CORTEX 48 (2012) 46–57

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Special issue: Review

The prefrontal cortex: Comparative architectonic organization in the human and the macaque monkey brains

Michael Petrides [a,*], *Francesco Tomaiuolo* [b,c], *Edward H. Yeterian* [d,e,f] *and Deepak N. Pandya* [e,f,g]

[a] *Montreal Neurological Institute, Department of Neurology and Neurosurgery, and Department of Psychology, McGill University, Montreal, QC, Canada*
[b] *Auxilium Vitae Volterra, Volterra, Pisa, Italy*
[c] *Department of Internal Medicine and Public Health, University of L'Aquila, Italy*
[d] *Department of Psychology, Colby College, Waterville, ME, USA*
[e] *Edith Nourse Rogers Memorial VA Medical Center, Bedford, MA, USA*
[f] *Boston University School of Medicine, Boston, MA, USA*
[g] *Beth Israel Deaconess Medical Center, Boston, MA, USA*

ARTICLE INFO

Article history:
Received 23 February 2011
Reviewed 18 March 2011
Revised 7 April 2011
Accepted 19 July 2011
Published online 29 July 2011

Keywords:
Prefrontal cortex
Cytoarchitecture
Fiber pathways

ABSTRACT

Detailed cytoarchitectonic studies of the human cerebral cortex appeared during the first quarter of the 20th century. The incorporation of the cytoarchitectonic map by Brodmann (1909) in the Talairach proportional stereotaxic space (Talairach and Tournoux, 1988) has established the Brodmann numerical nomenclature as the basis for describing the cortical location of structural and functional findings obtained with modern neuroimaging. In experimental anatomical and physiological investigations of the macaque monkey performed during the last 50 years, the numerical architectonic nomenclature used to describe findings in the prefrontal cortex has been largely based on the map by Walker (1940). Unfortunately, the map by Walker was not based on a comparative investigation of the cytoarchitecture of the human and macaque monkey prefrontal cortex and, as a result, the nomenclature and the criteria for demarcating areas in the two primate species are not always consistent. These discrepancies are a major obstacle in the ability to compare experimental findings from nonhuman primates with results obtained in functional and structural neuroimaging of the human brain. The present article outlines these discrepancies in the classical maps and describes comparative investigations of the cytoarchitecture of the prefrontal cortex of the macaque monkey and human (Petrides and Pandya, 1994, 1999, 2002a) in order to resolve these discrepancies and enable easy translation of experimental research in the monkey to findings in the human brain obtained with modern neuroimaging.

* *Corresponding author*. Montreal Neurological Institute, Department of Neurology and Neurosurgery, 3801 University Street, Montreal, Quebec, Canada H3A 2B4.
E-mail address: michael.petrides@mcgill.ca (M. Petrides).
0010-9452/$ – see front matter © 2011 Elsevier Srl. All rights reserved.
doi:10.1016/j.cortex.2011.07.002

The cerebral cortex can be divided into several distinct cytoarchitectonic areas on the basis of differences in cell size and type and in the arrangement of the neurons in the various cortical layers, such as differences in cell density, the presence or absence of certain layers, and the relative thickness of the layers. The first complete cytoarchitectonic maps to be published were those of Campbell (1905), who divided the human cerebral cortex into a few general regions, and the map of the monkey (*Cercopithecus*) cerebral cortex published by Brodmann (1905). A little later, Brodmann (1908, 1909, 1914) published his famous map of the human cerebral cortex. In Brodmann's maps, several cortical areas were identified and labeled with distinct numbers (Figs. 1A and 2A). In 1925, Economo and Koskinas published a major atlas of the human cerebral cortex in which the different architectonic areas were labeled with letters (Fig. 1B) and provided a detailed description of the different areas and excellent photomicrographs. In the 1950s, the maps of Bailey and Bonin (1951) and Sarkissov et al. (1955) appeared, the latter map being a modified version of the Brodmann map based on the examination of several brains. Various maps focused on the cytoarchitecture of the human frontal lobe, such as the map by Sanides (1962), the map of the orbital frontal region by Beck (1949), the dorsolateral frontal areas 9 and 46 by Rajkowska and Goldman-Rakic (1995), Broca's region by Amunts et al. (1999), and areas 10 and 13 by Semendeferi et al. (1998, 2001). Apart from the cytoarchitectonic studies mentioned above, some investigators described the architecture of the cerebral cortex based on myelin (Vogt, 1910; Vogt and Vogt, 1919) or pigment architecture (Braak, 1979).

Architectonic studies of the human cerebral cortex were of relatively limited interest until the emergence of modern functional neuroimaging in the 1980s. The demonstration with positron emission tomography (PET), initially, and a little later with functional magnetic resonance imaging (fMRI) that focal changes in cortical activity could be detected in relation to various aspects of motor and cognitive performance required a stereotaxic map to describe the location of these changes and to identify the cytoarchitectonic areas within which they were located. The stereotaxic map of Talairach (Talairach and Tournoux, 1988) was adopted by the functional neuroimaging community to provide a standard proportional stereotaxic space within which all brains could be transformed in order to correct, partially, for differences in size and shape and permit reporting of the structural or functional neuroimaging findings in a common stereotaxic space (see Brett et al., 2002). Gradually, the Talairach stereotaxic space, which was based on one brain, evolved into the Montreal Neurological Institute (MNI) standard proportional stereotaxic space (MNI space) that was based on several brains (Collins et al., 1994). The Talairach space and its modern development, the MNI space, constitute now the common stereotaxic framework within which specific activity changes in functional neuroimaging studies and/or morphological changes in the brain as a result of training or disease are described. The use of the Brodmann (1909) cytoarchitectonic numbers to describe the different areas of the cerebral cortex in the Talairach and Tournoux (1988) atlas also meant the wide adoption of the Brodmann cortical scheme by the functional neuroimaging community in the description of functional and morphological changes in the human cerebral cortex.

The identification of the cytoarchitectonic area within which the functional activity occurred is a complex issue that requires careful consideration of many factors. Probability maps which provide quantitative information about the location of particular structures in the Talairach or MNI space have been published to aid the investigator in making decisions about the locus of the activation. These probability maps have been of particular cytoarchitectonic areas (e.g., Amunts et al., 1999) or morphological structures, such as the pars opercularis (e.g., Tomaiuolo et al., 1999) or the orbitofrontal sulci (e.g., Chiavaras et al., 2001). In the latter case, the assumption has been that architecture maintains a more-or-less stable relation to certain morphological entities, which is known to be the case for some structures. For instance, the primary visual area (the striate cortex) is known to lie within the banks of the calcarine sulcus, the primary motor cortex (area 4) always lies in the anterior bank of the central sulcus

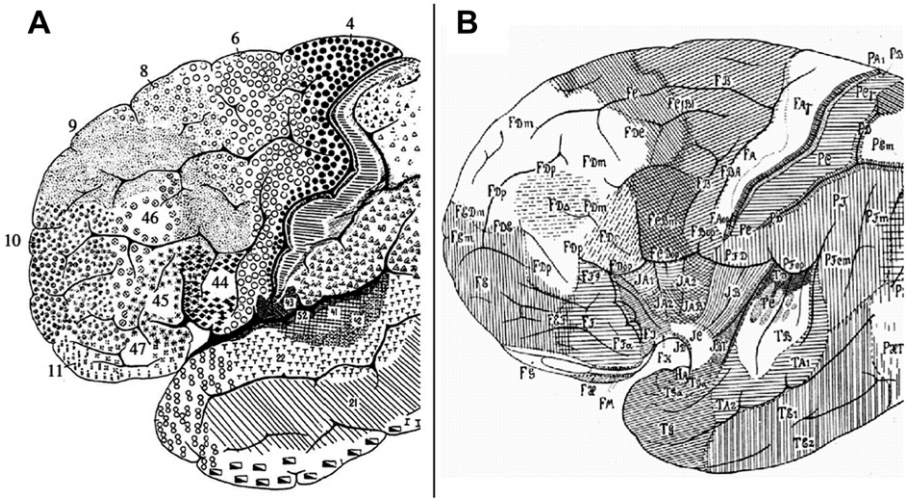

Fig. 1 – The frontal cortex of the human brain as parcellated in the cytoarchitectonic maps of (A) Brodmann (1909) and (B) Economo and Koskinas (1925).

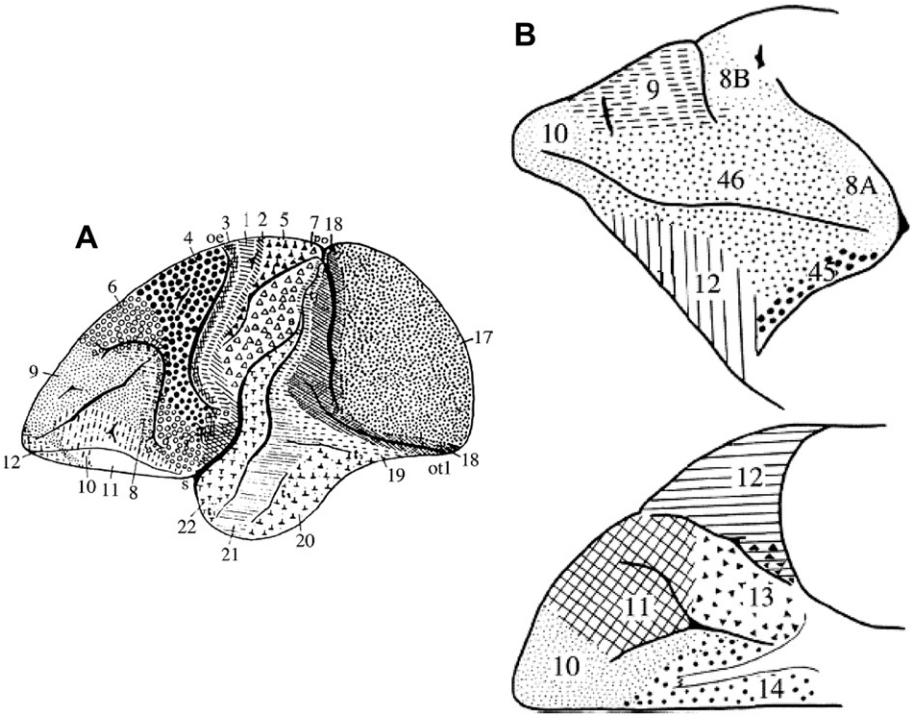

Fig. 2 – Cytoarchitectonic map of the monkey cerebral cortex by (A) Brodmann (1905) and the prefrontal cortex by (B) Walker (1940).

and the primary somatosensory cortical area 3 always lies in the posterior bank of the central sulcus. When such relations are known, a reasonable inference can be made of the architectonic location of certain functional changes. Nowadays, cortical activation foci can be detected even in individual subjects and, therefore, the functional activations can be related easily to particular sulci/gyri in an individual subject (e.g., Amiez et al., 2006).

The frontal cortex, which is the focus of the present article, comprises several architectonic areas in both the human and the monkey brain (e.g., Barbas and Pandya, 1989; Brodmann, 1905, 1908, 1909, 1914; Economo and Koskinas, 1925; Petrides and Pandya, 1999, 2002a; Sarkissov et al., 1955; Walker, 1940). Experimental anatomical studies in the monkey have shown that the afferent and efferent connections of these areas are quite distinct (for review of cortico-cortical connections, see Yeterian et al., 2011, and for the pathways used, see Petrides and Pandya, 2002b). Afferent connections provide a particular frontal area with information about perceptual and memory processing occurring in specific cortical and subcortical areas, while efferent connections provide the means by which a particular frontal cortical area can control information processed in other cortical and subcortical areas. Neuroimaging studies in the human brain can provide some evidence about the functional contribution of these areas by demonstrating overall increases in activity within particular regions (indirectly estimated via the blood oxygenation level) in relation to various aspects of cognitive processing (i.e., the so-called "activations"). However, studies in the monkey are necessary to link unambiguously particular functional contributions to specific architectonic areas by means of analysis of the cognitive effects of lesions *restricted* to these areas. In addition, since the overall activity changes demonstrated by neuroimaging within a region do not provide any information about the actual neuronal computations that underlie particular functional contributions, examination of the physiological and pharmacological properties of neurons recorded in these areas in alert behaving animals are necessary.

Since the 1950s, the development of experimental anatomical methods to study the connections between different brain areas, such as the silver degeneration (Fink and Heimer, 1967; Nauta, 1957), initially, and later the anterograde tracer methods (e.g., autoradiography, Cowan et al., 1972), made it possible to identify axonal fiber tracts in experimental animals. In such material, one can identify the precise course and termination of commissural and association cortico-cortical axonal pathways, as well as the cortico-subcortical projection axons leading to structures such as the striatum, thalamus, pons, reticular formation, tectum, and spinal cord. These anterograde axonal tracing methods can be supplemented with retrograde tracer techniques, using horseradish peroxidase (Mesulam, 1978) or fluorescent dyes (Keizer et al., 1983; Kuypers et al., 1980), which provide detailed information not only about the precise cortical area within which specific pathways originate, but also the precise neurons in particular cortical layers that give rise to the axonal connections. This experimental methodology gave rise to the golden era of experimental neuroanatomy during which detailed information about the connections of the different cortical areas of the primate cerebral cortex was gathered based on studies on various nonhuman primate species, in particular the macaque monkey.

During the last 10 years, major developments in imaging have permitted the reconstruction and visualization of

pathways in the human brain using diffusion MRI (e.g., Catani et al., 2005; Frey et al., 2008; Makris et al., 2005, 2007; Mori and Zhang, 2006; Saur et al., 2008; see Jones, 2008, for review of the methodology). Diffusion MRI has provided an important new tool to explore the connections of the human brain and is already beginning to play an important role in clinical practice, such as in the evaluation of potential impairments in white matter pathways in abnormalities of the nervous system (see, Johansen-Berg and Behrens, 2006). Although undoubtedly diffusion MRI is a major development in the study of the white matter pathways and their abnormalities in the human brain, one must be aware of the limitations of this method. Diffusion MR imaging permits the delineation of the stems of the major white matter association pathways that link various cortical regions together and the projection fiber pathways that connect cortical regions with subcortical nuclei. However, present limitations of the method do not permit the delineation of the precise origins within particular cortical areas of axonal pathways and the precise terminations of axons within specific architectonic cortical areas (for an excellent discussion of limitations even with 9.4 T scanning to resolve the details of the optic chiasm, see Roebroeck et al., 2008). The limitations of diffusion imaging for tractography are the result of partial volume averaging in single voxels of complex fiber relations, such as the crossing of fibers, close juxtaposition of distinct fiber tracts ("kissing"), and the presence of sharp curves. Other current limitations of diffusion MRI for tractography stem from the models used to estimate fiber orientations, such as the classical tensor model which has problems when there are two or more fiber orientations (Catani and Stuss 2012, this issue; Catani et al., in press). The distance from seed to target and how tortuous a pathway may be also affect the reliability of tractographic results (for an overview of the method, see Johansen-Berg and Behrens, 2006, and Jones, 2008).

As an example, suppose that a group of axons originate in cytoarchitectonic area PF of the rostral inferior parietal lobe and another group originate from the immediately and caudally adjacent area PFG and these axons run in close proximity to each other in the superior longitudinal fasciculus in the white matter of the inferior parietal lobule. Diffusion tensor imaging (DTI) can reconstruct the overall major stem of the superior longitudinal fasciculus but cannot distinguish the axon group that originated from PF as opposed to the axon group that originated from PFG since these distinct axon groups will be running in close juxtaposition ("kissing") and giving essentially the same diffusion profile. Similarly, although the stem of the major pathways can be reconstructed, there are limitations in correctly deriving the presence or absence of the terminations of the axons within particular cortical areas. Let us continue with the example above of the two groups of axons one of which originated from area PF of the inferior parietal lobule and the other from area PFG that is just caudal to the first one. Both these axon groups run in close proximity as part of the superior longitudinal fasciculus and one of them is directed to rostroventral premotor area 6, while the other is directed to area 44. Since both these axonal groups will be running in close proximity and both will enter the white matter of the ventral precentral gyrus, can DTI resolve those that terminate in premotor area 6 (including their origin) from those that terminate in area 44 (and their origin)? Since information is lost in voxels with convergence of axons (distinct fiber bundles that come close together) and divergence of axons (some fibers leave while others remain), it will be difficult to estimate these two fiber bundles with accuracy. Thus, DTI can reconstruct the major stem of the superior longitudinal fasciculus bringing information from inferior parietal areas to the ventral frontal region (e.g., Catani et al., 2005; Frey et al., 2008; Makris et al., 2005; Thiebaut de Schotten et al., 2012, this issue), but cannot estimate with accuracy which fibers terminate in rostroventral area 6 and which ones terminate in ventrolateral prefrontal areas 44 or 45. This precise differentiation can be achieved with anterograde tracer studies in the macaque monkey because labeled axons can be seen to emerge from the cortical area that was injected and can be traced all the way to their synaptic terminations in another distant cortical area (for an example, see Petrides and Pandya, 2009).

The above considerations indicate that, although the stems of the major pathways can be visualized with DTI in the human brain, detailed information about the precise cortical origins of axons and their precise cortical terminations must be derived from anterograde and retrograde tracer studies in the macaque monkey. In the companion article in the present issue by Yeterian et al. (2011), we review the cortico-cortical connectivity of the various prefrontal architectonic areas as shown in experimental anatomical studies in the macaque monkey. However, the success of such an endeavor to inform issues of connectivity in the human brain will be critically dependent on the extent to which architectonic areas have been defined by the same criteria in the monkey and the human frontal cortex. Cytoarchitectonic studies of the cortex of the monkey appeared at about the same time as those of the human cortex, but unfortunately the numerical designations employed did not always refer to areas with comparable architectonic features and location (see Petrides and Pandya, 1994, 1999, 2002a, for detailed discussion of this problem). For instance, Brodmann published a map of the cortex of the monkey in 1905 (Fig. 2A), but the numerical designations he used were not consistent with those used in his map of the human brain that was published later in 1908 and 1909 (Fig. 1A). He did not identify area 46 in the monkey and used the number 12 for the frontopolar region in contrast to his map of the human brain where the frontopolar region was identified with the number 10 (compare Fig. 1A with Fig. 2A). Furthermore, the number 10 was used by Brodmann to identify a part of the ventrolateral frontal region in the monkey. These are only some of the discrepancies in the two maps. Brodmann expressed considerable uncertainty about his subdivisions of the frontal cortex and expressly stated, in his famous monograph of 1909, that the numbers he used do not always denote homologous areas in different species.

The discrepancies in architectonic delineations and the uncertainty expressed by Brodmann about his demarcation of frontal cortical areas led to abandonment of his monkey map. In 1940, Walker published a map of the cytoarchitecture of the frontal cortex of the macaque monkey (Fig. 2B) and attempted to use, as far as possible, the numerical nomenclature used by Brodmann in the human brain. For instance, he designated the frontopolar cortex of the monkey as area 10 (as was the case in

the map of the human brain by Brodmann) and identified an area 46 and an area 45 that were missing from Brodmann's map of the monkey frontal cortex. Walker's map became the basis of subsequent cytoarchitectonic investigations of the macaque monkey frontal cortex. The Walker scheme, with some modifications introduced by Barbas and Pandya (1989) and Preuss and Goldman-Rakic (1991), provided the basis for the description of the results of anatomical connectional studies on macaque monkeys with various anterograde and retrograde tracers during the golden era of experimental neuroanatomy. Similarly, the location of recording and microstimulation sites in physiological studies and the placement of lesions in behavioral investigations of the frontal cortex in the monkey were often guided by Walker's map.

But there was a major problem. Although Walker (1940) harmonized the designations of some of the areas of the monkey prefrontal cortex with those used by Brodmann in his map of the human brain, he did not compare the cytoarchitecture of the human and the macaque monkey frontal lobe. Thus, several issues arise. Walker identified a large region within the banks of the sulcus principalis and the cortex immediately surrounding it as area 46, but he left open the question whether all of it or part of it corresponded to area 46 as identified by Brodmann in the human brain. Walker introduced an area 45 along the inferior branch of the arcuate sulcus, but, since he had not compared its architecture with that in the human brain, he repeatedly pointed out that he was not certain whether it corresponded to Brodmann's area 45 in the human brain. Furthermore, Walker introduced terms that were discrepant with those used by Brodmann in the human brain. He labeled the most ventral part of the macaque ventrolateral prefrontal region, where it continues into the orbital frontal cortex, as area 12 and used the term area 13 for the caudal orbitofrontal region. These numbers are discrepant with those of Brodmann who, in the human brain, used the number 47 to identify a part of the ventrolateral prefrontal region as well as most of the caudal orbital frontal region, while acknowledging that this huge region is architectonically heterogeneous.

The above discrepancies are a serious problem for modern neuroscience because they impede the ability to compare experimental findings from nonhuman primates with results obtained in functional and structural neuroimaging of the human brain. As pointed out above, although advances in structural neuroimaging (e.g., DTI) permit reconstruction of the major pathways of the human brain, these reconstructions cannot reveal the precise origins and terminations of the axonal connections (as can be done in the experimental tracer studies in the monkey). Although attempts are sometimes made to infer these terminations in the human brain with probabilistic DTI tractography (e.g., Behrens et al., 2007) or functional connectivity analysis (e.g., Margulies et al., 2009; van den Heuvel et al., 2009), these must be interpreted with caution and in the context of the experimentally studied pathways in the macaque monkey (Berlucchi 2012, this issue).

In the 1990s, we began a strictly comparative re-examination of the architecture of the macaque monkey and the human frontal cortex (Petrides and Pandya, 1994, 1999, 2002a). The aim of this research was to define the various prefrontal areas in the two species using the same cytoarchitectonic and topographical criteria so that a meaningful crosstalk between experimental anatomical, physiological and lesion-behavior research on monkeys and functional and structural neuroimaging in the human brain could proceed. This comparative examination yielded a parcellation of the prefrontal cortex that is comparable in the two species (Fig. 3), thus resolving the major problems that had arisen from discrepant parcellations in the classic maps.

There is no doubt that the basic architectonic plan is the same in these two primate species. It is often claimed that the prefrontal cortex has undergone disproportionate expansion in the human brain (Passingham, 1973; Schoenemann et al., 2005), but this claim has been challenged more recently. Semendeferi et al. (2002) have used MRI to examine the size of the frontal cortex in several primates and report that the relative size of the human frontal cortex is that expected for a primate of the human size. Furthermore, their results demonstrated that the human frontal cortex is not disproportionately large relative to that of the great apes, although it is larger in comparison with that of the lesser apes and monkeys. In addition, Smaers et al. (2011) provided evidence that neither the white matter nor the gray matter of the frontal lobe is disproportionately expanded in the human brain. They suggest, instead, that there might have been a left prefrontal ape specialization in relative white to gray matter volume and that humans may be the extreme case in this evolutionary trend. Thus, greater connectivity of the left prefrontal cortex (and hemisphere) and, perhaps, Broca's region, may have been a factor in language evolution, rather than the appearance of new architectonic areas (Thiebaut de Schotten et al., 2012, this issue). The left prefrontal specialization suggested by the data discussed above is of interest in relation to evidence from intrinsic functional connectivity by Liu et al. (2009) that asymmetry of the human brain is controlled by various factors, one of which appears to be a left-lateralized factor that includes certain prefrontal and temporal areas related to semantic processing. At present, only for frontopolar area 10 is there some evidence that it may be larger in the human brain than in apes (Semendeferi et al. 2001).

In the present article, we shall not provide an exhaustive description of the architectonic features of the various areas since this can be found in our primary research reports (Petrides and Pandya, 1994, 1999, 2002a). We shall instead guide the reader through the problems that were raised by the discrepancies in the classic maps and their resolution. In this manner, the reader will appreciate the changes made to the classic maps and will be provided with a key to the companion article by Yeterian et al. (2011) which describes the connections in the macaque monkey in the context of the Petrides and Pandya comparative map of the frontal cortex.

1. Architectonic correspondence issues in the dorsolateral frontal cortex of the macaque monkey and the human brain: the problem of areas 9, 46, and 9/46

In the macaque monkey, Walker (1940) labeled the highly granular cortex within and around the sulcus principalis as area 46. In the posterior end of the sulcus principalis, area 46 is

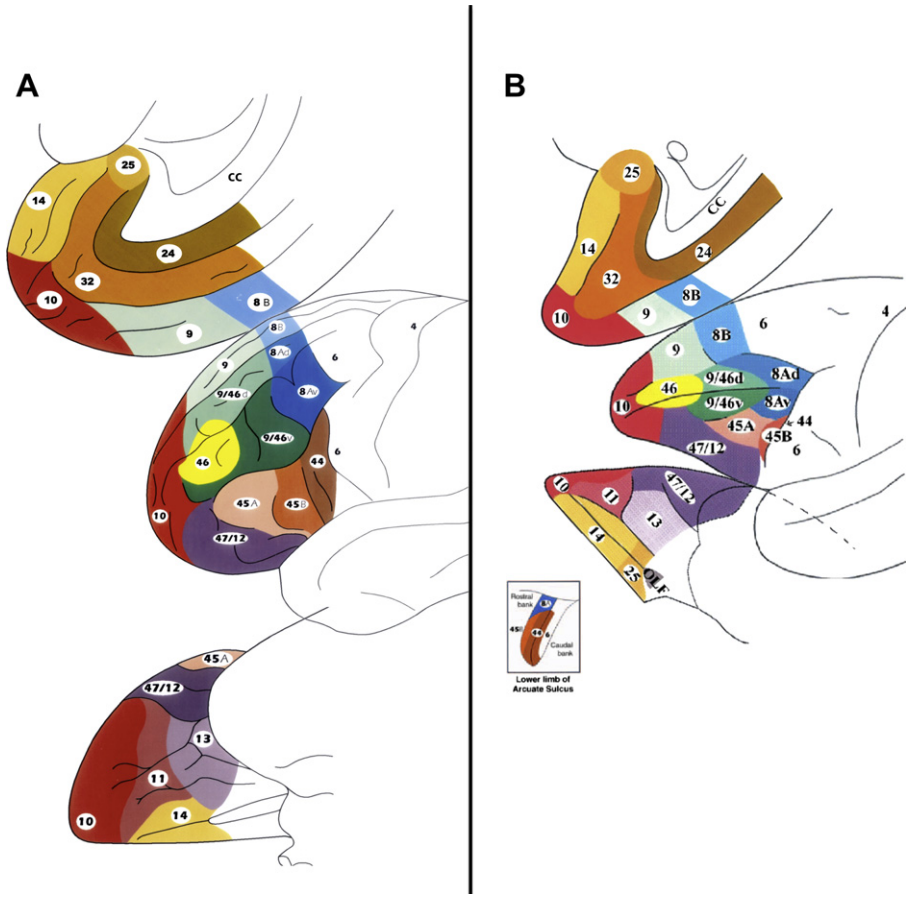

Fig. 3 – Cytoarchitectonic maps of the lateral, medial, and orbital surfaces of the frontal lobe of the human (A) and the macaque monkey (B) brains as parcellated by Petrides and Pandya (1994). In B, the inset diagram displays the region within the lower limb of the arcuate sulcus to show the cytoarchitectonic areas lying within its banks.

replaced by area 8 and in the rostralmost end by area 10 (see Fig. 2B). This definition of area 46 in the macaque monkey has dominated the anatomical and physiological literature in the description of cortical connections and interpretation of the location of physiological recordings and excisions to examine structure-to-function relations. However, Walker (1940) and many investigators (e.g., Barbas and Pandya, 1989; Preuss and Goldman-Rakic, 1991), subsequently, acknowledged that this large region labeled as area 46 is not homogeneous in its cellular structure. Which one of the different parts of Walker's area 46 in the monkey is homologous to Brodmann's area 46 in the human brain?

In the human brain, area 46 of Brodmann (equivalent to area FDΔ of Economo and Koskinas) is separated from area 8 on the middle frontal gyrus by area 9, but in Walker's monkey map it is not (compare Fig. 1A with Fig. 2B). Furthermore, Brodmann identifies area 9 also on the superior frontal gyrus above area 46 (see Fig. 1A). In our comparative architectonic investigation, we noted that area 9 on the superior frontal gyrus of the human brain has a poor layer IV (similar to the poor layer IV that one encounters in Walker's area 9 in the monkey), but area 9 on the middle frontal gyrus has a well developed layer IV and, in this respect, it is more similar to area 46 than to area 9 on the superior frontal gyrus. Furthermore, the very granular cortical area 9, which is interspersed between area 46 and area 8 on the middle frontal gyrus of the human brain, is comparable to the cortex in the posterior half of the principal sulcus of the monkey that Walker labeled as area 46. Although this portion of the cortex on the middle frontal gyrus that Brodmann labeled as area 9 shares with area 46 a well developed layer IV, it can be distinguished from area 46 by the presence of large, deeply stained pyramidal neurons in the lower part of layer III which are found in area 9 of the middle frontal gyrus but not in area 46. Area 46 has a layer III that contains small to medium pyramidal neurons giving it a rather uniform appearance.

In our comparative examination of the architecture of the human and the monkey frontal cortex, we noted that only the anterior part of Walker's area 46 in the monkey exhibits the characteristics of area 46 on the human middle frontal gyrus. We have therefore restricted the designation area 46 only to this cortical region of the monkey (area marked in yellow in Fig. 3). The cortex on the lips of the caudal portion of the sulcus principalis, which Walker also included in his area 46 (see Fig. 2B) but which has features characteristic of that part of area 9 that lies on the middle frontal gyrus of the human brain, we have labeled as area 9/46 in both species (area marked in dark green in Fig. 3). Although the connectivity of these subdivisions shares certain features, there are also striking differences, especially regarding connections with the

inferior parietal cortex. For instance, the caudal and ventral parts of the sulcus principalis (area 9/46v) have major somatomotor inputs that are not shared by area 9/46d or area 46 proper (see Petrides and Pandya, 1999, 2002a, 2009; reviewed in Yeterian et al., 2011, in this issue).

2. Architectonic correspondence issues in the ventrolateral frontal cortex of the macaque monkey and the human brain: the problem of areas 44, 45 and 47

Major discrepancies exist between the classical cytoarchitectonic maps of the human ventrolateral frontal cortex and those of the macaque monkey. In the map of the human brain by Brodmann (Fig. 1A), the ventral part of the precentral gyrus is occupied by areas 4 and 6. In front of premotor area 6, on the inferior frontal gyrus, three areas are identified: area 44 on the pars opercularis, area 45 on the pars triangularis, and part of area 47 on the pars orbitalis of the inferior frontal gyrus. The presence of the agranular motor (area 4) and premotor (area 6) cortical regions in the ventral part of the precentral gyrus of the monkey and the human cortex has not been the subject of much debate (compare Figs. 1A and 2A). By contrast, the identification of areas 44, 45 and 47 has been controversial. Brodmann (1905) did not identify these areas on the ventrolateral frontal cortex of the monkey (Fig. 2A) and Walker (1940) labeled a small strip of the cortex along the inferior branch of the arcuate sulcus as "area 45" (Fig. 2B) and the remainder of the inferior frontal region as "area 12" and more dorsally as part of area 46. However, Walker only tentatively suggested that the strip of cortex that he labeled as "area 45" in the monkey (Fig. 2B) may correspond to the cortical area 45 in the human brain as labeled by Brodmann (Fig. 1A) because he had not carried out a comparative examination of the monkey and the human ventrolateral frontal cortex (see Walker, 1940, p. 67). The issue of the definition of area 45 in the human and the macaque monkey brains was further complicated in the 1990s when some physiologists adopted the term "area 45" to refer to the ventral part of the frontal eye field in the macaque monkey. This is the part of the frontal eye field from which small amplitude saccades can be evoked with electrical microstimulation, in contrast to the more dorsal part of the frontal eye field, referred to as area 8, where large amplitude saccades are evoked (e.g., Schall et al., 1995). This usage emerged because, in Walker's map, area 45 is shown to start just below area 8A in the dorsal part of the inferior branch of the arcuate sulcus (Fig. 2B). However, area 45 as shown by Walker extends all the way to the ventralmost tip of the inferior branch of the arcuate sulcus (Fig. 2B) from where oculomotor responses have never been evoked. In addition, area 45 of the human brain has never been linked to oculomotor function, but rather to verbal and non-verbal retrieval from long-term memory (e.g., Petrides et al., 1995; Petrides, 1996). Thus, in our comparative examination of the architecture of the ventrolateral frontal region of the macaque and the human frontal cortex (Petrides and Pandya, 1994, 2002a), we had to address the following questions: (1) Is there an area 44 in the ventrolateral frontal cortex of the macaque monkey that lies immediately in front of agranular premotor area 6? (2) Is there an area in the macaque monkey frontal cortex that exhibits the characteristics of area 45 of the *human brain* and is this area in the monkey the same as "area 45" of Walker? Note that Walker's area 45 was not defined as a result of comparative architectonic examination. (3) Is there a cortical area in the ventrolateral frontal region of the monkey cortex that exhibits the characteristics of the part of Brodmann's area 47 that occupies the ventrolateral frontal region of the human brain? Note that Brodmann's area 47 in the human brain occupies the most ventral part of ventrolateral frontal cortex and extends to most of the caudal orbital frontal region and that Brodmann (1909) explicitly stated that it is a heterogeneous region that could be further subdivided.

The cortex occupying the pars opercularis of the human brain and labeled as area 44 by Brodmann (Fig. 1A) and area FCBm by Economo and Koskinas (Fig. 1B) is a dysgranular frontal region that exhibits a narrow and interrupted layer IV, and large pyramidal neurons in the lower part of layer III and in layer V. This dysgranular region emerges just in front of premotor area 6. Because the inferior branch of the arcuate sulcus is more-or-less vertically oriented and its architecture severely distorted in standard coronal sections, we examined several monkey brains in which the inferior branch of the arcuate sulcus was sectioned perpendicular to the direction of the sulcus, i.e., in a direction optimal for architectonic analysis. The results showed that, anterior to ventral area 6 and buried mostly in the most ventral part of the posterior bank and in the fundus of the inferior branch of the arcuate sulcus, there is a dysgranular cortical area that exhibits the characteristics of area 44 of the human brain (Fig. 3B inset; see Petrides and Pandya, 2002a, 2009; Petrides et al., 2005). Immediately rostral to this area, starting in the anterior bank of the inferior branch of the arcuate sulcus, there is another cortical area that exhibits the characteristics of area 45 of the human brain (Fig. 3B). Brodmann's area 45 (or area FDΓ according to the nomenclature of Economo and Koskinas) is a typical lateral prefrontal area exhibiting a very well developed layer IV (in sharp contrast to dysgranular area 44). In addition, there is a characteristic of area 45 that sets it apart from other lateral prefrontal areas: it is populated by clusters of unusually large and deeply stained pyramidal neurons in the deepest part of layer III (Amunts et al., 1999; Economo and Koskinas, 1925; Petrides and Pandya, 1994, 2002a). These were the characteristics that we observed in the macaque monkey cortex starting approximately in the anterior bank of the ventral part of the inferior arcuate sulcus and continuing on the ventrolateral frontal cortex for a considerable distance up to a small dimple that we labeled the infraprincipal dimple (Fig. 3B). Note that this area as defined by Petrides and Pandya (1999, 2002a) using the criteria of area 45 of the human brain is not coincidental with that labeled as area 45 by Walker (1940); although it includes part of Walker's area 45 (compare Fig. 3B with Fig. 2B).

Because the term area 45 has also been used in physiological studies in the monkey to refer to the most ventral part of the frontal eye field which lies on the dorsal part of the inferior branch of the arcuate sulcus close to area 8A (e.g., Schall et al., 1995), we carried out a study to examine whether electrical microstimulation along the part of the inferior arcuate sulcus defined as area 45 by the criteria of the human brain resulted in oculomotor responses (Petrides et al., 2005).

The results showed that oculomotor responses could only be obtained from the more dorsal part of the inferior branch of the arcuate sulcus, the part which does not exhibit the characteristics of human area 45. Thus, we concluded that both the large and the small saccade amplitude parts of the frontal eye field of the monkey lie at the interface of area 6 with area 8 and do not include area 45 if the latter is defined by the criteria used to identify area 45 in the human brain (Petrides et al., 2005). Furthermore, we were able to show that neuronal activity in macaque area 45 when defined by the criteria of the human brain is involved with active retrieval as is the case with human area 45 (see Cadoret and Petrides, 2007). This conclusion is consistent with everything known about areas 44 and 45 of the human brain, which have never been linked to oculomotor function and instead have been linked to controlled memory retrieval (see Petrides, 1996).

Finally, we addressed the question of the part of the macaque monkey ventrolateral frontal region that corresponds to the ventrolateral part of Brodmann's area 47 in the human brain. Here we should emphasize that the designation "area 47" was used by Brodmann (1909) to refer to a very large and architectonically heterogeneous zone that not only included the ventralmost part of the ventrolateral frontal region, but also extended on the caudal orbital surface as far as the medial orbital sulcus (see Fig. 1A). The designation "area 47" has not been used in any of the maps of the monkey brain, but Walker (1940) labeled a large part of the ventrolateral frontal region as "area 12" (see Fig. 2B). Medial to area 12 on the orbital frontal region, Walker labeled the cortex as "area 13", caudally, and "area 11", rostrally. Our comparative architectonic analysis of the ventrolateral and orbital region in the macaque monkey and the human brain established that Walker's area 12 corresponds to only a part of Brodmann area 47, namely the part that covers the ventralmost portion of the ventrolateral frontal region and extends as far as the lateral orbital sulcus. We therefore labeled this part of Brodmann's area 47 as "area 47/12" to acknowledge the architectonic correspondence between these cortical regions in the two primate brains (Fig. 3). The part of Brodmann's area 47 that extends further medially onto the caudal orbital region corresponds to area 13 of Walker in the monkey (Mackey and Petrides, 2009; Petrides and Pandya, 1994, 2002a).

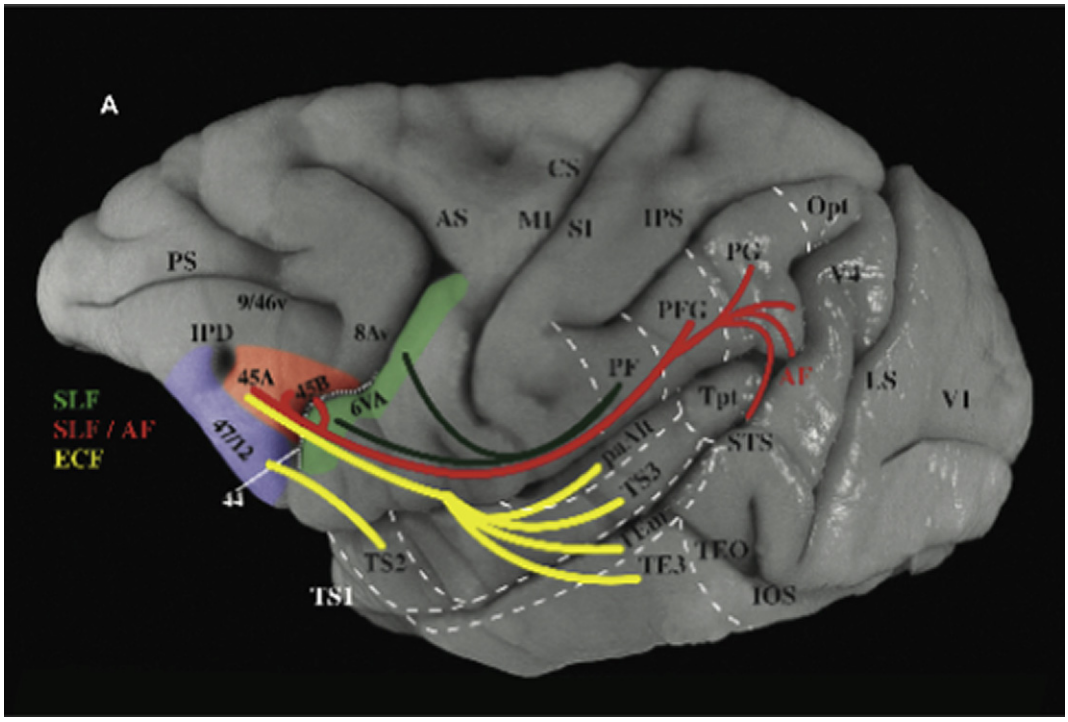

Fig. 4 – The dorsal (superior longitudinal fasciculus and arcuate fasciculus) and the ventral (extreme capsule fasciculus) pathways linking perisylvian parietal and temporal cortical regions with the homologues of Broca's region in the macaque monkey brain. The dorsal pathway (in red) is the superior longitudinal fasciculus (SLF) which originates from cortical areas of the inferior parietal lobule and terminates in areas 44, 45B, and 45A of Broca's region. Fibers originating from the caudal part of the superior temporal sulcus arch around the caudal end of the lateral fissure forming the arcuate fasciculus (AF) and blend with the fibers of the superior longitudinal fasciculus in the white matter of the inferior parietal lobule. The ventral premotor cortex (area 6), which controls the orofacial musculature, receives its strongest input from the most rostral part of the inferior parietal lobule (area PF) via a part of the superior longitudinal fasciculus (in green). The ventral pathway (in yellow) is the extreme capsule fasciculus (ECF) which originates from cortical areas of the intermediate and anterior superior temporal region, courses through the extreme capsule, and terminates primarily in area 45. Abbreviations: AF, arcuate fasciculus; AS, arcuate sulcus; CS, central sulcus; ECF, extreme capsule fasciculus; IOS, inferior occipital sulcus; IPD, infraprincipal dimple; IPS, intraparietal sulcus; LS, lunate sulcus; PS, sulcus principalis; SLF, superior longitudinal fasciculus; STS, superior temporal sulcus.

Areas 44 and 45 in the left hemisphere of the human brain are considered to constitute the anterior language region, often known as Broca's region (Amunts et al., 1999; Petrides and Pandya, 2002a). Besides the theoretical importance for language evolution of the demonstration of areas 44 and 45 in the ventrolateral frontal cortex of the macaque monkey, this research opened up the possibility of examining in detail the axonal pathways that bring input into the macaque areas that are homologs of Broca's region. We therefore re-examined the parietal and temporal inputs of these newly defined ventrolateral frontal cortical areas using the autoradiographic technique which permits the precise delineation of not only the course of the axons but also their precise termination (Petrides and Pandya, 2009). The results indicated two independent streams of connections that bring information from parietal and temporal cortex to the homologs of Broca's region. The rostralmost inferior parietal lobule area PF projects via the third branch of the superior longitudinal fasciculus to the ventral part of the premotor cortex. By contrast, most of the parietal input to areas 44 and 45 arises from areas PFG and PG, with a gradation such that area PFG projects strongly to area 44 and area PG projects more strongly to area 45. These parietal inputs are conveyed via the superior longitudinal fasciculus and there is a smaller input from the caudalmost temporal region via the arcuate fasciculus (Fig. 4). In addition to these parietal and posterior temporal inputs, the homologs of Broca's region receive input from the mid-lateral temporal region via the extreme capsule (Fig. 4). The extreme capsule fasciculus was first demonstrated by Petrides and Pandya (1988) but, in the earlier study, we had not described the ventrolateral frontal inputs as terminating in areas 44 or 45 since these areas had not been defined at the time. In our re-examination of these inputs in 2009, it was clear that most of the axons coursing through the extreme capsule from the temporal region terminated in area 45, with a minor contingent terminating in area 44. None of these connections terminated in premotor area 6 (Petrides and Pandya, 2009). The parietal inputs to Broca's region via the superior longitudinal fasciculus may correspond to the contingent arising from Geschwind's region as described by Catani et al. (2005) (Bizzi et al., 2012). The specificity of the connections of the different post-Rolandic cortical areas suggests that it would be better, when possible, to refer to specific cortical areas rather than general regions, such as posterior parietal or temporo-parietal junction when referring to cortico-cortical connectivity and function.

We have recently used functional connectivity analyses of resting state fMRI data, which detect coherent low-frequency fluctuations in the BOLD signal, in order to examine predictions about the connections of Broca's region in the human brain based on the macaque monkey data (Kelly et al., 2010). In

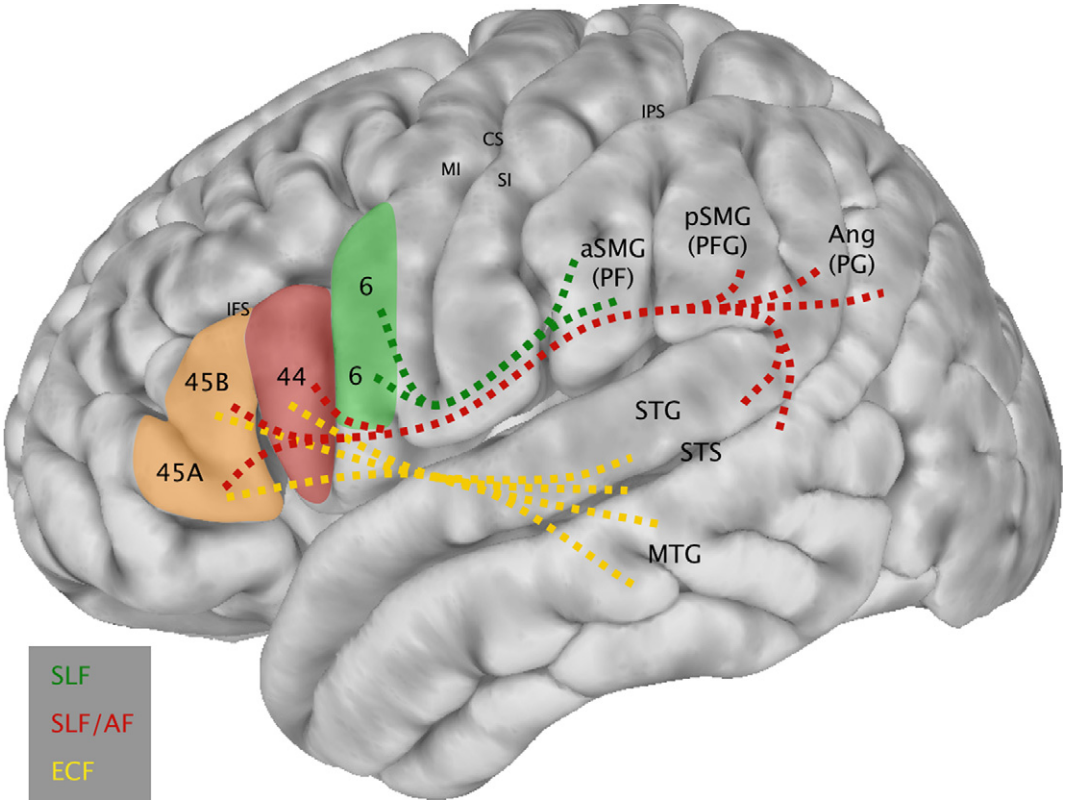

Fig. 5 – Schematic diagram integrating functional connectivity results between ventral area 6, area 44 and area 45 with perisylvian inferior parietal and temporal cortical regions (Kelly et al., 2010) with information concerning white matter tracts that join these regions as studied in the macaque monkey (Petrides and Pandya, 2009). Abbreviations: AF, arcuate fasciculus; Ang, angular gyrus; aSMG, anterior supramarginal gyrus; CS, central sulcus; ECF, extreme capsule fasciculus; IFS, inferior frontal sulcus; IPS, intraparietal sulcus; MTG, middle temporal gyrus; pSMG, posterior supramarginal gyrus; SLF, superior longitudinal fasciculus; STG, superior temporal gyrus; STS, superior temporal sulcus.

this study with normal human subjects, we used two methods to test hypotheses concerning differential connectivity of ventral area 6, area 44 and area 45 based on the anatomical tracing study (Petrides and Pandya, 2009) that established the connectivity of homologous regions in the macaque monkey: (1) manual selection of seed regions-of-interest within ventrolateral frontal cortex, on the basis of local sulcal and gyral anatomy, and (2) data-driven partitioning of ventrolateral frontal cortex into regions exhibiting distinct connectivity patterns, using a spectral clustering algorithm. We found that the findings from the monkey research predicted very well the functional connectivity (i.e., correlations) between parietal and temporal cortical areas and areas 6, 44, and 45 in the human brain. The results demonstrated functional connectivity of ventral premotor area 6, which is involved in the control of orofacial musculature, with somatomotor cortical areas and the rostral supramarginal gyrus (corresponding to area PF) (Fig. 5). By contrast, adjacent areas 44 and 45 (Broca's region) were connected with the caudal supramarginal gyrus (area PFG) and the angular gyrus (area PG). Area 45 had stronger connectivity with the angular gyrus (area PG) and the mid-lateral temporal cortex (Fig. 5). The findings suggest that the basic pattern of anatomical connectivity has been preserved between the non-linguistic macaque monkey brain and the human brain, raising interesting issues with regard to the evolution of language. In addition, they indicate rich, differential connectivity patterns between the three ventrolateral frontal areas controlling language production and the temporo-parietal perisylvian areas that are in contrast to the classical notion that focused on the posterior temporal to anterior language zone connection.

3. Conclusion

The studies reviewed above indicate that the basic organization of the frontal cortex cytoarchitecture in the human and macaque monkey brains, as well as the anatomical connectivity of the various architectonic areas that comprise it, is comparable. The macaque monkey cortex remains an excellent model to study in detail issues that arise in structural and functional investigations of the human brain. In addition, the experimental anatomical and physiological findings obtained in the macaque monkey with methods that are not possible in the human brain provide important hypotheses to be tested at the level of the human brain and, importantly, constrain the interpretation of findings in the human brain that may be artifacts due to the limitations of the methods used. With regard to the issue of the connectivity of the human cerebral cortex, the findings with resting state functional connectivity, which are consistent with some of the demonstrated structural connectivity of homologous areas in macaque monkey, support the claim that the method may reflect, at least partly, underlying structural connectivity (Kelly et al., 2010). Of course, it should be emphasized that resting state functional connectivity also reveals connections between regions of the cortex that lack direct anatomical connections (see Vincent et al., 2007; Di Martino et al., 2008). Thus, findings from the two methods available to examine the connections of the human brain, namely resting state functional connectivity and diffusion MRI, must be interpreted with caution and in the context of hypotheses derived from data obtained with experimental tracing methods in the monkey.

Acknowledgments

The research was supported by NSERC Grant RGPIN 7466.

REFERENCES

Amiez C, Kostopoulos P, Champod A-S, and Petrides M. Local morphology predicts functional organization of the dorsal premotor region in the human brain. *Journal of Neuroscience*, 26(10): 2724–2731, 2006.

Amunts K, Schleicher A, Burgel U, Mohlberg H, Uylings HBM, and Zilles K. Broca's region revisited: Cytoarchitecture and intersubject variability. *Journal of Comparative Neurology*, 412(2): 319–341, 1999.

Bailey P and Bonin G. *The Isocortex of Man*. Urbana: University of Illinois Press, 1951.

Barbas H and Pandya DN. Architecture and intrinsic connections of the prefrontal cortex in the rhesus monkey. *Journal of Comparative Neurology*, 286(3): 353–375, 1989.

Beck E. A cytoarchitectural investigation into the boundaries of cortical areas 13 and 14 in the human brain. *Journal of Anatomy*, 83(2): 147–157, 1949.

Behrens TE, Johansen Berg H, Jbabdi S, Rushworth MFS, and Woolricha MW. Probabilistic diffusion tractography with multiple fibre orientations: What can we gain? *NeuroImage*, 34(1): 144–155, 2007.

Berlucchi G. Frontal callosal disconnection syndromes. *Cortex*, 48(1): 35–44, 2012.

Bizzi A, Nava S, Ferrè F, Castelli G, Aquino D, Ciaraffa F, et al. Gliomas infiltrating the ventrolateral frontal region: clinical anatomo-functional language assessment with neuropsychology, diffusion MR tractography and functional MR imaging. *Cortex*, doi:10.1016/j.cortex.2011.11.015.

Braak H. The pigment architecture of the human frontal lobe. I. Precentral, subcentral, and frontal region. *Anatomy and Embryology*, 157(1): 35–68, 1979.

Brett M, Johnsrude IS, and Owen AM. The problem of functional localization in the human brain. *Nature Reviews Neuroscience*, 3(3): 243–249, 2002.

Brodmann K. Beitraege zur histologischen Lokalisation der Grosshirnrinde. III. Mitteilung. Die Rindenfelder der niederen Affen. *Journal für Psychologie und Neurologie*, 4: 177–226, 1905.

Brodmann K. Beitraege zur histologischen Lokalisation der Grosshirnrinde. VI. Mitteilung: Die Cortexgliederung des Menschen. *Journal für Psychologie und Neurologie*, 10: 231–246, 1908.

Brodmann K. *Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues*. Leipzig: Barth, 1909.

Brodmann K. Physiologie des Gehirns. In Bruns P (Ed)Neue Deutsche Chirurgie. Stuttgart: Enke, 1914: 85–426.

Cadoret G and Petrides M. Ventrolateral prefrontal neuronal activity related to active controlled memory retrieval in nonhuman primates. *Cerebral Cortex*, 17(1): i27–i40, 2007.

Campbell AW. *Histological Studies on the Localisation of Cerebral Function*. Cambridge: University Press, 1905.

Catani M and Stuss DT. At the forefront of clinical neuroscience. *Cortex*, 48(1): 1–6, 2012.

Catani M, Dell'Acqua F, Vergani F, Malik F, Hodge H, Roy P, et al. Short frontal lobe connections of the human brain. *Cortex*, doi:10.1016/j.cortex.2011.12.001.

Catani M, Jones DK, and ffytche DH. Perisylvian language networks of the human brain. *Annals of Neurology*, 57(1): 8–16, 2005.
Chiavaras MM, LeGoualher G, Evans A, and Petrides M. Three-dimensional probabilistic atlas of the human orbitofrontal sulci in standardized stereotaxic space. *NeuroImage*, 13(3): 479–496, 2001.
Collins DL, Neelin P, Peters TM, and Evans AC. Automatic 3D intersubject registration of MR volumetric data in standardized Talairach space. *Journal of Computer Assisted Tomography*, 18(2): 192–205, 1994.
Cowan WM, Gottlieb DI, Hendrickson AE, Price JL, and Woolsey TA. The autoradiographic demonstration of axonal connections in the central nervous system. *Brain Research*, 37(1): 21–51, 1972.
Di Martino A, Scheres A, Margulies DS, Kelly AM, Uddin LQ, Shehzad Z, et al. Functional connectivity of human striatum: A resting state FMRI study. *Cerebral Cortex*, 18(1): 2735–2747, 2008.
Economo C and Koskinas GN. *Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen*. Wien: Springer, 1925.
Frey S, Campbell JS, Pike GB, and Petrides M. Dissociating the human language pathways with high angular resolution diffusion fiber tractography. *Journal of Neuroscience*, 28(45): 11435–11444, 2008.
Fink RP and Heimer L. Two methods for selective silver impregnation of degenerating axons and their synaptic endings in the central nervous system. *Brain Research*, 4(4): 369–374, 1967.
Johansen-Berg H and Behrens T. Just pretty pictures? What diffusion tractography can add in clinical neuroscience. *Current Opinion in Neurology*, 19(4): 379–385, 2006.
Jones DK. Studying connections in the living human brain with diffusion MRI. *Cortex*, 44(8): 936–952, 2008.
Keizer R, Kuypers HG, Huisman AM, and Daan O. Diamidino yellow dihydrochloride (DY-2 HCl): A new fluorescent retrograde neuronal tracer which migrates only very slowly outside of the cell. *Experimental Brain Research*, 51(2): 179–191, 1983.
Kelly C, Uddin LQ, Shehzad Z, Margulies DS, Xavier Castellanos F, Milham MP, et al. Broca's region: Linking human brain functional connectivity data and non-human primate tracing anatomy studies. *European Journal of Neuroscience*, 32(3): 383–398, 2010.
Kuypers HG, Bentivoglio M, Catsman-Berrevoets CE, and Bharos AT. Double retrograde neuronal labelling through divergent axon collaterals, using two fluorescent tracers with the same excitation wavelengths which label different features of the cell. *Experimental Brain Research*, 40(4): 383–392, 1980.
Liu H, Stufflebeam SM, Sepulcre J, Hedden T, and Buckner RL. Evidence from intrinsic activity that asymmetry of the human brain is controlled by multiple factors. *Proceedings of the National Academy of Sciences USA*, 106(48): 20499–20503, 2009.
Mackey S and Petrides M. Architectonic mapping of the medial region of the human orbitofrontal cortex by density profiles. *Neuroscience*, 159(3): 1089–1107, 2009.
Makris N, Kennedy DN, McInerney S, Sorensen AG, Wang R, Caviness Jr VS, et al. Segmentation of subcomponents within the superior longitudinal fascicle in humans: A quantitative, in vivo, DT-MRI study. *Cerebral Cortex*, 15(6): 854–869, 2005.
Makris N, Papadimitriou GM, Sorg S, Kennedy DN, Caviness VS, and Pandya DN. The occipitofrontal fascicle in humans: A quantitative, in vivo, DT-MRI study. *NeuroImage*, 37(4): 1100–1111, 2007.
Margulies DS, Vincent JL, Kelly C, Lohmann G, Uddin LQ, Biswal BB, et al. Precuneus shares intrinsic functional architecture in humans and monkeys. *Proceedings of the National Academy of Sciences USA*, 106(47): 20069–20074, 2009.
Mesulam MM. Tetramethyl benzidine for horseradish peroxidase neurohistochemistry. A non-carcinogenic blue reaction-product with superior sensitivity for visualizing neural afferents and efferents. *Journal of Histochemistry and Cytochemistry*, 26(2): 106–117, 1978.
Mori S and Zhang J. Principles of diffusion tensor imaging and its applications to basic neuroscience research. *Neuron*, 51(5): 527–539, 2006.
Nauta WJH. Silver impregnation of degenerating axons. In Windle WF (Ed), *New Research Techniques of Neuroanatomy*. Springfield, Illinois: Charles C. Thomas, 1957: 17–26.
Passingham RE. Anatomical differences between the neocortex of man and other primates. *Brain Behavior and Evolution*, 7(5): 337–359, 1973.
Petrides M. Specialized systems for the processing of mnemonic information within the primate frontal cortex. *Philosophical Transactions of the Royal Society, London B*, 351(1346): 1455–1462, 1996.
Petrides M and Pandya DN. Association fiber pathways to the frontal cortex from the superior temporal region in the rhesus monkey. *Journal of Comparative Neurology*, 273(1): 52–66, 1988.
Petrides M and Pandya DN. Comparative architectonic analysis of the human and the macaque frontal cortex. In Boller F and Grafman J (Eds)Handbook of Neuropsychology. Amsterdam: Elsevier, 1994: 17–58.
Petrides M and Pandya DN. Dorsolateral prefrontal cortex: Comparative cytoarchitectonic analysis in the human and the macaque brain and corticocortical connection patterns. *European Journal of Neuroscience*, 11(3): 1011–1036, 1999.
Petrides M and Pandya DN. Comparative architectonic analysis of the human and the macaque ventrolateral prefrontal cortex and corticocortical connection patterns in the monkey. *European Journal of Neuroscience*, 16(2): 291–310, 2002.
Petrides M and Pandya DN. Association pathways of the prefrontal cortex and functional observations. In Stuss DT and Knight RT (Eds), *Principles of Frontal Lobe Function*. New York: Oxford University Press, 2002: 31–50.
Petrides M and Pandya DN. Distinct parietal and temporal pathways to the homologues of Broca's area in the monkey. *PLoS Biology*, 7(8): e1000170, 2009.
Petrides M, Cadoret G, and Mackey S. Orofacial somatomotor responses in the macaque monkey homologue of Broca's area. *Nature*, 435(7046): 1235–1238, 2005.
Petrides M, Alivisatos B, and Evans AC. Functional activation of the human ventrolateral frontal cortex during mnemonic retrieval of verbal information. *Proceedings of the National Academy of Sciences USA*, 92(13): 5803–5807, 1995.
Preuss TM and Goldman-Rakic PS. Myelo- and cytoarchitecture of the granular frontal cortex and surrounding regions in the strepsirhine primate galago and the anthropoid primate macaca. *Journal of Comparative Neurology*, 310: 429–474, 1991.
Rajkowska G and Goldman-Rakic PS. Cytoarchitectonic definition of prefrontal areas in the normal human cortex. *Cerebral Cortex*, 5(4): 307–322, 1995.
Roebroeck A, Galuske R, Formisano E, Chiry O, Bratzke H, Ronen I, et al. High-resolution diffusion tensor imaging and tractography of the human optic chiasm at 9.4T. *NeuroImage*, 39(1): 157–168, 2008.
Saur D, Kreher BW, Schnell S, Kümmerer D, Kellmeyer P, Vry M-S, et al. Ventral and dorsal pathways for language. *Proceedings of the National Academy of Sciences USA*, 105(46): 18035–18040, 2008.
Sanides F. *Die Architektonik des Menschlichen Stirnhirns*. Berlin: Springer-Verlag, 1962.
Sarkissov SA, Filimonoff IN, Kononowa EP, Preobraschenskaja IS, and Kukuew LA. *Atlas of the Cytoarchitectonics of the Human Cerebral Cortex*. Moscow: Medgiz, 1955.
Schall JD, Morel A, King DJ, and Bullier J. Topography of visual cortex connections with frontal eye field in macaque: Convergence and segregation of processing streams. *Journal of Neuroscience*, 15: 4464–4487, 1995.

Schoenemann PT, Sheehan MJ, and Glotzer LD. Prefrontal white matter volume is disproportionately larger in humans than in other primates. *Nature Neuroscience*, 8(2): 242–252, 2005.

Semendeferi K, Lu A, Schenker N, and Damasio H. Humans and great apes share a large frontal cortex. *Nature Neuroscience*, 5(3): 272–276, 2002.

Semendeferi K, Armstrong E, Schleicher A, Zilles K, and Van Hoesen GW. Limbic frontal cortex in hominoids: A comparative study of area 13. *American Journal of Physical Anthropology*, 106(2): 129–155, 1998.

Semendeferi K, Armstrong E, Schleicher A, Zilles K, and Van Hoesen GW. Prefrontal cortex in humans and apes: A comparative study of area 10. *American Journal of Physical Anthropology*, 114(3): 224–241, 2001.

Smaers JB, Steele J, Case CR, Cowper A, Amunts K, and Zilles K. Primate prefrontal cortex evolution: Human brains are the extreme of a lateralized ape trend. *Brain, Behavior and Evolution*, 77(2): 67–78, 2011.

Talairach J and Tournoux P. *Co-planar Stereotaxic Atlas of the Human Brain*. New York: Thieme, 1988.

Thiebaut de Schotten M, Dell'Acqua F, Valabregue R, and Catani M. Monkey to human comparative anatomy of the frontal lobe association tracts. *Cortex*, 48(1): 81–95, 2012.

Tomaiuolo F, MacDonald JD, Caramanos Z, Posner G, Chiavaras M, Evans AC, et al. Morphology, morphometry and probability mapping of the pars opercularis of the inferior frontal gyrus: An in vivo MRI analysis. *European Journal of Neuroscience*, 11(9): 3033–3046, 1999.

van den Heuvel MP, Mandl RC, Kahn RS, and Hulshoff Pol HE. Functionally linked resting-state networks reflect the underlying structural connectivity architecture of the human brain. *Human Brain Mapping*, 30(10): 3127–3141, 2009.

Vincent JL, Patel GH, Fox MD, Snyder AZ, Baker JT, Van Essen DC, et al. Intrinsic functionally architecture in the anaesthetized monkey brain. *Nature*, 447(7140): 83–86, 2007.

Vogt O. Die myeloarchitektonische Felderung des menschlichen Stirnhirns. *Journal für Psychologie und Neurologie*, 15: 221–232, 1910.

Vogt C and Vogt O. Allgemeinere Ergebnisse unserer Hirnforschung. *Journal für Psychologie und Neurologie*, 25: 279–462, 1919.

Walker AE. A cytoarchitectural study of the prefrontal area of the macaque monkey. *Journal of Comparative Neurology*, 73(1): 59–86, 1940.

Yeterian EH, Pandya DN, Tomaiuolo F, and Petrides M. The cortical connectivity of the prefrontal cortex in the monkey brain. *Cortex*, 48(1): 57–80, 2012.