

simple allometric scaling to maintain functional interconnectedness at a larger overall brain size. Specialization of cortical neuron types⁸ and elevated gene expression associated with metabolism and synaptic plasticity⁹ in humans suggest that subtle modifications of architecture, function and connectivity¹⁰ may have been critical in the evolution of human cognitive capacities.

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1. Schoenemann, P.T., Sheehan, M. J. & Glotzer, L. D. *Nat. Neurosci.* **8**, 242–252 (2005).
2. Semendeferi, K., Lu, A., Schenker, N. & Damasio, H. *Nat. Neurosci.* **5**, 272–276 (2002).
3. Bailey, P., von Bonin, G. & McCulloch, W.S. *The Isocortex of the Chimpanzee* (Univ. of Illinois Press, Urbana, Illinois, 1950).
4. Mauss, T. J. *Psychol. Neurol.* **18**, 410–467 (1911).
5. Holloway, R.L. & Post, D.G. in *Primate Brain Evolution: Methods and Concepts* (eds. Armstrong, E. & Falk, D.) 57–76 (Plenum, New York, 1982).
6. Harvey, P.H. & Krebs, J.R. *Science* **249**, 140–146 (1990).
7. Zhang, K. & Sejnowski, T.J. *Proc. Natl. Acad. Sci. USA* **97**, 5621–5626 (2000).
8. Nimchinsky, E.A. *et al. Proc. Natl. Acad. Sci. USA* **96**, 5268–5273 (1999).
9. Cáceres, M. *et al. Proc. Natl. Acad. Sci. USA* **100**, 13030–13035 (2003).
10. Holloway, R.L. *Am. J. Phys. Anthropol.* **118**, 399–401 (2002).

Schoenemann *et al.* reply:

Sherwood *et al.* find the prefrontal volume proxy we used problematic, even though it has been widely used in the neuropsychological literature for many years^{1–4}, and it (or variants) have also been applied to non-human primates^{5,6}. Sherwood *et al.* believe this proxy specifically underestimates the size of ape values, yet the frontispiece of one of the sources they cite⁷ clearly shows any underestimation is minor compared to that found in humans.

Taking refs. 7 and 8 together, we see that the degree of underestimation using this method increases as one gets closer to humans. An image highlighting the approximate degree of underestimation based on cytoarchitectural maps^{7,8} is posted on our web site, so interested readers may judge for themselves (<http://www.sas.upenn.edu/~ptschoen/Pics/prefrontal-delineation.jpg>).

Furthermore, using a proxy for prefrontal volume on MRI data is exactly what Semendeferi *et al.* have reported in this same journal⁹. Their proxy was total frontal volume minus precentral gyrus volume, which also does not follow cytoarchitectural boundaries but leads to a varying degree of overestimation of prefrontal size across species. Nevertheless, the authors argue their data “...goes against the large relative differences in the prefrontal cortex between humans and great apes reported in previous publications...” (p. 274) and “...should prove useful until more definitive data become available...” (p. 273). Our proxy is no less valid; it simply focuses on more anterior regions of the frontal cortex. Together, these studies suggest that as one looks at increasingly anterior regions, humans seem increasingly disproportionate. Comparing Figures 2 and 3 from ref. 9 to our Figures 2 and 4 makes this abundantly clear.

Sherwood *et al.* believe the strongest case for specialized enlargement of prefrontal white matter would be to show that it is disproportionate relative to prefrontal gray matter. On the contrary, given that the role of the prefrontal cortex includes executive oversight of posterior regions, the interesting question is how extensively it interconnects relative to non-prefrontal regions. Our data show that the distribution of white matter is peculiar in humans, even though it scales with prefrontal gray matter.

Sherwood *et al.* also argue that great apes alone are the only valid comparison group. The problem is that only four data points can be used to estimate this relationship, thereby vastly reducing confidence in the regression prediction. (Humans would have to be more than 950% larger than predicted in order to be significantly larger.) Thus, it is an open question whether humans have more prefrontal

white matter with respect to non-prefrontal white matter than great ape data predict, but it is not an open question regarding primates as a whole (at least from our data).

How humans differ from primates as a whole, versus how they differ from great apes alone, are really two different, equally important questions. Brodmann's original data show that chimpanzees have 56% more prefrontal surface area than predicted from non-prefrontal surface area. This, combined with our data suggesting an increased slope within great apes, may suggest that prefrontal elaboration accelerated in great apes.

The most interesting question is what all these patterns mean behaviorally. It is important to recognize that both behavioral selection and developmental constraint explanations exist for allometric scaling. Showing that allometry statistically explains some pattern does not indicate that it is therefore behaviorally irrelevant.

Semendeferi *et al.* note, “In a previous study, we found that the relative volume of white matter underlying prefrontal association cortices is larger in humans than in great apes”⁹. We believe our study is consistent with this statement.

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1. Zipursky, R.B., Lim, K.O., Sullivan, E.V., Brown, B.W. & Pfefferbaum, A. *Arch. Gen. Psychiatry* **49**, 195–205 (1992).
2. Sax, K.W. *et al. Am. J. Psychiatry* **156**, 139–141 (1999).
3. Laakso, M.P. *et al. Psychiatry Res.* **114**, 95–102 (2002).
4. Raz, N. *et al. Cereb. Cortex*; published online 9 February 2005 <<http://cercor.oupjournals.org/>>.
5. Lyons, D.M., Afarian, H., Schatzberg, A.F., Sawyer-Glover, A. & Moseley, M.E. *Behav. Brain Res.* **136**, 51–59 (2002).
6. McBride, T., Arnold, S.E. & Gur, R.C. *Brain Behav. Evol.* **54**, 159–166 (1999).
7. Bailey, P., von Bonin, G. & McCulloch, W.S. *The Isocortex of the Chimpanzee*. (Univ. of Illinois Press, Urbana, Illinois, 1950).
8. Brodmann, K. *Anat. Anz.* **41** (suppl.), 157–216 (1912).
9. Semendeferi, K., Lu, A., Schenker, N. & Damasio, H. *Nat. Neurosci.* **5**, 272–276 (2002).
10. Holloway, R.L. *Am. J. Phys. Anthropol.* **118**, 399–401 (2002).