Perspectives

From mice to men: the evolution of the large, complex human brain

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1. Introduction

My interest in brain evolution developed because I had the opportunity to study with two outstanding neuroscientists who studied how brains of different mammals were similar and different. As a graduate student, I worked with Irving Diamond at Duke University where his laboratory studied brain organization and behaviour in such seldom investigated mammals as tree shrews, squirrels, hedgehogs, and opossums. I continued with postdoctoral training at the University of Wisconsin where Clinton Woolsey was describing the organization of sensory and motor areas of neocortex in rabbits, cats, and monkeys. For a while, I concentrated on studies of visual cortex organization in New World owl monkeys. After I was appointed as an associate professor at Vanderbilt University, I was able to gradually expand my research, with the help and leadership of a talented group of graduate students and postdoctoral fellows, to include investigations of the somatosensory, auditory and motor systems. Over time we were able to study these systems in a range of mammals, including a number of species of prosimian and simian primates, as well as study brain material obtained after natural death from apes and humans. We also studied hedgehogs, tenrecs, shrews, moles, rats, squirrels, cats, and tree shrews, but the general goal was to see how brains were similar and different, and use this information to infer the course of brain evolution from early mammals to present-day humans. Like exploring the universe, the task is so enormous that we will never be done, but the fun is in the journey, and we feel that we have made great progress. The future is especially bright, as I started this journey when few methods were available to reveal brain organization and function. Gradually, more-powerful methods emerged, and we now seem to be in an explosion of technical advances. The brief outline of brain evolution that follows will be replaced by a much more detailed description in 10 years.

Humans are known for their curiosity, and they are especially curious about themselves. All cultures have stories about human origins and history. Most of us are extremely interested in human behaviour. We watch and listen to others, read books about others, and watch plays and movies about others. We see similarities and differences in our behaviour and those of other mammals, and seek to understand these similarities and differences. Because all our thoughts, actions, and feelings are generated by our brains, and the very concept of self depends on our brain, it is natural to wonder how our brain works. And if we reflect on our impressive range of human abilities, and compare these to those of other species, especially other primates, one might wonder about how brains differ, and how our unusually large and complex brain evolved.

Scientists have long been interested in these questions, but until recently, very little was known about brains. Of course, it was realized that brains of different species vary greatly in size and shape, and that large mammals tend to have large brains. Thus, elephants and whales have even bigger brains than humans. After a period of uncertainty, early scientists also understood that different parts or regions of the brain had different functions, as this could be quite obvious after certain lesions of the brain (damage to specific brain areas resulted in the loss of specific abilities). A critical advance occurred when observations of 100 years ago led to the adoption of the neuron doctrine, the concept that the basic element of brain function was the neuron, a morphologically distinct unit, rather than a nerve net of conjoined neurons. Since neurons do not become huge in large brains, one obvious difference between the brains of "mice and men" is that we have many more neurons. Gradually, and then with an accelerating pace, more became known about brains, as technical advances and research funding made progress even more possible. Because of these advances, it is now possible to portray the broad outlines of brain organization

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and function in humans, and trace the probable course of brain changes from early mammals to current humans.

2. How do we chart the course of human brain evolution?

Perhaps the most challenging of the pursuits in neuroscience is that of reconstructing the evolutionary history of our brains. Our large, complex brains evolved from a much simpler, smaller bilateral pattern found in the early vertebrates over 400 million years ago (mya). A major advance occurred with the emergence of early mammals over 200 mya when the thin dorsal cortex of the brain of reptiles was modified to form the thicker, layered neocortex of mammals (Northcutt and Kaas 1995). As a result of 200 million years of divergent evolution, mammalian species now vary greatly in amount of neocortex and overall brain size (figure 1). The large human brain is dominated by a huge, highly folded sheet of neocortex that covers the rest of the brain. Because the neocortex is the most enlarged part of the human brain, compared to most other mammals, the focus here is on how this important part of the brain evolved. The answer is not known in detail, but the broad outlines of this story are now clear.

An obvious problem in studying the course of brain evolution is that brains do not fossilize, so we cannot directly study the brains of a sequence of ancestors and chart the changes over time. Yet, we can learn something from the fossil record, as skulls do fossilize, and the size and shape of the brain can be closely estimated from the inside dimensions of the brain case of fossilized skulls or the preserved natural endocasts of the brain case of extinct mammals. For example, by reconstructing the brain from the brain case of a 147 million year old Archaeopteryx skeleton, the oldest and most primitive of fossil birds, it was possible to conclude that the brain was large for a reptile, but small for a bird, while still bird-like in shape (Dominguez *et al* 2004). Thus, early birds had modified brains in external appearance in ways that suggested neurological adaptations for flight, but the small size of the brain indicates that the adaptation to the bird niche was incomplete. We know from such historical fossil evidence that early mammals were small and had small brains with little neocortex (Jerison 1973). In external appearance, the brains of early mammals did not look much different from the brains of a number of small-brained mammals that continue to exist today. We know that brain size increased relative to body size in many branches of mammalian evolution, including the primate line leading to humans. In particular, human brains increased 3–4 times in size from our ancestral apes over the course of the last 5 million years, mainly in the last 2 million years (Kaas and Preuss 2003). Thus, it is certain that one feature of brains, size, varied over time and our history from the first mammals to the present time was characterized by a dramatic increase in brain size, slowly at first and very rapidly in recent times. When behavioural range and capacity is related to brain size across mammalian species, clearly brain size is a very important factor (Roth 2001). This makes intuitive sense, as large brains with more neurons should have more computational power.

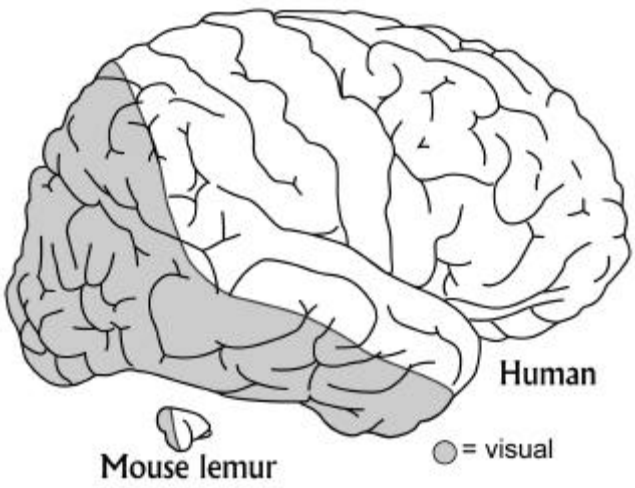

Figure 1. The brains of primates vary greatly in size, from the huge human brain (above) with many fissures, to the small brain of the mouse lemur (below), a member of the prosimian radiation in Madagascar. As for several other small-brained primates, the mouse lemur cortex has only two fissures, the lateral or Sylvian fissure, and the calcarine fissure of the medial cortex (not shown). The estimated proportion of cortex devoted to processing visual information is shaded.

Yet brain size is only part of the story. Brains are made up of functionally distinct parts or "organs", usually called nuclei for subcortical parts, and areas or fields for cortical parts. Parts are interconnected to form systems that process information from receptors, store information from the past, and organize and control behaviour. Such systems have some features in common across mammalian species, but they are also extremely varied as they have been modified in evolution to address the cognitive and behavioural needs of mammals as they adapted to different environmental niches. Simply put, it is not our larger brain alone that makes our behaviour different from that of a cat or tiger, but also differences in brain organization. If dead brains rapidly rot and disappear, how can we ever know how the brains of our long dead ancestors were organized? The answer is to infer the organization of the brains of ancestors from the organization of the brains of living (extant) species where detailed studies of brain organization are possible. But what is the logic of such an approach?

Early investigators (e.g. Clark 1959) made inferences about the course of human brain evolution by assigning related extant species to a series of levels, basically assuming that such relatives constitute "living ancestors". Thus, small brained tree shrews, a squirrel-like relative of primates once thought to be a primitive primate, were at the base of the primate tree of evolution, with prosimian primates, smaller monkeys, larger monkeys, and apes forming the successive steps on the ladder of levels to humans. While this approach did provide a rough description of the course of human brain evolution, there was no obvious way to distinguish brain specialization unique to the representative species or taxa from primitive traits that we inherited from primate ancestors. Fortunately, this early approach has been refined and constrained by formal rules that apply broadly to the study of evolution (Hennig 1966).

The basic assumption of a phylogenetic or cladistic approach is that living mammals constitute a mixture of primitive traits or features that have been retained from a distant ancestor, and more derived or specialized traits that have been acquired more recently. A clade is a group of any size of related species. One could consider all mammals as a clade, all primates as a smaller clade, and extinct and living hominids as an even smaller clade. Traits that are common to all or most of the members of the clade are parsimoniously considered to be most likely inherited from a common ancestor, rather than independently evolved specializations, while uncommon traits are considered to be specializations that evolved in only a single line in the clade, possibly independently more than once in two or more lines.

To apply the cladistic method to the study of human brain evolution, we can infer the features of the brains of the first mammals some 200 mya by asking what brain features are found in most or all mammals. A thick neocortex with six layers would be one example. We can then jump forward to the advent of eutherian (placental) mammals some 135 mya, and find that all eutherian mammals have a corpus callosum, but all the other mammals (metatherian and prototherian mammals) do not. Thus, this feature of the human brain evolved over 135 mya. We can then ask what all primate brains have in common (the middle temporal area, MT, of visual cortex, for example), what all or most anthropoid (monkeys, apes and humans) brains have in common (an area 2 of somatosensory cortex for example), and so on. The approach is simple in concept, but difficult to realize for several reasons.

One obvious difficulty is that humans are the only surviving species of the hominid clade. Other members of the genus *Homo*; *H. erectus*, *H. neanderthalensis*, *H. habilis*, etc. are extinct and only their brain endocasts can guide us. The same is true for the varied members of the genus *Australopithecus* and the genus *Paranthronus*. Another problem is that many extant primate species are rare and protected, and we can learn very little about their brains. Furthermore, for ethical reasons, we can learn about brain organization in apes only from non-invasive procedures, and in humans only from non-invasive procedures or invasive procedures that relate to medical treatment. Finally, brain studies are often costly, labour intensive, and difficult to interpret. Thus, a full-scale cladistic approach is seldom practical. In the end, many of the inferences about human brain evolution are based on information obtained from a few well-studied species. Thus, in practice, modern inferences are based on an approach that more closely reflects the ladder of levels approach of early neuroscientists than a conceptually rigorous cladistic approach (see Kaas 2002). As a result, many conclusions remain tentative, but they are open to challenge and new interpretations as the database is expanded. Present results allow the overall sketch that follows.

3. The brains of our early mammalian ancestors

In principle, one would reconstruct the brain of an early ancestral mammal by determining brain organization in extant species in as many branches of the mammalian radiation as possible. To be practical, however, it is useful to carefully select a smaller number of especially informative species for intensive study. As early mammals had small brains with little neocortex, it is logical to study extant mammals with small brains and little neocortex (Jerison 1973), because these brains may have changed the least from those of early ancestors. We want to study such small-brained mammals from as many major clades as possible to see what they have in common. Fortunately, recent efforts to incorporate molecular data sets (Murphy *et al* 2001) into the analysis of phyletic relationships have led to new and detailed proposals of how mammals evolved (figure 2). These proposals include six major clades or superorders, and they place members of the previous Insectivore order in two different superorders. Insectivores were previously grouped in a single order because they share a number of primitive features. The insectivore, tenrecs, from Madagascar are now recognized as members of the superorder, Afrotheria, and they are not closely related to the insectivore hedgehogs, shrews and moles of the superorder, Laurasiatheria. Thus, shared features of both groups of Insectivores are likely to be retained from early mammals, rather than specializations of an insectivore clade.

What features of neocortex were likely present in the brains of early mammals? A cladistic analysis of members of the six superorders suggests that the brain was much like that of extant tenrecs (figure 3). Consistent with

the fossil record on brain size and proportions in early mammals, tenrecs have a small brain with little neocortex. Much of this small brain is dominated by structures that process olfactory information (olfactory bulb, olfactory tubercle, pyriform cortex). The hippocampus (not shown), which is critical for spatial memory and other adjustments to the environment, is nearly as large as all neocortex. The small neocortex is dominated by a few areas for processing sensory information, especially the primary visual (V1), auditory (A1), and somatosensory (S1) areas that characterize the brains of all or nearly all mammals. In addition, S1 is bordered by additional somatosensory areas rostrally, caudally, and laterally, forming a system with five cortical areas. A1 may have additional associated auditory fields, and V1 is bordered by a second visual area, V2, and a small temporal visual region. Cortex of the medial wall contains several (3–4) subdivisions of limbic cortex, while frontal cortex has a primary motor area, M1, a visuomotor area, and orbital frontal cortex for evaluating the hedonistic value of taste and other sensory stimuli. Altogether, the small cap of neocortex of tenrecs has on the order of 15 or so functionally distinct areas of cortex (Krubitzer *et al* 1997). Most of these areas have also been identified in the members of the other five superorders of mammals. The most notable exception is that a separate motor area does not exist in the frontal cortex of opossums of the marsupial superorder (Beck *et al* 1996; Catania *et al* 2000b). While a motor area has been claimed for some marsupials and some monotremes, the bulk of the evidence suggests that members of these two early branches of the mammalian tree (prototherian monotremes diverged about 180 mya; metatherian marsupials, about 135 mya) do not have a separate motor area (M1), while all members of the four superorders of eutherian (placental) mammals do. Thus, the eutherian ancestors of primates were characterized by a brain that had a primary motor area, and most of the features found in the brains of extant tenrecs (Krubitzer *et al* 1997), hedgehogs (Kaas *et al* 1970; Catania *et al* 2000a) and shrews (Catania *et al* 1999).

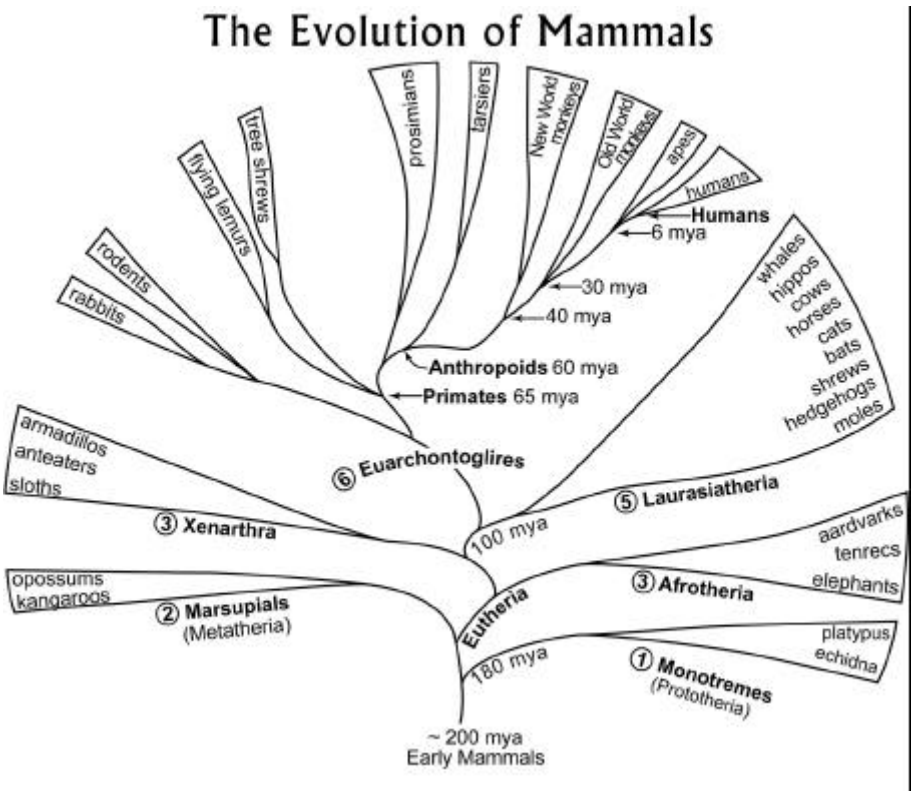

Figure 2. The evolutionary history of mammals. Recent molecular studies of phylogenetic relationships of mammals have reorganized the phylogenetic tree to include six superorders. Therian reptiles evolved into early mammals and then diverged into the prototherian monotreme superorder, the metatherian marsupial superorder, and four superorders of eutherian (placental) mammals. Humans are in the superorder, Euarchontoglires with other primates and the tree shrews (Scandentia), flying lemurs (Dermoptera), rodents (Rodentia), and rabbits and pikas (Lagomorpha). Based on Murphy *et al* (2001).

4. Early primates

Primates constitute one branch of a superorder that includes rodents, lagomorphs, flying lemurs, and tree shrews (figure 2). Judging from what these mammals have in common, the early members of this superorder had a slightly expanded neocortex, a somewhat expanded visual system that included a larger visual domain in occipital and temporal cortex, and an enhanced cortical motor system with possibly a single premotor area, M2, in addition to M1 (Sur 1980; Sur *et al* 1980; Gould *et al* 1986; Krubitzer *et al* 1986; Li *et al* 1990; Lyon *et al* 1998). While the brains of tree shrews, as close relatives of primates, have been extensively studied, the brains of flying lemurs, as the next closest relative, have not. The most impressive difference in neocortex between tree shrews and primitive mammals is the considerable expansion of visual cortex, which is divided into at least eight visual areas (Lyon *et al* 1998). In contrast, auditory, somatosensory and motor regions were much less expansive and contained fewer subdivisions. All primates also have an expanded visual system, and thus it appears likely that the common ancestor of tree shrews and primates had already started to emphasize vision by expanding and subdividing visual cortex.

Early primates were small, nocturnal predators, living on insects and other invertebrates, small vertebrates, fruit and plants (Ross 1996). They depended more on vision for detecting food, and manipulating food items with the forepaw. The fossil record indicates that their visual system was characterized by orbital convergence, suggesting an increase in the importance of binocular vision and stereoscopic vision that could assist prey detection (Cartmill 1974) and the manipulation of small food items (Barton 2004). The early primates had brains that were smaller compared to body size than most extant primates (Radinsky 1975). However, their brains were similar in size and shape to those of present-day prosimian lemurs, galagos, and lorises, suggesting that these primates have retained many ancestral brain features from early primates.

Soon after the first primates emerged over 65 mya (this is a conservative estimate; other estimates go back as far as 90 mya; see Arnason *et al* 1998) the primate line divided into three major branches. In terms of brain size and shape, the prosimians noted above changed the least. Another distinct branch, one that was relatively unsuccessful, led to present-day tarsiers. They shared a diurnal ancestor with adaptations for diurnal vision with the third major branch of anthropoid primates (monkeys, apes and humans), but later reverted to nocturnal life (Ross 1996). This required tarsiers to re-adapt for dim light by evolving huge eyes. The visual system of tarsiers also became specialized for detecting small prey. They are the only extant primates that eat no plants. Because they are rare,

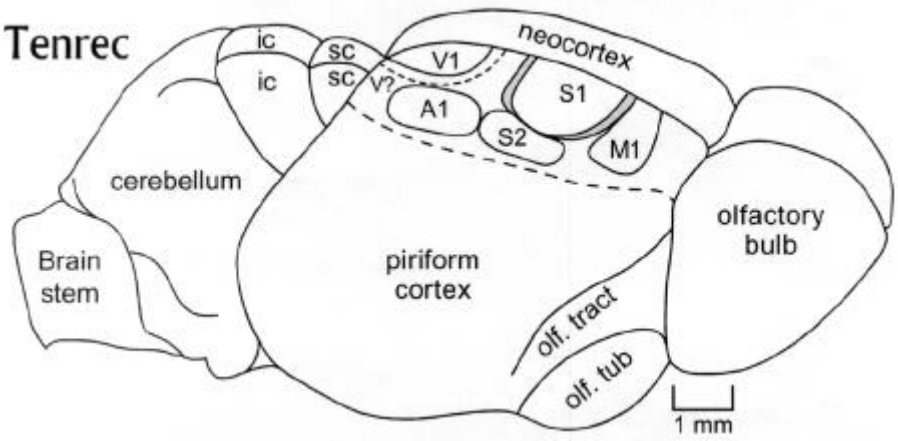

Figure 3. A dorsolateral view of the brain of a small Afrotherian mammal, the Madagascar tenrec (*Echinops telfair*). The most notable feature of the brain is that the neocortex is so small. The forebrain is dominated instead by a large olfactory bulb and other parts of the olfactory brain (olfactory tract, tubercle, and piriform cortex). In most mammals, neocortex is more expansive so that it covers the midbrain and part of the cerebellum (compare with figure 1). In tenrecs, the midbrain, with the inferior colliculus (IC) and superior colliculus (SC) of the tectum, is not covered by the neocortex. The small neocortex of tenrecs does have at least two visual areas, V1 and V2, a primary auditory area, A1, a primary somatosensory area, S1, a second somatosensory area, S2, bands of secondary somatosensory cortex just rostral and just caudal to S1, and a primary motor area, M1. There are a few other areas, perhaps 15, but neocortex is dominated by a few sensory and motor areas. See Krubitzer *et al* (1997) for further details.

and protected, little is known about the details of their brain organization, so few comparisons with other primates are possible. In contrast, brain organization has been extensively studied in several species of New World monkeys, and in Old World macaque monkeys, two major branches of anthropoid primates. Apes evolved from Old World monkeys, and hominoids from apes.

The well-studied brain of galagos reflects many of the features of cortical organization (figure 4) that are shared with other primates. First, galagos and all other primates have two fissures in common, the lateral (or Sylvian) fissure and the calcarine fissure on the medial surface of the hemisphere (not shown). Other fissures are variably present across primate taxa. Second, visual cortex is well developed and it includes a number of visual areas that are also recognized in anthropoid primates. In addition to V1 and V2 of the early mammals, there is a V3 and a middle temporal visual area, MT. These areas appear to be new with primates, but this is not completely certain. Other visual areas are less well established, and proposals differ in the names of some areas, but all primates appear to also have a dorsolateral visual area, DL or V4 (which may have subdivisions), a dorsomedial visual area, DM or V3a, a MT crescent (MTc), MST, FST with dorsal and ventral subdivisions, several divisions of inferior temporal cortex that are visual, and two or more visuomotor areas in posterior parietal cortex (Kaas 2003). In the frontal lobe, there is a distinct frontal eye field (FEF), for directing eye movements and fixation on objects of interest (Wu *et al* 2000). Auditory cortex has several subdivisions including A1, R, and CM of other primates (Kaas and Hackett 2000). Somatosensory cortex includes S1 (areas 3b, 3a, 1, PV and S2 of other primates, Wu and Kaas 2003), and motor cortex is well developed to include M1, a dorsal premotor area, PMD, a ventral premotor area, PMV, and a supplementary motor area, SMA, as well as at least two cingulate motor areas on the medial surface of the hemisphere (Wu *et al* 2000). A clear granular prefrontal region exists which functions in working memory for anthropoid primates (Preuss and Goldman-Rakic 1991). From these comparisons, it is obvious that early primate brains were already highly specialized, and a distinct primate pattern has been retained in prosimian and anthropoid primates. Although studies of other prosimians

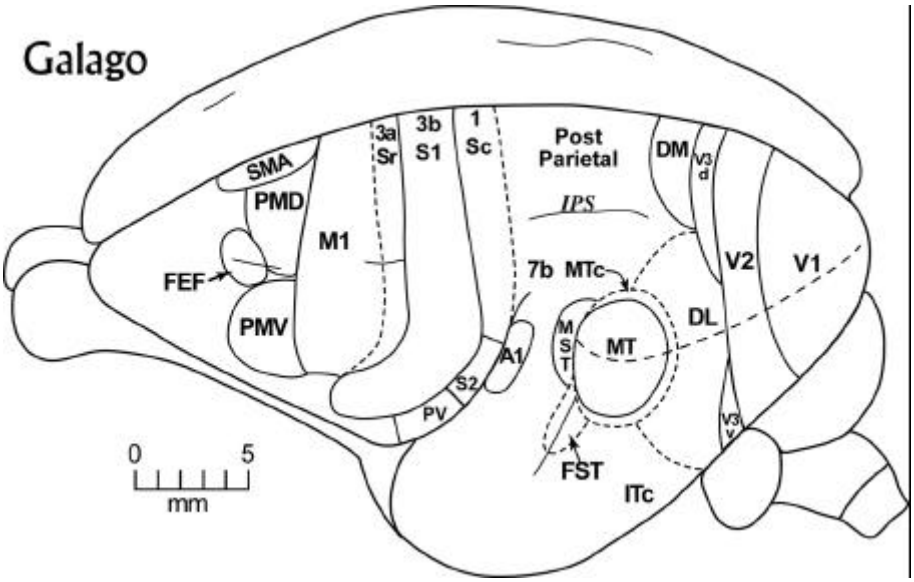

Figure 4. A dorsolateral view of the brain of a galago, a cat-size African prosimian primate. Primary visual (V1), somatosensory (S1 or area 3b), auditory (A1), and motor (M1) areas are outlined. Compare with figure 3. Other visual areas include the second area (V2), the third area (V3) with dorsal (d) and ventral (v) halves, the dorsolateral (DL) area, the middle temporal area (MT), the middle temporal crescent (MTc), the fundal superior temporal (FST) area, the caudal inferior temporal (ITc) area, and the dorsomedial (DM) area. Posterior parietal cortex around the inferior parietal sulcus (IPS) contains several multisensory and sensorimotor areas. Somatosensory cortex includes areas rostral (Sr or area 3a) and caudal (Sc or area 1) to S1, the second area (S2), the parietal ventral area (PV), and a region termed 7b. Premotor cortex includes the ventral premotor area (PMV), dorsal premotor area (PMD), the supplementary motor area (SMA), and premotor areas in the cortex between the two hemispheres. Areas PV and S2 extend into the lateral sulcus.

have been limited, it appears that most or all prosimian primates have diverged little in the organization of neocortex, and they closely reflect the organization of neocortex of early primates.

Early anthropoid primates were monkeys that emerged in Africa over 60 mya. Somehow, most probably by rafting, some of these early simians got to South America where they diverged into two main lines, the marmosets and tamarins (Callithrichidae) and the (Cebidae) cebus, squirrel, howler, owl, spider and other New World monkeys. These platyrrhine monkeys occupy a diverse array of ecological niches. Owl monkeys are the only nocturnal anthropoid, and they have large eyes as an adaptation to dim light. The marmosets and tamarins are very small

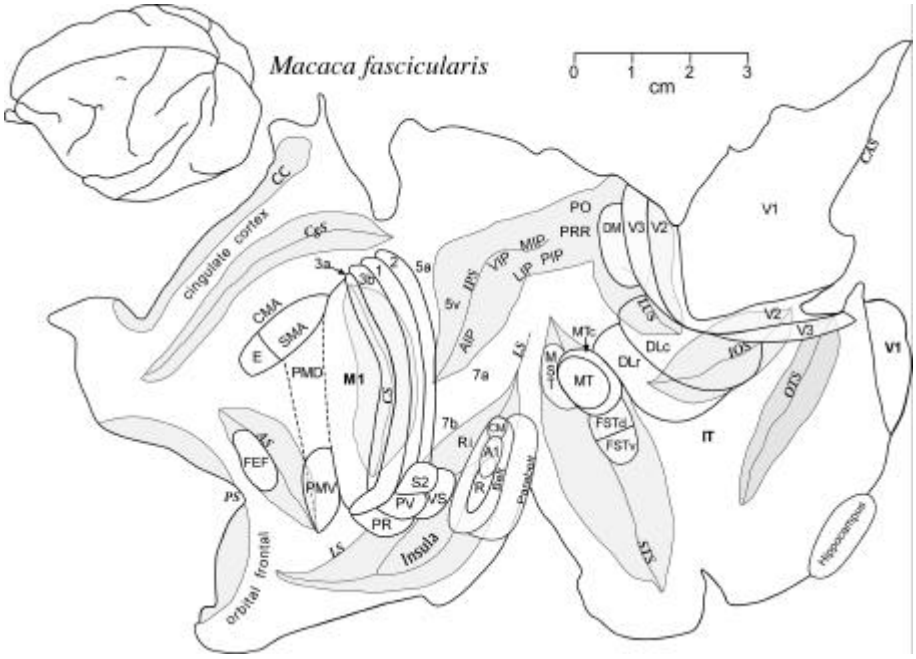

Figure 5. Some of the proposed subdivisions of neocortex in macaque monkeys. Because the cortex of the large macaque brain is folded into a number of fissures (upper left), many areas are not visible on the surface until the cortex is separated from the underlying fibers and flattened as a large sheet (with some cuts and tears). This exposes cortex of the medial wall of the cerebral hemisphere, including cingulate cortex and the banks of the cingulate sulcus (CgS), along with the corpus callosum. In the frontal lobe, the principal sulcus (PS) is split and the arcuate sulcus (AS) is opened. More caudally, the central sulcus is opened, and laterally the lateral sulcus (LS) is opened to reveal the insula at the floor of the sulcus. The superior temporal sulcus (STS) in the temporal lobe, the intraparietal sulcus in the parietal lobe, is also opened. In the occipital lobe, primary visual cortex is torn and unfolded from the calcarine sulcus (CAS) of the cortex of the medial wall, and the lunate sulcus (LUS), inferior occipital sulcus (IOS), and occipital temporal sulcus are opened. Visual areas include V1, V2, V3, MT, MTc, MST, FST, DL, and DM of galagos (see figure 4 for abbreviations), but DL has rostral (r) and caudal (c) subdivisions, and FST has dorsal (d) and ventral (v) subdivisions. In the IPS, anterior (AIP), lateral (LIP), medial (MIP) and posterior (PIP) intraparietal areas have been proposed, along with a parietal reach area (PRR), and a parieto-occipital area (PO). Other regions of parietal cortex are numbered according to the classical scheme of Brodmann (5a, SV, 7a, 7b). Auditory cortex includes a primary area (A1), a rostral area (R), a belt of 7–8 additional areas including the caudomedial area (CM), and a parabelt of at least two areas. Somatosensory cortex includes S1 (area 3b) and areas 3a, 1 and 2, as well as S2, PV, the parietal rostral area (PR), the ventral somatosensory area (VS), a retroinsular region (Ri) and other fields. Motor cortex includes dorsal and ventral premotor fields (PMD, PMV), the supplementary motor area, SMA, visuomotor frontal eye field (FEF), a supplementary eye field (E), and cingulate motor areas (CMA). The hippocampus is attached to a caudal portion of cortex. The rest of neocortex has been divided further into areas, many of which are poorly defined and uncertain, but macaques clearly have a large number of cortical areas, as well as basic primate areas shared with galagos.

monkeys that have a number of derived specializations related to their small size. Old World catarrhine monkeys are generally much larger than New World monkeys, and they include species more adapted to terrestrial life. All Old World monkeys can be identified by their well-developed sitting pads. Their radiation includes the main branches or subfamilies of the predominantly African cercopithecoids (macaques, baboons, and mangabeys). The leaf-eating colobine monkeys of Africa and Asia form the second subfamily of Old World monkeys.

Most of what is known about the brains of New World monkeys comes from studies of owl monkeys, squirrel monkeys, and marmosets, with some information from the larger cebus monkeys. Most of the information from Old World monkeys comes from a few species of macaque monkeys. There appear to be some differences in cortical organization between the smaller New World monkeys and the larger Old World macaques in that macaques have more expansive temporal lobes, posterior parietal regions, and prefrontal and orbitofrontal cortex, but uncertainties exist about how these regions of cortex are divided into areas.

A parcelation of much of the neocortex of Old World macaque monkeys demonstrates some of the common features of primate brains and some of the differences between prosimian and Old World primates (figure 4). The basic areas of early mammals (S1, S2, M1, A1, V1, V2) have been retained. They are greatly enlarged in this large brain, but they occupy proportionally much less of the cortical sheet. Areas have also been retained from the first primates, including V3, DL (V4), MT, FSTd, FSTv, 3a, 1, PV, VS, R, PMv, PMd and others. In addition, there has been a huge expansion of temporal, posterior parietal, and frontal regions of cortex, where a number of new areas have been proposed and others are likely to be yet identified. The clear conclusion is that large brains of Old World macaques (and other Old World monkeys) have more cortical areas than prosimian primates (and at least most New World monkeys). Thus, the number of cortical areas increased with brain size in the evolution of Old World Anthropoid primates. With more cortical areas, the processing of sensory information, and the systems for planning movements and motor control became more complex, and included more stages of processing.

5. Recent steps toward evolving the human brain: Apes and hominids

About 30 mya (possibly, 50 mya), one line of Old World monkeys gave rise to apes, which are characterized by a lack of a tail, a number of skeletal features including long upper limbs, and longer gestation and first reproduction times than Old World monkeys. The longer gestation times and slower maturation allowed brains to grow bigger. Early apes were diverse and abundant, but monkeys later became more dominant, and only modern humans remain from the hominoid line (apes and hominids) as an abundant species. Relatively recently, about 4 or 5 million years ago, one line of apes gave rise to hominids, the bipedal anthropoids. While apes had quite large brains compared to monkeys (figure 6), early hominids were bipedal, but had brains of about the same size as apes. This remained true for members of the *Australopithecus* and *Paranthropus* radiations, but soon after the Homo genus emerged about 2·5–3 mya, brains of our ancestors rapidly increased in size, especially over the last 1 million years, from 500–800 cm^3 of *Homo habilis* to 1200–1400 cm^3 of modern humans, *Homo sapiens*. The transformations in brain organization that occurred over that time are largely uncertain because until recently it was difficult to obtain much information about the organization of the human brain, we know about the brains of our hominid ancestors only from the fossil brain endocasts,

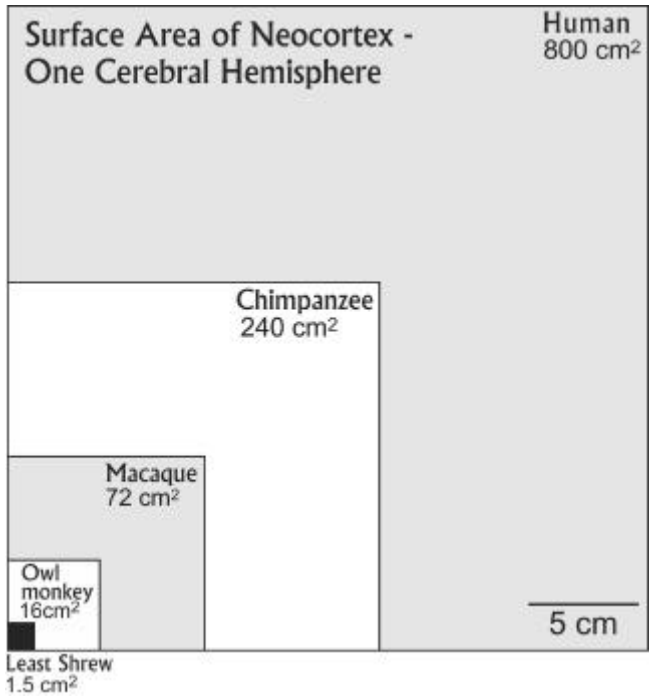

Figure 6. Humans have much more neocortex than other primates or small-brained mammals such as the least shrew (or tenrec, figure 2). Here the proportional sizes and numerical values of the surface area of the neocortex one of the two cerebral hemispheres are indicated for human, chimpanzee, macaque monkey, owl monkey, and least shrew. The volume differences are even greater as the human cortex is more than twice as thick as that of the shrew. Because of scaling problems (see text), the human brain cannot be simply a greatly enlarged version of the small brain of an ancient mammalian ancestor.

and we know very little about the brains of living (extant) apes. As we know quite a bit about the organization of the brain in extant macaque monkeys (figure 5), some investigators assume that the human brain is basically an enlarged version (12–15 times the neocortical surface area) of the macaque brain in organization. However, there are reasons to question this assumption. First, humans have obvious specializations of the two cerebral hemispheres that monkeys do not have. Most notably, a large portion of the temporal lobe and parts of the frontal lobe of the left cerebral hemisphere are specialized for language abilities in humans, and a large portion of the posterior parietal region of the right hemisphere is specialized for mathematics, music, and spatial reasoning (Gazzaniga 1995; Corballis 1998). Part of the ventral temporal lobe is specialized for recognizing the faces of individuals (Gauthier 2004), and we can distinguish and remember hundreds of faces, something very important for a highly social species. Our frontal lobes are specialized for recognition of self, an appreciation of the intentions and thoughts of others (a theory of mind) and an appreciation of the impact of our acts on our future (Povinelli and Preuss 1995). Our parietal-frontal motor guidance and planning system mediates an intuitive sense of tool use, and the ability to acquire great skill in tool use. These brain-mediated traits distinguish us from monkeys, and there are only traces of them in apes.

Human brains are asymmetrical in shape because of these hemispheric specializations. Because of the focus of language in the left hemisphere, and the association of language with sound, the auditory system of the upper temporal lobe and cortex of the upper bank of the lateral (Sylvian) fissure has apparently expanded in the left hemisphere, altering the slope and shape of fissures. Surprisingly, the extant great apes (gorillas and chimps) also have this asymmetry (Yeni-Komshian and Benson 1976; Gannon *et al* 1998), although to a lesser extent, and this asymmetry can be identified in the fossil endocasts of the brains of our hominid ancestors (Corballis 1989). Likewise, the ventral premotor region of the frontal lobe that is enlarged and specialized as Broca's area is in the left cerebral hemisphere of humans, and this region is also enlarged in apes (Cantalupo and Hopkins 2001). Thus, the trend toward an asymmetrical brain clearly predates the advent of modern humans, although modern language abilities likely did not. Therefore, the adaptive forces that led to hemispheric specialization related to functions other than language, at least initially. Because human language may have a gestural origin, humans and our hominid ancestors are predominately right handed, and centers for visuomotor guidance of hand use are near the junction of inferior parietal cortex with upper temporal cortex, left hemisphere specialization for hand use and gesture might have led to the initial asymmetry.

Another reason to suppose that the human brain is more than an enlarged monkey brain is that large brains present design problems that seem to require alterations in organization. This review started with the statement that as brains increase in size, neurons fail to keep pace. Although the pyramidal cells of neocortex do vary in size, branching pattern, spine density and spine number across species, cortical areas, and brain sizes (Elston *et al* 2004), such variation is limited and sometimes counter intuitive. Thus, pyramidal neurons in V1 of small marmosets and large macaque monkeys are very similar, even though V1 is five times larger in surface area in macaques. As neurons do not enlarge proportionally with brains, the major difference in large and small brains is in the number of neurons. While accurate measures are difficult to obtain, a rough estimate is that the small cortex of a mouse contains about 10 million neurons and the cortex of a human about 100 billion, an increase of 10,000 times (Schüz and Palm 1989). The difference would be even greater, except for the connection problem (Kaas 2000). If large brains are to work in approximately the same way as small brains, then each neuron should maintain its connections with the same proportion of other neurons as brain size increases. However, this would mean connections with even more neurons. In addition, the connections would get longer and longer as neurons became spaced further and further apart. Thus, more and more of the brain would be devoted to connections rather than neurons, and the rate of increase in number of neurons would be less and less with further increases in brain size. Without redesign of the brain, there would be little point in having brains much larger than ours, as so few neurons compared to connections would be added (Cherniak 1990). While larger brains devote more of their mass to connections (Allman 1999), they do so far less than predicted from a model of maintained connectivity. Thus, there are fewer connections than predicted.

There are several ways in which the organizations of brains can be changed to reduce the impact of the connection problem. One is to increase the number of processing areas because a large proportion of connections are intrinsic to an area, and connection distances and numbers of target neurons would be less in the smaller areas that would result from dividing cortex into more areas. If we assume that the evolution of the large human brain effectively addressed the scaling problem, there should be a considerable increase in the number of cortical areas, the functionally unique subdivisions in the human brain. Much of the current wealth of fMRI data on the human brain is starting to substantiate this view. Second, areas of related function that need to communicate with each other need to be kept close to each other. In practice, most connections between cortical areas are between adjacent or nearly adjacent areas (Young *et al* 1995). Third,

as distance is time in the brain, and time in neural computations is very important, the need for long connections can be reduced by concentrating functions in one cerebral hemisphere or the other (Ringo *et al* 1994). This is most obvious in the specializations of the two hemispheres in the human brain. It would be too costly to have large numbers of thick, rapidly conducting axons communicating between paired auditory-language centers in the large human brain, so language is mediated mostly in the left hemisphere. The number of thick, rapidly conducting axons in the corpus callosum connecting the two cerebral hemispheres is much less in the human brain than predicted by scaling up a mouse or small primate brain. Thus, we expect the large human brain to differ from the smaller brain of Old World monkeys by having more cortical areas, larger clusters of areas that mediate related functions via interconnections, and hemispheric specializations that reduce the need for long connections between the cerebral hemispheres.

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