Comparing Brains

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Some animals have larger brains than others, but it is not yet known why. Species differences in life-style, including dietary habits and patterns of development of the young, are associated with variation in brain weight, independently of the effects of body weight and evolutionary history. Taken together with behavioral and neuroanatomical analyses, these studies begin to suggest the evolutionary pressures that favor different sized brains and brain components.

WE HUMANS SET OURSELVES APART FROM THE REST OF the animal kingdom by our superior intellect, a physical manifestation of which is often considered to be the large size of our brains. Perhaps important clues to the reasons for humans having such large brains can be gleaned from studies that compare the brains of different species. Just as gut size and morphology have been successfully related to the feeding habits of different animal species, so we might expect brain size and morphology to be related to information processing, storage, and retrieval needs. What life-styles have favored the evolution of larger brains, and why? Have different components of the brain evolved independently of each other in response to particular environmental demands? We do not yet know the answers to these critical questions, but in recent years some clear patterns and generalizations have emerged, which point to ways of integrating ecological, evolutionary, physiological, and neuroanatomical studies.

In fact, the human brain is not so very large. Weighing in at about 1.3 kg, our brains are dwarfed by those of some other mammals. For example, the brains of several baleen whale species and the toothed sperm whale weigh between 5 and 8 kg, and those of the African and Indian elephants also weigh more than 5 kg. Whales and elephants are heavier than humans and, the argument generally runs, the human brain is heavy in relation to the weight of the body. It is because heavier bodied species have heavier brains that comparative studies of brain volume or weight are sometimes made among species of similar body weight. Alternatively, comparisons are more often made after controlling statistically for the effects of body weight or some other size-related reference variable. Encephalization, a comparative concept, is measured as a species' deviation from some observed or expected relation between brain mass and body mass in a reference group.

Several problems are associated with both the concept and measurement of encephalization, including the choice of a reference variable, the choice of a reference taxonomic or phylogenetic group, and the choice of a reference curve or line. In each case, the estimate of encephalization obtained depends on the procedure used.

Body Weight as a Reference Variable

The finding that brain weight increases with overall body weight does not necessarily imply a cause and effect relation. Many components of the body increase with body weight and, for the most part, body weight is employed as a surrogate measure for some (perhaps unidentified) underlying variable.

In fact, body weight may be a particularly unsuitable reference variable for some purposes because it varies so much, both among individual adults at any one time and within individuals from time to time. Brain weight, which varies very little during an adult's lifetime, may be more highly correlated with some morphological, life history, or environmental variable than is body weight simply because the body weights are unrepresentative, being derived in part from pregnant, obese, or emaciated animals. Sacher (*1*) found that maximum recorded life-span was more highly correlated with adult brain weight than with adult body weight across a sample of mammal species. As a consequence, life-span increased with brain weight when the effects of body weight were held constant, leading Sacher to suggest that the brain somehow controls maximum life-span. In response, Economos (*2*) pointed out that species differences in life-span are more highly correlated with the weight of the adrenal gland than with brain size. Instead of arguing that the adrenal gland influences life-span, Economos pointed out that intraspecific variation in adrenal gland size is very small indeed. The implication was that adrenal gland weight may provide a less variable measure than either brain or body weight.

This statistical problem is most serious when the comparative analysis requires that the influence of body weight should be removed from both brain weight and the variable with which brain weight is being correlated because, in such a case, a correlated source of statistical error is added to both variables. When such an analysis is necessary, one way of eliminating the problem is to demonstrate that some independent estimate of size, derived from a different sample of individuals, produces similar taxonomic correlates of encephalization.

Choice of Reference Group

Bauchot and Stephan (*3*) and many since have used a group of extant insectivore mammal species, the so-called "basal insectivores," as a reference group for mammals on the assumption that their brains are similar in structure to those of early mammals. For similar reasons, Portmann (*4, 5*) used the extant Galliformes as a reference

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group for birds. Under such schemes, encephalization is presumably meant to refer in some sense to a measure of "evolutionary progression." Rather than attempting the dubious exercise of describing evolutionary progression from extant species, it is more common nowadays to seek life-style correlates of encephalization that have evolved independently in different phylogenetic lineages. In such cases, the reference group from which encephalization is calculated usually consists of all extant species derived from a particular common ancestor—a monophyletic group in Hennig's sense of the term (*6*). Encephalization varies with the reference group used. For example, almost all primates are highly encephalized when mammals are used as the reference group, but about half the primate species inevitably lie below the reference line when primates themselves are used as the reference group.

Expected Versus Observed Reference Lines

Expected lines. It has been fairly common practice to impose a line with a predetermined exponent through the reference taxon on the graph of brain weight versus body weight. For example, after reviewing several alternatives, Jerison (*7*) argued for the use of a two-thirds exponent because "2/3 implies a surface:volume relationship and may, therefore, be the basis for theorizing on the significance of the brain size" (*7*, p. 49). As we understand Jerison's subsequent formalization of the idea (*8*), the brain is considered to carry two-dimensional projections of a three-dimensional world and, therefore, the brain may be viewed as a series of sheets of cells. The three-dimensional world is represented by an animal's body (in an unspecified fashion) and, therefore, the square root of brain weight should be proportional to the cubed root of body weight. If that is so, brain weight should scale on body weight with a power of two-thirds. Jerison's model originally assumed that the sheets of cells of which the brain is composed are of equal thickness but, taking into account the fact that larger bodied animals have a thicker neocortex, Jerison went on to argue that a somewhat steeper exponent might be expected (*9*).

Another expected line is that defined by the genetic covariance between brain and body weight (*10*). For example, selection for changed body weight would result in a correlated response in brain weight, partly because some genes whose products influence the weight of one character may also influence the other (for example, generalized growth hormones). Similarly, genetic drift may produce an evolutionary correlation between brain and body weight. The correlated genetic response may produce animals with brain sizes that cause them to leave less offspring than larger or smaller brained alternatives of the same body weight. In such cases, natural selection may be expected to break the evolutionary allometry by favoring alleles whose products lead to changes in either brain weight or body weight, but not both.

Observed lines. An alternative to using curves with fixed exponents, which convert to straight lines with fixed slopes when the brain and body weight data are logarithmically transformed, is to use a reference line of best fit to the available data, although calculating such a line produces two problems. First, species cannot be treated as independent points in a comparative analysis because closely related species tend to be similar by descent from a common ancestor (*11–13*). Second, the statistical procedure for producing a best fit line will usually determine its form. We consider each problem in turn.

If our reference taxon was the apes, there would be four species of great apes (two chimpanzees, the gorilla, and the orangutan), humans, and about eleven lesser apes (ten gibbon species and the siamang). The lesser apes would contribute excessively to an estimate of the line of best fit. Since the lesser apes have small bodies and small brains for their body weights in comparison with the other apes, the line calculated across all species points would have a steeper slope and lower overall elevation than if lesser apes were either excluded from its calculation or used as a single point. Should we use genus values calculated from constituent species averages as our independent data points for estimating the reference line? The answer must be no because, just as closely related species values cannot be considered as independent points for a statistical analysis, so genera within taxonomic families (for example, gibbon and siamang) are likely to be more similar to each other than are genera from different families (gibbon and gorilla). One reason for this taxonomic dependence is that evolutionary changes occurring in the past are likely to be inherited by present-day descendants. For example, a rapid increase in brain size in the most recent common ancestor of the great apes might be inherited by all descendent species.

One solution to the problem of taxonomic dependence was provided by Felsenstein (*13*) who pointed out that, given a phylogenetic tree, differences between daughter taxa emanating from the same node will have evolved independently of differences elsewhere on the phylogenetic tree. Given a bifurcating tree (two daughter taxa emanating from every node), there will be $n - 1$ independent comparisons, where n is the number of extant species. However, phylogenetic trees are not accurately known, and many trees contain nodes with more than two daughter taxa (for example, three or more species per genus). Various methods have been devised for deriving near independent comparisons from such coarsened trees (*12, 14–16*). When comparisons for brain weight are plotted against those for body weight, we can identify cases where the evolved difference in brain weight is either smaller or larger than is typical for the observed difference in body weight (Fig. 1).

When brain and body weight data have been logarithmically transformed, the relation between the two variables is roughly

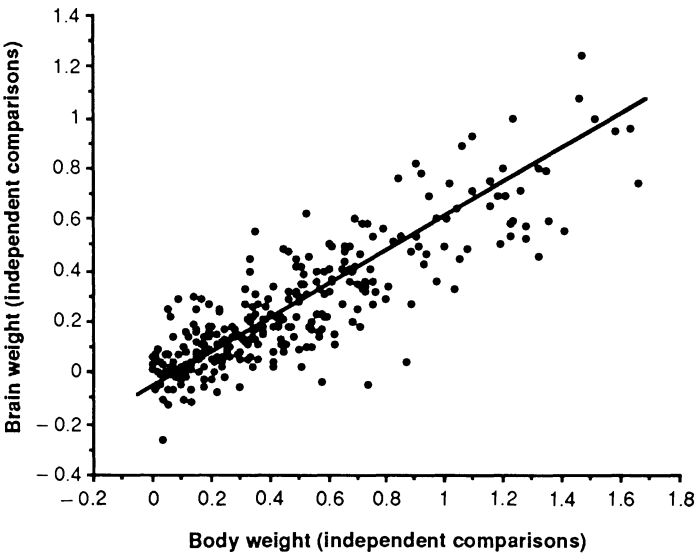


Fig. 1. Plot of contrasts on brain weight against contrasts on body weight (n = 308) obtained from an analysis of 917 mammal species. Each point represents a comparison among different daughter taxa, so that for each node of the taxonomic tree (assumed to be a phylogenetic tree) a single comparison is calculated to provide a weighted average [more strictly, a linear contrast (*60*)] of differences in body and brain weight among daughter taxa (*14*). The slope of the line, fitted by the structural relations model with $\lambda = 0.20$, is approximately 0.69 (see text). Many early analyses suggested a 0.67 slope, whereas comparisons across species from different orders suggested a slope of 0.75. The graph given here incorporates comparisons from all taxonomic levels. Data from (*12, 21*).

linear. However, if the correlation is not very large (that is, if it lies between 0.98 and −0.98), the form of the line of best fit is rather sensitive to the method of curve-fitting used. The three methods in common use, model 1 regression (the ordinary least squares method in which the independent variable is regarded as having been estimated without error), major axis, and reduced major axis, are special cases of the general structural relations model (*17, 18*) that make different assumptions about the relative amount of statistical error variance associated with estimates of brain and body weight. Apart from measurement error, which is generally small, statistical error variance arises from real biological differences. One major source of such variance is the difference among individuals of a species, with the ratio of variance in brain weight to variance in body weight among adults (on logarithmically transformed data) being about 0.2 (*19–22*). When small samples of individuals are used to estimate the species-typical weights (fewer than five individuals are frequently used), the higher variance among individuals in body weight may lead to inaccurate estimate of the species average body weight. Model 1 regression assumes that there is no such statistical error variance in body weight; major axis assumes that the ratio of error variances in brain to body weight is 1.0; and reduced major axis assumes that the ratio of error variances in brain to body weight is the same as the ratio of the true variances. The structural relations model with estimated error variances is to be preferred over each of these special cases for defining the functional relation (*18*). However, if encephalization quotients are required to be uncorrelated with body weight, deviations from the model 1 regression line will, by definition, provide such measures.

Explaining Exponents

The exponent linking overall brain weight to body weight across samples of vertebrate species has been of considerable interest in its own right. In 1975, Gould wrote that brain weight "generally scales to the two-thirds power of body weight (an immense number of sources ranging from Snell, 1891 [*23*] to Jerison, 1973 [7]); a relationship between brain weight and body surfaces is here implicated, but it has never been satisfactorily explained" (*24*, p. 248). Subsequently when data sets containing information from more species were used, it became generally acknowledged that the exponent across samples from all orders of mammals was somewhat higher, probably nearer to 0.75 (*25–28*). Whereas a two-thirds exponent had been thought by Gould to implicate body surface areas (which increase approximately with the two-thirds power of body weight), so a three-quarters exponent suggested to others an energetic explanation for the scaling of brain on body weight (basal metabolic rates increase approximately with the three-quarters power of body weight).

Three attempts have been made to explain the three-quarters exponent in terms of energetics. First, Armstrong (*29*, p. 1303) argued that "among extant mammals an increase in brain size keeps pace with an increase in body size when the size is adjusted for the availability of energy." It is not clear why mammals should have been selected to supply a constant proportion of their daily basal energy turnover to the brain, nor why the primates should have been selected to allocate a higher proportion (9 to 20%) of their daily energy turnover to their enlarged brains than do typical mammals (about 5%). In a sense, Armstrong's argument was nothing more than a restatement of the then known facts (*27*).

The second energetic explanation was proposed by Martin (*26, 30*) who had presaged Armstrong's hypothesis and dismissed it on the grounds that it lacked generality—the exponent linking brain and body weight across birds and across reptiles was 0.56 and not 0.75 (*31*). Martin used the fact that 0.75 squared is about 0.56 to suggest that brain size is limited in birds and reptiles by two consecutive metabolic processes but that in mammals only a single limiting metabolic stage is involved. In our summary of Martin's argument below, the subscript m refers to mammals, and b to birds and reptiles. According to Martin, metabolic rate (M) in mammals increases with the 0.75 power of adult body weight (B), and the weight of the neonate's brain (N) is determined by the mother's metabolic rate. Therefore, neonatal brain weight scales to the 0.75 power of maternal body weight. All neuronal division is complete at birth, so that postnatal brain development consists of the expansion of existing neurons and the addition of glial cells. This means that adult brain weight (A) is a body-size–independent multiple of neonatal brain weight and therefore scales with the 0.75 power of adult body weight.

$$M_m \propto B_m^{0.75} \quad (1)$$

and

$$N_m \propto M_m \quad (2)$$

therefore

$$N_m \propto B_m^{0.75} \quad (3)$$

$$A_m \propto N_m \quad (4)$$

therefore

$$A_m \propto B_m^{0.75} \quad (5)$$

Martin suggests that a two-stage metabolic process limits brain weight in birds and reptiles because the mother must produce an egg, and the egg must produce the neonatal brain. Martin's argument goes that, as with mammals, maternal metabolic rate scales with the 0.75 power of her body weight. Egg weight (E) is determined by maternal metabolic rate, so egg weight scales with the 0.75 power of maternal body weight. The metabolism of the egg (P) scales on egg weight with the 0.75 power, and hatchling brain weight (H) is directly proportional to the metabolism of the egg. It then follows that hatchling brain weight scales with the 0.56 power of maternal body weight. Since neuronal division determining the size of most components of the adult brain is complete at birth (*32*), to a good approximation adult brain weight is a multiple of hatchling brain weight and, therefore, scales with the 0.56 power of adult body weight.

$$M_b \propto B_b^{0.75} \quad (6)$$

$$E_b \propto M_b \quad (7)$$

therefore

$$E_b \propto B_b^{0.75} \quad (8)$$

$$P_b \propto E_b^{0.75} \quad (9)$$

$$H_b \propto P_b \quad (10)$$

therefore

$$H_b \propto (B_b^{0.75})^{0.75} = B_b^{0.56} \quad (11)$$

$$A_b \propto H_b \quad (12)$$

therefore

$$A_b \propto B_b^{0.56} \quad (13)$$

There are many unexplained assumptions built into Martin's theory. Why should birds, mammals, and reptiles be selected to have as large a brain as their metabolic rates will allow? Why should the proportion of metabolic turnover which is allocated to the neonate's brain be the same, irrespective of species differences in adult body weight? Why should hatchling brain weight scale in proportion to the

metabolic rate of the egg, which must not only provide for the chick at the time it hatches but also for the developing embryo? However, even if we accept the assumptions and the exponents as stated, Martin's hypothesis fails against a number of its own predictions. For example, mammals with high basal metabolic rates for their body size do not produce large brained young (*33*), as would be predicted if the brain size of the young was determined by the metabolic rate of its parent (Eq. 2). Furthermore, when total litter brain mass is plotted against basal metabolic rate, the exponent is about 0.85 instead of the predicted 1.0 (also Eq. 2) (*33*). Among birds, hatchling brain weight scales on maternal body weight with an exponent of about 0.4, which is significantly below 0.56 (predicted by Eq. 11), whereas adult brain weight scales on hatchling brain weight with an exponent of about 1.45, which is significantly above 1.0 (predicted by Eq. 12) (*34*). Other problems with the hypothesis are discussed elsewhere (*33, 34*).

The third explanation for the 0.75 exponent in mammals is Hofman's (*35*) proposal that maternal metabolic turnover constrains gestation length and thereby limits neonatal brain size. Hofman's suggestion is a variant of Martin's because it proposes that neonatal brain weight is limited by the mother's metabolic rate, albeit indirectly (*26, 30*). But, as we have already mentioned, mammals with high metabolic rates for their body weight do not produce large brained young. Furthermore, when body weight is held constant, species with long gestation lengths do not have particularly high metabolic rates (*33*). However, as we shall see below, there are indications that different patterns of neonatal development can be associated with different neonatal and adult brain weights.

Correlates of Encephalization: The Whole Brain

A number of studies have sought life history, ecological, and morphological correlates of encephalization. Despite an enormous literature on the topic with a variety of encephalization quotients, relatively few consistent patterns have emerged that are independent of phylogenetic associations. It has not been unusual to seek associations between encephalization and more than 20 variables that summarize the life-styles of the various species in a focal taxon. In such cases, we should expect at least one variable to show a significant association at the 5% probability level, simply by chance. Accordingly, we focus our attention on associations that are either highly significant or recur within several different taxa. There are two sets of such consistent correlates: the first is with diet in mammals and the second with pattern of development in birds. Neither has been satisfactorily explained, and investigations have yet to proceed from the identification of patterns in the data to the formulation of testable hypotheses that might explain them.

Diet in mammals and development in birds. Fruit-eating bats have larger brains for their body weights than do insectivorous species (*36, 37*). Eisenberg and Wilson (*37*) speculated that the difference may be a consequence of the greater foraging demands faced by the frugivorous (fruit-eating) species. Taken alone, the dietary association with encephalization in the bats would not be particularly impressive because it is associated largely with members of a single fruit-eating family—the Pteropodidae—having relatively large brains. However, dietary correlates of encephalization have been identified in two other orders of mammals, the rodents and the primates (*38, 39*). When separate comparisons were made on species belonging to nine different families, in each case, leaf-eating primates and rodents were found to have smaller brains for their body weights than did their closest relatives that do not feed on leaves. It is not likely that these differences can be attributed to the relatively large guts of the leaf-eating mammals, but they do seem to be associated with differences in ranging behavior, with the leaf-eating mammals having smaller home ranges.

These associations in primates, small mammals, and bats have led to the suggestion that differences in encephalization arise through variation either in the range of stimuli that need to be processed for feeding or in the associated information storage and retrieval systems, rather than through the nature of the food resource. Ecologically monotypic families allow a further insight (*40*). If the range of sensory stimuli in an animal's environment relates to selection for increased brain weight, we might expect fossorial (burrowing) families to have especially small brains for their body weight, which, for the most part, they do. Although differences in encephalization among primates and rodents are associated with diet, they seem to be uncorrelated with other aspects of life-style such as activity timing (nocturnal, diurnal, or crepuscular), breeding system, habitat, and degree of independence of the young at birth (*34, 39*).

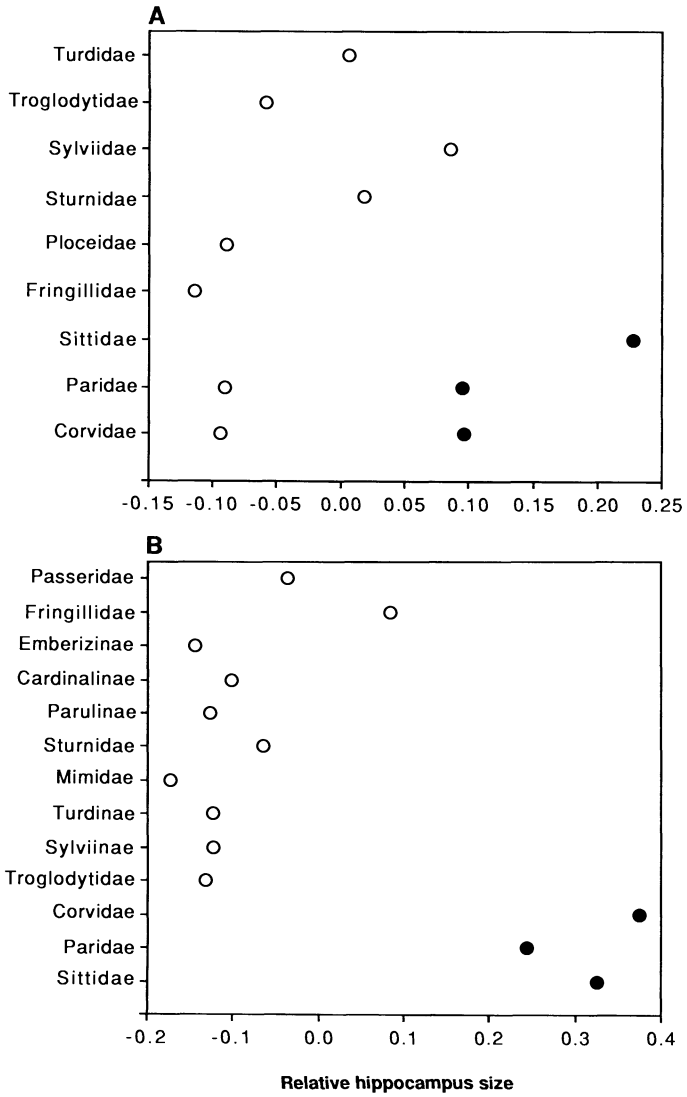
The dietary correlates of encephalization may, it seems, have helped to explain one of the oldest puzzles in the study of brain weight allometry (*21*). Exponents relating brain to body weight among adults of closely related species were found to be much shallower than similar exponents for more distantly related species. It was often claimed that species from the same genus were linked with an exponent of between 0.2 and 0.4, whereas the exponent for species from different orders was typically between 0.67 and 0.75. Recent analyses suggest that part of the difference resulted from the use of inappropriate statistics. For example, because the ratio of error to real variance is greater among species of more similar body weights, model 1 regression analysis on logarithmically transformed data provides consistently greater underestimates of the true slope for samples of more closely related species (*28*). Simulation studies showed that major axis and reduced major axis analysis would also produce an artifactual pattern of increasing slope with taxonomic level of analysis (*20*). When the more appropriate structural relations model was used, there was little if any general pattern of increased slope with taxonomic level (*21, 41*). Furthermore, there is evidently considerable variation among orders of mammals in the magnitude of slopes calculated from independent comparisons within those orders, varying from 0.46 for cetaceans, through 0.70 for marsupials, to 0.92 for primates (*12*). The latter finding casts considerable doubt on the existence of a universal or general exponent for the mammals and, therefore, on the value of the attempts discussed in the previous section aimed at interpreting empirical exponents calculated across samples of mammals from different orders. The three orders within which slopes markedly increased with the taxonomic level of comparison were the bats, the rodents, and the primates. Controlling for dietary differences with the use of partial regression removed the effect from those orders also (*21*).

These recent analyses do not rule out the possibility of low exponents among adults from closely related species. [Indeed, at a lower level of comparison, within species, there is often little if any relation between brain weight and body weight among adults of the same sex (*28*).] There is a clear need for careful statistical analyses of appropriate data that will apportion the sources of statistical error variance to their appropriate biological and nonbiological sources (*10, 42*). For example, differences in adult brain weight and in adult body weight among closely related species may result from selection acting on brain weight, on body weight, or on both. If there is a genetic correlation between characters, selection on one character may produce a correlated evolutionary change in the other. There is also the associated ontogenetic perspective (*24, 42*). When differences in adult body weight among closely related species result from differences in the period of prenatal or early infant growth, we might

expect marked differences in adult brain size because the brain grows much faster in relation to the body during early development. In contrast, when differences in adult body weight result from prolonged periods of juvenile or subadult growth, we should expect to see relatively smaller differences in adult brain than body weight.

A lack of association between encephalization and patterns of juvenile development among the mammals contrasts strongly with findings from birds—precocial mammals, defined as those with their eyes open at birth or shortly afterwards, do not have smaller brains as adults than altricial species (*34*). In contrast, Adolf Portmann, using Galliformes as a reference group from which to record encephalization, found that patterns of development of the young are correlated with differences in brain weight among adult birds: altricial species, defined here as those born with their eyes closed and without down, have larger brains as adults than do precocial species (*4, 5*). Bennett and Harvey (*43*) confirmed Portmann's findings for the whole brain (as well as for the brain stem, optic lobes, cerebellum, and hemispheres) in analyses that controlled for both taxonomic association and the potential confounding influence of many other behavioral and ecological variables (including diet, which was not associated with taxonomic differences in encephalization among birds).

The difference in correlates of encephalization between birds and mammals remains puzzling. In summary, encephalization in mammals is often associated with dietary differences, whereas in birds it is associated with varying patterns of hatchling development (*44*). A comparison of brain development of the two groups may prove profitable. In relation to adult body size, altricial birds have smaller brained hatchlings than do precocial species, but grow to have larger brains as adults (*34, 43*). Much more of an altricial bird's brain growth is done in the nest after hatching, which possibly facilitates the development of a larger adult brain, whereas precocial birds are hatched more nearly wired up and ready to go. Among mammals the picture is slightly different. Species with long gestation lengths for their body size do give birth to relatively large brained young, both in relation to the size of the mother and to the size of the neonate (*33, 45, 46*), but postnatal brain growth is reduced so that relative gestation length is not correlated with encephalization among adults. Gestation length is closely tied to neonatal brain weight, which itself helps define an altricial-precocial axis for mammals. The reasons why precociality is favored in only some species is not properly understood, but is probably related to species differences in age-specific mortality patterns (*46, 47*).



Correlates of Encephalization: Parts of the Brain

It may be difficult to evaluate the significance of a correlation between the size of the whole brain and an ecological variable, because the brain is a heterogeneous structure in which different parts serve different functions. Instead it may be more revealing to look for associations between ecology or behavior and well-defined regions of the brain with known functions. Take, for example, the correlation between diet and encephalization in the three mammal orders referred to earlier. As described in the last section, the generally accepted account of this association is that leaf-eaters do not need to remember as much about the temporal and spatial distribution of their food as do frugivores and seed-eaters. Although it is possible that the greater requirements for information processing arising from a diet of fruit or seeds have resulted in a nonspecific increase in brain size and "intelligence" (*48*), it is perhaps more plausible to hypothesize that the demands of remembering temporal and spatial patterns of food have led during evolution to selective enlargement of the specific brain regions concerned with this kind of processing. Most studies of encephalization have not considered specialization of brain and behavior at this level. There are several examples of correlations between behavior or ecology and enlargement of particular brain regions [for example, bird song and certain

Fig. 2. Two studies in which the volume of the hippocampal region (dorsomedial cortex) of food-storing and non–food-storing passerine birds was compared. (**A**) Krebs *et al.* (*51*) measured the volume of the hippocampus and telencephalon of 52 individuals belonging to 35 species or subspecies of (primarily) European passerines in nine different families. (**B**) Sherry *et al.* (*52*) measured 28 individuals belonging to 23 species of North American passerines in 13 different subfamilies (these authors analyzed their data at the subfamily level, whereas Krebs *et al.* used families). In both studies, multiple regression was used to remove the effects of body size and telencephalon volume. Storer/nonstorer was coded as a dummy variate and other possible confounding ecological variables were examined in a similar way. The graphs show deviations from the regression line fitted to a plot of residual variation in hippocampal volume on body weight against residual variation in telencephalon volume on body weight. In other words, the average hippocampus size relative to body and telencephalon size is shown for each family. In the study of Krebs *et al.* (*51*), members of the Corvidae and Paridae were divided into those species which store food and those which do not; hence there are two points for each of these families. In both studies, the effect of food storing on hippocampal volume was highly significant after removing effects of body mass and telencephalon volume.

telencephalic nuclei (*49*); use of touch for feeding and trigeminal projection nuclei in shorebirds (*50*)] but for the most part these studies have not examined more than a few species, nor have they corrected for effects of body size or other confounding variables.

Two recent examples illustrate the potential of comparative studies of encephalization of specific brain regions. Krebs *et al.* (*51*) and Sherry *et al.* (*52*) showed that among European and North American passerine birds, respectively, there is an association between the volume of the hippocampal region (dorsomedial cortex), relative to body and telencephalon volume, and a particular behavioral trait, namely food-storing (Fig. 2). Among the passerine birds, some species in three families, the Paridae (titmice), Sittidae (nuthatches), and Corvidae (crows) store food in many thousands of sites in their home range. Behavioral studies have shown that these birds use a long-lasting, accurate spatial memory to retrieve their hoards (*53*). Furthermore, the food-storing species have a longer lasting spatial memory when compared with closely related nonstorers in certain laboratory tasks (*54*). The hippocampal region of birds, as in mammals, plays a role in processing certain kinds of memory including spatial memory (*55*). It seems likely, therefore, that food-storing has resulted in an adaptive specialization of memory and a concomitant enlargement of the hippocampus. Similarly, Healy and Guilford (*56*) have shown that in 12 of 13 independent taxonomic comparisons, nocturnal birds tend to have a larger olfactory bulb, relative to overall brain and body size, than do diurnal families (*57*). As in the study of hippocampal volume, possible confounding ecological variables were examined and found to be unimportant. The inference from this study is that nocturnal birds rely more heavily than do diurnal species on olfactory cues for orientation, location of food, and so on, and have hence evolved a larger sensory apparatus for acquisition of olfactory information.

A notable feature of both these examples is that, although one brain region is enlarged, the whole brain is not: food-storers do not have a larger telencephalon, relative to body size, than do nonstorers, they simply have a larger hippocampus. This implies either (i) that some other part of the telencephalon must be smaller in food-storers than in other species, or (ii) that the hippocampus is such a small part of the telencephalon that taxonomic differences in hippocampus size do not contribute significantly to differences in telencephalon size. In either case, it raises the question, discussed earlier, of what constrains overall brain size. If overall size is constrained, for reasons not yet understood, it may well be that specialized enlargement of one region has to be associated with reduction in size of another area. An early suggestion of such a constraint is due to Mark Twain: "I never could keep a promise. I do not blame myself for this weakness, because the fault must lie in my physical organization. It is likely that such a liberal amount of space was given to the organ which enables me to make promises that the organ which should enable me to keep them was crowded out" (*58*, p. 148). In other words, there may be trade-offs in the evolutionary specialization of the brain. As yet these trade-offs have still to be identified (*59*), let alone understood in terms of their behavioral consequences. Further studies of allometry of particular brain regions in relation to behavior may help to provide the answers.

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62. We gratefully acknowledge grants from the Commission of the European Communities [to P.H.H., SCI*.0184.C(JR)], the Royal Society (to J.R.K.), and the Science and Engineering Research Council (to J.R.K.), which helped finance our recent contributions to the work described in this article. We thank S. Healy, A. Read, and B. Riska for helpful comments on a draft of this manuscript. B. Riska suggested the quotation from Mark Twain.

Research Article

Soluble Human Complement Receptor Type 1: In Vivo Inhibitor of Complement Suppressing Post-Ischemic Myocardial Inflammation and Necrosis

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The complement system is an important mediator of the acute inflammatory response, and an effective inhibitor would suppress tissue damage in many autoimmune and inflammatory diseases. Such an inhibitor might be found among the endogenous regulatory proteins of complement that block the enzymes that activate C3 and C5. Of these proteins, complement receptor type 1 (CR1; CD35) has the most inhibitory potential, but its restriction to a few cell types limits its function in vivo. This limitation was overcome by the recombinant, soluble human CR1, sCR1, which lacks the transmembrane and cytoplasmic domains. The sCR1 bivalently bound dimeric forms of its ligands, C3b and methylamine-treated C4 (C4-ma), and promoted their inactivation by factor I. In nanomolar concentrations, sCR1 blocked complement activation in human serum by the two pathways. The sCR1 had complement inhibitory and anti-inflammatory activities in a rat model of reperfusion injury of ischemic myocardium, reducing myocardial infarction size by 44 percent. These findings identify sCR1 as a potential agent for the suppression of complement-dependent tissue injury in autoimmune and inflammatory diseases.

ACTIVATION OF THE COMPLEMENT SYSTEM CAUSES TISSUE injury in animal models of autoimmune diseases, such as immune complex–induced vasculitis (*1*), glomerulonephritis (*2*), hemolytic anemia (*3*), myasthenia gravis (*4, 5*), type II collagen-induced arthritis (*6*), and experimental allergic neuritis (*7*), and in two nonimmunologically mediated forms of primary tissue damage, burn (*8*), and ischemia (*9, 10*). The pathobiologic effects of complement are mediated directly by C5b, C6, C7, C8, $C(9)_n$, the cytolytic membrane attack complex, and indirectly by the fragments of activated C3 and C5 that stimulate a range of proinflammatory responses from mast cells and leukocytes (*11*). Indeed, if animals are transiently depleted of C3 and C5 by treatment with cobra venom factor, they are protected from tissue injury in each of these disease models. Our studies provide evidence for the potential therapeutic