Supporting Information

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Delineating Cortex Across Species

Here, we summarize evidence for the inclusion of cortical areas in either our conservative (cytoarchitecturally granular/dysgranular) or liberal (agranular but implicated in cognitive function) delineations of PFC. Tables S2 and S3 detail human and macaque areas, respectively, and include cytoarchitectural designations of granular (G), lightly granular (LG), dysgranular (D), or agranular (A) as reported by previous studies. Human areas correspond to those in the HCP_MMP1.0 parcellation (1), while macaque areas are a composite of those from Ferry et al. (2), Paxinos et al. (3), and Lewis and Van Essen (4) cytoarchitectural parcellations.

Human Liberal PFC Delineations. For humans, areal functional properties were primarily drawn from Glasser et al. (1), which describes such properties in detail. An instructive starting example is human area 55b, which lies within a strip of premotor areas but, on multiple grounds, can be considered part of liberal PFC. More specifically, area 55b is bounded medially and laterally by the frontal and premotor eye fields (FEF/PEF), posteriorly by primary motor cortex (4), and anteriorly by ventral premotor cortex (6v) and conservative PFC areas 8C and 8Av. Area 55b exhibits several distinctive features: (*i*) light myelination compared with moderately myelinated FEF/PEF and heavily myelinated primary motor cortex; (*ii*) strong functional connectivity with a seed in the Peri-Sylvian Language area (PSL); and (*iii*) strong activation in contrasts of cognitive-related tasks relative to surrounding areas. Specifically, area 55b exhibited left lateralized activation in the Language Story and Relational–Match tasks and right lateralized activation in the social cognition [Theory of Mind (ToM) –Random] task [tasks and resulting parcellation are detailed in Glasser et al. (1)]. Whether cortical area 55b meets the architectonic criteria for dysgranular or granular cortex warrants closer examination, but we consider it appropriate for our liberal delineation based on its specific cognitive-related task contrasts.

Areas 44 and 45 correspond to Broca's area (5) and show strong activations in task contrasts Language Story and Story–Math. Area SFL is part of the larger language network and shows functional activation in Language Story and Relational–Match contrasts. Areas IFJp and IFJa show greater activation in task contrasts ToM–Random and Faces–Shapes relative to posterior premotor neighbor 6r. Transitional areas i6-8 and s6-8 show a gradual change in activation from posterior premotor cortex anteriorly, exhibiting relative activation during working memory task contrasts compared with neighbors. Areas a24 and 24p exhibit relative deactivations for task contrasts Language Story, ToM–Random, and Faces–Shapes relative to neighboring areas. Areas a32pr, d32, p32, and s32 show activations/deactivations relative to neighbors in Math–Story and/or Faces–Shapes task contrasts and the Language task category. Finally, area 25 is in an orbitofrontal region where functional imaging signal quality is reduced; however, we believe that its adjacency to areas orbitofrontal cortex and pOFC and similar structural properties warrants its inclusion in human liberal PFC.

FEFs were excluded from prefrontal cortex, as Glasser et al. (1) placed it in superior premotor cortex (along with areas 6d and 6a). See *Supplementary anatomical results*, particularly figure 10, in ref. 1, for explicit details about areal boundaries and classifications.

Macaque Liberal PFC Delineations. When considering agranular areas in the macaque frontal lobe, we consulted the literature for evidence of cognitive-related function and attempted to maintain PFC designations among putatively homologous areas shared with humans (e.g., areas 24, 25, and 32).

Area 24 is typically subdivided into areas 24a, 24b, and 24c. While the Ferry et al. (2) parcellation of these areas is limited in its posterior extent due to tissue coverage limitations, the Paxinos et al. (3) whole-cortex parcellation allows extension of these areas to their posterior extent. We first created composite versions of these two different parcellations, resulting in areas 24a′, 24b′, and 24c′. As described in Ferry et al. (2), while these regions are generally considered part of their medial prefrontal network, more posterior/dorsal portions could be considered part of premotor cortex. For this reason, we chose to subdivide these areas further into anterior and posterior portions, primarily guided by anterior–posterior delineations of adjacent dorsal areas. Although a finer-grained functional delineation of this region could help to refine our liberal PFC, we note that modifications of these areas are unlikely to change the main conclusions of this study.

Medial areas 25 and 32 and orbitofrontal areas 13a and 14c, although cytoarchitecturally agranular, are outlined by Carmichael and Price (6) as members of either cognitive or affect functional domains and thus warrant inclusion in liberal PFC.

Delineating Chimpanzee PFC. Analysis of chimpanzee PFC architectonics was informed by comparisons of myelin maps and gradients with those in the human and macaque but also by previously published cyto/myeloarchitectonic studies/parcellations (7, 8). Chimpanzees share with humans and macaques the structural landmark of a heavily myelinated motor strip, the border of which is outlined with a black contour in Fig. 2 and in Fig. S4. Anterior to this border, one would expect to find premotor cortex corresponding to Brodmann area 6, followed more anteriorly by cognitive-related PFC. We consider the pink contour in Fig. 2 to be a plausible candidate for a conservative delineation of chimpanzee PFC and note that it runs generally posterior to the genu-based border (white contour). The medial aspect of our chimpanzee PFC delineation includes areas FDL, FH, and FG while excluding areas LA and FL. Based on reported cytoarchitecture, we consider Bailey areas FDL, FH, and FG to be plausible homologs of Brodmann (9) areas 32, 25, and 11, respectively. We similarly consider Bailey areas LA and FL to be plausible homologs of Brodmann areas 24 and 25, respectively.

We adapted Bailey et al.'s (7) cytoarchitectonic map of chimpanzee cortex (Fig. S1, *Right*) to a single chimpanzee subject using the atlas's labeled coronal slices (Fig. S2). Bailey et al. color the motor strip along the precentral gyrus in yellow (area FA, equivalent to Brodmann area 4 in other primates), which corresponds with the heavily myelinated region (red) represented in our myelin map. Immediately rostral is premotor area FB (equivalent to Brodmann area 6), followed further rostrally by FC, which corresponds most closely to Brodmann area 8. Bailey et al.'s FB and FC correspond to the moderately myelinated regions (yellow/green) of our myelin maps immediately rostral to the motor strip. Putative frontal eye fields were specifically labeled by Bailey et al. as FDΓ, which may correspond to the rostral-most finger of moderately myelinated frontal cortex most easily observed on an inflated surface (Fig. 2, *Top Row*). By visual inspection, our cortical myelin-based PFC border shows good agreement with the premotor/prefrontal borders illustrated in Bailey et al.'s (7) cytoarchitectonic map and Walker's (10) thalamocortical connectivity map.

Statistical Analyses

Fig. S3 illustrates box-and-whisker plots of individual variances in ratios of total cortical volume devoted to PFC or areal delineations reported for each species in Table 1. Panels *A–C* show no overlap for gray matter volume between human and macaque for any delineation of PFC, while both human and macaque values overlap with chimpanzee for conservative and genu-based PFC delineations. Similarly, there is no overlap for white matter volume between human and macaque using the genu-based proxy. Panels *E–G* show no overlap between the three species for cortical areas V1 and 4; however ratios of area FEF/45b were not statistically significant across humans and macaques.

To test whether scaling regression slopes reported in Fig. 4*A* were significantly different, we performed an ANCOVA and report F statistics and *P* values for comparisons across the three regression slopes. Resulting *P* values suggest that each slope is significantly different from the others ($P < 0.05$).

Cortical Thickness Maps

Cortical thickness and thickness gradient maps for each species are shown in Fig. S4. To summarize our qualitative assessment: Macaque dorsolateral frontal cortex has relatively thick anterior frontal cortex (green) and even thicker premotor/motor cortex (red) separated by a strip of thin cortex (blue). A similar pattern is discernible, although less pronounced, in the chimpanzee and perhaps also in human. The macaque cortical thickness gradient (Fig. S4, *Second* and *Bottom Rows*) more clearly illustrates the cortical thickness transitions on which the conservative and liberal PFC borders lie, although such a pattern is less obvious in the human and chimpanzee. Human anterior insular cortex contains a prominently thick patch with corresponding anterior gradient ridges; however, this pattern is less obvious in the chimpanzee and is nonexistent in the macaque. However, cortical segmentation of this region was problematic in the nonhuman primate species, suggesting this may reflect a methodological artifact rather than a neuroanatomically significant interspecies difference. As with insular myelin content and gradients, all PFC delineations lie anterior to this region. Thickness maps in macaque medial frontal cortex include a patch of thick cortex posterior to the previously described myelin gradient ridge. In both macaque and human, relatively thin anteromedial frontal cortex becomes thicker posteriorly as it approaches the medial wall; the thicker posterior region is included only in our liberal PFC delineation.

1. Glasser MF, et al. (2016) A multi-modal parcellation of human cerebral cortex. *Nature* 536:171–178.
2. Ferry AT, Ongür D, An X, Price JL (2000) Prefrontal cortical projections to the striatum in macaque monkeys: Evidence for an organization related to prefrontal networks. *J Comp Neurol* 425:447–470.
3. Paxinos G, Huang X-F, Toga A (2000) *The Rhesus Monkey Brain in Stereotaxic Coordinates* (Academic, San Diego).
4. Lewis JW, Van Essen DC (2000) Mapping of architectonic subdivisions in the macaque monkey, with emphasis on parieto-occipital cortex. *J Comp Neurol* 428:79–111.
5. Geschwind N (1965) Disconnexion syndromes in animals and man. I. *Brain* 88: 237–294.
6. Carmichael ST, Price JL (1994) Architectonic subdivision of the orbital and medial prefrontal cortex in the macaque monkey. *J Comp Neurol* 346:366–402.
7. Bailey P, Bonin GV, McCulloch WS (1950) *The Isocortex of the Chimpanzee* (Univ of Illinois Press, Urbana, IL).
8. Walker AE (1940) A cytoarchitectural study of the prefrontal area of the macaque monkey. *J Comp Neurol* 73:59–86.
9. Brodmann K (1912) Neue Ergebnisse über die vergleichende histologische Lokalisation der Grosshirnrinde mit besonderer Berücksichtigung des Stirnhirns. *Anat Anz* 41: 157–216.
10. Walker AE (1938) The thalamus of the chimpanzee: IV. Thalamic projections to the cerebral cortex. *J Anat* 73:37–93.

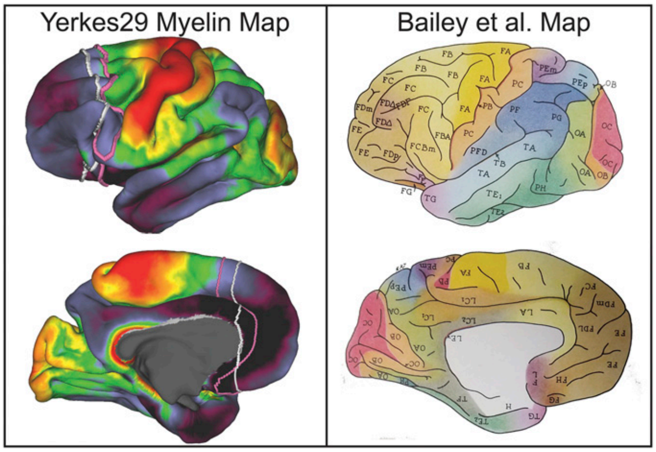

Fig. S1. A candidate boundary for conservative PFC in the chimpanzee. (*Left*) Maps of group-average chimpanzee cortical myelin maps overlaid on group-average pial (i.e., folded) surfaces. The pink contour drawn on the surface serves as a candidate boundary for a conservative delineation of the PFC. The genu-based PFC delineation is marked with a white contour for reference. (*Right*) Bailey et al.'s (1) cytoarchitectonic drawings are reproduced (with the medial view mirror-flipped to match the *Left*). Data are available at https://balsa.wustl.edu/76Lm. Adapted with permission from ref. 1. From *The Isocortex of the Chimpanzee*. Copyright 1952 by the Board of Trustees of the University of Illinois. Used with permission of the University of Illinois Press.

1. Bailey P, Bonin GV, McCulloch WS (1950) *The Isocortex of the Chimpanzee* (Univ of Illinois Press, Urbana, IL).

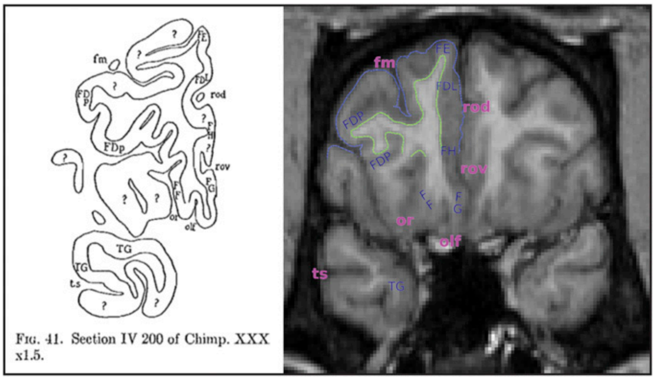

Fig. S2. Mapping Bailey et al.'s (1) cytoarchitectonic atlas to chimpanzee structural MRI. A recreation of a labeled obliquely angled slice from Bailey et al.'s atlas (*Left*), which was mapped to an individual chimpanzee subject that shared cortical folding patterns (*Right*). Pink and green outlines in the MRI slice correspond to white matter and pial surface segmentations, respectively. Data are available at https://balsa.wustl.edu/67GG. Reprinted with permission from ref. 1. From *The Isocortex of the Chimpanzee*. Copyright 1952 by the Board of Trustees of the University of Illinois. Used with permission of the University of Illinois Press.

1. Bailey P, Bonin GV, McCulloch WS (1950) *The Isocortex of the Chimpanzee* (Univ of Illinois Press, Urbana, IL).

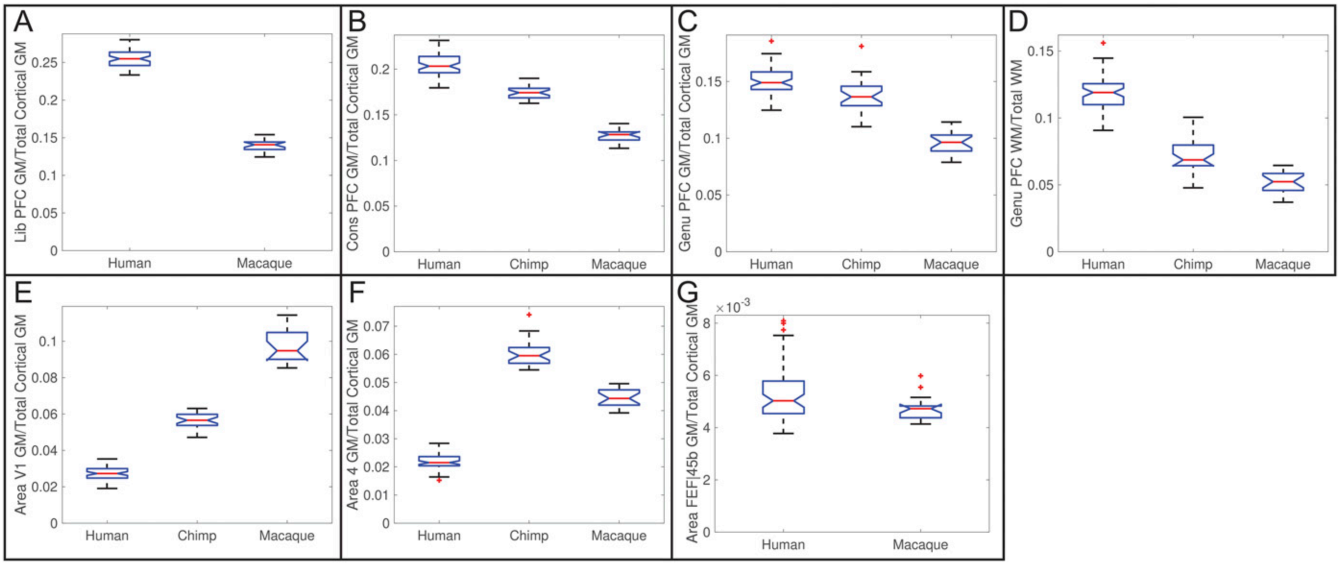

Fig. S3. (*A–G*) Box plots of ratios of prefrontal and areal cortical gray matter volume to total cortical gray matter volume. For each species, the median value is indicated by a red line, and the bottom and top edges of the box indicate the 25th and 75th percentiles, respectively. Whiskers extend to the most extreme data points not considered outliers. Outliers are plotted individually with a plus symbol. The notched portion of boxes indicates the overlap region outside of which the difference in median value is statistically significant.

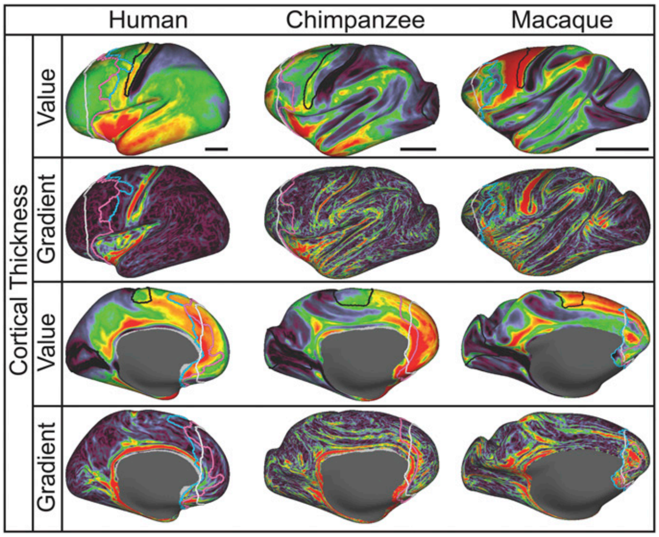

Fig. S4. Relation of cortical thickness to PFC delineations. Left hemisphere frontal cortex of each primate species displaying cortical thickness (*Top* and *Third Rows*) and its corresponding spatial gradient (*Second* and *Bottom Rows*). The white line overlying each map represents the group-average location of the coronal slice at the corpus callosum genu (see also Fig. 3); pink and blue lines represent group-average conservative and liberal PFC delineations, respectively. Primary motor area 4 and primary visual area V1 are bounded by black contours in the parietal and occipital cortex, respectively. Black bars indicate the relative scale of the group-average inflated surfaces for each species. Data are available at https://balsa.wustl.edu/104j.

Table S1. ANCOVA of interspecies scaling regression slopes

ANCOVA	F	*P*
Conservative PFC vs. non-PFC	44.6	0.022
Non-PFC vs. V1	112.4	0.009
Conservative PFC vs. V1	156.8	0.006

ANCOVA of scaling regression slopes reported in Fig. 4*A*. A value of $P < 0.05$ was considered statistically significant.

Table S2. Human cortical areas included in PFC delineations

Area name	Area if different (ref.)	Histology G/D/A and area if different (ref.)
i6-8	(1)	
s6-8	(1)	
8Ad	8 (2, 3)	G 8 (3); D 8 (4)
8Av	8 (2, 3)	G 8 (3); D 8 (4)
8BL	8, (2, 3)	G 8 (3); D 8 (4)
8BM	8 (2, 3)	G 8 (3); D 8 (4)
8C	8 (2, 3)	G 8 (3); D 8 (4)
9–46d	9/46 (2, 3)	G 9/46 (3)
a9-46v	9/46 (2, 3)	G 9/46 (3)
p9-46v	9/46 (2, 3)	G 9/46 (3)
9a	9 (2); 9 (3)	G 9 (3); G 9 (2, 4)
9m	9 (2); 9 (3)	G 9 (3); G 9 (2, 4)
9p	9 (2); 9 (3)	G 9 (3); G 9 (2, 4)
10d	10 (2); 10 (3)	G 10 (3); G 10p, 10r, 10m (4)
10pp	10 (2); 10 (3)	G 10 (3); G 10p (4)
10r	10 (2); P10 (3)	G 10 (3); G 10r (4)
10v	10 (2); 10 (3)	G 10 (3); G 10p, 10r, 10m (4)
a10p	10 (2); 10 (3)	G 10 (3); G 10p (4)
p10p	10 (2); P10 (3)	G 10 (3); G 10p (4)
11l	11 (2); 11 (3)	G 11 (3); G 11l (4)
13l	13 (2); rostral 13 (3)	D (5); G rostral 13 (3, 4)
a24	24 (1, 3)	A 24 (3); A 24/AC (4)
p24	24 (3)	A 24z (3)
25	(1, 3)	A 25/IL (4)
a32pr	32; GI (1, 3)	A 32 (3); A 32/AC, 32/PL (4)
d32	32 (3)	A 32 (3); A 32/AC, 32/PL (4)
p32	32 (3)	A 32 (3); A 32/AC, 32/PL (4)
s32	32 (3)	A 32 (3); A 32/AC, 32/PL (4)
44	(2)	G/A (4); G (6)
45	(2)	
46	(2)	
47l	47/12 (2); 47 (3)	G 47 (3)
47m	47/12 (2); 47 (3)	G 47 (3)
47s	47/12 (2); 47 (3)	G 47 (3)
a47r	47/12 (2); 47 (3)	G 47 (3)
p47r	47/12 (2); 47 (3)	G 7 (3)
55b	(1)	
IFJa	(1)	
IFJp	(1)	
IFSa	(1)	
IFSp	(1)	
OFC	11, 13, 14 (2); 11, 13, 14 (3)	G 1, rostral 13 + 14, A caudal 13 + 14, agranular insular cortex (3); LG 11m, D/A 13l, 13m, 13b, A 13a, 14c (4)
pOFC	13, 14 (2); rostral 13 + 14; caudal 13 + 14 (3)	G 11, rostral 13 + 14, A caudal 13 + 14, agranular insular cortex (3)
SFL	(1)	

Conservative PFC areas are colored in red; liberal PFC areas are colored in blue. Histological abbreviations: A, agranular; D, dysgranular; G, granular; LG, lightly granular.

1. Glasser MF, et al. (2016) A multi-modal parcellation of human cerebral cortex. *Nature* 536:171–178.
2. Petrides M, Pandya DN (1999) Dorsolateral prefrontal cortex: Comparative cytoarchitectonic analysis in the human and the macaque brain and corticocortical connection patterns. *Eur J Neurosci* 11:1011–1036.
3. Passingham RE, Wise SP (2012) *The Neurobiology of the Prefrontal Cortex: Anatomy, Evolution, and the Origin of Insight* (Oxford Univ Press, Oxford).
4. Wise SP (2008) Forward frontal fields: Phylogeny and fundamental function. *Trends Neurosci* 31:599–608.
5. Ongür D, Ferry AT, Price JL (2003) Architectonic subdivision of the human orbital and medial prefrontal cortex. *J Comp Neurol* 460:425–449.
6. Petrides M, Pandya DN (2002) Comparative cytoarchitectonic analysis of the human and the macaque ventrolateral prefrontal cortex and corticocortical connection patterns in the monkey. *Eur J Neurosci* 16:291–310.

Table S3. Macaque cortical areas included in PFC delineations

PFC area	Primary atlas areas	Area name if different (ref.)	Histology G/D/A and area if different (ref.)
8ad	8ad_PHT00	8 (1, 2)	G 8 (2)
8av	8av_PHT00	8 (1, 2)	G 8 (2)
8b	8b_PHT00	8 (1, 2)	G 8 (2)
8/32	8/32_PHT00	8, 32 (1); 8, 32 (2)	G 8, A 32 (2); A 32/PL (3)
9/46d	9/46d_PHT00	9/46 (1, 2)	G 9/46 (2)
9/46v	9/46v_PHT00	9/46 (1, 2)	G 9/46 (2)
9/46	9/46_PHT00	9/46 (1, 2)	G 9/46 (2)
9l	9l_PHT00	9 (1); 9 (2)	G 9 (2); G 9 (3)
9m	9m_PHT00	9 (1); 9 (2)	G 9 (2); G 9 (3)
9/32	9/32_PHT00	9, 32 (1); 9, 32 (2)	G 9, A 32 (2); G 9, A 32/PL (3)
10d_pr	10d_PHT00	10 (1); 10 (2)	G (4); G 10 (2); G 10m, 10o (3)
10m_pr	10m_FOA00; 10m_PHT00	10 (1); 10 (2)	G (4); G 10 (2); G (3)
10°	10o_FOA00	10 (1); 10 (2)	G (4); G 10 (2); G 10m, 10o (3)
11l	11l_FOA00	11 (1); 11(2)	G (4); G 11 (2); G (3)
11m	11m_FOA00	11 (1); 11(2)	G (4); G 11 (2); G (3)
12l_pr	12l_FOA00; 47(12)L_PHT00	47/12 (1); (5)	G (4); G 11 (2); G (3)
12m	12m_FOA00	47/12 (1); 9 (5)	G (4)
12°	12o_FOA00	47/12 (1); (5)	G (4)
12r_pr	12r_FOA00; 47(12)_PHT00	(5)	D (4)
13a	13a_FOA00	13 (1); 13 (2)	A (4); G rostral 13, A caudal 13 (2); A (3)
13b	13b_FOA00	(4)	D (4)
13l	13l_FOA00	13 (1); 13 (2)	D (4); G rostral 13, A caudal 13 (2); LG (3)
13m	13m_FOA00	13 (1); 13 (2)	D (4); G rostral 13, A caudal 13 (2); LG (3)
14c	14c_FOA00	14(1); 14 (2)	A (4); G rostral 14, A caudal 14 (2); LG rostral 14, A caudal 14 (3)
14r	14r_FOA00	14 (1); 14(2)	D (4); G rostral 14, A caudal 14 (2); LG rostral 14, A caudal 14 (3)
(3)(3)24aa	24a_FOA00; 24a_PHT00	24, frontal (1); 24 (2)	A (4); A 24 (2); A 24a/AC (3)
24ba	24b_FOA00; 24b_PHT00	24, frontal (1); 24 (2)	A (4); A 24 (2); A 24b/AC (3)
24ca	24c_PHT00	(4)	A (4)
25	25_FOA00	(1); (2)	A (2); A 25/IL (3)
32_pr	32_FOA00; 32_PHT00	Frontal (1); (2)	A (4); A (2); A 32/PL (3)
44	44_PHT00	(6)	D (6)
45a	45a_PHT00	(1); 45 (2)	G 45 (1); G 45 (2)
46d_pr	46d_PHT00	46 (1); 46 (2)	G 46 (2)
46v_pr	46v_PHT00	46 (1); 46 (2)	G 46 (2)

Conservative PFC areas are colored in red; liberal PFC areas are colored in blue. Histological abbreviations: A, agranular; D, dysgranular; G, granular; LG, lightly granular.

1. Petrides M, Pandya DN (2002) Comparative cytoarchitectonic analysis of the human and the macaque ventrolateral prefrontal cortex and corticocortical connection patterns in the monkey. *Eur J Neurosci* 16:291–310.
2. Passingham RE, Wise SP (2012) *The Neurobiology of the Prefrontal Cortex: Anatomy, Evolution, and the Origin of Insight* (Oxford Univ Press, Oxford).
3. Wise SP (2008) Forward frontal fields: Phylogeny and fundamental function. *Trends Neurosci* 31:599–608.
4. Carmichael ST, Price JL (1994) Architectonic subdivision of the orbital and medial prefrontal cortex in the macaque monkey. *J Comp Neurol* 346:366–402.
5. Petrides M, Pandya DN (1999) Dorsolateral prefrontal cortex: Comparative cytoarchitectonic analysis in the human and the macaque brain and corticocortical connection patterns. *Eur J Neurosci* 11:1011–1036.
6. Frey S, et al. (2011) An MRI based average macaque monkey stereotaxic atlas and space (MNI monkey space). *Neuroimage* 55:1435–1442.

Other Supporting Information Files

Dataset S1 (PDF)