

## Frontal Cortex Evolution in Primates

**E C Bush**, Harvey Mudd College, Claremont, CA, USA  
**J M Allman**, California Institute of Technology,  
 Pasadena, CA, USA

© 2009 Elsevier Ltd. All rights reserved.

### Primate-Specific Adaptations

The frontal cortex can be defined as the neocortex anterior to the motor somatosensory–cortex border. This is a large region in primates, containing areas involved directly or indirectly in the control of almost every behavior. It has long been thought that the frontal cortex played an important role in primate evolution. Modern evidence supports this view. Indeed, given the diversity of functions in the region and the variety of unique behaviors exhibited by primates, it would be surprising if the frontal cortex had not evolved unique adaptations.

The common ancestor of eutherian mammals probably had a small body and a small brain. Comparative work in modern mammals suggests it had a basic complement of cortical areas including primary visual, auditory, and somatosensory areas. It also probably had a primary motor area (M1). This means that we could define a frontal cortex in that mammal and that the region of the frontal cortex in modern eutherians (taken as a whole) can be thought of as being homologous.

It is likely however that this broad homology obscures substantial differences in frontal cortex structure between primates and nonprimates. One piece of evidence to this effect is that the frontal cortex scales differently in primates and nonprimates. In primates, the frontal cortex hyperscales with the brain size. This can be seen in the reconstructions in [Figure 1](#) which show the brain of a small primate, the galago, and a larger primate, the macaque. A primate with a larger brain tends to have a disproportionately large frontal cortex. In contrast, in a nonprimate order, carnivores, the frontal cortex size does not vary systematically with brain size. This suggests that the structure and development of the frontal cortex differs substantially in the two orders.

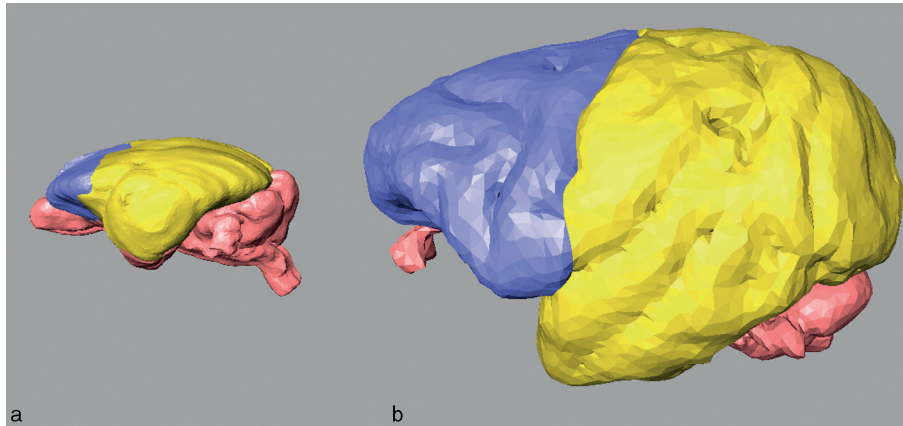
When we focus on specific cortical areas and regions, we again find that the primate frontal cortex differs in important ways from that found in other orders. A variety of evidence suggests that the two main branches of primates, strepsirrhines and anthropoids, share up to ten motor areas in the frontal cortex. Of these, only one or two have clear homologs outside primates. Most eutherians have an agranular M1,

with large layer 5 pyramidal cells, somatotopy, and relatively low thresholds of stimulation. Rostral and medial to M1 is a supplementary motor area (SMA, also called M2) in primates. It is also somatotopically organized, and has slightly smaller layer 5 pyramidal cells than M1. This area may have homologs in other mammals such as rats.

The remaining motor areas which are shared among primates appear not to have one-to-one homologs in other orders. Among these areas are several cingulate motor areas and a number of premotor areas involved in higher-level coordination of movement. Several of these are particularly interesting. The frontal eye field (FEF) is connected with both the sensory visual areas and the prefrontal cortex. Microstimulation here produces saccadic and smooth pursuit eye movements. The FEF may be involved in the voluntary control of eye movements, an attribute of great importance for highly visual primates. Strepsirrhines and haplorhines also share a ventral premotor area (PMV), which appears to have representations of the upper body. One possibility is that PMV is involved in the visually guided grasping of objects, something that would be especially important to a small visual predator. Early primates are thought to have been small arboreal visual predators, and it is tempting to view the evolution of primate motor areas in this light. These areas could be seen as motor adaptations of the earliest primates for a very demanding arboreal niche.

A frontal region of particular interest in primate evolution is the prefrontal cortex. This region has a wide variety of connections with other brain regions, and patients with prefrontal damage show deficits in the ability to plan and organize behavior. This suggests that it is involved in aspects of behavior which have been important in primate evolution.

The question of whether the prefrontal cortex is unique to primates has been controversial. Brodmann originally argued that it was, identifying prefrontal cortex with the well-developed granular layer 4 which is seen in primates. This was later disputed based on connectivity data. Today, there is general agreement that neither of these two types of data alone provides an adequate answer. However, there is less consensus on whether the prefrontal cortex is unique to primates. What is clear, however, is that even if a broadly homologous prefrontal cortex exists in other mammals, it is substantially different from that found in primates. There is no evidence that rats possess anything like the diversity of prefrontal areas found in primates, and many of the details of the primate prefrontal cortex are likely to be unique to the order.



**Figure 1** Reconstructions of the brains: (a) *Galago senegalensis*; (b) *Maccaca mulatta*. Frontal cortex is indicated in blue. The position of the motor-somatosensory cortex border was used to delineate frontal cortex. The two brains are shown here in their proper proportions relative to one another.

## Specializations within Primates

### Anthropoids versus Strepsirrhines

There is also important variation in frontal cortical structure between the two large divisions of primates, anthropoids and strepsirrhines (represented by the macaque and galago, respectively). Among the premotor areas we have discussed, area PMV appears to have developed interesting adaptations in anthropoids. In monkeys, it seems to have an increasing representation of distal forelimb movements. At the same time, it has strong connections to parts of somatosensory cortex which represent information from the cutaneous receptors of the hands. Such information is particularly useful for reaching and grasping motions. These differences have led to the suggestion that anthropoid PMV evolved mechanisms for the improved guidance of reaching and grasping.

In terms of the broader arrangement of areas, however, the premotor cortices in the two groups have many similarities. As already mentioned, electrophysiological data suggest that the motor and premotor regions of anthropoids and strepsirrhines share up to ten areas. Architectonic evidence supports this view. This broad similarity in the arrangement of areas can be found in several other frontal regions. Comparisons in cytoarchitecture and myeloarchitecture suggest that anthropoids and strepsirrhines have a similar arrangement of areas in the orbital and medial regions of the frontal cortex.

In contrast, it seems that there are important differences between the two groups in the prefrontal cortex. Macaques appear to have a much larger number of areas in this region than galagos do. This is suggested by patterns of connectivity between the prefrontal cortex and other regions. Labeling experiments show

that the prefrontal cortex in both species has numerous connections with other parts of the cortex. But the pattern of connectivity suggests that galago has fewer prefrontal areas. For example, tracer injections in regions of the parietal cortex produce fewer discrete zones of labeling in the galago prefrontal cortex than in the macaque. A similar result has been found in comparisons of architectonic parcelations in the two species.

Current architectonic and connective data suggest that most prefrontal areas in galagos can be identified with a homologous area in the macaque. For example, the posterior-most prefrontal areas in galago appear to have homologs in the macaque arcuate cortex region. These conclusions reflect similarities in cell density and size, fiber-staining patterns, and connections to the parietal, superior temporal, and inferotemporal cortices. Similar conclusions have been reached about other areas in the galago prefrontal cortex (e.g., areas in the superior, polar, and ventral parts of the prefrontal cortex).

However, there are a number of areas in the macaque which have no clear homolog in galagos. These areas are concentrated especially around the principal sulcus in macaques, and they may represent anthropoid-specific specializations. This region of the cortex, often referred to as the dorsolateral prefrontal cortex, is thought to be involved in working memory. Classic lesion studies showed that monkeys with lesions in this region have deficits on delayed-response tasks. Such tasks may involve spatial working memory, for example, requiring the monkey to remember a physical position where food was last given. They can also involve nonspatial problems which require the monkey to remember an object's identity over a delay. Working memory of this type is thought to

play an important role in cognition, and in light of this, it is especially interesting that the dorsolateral prefrontal cortex appears to have anthropoid-specific specializations. Also, it is interesting to note that area PMV has developed connections to the dorsolateral prefrontal cortex which are especially prominent in Old World monkeys.

### Great Apes and Humans

The fronto-polar cortex (Brodmann's area 10) expands in apes and especially in humans both absolutely and relative to total cortical size. Functional imaging studies indicate that area 10 is activated in the retrieval of episodic memory, in the receipt of monetary rewards, in weighing cost versus benefit, in the formulation of auction bids, in deciding how much to spend to punish cheaters, and in moral decision making. The retrieval of specific past episodes contributes to the complex deliberative socioeconomic decision making that this structure participates in. The slow deliberative nature of this form of cognition stands in contrast to rapid intuition, which another hominoid specialization, the von Economo neurons (VENs) may participate in.

The VENs are large bipolar cells located in anterior cingulate (aCC) and fronto-insular (FI) cortex. They are distinguished from pyramidal cells because they have only a single, large, basal dendrite, whereas pyramidal cells have an array of smaller basal dendrites extending from the cell body. The VENs are present only in humans and great apes and are far more abundant in humans than in apes.

The apical dendrites of VENs are very similar to those of the apical dendrites of neighboring pyramidal cells. The radial orientation and narrow width of the dendritic arborization indicate that the VENs sample a sharply circumscribed cylinder of cortex, possibly corresponding to a minicolumn. They may thus constitute a fast-fire output from minicolumns that provides a rapid relay to other parts of the brain. VEN functions are revealed by immunocytochemical staining with antibodies to neurotransmitter receptors. The VENs are strongly labeled with antibodies to the dopamine D3 receptor, which may signal the expectation of reward under uncertainty. The activation of the FI and aCC increases with the degree of uncertainty. FI and aCC activity is coupled to situations in which the subject sustains a gambling loss (punishment) and then switches to a different behavioral strategy, implying that in normal subjects these areas are involved in adaptive decision making and cognitive flexibility.

The VENs may participate in intuition, a form of cognition in which many variables are rapidly evaluated to yield a fast decision. Typically we are

unaware of the logical steps or assumptions underlying the process although intuition is based on experience-based probabilistic models. We experience the intuitive process at a visceral level. Intuitive decision making enables us to react quickly in situations that involve a high degree of uncertainty, which commonly involve social interactions. Frequently we do not have the luxury of sufficient time to perform a deliberative cost-benefit analysis to determine the most appropriate course of action but, instead, must rely on rapid intuitive judgments. The aCC and FI are active when subjects make decisions under a high degree of uncertainty. These areas are also active when subjects experience guilt, experience embarrassment, and engage in deception. The aCC and FI are also active in humor, trust, empathy, and the discrimination of the mental states of others. All these social emotions are influenced by the degree of uncertainty involved. Their large size suggests that the VENs may relay a fast intuitive assessment of complex social situations to allow the rapid adjustment of behavior in quickly changing social situations. For example, humor, which activates the FI and aCC in proportion to subjective ratings of funniness, may serve as a way to recalibrate intuitive judgments in changing social situations, thus resolving uncertainty and relieving tension. The VENs can thus be seen as an adaptation supporting the increased complexity of hominoid and especially human social networks.

*See also:* Brodmann's Areas; Frontal Eye Fields; Humans; Orbitofrontal Cortex: Visual Functions; Prefrontal Cortex: Structure and Anatomy; Prefrontal Contributions to Reward Encoding; Prefrontal Cortex; Reward Neurophysiology and Orbitofrontal Cortex.

### Further Reading

- Allman JM, Hakeem A, and Watson K (2002) Two phylogenetic specializations in the human brain. *Neuroscientist* 8: 335–346.
- Allman JM, Watson K, Tetreault N, and Hakeem A (2005) Intuition and autism: A possible role for von Economo neurons. *Trends in Cognitive Sciences* 9: 367–373.
- Bush EC and Allman JM (2004) The scaling of frontal cortex in primates and carnivores. *Proceedings of the National Academy of Sciences of the United States of America* 101: 3962–3966.
- Kaas JH and Preuss TM (2003) Human brain evolution. In: Squire L, Bloom F, Landis SR, and Zigmond M (eds.) *Fundamental Neuroscience*, 2nd edn., pp. 1147–1166. San Diego, CA: Academic Press.
- Nimchinsky EA, Gilissen E, Allman JM, Perl DP, Erwin JM, and Hof PR (1999) A neuronal morphologic type unique to humans and great apes. *Proceedings of the National Academy of Sciences of the United States of America* 96: 5268–5273.

- Preuss TM and Goldman-Rakic PS (1991) Ipsilateral cortical connections of granular frontal-cortex in the strepsirhine primate galago, with comparative comments on anthropoid primates. *Journal of Comparative Neurology* 310: 507–549.
- Preuss TM and Goldman-Rakic PS (1991) Myeloarchitecture 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.
- Semendeferi K, Armstrong E, Schlechter A, Zilles K, and Van Hoesen G (2001) Prefrontal cortex in humans and apes: A comparative study of area 10. *American Journal of Physical Anthropology* 114: 224–241.
- Stepniewska I, Preuss TM, and Kaas JH (2006) Ipsilateral cortical connections of dorsal and ventral premotor areas in new world owl monkeys. *Journal of Comparative Neurology* 495: 691–708.
- Watson K, Matthews B, and Allman J (2007) Brain activation during sight-gags and language-dependent humor. *Cerebral Cortex* 17(2): 314–324.
- Wu CW, Bichot NP, and Kaas JH (2000) Converging evidence from microstimulation, architecture, and connections for multiple motor areas in the frontal and cingulate cortex of prosimian primates. *Journal of Comparative Neurology* 423: 140–177.