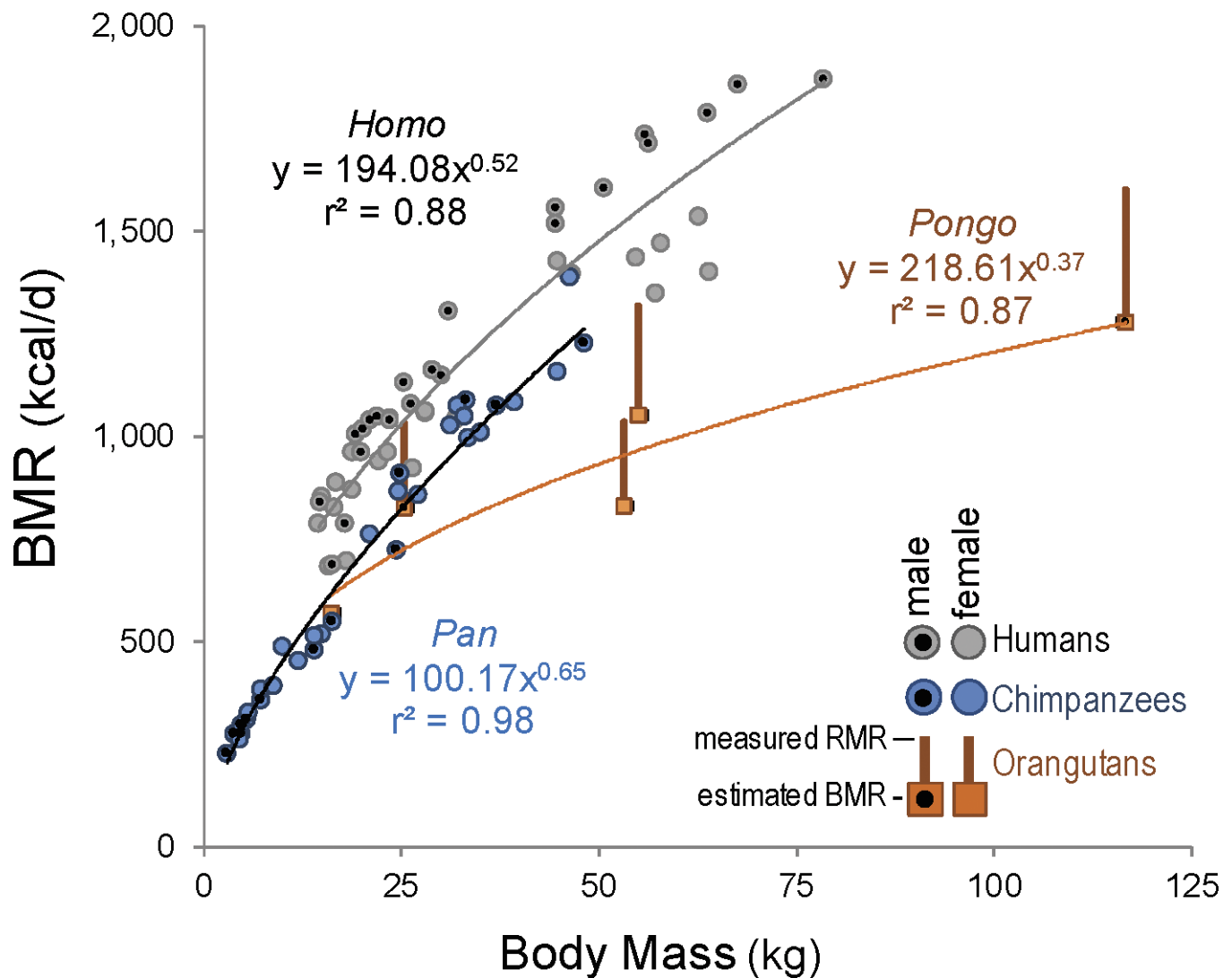
BMR. Published respirometry measurements of BMR for chimpanzees^{15,16} (age: 2 months to 15 years) and comparably aged humans¹⁴ (3–18 years) were ln-transformed and analysed using multiple regression²⁶ controlling for sex, age, and ln-transformed body mass. Humans had higher BMRs than chimpanzees ($P < 0.001$) in all analyses (Supplementary Table 3). These data, along with the few available data for orangutan BMR^{16,17}, are plotted in Extended Data Fig. 2. Allometric regressions for chimpanzees and orangutans (Extended Data Fig. 2) were used to estimate BMR for the *Pan* and *Pongo* cohorts (Table 1). Published BMR prediction equations for adult humans²⁷ were used for the *Homo* cohort in Table 1.

26. R Core Team. R: A language and environment for statistical computing. (R Foundation for Statistical Computing, Vienna, Austria, 2013).

27. Henry, C. J. Basal metabolic rate studies in humans: measurement and development of new equations. *Public Health Nutr.* **8**, 1133–1152 (2005).



Extended Data Figure 1 | The human energetic paradox. Humans achieve greater reproductive output (g year^{-1} ; black bar) and have larger brains (g ; blue bar) relative to female metabolic mass ($\text{kg}^{0.75}$) than any of the great apes, yet also achieve longer lifespans (grey bar). Human data are from traditional hunter-gatherer and subsistence farming populations; ape data are from populations in the wild¹ (see Supplementary Table 2).



Extended Data Figure 2 | BMRs for humans, chimpanzees and orangutans. Available BMR data for chimpanzees^{15,16} are primarily from juveniles (age: 2 months to 15 years), and are shown here against comparably aged humans¹⁴ (3–18 years). Humans have greater BMRs than chimpanzees in a general linear model of ln-transformed BMR and mass controlling for age and sex ($P < 0.001$; Supplementary Table 3). Note that in humans (but not chimpanzees), males have greater BMRs for a given body mass, reflecting their greater proportion of FFM (that is, lower body fat percentage). The available data for orangutan BMR consists of one juvenile individual¹⁶ (no age reported, mass 16.2 kg).

Resting metabolic rates (RMRs; kcal day⁻¹), measured in alert orangutans while sitting¹⁷, are also shown. The top of the bar indicates the measured RMR for those individuals, and the bottom square indicates estimated BMR based on those measurements¹⁷, assuming BMR = 0.8RMR. No BMR data are available for gorillas. Symbols marked with black circles are males. Allometric regressions shown for *Pan* ($y = 100.17x^{0.65}$) and *Pongo* ($y = 218.61x^{0.37}$) were used to estimate BMR for the adult cohorts in Table 1. Human BMR in Table 1 was estimated from published, sex-specific predictive equations for adults²⁷.