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THE HUMAN BRAIN EVOLVING:
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Editors

Douglas Broadfield
Florida Atlantic University

Michael Yuan
Columbia University

Kathy Schick
Stone Age Institute & Indiana University

Nicholas Toth
Stone Age Institute & Indiana University

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FRONT COVER CAPTIONS

Center: Portrait of Ralph L. Holloway.
Upper left: A modern human brain.
Upper right: Ralph measuring landmarks on an endocast ca. 1976.
Lower right: Homo habilis cranium KNM-ER-1813 from Koobi Fora, Kenya (photo by Holloway).
Lower left: Ralph with an endocast of the Flores "hobbit" cranium.

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CHAPTER 9

BRAIN REORGANIZATION IN HUMANS AND APES

KATERINA SEMENDEFERI, NICOLE BARGER AND NATALIE SCHENKER

ABSTRACT

This paper examines evidence from comparative neuroanatomical studies of humans and apes to address Holloway’s ideas (Holloway, 1968, 1979, 2001) about reorganization in hominoid and hominid evolution. Specifically, work accomplished mostly in our laboratory supports the theory of reorganization for some brain areas but not others. Quantifiable parameters of selected gross anatomical regions, individual cortical areas, and subcortical nuclei point to selective reorganization in both human and great ape brains. Much of this accumulated evidence is based on species differences between gross measures of the frontal lobe (e.g., overall volume or the amount of white matter or cortex) and functionally relevant subregions within it (such as the dorsal, mesial, and orbital sectors). Further support is derived from analyses of regions neighboring the frontal lobe, such as the frontal insular cortex, using histological measurements of size of cortical areas and neuronal densities. Evidence for reorganization in the temporal lobe includes distribution of white matter, and the organization of a major subcortical structure, the amygdala. These findings are a starting point for studying and understanding reorganization in these and other parts of the brain.

INTRODUCTION

Most regions of the primate brain conform to regular scaling relationships (Jerison, 1973; Finlay et al., 2001), but there are some exceptions to this regularity across species. For example, Holloway hypothesized (1968) that the human brain is not an enlarged ape brain, and that ape and monkey brains are not enlarged or reduced versions of each other. It is likely that different regions of the brain are differentially increased or decreased depending on the adaptive forces present in the evolutionary environment. For example, animals that rely heavily on a particular sensory modality (e.g. audition, vision, somatosensory) have differentially enlarged cortical territories (Figure 1) that are involved in such functions (Krubitzer and Kahn, 2003). Although information supporting Holloway’s hypothesis is now available for smaller mammals, comparisons of humans and apes remain scarce. Neuroanatomical comparisons of extant ape and human brains can identify features that are either shared among hominoids, i.e., humans and apes, or are unique to humans and thus may have arisen specifically during hominid evolution. Our laboratory has focused on these issues and we have modified and expanded upon previous hypotheses, many of which were originally based on limited empirical information. While advanced human cognitive abilities might be attributable in part to an increase in total brain size (Gibson, 2002; Passingham, 2002), they might also arise from discrete modifications in the relative size of specific neural systems that accompany absolute brain size increases. Species-specific cognitive abilities might also exist independently of changes in absolute brain size (Figure 2) and thus may be differentially present in primates that have similarly sized brains (e.g. great apes). To address this latter possibility, our studies have been aimed at understanding the organization and size of individual cortical areas and subcortical regions across hominoids.

In human and ape species few detailed evolutionary studies of the brain exist and even fewer studies include analyses of isolated regions of the brain. Unlike
The majority of previous analyses, our data are drawn from a sample that includes multiple individuals of each hominoid species. We use both in vivo structural magnetic resonance images (MRI) and histological sections of postmortem specimens (donated by zoological and research facilities) in our analyses. With these samples we isolated different cortical areas to determine the extent to which they have expanded or become diminished in each hominoid species, resulting in distinct neural organizations. Differences in the size and organization of the whole brain and specific subregions might reflect species-specific adaptations, functional specializations, and/or major evolutionary events relating to changes in the organization of the hominoid brain (Armstrong, 1990). From a neuroscientific perspective, comparisons of specific neural circuits or cortical areas in closely related species are necessary for understanding the species-specific adaptations and neural circuitry underlying behavior. Studies of relationships such as total brain size to body size are insufficient for the understanding of species-specific adaptations in behavior and underlying neural circuitry.

With a diverse sample of hominoids, we tested the assumptions of longstanding hypotheses about human brain evolution using larger samples and more rigorous experimental techniques. The frontal lobe has long been considered the most likely candidate for evolutionary expansion in the human line, because it plays a central role in higher order cognitive functions like planning for the future, abstract symbolic processing, and categorization (Damasio, 1985). Until recently, many evolutionary reconstructions assumed an enlarged frontal cortex in humans (Deacon, 1997). Early data from Brodmann (1909) and Blinkov and Glezer (1968) supported the notion that human frontal lobes were disproportionately enlarged compared to other primates. Unfortunately, it is difficult to accept these data as reliable, because only a few hominoid species were represented, and the sample size often included only one or two hemispheres per species. Furthermore, the organization of the primate frontal cortex is complex (Goldman-Rakic, 1984; Barbas and Pandya, 1989), comprising many diverse territories with distinct functional properties. Addressing the frontal

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Figure 1. Three mammalian species with cortical sheets of similar size representing different sensory adaptations (modified from Krubitzer & Kahn, 2003)
lobe only as a whole elides this functional heterogeneity. Few studies have addressed comparative morphometric differences in subregions of the frontal lobe or the organization of this sector from an evolutionary perspective (Fuster, 1997; Holloway, 1968; Jerison, 1997). We have used this novel approach in the laboratory and we discuss our findings below.

Another theoretical tenet in the study of brain evolution is that the limbic system is a conserved region and therefore less likely to exhibit evolutionary change. This notion has been questioned by recent comparative research. The limbic system, also referred to as the “paleomammalian” brain (MacLean, 1990), has long been considered to mediate primarily basic functions such as drives and emotions. Because of this association, it is sometimes viewed as primitive and thus unlikely to be evolutionarily effected in the human brain, in contrast to the proposed enlargement of association areas like the prefrontal cortex that are known to be involved in abstract thinking and language (Foundas, 2001). Contrary to this prediction, several limbic structures exhibit evolutionary reorganization in humans, specifically, the thalamus, the orbitofrontal cortex, and the amygdala. These latter two structures are also considered central components in the neural system subserving social affiliation. In humans and several species of primates, lesions of the amygdala and certain frontal cortical regions alter normal social behaviors (Kling and Brothers, 1992). Humans with frontal trauma are impaired in their ability to process socio-emotional information and to follow social rules (Adolphs, 1999). Nonhuman primates with amygdala lesions show atypical behaviors in social interactions such as the tendency to be either socially disinhibited (Emery, et al., 2001) or socially fearful (Kling, 1986). The fact that the portions of the neural system subserving social behavior show evolutionary reorganization in humans and apes is striking given the increasing popularity of arguments which posit that the pressure of living in complex social environments has had considerable influence on primate brain evolution. Despite an increased interest in social cognition across scientific fields, though, our understanding of the evolution of associated neural structures in humans and the apes is in its infancy.

Thus, there is some evidence to support the idea that, beyond the presumed influence of gross increases in overall isocortical or frontal lobe volume, systems and regions of the brain that are explicitly associated with certain behaviors, especially social behaviors, have been the targets of evolutionary reorganization. Still, it is unclear whether and to what extent neural systems involved in social cognition vary among primate species. We are just beginning to address how the neural systems that determine how individuals relate to conspecifics and make decisions about social interactions are organized and reorganized through evolutionary processes. Here we will examine evidence from our laboratory that supports Holloway’s ideas on mosaic evolution and brain reorganization in limbic and isocortical structures associated with social behavior. We will also present findings

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**Figure 2.** Lateral and orbital views of ape and human brains in a phylogenetic tree. Brains are not in scale, but are either enlarged (gibbon) or reduced (human) to match in size.
suggesting that regions in the frontal lobe show a more conservative pattern of evolution across hominoids.

**In Vivo Investigations of the Frontal Lobe**

The central role assigned to the frontal lobe in human evolutionary reconstructions is based largely on its involvement in complex cognitive functions such as symbolic thought, cognitive planning, decision making, and language production (Owen et al., 1996; Bechara et al., 2000; Foundas, 2001; Pochon et al., 2001). The frontal lobe is also associated with perception, response selection, working memory, problem solving (Owen, 1997; Bechara et al., 1998; Petrides, 2000; Pochon et al., 2001), processing emotional stimuli, the production of affective responses (Cummings, 1993; Rezai et al., 1993), planning and initiation of voluntary motor sequences (Tanji and Mushiake, 1996), theory of mind (Fletcher et al., 1995; Gallagher et al., 2000; Stuss et al., 2001), attention management (Carter et al., 1999; Dagher et al., 1999), and the evaluation of actions based on emotional reinforcers (Damasio, 1994; Stone et al., 1998; Rolls, 2000). Large lesions of the frontal lobe produce the delayed response deficit, which is characterized by a lack of initiative or, in other words, the impairment of “interest and hence sustained attention and initiative” (Sanides, 1964; Harlow et al., 1964; Rosvold et al., 1964).

**Whole frontal lobe**

The frontal lobe is located anterior to the parietal and temporal lobes (Figure 3) and is bounded in all primates by the central and lateral sulci. In a series of comparative morphometric investigations we used three dimensional reconstructions of MRI scans (Semendeferi et al., 1997; Semendeferi and Damasio, 2000) to investigate the size of the frontal lobe in postmortem and living humans (n=11), great apes (n=19), and other primates (Hylobates sp. n=5; Macaca mulatta n=1). Although in absolute volume the human frontal lobe is larger than the frontal lobe of other primates, allometric analyses suggest that the human frontal lobe is as large as expected for an anthropoid brain of human size (Semendeferi et al., 1997; Semendeferi and Damasio, 2000). Because both humans and great apes have a large frontal lobe relative to the rest of the brain, human brain evolution and the evolution of complex cognitive capabilities cannot simply be attributed to differential enlargement of the frontal lobe as a whole.

We hypothesized that differences in the neural substrates underlying complex cognitive functions in humans may instead be present in subregions of the frontal lobe at gross anatomical and/or microscopic levels. The frontal lobe includes parts of subcortical structures such as the basal ganglia as well as gray matter (cortex) and white matter (connective fibers) (Figure 3). A number of morphometric studies have addressed the size of individual gross anatomical regions of the frontal lobe in normal (Caviness et al., 1996) and pathological human brains (Andreasen et al., 1994; Mitelman et al., 2003; Carper and Courchesne, 2005). Using landmarks that are consistently present across hominoids, we identified three such regions: the dorsal, mesial, and orbital sectors of the frontal lobe (Semendeferi et al., 1997; Schenker et al., 2005). We made volumetric assessments of the frontal lobe and these three sectors. We also segmented them into both gray matter and white matter for separate quantifications.

**Frontal cortex**

Like the frontal lobe as a whole, the frontal cortex in humans is as large as expected for an ape of human brain size (Semendeferi et al., 2002) (Figure 4). It occupies a similar proportion of total cerebral cortex in humans and in great apes, but a smaller proportion in smaller-brained primates (Figure 5). This is also true for

Figure 3. Lateral view of a human brain highlighting the frontal and temporal lobes that were targeted in our comparative studies. Vertical bar represents the location of a cross section (shown on the right) which reveals the presence of the cortex (gray) and white matter (white).
the orbital, mesial, and dorsal sectors of the human frontal lobe (Figure 6). These three sectors maintain a lawful relationship with increasing brain size in humans and in most hominoids.

**White matter**

Classical investigations of the frontal lobe focused mostly on measurements of the cortex, but more recent studies have recognized that species differences in white matter volumes may be of functional and morphological importance. We identified and measured the volume of the white matter in the frontal lobe (Figure 3) and found that, as expected, white matter has a positive allometric relationship with increasing brain size (Schenker et al., 2005). Like the frontal cortex, total white matter volume in the frontal lobes are as large as expected in hominoids (Schenker et al., 2005). Our findings support the long established idea that larger brains tend to have a larger percentage of white matter than smaller brains and are consistent with expected values for humans and apes in gross frontal lobe measures (Frahm et al., 1982; Prothero and Sundsten, 1984; Hofman, 1989; Rilling and Insel, 1999; Zhang and Sejnowski, 2000; Bush and Allman, 2004).

Nonetheless, because white matter is a complex territory comprising numerous, distinct fiber systems, humans might show variation in the distribution of white matter amongst these subsectors. Commissural systems such as the corpus callosum provide communicative pathways between the hemispheres. Projection fiber systems such as the corona radiata link isocortex with non-isocortical neural structures and the periphery. Long association fibers mediate intrahemispheric communication between distant cortical areas. There are also short association fibers that function as connections between topographically adjacent regions. The overall spatial arrangement of the fiber systems reflects the topographic relationship between the origins and targets of the connections (Dejerine, 1895; Heimer, 1995). While it is not possible to distinguish all specific fiber systems in gross brain scans, a number of morphometric studies in humans (using structural MRI scans) have parcellated the white matter to measure the volume of its subdivisions (Makris et al., 1997; Herbert et al., 2004). One subdivision is the gyral white matter which includes the white matter immediately underlying cortical territories; another subdivision is the core, which includes all remaining white matter in the frontal lobe (Figure 7). The gyral white matter immediately underlying cortical territories generally includes, in addition to long projection fibers, also short corticocortical association fibers that link neighboring cortical regions (Heimer, 1995). Gyral white matter volume approximates the size of connections between regions that lie in close proximity, whereas core white matter reflects more the degree of connectivity between distant regions.

The relationship between gyral white matter and core white matter is different in humans compared to other primates (Schenker, et al., 2005). Most human values for gyral white matter are larger than expected in the frontal lobe (Figure 8), while the average percent residuals of human values for the frontal gyral white matter are more than 26%. Enlarged gyral white matter in humans suggests increased interconnectivity within and between neighboring cortical regions, many of which support complex cognitive behaviors. Thus an increased ratio of gyral white matter to core white matter is likely to reflect an increased emphasis on short, intrahemispheric, cortico-cortical associations. Nevertheless, the volume of the white matter, whether core or gyral, can increase as
a function of several parameters, including numbers of fibers, size of fibers and/or degree of myelination (Hararrison et al., 2002).

Developmentally there are differences in the myelination of gyral versus core white matter. White matter in closer proximity to the cortex myelinates after core white matter, and occurs late in the first year of life or later, especially in the frontal cortex (Yakovlev and LeCours, 1967). Similar differences might exist across species, but no cross species comparisons exist regarding the degree of myelination. Thus, speciesspecific differences might include increased numbers of axons, increased crosssectional area of axons, or increased myelination between cortical areas resulting in faster information processing, facilitating complex cognitive function (Harrison et al., 2002). Other studies of fiber systems based on structural MRI and diffusion tensor imaging (Rilling and Insel, 1999; Glasser and Rilling, 2008) also suggest that some fiber systems are represented in different proportions in selected primates, supporting the idea of the presence of selective reorganization in the white matter.

**Reorganization and the human frontal lobe**

There is no evidence for brain reorganization based on the size of the frontal lobe and the frontal cortex as a whole. Homogeneity in the scaling relations of some of the major sectors in the brain was suggested previously (Jerison, 1973; Clark, et al., 2001; Finlay and Darlington, 1995), and our results show that homogeneity also exists with respect to the size of the hominoid frontal cortex. Our findings support Bonin’s (1948), Holloway’s (1968), and Jerison’s (1973) long standing ideas regarding the evolution of the frontal cortex and frontal lobe as a whole, which received additional support more recently (Bush and Allman, 2004), namely that “man has precisely the frontal cortex which he deserves” (Bonin, 1948). Nevertheless our morphometric results challenge the two data sets collected by Brodmann (1912) and Blinkov and Glezer (1968) and the dominant dogma derived from their data that views human cognitive evolution as largely driven by a differential enlargement of the frontal lobe and frontal cortex (Deacon, 1997; Fuster,
1997). How can we account for the difference between our morphometric results and those of Brodmann (1912) and Blinkov and Glezer (1968)?

The frontal cortex includes prefrontal cortex, motor cortex, and premotor cortex. Brodmann (1912) measured the frontal cortex as a whole and also its subcomponent, the prefrontal cortex. He reported that both the frontal cortex and the prefrontal cortex are larger in the human brain than in the chimpanzee. Our findings are directly comparable to what Brodmann (1912) and Blinkov and Glezer (1968) reported for frontal cortex. The frontal cortex can be measured and directly compared across individuals and species in a consistent manner using reliable and reproducible landmarks. Additionally, use of MRI scans of living individuals provides a solid basis for morphometric studies widely used today, free of concerns regarding shrinkage or manipulation of post-mortem tissue (which was the case with all quantitative studies in the early and mid-20th century). According to Brodmann, the frontal cortex occupies 6% more of the surface of the brain in the human than in the chimpanzee. His data set includes a single human hemisphere and a single chimpanzee hemisphere with no representation of the other great apes (Figure 5). Our data set includes several individuals per species (see Figure 5) and the range of values for each species is considerable. An examination of our sample reveals that if only one human from the upper end of the species range were compared to only one chimpanzee from the lower end of the species range then the presence of species differences could be supported. This could easily have been the case with the individual subjects used in previous studies, and the previous findings may therefore reflect a sampling bias.

The limited number of primate species and an under-representation of the great apes might also account for the discrepant results between our findings and previous findings. Previous studies focused on human versus nonhuman primate comparisons, while our studies focus on how humans compare to our closest relatives, the great apes. If our studies had excluded most of the great apes, the results would have been more consonant with the previous findings, because gibbons and monkeys do, in fact, have relatively smaller frontal cortices than humans (Figure 5).

Additionally, we calculated volumes for the cortical regions of interest, while earlier studies (Brodmann, 1912; Blinkov and Glezer, 1968) used surface estimates. This is unlikely to account for much of the variance, however, because cortical volume is highly correlated with the surface of the cortical sheet. We conclude that sample size, sample composition, and the presence of intraspecific variation across species are the most likely factors underlying the differences between previous and recent studies of the frontal cortex.

Figure 6. Log-log regressions through humans and apes of dorsal cortex, mesial cortex, and orbital cortex in the frontal lobe (modified from Schenker et al., 2005).
The fact that the relative size of the frontal cortex is similar in humans and great apes does not mean that the frontal cortex is less critical to hominid cognitive specialization than has been suggested (Goldman-Rakic, 1984; Fuster, 1997; Damasio, 1994). The frontal cortex could support the outstanding cognitive capabilities of humans without undergoing a disproportionate overall increase in size because: 1) mere differences in absolute brain size could provide an explanation (Passingham, 2002); 2) subsectors of the frontal lobe may be reorganized and differentially enlarged. In comparative and evolutionary studies of the brain, large anatomical territories have been commonly treated as uniform entities, despite their heterogeneity. The frontal cortex is not functionally homogenous and comprises anatomical subdivisions with distinct functional attributes. These anatomical subdivisions are identifiable at various levels of analysis. We have no direct findings from in vivo studies that address what Brodmann (1912) and Blinkov and Glezer (1968) reported for prefrontal cortex because the boundaries of the prefrontal cortex are difficult to define on MR images. It is likely, though, that their calculations for a subregion of the frontal cortex (the prefrontal cortex) may be affected by the same sampling biases as their calculations for whole frontal cortex. In the following section we provide empirical support for the idea that selected parts of the human prefrontal cortex are enlarged.

**Reorganization in the frontal cortex of other hominoids**

The relative enlargement of the frontal cortex may be one of several reorganizational features present in Plio-Pleistocene hominoid precursors, which distinguish the brains of extant hominoids from those of the smaller primates, such as gibbons and monkeys including baboons (McBride, et al., 1999). The smaller primates have a smaller percentage of their total cortex devoted to frontal cortices (Figure 5), and the range of their values does not overlap with the values of the larger hominoids. These findings point to a possible great ape/human specialization for an enlarged frontal cortex that may set larger hominoids apart from other anthropoid primates (Radinsky, 1974).

Notable anatomical variations are present in selected hominoid species. For example, all orangutans in our studies have significantly smaller orbital sectors than predicted for an ape brain of their size. In spite of having some of the largest brains in our sample of great apes,
orangutans have some of the smallest absolute values for the orbital sector and the smallest relative size, with no overlap in individual values with any of the other ape species (Figure 9). Additional observations come from previous studies involving postmortem material and parameters such as total length of orbitofrontal cortex (Semendeferi, 1994; Semendeferi et al., 1997). Overall we examined this sector in a total of 12 hemispheres of orangutan brains, and compared them to a total of 32 hemispheres representing the other great apes in our sample (Semendeferi et al., 1997, 1998, 2001; Schenker et al., 2005). Orangutans stand out consistently across studies for their smaller orbital sector.

The ratio of gyral white matter to cortex within each sector does not distinguish humans from other apes, but the ratio in the dorsal sector distinguishes apes from one another. Within the dorsal sector, the ratio of gyral white matter to cortex is larger in Pan (Figure 10) than in either Gorilla or Pongo. While it is expected for primates with larger brains to have an increased ratio of white to gray matter, chimpanzee and bonobo brains are smaller than gorilla and orangutan brains, not larger. Furthermore, this relationship is only present in the dorsal sector of the frontal lobe. Additionally, within Pan, chimpanzees have a relatively larger dorsal sector than bonobos. This difference is largely driven by an increased amount of gyral white matter (Figure 11), not cortex (Schenker et al., 2005). Orangutans also have a relatively large dorsal cortex and gyral white matter, but individual values overlap with those of other apes.

Our findings further suggest that although most gross anatomical sectors in the frontal lobe are as large as expected, morphometric differences exist in selected sectors and selected species. Our data suggest that the inclusion of closely related species and larger numbers of individuals per species may reveal that certain areas of the brain present modifications expressed even at the gross level (de Winter and Oxnard, 2001). The traditional notion that disproportionately large frontal lobes and frontal cortices are the hallmark of hominid brain evolution is not supported by our findings, but there is evidence that the frontal lobe has undergone reorganization. Apes are distinguishable from each other in the orbital sector and the dorsal sector. Humans exhibit unique patterns of white matter distribution in the frontal lobe, suggesting that specializations relating to connectivity occurred during hominid evolution. The rest of the paper will review evidence supporting the hypothesis that specific subsectors have been reorganized.

Figure 8. Gyral white matter versus core for the frontal lobe; solid and dashed lines represent the regression lines and their confidence intervals, respectively.
Prefrontal Cortex

At the cytoarchitectonic level, the frontal cortex (Figure 12) can be subdivided into motor related cortex (primary and supplementary) and prefrontal cortex. The prefrontal cortex is located anterior to the motor and premotor cortices. It is also called the frontal association cortex or the frontal granular cortex, referring to its functional and structural attributes, respectively. The primate prefrontal cortex has been the focus of a host of studies for the past century. Like the rest of the cortex, it has been further subdivided qualitatively into smaller architectonic regions on the basis of their distinct neuronal organization, such as the number and size of the cortical layers, the size, shape, and density of the neurons, and the degree of axon myelination. In addition, support for this more refined cortical parcellation comes from the distinct connections of cortical areas with the various subdivisions of the mediodorsal nucleus of the thalamus and other cortical and subcortical structures (e.g., the temporal and parietal lobes, the hypothalamus, the amygdala, and the hippocampal formation) (Rempel-Clower and Barbas, 2000). The prefrontal cortex includes Brodmann’s areas 8, 9, 10, 11, 44, 45, 47, and 46 (“frontal region”, Brodmann 1909). It is bordered on the dorsolateral surface by Brodmann’s areas 4 and 6 (“precentral region”), on the mesial surface by Brodmann’s areas 24, 32, 33, 25, 23, and 31 (“cingulate region”) as well as the mesial extension of areas 4 and 6, and on the orbital and lateral surface by the “anterior insular region”.

Since Brodmann’s map of the human cortex was originally published, efforts have been made to remap and characterize selected cortical areas in the human brain (Amunts et al., 1995; Amunts et al., 1996; Amunts et al., 1999; Amunts et al., 2003; Bailey and von Bonin, 1951; Blinkov and Glezer, 1968; Braak, 1980; Donoghue and Sanes, 1994; Hof et al., 1995; Öngür et al., 2003; Petrides and Pandya, 1999; Petrides and Pandya, 2002; Rademacher et al., 2001; Rajkowska and Goldman-Rakic, 1995a,b; Semendeferi et al., 1998; Semendeferi et al., 2001; Vogt et al., 1995; von Economo, 1929; Zilles et al., 1995). Multiple efforts have been made to map the frontal cortex in the commonly used experimental primates, mostly rhesus monkeys and other species of macaques (Barbas and Pandya, 1987; Burman et al., 2006; Carmichael and Price, 1994; Donoghue and Sanes, 1994; Dusser de Barenne et al., 1941; Fogassi et al., 1994; Gebhard et al., 1985; Matelli et al., 1985, 1986; Petrides and Pandya, 1999; Petrides and Pandya, 2002; Preuss and Goldman-Rakic, 1991; Rosabal, 1967; Stepniewska et al., 1993; von Bonin and Bailey, 1947; Walker, 1940; Watanabe-Sawaguchi et al., 1991; Zilles et al., 1982, 1986). A few studies have also demonstrated the organization of the frontal cortex in apes at the histological level (Bailey et al., 1950; Hakeem et al., 2004; Semendeferi et al., 1998, 2001; Raghanti et al., 2008).

The size of the prefrontal cortex (after excluding motor, premotor and limbic cortices from the rest of the frontal lobe) is a subject of long debate. Brodmann (1912) reports as much as a 12% enlargement of the human prefrontal cortex compared to the chimpanzee (the only ape included in his data set). Despite the longstanding debate, no new data have been collected on the size of the prefrontal cortex as a whole in more than five decades. Deacon (1997), based on the quantitative measures obtained earlier in the 20th century (Brodmann, 1912; Blinkov and Glezer, 1968) argues that the relative size of the prefrontal cortex in humans is 202% more.
Figure 10. Ratio of gyral white matter to cortex in the dorsal sector of the frontal lobe.

Figure 11. Ratio of gyral white matter in the dorsal sector in relation to the rest of frontal lobe.
Figure 12. Lateral view of the human brain showing extent of the frontal and prefrontal cortex including cortical areas as assigned by Brodmann.

Figure 13. Upper left: Lateral view of the human brain with vertical bar cutting through Brodmann’s area 10. Lower part: Cross sections through the prefrontal cortex in the human and ape brains showing location and extent of Brodmann’s area 10.
than expected for a nonhuman primate brain of the human size. Bonin (1948) and Holloway (1968) analyzed the same data sets and instead conclude that humans have a frontal lobe as large as expected for a primate brain of human size.

Proper identification of the prefrontal cortex requires analysis of the microscopic features that define its boundaries with neighboring areas. For that, histological investigations are necessary. No gross morphological criteria are sufficiently accurate to replicate Brodmann’s definition, because no sulcal landmarks can reliably establish the transition of prefrontal cortex to premotor cortex or the borders of individual cortical areas. Consequently, this issue can only be resolved using cytoarchitectonic criteria in combination with quantitative studies based on histological sections. To date, no such studies exist.

The only segment of the frontal cortex that can be identified reliably based on gross morphology, and that if removed, can bring the size of the remaining frontal cortex closer to prefrontal cortex, is the precentral gyrus, which is largely occupied by Brodmann’s area 4 (Figure 12). We found that even after removing the precentral gyrus from our analysis, the remaining human frontal cortex is as large as expected for an ape of their brain size (Semendeferi et al., 2002). The relative size of the frontal cortex after excluding the precentral gyrus ranges from 28.8% to 33% in humans, 25.5% to 29.7% in great apes, and 22.0% to 23.8% in gibbons. All African ape species overlap with humans, and there is extensive overlap among the great apes themselves. While definitive statements about the size of the prefrontal cortex can come only from comparative cytoarchitectonic studies of the brains of extant ape species and humans, small sample size and under-representation of great apes in the studies of Brodmann (1912) and Blinkov and Glezer (1968) place any definitive conclusions in favor of an enlarged prefrontal cortex in humans into question. The frontal lobe as a whole, unlike what the above studies suggest, is not enlarged in humans. Finally, if the quantitative data for the whole frontal cortex in the above studies cannot be replicated, then the data provided by the same sources for a fraction of the whole frontal, i.e. for the prefrontal cortex are likely not reliable either. A large-scale cytoarchitectonic study is necessary to resolve this issue.

While maps and comparisons of the primate cortex are generally qualitative in their approach, several recent studies have also quantified different areas (Domrowski et al., 2001; Hof et al., 1995; Semendeferi et al., 1998). These quantification efforts target selected neurobiological parameters, including numbers and densities of neurons (Rajkowska and Goldman-Rakic, 1995a,b;
Semendeferi et al., 1998; Semendeferi & Damasio, 2000; Uylings et al., 2006), density of subpopulations of immunoreactive neurons (Raghanti et al., 2008), density of glia cells (Sherwood et al., 2006), size of neurons (Nimchinsky et al. 1999), as well as size of individual cortical areas (Semendeferi et al., 1998, 2001). Of particular interest are studies that document the strong quantitative signatures of individual cortical regions. Amunts and colleagues (Amunts et al., 1999; Schepersjans et al., 2008; Schleicher and Zilles, 1999) used automated quantitative techniques based on statistical algorithms to identify microstructural boundaries between cortical areas. Because the boundaries are defined using a computer algorithm that analyzes structural density patterns, the boundaries are observer-independent and reproducible. Furthermore, their consistency across adjacent sections provides evidence that these boundaries are not the result of random events. Dombrowski et al. (2001) demonstrated that quantitative architecture can be used to distinguish prefrontal cortical areas in rhesus monkeys. The prefrontal cortical areas they analyzed are well characterized by their connectivity patterns within and outside the frontal lobe (Rempel-Clower and Barbas, 2000). This suggests that quantitative cytoarchitecture provides reproducible criteria for the identification of cortical systems relevant to function. This approach does not require the invasive procedures involved in acquiring tissue from experimental animals or the use of multiple immunohistochemical markers to characterize a cortical territory and thus is a useful approach in the study of the human and ape brains.

**Brodmann’s areas 10 and 13**

Even though the frontal lobe and frontal cortex as a whole are not differentially enlarged in humans, some of the lobe’s constituent areas seem to vary differentially in size across the hominoids. Morphometric studies of histological sections using cytoarchitectonic criteria suggest that the size and organization of individual cortical areas in the hominoid prefrontal cortex, and not the prefrontal cortex as a whole, may set humans apart from the great apes. Within the prefrontal cortex, selected areas are differentially enlarged or diminished (Semendeferi et al., 1998, 2001). We examined two areas, areas 10 and 13, in terms of size and structural organization at the histological level. Our findings provide evidence for mosaic evolution within the prefrontal cortex.

Brodmann’s area 10 is involved with the planning of future actions, the undertaking of initiatives, and working memory and attention (Okuda et al., 1998; Lepage et al., 2000; Daffner et al., 2000). In humans, lesions of the anterior portion of the prefrontal cortex that include area 10 are associated with impairment in highercognitive abilities that facilitate extraction of meaning from ongoing experiences, the organization of mental contents that control creative thinking and language, and the artistic expression and planning of future actions (Damasio, 1985). In contrast, area 13, part of the posterior orbital region, supports behaviors related to responses to social stimuli and complex aspects of social cognition, (Damasio and Van Hoesen, 1983). In macaque monkeys, changes in emotional states and disinhibition of emotional reactions are associated with lesions including area 13. Removal of this cortex enhances aversive reactions and reduces aggressive reactions in threatening situations. These emotional alterations have been interpreted on the basis of the close relationships between the posterior orbital cortex and limbic structures, especially the mediodorsal nucleus of the thalamus and the amygdala (Butter and Snyder, 1972).

Brodmann’s areas 10 and 13 form the frontal pole and the core posterior orbitofrontal region respectively. Their cytoarchitecture and connectivity have been well described in the macaque monkey (Barbas and Pandya, 1989; Preuss and Goldman-Rakic, 1991; Morecraft et al., 1992; Carmichael and Price, 1994). Less was known about them in the human brain (area 13 was not identified as a separate cortical area by Brodmann) or the brain of the apes prior to our comparative studies (Semendeferi et al., 1998, 2001). In Asian and African large-bodied hominoids, area 10 is present in orangutans, chimpanzees, bonobos, and humans and occupies the entire frontal pole (Semendeferi et al., 2001). In smaller primates such as gibbons, area 10 occupies only a restricted location in the orbital part of the frontal pole (Figure 13). In contrast, area 13 shares a similar topographic and topological location across all of the species examined (Figure 14).

Area 10 in the human brain presents some specialized features (Semendeferi et al., 2001); one such feature involves the considerable increase in its overall size in the human brain (Figure 15). Area 10 is larger in the human brain than in the other hominoids, even in relative terms. It is twice as large in the human brain (1.2% of brain volume) than in the brains of great apes (0.46–0.74% of brain volume). Although the increase is considerable in terms of the percentage the area occupies in the brain, more data are required to test whether the area is larger than expected for a brain of human size (Holloway, 2002). Area 13 is present in all hominoids, but is reduced in humans and bonobos (Semendeferi et al., 1998). This reduction might be the result of a proliferation of other cortical areas or subdivisions within the orbitofrontal cortex of these species. In orangutans, however, the orbitofrontal cortex is relatively homogeneous, with area 13 occupying a larger portion of this region than in the other great apes. The total volume of area 13 in the right hemisphere of the great apes and humans is very similar, ranging from 269.9 mm3 in the chimpanzee to 366.2 mm3 in the human. An exception is the bonobo, which has a volume of 110.5 mm3. However, relative to brain size, the human and bonobo have a small area 13 (0.03%), while in the gibbon and the other great apes area 13 occupies a greater percentage of the brain (0.06–0.09%). Across hominoid species, areas 10 and 13 do not vary in size in coordination with one another.
Another specialized feature of area 10 involves the neuropil, or the space between cell bodies, which is largely devoted to axons and dendritic processes within the cortex (Semendeferi et al., 1998, 2001). Unlike area 13, neuropil is increased in area 10 of the human brain in layers that are primarily connected to other higher-order cortical areas of the same and opposite hemispheres (Figure 16). This is of interest given that the volume of gyral white matter is larger than expected in humans and primarily represents connectivity between closely located higher order cortical areas. Other lines of evidence also support the idea that parts of the prefrontal cortex have increased dendritic arborization in humans compared to macaques (Elston et al., 2006).

Studies in macaques have demonstrated an anterior-posterior gradient in neuronal density across frontal cortical areas (Dombrowski et al., 2001). Our data also demonstrate this trend (Figure 17). Across species, with the exception of the gorilla, the density of neurons in area 10, located in the frontal pole, is greater than the density in area 13, located in posterior orbital cortex. In both areas, the density of neurons is considerably lower in humans than in the apes. However, within the apes, neuron densities in area 10 and area 13 do not vary in coordination with each other. For instance, while the orangutan has the lowest neuron density in area 13, it has the second highest density in area 10. Variation among species in the neuron densities in these areas provides some evidence for the mosaic evolution of cortical areas in the prefrontal cortex.

Area 13 is relatively conserved, particularly in terms of its absolute size. A hypothetical reconstruction of the Plio-Pleistocene hominoid brain would place area 13 in a restricted area, occupying the most posterior parts of the medial orbital gyrus and the posterior orbital gyrus, with structural features similar to those in the extant species. In general, area 10 in the human brain appears to be specialized in size and organization, which suggests that
functions associated with this part of the cortex have become particularly important during hominid evolution. Planning and initiating actions are hallmarks of human behavior, and although these features are present to some extent in other hominoids and possibly other primates, they became fully expressed in the Plio-Pleistocene hominids.

There is variation in the size and in aspects of the organization of the frontal lobes among the hominoids (Semendeferi et al., 1997). These differences might reflect species-specific adaptations, functional specializations, and/or major evolutionary events relating to changes in the organization of the hominoid brain. Relationships such as total brain size to body size is not sufficient for understanding species-specific adaptations in behavior and underlying neural circuitry. An analysis of two regions of prefrontal cortex reveals differences in the organization of parts of the limbic frontal cortex, involved in social cognition, between species that have very similar absolute brain sizes (orangutan versus chimpanzee) (Semendeferi and Damasio, 2000). It is clear that specific neural circuits or cortical areas have to be compared among closely related species.
Brodmann's areas 44 and 45 (Broca's area)

Two other cytoarchitectonic areas in the prefrontal cortex, Brodmann's areas 44 and 45, comprise what is known as Broca's area, and typically occupy part of the inferior frontal gyrus in the human brain (Figure 18). In all hominoids, Brodmann's areas 44 and 45 are located within the inferior frontal gyrus, anterior to the inferior precentral sulcus (Schenker et al., 2008). The two areas can be distinguished by differences in the prominence of layer IV and the total thickness of cortex (Figure 19).

They also exhibit certain differences in overall cortical thickness and in relative laminar width among species, with gorillas and orangutans displaying less difference in thickness between the two areas than chimpanzees and bonobos.

Within areas 44 and 45, we investigated the minicolumnar organization of the cortex (Schenker et al., 2008). Minicolumns are vertically-oriented aggregates of cells with strong vertical interconnections among layers, forming fundamental structural and functional units within cortex (Douglas and Martin, 1992; Mountcastle,
Their organization in the adult brain is thought to be derived from ontogenetic columns and the migration of cells into radial columns during development (Rakic, 1995). Minicolumns comprise rows of neurons traversing layers II-VI (Buxhoeveden and Casanova, 2002; Mountcastle, 1997) and are assumed to be one cell wide in layers III, V, and VI (Seldon, 1981).

Minicolumns in Broca’s area are larger in humans than in great apes (Figure 21). This pattern is similar to the pattern reported previously for the planum temporale (area Tpt, Buxhoeveden et al., 2001). Nevertheless, even though spacing between minicolumns in humans is larger in absolute terms, it is smaller relative to total brain volume (Figure 22). This indicates that despite the increased width of minicolumns, a human’s cortex contains more minicolumns than the cortex of a great ape.

It is not yet clear whether larger minicolumns in humans is a specific characteristic of cortical areas involved in language function (Broca’s area and area Tpt), or if larger minicolumns exist throughout the human cortex regardless of functional attributes. To date, comparative studies of minicolumns in humans and great apes have focused on cortical regions that are active in linguistic functions. Therefore, these findings may be evidence either of differential changes in the inferior frontal gyrus and the superior temporal gyrus or a cortex-wide difference in humans. Further conclusions await data from minicolumns in additional regions of cortex.

Frontoinsular cortex

Neuroanatomists in the late 19th and early 20th centuries described the presence of an unusual cell in the human cortex (von Economo and Koskinas, 1925). These cells were named spindle neurons based on their characteristic bipolar shape and large size, which is approximately four times larger than pyramidal neurons. Spindle neurons were identified in a specific layer (layer Vb) of two areas of the frontal part of the brain, the anterior cingulate and the frontoinsular cortex (von Economo & Koskinas, 1925 or “anterior insular” according to Brodmann, 1909).

Contemporary studies replicated the early reports in the human brain and also identified the presence of this neuronal phenotype in the anterior cingulate cortex of some mammals. Spindle cells were found in the human, gorilla, bonobo, chimpanzee and orangutan anterior cingulate cortex, but were not found in 22 other primate species or 30 other mammals examined (Nimchinsky et al., 1995; Nimchinsky et al., 1999). Spindle neurons are larger in humans and chimpanzees and smaller in gorillas and orangutans. Spindle neuron volume correlates with encephalization, while the volume of other neurons in layers V (pyramidal) and VI (fusiform) does not (Nimchinsky et al., 1999).

We have used stereological sampling to determine the number of spindle neurons in the “anterior insular region” (Brodmann, 1909) also known as the frontoinsular cortex (area F1) (von Economo and Koskinas, 1925),

Figure 20. Minicolumnar organization in the cortex of Brodmann’s areas 44 and 45 in a chimpanzee and orangutan brain. Scale bar equals 100 μm.
Figure 21. Mean horizontal spacing distance (A) and gray level index (B) by individual and area for the human and ape brains in Brodmann's areas 44 and 45 (modified from Schenker et al., 2008)
in humans and African apes (Hakeem et al., 2004; Kennedy et al., 2007). The frontoinsular cortex is agranular cortex that makes up the anterior portion of the insula (von Economo & Koskinas, 1925; Mesulam & Mufson, 1982). Two cytoarchitectural features unmistakably define area FI (von Economo and Koskinas, 1925). First, FI is agranular cortex, with very few cells in layer II creating a discontinuous appearance, and a near complete or complete absence of layer IV. Second, layer Vb contains large bipolar spindle neurons (Fig. 23), which make identification of the boundaries of FI unambiguous.

After close examination of the orbitofrontal and insular cortex in 25 primate species, only humans and African apes exhibit spindle neurons. We did not identify spindle neurons in the Asian apes (orangutans and gibbons), in Old and New World monkeys, or in prosimians (Hakeem et al., 2004). The FI spindle neurons are approximately 30% more numerous in the right hemisphere of both humans and apes. It is very likely that spindle neurons are a specialization found in humans and great apes, and their presence in area FI is a phylogenetic specialization of the clade comprised more specifically of humans and African apes. Since they are present in all members of this clade, they are likely to have been present in the last common ancestors of the clade, which lived less than 10 million years ago.

Given this evolutionary scenario and the functional properties of the areas containing spindle neurons, this hemispheric specialization might have arisen before the evolution of language and might be relevant to the domains of emotion and social cognition. Based on the functions normally attributed to the rostral anterior cingulate and FI and the evolutionary uniqueness of spindle neurons, researchers have suggested that these neurons might play a key role in socioemotional and higher-order cognitive processing (Watson et al., 2007; Allman et al., 2005; Nimchinsky et al., 1999), leading many to speculate that they may be dysfunctional in autism (Allman et
Allman and colleagues (2005) proposed that the spindle neurons relay to other brain structures signals concerning value judgments in situations involving risk or uncertainty, especially in social bonding and economic decision-making. Furthermore, several species of whales have been shown to possess spindle neurons, and this might be an example of convergent evolution (Hof and Van Der Gucht, 2006).

Although the human frontal cortex as a whole is not differentially enlarged compared to apes, there is variation in aspects of the organization of the frontal cortex among the hominoids. There is some support for the idea that brain enlargement has been accompanied by a reorganization of specific connectivity patterns and that individual species may process information differently. Instead of an overall enlargement of this part of the brain relative to the rest of the brain, specific cortical areas have changed in size. Some areas are enlarged in humans, while others are smaller; similar differences are present across the apes. Additionally

**Temporal Lobe**

While the frontal lobe is featured in the study of human evolution because of its functional properties, increasing comparative evidence suggests that temporal cortical and subcortical structures are undergoing considerable evolutionary change, perhaps even more so than the frontal lobe. The temporal lobe (Figure 3) is recruited in many essential cognitive processes such as the formation and processing of declarative memory (Squire et al., 2004), auditory processing (Poremba et al., 2003), self-recognition (Kircher et al., 2001), visual processing (Mishkin et al., 1983), and the detection of biological motion that underlies theory of mind (Frith and Frith, 1999). Similarly, while species-specific vocalizations activate only cells in the superior temporal sulcus in non-human primates, language processing occurs throughout the temporal lobe (Damasio et al., 1996; Price, 2000; Gorno-Tempini and Price, 2001; Grabowski et al., 2001; MacSweeney et al., 2002; Rilling and Seligman, 2002).

MRI data from two independent studies, Semendeferi and Damasio (2000) and Rilling and Seligman (2002), indicate that the human temporal lobe is, on average, larger than would be predicted for an ape of human brain size. Using at least two individuals per species, both studies concluded that human residuals were predominantly positive and in many cases significantly so. In Rilling and Seligman’s (2002) study, the average temporal lobe volume, as well as the temporal cortical surface area of their six human brains was larger than predicted by the regression line drawn through the apes (Figure 24). Similarly, all 10 of the human specimens measured by Semendeferi and Damasio (2000) fall above the ape regression line, and the mean human value
falls outside of the prediction interval (Figure 24). Regressing the ape temporal lobe volumes from Semendeferi and Damasio (2000) against brain volumes produces a slope of less than one, suggesting temporal lobe volume and whole brain volume are negatively allometric in the apes. When humans are added to the ape sample, the slope of the line closely approaches isometry (slope = 0.979). In the apes, then, the rate of temporal lobe increase lags behind expansion of the entire brain, but temporal lobe size increases at approximately the same rate as the whole brain when human data are included. Thus, these studies suggest that, in contrast to the frontal lobe, the temporal lobe as a whole shows evolutionary expansion in the human lineage.

In contrast to findings in human temporal cortex, our data suggest that temporal lobe white matter has not undergone evolutionary expansion (Schenker et al., 2005). Larger brains contain a greater ratio of white to gray matter than smaller brains (Frahm et al., 1982; Prothero and Sundsten, 1984; Hofman, 1989; Rilling and Insel, 1999; Zhang and Sejnowski, 2000; Bush and Allman, 2004), and total temporal lobe white matter volume shows a positive allometric relationship with temporal lobe volume across hominoids. The ratio of temporal white matter to cortex is not greater in humans than would be expected based on temporal lobe volume; however, analyses of subdivisions of the white matter suggest reorganization similar to the frontal lobes. As with the frontal lobes, the ratio of gyral to core white matter in the human temporal lobe is larger than would be predicted from ape values (Figure 24). The human values for this measure fall above the confidence interval in half of the cases and show average percent residuals greater than 45% (Schenker et al., 2005). A differentially enlarged volume of gyral white matter, as opposed to core white matter, in humans allows for increased interconnectiv-
Amygdala

The temporal lobe comprises subcortical structures essential to both simple and complex behaviors, including central components of the limbic system. The idea that the production and mediation of complex behavior falls exclusively under the purview of the isocortex has been challenged. The challenge comes from the perspective that interactions between multiple cortical territories, including both “basic” emotional processing mediated by limbic structures and “higher order” isocortical cognitive processing, are important for the production of complex behaviors, especially in the social domain (e.g., Damasio, 1994). One such structure, the amygdala or amygdaloid complex (Figure 25), has traditionally been associated with emotional regulation but has more recently received scientific attention for its central role in mediating social cognition and affiliation (Kling, 1986; Brothers, 1990; Adolphs, 1999; Brothers and Ring, 1992; Kling and Brothers, 1992; Adolphs, 2003). The amygdala modulates emotional, neural, and bodily responses to external stimuli and directs an individual’s attention on the emotional significance of the stimulus to produce a context appropriate response (Adolphs, 1999). Although implicit associative learning, attending to salient stimuli, memory consolidation (Phelps, 2005), and environmental appraisal (Emery, 2000) are undoubtedly central to many social cognitive skills, the amygdala is also associated with mediating and evaluating explicitly social stimuli. Some examples from neuroimaging studies include the processing of emotional vocal, facial, and full body expressions (Yang et al., 2002; Hadjikhani and de Gelder, 2003; Giascher et al., 2004; Sander et al., 2005), evaluating trustworthiness in others (Grezes et al., 2004; Singer et al., 2004), and deciding whether to conform to peers’ suggestions (Berns et al., 2005).

At the cellular level, neurons in the macaque amygdala are activated by both dynamic social behaviors such as social interaction (Brothers and Ring, 1992, 1993) and social approach (Kling et al., 1979) and static representations such as images of faces (Brothers, 1990). In the rapidly changing, complex social environments inhabited by primates (Humphrey, 1988; Whiten and Byrne, 1988; Dunbar, 2003), the sorts of processes subserved by the amygdala might provide an individual with essential tools for evaluating conspecifics and navigating the social milieu. Given its importance in social cognition, a possible “prime mover” in primate cognitive evolution, the amygdala could be a target for evolutionary change or reorganization. Moreover, mounting evidence suggests that not only isocortical but also subcortical or allocortical regions of the human brain undergo evolutionary adaptation. For example, the nuclei of the thalamus, another subcortical limbic structure, show differential volumetric increase across primate species which suggests evolutionary reorganization (Armstrong, 1986).

The amygdala is a heterogenous structure comprising numerous highly interconnected nuclei. While a significant number of these nuclei share connections with non-isocortical structures, the lateral, basal, and accessory basal nuclei have strong reciprocal connections with the isocortex. These three nuclei are collectively referred to as the basolateral division of the amygdaloid complex (Figure 26). The basolateral division, together with its extensive interconnections with the isocortex, is important for pairing affective values with incoming stimuli, associative learning (Sah et al., 2003), and memory consolidation (McIntyre et al., 2003). Although little is known about the evolution of the amygdala in primates, previous research suggests that a portion of the amygdala that includes the basolateral division shows evolutionary increase in primates when compared with other regions of the amygdala (Stephan and Andy, 1977; Stephan, et al., 1987). This differential change has been attributed to the influence of isocortical expansion on the connected basolateral nuclei. The volume of the expanded region correlates with social group size, and thus it is likely that this mosaic pattern in the evolution of the amygdaloid subcomponents is driven by social evolutionary pressures (Barton, et al., 2003; Barton & Aggleton, 2000). Unfortunately, these studies of the amygdala included few hominoid species, making it difficult to assess the role the amygdala has played in human evolution. To better understand the importance of the amygdala and its constituent nuclei in human and ape evolution in particular, we performed a morphometric analysis of the amygdala as a whole and also of the basolateral division (the accessory basal, basal, and lateral nuclei) using specimens from all hominoid species.

In the human brain, the amygdala is as large as expected in overall volume, although absolutely it is more than three times the size of the chimpanzee amygdala (Figure 27). In contrast, the basolateral division shows a unique pattern of organization. The lateral nucleus is clearly the largest of the basolateral nuclei in humans (Figure 28), while the basal nucleus is the largest in apes. Stereological analyses of the amygdala and the basolateral division performed on a large sample of human brains confirm our findings in humans (Schumann and Amaral, 2005). The basolateral nuclei of macaques (Amaral et al., 1992; control data in Emery et al., 2001) are organized more like apes, suggesting that humans may be derived compared with other Old World primates. The lateral nucleus in the human brain is also larger than would be predicted for an ape of human brain size (Figure 29). Thus, our data suggest that the organization of the human basolateral division is distinguished by a volumetric increase in the lateral nucleus, and that the lateral nucleus may be evolutionarily emphasized in the human amygdala.

It is very likely that the differential expansion of amygdaloid regions is influenced by the expansion of neuroanatomical regions that are strongly connected with the nuclei, as previously suggested for larger sub-
Figure 26. Diagram shows major components of the amygdala and related connections with rest of the brain.

Figure 27. Volume of the amygdala across species. Bars represent individual specimens used in the two studies presented.
Figure 28. Percentage of basolateral division of the amygdala occupied by the lateral, basal, and accessory basal nuclei in each species. (Data from Barger et al., 2007).

Figure 29. Regression of hemisphere volume against the volume of the lateral nucleus of the amygdala (modified from Barger et al., 2007).
components of this structure (Stephan and Andy, 1977). While information about the function of individual amygdaloid nuclei in the primate brain is limited, it has been hypothesized (Emery and Amaral, 2000; Stefanacci and Amaral, 2002) that polymodal and unimodal sensory information from the temporal cortex first enters the lateral nucleus, where it is received and categorized. This information passes to the basal nucleus where it is paired with information about the social context of the signal through its extensive connections with the orbitofrontal cortex. This highly processed information is then transferred to the striatum and the central nucleus (which subsequently targets hypothalamic and brainstem nuclei) to initiate the production of a context appropriate response. In humans, a preponderance of information from the elaborated temporal lobe would be flowing into the human amygdala via the lateral nucleus, increasing processing demands within the basolateral division. Given the functional and connective relationships between the temporal lobe and the lateral nucleus, it is likely that the unique organization of the human basolateral division is driven by information flowing from the enlarged human temporal lobe into the lateral nucleus (Stefanacci and Amaral, 2002).

Among the apes, the basolateral division of the gorilla and orangutan are most specialized (Barger, et al. 2007). The basal and accessory basal nucleus are exceptionally large in the gorilla, while the lateral nucleus is diminished, a more extreme manifestation of the pattern found among the other apes (Figure 28). If connected isocortical regions influence the elaboration of amygdaloid subcomponents, then this might account for the smaller than expected size of the gorilla temporal lobe (Semendeferi and Damasio, 2000; Rilling and Seligmann, 2002), which is an inverse of the human pattern. Orangutans show more extensive differences in amygdala volume compared to other apes. They have uniquely smaller total amygdala and basolateral division volumes compared to the other great apes (Figure 30). Within the basolateral division, the accessory basal nucleus is smaller in orangutans than would be predicted based on volumes in other hominoids (Figure 31). The basolateral division and especially the accessory basal nucleus receive considerable projections from the orbitofrontal cortex, including area 10 (Ghashghaei and Barbas, 2002; Stefanacci and Amaral, 2002), which is also smaller in orangutans, as discussed above (Figure 32). These data from the amygdala together with existing data on other neural structures provide new perspectives on the evolution of the amygdala and related neural systems (Barton and Harvey, 2000). While amygdaloid nuclei volumes in humans and gorillas might be influenced by the respective increase and decrease of predicted temporal lobe volumes, diminution in orangutan amygdala and amygdaloid nuclei volumes parallel decreases in the size of interconnected, limbic orbitofrontal regions.

Overall our findings largely support hypotheses of amygdala evolution that highlight the importance of

![Figure 30. Left: Relative volume of the amygdala (amygdaloid complex) across great apes. Right: Relative volume of the basolateral division across great apes (modified from Barger et al., 2007)](image)
functional networks within the brain and point to the importance of interconnected networks that might be influenced in a mosaic fashion characteristic of evolutionary reorganization. We found variation in limbic structures among hominoids, suggesting that parts of the human limbic system might be highly specialized. Along with the reorganization of the limbic orbitofrontal sectors of the isocortex, humans also show reorganization of the amygdala. These factors reinforce the idea that human emotional processes are not primitive relics of our evolutionary past but instead are highly evolved systems that complement higher order cognitive processes. Moreover, the associations between temporal lobe and amygdala expansion point to importance of social information processing in human brain evolution.

**Discussion**

While there are clear cognitive differences between humans and apes, the neural underpinnings of these differences are considerably less obvious. How do differences in the size and organization of the human brain produce the cognitive specializations found in our species? Have specific functional circuits been acted upon by evolutionary processes, or is overall size increase the only hallmark of human brain evolution? Anatomical studies comparing the human brain with the ape brain may give us a sense of the associated cognitive changes that might have occurred in ancestral hominids during the Plio-Pleistocene.

**The frontal lobes: Reorganization over enlargement**

Early students of hominid brain evolution identified the frontal lobe as a candidate region for evolutionary expansion given its involvement in higher order executive functions such as abstract thinking and planning and also its involvement in language production. Thus, unique human cognitive capabilities were thought to result from an overall increase in human brain volume accompanied by a disproportionate increase in frontal cortex volume, and this assumption received early empirical support from Brodmann's comparative studies. We addressed this question more recently using modern morphometric techniques and larger samples of hominoids, and found that complex human cognition could not be attributed to a relative increase in human frontal lobe volume. Although the size of the human frontal lobe is larger in absolute terms, frontal lobe volume is remarkably similar across hominoids when whole brain size is factored out. It is likely, then, that the relative size of the frontal lobes has not changed significantly during hominid evolution. These results contradict deep-rooted assumptions about the evolution of the human brain.

![Figure 31. Regression of hemisphere volume against the volume of the accessory nucleus of the amygdala (modified from Barger et al., 2007)](image)
Moreover, the degree of inter- and intra-specific variation we found in our own large sample merits a cautionary statement when interpreting the results of studies that rely exclusively on one or two hemispheres of only a few species. Similarly, frontal lobe measurements from individual hominid endocasts might represent extreme values from a highly variable territory. While expanded frontal lobes are not a unique human characteristic, other anthropoid primates have relatively smaller frontal lobes than both apes and humans, suggesting that this could be a hominoid specialization.

In regard to human evolution, specifically, our results demonstrate the need for new directions of investigation. While the frontal lobe as a whole is not differentially enlarged in humans, it might instead exhibit internal reorganization. This might be manifest at either the gross or the histological level. At the gross level, reorganization can be identified in the distribution of white matter and gray matter across species. At the histological level, reorganization of the frontal lobe may be indicated by the presence or absence of particular cortical areas or by species-specific variation in their size or structural features. Portions of the frontal lobe also exhibit modifications in local circuitry reflected in specific cytoarchitectonic patterns, as seen in areas 10 and 13. Like the entire frontal lobe, the relative size of the dorsal, mesial, and orbital sectors of the human frontal lobe do not stand apart from the apes. In contrast, discrete cytoarchitectonic regions evidence frontal lobe reorganization. Frontal polar area 10, which has dorsal and orbital components, is increased in humans. In contrast, area 13 in the posterior orbitofrontal cortex is reduced. It is possible that anterior components of the orbitofrontal cortex have become more emphasized in human evolution over more posterior portions. Likewise, because the relative size of the orbitofrontal cortex is similar in humans and apes but
area 13 is smaller in humans, the human orbitofrontal cortex might be more heterogeneous than the orbitofrontal cortex of most great apes.

The distribution of white matter in human brains is consistently different from the white matter of the apes. This suggests that differences in connectivity might contribute to human cognitive specializations. More white matter underlies gyral convolutions in humans than in other hominoids, possibly to allow for closely associated areas to communicate more efficiently with one another. Humans have more neuropil in the frontal lobe than other primates, indicating that more space for connectivity is available at the microstructural level. There is increased neuropil in the superficial layers (II/III) of frontal polar area 10, and in Broca’s areas, areas 44 and 45, as indicated by the size of minicolumns and gray level index measurements. Such differences in neuropil might not be uniformly distributed across cortical layers or regions as the data from apes and humans cluster together elsewhere in the cortex (Semendeferi et al., 2001).

Frontal lobe reorganization does not solely occur in humans; it also characterizes other hominoids. Like humans, bonobos have a relatively small area 13 and might have increased complexity in the orbitofrontal cortex due to an increase in the numbers of cytoarchitectonically distinct areas. In contrast, orangutans exhibit a particularly small orbital sector, which is more homogenous and predominantly comprises area 13. The cytoarchitecture of area 13 in orangutans appears more “prefrontal” than limbic, though the most “prefrontal” region of the orbital surface, area 10, is also much smaller in orangutans than in other apes. It is possible that portions of the orangutan orbital sector have shifted toward the lateral surface of the frontal lobe, because the dorsal cortex is relatively enlarged in orangutans. Because the functions of the orbitofrontal cortex are vital to social cognitive processing, the orangutan’s smaller orbitofrontal cortex might reflect the species’ less gregarious social structure and might be related to a reduced emphasis on limbic cortices in orangutan neuroanatomy. In the gorilla, area 10 is somewhat distinct from the other apes and appears to be either selectively reorganized or shifted to a different position in the frontal lobe. Thus, humans as well as several other hominoid species show differential increase in particular portions of the frontal lobe, despite the fact that measures of the whole frontal lobe are not relatively increased in any of the species. Contrary to long-standing dogma, evidence suggests that internal reorganization and not gross volumetric increase characterizes hominin frontal lobe evolution. It appears, in fact, that the most extensive evolutionary expansion has not occurred in the human frontal lobe but in the temporal lobe.

**Beyond the frontal cortex**

Despite these new findings for the frontal cortex, reorganization of the whole brain appears to have occurred over the course of human evolution. The human brain is not simply a scaled up version of an ape brain. At the gross level, the temporal lobe and temporal cortex are larger in relation to whole brain size than would be predicted for a primate of human brain size. From an evolutionary perspective, this is striking given the lack of a parallel increase in the frontal lobe or the primary visual cortex (Holloway, 1968). Unfortunately, it is difficult to conclude whether the temporal lobe is uniquely expanded, because there is little comparative information about the hominoid parietal lobe. Nevertheless, our preliminary unpublished observations on the size and morphology of the parietal lobes in apes and humans support Holloway’s (1968) conclusions favoring a differential expansion and reorganization of the inferior parietal lobule.

Within the temporal lobe, the amygdala exhibits intrinsic reorganization which appears to reflect the reorganization occurring in the whole brain. This pattern of coordinated change may indicate the influence of evolutionary pressures on specific networks, suggesting mosaic evolution (Barton et al., 2003; Barton and Harvey, 2000). The basolateral division of the amygdala has expanded over the course of primate evolution, and this is probably due to its strong connective relationship with the particularly enlarged primate isocortex (Stephan and Andy, 1977; Stephen et al., 1987). In contrast, the more conserved amygdaloid nuclei, which lie outside of the basolateral division, are interconnected with more conserved brainstem and olfactory regions. Strikingly, we found that humans are distinguished by an intrinsic reorganization of the basolateral division. This finding is consistent with our initial impressions that isocortical increases drive volumetric increases in the basolateral division of the amygdala. The ape basolateral division is characterized by a large basal nucleus followed in size by the lateral nucleus and the accessory basal nucleus, respectively. This organization is similar to the organization of the basolateral division of macaque monkeys. In humans the basolateral division is comparatively reorganized. The lateral nucleus is largest, followed in size by the basal and accessory basal nuclei, respectively. The three nuclei that constitute the basolateral division have distinct connections with specific portions of the isocortex. While the basal and accessory basal nuclei have a stronger connective relationship with the orbitofrontal cortex, the lateral nucleus shares the majority of its connections with the enlarged human temporal lobe (Stefanacci and Amaral, 2002). Both the temporal lobe and the lateral nucleus are enlarged in humans, while nuclei connected to regions that are not disproportionately enlarged in humans are not enlarged. As such, evolutionary mosaics present at gross levels of the human brain are reflected in the organization of the basolateral nuclei. This finding provides intriguing evidence that evolution might be acting upon neural systems rather than discrete structures yielding neuroanatomical mosaics.

While none of the ape specimens exhibited basolateral reorganization, there were some exceptional volu-
metric differences among the apes. Orangutans have a smaller total amygdala and a smaller basolateral division than the other great apes (Barger, et al. 2007). The basal and accessory basal nuclei are smaller than those of the other great apes, and the accessory basal nucleus is smaller than predicted for a hominoid of orangutan brain size. The basal and accessory basal nuclei are more connected to the orbitofrontal cortex than the lateral nucleus (Carmichael and Price, 1995; Stefanacci and Amaral, 2002), which is also smaller in orangutans. Given that these regions are limbic in nature, it is likely that limbic structures have been deemphasized in orangutan evolution.

In the inverse of the human pattern, the gorilla has a particularly small lateral nucleus relative to the other great apes and also has the smallest temporal lobe of the apes (Semendeferi and Damasio, 2000; Rilling and Seligman, 2002). The gorilla’s smaller lateral nucleus is associated with a larger accessory basal nucleus. Because the accessory basal nucleus shares strong connections with both the orbitofrontal cortex and the superior temporal gyrus (Stefanacci and Amaral, 2002), it is more difficult to resolve the issue of whether connectivity influences volume. While the temporal lobe is smaller in gorillas, the superior temporal gyrus is not similarly reduced (Rilling and Seligman, 2002). Thus, the superior temporal gyrus might be larger than expected based on overall temporal volume in gorillas. Similarly, the orbitofrontal cortex is only slightly larger in gorillas compared to other apes (Semendeferi et al., 1997), but portions of the orbitofrontal cortex contain a greater number of neurons than other apes (Semendeferi et al., 1998), indicating that there may be more information transfer between the orbitofrontal cortex and other portions of the brain such as the accessory basal nucleus. The amygdala has not only been reorganized over the course of hominid and hominoid evolution, but it also reflects other reorganizational events in functionally related portions of the brain.

Functional implications and neuroecological considerations

The results of the new body of comparative research presented here challenge long held theories about which cognitive properties drive human brain evolution. Limbic structures, traditionally held to be conserved, show evolutionary change in the human brain, while regions that subserve many higher-order cognitive functions, such as the frontal lobe, have not enlarged as a whole. Likewise, neither the frontal cortex nor the amygdala is disproportionately represented in the hominoid brain, although they might be expected to be larger or smaller in humans, respectively, due to their functional properties. Instead, there appears to be a species-specific reorganization of their circuitry, and our data suggest that these regions have evolved in a mosaic fashion.

Within the human frontal lobe, the increased size of area 10 (the frontal pole) and decreased size of area 13 (orbitofrontal limbic cortex) suggest an increased emphasis on executive functions. This reorganization supports previous hypotheses about human brain evolution, which predict human differences in portions of the brain that control executive functions. At the same time, however, a considerable portion of area 10 comprises the orbitofrontal cortex, which is complex, heterogeneous, and is characterized as limbic cortex. In humans, limbic cortices are not reduced appreciably in size in relation to the apes. This finding suggests that regions long associated with emotional processing are not diminished in humans. Furthermore, available data suggest that the size of the prefrontal sector, involved in higher order cognitive functions, may not be as large in humans as once thought. It is difficult to assess the importance of prefrontal cortex-mediated functions in human brain evolution because little histological data is available for the areas contained within the prefrontal cortex, although the results suggest that the story is more complex than previously envisioned. The available evidence indicates that the frontal lobe may have played a key role in hominoid brain evolution, while playing a supporting one in hominid evolution.

Our data suggest that volumetric increase or reorganization of specific neural areas (Semendeferi et al., 1998, 2001) are associated with concomitant changes in heavily interconnected areas (Barger, et al., 2007), and that these mosaic changes occur in specific neural systems. Specifically, portions of the brain that are critical for complex social behavior, such as the limbic frontal cortex and amygdaloid nuclei, show volumetric increase, reorganization, or both. Studies of social cognition among primates (DeWaal and Aureli, 1996; Ingmanson, 1996; Byrne, 1996; Van Schaik and Van Hooff, 1996) emphasize species-specific patterns in how individuals deal with conspecifics and the importance of this behavior for survival and reproduction. In humans, damage to the orbital and mesial frontal sector, i.e., the limbic frontal cortex, is associated with a variety of deficits in social behavior (Damasio, 1994). While orbitofrontal lesions do not necessarily impair basic cognitive abilities such as memory, attention, and language (Stuss and Benson, 1984; Damasio, 1994), the ability to learn social rules and engage in socially affiliative behaviors can be diminished. Numerous analyses suggest a connection between the orbitofrontal cortex and the evaluation of social context based on emotional reinforcers (Bechara et al., 2000; Northoff et al., 2000; Rolls, 2000; Schoenbaum and Setlow, 2001). An extensive body of neuroimaging research has linked both orbitofrontal cortical activation and amygdala activation with social appraisal processes (Emery, 2000; Emery and Amaral, 2000). Normal frontal lobe and amygdala development and function are compromised in autism, which is predominantly characterized by impaired socioemotional behavior. In autism, the frontal lobe and amygdala show abnormal overgrowth during early development (Schumann et al., 2004; Carper and Courchesne, 2005). It is striking that
these regions are all targeted in human evolution, suggesting that systems that influence social behavior are under selective pressure. Area FI has also been associated with socioemotional processing and it is tempting to view the unique cell types (spindle cells) found in this region as adaptations related to social processing. While the entire temporal lobe is not a dedicated social brain “module”, it is considerably entrenched in the processing of species-specific visual and auditory information and in encoding the identity of conspecifics (Kircher et al., 2001; Mishkin et al., 1983; Frith and Frith, 1999). The temporal polar region has also long been hypothesized to be an essential component of the neural system subserving primate social behavior in association with the orbitofrontal cortex and amygdala (Brothers, 1990). Neurons in the superior temporal gyrus respond to species-specific vocalizations, and portions of the superior temporal sulcus are involved in processing facial gestures. Visual information about conspecifics flows through the inferior temporal sulcus through the “what/who” pathway, conveying information about the identity of a stimulus, and complex multimodal social information is processed in the temporal polar region (Brothers, 1990). Further, Rilling and Seligman (2002) point to the temporal lobe’s extensive role in language processing and suggest that the human temporal lobe increase reflects this particular social communicative adaptation.

From this perspective, our orangutan findings are particularly relevant because orangutans are the only semi-solitary ape (Delgado and van Schaik, 2000). Both of the structures that are most reduced in orangutans, the orbitofrontal cortex and the amygdala, are limbic structures that have long been considered central components of the neural system subserving primate social behavior (Adolphs, 1999; Brothers, 1990). Our neuroanatomical findings give rise to behavioral predictions that can be tested by comparative studies of socioemotional differences across ape species. Although to date such studies are rare, one relevant case found that orangutans behave less impulsively than chimpanzees in a numerical ordination task that required them to evaluate edible stimuli (Shumaker et al., 2001). The authors suggested that this difference is related to reduced feeding competition in the orangutan’s social environment compared to the chimpanzee. While orangutans are gregarious and share close bonds with group mates in rehabilitation centers (Russon, 2000, 2002), the high costs of feeding competition in the wild keeps party sizes small, averaging around two individuals per party (Delgado and van Schaik, 2000). Increased emphasis on limbic components such as the orbitofrontal cortex and amygdala might be necessary in situations where competition is high, and less so for situations involving reduced competition. In support of this idea, amygdala volume is actually increased in early autism. An enlarged amygdala might account for the increased social anxiety experienced by autistic children (Schumann et al., 2004). It is possible that less impulsivity or reduced anxiety about the behavior of conspecifics might be adaptive for a solitary great ape species, given that social learning plays a critical role in hominoid development and the opportunities to do so would be reduced in a solitary species.

Our accumulated neuroanatomical findings provide support for the idea that even though most brain components enlarge in a lawful manner across species of various brain sizes, selected neural systems have been reorganized in a mosaic fashion in ways that might reflect the evolutionary socioecology of each species. While addressing hypotheses about human brain evolution such as the theory of neural reorganization put forth by Holloway, this research also has implications for emerging fields such as neuroecology, which attempts to connect the neural substrates of behavior with species-specific socioecological adaptations. In some ways, Holloway’s ideas on reorganization were a prelude to neuroecology, and our data suggest that both perspectives may serve as useful frameworks for the study of human brain evolution. Although further empirical investigations are necessary to fully test his early predictions, a considerable amount of information is fast accruing in favor of Holloway’s pioneering ideas about primate brain evolution made almost a half a century ago.

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