Ashley N. Parks and Jeroen B. Smaers

Abstract

In 1912, Korbinian Brodmann suggested that the "regio frontalis" (i.e., the prefrontal cortex) of the human brain was exceptionally large in comparison to other primates. His observations sparked over a century of neuroscientific inquiry into the frontal lobe and the prefrontal cortex in particular. Later work describing the role of the prefrontal cortex in human intelligence drove anthropologists and evolutionary neuroscientists to study its evolution as a means of revealing the evolutionary history of unique cognitive capacities of humans. Here we discuss the results of investigations into the frontal cortex from the perspectives of multiple disciplines: paleoneurology, comparative neuroanatomy, and phylogenetic comparative neuroanatomy. We will describe the different pieces of the puzzle that each of these disciplines contributes to forming a detailed picture of the evolution of the human frontal lobe. We then hone in on phylogenetic comparative approaches in order to investigate changes in frontal lobe scaling across anthropoids. We find that human frontal lobe enlargement is driven specifically by an expansion of the prefrontal cortex, not the frontal motor areas. These results are confirmed by comparisons of regions within the frontal lobe that indicate the human prefrontal cortex has expanded drastically in comparison to frontal motor areas. Furthermore, evolutionary rate analyses reveal that the rate of evolution of the prefrontal cortex size is higher than for the relative sizes of the frontal lobe or the frontal motor cortex. Overall, phylogenetic comparative analyses converge on the observation that different areas of the frontal lobe evolved at different rates of evolution, favoring exceptional enlargement of the prefrontal cortex, but not necessarily the frontal lobe as a whole. These perspectives thus confirm that the human brain is more than a scaled-up version of the monkey brain and that the putative unique expansion of the "regio frontalis" is indeed an important feature that may support human's unique cognitive abilities.

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14.1 Introduction

The search for the neural substrate of human intelligence is a prevailing topic in the neurosciences. Ever since the landmark cytoarchitectonic mapping of the cerebral cortex by Brodmann (1912), a particular focus has been on the "regio frontalis." Brodmann noted that the prefrontal cortex is

disproportionately larger in humans compared to nonhuman primates, suggesting this region may have been subject to an exceptional evolutionary expansion. At the time, the functional underpinnings of the prefrontal cortex were, however, piecemeal. Subsequent neuroscientific work has demonstrated that this region is associated with a plethora of behavioral features that contribute to measures of general intelligence in humans (e.g., language, decision-making, theory of mind, reaching higher level goals (Asplund et al. 2010), planning (Rowe et al. 2001), introspection (Fleming et al. 2010), imagination, social information processing (Adolphs 2009)).

Considering the central role of the frontal lobe, and the prefrontal cortex in particular, for human intelligence, anthropologists and evolutionary neuroscientists have sought to study its evolution in the hope of unraveling the evolutionary history of humans' exceptional cognitive capacities (Passingham 1973). Here we discuss the findings of this endeavor as approached from different disciplines. Comparative neuroscientists utilize neuroimaging techniques to detail differences among humans, chimpanzees, and macaques (Avants et al. 2006; Van Essen and Dierker 2007; Glasser and Van Essen 2011). Paleoneurologists use fossil endocasts to track putative differences among hominin species (Neubauer 2014). Lastly, phylogenetic comparative neurobiologists study differences across a wide sample of extant species in order to map detailed patterns of change along individual lineages of the tree of life (Smaers and Soligo 2013).

In paleoneurological and phylogenetic comparative studies, the study of the prefrontal cortex is often proxied by the frontal lobe (the larger neuroanatomical region that subsumes the prefrontal cortex) (Bush and Allman 2004; Bruner et al. 2013; Falk 2014). To make an adequate distinction between the frontal lobe and prefrontal cortex, a brief anatomical and functional description of the frontal lobe and its constituent regions will first be provided. Throughout, a clear distinction will be maintained between studies that focus on the frontal lobe and those that focus on the prefrontal cortex.

14.2 Anatomy and Function of the Frontal Lobe

The human frontal lobe comprises the most anterior portion of the neocortex. It extends from the frontal pole anteriorly to the central sulcus posteriorly. It borders posteriorly with the postcentral gyrus of the parietal lobe, and it is separated from the temporal lobe by the lateral sulcus. The boundary between the primary motor cortex (area 4) of the frontal lobe and the somatosensory cortex (area 3) of the parietal lobe is also distinguished by clear differences in cytoarchitecture

(cellular structure). The primary motor cortex is agranular, contains large pyramidal neurons, and is marked by generally diffuse lamination, whereas the primary somatosensory cortex (area 3) has a granular layer IV and is clearly differentiated from the frontal lobe by its sharply defined layers (Bucy 1937). The frontal lobe is functionally and structurally heterogeneous, as it contains multiple subdivisions that are the structural basis of different aspects of both motor and higher cognitive processing. The general functional subdivisions of the frontal lobe are the primary motor cortex, the premotor and supplementary motor areas, and the prefrontal cortex (Fig. 14.1).

The primary motor area occupies a strip of cortical tissue in the precentral gyrus, primarily in the anterior wall of the central sulcus. Its distinct cytoarchitecture is marked by the presence of large pyramidal neurons located in layer V called Betz motor cells. The primary motor cortex contains many cells of origin of descending motor pathways that are involved in the initiation of voluntary movements. Before the topographic organization of motor representation in area 4 had been confirmed using electrical studies, the mid-nineteenth century neurologist Hughlings Jackson predicted the pattern in which movements are mapped on to the primary motor cortex based on his observations of the predictable spread of tremors in epileptic patients (Jackson 1867). Jackson observed that partial seizures produced abnormal movements that progressed in a predictable manner from one part of the body to the next, i.e., from fingers to the hand, arm, shoulder, and, eventually, face. This sequence corresponds to the motor homunculus—a physical representation of the human body located in the precentral gyrus (Sira and Mateer 2014). Stimulation of the primary motor area elicits contralateral contraction in the muscles of the corresponding anatomical area (Fuster 2002; Sira and Mateer 2014).

Electrical stimulation of the premotor cortex, or Brodmann's area 6, also elicits muscle contraction, albeit at a higher threshold. The premotor area and supplementary motor areas are located anterior to the primary motor area. Originally, Brodmann (1909) determined that the premotor area and the primary motor cortex both lacked an internal granular layer IV and were thus determined to be architectonically agranular. However, it was later discovered that the premotor cortex is *dysgranular*, as it contains a faint granular layer IV. Unlike the sharp boundary between Brodmann's areas 3 and 4, the border between the premotor cortex (area 6) and the primary motor cortex (area 4) is somewhat more diffuse and is marked by the absence of Betz cells (Bucy 1937) as well as a faint granular layer IV in area 6. Both the number and size of Betz cells taper toward the anterior boundary of area 4, yet they remain larger than the pyramidal cells found in the premotor cortex.

The prefrontal cortex occupies the most anterior portion of the frontal lobe, although its precise delineation is a matter of contention. This region was originally coined the
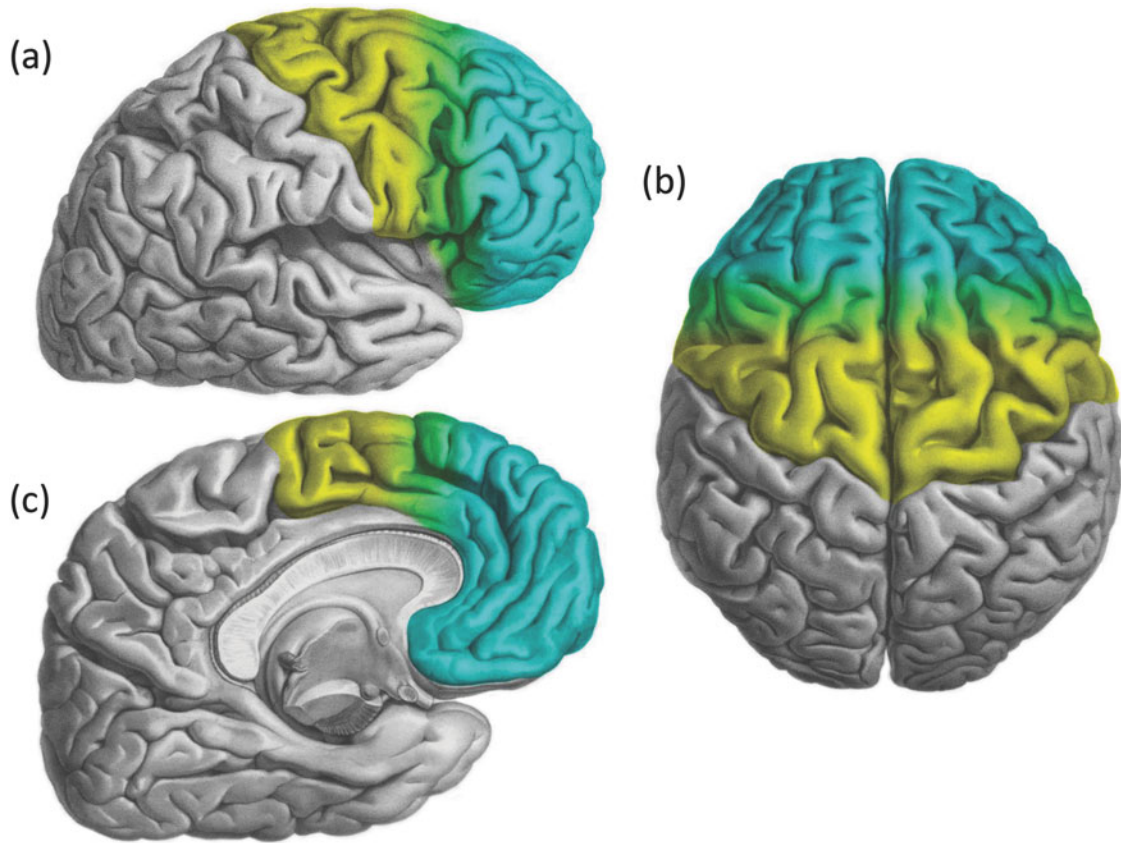
Fig. 14.1 Lateral (**a**), dorsal (**b**), and medial (**c**) view of the human brain illustrating the regions under consideration. Colors illustrate the approximate boundaries of the primary motor cortex (*yellow*), premotor cortex and supplementary motor cortex (*green*), and prefrontal cortex (*blue*) (Figure adjusted from Foville 1864)

"granular frontal cortex" or *regio frontalis*, by Brodmann, and was later referred to as the "prefrontal cortex" by subsequent researchers (Preuss 1995), although Brodmann originally reserved the term "prefrontal cortex" for a single area (area 11) within this region. In the mammalian brain, the prefrontal cortex is conventionally defined based on a combination of cytoarchitectonic and connectivity criteria, including a prominent granular layer IV and reciprocal connectivity with the mediodorsal nucleus (MD) of the thalamus (Rose and Woolsey 1948; Fuster 2002). While some researchers maintain that the use of MD projection and granularity for delineating the border of the prefrontal cortex ultimately converges on similar anatomical definitions of the region, these criteria are challenged in later works for their lack of diagnostic power (Preuss 1995). In primates, the prefrontal cortex has three major anatomical aspects: the lateral, medial, and ventral or orbital prefrontal cortex. Each prefrontal region is further divided into functionally and cytoarchitectonically distinct areas, such that there is considerable structural and functional variance within the prefrontal cortex itself. Each of these prefrontal areas plays a distinct role in the organization and control of behavioral, linguistic, and higher cognitive functions associated with intelligence (for more information, see Fuster 2008; Passingham and Wise 2012; Passingham et al. 2017). Unfortunately, no broad-scale comparative dataset of cytoarchitectonically distinct prefrontal subdivisions currently exists, prohibiting a detailed phylogenetic comparative analysis (though see Semendeferi et al. 2001 for an analysis of area 10 in apes).

14.3   A Paleoneurological Perspective

Paleoneurologists study the evolution of the frontal lobe in the hominin lineage by examining variation in such features as sulcal patterns, curvature of the frontal bone, and breadth of the anterior cranial fossae of the endocranial cavities of fossil specimens. Using endocasts, measurements of frontal gyri are derived from the imprints of sulcal patterns. The degree of sulcal preservation is, however, impacted by such variables as species, age of the individual, and geological conditions, such that sulcal imprints are typically poorly preserved in hominin fossils

(Falk 2014). In addition to sulcal patterns, several studies quantify the shape and proportions of the anterior cranial fossa, with particular regard to both the anterior curvature of the frontal bone and the diameter of the anterior cranial fossa at its widest aspect. Although frontal "bulging" and lateral widening have been used as proxies for frontal lobe expansion, the relationship between structural changes in the anterior cranial fossa and the underlying neural tissue is not straightforward, leading to conclusions that such features cannot provide unequivocal information on frontal lobe expansion (Bruner 2017). Nevertheless, three endocranial traits in particular have been discussed in the context of frontal lobe expansion: sulcal pattern variation, frontal bulging, and lateral widening.

Sulcal patterns in the frontal lobe have been a principal focus in the study of hominin endocasts. In the case of the genus *Homo*, every specimen displays sulcal patterns associated with the inferior frontal gyrus (including an outward protrusion at Broca's area) (Tobias 1987; Bruner and Holloway 2010). Frontal sulcal patterns in earlier specimens of *Homo*, such as *Homo habilis* and *Homo erectus*, have been reported to be markedly similar to those of modern *Homo sapiens* (Tobias 1987; Bruner and Holloway 2010). However, it is not clear how these patterns contrast with australopithecines due to sample size constraints. Indeed, evidence of frontal gyri in australopithecine endocasts are often observed in single, fragmentary specimens that are difficult to interpret in a broader phylogenetic context (Bruner 2017). For example, it has been suggested that a convexity in the anterior portion of the frontal lobe of specimen MH1 (*Australopithecus sediba*) represents the initial evolutionary stages of a more humanlike inferior frontal gyrus (Carlson et al. 2011; Falk 2012, 2014; Falk et al. 2012). More specimens are needed in order to characterize frontal sulcal patterns across australopithecine genera.

Additionally, modern human crania exhibit a characteristic anterior bulging of the frontal bone (Bruner et al. 2013). Although there is overlap in the degree of "frontal bulging" across a wide range of earlier and modern species of *Homo* (Bookstein et al. 1999), it has been suggested that the accentuated curvature of the frontal bone reflects underlying changes in cortical tissue (Lieberman et al. 2002). However, both the face and the vault of the skull contribute to formation of frontal bone morphology; thus, causality of frontal bulging is obscured by structural interactions between the neurocranial and splanchnocranial elements (Bookstein et al. 1999; Bruner et al. 2013; Bruner 2017). Indeed, the frontal bone comes into direct contact with the orbits, rendering frontal bone morphology susceptible to vertical constraints on facial growth (Enlow 1990). Thus, it is plausible that anterior bulging of the frontal bone is a structural by-product of spatial constraints that stem from changes to the hominin facial shape (Bruner 2017).

Lastly, the anterior cranial fossae of modern humans and Neanderthals have undergone a lateral widening (Bruner and Holloway 2010). In comparison to *Homo erectus* and australopithecines, modern humans and Neanderthals exhibit an evolutionary grade shift in the proportion of the anterior cranial fossa width relative to the width of the posterior portion of the cranium (Bruner and Holloway 2010). The frontal lobes are absolutely and relatively wider in Neanderthals and modern humans than in more archaic species. As Neanderthal and modern humans are the only two species whose frontal lobes lie directly on top of the orbits, it is possible that cranial constraints from direct contact with the orbits have caused a shift in proportions toward a greater maximum brain width (Bruner 2017).

Three hypotheses have been suggested to account for changes in the form and proportion of the anterior cranial fossa (Bruner and Holloway 2010; Bruner 2017): (1) Neanderthals and modern humans underwent a redistribution of cortical volume as a secondary consequence of structural constraints from having the frontal lobes lie directly on top of the orbits (Bookstein et al. 1999; Bruner and Manzi 2005; Bruner 2017); (2) underlying changes in cortical organization, specifically via the expansion of Broca's area and the evolution of language and complex cognition, have caused a lateral expansion of the anterior endocranial cavity; and (3) cranial constraints caused lateral widening, providing the spatial dimensions that would be exapted for new neural functions (i.e., new connections to Broca's area in association with language). Evidence thus far seems to favor that a geometric reconfiguration of frontal cortical mass was largely a secondary by-product of structural changes to the face and skull (Bruner and Holloway 2010; Bruner 2017). In sum, the fossil record does not provide evidence that directly addresses frontal expansion (Bruner 2017). Moreover, because internal brain reorganization cannot be deduced from shifts in the gross proportions of the cranium, the expansion of the human frontal lobe and consequent changes in cognition evade fossilization in the paleoanthropological record. Insights from other disciplines are necessary in order to address purported changes in human frontal lobe evolution.

14.4 A Comparative Neuroanatomical Perspective

Elucidating the nature of differences between the prefrontal cortex of humans and other animals has been an enduring question driving comparative neuroanatomical enquiry for over a century (Preuss and Goldman-Rakic 1991; Fuster 2002; Sherwood and Smaers 2013). Brodmann's (1909, 1912) seminal work highlighted the significance of the "regio frontalis" in primates, with a specific emphasis on

the unique qualities of the human prefrontal cortex. Brodmann conducted a broad survey of mammalian cytoarchitecture and concluded that the granular frontal cortex (the area now referred to widely as the prefrontal cortex) is unique to primates and that the human prefrontal cortex is disproportionately large in comparison to that of nonhuman primates. Brodmann's work instigated an ongoing stream of research regarding the evolutionary significance of the prefrontal cortex, including whether or not new regions have evolved within the frontal lobe throughout the course of primate brain evolution.

Brodmann's first major hypothesis was that the granular frontal cortex (the prefrontal cortex) is unique to primates and is rudimentary or absent in all mammals. In support of Brodmann's hypothesis, several researchers have argued that the evolution of the frontal lobe in primates involved the addition of new functionally and cytoarchitectonically distinct areas that comprise the prefrontal cortex (Sanides 1964, 1970; Pandya et al. 1988). However, arguments against the evolutionary distinctiveness of the primate prefrontal cortex have been made by emphasizing similarities in connectivity patterns across mammals (Rose and Woolsey 1948). Specifically, the bidirectional connectivity of the mediodorsal (MD) nucleus projects similarly to the granular portion of the frontal lobe (the prefrontal cortex) in primates and to the nongranular cortex in other mammals. As an extension of this hypothesis, it has been argued that the MD-projection cortex in nonprimates is homologous to the prefrontal cortex of primates (Akert 1964). Lesion studies of the MD-projection cortex of rats provided support for the homology in the functional organization of the prefrontal cortex (Eichenbaum et al. 1983; Kolb 1984). It is now generally accepted that homologues of the orbital and cingulate portions of the prefrontal cortex exist in some nonprimate mammals (Ongür and Price 2000), while the dorsolateral prefrontal regions are not found outside of primates (Preuss 1995).

Brodmann's second major hypothesis was that the prefrontal cortex underwent considerable expansion throughout the course of human evolution, including the possible addition of new areas within the prefrontal cortex. Brodmann remarked that the prefrontal regions were not identical in human and nonhuman primates, noting that homologies between the monkey and human prefrontal regions were unclear. While many early works regarded the primate prefrontal cortex as a homogenous unit that lacked internal functional subdivisions (Lashley and Clark 1946; Von Bonin 1948), it is now well established that there is a high degree of functional and structural parcellation within the prefrontal cortex (Cavada and Goldman-Rakic 1989; Preuss and Goldman-Rakic 1989, 1991; Seltzer and Pandya 1989).

However, whether or not the monkey prefrontal cortex contained a full complement of structurally and functionally distinct regions as the human prefrontal cortex was less clear. Walker (1940) created new cytoarchitectonic maps of the macaque brain in which he described new areas on the posterior orbital surface of the monkey prefrontal cortex. Modifications to Brodmann's original parcellation of the human prefrontal cortex were proposed to account for areas that Brodmann originally only identified in humans (Beck 1949; Petrides and Pandya 1994). It is now generally accepted on the basis of cytoarchitectonic evidence that the human orbital prefrontal cortex is homologous to the orbital prefrontal cortex of nonhuman primates (Semendeferi et al. 1998; Ongür and Price 2000). Similarly, the lateral prefrontal cortex of the macaque monkey has been argued to contain the same complement of cytoarchitectonic regions as that found in humans (Petrides 2005).

Whether or not the prefrontal cortex of humans is exceptionally enlarged, as suggested by Brodmann, or is to be expected for a primate of human body size, has been addressed in several comparative neuroimaging studies (Avants et al. 2006; Van Essen and Dierker 2007; Glasser and Van Essen 2011). For example, neuroimaging methods have been used to demonstrate that the relative size of the prefrontal cortex of humans is twice as large in comparison to that of chimpanzees (Avants et al. 2006). Furthermore, differences in the relative size of regions within the prefrontal cortex have been documented, such as the exceptional expansion of the human lateral prefrontal cortex in comparison to macaques (Van Essen and Dierker 2007). Distinctions in the connectivity patterns of the prefrontal cortex in humans and other primates have also been demonstrated using neuroimaging techniques. For example, unlike in chimpanzees and macaques, the human left ventral premotor cortex is strongly connected with the left middle and inferior temporal gyrus by means of the arcuate fasciculus (Rilling et al. 2008). Additionally, humans, but not macaques, exhibit strong functional connectivity between the anterior prefrontal cortex (aPFC) and the inferior parietal lobe (Mars et al. 2011).

In sum, comparative neuroanatomists have used direct comparisons of neuroanatomical variation between species in order to advance our knowledge of the evolution of the human frontal lobe and the prefrontal cortex in particular. Firstly, comparative neuroanatomical studies largely reject Brodmann's notion that the prefrontal cortex is unique to primates among mammals with the exception of the primate dorsolateral prefrontal cortex. The orbital and cingulate portions of the prefrontal cortex, on the other hand, are found in many other mammalian species. Secondly, the human prefrontal cortex has undergone considerable expansion in comparison to nonhuman primates, although it is

generally accepted that the prefrontal cortex of humans and nonhuman primates contains the same complement of cyto-architectonic regions. Thus, it is unlikely that the human prefrontal cortex expanded by the addition of new regions that are not found in other primates.

14.5 A Macroevolutionary Perspective

In order to make inferences about the evolutionary context in which the human brain evolved, comparative neuro-anatomists often rely upon direct comparisons between humans and our closest living relatives, chimpanzees and bonobos. Implicit in this comparison is the notion that the neural architecture of the chimpanzee has not changed throughout the course of the evolution of *Pan*, such that the chimpanzee brain can function as a stand-in for the brain of the last common ancestor of chimpanzees and humans. This underlying assumption is problematic considering that both chimpanzees and humans have evolved for around 6 million years since their last common ancestor. This leaves the possibility that chimpanzees may also have evolved traits that are unique to their lineage. Several recent studies have indeed shown this to be the case (Sayers et al. 2012; Almécija et al. 2015). It is clear that any derived morphological traits of the chimpanzee brain will confound the results of an evolutionary analysis based off direct comparisons between the two species.

Additionally, the direct comparison of chimpanzee and human brains fails to take allometry into account, confounding interpretations of proportionality (Passingham 1973). Comparisons of proportions assume that variables scale at a ratio of one-to-one (i.e., isometry). It is, however, well established that many neural structures do not scale in a ratio of one-to-one but, rather, are found to scale allometrically with size (Finlay and Darlington 1995). Allometric scaling trends are critically important to the understanding of the evolution of human neural architecture, as shared allometries may reflect shared functional, genetic, and developmental constraints (Smaers et al. 2017). Departures from shared allometries, in particular, are evolutionarily informative because they reveal deviations from integration that highlight shifts in the functional, genetic, and/or developmental bauplan of animals. Such information is crucial to identify instances where brain organization shifts away from the generally integrated building plan of the vertebrate brain (Sylvester et al. 2010). A renewed effort to collect data for comparisons across a broad range of species (e.g., MacLeod et al. 2003; Sherwood et al. 2005a; Smaers et al. 2010, 2011b, 2013; Bauernfeind et al. 2013), in conjunction with ongoing advancements in comparative methods, permits a macroevolutionary account of brain evolution that is able to characterize allometric scaling trends

(and species- or clade-specific deviations from allometry) in brain structures throughout a vast array of species in a primate phylogenetic tree.

In order to develop a macroevolutionary context of the human brain, statistical methods are used that incorporate the phylogenetic relatedness among the species under study in techniques that answer questions regarding the coevolution of traits, the scaling patterns of traits, and the tempo and mode of evolution of traits (Venditti et al. 2011; Khabbazian et al. 2016; Smaers and Rohlf 2016; Smaers et al. 2016). These approaches are of particular relevance to elucidating the evolution of the human frontal lobe because they address issues of allometry and putative human "uniqueness." It is clear, however, that these methods require information from a wide range of species. One advantage of comparing trait variation across a broad comparative sample is that it alleviates the issues presented by apomorphies in the direct comparison of two species.

A principal issue limiting the collection of prefrontal information across a wide range of species is that there is no standard method for delineating prefrontal boundaries across species (Sherwood and Smaers 2013). Different delineations of the prefrontal and frontal regions have been used across datasets, confounding the interpretability of comparisons of these prefrontal measurements. Some studies rely on gross anatomical landmarks, such as the genu of the corpus callosum, in order to delimit the boundaries of the prefrontal cortex (McBride et al. 1999; Schoenemann et al. 2005), while other researchers insist upon the use of cyto-architectonic criteria for an accurate demarcation of prefrontal boundaries (Semendeferi et al. 2001; Sherwood et al. 2005b). Of the available datasets, only two provide information on the prefrontal cortex based on cytoarchitectonic criteria (Brodmann 1912; Smaers et al. 2011a). Brodmann (1912) provides information for 13 species (including humans) on total area of the granular frontal cortex, agranular cortex, neocortex, and striate cortex. Brodmann's delineation of the granular frontal cortex (i.e., the prefrontal cortex) is defined as all subregions of the frontal lobe that contain a prominent granular layer IV (including areas 8, 9, 10, 11, 44, 45, 46, and 47 in the human brain). Brodmann's cytoarchitectonic maps can be regarded as the most reliable dataset, with subsequent cytoarchitectonic maps providing highly similar impressions (von Economo and Koskinas 1925; Bailey et al. 1950; Bailey and Von Bonin 1951), including recent maps based on the difference in myelination between association cortex and other areas (Glasser and Van Essen 2011). Smaers et al. (2011a) provided a proxy of prefrontal volume across a wider range of species ($N = 19$) by employing a volumetric bootstrapping procedure along the frontal pole relative to the cytoarchitectonic borders between the frontal lobe and the parietal lobe. First, the borders between the frontal and parietal lobes were delineated based on

cytoarchitectonic criteria (using 20 section intervals). Then, the cumulative volume of the first five anterior sections along the frontal pole were considered as a proxy for prefrontal volume, while the last five posterior sections were considered as a proxy of frontal motor area volume. For more information, see Smaers et al. (2011a, 2012, 2017). While the Brodmann dataset provides a more accurate delineation of the prefrontal cortex as defined by the presence of a prominent granular layer IV, the Smaers dataset provides a proxy for prefrontal size that underestimates possible exceptional expansion in great apes and humans (see more information in Smaers et al. 2017). Here we discuss the Brodmann and Smaers datasets only because they are the only two datasets that provide prefrontal information based on cytoarchitectonic criteria.

In order to test whether the human frontal lobe deviates significantly from allometric predictions, we performed a phylogenetic analysis of covariance (Smaers and Rohlf 2016). This procedure tests whether different groups in the sample indicate significant differences in the slope and intercept of the regression. Specifically, this procedure evaluates whether a model that includes separate slopes or intercepts for different groups provides a better fit for the data than a model with a single intercept. A phylogenetic ANCOVA test for differences in intercepts between groups for frontal lobe size versus brain size hereby constitutes a test on whether these different groups have significantly different values for relative frontal lobe size. Results (Table 14.1) indicate that human frontal cortex expansion (relative to the rest of the

neocortex) is approaching significance in humans for both datasets (P is just below 0.05 for the Smaers data and non-significant for the Brodmann data). Similarly, human prefrontal cortex expansion relative to the rest of neocortex size nears significance ($P = 0.058$ for the Smaers data and $P < 0.014$ for the Brodmann data). Frontal motor area expansion is, however, not significant. Importantly, prefrontal expansion relative to frontal motor expansion is highly significant ($P < 0.01$ for the Smaers data and $P < 0.001$ for the Brodmann data).

These results support the conclusion that frontal motor areas have not significantly expanded in the human brain but, rather, that the prefrontal cortex has (Passingham 1975; Buckner and Krienen 2013; Glasser et al. 2014; Smaers et al. 2017). Results reveal that any enlargement in the frontal lobe is due to expansion in the prefrontal cortex, not the frontal motor areas. This is confirmed in a comparison of prefrontal to frontal motor areas indicating that the human prefrontal cortex has expanded dramatically relative to frontal motor areas. Together, our results suggest that the expansion of the frontal lobe is due to the exceptional expansion of the prefrontal cortex. Thus, a grade shift within the human frontal lobe is evident (frontal motor areas have not expanded significantly, even decreased in relative size, while prefrontal cortex size has expanded significantly). It should be noted that the current measure of frontal motor areas does not differentiate between primary motor areas and premotor areas. In alignment with previous suggestions (Blinkov and Glezer 1968; Passingham and Ettlinger 1974; Preuss 2004),

Table 14.1 Results from a phylogenetic analysis of covariance. Results relate to tests of differences in intercept among groups with the slope held constant. "Others" refers to all non-great ape primates in the sample. The analysis includes the comparison of multiple treatment groups (group a "v" group b) to a control group ("|" group c)

| Y	X	Grouping	Smaers data			Brodmann data		
		PGLS ANCOVA	F	P		F	P	
Frontal	Rest of the neocortex	Among groups	2.651	0.103		3.384	0.118	
		Humans v others|great apes v others	5.085	0.040	*	4.160	0.097	
		Humans v great apes|others	4.789	0.045	*	0.202	0.672	
		Great apes v others|humans	1.380	0.258		4.015	0.101	
Prefrontal	Frontal motor	Among groups	4.842	0.024	*	24.911	0.003	**
		Humans v others|great apes v others	9.098	0.009	**	49.820	0.001	***
		Humans v great apes|others	5.051	0.040	*	23.080	0.005	**
		Great apes v others|humans	5.994	0.027	*	2.316	0.189	
Prefrontal	Rest of the neocortex	Among groups	2.109	0.156		7.110	0.035	*
		Humans v others|great apes v others	4.207	0.058		13.678	0.014	*
		Humans v great apes|others	3.349	0.087		3.895	0.105	
		Great apes v others|humans	1.710	0.211		5.995	0.058	
Frontal motor	Rest of the neocortex	Among groups	0.930	0.416		1.772	0.262	
		Humans v others|great apes v others	1.257	0.280		1.425	0.286	
		Humans v great apes|others	0.345	0.566		3.458	0.122	
		Great apes v others|humans	1.768	0.204		1.383	0.293	
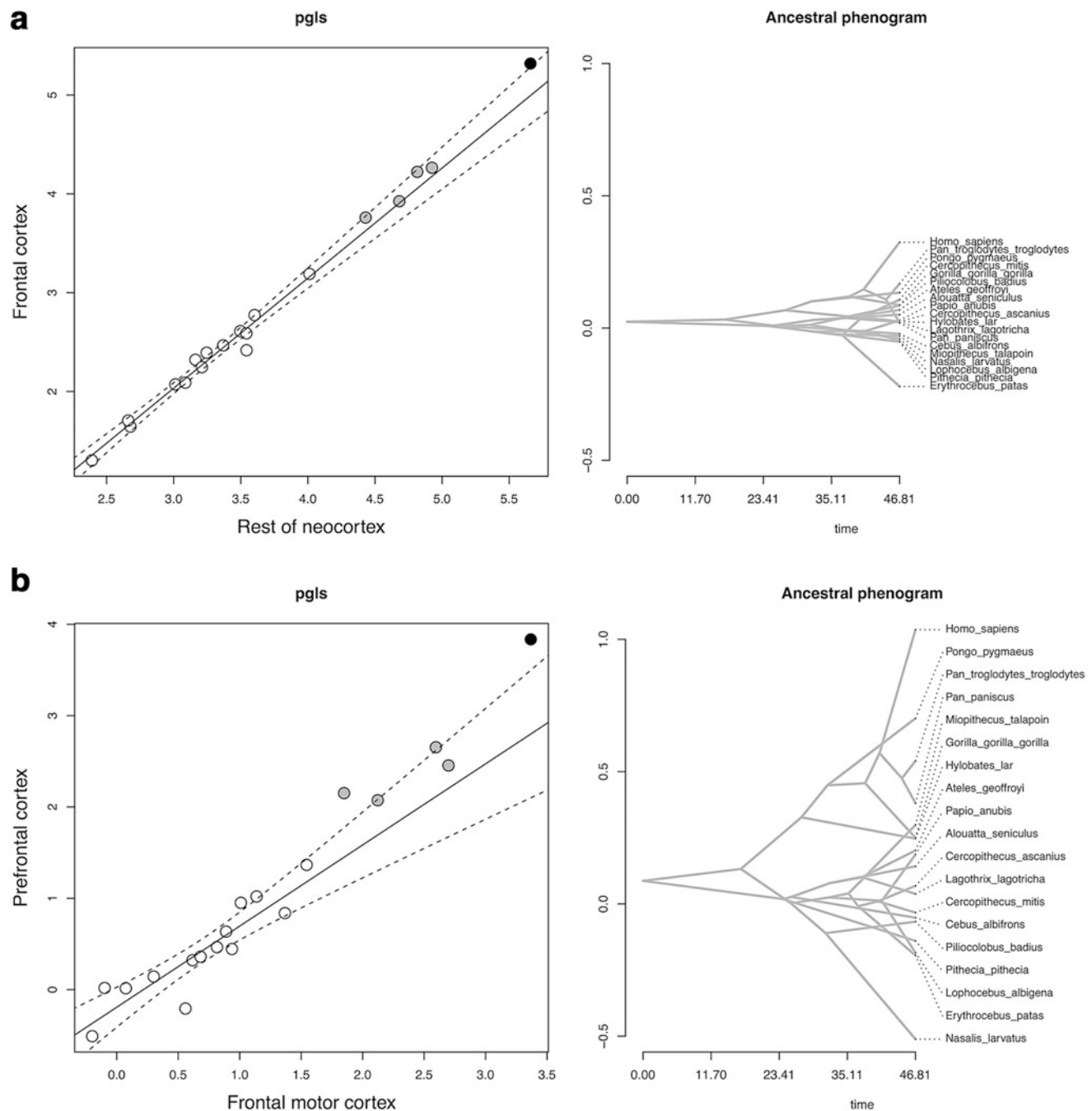
Fig. 14.2 Phylogenetic generalized least-squares analysis of the Smaers data. Confidence intervals (*dashed lines*) indicate the uncertainty in the estimation of the scaling parameters (i.e., the slope and intercept of the regression). Regression parameters are based on the scaling pattern of the non-hominoid sample. *Black circles* represent human values, whereas *gray circles* reflect great ape values. All other primates are indicated by *white circles*. *Scaling patterns* are displayed for four comparisons: (**a**) scales the frontal cortex to the rest of the neocortex (defined as the neocortex minus the frontal cortex); (**b**) the prefrontal cortex to frontal motor cortex; (**c**) the prefrontal cortex to the rest of the neocortex (defined as the neocortex minus the frontal cortex); (**d**) frontal motor cortex to the rest of the neocortex (defined as the neocortex minus the frontal cortex). *** indicates $P < 0.001$, ** $P < 0.01$, *$P < 0.05$. Ancestral phenograms depict estimations of trait evolution across independent lineages of a phylogeny (Smaers et al. 2016), such that both increases and decreases in the rate of evolution of relative brain structure volumes can be visualized

it is expected that the non-enlargement of human frontal motor areas applies particularly to the primary motor cortex, not necessarily to the premotor areas.

In addition to testing for scaling patterns, phylogenetic comparative methods can also be used to map the evolution

of biological traits. Figures 14.2 and 14.3 display the scaling patterns of the frontal lobe and prefrontal cortex and the ancestral phenograms of relative frontal lobe and prefrontal cortex size. Ancestral phenograms display a best estimate of how relative frontal lobe and prefrontal cortex size have
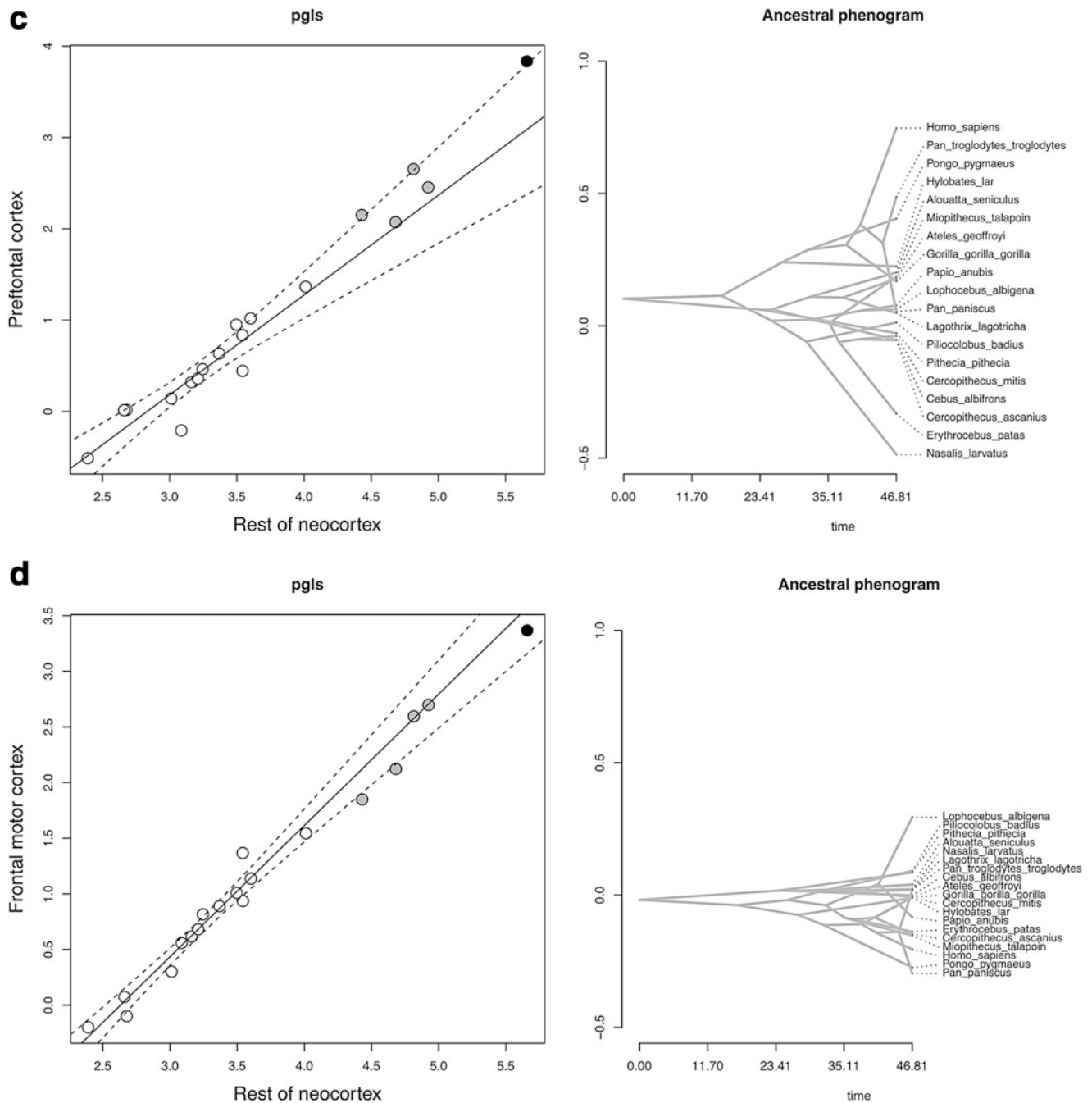
Fig. 14.2 (continued)

changed through time across the individual lineages of the phylogenetic tree. Results are indicated for both the Smaers (Fig. 14.2) and Brodmann (Fig. 14.3) datasets and lead to the same conclusion with regard to frontal and prefrontal cortex evolution. The specific measure of relative size matches the analyses performed in (a–d). Ancestral phenograms were computed using a multiple-variance Brownian motion procedure (Smaers et al. 2016) (equivalent results were obtained using a constant-variance Brownian motion procedure).

From the ancestral phenograms, it is clear that most of the cross-species variation that occurs in the frontal lobe is accounted for by changes in relative prefrontal cortex size. This is further confirmed by a rate analysis demonstrating that the rate of evolution of relative prefrontal cortex size is higher than that in the relative sizes of either frontal cortex or frontal motor areas (Fig. 14.4). The rate is hereby quantified as the Brownian motion rate parameter (σ^2) of a multiple-variance Brownian motion model (also here equivalent results were obtained using a constant-variance Brownian

Fig. 14.3 Phylogenetic generalized least-squares analysis of the Brodmann data. Conventions as in Fig. 14.2
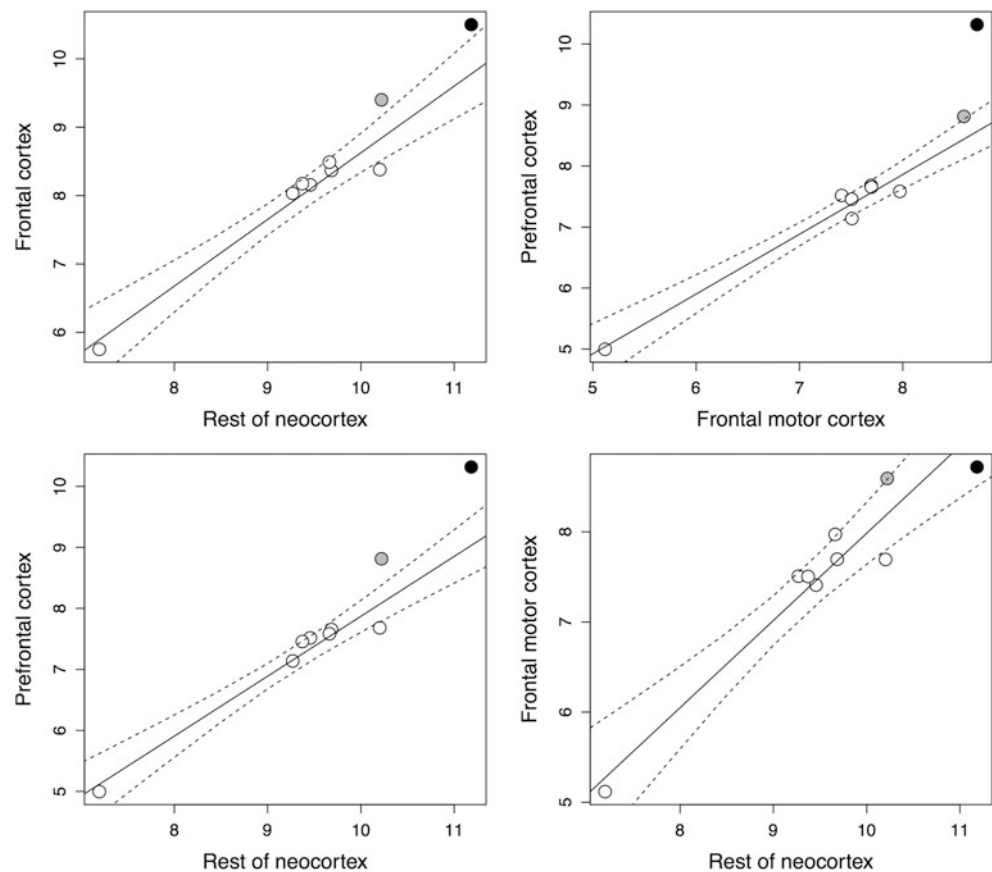
motion model) and calculated using a Bayesian MCMC procedure (with 10^6 iterations and a 20% burnin). The Brownian motion rate parameter is directly related to the amount of observed trait variation within a given time span. Traits with a higher rate of evolution are traditionally interpreted as being under a higher selective pressure. These results again confirm that comparative variation in frontal lobe volume is primarily a matter of variation in prefrontal volume.

Overall, phylogenetic comparative analysis of the frontal and prefrontal cortex thus demonstrates a grade shift within the frontal lobe toward more than predicted prefrontal cortex expansion. The traditional view that humans are an extension of the nonhuman primate allometric trend in terms of frontal (or prefrontal) evolution is not supported. Humans, great apes, and non-hominoid primates thus form three distinct grades in frontal lobe evolution (Passingham and Smaers 2014; Smaers et al. 2017). Evidence thus suggests that non-allometric expansion of the prefrontal cortex occurred at the dawn of great apes (~19–15 mya), such that selective pressures for higher cognitive functions underlie frontal lobe organization in both great apes and humans (Smaers et al. 2017). Exceptional expansion of the prefrontal cortex converges with

functional data from cognitive neuroscience and primatology indicating that both great apes and humans are characterized by complex social cognition (Adolphs 2003, 2009) and the concomitant evolution of cultural traditions (van Schaik et al. 2003).

14.6 Discussion

Unpacking the biological basis of distinctly human cognitive and behavioral capacities is a major force of compelling scientific inquiry. Korbinian Brodmann's cytoarchitectonic maps of the cerebral cortex highlighted the significance of the "regio frontalis" in humans. His conclusion that the prefrontal cortex was especially enlarged in humans compared to nonhuman primates inspired over a century of neuroscientific research. Due to its fundamental role in human intelligence, it is no wonder that the investigation into the evolutionary history of the prefrontal cortex has involved a multidisciplinary approach. When insights from paleoneurology, comparative neuroanatomy, and phylogenetic comparative methods are taken in summation, a much more complete picture of the evolution of the frontal lobe, and the prefrontal cortex in particular, begins to emerge.
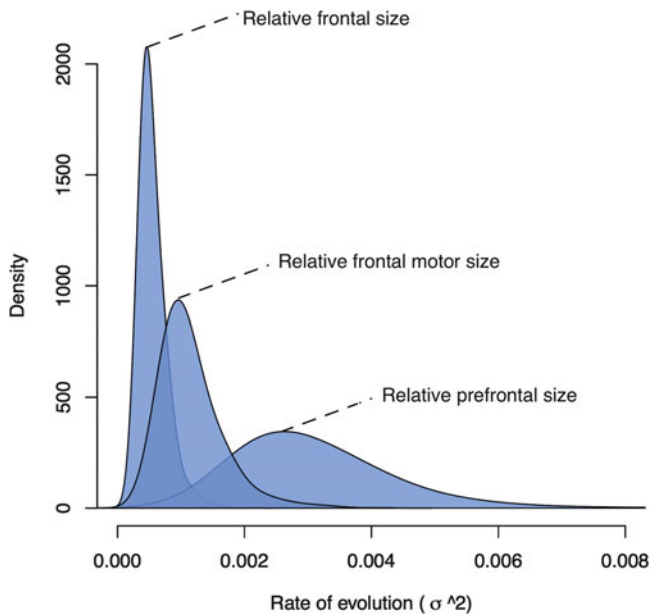
Fig. 14.4 Results from a rate analysis on the Smaers dataset. Rates are quantified as σ^2 (i.e., the Brownian motion rate parameter). Traits with a higher rate are commonly interpreted as being under a higher selective pressure. Rates are displayed for the expansion of the frontal cortex, prefrontal cortex, and frontal motor areas, each relative to the rest of the neocortex (defined as the neocortex minus the frontal cortex)

Paleoneurological studies provide the only direct evidence of changes in brain structure since our last common ancestors with chimpanzees. While evidence strongly suggests that there have been changes in the form and proportions of the anterior cranial fossa, it is unclear whether these structural differences reflect variations in underlying cortical organization. Modern human crania exhibit (a) enhanced curvature of the frontal bone and (b) a larger diameter of the anterior cranial fossa (i.e., "lateral widening"). it is not currently possible to determine whether or not these changes are driven specifically by the expansion of the frontal lobe. Moreover, internal changes in the relative sizes of structures within the frontal lobe are not revealed by gross changes in the form of the anterior cranial fossa. Thus, insights from other perspectives must be integrated in order to elucidate the nature of changes in underlying cortical organization. For example, genetic evidence suggests that the human prefrontal cortex underwent the majority of its exceptional expansion only since the emergence of anatomically modern humans (Shulha et al. 2012; Somel et al. 2014). More multidisciplinary evidence is needed to interpret structural changes in the anterior cranial fossa and whether this might reflect exceptional expansion of specific components within the frontal lobe since the last common ancestor of chimpanzees and humans.

Phylogenetic comparative studies provide a broader evolutionary picture, as they place the evolution of the hominin frontal lobe in a broader macroevolutionary context. Such studies analyze phylogenetic trees in association with data from many species in order to investigate the tempo, mode, and scaling patterns that underlie variation in the frontal lobe across a wide range of different species. Results of macroevolutionary analyses presented here demonstrate that the frontal cortex is expanded in comparison to the rest of the neocortex, but that this is due principally to the extraordinary expansion of the human prefrontal cortex. Comparisons of prefrontal and frontal motor areas confirm these results, demonstrating that the human prefrontal cortex has expanded dramatically relative to frontal motor areas. This is further confirmed by a rate analysis demonstrating that the rate of evolution of relative prefrontal cortex size is far higher than that in the relative sizes of either frontal cortex as a whole and frontal motor areas. These results also are in accordance with previous phylogenetic comparative analyses that demonstrate how humans, great apes, and other primates form three distinct grade shifts in prefrontal cortex expansion among primates that differ significantly from each other (Passingham and Smaers 2014; Smaers et al. 2017). Thus, phylogenetic comparative methods indicate that there has been significant reorganization within the frontal lobe throughout the course of human evolution that is driven primarily by prefrontal expansion.

Thus, multiple lines of evidence converge upon the observation that different areas of the human frontal lobe have evolved at different rates favoring prefrontal expansion. The different perspectives discussed here reveal unique pieces of this puzzle. Paleoneurology is unique in its ability to demonstrate structural changes of the anterior cranial fossa within the human lineage, comparative neuroanatomy provides a detailed picture of differences in cytoarchitecture and connectivity between humans and other primates, and phylogenetic comparative methods place these neuroanatomical differences in a larger macroevolutionary context. Together, these perspectives indicate that the human brain is more than a scaled-up version of the monkey brain and that the putative unique expansion of the "regio frontalis" is indeed an important feature that may support human's unique cognitive abilities. Future analyses would benefit from a continued effort to expand available datasets on cytoarchitectonically distinct areas of the cerebral cortex (Zilles et al. 2011). Furthermore, given the functional contribution of the frontoparietal (Genovesio et al. 2014; Caminiti et al. 2015) and cortico-cerebellar systems (Kelly and Strick 2003; Ramnani 2006; Koziol et al. 2014) and their contribution to explaining the evolution of brain organization in primates (Smaers et al. 2011b, 2013; Smaers and Soligo 2013; Smaers 2014), future research should also look to emphasize prefrontal connectivity and the targets of its various projections.

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