PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

# Comparison of Prefrontal Architecture and Connections [and Discussion]

D. N. Pandya, E. H. Yeterian, S. Fleminger and S. B. Dunnett

*Phil. Trans. R. Soc. Lond. B* 1996 **351**, 1423-1432
doi: 10.1098/rstb.1996.0127

# Comparison of prefrontal architecture and connections

D. N. PANDYA[1] AND E. H. YETERIAN[2]

[1] *Department of Anatomy and Neurobiology, Boston University School of Medicine, 80 East Concord Street, Boston, MA 02118, U.S.A.*
[2] *Department of Psychology, Colby College, 5557 Mayflower Hill, Waterville, ME 04901–8855, U.S.A.*

## SUMMARY

The advent of new technology has led to a proliferation of studies examining the functional roles of discrete prefrontal cortical areas. This has created a need for more precise information regarding the morphological characteristics of this region. Existing architectonic maps of human and monkey brains are not compatible with regard to areal delineations and topography, creating significant difficulty in interpreting comparative data. Therefore, we have re-examined the comparative morphological organization of the prefrontal cortex in humans and rhesus monkeys. Our analysis indicates that the architectonic areas in both species correspond in terms of morphological features as well as topographical locations. We have developed a common organizational schema for these areas, thereby allowing for a resolution of previous discrepancies. Moreover, in monkeys a connectional analysis has revealed that each of the newly designated areas is characterized by a unique pattern of cortical relationships. The present organizational schema provides a framework for interrelating findings such as those obtained from human brain imaging studies with those from behavioural investigations of non-human primates.

## 1. INTRODUCTION

The various areas of the prefrontal cortex (PFC) seem to contribute to specific and differential functions. In the human, on the basis of clinical syndromes as well as brain imaging studies, it has been suggested that whereas the ventromedial PFC is involved in decision-making processes, the lateral portion has a role in working memory, planning and sequencing of behaviour, language, and attention. Likewise, in non-human primates, experimental studies have shown that the ventrolateral PFC has a role in response inhibition, whereas the dorsolateral PFC is implicated in spatial processes, working memory and sequencing of behaviour. The caudal PFC is reported to be involved in attentional mechanisms (e.g. Goldberg & Bruce 1985). Some of these functions are limited to one or two specific architectonic areas (e.g. Fuster 1989; Damasio & Anderson 1993; Wilson *et al.* 1993).

The areal designations in architectonic maps of PFC in monkeys and humans do not coincide in certain cases. Thus, it becomes difficult to relate results obtained from animal experimentation to findings in humans. To address this problem, Petrides & Pandya (1994) reanalysed and compared the architecture of PFC in human and monkey brains. Their results show that there is overall correspondence among all PFC areas in these brains. To facilitate such comparison, existing numbering schemas have to be modified, albeit maintaining common nomenclature in the two species.

The functional role of a given cortical area *per se* in either human or monkey brains can be revealed by using imaging techniques or by experimental approaches. However, to understand more fully the contributions of a given cortical region to specific processes, it is important to know how that region is connected with other cerebral cortical areas. Substantial connectional data have been gathered by several investigators during the past three decades in non-human primates. Evidence of architectonic areal correspondence as described below allows one to extrapolate connectional relationships from monkeys to humans. We will describe connectional information from experiments in monkeys specifically designed to reveal afferent connectivity of prefrontal regions, and will briefly discuss functional implications.

## 2. ARCHITECTONICS

Several investigators have developed architectonic maps of PFC in humans and monkeys (Brodmann 1905, 1909; Vogt & Vogt 1919; Economo & Koskinas 1925; Walker 1940; Bonin & Bailey 1947; Sarkissov *et al.* 1955; Barbas & Pandya 1989; Preuss & Goldman-Rakic 1991). An examination of Brodmann's (1905, 1909) maps (figures 1*a*, *b*) reveals correspondence in nomenclature and location only for certain areas, namely 24, 25 and 32. Walker (1940; figure 1*c*) reinvestigated the architectonic organization of PFC in macaque monkeys, with the intent of resolving some of the differences in nomenclature and location of areas with regard to Brodmann's human map. For example, consistent with Brodmann's map of the human brain, Walker localized area 10 in the monkey to the medial and lateral aspects of the frontal pole. However, the

*Phil. Trans. R. Soc. Lond.* B (1996) **351**, 1423–1432
*Printed in Great Britain*

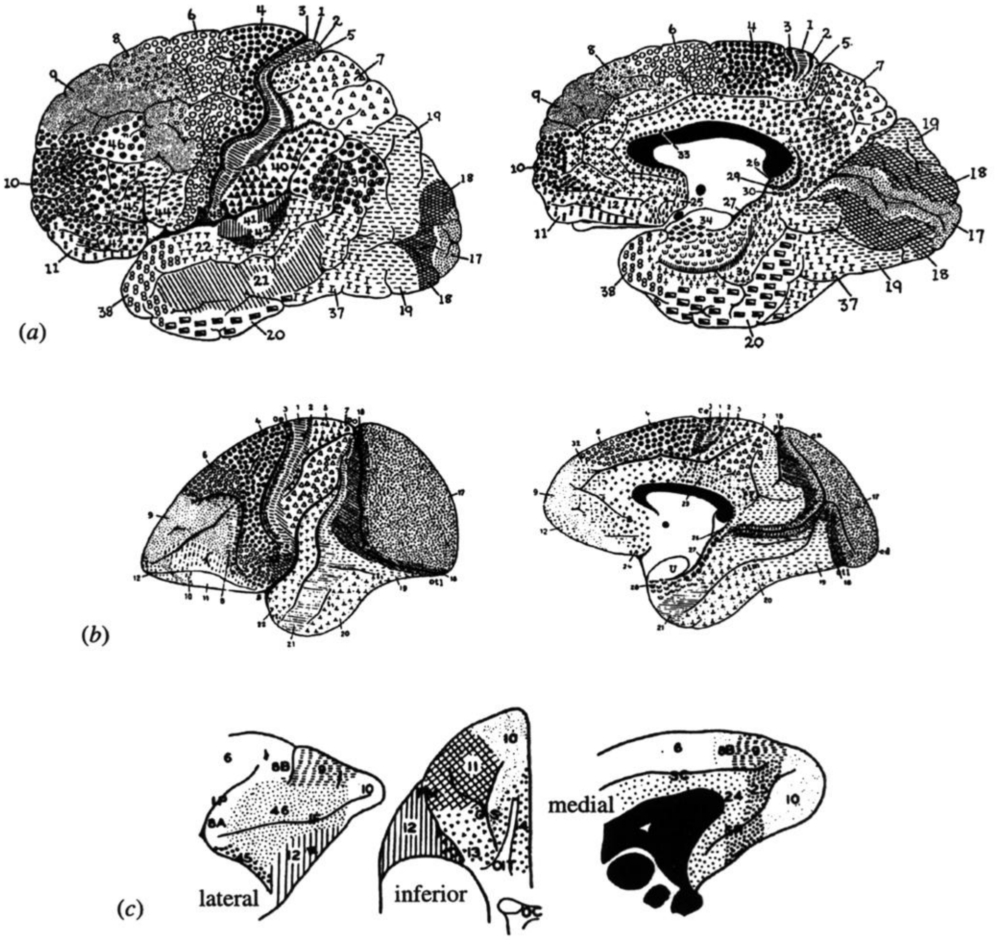

Figure 1. (*a*) Cytoarchitectonic map of the human cerebral cortex by Brodmann (1909); (*b*) cytoarchitectonic maps of the cerebral cortex in monkeys by Brodmann (1905); (*c*) cytoarchitectonic maps of the prefrontal cortex in monkeys by Walker (1940).

locations of other areas in Walker's map differ significantly from those of Brodmann. For example, Walker designated area 12 in the ventrolateral prefrontal region. In contrast, Brodmann termed a corresponding region in the human brain as area 47. Moreover, the relative size and extent of Walker's areas 9, 8 and 46 were different compared to areas of the same names designated by Brodmann in humans. The locations of areas 14, 13 and 11 were also inconsistent in Brodmann's human and Walker's monkey maps. Our maps, based on a reanalysis of architectonic features of PFC, attempt to resolve these differences (figure 2). We will provide only a brief summary of comparative architectonic descriptions below. A detailed presentation has been given elsewhere (Petrides & Pandya 1994).

### (*a*) *Area 44*

In the human brain, this area is located in the pars opercularis, and constitutes the major portion of Broca's area. Architectonically, area 44 appears dysgranular, with large pyramidal neurons in deep layer III. Although well documented in humans, this area has not been delineated previously in monkeys (figure 1). According to our findings, an area with architectonic features corresponding to area 44 in the human brain is found in the caudal bank of the lower limb of the arcuate sulcus in monkeys (figure 2*b*). We have designated this cortical subregion in the monkey as area 44.

### (*b*) *Area 8*

In both humans and monkeys, area 8 lies on the dorsolateral PFC, caudal to area 9 and rostral to area 6. Walker (1940) specified two subdivisions of this area, 8A in the concavity of the arcuate sulcus, and 8B located dorsally and extending toward midline (figure 1*c*). Although historically in the human brain this area has been delineated as a single entity, our findings indicate that it comprises two major subdivisions as in the monkey, designated 8A and 8B, based on architectonic features. Moreover, in both species, area 8A can be divided into dorsal (8Ad) and ventral (8Av) sectors (figure 2).

### (*c*) *Area 45*

In the human brain, this area is located in the pars triangularis, in the inferior frontal gyrus. Walker (1940) placed area 45 in the monkey mainly within the rostral bank of the lower limb of the arcuate sulcus (figure 1*c*). According to our findings, area 45 is

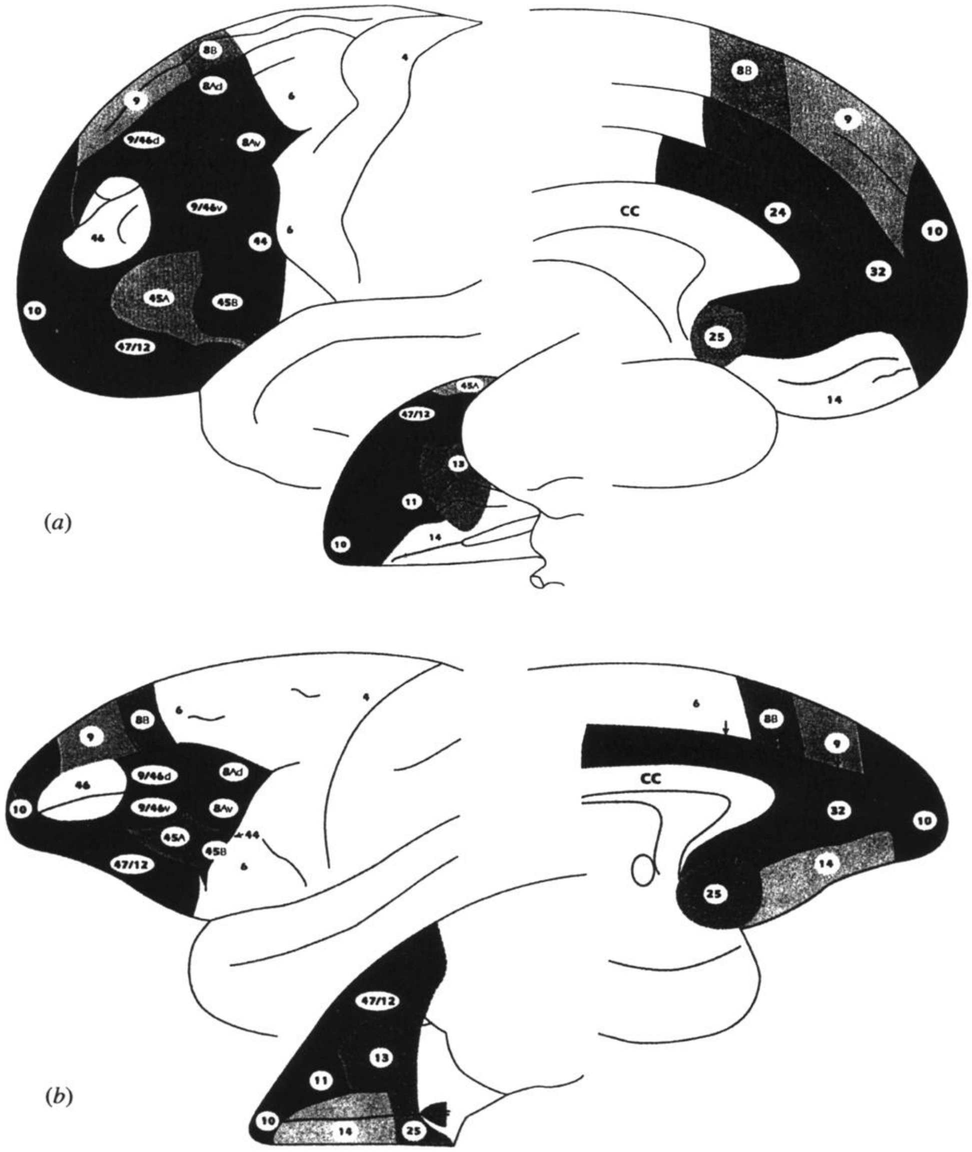

Figure 2. Cytoarchitectonic maps of the lateral, medial, and ventral surfaces of the cerebral cortex of the human (*a*) and monkey (*b*) brain by Petrides & Pandya (1994).

located not only within the sulcus, but also extends further rostrally on to the inferior prefrontal convexity. Moreover, on the basis of architectonic differences, we have divided this area into two sectors, 45A rostrally and 45B caudally, as in the human brain (figure 2).

### (*d*) *Areas 9 and 46*

In both humans and monkeys, these areas occupy the mid-dorsolateral sector of the PFC. In the monkey brain, they appear to have a simple topographic relationship to one another, with area 9 dorsal to area 46 (figure 1*c*). In contrast, in the human brain, area 9 has been shown to encircle area 46, except for the rostral portion of the latter area (figure 1*a*). In the monkey, area 46 has been localized in and around the principal sulcus, and has been reported to have further subdivisions (Barbas & Pandya 1989; Preuss & Goldman-Rakic 1991). According to our analysis, area 9 in both the human and the monkey brain is located dorsal to area 46, and extends medially to the cingulate region. In the human brain, the part of area 9 caudal and ventral to area 46 has architectonic characteristics similar to caudal area 46 of the monkey. Therefore, this region previously delineated as ventral area 9 in the human brain and as caudal area 46 in the monkey brain has been designated as area 9/46 in both species (figure 2). Furthermore, we have subdivided area 9/46 into dorsal and ventral divisions, areas 9/46d and 9/46v, respectively.

### (*e*) *Areas 47 and 12*

Brodmann (1909) described area 47 in the human brain as a region located ventral to area 45 and caudal to area 10, extending on to the lateral orbital surface (figure 1*a*). In the monkey, Walker (1940) outlined a topographically similar region, but designated it as area 12 (figure 1*c*). On the basis of their topographic as well as architectonic similarity, we have labelled these regions as area 47/12 in both species (figure 2).

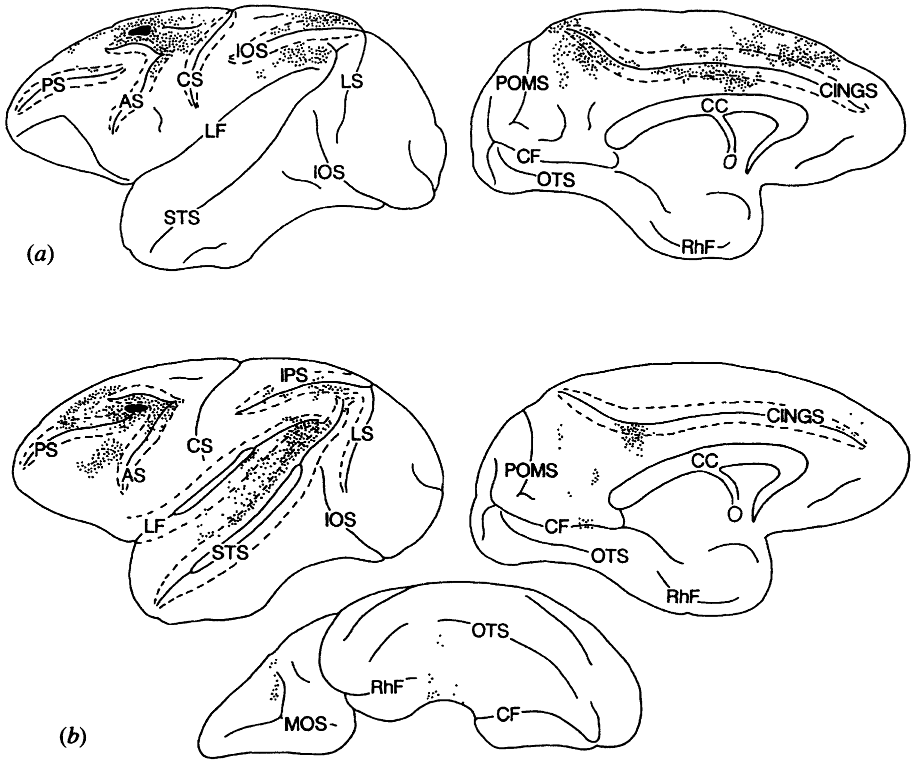

Figure 3. Diagrammatic representations of the injection sites (shown in black) in (*a*) case 1 and (*b*) case 2, and the distribution of retrogradely labelled cells (shown as dots) on the lateral, medial, and ventral surfaces of the cerebral hemispheres. (Abbreviations in this and subsequent figures: AS, arcuate sulcus; CC, corpus callosum; CF, calcarine fissure; CING S, cingulate sulcus; CS, central sulcus; IOS, inferior occipital sulcus; IPS, intraparietal sulcus; LF, lateral fissure; LS, lunate sulcus; MOS, medial orbital sulcus; OTS, occipitotemporal sulcus; POMS, medial parieto-occipital sulcus; PS, principal sulcus; RhF, rhinal fissure; STS, superior temporal sulcus.)

### (*f*) *Area 13*

Although Walker (1940) identified this area in the monkey as occupying the caudal part of the orbitofrontal cortex, in the human brain it has been subsumed within area 47 (figures 1*a*,*c*). According to our observations, this caudal orbital region has common architectonic features in both species. Therefore, on the basis of similar topography as well as morphology, we have labelled this region area 13 in the human brain (figure 2).

### (*g*) *Area 11*

In the monkey, area 11 occupies a location between areas 13 and 10 on the orbital surface (figure 1*c*). In the human, in contrast, the region designated as area 11 has been localized within the gyrus rectus on the ventromedial surface of the hemisphere by Brodmann (1909; figure 1*a*). We have identified a region in the human brain with similar architectonic characteristics as area 11 in the monkey, located between areas 10 and 13 on the orbital surface, and have designated it as area 11 (figure 2).

### (*h*) *Area 14*

This area in the monkey has been shown to occupy the gyrus rectus, and to be bordered by area 10 rostrally and area 25 caudally (figure 1*c*). In the human as mentioned above, the cortex in the area of the gyrus rectus has been delineated as areas 11 and 12. On the basis of topographic and architectonic similarities, we have designated this cortical region as area 14 in both species (figure 2).

## 3. CORTICOCORTICAL CONNECTIONS

One approach that can be used to support the existence of discrete architectonic areas is to establish specific patterns of cortical connectivity for those areas. As a number of investigators have outlined the connections of PFC on the basis of earlier maps, we will restrict our discussion to differential inputs to some of the newly defined prefrontal areas, as revealed by the fluorescent retrograde tracing method.

### (*a*) *Dorsal prefrontal areas*

In case 1, a fluorescent tracer (diamidino yellow, DY) was placed in dorsal area 6, rostral to the superior precentral dimple (figure 3). The retrograde labelling revealed a unique overall pattern of cortical inputs, both locally within the frontal lobe as well as distally from the post-Rolandic cortex. Thus, this area receives projections from areas 8B and 9 rostrally, and dorsal areas 6 and 4 caudally. Other inputs arise from the supplementary motor area (MII), the cortex in the depths of the cingulate sulcus corresponding to cingulate motor regions (e.g. He *et al.* 1995; Morecraft & Van Hoesen 1993) and area 24. This area receives post-Rolandic projections from the medial parietal

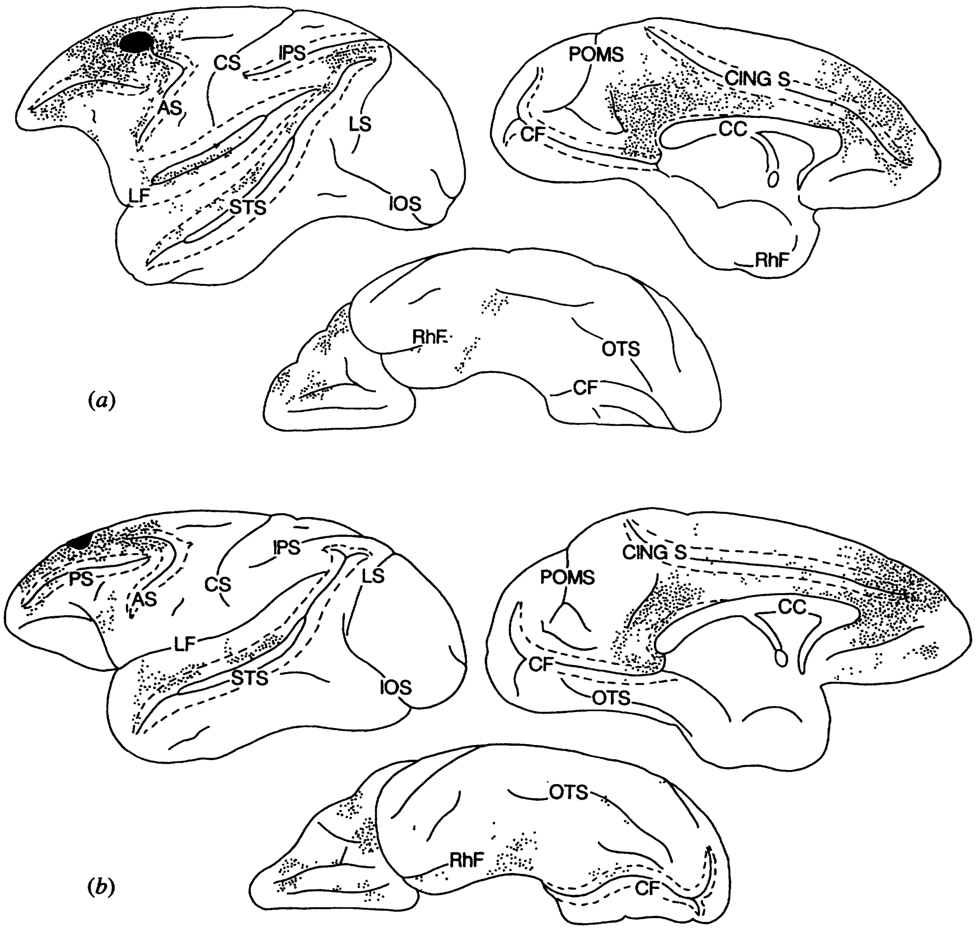

Figure 4. Diagrammatic representations of the injection sites in (*a*) case 3 and (*b*) case 4, and the distribution of retrogradely labelled cells.

region, including areas 31 and the supplementary sensory area (Murray & Coulter 1981). Another source of input is the caudal superior parietal lobule, and area 7A of the inferior parietal lobule (IPL).

In case 2, a retrograde tracer (Fast Blue, FB) was injected in area 8Ad in the dorsal concavity of the arcuate sulcus (figure 3). Local connections to this region are derived from areas 8B, 9, 9/46 and 45. Distant projections arise from area 31 on the medial surface and the caudal part of the lower bank of the intraparietal sulcus (IPS). Significant input to area 8Ad seems to come from the caudal superior temporal gyrus (STG), and from the caudal superior temporal sulcus (STS), including the multimodal area of the STS (MM-STS) and area MST.

An injection (FB) in area 8B revealed local connections from areas 8Ad, 9/46d, 9, and 6 (case 3, figure 4). This region also receives projections from areas 45, 47/12 and 46v, as well as area 11 on the orbital surface. From the medial surface, inputs are derived from areas 8B and 9, as well as from rostral area 24. Distant projections to this prefrontal region arise from caudal area 23, area 31 and the rostral part of medial area 19. Area 8B also receives input from the caudal IPL, rostral insular cortex, MM-STS and area TH of the parahippocampal gyrus.

An injection (DY) in lateral area 9 demonstrated local connections from rostral area 9, area 8B, dorsal area 6 and area 8Ad (case 4, figure 4). Within the frontal lobe, areas 47/12, 11, 14, 13 and orbital area Pro (proisocortex) also project to lateral area 9. Substantial input is derived from the adjacent medial surface, including areas 8B, 9, 32 and rostral area 24. Distant projections originate from caudal area 23, retrosplenial cortex, rostral MM-STS and rostral STG. Finally, lateral area 9 receives input from area TH.

In case 5, an injection (FB) was placed in dorsal area 9/46 (figure 7). The basic pattern of afferent projections to this region was similar to that of the preceding case, with some minor variations. Thus, local projections originate rostrally from area 46, and caudally from areas 8B, 8Ad and 6. Other frontal afferents arise from the orbital surface, mainly from area 11. On the medial surface, areas 9, 32 and 24 send projections to dorsal area 9/46. Distant inputs to this region arise from area 23, retrosplenial cortex, the ventral part of the medial parietal region and medial area 19. Some projections also are derived from rostral MM-STS, rostral STG, and area TH.

### (*b*) *Ventral prefrontal areas*

In case 6, an injection (DY) was placed in area 44 of the caudal bank of the inferior limb of the arcuate sulcus (figure 5). Local projections to this region arise

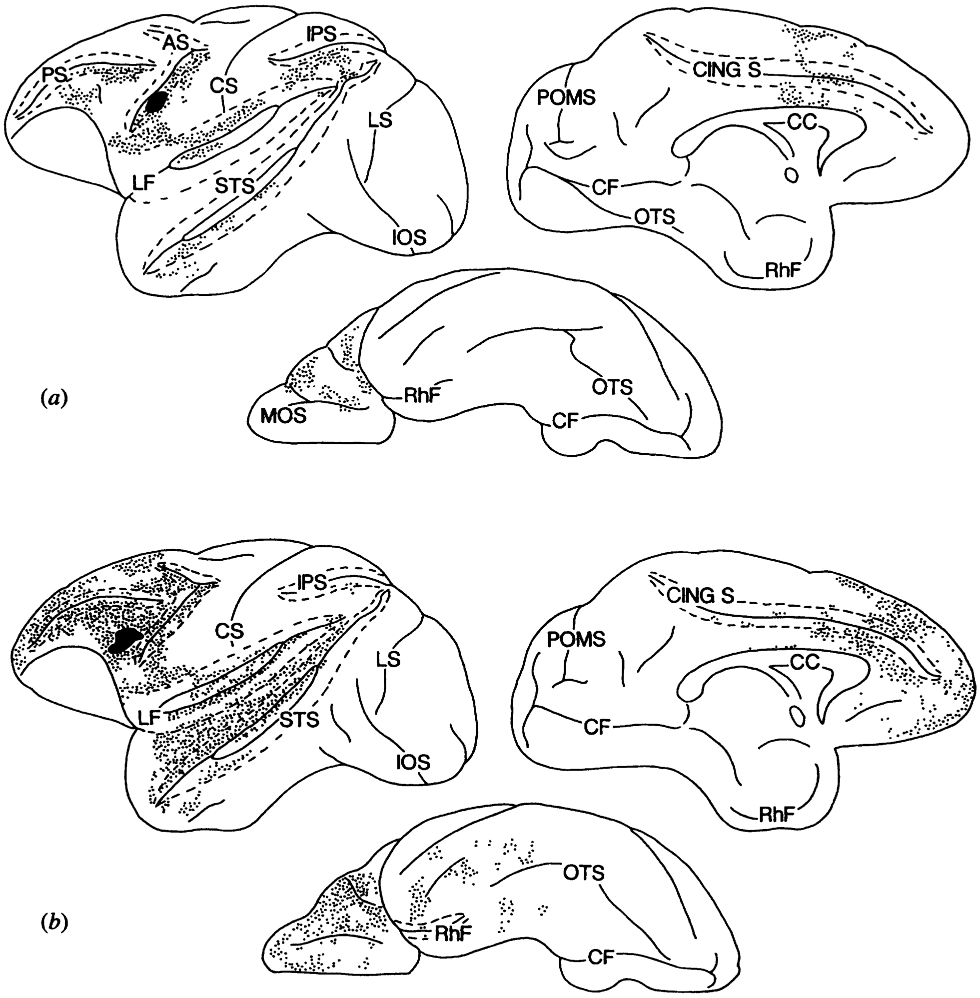

Figure 5. Diagrammatic representations of the injection sites in (*a*) case 6 and (*b*) case 7, and the distribution of retrogradely labelled cells.

from areas 9/46v, 47/12, 13, orbital area Pro and ventral area 6. Area 44 also receives input from the dorsal part of area MII, the cingulate motor region and caudal area 24. Distant projections are derived from the dorsal Sylvian opercular cortex including areas proM and SII, and from the rostral insula. Substantial connections also arise from the rostral and middle IPL. Some projections are derived from the rostral part of the lower bank of the STS.

In case 7, an injection (FB) was placed in area 45 (figure 5). This area receives projections from virtually all divisions of the prefrontal cortex, with the exception of most of area 9/46d. Unlike the preceding case, a significant amount of input is derived from the entire STG, and the cortex of the circular sulcus. Area proM and the precentral portions of areas 2 and 1 also seem to give rise to projections to this region. A notable amount of input is derived from the caudal insular cortex, the entire extent of MM-STS and area MST. Other connections originate from the rostral inferotemporal region, and from the rostral parahippocampal gyrus, mainly area TL (Rosene & Pandya 1983).

An injection (DY) in area 47/12 (case 8, figure 6) revealed local projections arising from areas 45 and 9/46v caudally, and from area 10 rostrally. Area 47/12 also receives input from dorsal area 46 and from area 9. Distinct foci within areas 14, 10, 11 and 13 on the orbital surface, and areas 14, 32 and 9 on the medial surface, send projections to this area. Distant connections arise from the rostral temporal lobe, including rostral area TL, the inferotemporal region, rostral MM-STS, and rostral STG.

An injection (FB) was placed in area 8Av in the lower bank of the arcuate sulcus (case 9, figure 6). Local afferent projections are relatively sparse and are derived from areas 8Ad and 8B dorsally, and 45, 47/12 and 46 rostrally. Distant projections originate from the lower bank of IPS, the lower bank and depths of STS and caudal MM-STS. Other connections arise from the caudal inferotemporal area and from lateral area V4.

Finally, an injection (DY) was placed in area 9/46v (case 10, figure 7). Local projections are derived from rostroventral area 46, and areas 47/12, 11 and 13. Distant connections arise from ventral area 6, area proM, opercular area SII, rostral IPL and rostral insula.

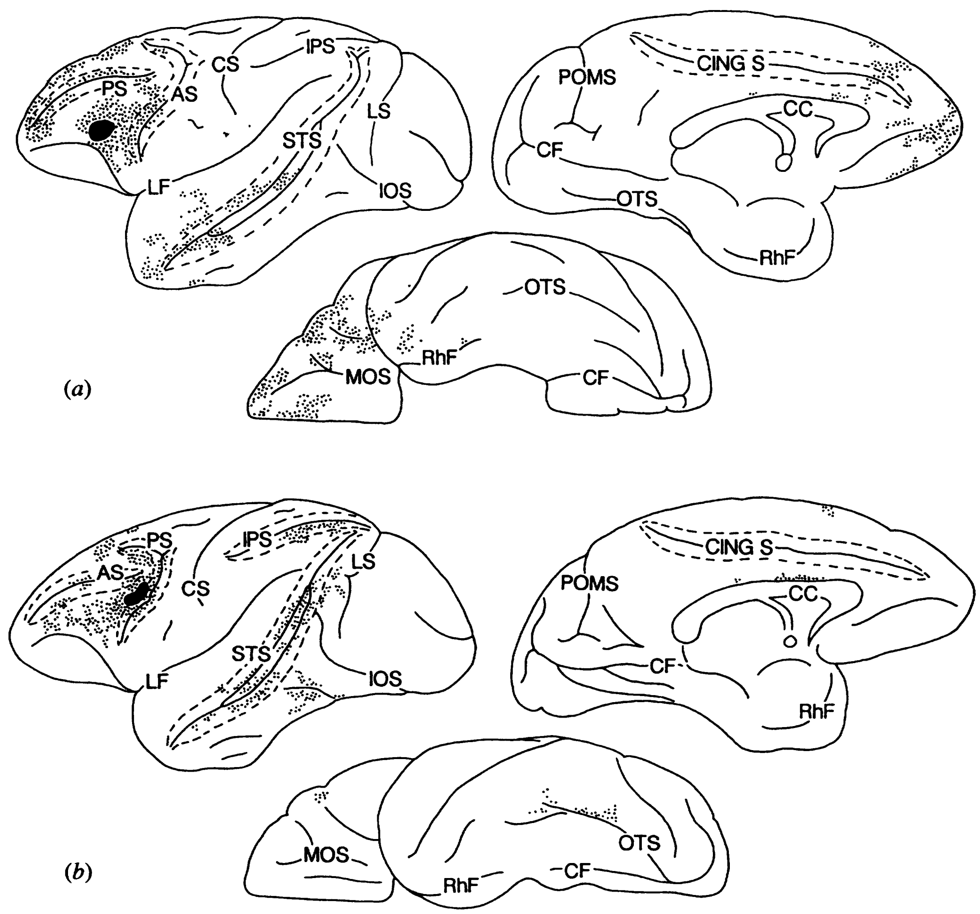

Figure 6. Diagrammatic representations of the injection sites in (*a*) case 8 and (*b*) case 9, and the distribution of retrogradely labelled cells.

## 4. CONCLUSION

The architectonic areas that have been redesignated to correspond to each other in the monkey and the human brain appear to have common morphological features. It should be emphasized that although there are common patterns of laminar distribution of neurons for any pair of corresponding areas in the human and the monkey brain, this should not be construed as implying that these areas have identical cellular composition.

Each architectonically distinct prefrontal region, as studied in the monkey brain, has been shown to have a distinctive overall pattern of cortical connectivity. In regard to local (intrinsic prefrontal) connections, areas above the principal sulcus tend to have input mainly from dorsal and medial prefrontal regions, whereas those below the principal sulcus have input predominantly from ventrolateral and orbital cortices. There is evidence for certain prefrontal areas having much more diverse local afferents, e.g. area 45 receives significant input from dorsal and medial as well as ventrolateral and orbital prefrontal regions. Likewise, dorsal areas 9 and 9/46 have significant connections from various orbital regions.

With regard to post-Rolandic inputs to PFC, architectonically distinct areas have differential connectional relationships. For example, dorsal area 6 has inputs predominantly from sensory-motor regions (frontal, parietal and cingulate), as well as from area 7A involved in visuospatial functions, and limbic input from area 24. In contrast, lateral area 9 has a different pattern of afferent connectivity. Thus, this region has its main inputs from limbic-related areas, such as area 32, rostral area 24, area 23, caudal orbitofrontal cortex, retrosplenial cortex and parahippocampal gyrus, as well as from multimodal cortex (MM-STS). Area 9/46d has a pattern of afferent connections basically similar to that of lateral area 9, except that it has much stronger inputs from orbitofrontal area 11, from retrosplenial cortex and from medial area 19 (visuospatial input).

On the basis of architectonic studies, three subdivisions have been demarcated for area 8 in both the human and the monkey brain. In terms of connections, area 8B, which is situated between area 6 caudally and area 9 rostrally, has different inputs compared to both adjoining areas as well as other subdivisions of area 8. Thus, major inputs to area 8B are derived from limbic regions such as rostral area 24, area 23, retrosplenial cortex, parahippocampal gyrus and rostral insula. Area 8B receives other inputs of a visuospatial nature from medial area 19 and caudal IPL, as well as inputs from MM-STS. Area 8Ad, like area 8B, receives projections from visuospatial regions, namely caudal IPL. However, it receives little input from limbic-

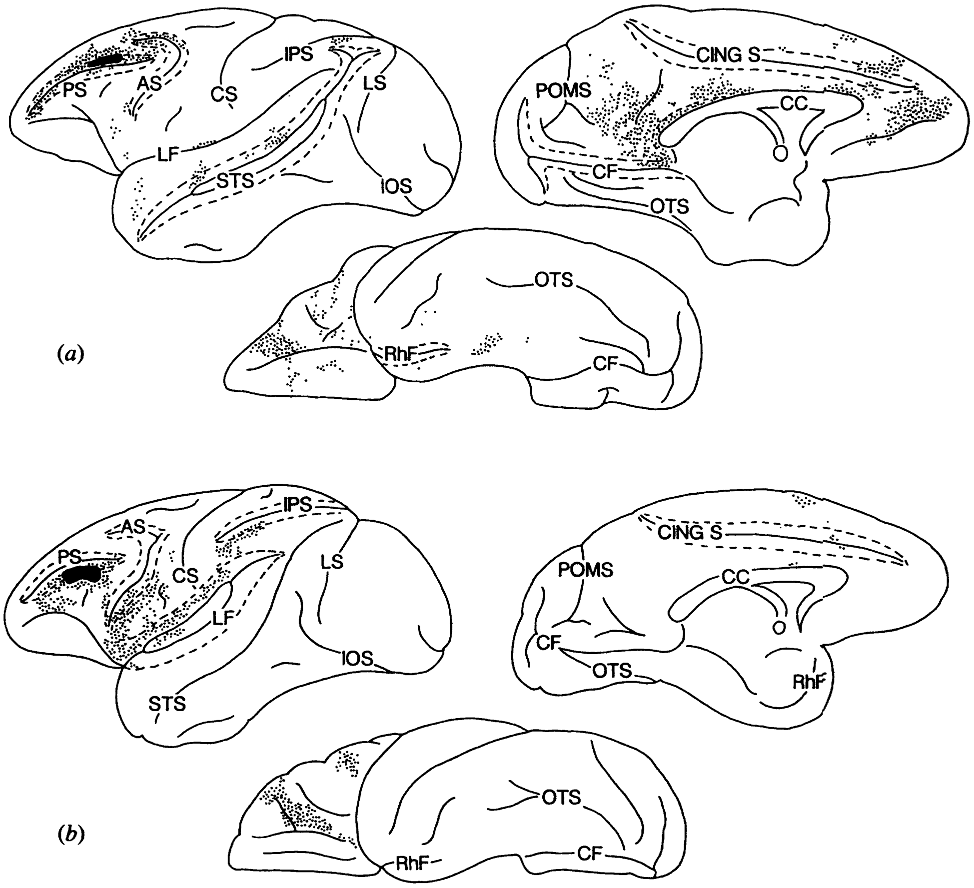

Figure 7. Diagrammatic representations of the injection sites in (*a*) case 5 and (*b*) case 10, and the distribution of retrogradely labelled cells.

related areas. Additionally, area 8Ad has significant afferents from auditory-related areas of STG, visually-related area MST and caudal MM-STS. In contrast to the other divisions of area 8, area 8Av has inputs mainly from visually-related cortices, in the lower bank of IPS and in STS, and in the lateral extrastriate and caudal inferotemporal regions. In short, area 8B has preferential connections from limbic-related areas, 8Ad from visuospatial and audiospatial areas, and 8Av from areas relating to central as well as peripheral vision. It should be pointed out that in a recent review, Paus (1996) has challenged the notion that area 8 in the human brain represents the location of the frontal eye field, although such a relationship appears to be the case in monkeys. Therefore, further studies are needed to address the functional role of area 8 in humans.

Within the ventral prefrontal region, there appear to be different overall patterns of afferent inputs to areas 44, 45 and 47/12. Connections to area 44, the homologue of Broca's area pars opercularis in humans, arise mainly from somatosensory-related regions in the Sylvian operculum – area SII, as well as rostral IPL corresponding to the supramarginal gyrus. Area 44 receives only minor projections from the visually related areas of the inferotemporal region. In contrast, input to area 45, the homologue of Broca's area pars triangularis in the human brain, is derived mainly from auditory association areas of STG and the cortex of the circular sulcus, and from MM-STS. Area 45 has minor connections from the somatosensory cortices of the rostral Sylvian operculum, and from visual areas of the rostral inferotemporal region. Finally, this area receives connections from limbic regions – area 24, insular cortex and area TL. Area 47/12 also is considered to belong to the rostral part of Broca's area, pars orbitalis, in the human brain. Inputs to this region are derived from somatosensory area SII and from visual inferotemporal areas. Area 47/12 has only minor inputs from limbic-related cortices. Finally, inputs to area 9/46v, compared to those of Broca's related areas, are derived predominantly from somatosensory regions of the Sylvian operculum and from rostral IPL. Thus, each architectonically distinct area below the principal sulcus has a unique overall pattern of cortical connectivity.

The overall executive role of PFC undoubtedly depends on the integrated activity of diverse architectonic regions. Nevertheless, a consideration of connectional relationships of various morphologically distinct prefrontal areas suggests the existence of two broad categories. In general, prefrontal areas above the principal sulcus are related preferentially to post-Rolandic cortices located on the medial surface as well as dorsolaterally. In contrast, prefrontal areas below the principal sulcus are linked strongly with post-Rolandic regions located ventrolaterally and ventromedially. Within each of these categories of frontal regions, there seem to be differing patterns of cortical connectivity as one progresses farther rostrally within PFC. The caudolateral frontal region above the principal sulcus (areas 6 and 8Ad) receives input mainly from somatomotor association areas relating to the trunk and limbs, and from areas involved in visuospatial and audiospatial processes. In contrast, more rostral areas (9 and 9/46d) receive input predominantly from limbic regions and multimodal areas. Consistent with their morphological and connectional specificity, these dorsal frontal regions appear to have different overall functional roles. Thus, whereas caudal regions are involved in conditional response tasks and in attentional processes, more rostral regions have a role in spatial functions and in working memory (e.g. Goldman-Rakic 1987; Petrides 1987, 1991; Wilson *et al.* 1993).

Similar differential anatomical and functional correlations can be observed for frontal regions below the principal sulcus. Thus, the caudal region receives input mainly from modality-specific regions – area 44 from somatomotor association areas relating to the head, neck and face, as well as from inferior parietal association areas, and area 8Av from areas relating to central vision. Functionally, area 44 has been shown to have a role in higher-order programming of orofacial movement, whereas area 8Av is involved in visual attentional processes regarding objects (Suzuki 1985; Rizzolatti *et al.* 1988). In contrast, area 47/12 receives its main input from the rostral inferotemporal area, and appears to be involved in a number of functions, including response inhibition and the appreciation of the behavioural significance of stimuli (e.g. Iversen & Mishkin 1970; Suzuki & Azuma 1977). Area 9/46v has inputs predominantly from area SII and from insular and somatomotor association areas, and has been proposed to have a role in working memory for orofacial functions (Preuss & Goldman-Rakic 1989). Finally, area 45 has a distinctive pattern of connections, and receives significant input from auditory association areas, as well as from somatomotor and visual regions. This area also receives substantial projections from multimodal areas and from the insula. Although the precise functional nature of this region in monkeys is not well understood, area 45 corresponds to the pars triangularis of Broca's area in the human brain, which is known to have a role in language function. The fact that area 45 in the monkey receives strong input from the superior temporal region is suggestive of involvement in non-verbal communication.

Exactly how discrete prefrontal architectonic regions and their differential connections contribute to the executive role of the frontal lobe remains to be determined. Nevertheless, processes such as attention, working memory and response inhibition can be viewed as key components of a general capacity for effecting appropriate behaviour. To that end, our results are consistent with an overall dichotomy between dorsal and ventral frontal regions, with the former involved in spatial functions and the latter in processes in which specific stimuli are the focus of behaviour (e.g. Fuster 1989; Wilson *et al.* 1993). Alternatively, Petrides (1994, 1995) has suggested that ventrolateral PFC areas play a role in active encoding and retrieval of specific information held in visual, auditory and somatosensory association areas with which they are connected. This would allow for selection, comparison and decision processes regarding information held in short- and long-term memory. The mid-dorsolateral PFC, in contrast, is thought to be involved when information that has been retrieved must be monitored and manipulated in the planning and execution of behaviour. It may be the combination of these various processes that underlies the full executive function of PFC.

## REFERENCES

Barbas, H. & Pandya, D. N. 1989 Architecture and intrinsic connections of the prefrontal cortex in the rhesus monkey. *J. Comp. Neurol.* **286**, 353–375.

Bonin, G. von & Bailey, P. 1947 *The neocortex of the Macaca mulatta.* Urbana, IL: University of Illinois Press.

Brodmann, K. 1905 Beitraege zur histologischen Lokalisation der Grosshirnrinde: III. Mitteilung. Die Rindenfelder der niederen Affen. *J. Psychol. Neurol.* **4**, 177–206.

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

Damasio, A. R. & Anderson, S. W. 1993 The frontal lobes. In *Clinical neuropsychology*, 3rd edn (ed. K. M. Heilman & E. Valenstein), pp. 409–460. New York: Oxford University Press.

Economo, C. von & Koskinas, G. N. 1925 *Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen.* Berlin: Springer.

Fuster, J. M. 1989 *The prefrontal cortex*, 2nd edn (*Anatomy, physiology, and neuropsychology of the frontal lobe*). New York: Raven Press.

Goldberg, M. E., & Bruce, C. J. 1985 Cerebral cortical activity associated with the orientation of visual attention in the rhesus monkey. *Vision Res.* **25**, 471–481.

Goldman-Rakic, P. S. 1987 Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In *Handbook of physiology*, vol. 5, pt *1* (ed. V. B. Mountcastle & F. Plum), pp. 373–417. Bethesda, MD: American Physiological Society.

He, S., Dum, R. P. & Strick, P. L. 1995 Topographic organization of corticospinal projections from the frontal lobe: motor areas on the medial surface of the hemisphere. *J. Neurosci.* **15**, 3284–3306.

Iversen, S. D. & Mishkin, M. 1970 Perseverative interference in monkeys following selective lesions of the inferior prefrontal convexity. *Exp. Brain Res.* **11**, 376–386.

Morecraft, R. J. & Van Hoesen, G. W. 1993 Frontal granular cortex input to the cingulate (M3), supplementary (M2) and primary (M1) motor cortices in the rhesus monkey. *J. Comp. Neurol.* **337**, 669–689.

Murray, E. A. & Coulter, J. D. 1981 Supplementary sensory area: The medial parietal cortex in the monkey. In *Cortical sensory organization*, vol. 1 (*Multiple somatic areas*) (ed. C. N. Woolsey), pp. 167–195. Clifton, NJ: Humana Press.

Paus, T. 1996 Location and function of the human frontal eye-field: a selective review. *Neuropsychologia* **34**, 475–483.

Petrides, M. 1987 Conditional learning and the primate frontal cortex. In *The frontal lobes revisited.* (ed. E. Perecman), pp. 91–108. New York: The IRBN Press.

Petrides, M. 1991 Functional specialization within the dorsolateral frontal cortex for serial order memory. *Proc. R. Soc. Lond.* B **246**, 299–306.

Petrides, M. 1994 Frontal lobes and working memory. In

*Handbook of neuropsychology*, vol. 9 (ed. F. Boller & J. Grafman), pp. 59–82. Amsterdam: Elsevier Science B.V.

Petrides, M. 1995 Functional organization of the human frontal cortex for mnemonic processing: Evidence from neuroimaging studies. *Ann. N.Y. Acad. Sci.* **769**, 85–96.

Petrides, M. & Pandya, D. N. 1994 Comparative architectonic analysis of the human and macaque frontal cortex. In *Handbook of neuropsychology*, vol. 9 (ed. F. Boller & J. Grafman), pp. 17–58. Amsterdam: Elsevier Science B.V.

Preuss, T. M. & Goldman-Rakic, P. S. 1989 Connections of the ventral granular frontal cortex of macaques with perisylvian premotor and somatosensory areas: anatomical evidence for somatic representation in primate frontal association cortex. *J. Comp. Neurol.* **282**, 293–316.

Preuss, T. M. & Goldman-Rakic, P. S. 1991 Myelo- and cytoarchitecture of the granular frontal cortex and surrounding regions in the strepsirhine primate *Galago* and the anthropoid primate *Macaca*. *J. Comp. Neurol.* **310**, 429–474.

Rizzolatti, G., Camarda, R., Fogassi, L., Gentilucci, M., Luppino, G. & Matelli, M. 1988 Functional organization of inferior area 6 in the macaque monkey: II. Area F5 and the control of distal movements. *Exp. Brain Res.* **71**, 491–507.

Rosene, D. L. & Pandya, D. N. 1983 Architectonics and connections of the posterior parahippocampal gyrus in the rhesus monkey. *Soc. Neurosci. Abstr.* **9**, 222.

Sarkissov, S. A., Filimonoff, I. N., Kononowa, E. P. & Preobraschenskaja, I. S. 1955 *Atlas of the cytoarchitectonics of the human cerebral cortex*. Moscow: Medgiz.

Suzuki, H. 1985 Distribution and organization of visual and auditory neurons in the monkey prefrontal cortex. *Vision Res.* **25**, 465–469.

Suzuki, H. & Azuma, M. 1977 Prefrontal unit activity during gazing at a light spot in the monkey. *Brain Res.* **126**, 497–508.

Vogt, C. & Vogt, O. 1919 Allgemeinere Ergebnisse unserer Hirnforschung. *J. Psychol. Neurol.* **25**, 279–462.

Walker, A. E. 1940 A cytoarchitectural study of the prefrontal area of the macaque monkey. *J. Comp. Neurol.* **73**, 59–86.

Wilson, F. A. W., Scalhaide, S. P. O. & Goldman-Rakic, P. S. 1993 Dissociation of object and spatial processing domains in primate prefrontal cortex. *Science Wash.* **260**, 1955–1958.

## *Discussion*

S. Fleminger (*Academic Department of Psychological Medicine, St Bartholomew's and the Royal London School of Medicine and Dentistry, Turner Street, London E1 2AD, U.K.*). A fundamental question regarding cytoarchitectonic areas is whether they determine the distribution of afferent connections to the cerebral cortex or whether simply spatial location across the cortex determines the distribution of afferents. If the latter is correct then if you move across the cerebral cortex efferents change regardless of whether or not cytoarchitectonic structure has changed. Your demonstration that afferent connections vary across the cytoarchitectonic areas is compatible with either formulation. To demonstrate that the distribution is specific to cytoarchitectonic area it is also necessary to demonstrate that two sites located at a distance from one another, but within the same architectonic area, always have the same pattern of distributions. Has this experiment been done?

D. N. Pandya. Your question is very well taken, and has always been an issue as we have attempted to interpret our results. We would like to point out that the overall conclusion from our studies as well as those of several other investigators, strongly suggests that any portion of a given architectonic area has qualitatively similar connectional relationships with other brain regions. However, the quantity of connections may vary according to the size of the area covered.

S. B. Dunnett (*MRC Cambridge Centre for Brain Repair, The E. D. Adrian Building, Forvie Site, Robinson Way, Cambridge CB2 2PY, U.K.*). A classic criterion for defining prefrontal cortex has been in terms of inputs from the mediodorsal nucleus of the thalamus. To what extent have inputs from discrete subdivisions of this thalamic nucleus been informative in defining the borders between subdivisions of prefrontal cortex?

D. N. Pandya. The answer to your question is that indeed the connections of specific parts of the mediodorsal nucleus help to outline the major divisions of the prefrontal cortex. For example, the magnocellular portion is related to the medial and orbital sectors of the prefrontal cortex, whereas the multiform portion is linked with the caudal prefrontal region. The parvocellular portion is connected with the intermediate cortex comprising the dorsolateral region and the inferior prefrontal convexity. Moreover, the dorsal portion of the mediodorsal nucleus is related to the dorsal and medial sectors of the prefrontal cortex, and the ventral portion to the inferior and orbital prefrontal regions. However, within this broad connectional topography, it should be pointed out that each specific portion of the mediodorsal nucleus is connected with more than one architectonic region of the prefrontal cortex. Therefore, to demonstrate the existence of specific architectonic areas at a finer level, it is necessary to examine cortical morphological features in relation to corticocortical as well as thalamic connectivity.