neocortex, these two nuclei are among the brain structures that show the largest increase in primates. This interconnect-

edness between the two cortices does not appear in the measurements of Clark and colleagues.

I have considered cortical surface areas, rather than volumes, as a potentially more appropriate measure of the computational capacity of sheet-like formations, and observe a linear relation between telen-

cephalon and cerebellum over a wide range of different mammals (Fig. 1). As the cerebellum is a highly folded cortex of almost uniform thickness in all species, the increase in cerebellar size can also be measured in terms of cortical surface area.

How did brains evolve?

Three reports on mammalian brain evolution1-3 analyse the same comparative data on brain component volumes5 but come to partially conflicting conclusions. Clark et al.3 conclude from their analysis of volumetric brain proportions (“cerebrotypes”) that cerebellum size is invariant across mammalian taxonomic groups, the neocortex and cerebellum do not co-vary in size (in contradiction to ref. 1), and cerebrotype-based measures identify direc-
tional changes in brain architecture. Here I provide evidence that calls each of these conclusions into question. The failure of the cerebrotype measure to identify species differences in brain architecture that are independent of gross brain size undermines the proposal by Clark et al. that it could be useful for detecting evolutionary patterns and phylogenetic relationships.

In attempting to establish uniformity of cerebellum size, Clark et al. do not use a multiple-comparisons procedure, instead carrying out t-tests for each taxon against all the other taxa, thereby pooling taxa with smaller- and larger-than-average cerebellum size. In contrast, analysis of variance (ANOVA) on cerebellum volume proportion in nine mammalian orders5 (not including two eulachonic taxa said to deviate from cerebellar constancy6) indicates significant variance (F = 18.8, d.f. = 7, 81, P < 0.0001, 15 of 28 pairwise comparisons significant). What Clark et al. have observed is that neocortex size varies more than cerebellum size, so that variation in the latter is small as a propor-
tion of the whole. This does not, however, contradict an important evolu-
tionary relationship between them.

The fact that, as the neocortical fraction of brain size increases, the cerebellum does not, like all the other structures, decrease as a proportion of total brain volume5, suggests that the cerebellum and neocortex evolved together, but with the cerebellum evolving more slowly. When variation in the size of other brain structures is part-
tailed out, there is a significant correlation between cerebellum and neocortex size (Fig. 2). This correlation is not dependent on using residuals from linear regression, as it is also found using simple ratios of cerebellum and neocortex size to the size of the rest of the brain (across taxa, r^2 = 0.87, d.f. = 1, 91, P < 0.0001). Neither is it an artefact of taxonomic effects such as ‘grade shifts’8, as it is apparent using the method of phylogenetically independent contrasts8, which controls for such effects (primates, r^2 = 0.33, d.f. = 1, 39, P < 0.0001; insectivores, r^2 = 0.27, d.f. = 1, 32, P = 0.002). Data


correlations between cerebellum and neocortex size. The discrepancy between the results of

Clark et al.1 and the constant ratio of cerebral and cerebellar surface areas may also be due to their inclusion of the white matter in the volumes of neocortex and cerebellum. The human neocortex consists of nearly 42% white matter, a peak value for primates, in which, as in other mammals, larger brains have a greater proportion of white matter5. In contrast, the cerebellum has a more-or-

less constant proportion of white matter (30% in rats and 26% in humans). The increase in neocortical white matter during evolution7,8 probably reflects the need in larger brains to maintain the high connectivity required to operate associative networks5. The cerebellum, in contrast, lacks a system of intrinsic long-range connections and relies entirely on the opera-
tion of local short-range connections within the grey matter5. The cerebellar subcortical white matter is composed only of input and output fibres, the number of which is proportional to the surface area of the cortex.

Fahad Sultan

Department of Cognitive Neurology,
University of Tübingen, Auf der Morgenstelle 15,
72076 Tübingen, Germany

e-mail: fahad.sultan@uni-tuebingen.de

on bats also indicate a positive correlation between residual neocortex and cerebellum size ($n = 158$ species, $r^2 = 0.45, P < 0.0001$). Hence different analyses in several taxa all point to a relationship between relative neocortex and cerebellum size.

A problem with using volume proportions is that these correlate with overall brain size in all taxa studied, and hence confute allometric trends (nonlinear scaling) among brain components with variation in component size that is independent of whole-brain variation. Clark et al. mistakenly claim that volume fractions among insectivores do "not vary systematically with brain size for any principal developmental brain division". As in primates, neocortex proportion is positively correlated with brain size among insectivores (linear regression on log-transformed brain volume, $n = 50$ species; $r^2 = 0.18, P = 0.002$) and also in bats ($r^2 = 0.58, n = 158$ species, $P < 0.0001$), suggesting that this is not an unusual feature of primates associated with "directed selection pressure" in that taxon.

This conflation of brain size and size-independent structural differences limits the utility of the cerebrotype measure for evaluating adaptive patterns and phylogenetic relationships. For example, cerebrotypes place gibbons (Hylobates) with similarly sized Old World monkeys and not with their closest phylogenetic relatives, the other apes. Clark et al. suggest that selection has caused important shifts in brain proportions at the origin of major mammalian taxa, whereas constraints have resulted in "a relatively uniform cerebrotype" within each taxon. In contrast, another study concludes that mosaic brain organization is caused by selective adaptation within orders, whereas between orders there is an interplay between selection and constraints. However, it is unnecessary to postulate that constraints have been more active either at the origin of major taxa or during their subsequent evolutionary radiation. Clark et al. interpret the partly non-overlapping distributions of their multivariate representations of brain proportions as evidence that shifts in cerebrotype evolved at infrequent (about 10-million-year) intervals, followed by relative stasis. However, these distributions would be expected from an evolutionary pattern of gradual divergence and extinction of some intermediate forms. The most parsimonious assumption is that both selection and constraints operated similarly at different taxonomic levels.

Robert A. Barton

Evolutionary Anthropology Research Group, Department of Anthropology, University of Durham, Durham DH 1 3HN, UK

e-mail: r.a.barton@durham.ac.uk


Clark et al. reply — Sultan’s observations do not contradict our finding that, when normalized to the whole brain, cerebellar volume is relatively constant. To make interspecies comparisons, we used the volume fraction (the volume of a component divided by the total brain volume)3. Without this normalization, the dominant trend is variation in absolute size. This logic applies to surface areas as well, and Sultan’s interesting analysis reflects this principle.

Sultan points out that because cerebellum and neocortex differ fundamentally in their basic wiring structure, neocortical white matter should be excluded from our calculations. Doing this increases the effective cerebellar (cbl) volume fraction to $F_{cbl} = F_{cbl}/(1 - F_{cbl})$, where $F_{cbl}$ is the neocortical white-matter volume fraction. We made this correction in 44 species3 and found that its effect was negligible: $F_{cbl}$ is still relatively constant (0.16 ± 0.04, mean ± s.d., 13 taxa), whereas the corrected neocortical grey-matter volume fraction is not. The quantities are uncorrelated ($r^2 = 0.07, d.f. = 11, P = 0.4$). The cerebellar correction is largest in cetaceans ($F_{cbl} = 0.25 ± 0.06, 2$ species), emphasizing our finding that echolocating mammals have unusually large cerebellar volume fractions. Note that the use of a t-test (not ANOVA) was appropriate here because we wanted to know whether a taxon’s mean was outlying.

Barton’s allometric approach to quantifying size differences relies on fitting data to a single power law (a linear fit in log-log coordinates). He uses data on neocortical volume ($V$), cerebellar volume ($C$), and the rest of the brain ($B - N - C$). He fits for $log N$ and $log C$ against $log (B - N - C)$ by pooling primate and insectivore taxa; the fit slope is 1.62 for neocortex and 1.28 for cerebellum. But subtracting these fits discards the difference between these two baseline relationships, which constitutes the dominant size trend between neocortex and cerebellum. As the underlying reason for the fitted trend is unknown, it is unclear whether the resulting residuals are interpretable.

Calculating residuals creates another problem: pooled data from multiple taxa are generally not well fitted by a single power law.1,5 As a result, residuals calculated to a single line contain systematic errors (see Fig. 13 of ref. 1 and Fig. 4 of ref. 5). For instance, fits for different taxa often have similar slopes but different intercepts, a phenomenon known as grade shifting. This is apparent in Barton’s analysis, in which nearly all primates fall above the fit lines, causing neocortical and cerebellar residuals to be mostly positive for primates and negative for insectivores (Fig. 2), and leading to an artefactual correlation.

To remedy this, we considered the primates separately, dividing them into lemurs and lorises (haplorhines) and tarsiers, monkeys and apes (strepsirhines). After fitting each group to its own power law, we recalculated neocortical and cerebellar residuals and found that one set of residuals can explain only 9% of the variance in the other set ($r^2 = 0.09, 39$ d.f., $P = 0.1$). Recalculation including insectivores gives similar results, although classification of insectivores poses more difficulties than primates2. Therefore, the correlation reported by Barton does not exist within taxa; it largely (although indirectly) reflects differences in brain architecture among taxa. The same arguments also apply to his other analyses.

A third type of error arises when components are combined for analysis. The sum of two power laws of differing exponent can never yield a power law. Therefore any analysis (including Barton’s) that combines multiple components (for instance, the rest of the brain, or neocortex equals grey plus white matter) intrinsically contradicts the power-law assumption.

Underlying our disagreements with Barton is the fact that allometric relationships constitute ad hoc models that often provide only a rough fit to the data2. Where power-law phenomena have an explanation, such as in the circulatory system, the tissue in question is substantially more homogeneous than the whole brain. For this reason, using residuals based on subtracting approximate power-law trends may not be particularly effective at identifying relationships in the architecture of mammalian brains.

Samuel S.-H. Wang*, Partha P. Mitra†, Damon A. Clark††

Departments of Molecular Biology and †Physics, Princeton University, Princeton, New Jersey 08544, USA
e-mail: samwang@princeton.edu
† Bell Laboratories, Lucent Technologies, Murray Hill, New Jersey 07974, USA