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4.05 The Evolution of Parallel Visual Pathways in the Brains of Primates

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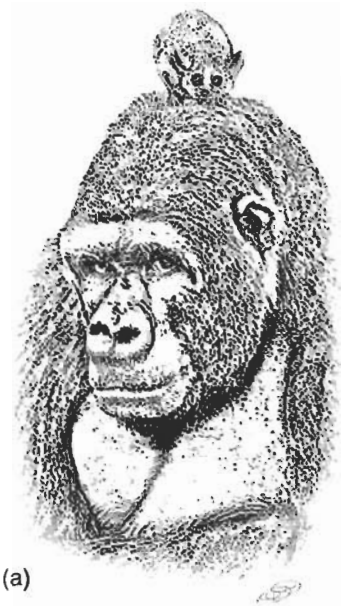
Glossary

analogy	Functional similarity between parts of different organisms due to parallel evolution, without common ancestral origin.
Brodmann	Brodmann (1909) developed a commonly accepted scheme for dividing V1 into six layers (I, II, IIIA, IIIB, IVA, IVB, IVCα, IVCβ, V, and VI).
Hässler	We have used a modification of a nomenclature devised originally by Hässler (1967). The latter allows for more appropriate cross-species comparisons. This nomenclature subdivides cortex into the following layers, with Brodmann's nomenclature in parentheses: I (I), II (II), IIIA (IIIA), IIIBα (IIIB) and IIIBβ (IVA), IIIC (IVB), IVα (IVCα), IVβ (IVCβ), V (V), and VI (VI).
homology	Similarity between parts of different organisms due to evolution from the same part of a common ancestor.
homoplasy	Correspondence between parts or organs as a result of evolutionary convergence.
K, M, P cells	Koniocellular (K), magnocellular (M), and parvocellular (P) cells found in different layers of the lateral geniculate nucleus of primates.
ON-/OFF-center cells	Retinal ganglion and lateral geniculate nucleus cells that respond with increases in response to either the onset or offset of light in the receptive field center.
ontogeny	Developmental progression of an organism from embryo to adult.

4.05.1 Introduction

The primate order to which we belong is quite heterogeneous in size, form, and lifestyle. Primate species range in size from some prosimians that can weigh as little as 100g (e.g., the mouse lemur, *Microcebus murinus*) to species of great apes, whose males can weigh more than 300kg (e.g., the gorilla; Figure 1). Such size differences can also be seen in the brain, which varies in weight from 1.73g in the mouse lemur to 1400g in humans (Bons *et al.*, 1998; Williams, 2002).

These differences in body/brain size and lifestyle of existing primate species can make it difficult to trace the evolutionary history of brain parts and connections, particularly since big differences in brain size and lifestyle result in both addition and deletion of brain parts, and changes in connections due to scaling issues (Kaas, 2004). Moreover, the clues about brain evolution left by ancestors are limited. These clues rely on incomplete fossil records, and genes whose rate of change cannot be predicted precisely, or (in most cases) be linked to specific brain parts. Finally, relevant visual pathway data have been gathered for relatively small numbers of existing primate species. None of these clues alone, including current powerful genetic approaches, offer sufficient evidence to trace the evolutionary history of specific brain components and connections in primate evolution. The strongest evidence for evolutionary relationships between brain parts and connections of different primates is likely to be the common presence of a feature in several distantly related primates. The difficulty lies in trying to determine

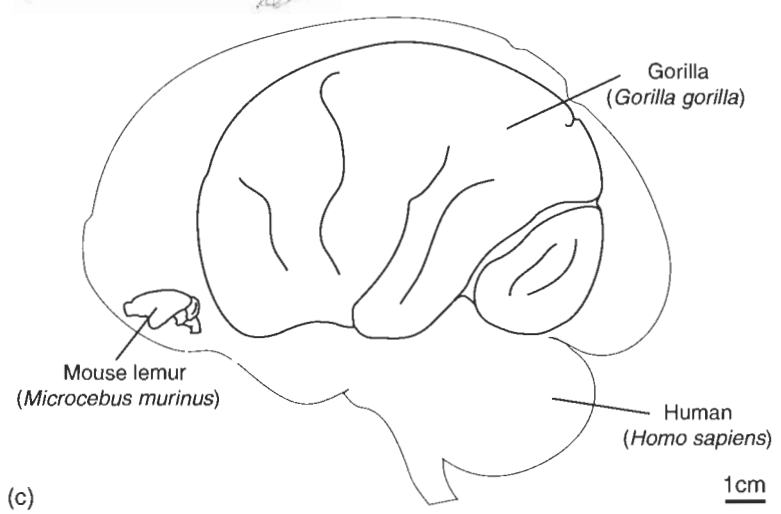


(a)

Relative body and brain sizes

Mouse lemur (*Microcebus murinus*)	Body:	0.06 kg
	Brain:	1.73 g
Gorilla (*Gorilla gorilla*)	Body:	175 kg
	Brain:	535 g
Human (*Homo sapiens*)	Body:	65 kg
	Brain:	1400 g

(b)



(c)

Figure 1 Relative sizes of primates and their brains. The primate order includes mammals that range widely in body and brain size from mouse lemur to gorilla and human. a, Artistic depiction of the relative size differences between a mouse lemur and a gorilla; b, comparison of body and brain weights of mouse lemurs, gorillas, and humans (Bons *et al.*, 1998; Williams, 2002); c, schematic representation of relative brain sizes of these primates. a, Reproduced by permission of David Royal.

the history of these brain parts and connections since similarities may simply reflect a form of parallel evolution (homoplasy) and not necessarily homologous relationships. Also, the fact that connections can be added, deleted, or evolve at different rates in a mosaic fashion magnifies the problem. Nevertheless, some inferences can be made by careful comparisons across existing species and by combining this information with emerging genetic maps of relationships between species.

Our goal in this article is to review relevant evidence from a variety of sources in an effort to reconstruct a reasonable scenario as to how parallel visual pathways might have evolved in primates. Given that visual system studies of living primates are limited to only a few of the many existing primate species, we must rely on work on other mammals, and even nonmammals, to construct a reasonable scenario of the evolution of the visual pathways in primates. Historically, it has been argued that the main parallel visual pathways to cortex in mammals are the retinocolliculopulvinar and retinogeniculo-V1 pathways (see Casagrande and Royal, 2004; Casagrande and Xu, 2004).

For this article, we have chosen to focus on channels passing to and through the lateral geniculate nucleus (LGN), since these pathways may have become differentially specialized in primates and

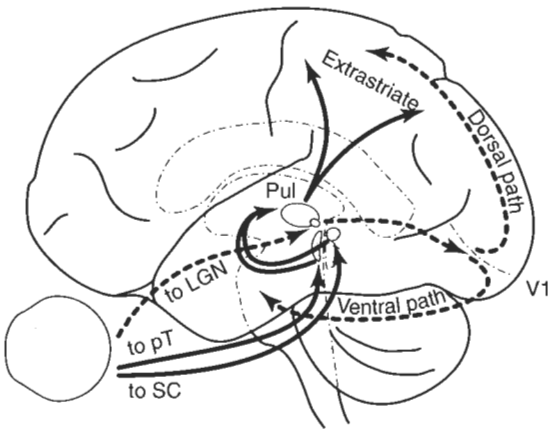


Figure 2 Parallel visual pathways from retina to cortex. In primates, visual information reaches cortex from retina via several pathways. The most studied, and important, is the pathway from the eye to the LGN to V1 (also called striate cortex or area 17), shown with dashed arrows. In V1, new pathways are constructed that enter two hierarchies of visual areas known as the dorsal and ventral paths or streams of processing, also referred to by some authors as the 'where stream' or vision for action stream and the 'what stream', respectively, in reference to their proposed function. Less studied is the pathway from retina (eye) via superior colliculus (SC) and pretectum (pT) to pulvinar (Pul). Pulvinar, in turn, sends widely distributed projections to most extrastriate visual areas to which the dorsal and ventral pathways also project.

are known to be the main pathways for conscious visual perception in primates (Figure 2). We have divided the article into eight sections, including this introduction. In Section 4.05.2, we define what we mean by parallel pathways and provide some other operational definitions that are used in the remaining sections. In Section 4.05.3, we consider whether magnocellular (M) and parvocellular (P) retinogeniculocortical pathways are homologous across primates and whether these pathways exist in nonprimates (e.g., Y and X streams in cats) as some have proposed (Casagrande and Xu, 2004). In Section 4.05.4, we address the controversies over whether the fine fiber system identified by Bishop (1933) in frog and rabbit optic nerve becomes the koniocellular (K) pathway in primates. Given that the K pathway is heterogeneous, we argue that the K pathway is actually made up of a number of pathways of which some are likely to have been present in the common ancestor of primates. A related issue, namely the evolution of chromatic channels and color vision in primates, is addressed separately in Section 4.05.5. Here we defend the position that one type of K pathway likely transmitted cone signals to the LGN even in the ancestors of primates, given that these cone signals have been found in K LGN cells in both New World and Old World primates and in some cat W cells (which share other features with primate K cells). In Section 4.05.6, we consider other properties that remain segregated in the LGN and cortex, such as input from the two eyes and whether it existed in the common ancestor of primates. We support the position that the laminar pattern of ocular segregation in the LGN and the columnar organization of ocular segregation in cortex show the same basic features across primates, suggesting that both were present in the common ancestor of primates. In Section 4.05.7, we examine the issue of whether parallel LGN pathways evolved as starting points for specific hierarchies of visual cortical areas that have been referred to as the dorsal and ventral streams of visual processing in the common ancestor of primates. In Section 4.05.7, we also consider the issue of whether such cortical streams are conserved across mammals or evolved separately in such species as cats. We take the position that the basic subdivisions into dorsal and ventral streams of visual processing at the cortical level can be identified in a diverse range of primates and so are likely to be homologous, but components may have been added, deleted, or modified in different primate lines. In Section 4.05.8, we provide a summary and also outline questions that need to be addressed in order to arrive at more definitive conclusions concerning the evolution of parallel visual pathways. We also outline some practical strategies for answering some of these questions.

4.05.2 Background and Some Definitions

In order to examine the issue of the evolution of parallel visual pathways we need to consider how to define the specifics of the problem. For example, how do we know if a visual pathway is homologous (derived from a common ancestor) or simply analogous (functionally similar but not inherited from a common ancestor)? Since parallel visual pathways are made up of cells at different levels of the neuraxis that differ in terms of neurochemistry, morphology, connections, and function, we need to clarify our level of analysis. For example, can we consider a pathway that carries chromatic signals from two cone types in the retina of a diurnal primate species as homologous to a pathway that appears similar in all other respects to one that carries signals from a single cone type in a monochromatic nocturnal species? We would argue that if this similarity extends to other defining features of the pathway and extends to several distantly related

species the answer should be yes. What would be useful is to understand which particular neural characters at any level in the pathway are conservative. It is likely that answers lie in the ontogeny of these pathways given that early embryological stages are quite conservative across mammals. Unfortunately, since there are almost no studies available comparing the neural development of the visual system of different primate species, we are unlikely to be able to identify such ontological characters, although some clues can be obtained by making comparisons between available primate and nonprimate developmental data. An additional related problem is that it is not clear how modifications at one level of the visual system (e.g., the retina) affect the development of more central target structures and vice versa. For example, Kaskan *et al.* (2005) have argued that major changes in retinal ganglion cell number or shifts in the proportions of rods and cones do not result in major differences in the size of the primary visual cortex (V1) which, instead, appears to scale with overall brain size (see Visual Cortex: Evolution of Maps and Mapping). This result implies that the developmental programs for visual areas in the telencephalon and diencephalon (forebrain) are relatively independent (at least at the early stages) from changes that occur in the original out-pocketing of the forebrain, the retina. If this is the case, then using the retina as the starting point for investigating the evolution of parallel visual pathways may be the wrong approach. Careful examination of V1, however, indicates that there may be differences in relative laminar development across primates that appear to correlate with changes in the eye. Examination of the thalamus, especially the LGN, also indicates that relative laminar development varies in predictable ways with phylogeny and visual niche in primates (Figure 3). Thus, examination of detailed structure (not just gross size) may offer more insights concerning the evolution of brain parts (see Elston *et al.*, 2001).

We argue that, although the programs of neural development that establish peripheral tissues and each level of the neuraxis can differ, they are never evolutionarily divorced from each other if they are connected in the adult. After all, the entire machine needs to run reasonably well for the adult organism to survive and reproduce and this requires that connections be made appropriately. Changes at one level can never be completely divorced from changes at the next level. The latter also raises the issue of epigenetic effects. Clearly, there are a number of epigenetic mechanisms, including neural activity/experience and competition for growth factors, that must be used to match neuronal populations at different levels in large brains since the number of synapses far exceeds the number of genes available for individual specification by a large margin. For example, in humans there are about 15×10^8 synapses per mm^3 of neuropil (DeFelipe *et al.*, 1999) compared with $26–38 \times 10^3$ genes (Venter *et al.*, 2001). Still, these epigenetic mechanisms must have a genetic base and must be selected in order to ensure that brain areas wire correctly (Easter *et al.*, 1985).

Another big question that must be answered before we can even begin thinking about evolution of parallel visual pathways is the question of why these pathways arose in the first place. Parallel pathways likely arise in evolution in response to incompatibilities. A cell cannot have a large dendritic field that integrates information across many receptors and have a small dendritic field capable of discrete fine grain sampling from just one or two receptors. Such incompatibilities could also provide an evolutionary drive for parallel pathway specialization. Parallel pathways presumably also arise from the constraints on the speed of transmission, particularly in relatively large mammalian brains. It seems likely then that true parallel visual pathways originate from ganglion cells that are clearly distinct in a number of ways. As argued eloquently by Rowe and Stone (1980), dividing ganglion cells into different classes needs to be based upon a parametric approach using a variety of criteria, given that it is difficult to prove that any single characteristic defines an entire class. A true class of ganglion cells should also tile the retina without visuotopic holes, otherwise differences may simply reflect natural variation within a cell class. Presumably once the number of ganglion cell types can be established then the number of parallel pathways to the brain/LGN will be limited to that number, assuming that each ganglion cell class projects to its own unique set of cells. In the case of the LGN, the number of different ganglion cells that provide input has still not been established, but, as explained more fully below, one can make comparisons between species based upon examination of some of the established pathways. Similarly, at the level of the LGN and V1, a true visual pathway should show anatomical segregation in terms of connections even if specific functional signatures cannot be traced from level to level. Beyond the first synapse in V1, however, it appears that a separate set of parallel pathways is established that links V1 to extrastriate areas (Casagrande and Kaas, 1994). The degree to which the geniculocortical pathways are actually linked directly to the pathways leading to extrastriate areas is a matter of debate given that most signatures of early pathways disappear at the level of V1

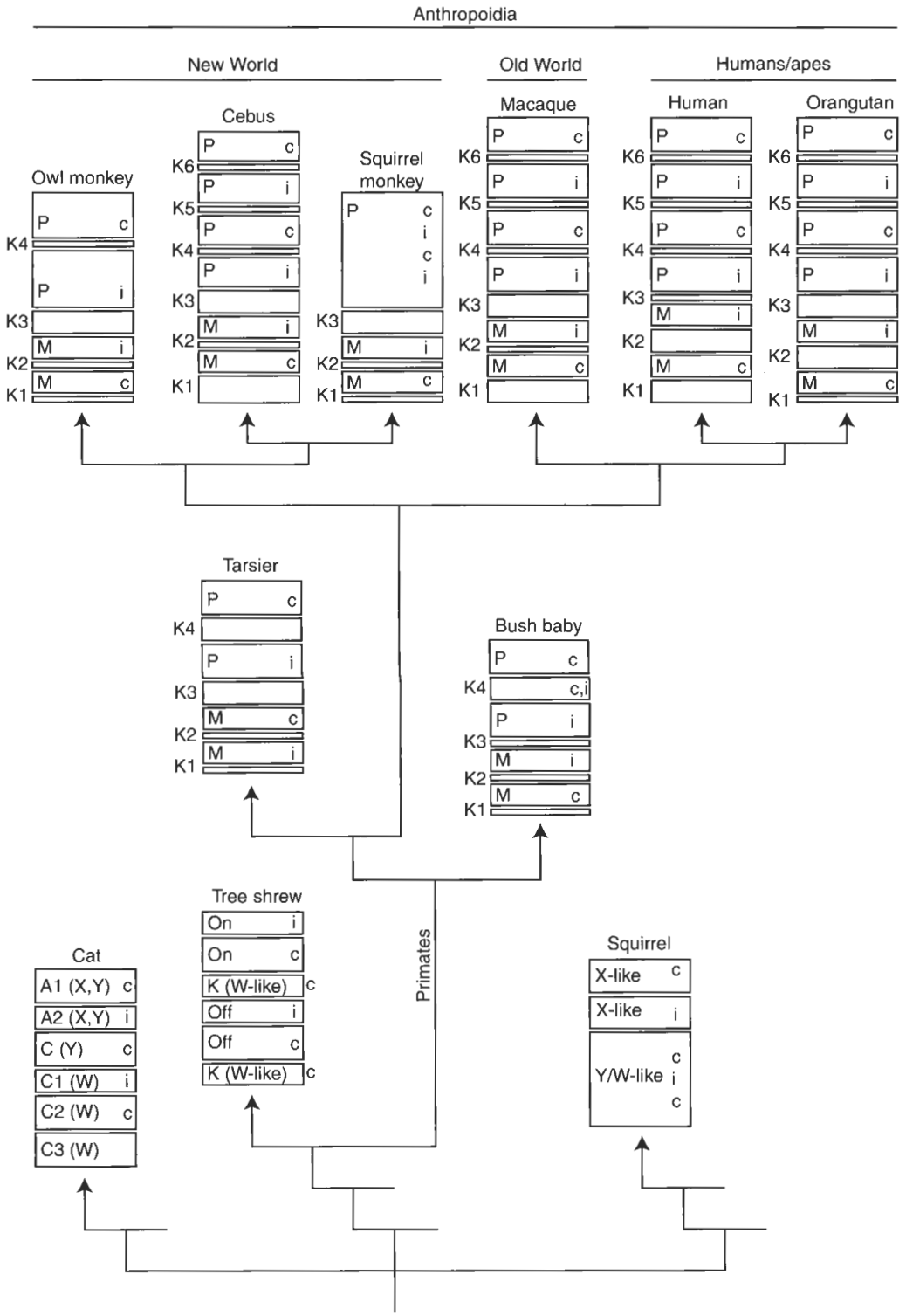


Figure 3 Laminar organization of the LGN in primates, tree shrews, squirrels, and cats. LGN cell layers for each species are indicated in boxes. The phylogenetic relationships between mammalian species are indicated by arrows, with the top branches indicating the relationships between primates. Only a few examples are shown. Note that in all primates the LGN is organized in a similar manner with two P layer and two M layers. In some primates (e.g., macaque monkeys), the P layers can split into four layers in a portion of the nucleus, and in others (squirrel monkeys) P cells exist as a cell mass where layers exist only based upon separate input from each eye. Tree shrews (Scandentia) are the closest living relatives of primates but have a very different LGN laminar organization as do squirrels (Rodentia) and cats (Carnivora). See text for details. c, contralateral retinal input; i, ipsilateral retinal input; K, koniocellular; M, magnocellular; P, parvocellular. Numerals refer to different K layers.

(Merigan and Maunsell, 1993; Casagrande and Xu, 2004). Nevertheless, similarities in the output of V1 to other cortical areas and their connections with each other allow us to ask whether similar hierarchies of visual areas are established across various primate species. As discussed in more detail below, it appears that V1 projects to the same areas in a range of primates (Casagrande and Kaas, 1994) but that, beyond V1, the evidence from connections, lesions, and behavior studies can support the idea that two major hierarchies of visual areas existed in a common ancestor of primates only in the broadest sense.

4.05.3 The Evolution of P and M Pathways

In almost all mammalian species so far examined, retinal and LGN cells can be physiologically classified into those that appear to convey information about higher spatial frequencies and respond in a more sustained manner, those that appear to respond better to higher temporal frequencies in a more transient manner, and those with slowly conducting axons and heterogeneous response properties (Stone, 1983; Lennie, 1993; Casagrande and Xu, 2004). In primate LGN, these classes correspond to P, M, and K neurons, respectively. In this section, we focus on the P and M pathways; the K pathway will be dealt with more fully in Section 4.05.4. Here, we consider the competing hypotheses that the P and M pathways (1) were present early in mammalian evolution and are thus homologous with similar pathways in nonprimates (e.g., X and Y cells in cats), (2) appeared early in primate evolution and their similarities with other mammalian species thus represent examples of parallel evolution, or (3) evolved independently in different primate lineages. Evidence for or against these hypotheses is sought from comparisons of response properties, anatomical organization, and neurochemistry in the retinogeniculocortical pathways of New World and Old World primates, cats, tree shrews, and rodents. Most of the nonprimate data come from cats, as their visual systems have been the most thoroughly studied of all nonprimate mammals.

In all primates, the M pathway originates from large retinal ganglion cells (parasol cells) which project to the M layers of the LGN, whereas the P pathway originates from smaller retinal ganglion cells (midget cells), which project to the P layers of the LGN (Figure 3). M cells in the retina and M LGN have larger receptive fields, lower preferred spatial frequencies, higher preferred temporal frequencies, and higher contrast sensitivities than their P counterparts. A similar dichotomy is found between Y and X cells in the cat retina and LGN (Table 1). Although X and Y cells in cats were first distinguished on the basis of a single criterion, linearity of spatial summation, the X versus Y classification was found to correspond to a host of other characteristics, and it is this extended sense of X and Y that is used here (Norton and Casagrande, 1982). Indeed, when W cells were described in cats, it was found that some were linear and some nonlinear, yet they were clearly a separate population based on the extended criteria that define X and Y cells (Table 1). Although it has been proposed that M and P cells are homologous to Y and X cells, respectively, an alternative hypothesis is that cat X and Y cells correspond to the linear and nonlinear subgroups of M cells, respectively, and that the P pathway is primate-specific (Kaplan and Benardete, 2001). X and Y cells, however, differ in many morphological and physiological characteristics in a similar way to M and P cells, while it is not clear that the linear and nonlinear M cells differ in characteristics other than linearity (see, however, Kaplan, 2004). It should be noted that linearity arises from a special mechanism that is added to the linear center surround mechanism present in all

Table 1 Comparison of primate M and P cells with cat X and Y cells

Attribute	*Primate M cells*	*Cat Y cells*	*Primate P cells*	*Cat X cells*
Cell size	Large	Large	Small	Small
Conduction velocity	Fast	Fast	Slow	Slow
Response dynamics	Transient	Transient	Sustained	Sustained
Spatial resolution	Lower	Lower	Higher	Higher
Temporal resolution	Higher	Higher	Lower	Lower
Contrast sensitivity	Higher	Higher	Lower	Lower
V1 projection	Upper tier of layer 4	Upper tier of layer 4	Lower tier of layer 4	Lower tier of layer 4
Linearity of spatial summation	Most linear, some nonlinear	Nonlinear	Linear	Linear
Chromatic opponency	No	No	Yes (in trichromatic primates)	No

retinal ganglion cells, so linearity of certain cell classes could be gained or lost in evolution without compromising other physiological properties.

Another physiological property that differs between primates and cats is color selectivity in that P cells have chromatic opponency, whereas X cells do not. However, this difference is affected by the fact that cats are dichromats, adapted for a nocturnal existence. As discussed more fully in the following sections, long-wavelength cones were gained (or, more likely, regained) independently in New World and Old World primates. The P cells of some dichromatic (or even monochromatic in the case of galagos and owl monkeys) primates also lack color opponency for similar reasons as cat X cells, yet they have all the other characteristics of P cells in trichromatic primates. Thus, P cells in all primate species should be considered homologous, regardless of color selectivity, because such differences can be explained by changes in single photopigment genes. By the same reasoning, lack of color opponency should not be used as evidence against homology of cat X cells and primate P cells (see Evolution of Color Vision and Visual Pigments in Invertebrates).

Although fewer data are available, distinct physiological classes, possibly corresponding to P and M pathways, have been found in other species. In gray squirrels, P-like cells with longer latencies, sustained firing, and linear spatial summation could be distinguished from M-like cells with short latencies, transient responses, and linear or nonlinear summation (Van Hooser *et al.*, 2003). In tree shrews, although linear and nonlinear cells have been found (Sherman *et al.*, 1975), it appears that the nonlinear cells are more like K or W cells than M cells, and that nonlinear M cells are lacking (Holdefer and Norton, 1995). A clear dichotomy between transient and sustained responses is found in the tree shrew, however (Sherman *et al.*, 1975; Lu and Petry, 2003).

Within the LGN, M and P cells are segregated into different layers. The standard primate laminar pattern consists of four layers: two M layers adjacent to the optic tract, followed internally by two P layers (Casagrande and Norton, 1991; Kaas, 2004). Each of these layers receives input from one hemiretina, with the first M layer receiving crossed (nasal hemiretina) input and the second M layer receiving uncrossed (temporal hemiretina) input. The P layer closest to the second M layer also receives an uncrossed retinal input, while the most internal P layer receives a crossed retinal input. The K layers, discussed in more detail below, lie mainly between or ventral to each of the P and M layers (Casagrande, 1994; Hendry and Reid, 2000; Casagrande and Xu, 2004). In some primates, the two P layers can split into four layers, but this occurs for only a topographically limited portion of the nucleus. For example, in macaque monkeys, four P layers can be identified only within the part of the nucleus representing about 2–3° to 17° of eccentricity (Malpeli *et al.*, 1996). In some humans, P layers split into as many as eight layers in some parts of the nucleus, but in other humans only two P layers exist across the whole extent of the LGN (Hickey and Guillery, 1979). In some primates, portions of the ipsilaterally innervated M layer can split off and form an extra layer next to the optic tract within a portion of the nucleus (Casagrande and Joseph, 1980). The latter is the standard condition for M layers in the tarsier, where it has been suggested that the ipsilaterally and contralaterally innervated M layers are reversed (Rosa *et al.*, 1996). Finally, in many New World primates (e.g., squirrel monkeys), P cells exist as an unlaminated cell mass where layers can only be defined based upon segregated input from the axons from the two eyes (Tigges and O'Steen, 1974; Fitzpatrick *et al.*, 1983). All of these differences, however, can easily be recognized as modifications of the basic primate laminar pattern (Figure 3).

In most nonprimate mammals with well-developed visual systems, three main subdivisions of the LGN can be recognized, progressing internally to externally (i.e., toward the optic tract): (1) a main contralateral layer receiving X- and Y-type input, (2) a main ipsilateral layer receiving X- and Y-type input, and (3) an outermost layer comprising sublayers receiving various combinations of contralateral Y-type input and ipsilateral and contralateral W-type input. The LGN of the cat, for example, consists of paired layers A and A1 receiving mixed X and Y inputs from the contralateral and ipsilateral eyes respectively, a magnocellular C layer receiving contralateral Y cell input, and several small-celled layers receiving either contralateral or ipsilateral W cell input. The LGN of sheep and other ungulates has a similar organization (Karamanlidis and Magras, 1972; Ebinger, 1975; Karamanlidis *et al.*, 1979; Clarke *et al.*, 1988). Additionally, carnivores and ungulates possess a medial interlaminar nucleus (MIN) which receives Y and W input. Layers A and A1 are subdivided into sublayers receiving input from either ON-center or OFF-center retinal ganglion cells in such mustelid carnivores as ferrets and mink (LeVay and McConnell, 1982; Stryker and Zahs, 1983). In squirrels, contralateral layer 1 and ipsilateral layer 2 receive X- and Y-like input (referred to by some as P-like and M-like; see above), while Y-like input is found in layers 1, 2, and especially 3, and W-like input is confined to layer 3 (Kaas *et al.*, 1972; Van Hooser *et al.*, 2003).

The primate LGN thus differs from the standard mammalian plan in having complete, not partial, segregation of different cell classes. As previously pointed out (Boyd and Matsubara, 1996; Matsubara and Boyd, 2002), a simple scenario for transitioning to the primate organization involves the coalescing of ipsilateral Y cells ventrally in layer A into a separate layer. The resulting lamination pattern would have the same contra-M, ipsi-M, ipsi-P, contra-P organization as seen in primates.

Interestingly, the tree shrew, which is considered phylogenetically closer to primates than the groups considered above, has a unique LGN organization which is unlike that in primates or other mammals. The tree shrew has a six-layered LGN with two layers containing W-like cells, and the remaining four layers segregated by both eye input and contrast sign (ON center vs. OFF center). Projections from sustained and transient retinal ganglion cells do not appear to segregate into different LGN layers in the tree shrew. The tree shrew visual system thus appears to have many derived characteristics that arose independently of those in primates (Rager, 1991; Kaas, 2002).

Another criterion that has been used to determine homology in the LGN is neurochemical content. M cells (but not P cells) in the LGN of primates and Y cells (but not X cells) in the LGN of cats are selectively labeled by antibodies against a cell surface antigen, Cat-301 (Hockfield and Mckay, 1983; Hockfield *et al.*, 1983; Hendry *et al.*, 1988), or against nonphosphorylated neurofilaments (Chaudhuri *et al.*, 1996; Bickford *et al.*, 1998). These molecular markers thus support the hypothesis of homologies between LGN cell classes in different mammalian lines.

Finally, the geniculocortical projections of the different classes of relay cells provide evidence for homology between different groups. In all primates, M cells project to the upper portion of layer IV, P cells project to the lower portion of layer IV, and K cells project above layer IV (Casagrande and Norton, 1991). In cats, the laminar segregation between X and Y cells is similar (though likely not as absolute) with X-cell terminations concentrated in lower layer IV and Y cell terminations concentrated in upper layer IV. W cells project outside of layer 4 (see Section 4.05.4 on K pathway for further discussion). In both cats and primates, the simple laminar dichotomy between X and Y cells is likely to be complicated by subclasses of X and Y cells and M and P cells. For example, the Y cells in layer C have larger receptive fields, higher contrast sensitivity, and more pronounced nonlinearities than A-layer Y cells (Frascella and Lehmkuhle, 1984; Yeh *et al.*, 2003). Their terminations are confined to the topmost third of layer IV and, moreover, selectively target cytochrome oxidase (CO) blob columns (Boyd and Matsubara, 1996). It has been argued that a similarly defined subclass of M cells exists in primates (Hawken *et al.*, 1988; Bauer *et al.*, 1999), although the evidence for this is not as conclusive.

The sublaminar organization of geniculocortical organization in other animals is not as well described as for cats and primates, but it can be noted that the layer 3 complex in squirrels, which contains Y-like and W-like cells, projects to the upper part of layer 4 and supragranularly, and these two projections likely come from Y-like and W-like cells, respectively (Weber *et al.*, 1977; Harting and Huerta, 1983). Tree shrews have a very different geniculocortical arrangement, whereby terminations from ON-center and OFF-center cells segregate within different sublamina of layer 4 (Fitzpatrick and Raczkowski, 1990). The W-like LGN layers, however, still terminate outside of layer 4.

The data reviewed here strongly support the hypothesis that the precursors to M and P cells were present in the earliest primates, so M and P cells in all primates are homologous. Moreover, the similarities in organization of the M and P pathways in primates and similar pathways in some other mammals provide some support for the hypothesis that the M versus P dichotomy arose prior to the divergence of primates from other mammals, with the unique differences found in tree shrews representing a derived condition, not primitive characteristics representative of early primates.

4.05.4 Is the K Pathway Evolutionarily Old?

In Section 4.05.3, we focused on the parallel M and P pathways connecting the retina with V1; in this section, we focus on a third parallel pathway, currently referred to as the koniocellular, or K, pathway (for reviews see Casagrande, 1994; Hendry and Reid, 2000; Casagrande and Xu, 2004). As for the M and P pathways, the K pathway consists of a distinct class (or classes, as K cells are heterogeneous) of retinal ganglion cells that project to distinct groups of cells in the LGN, which are in turn connected to distinct layers of V1. The K pathway has a constellation of features that distinguish it from the M and P pathways and that have led some to suggest that the K pathway is phylogenetically older than the M and P pathways. In this section, we review this hypothesis, while at the same time

reviewing the data for homologues of the K pathway in other mammalian species, particularly the W pathway in the cat, the nonprimate for which the greatest amount of data on the visual system is available.

The cat W pathway was relatively well studied years before the primate K pathway was closely examined (Stone, 1983), and indeed even before the extent and importance of the K pathway in primates was widely acknowledged. There are a large number of similarities between K and W pathways. At the level of the retina, both cat W and primate K retinal ganglion cells have small cell bodies, thin but extensive dendrites, and the thinnest most slowly conducting axons in the optic tract (Casagrande and Norton, 1991). There is evidence for a similar class of retinal ganglion cells in other mammals as well, including rats, rabbits, and tree shrews.

The geniculate projections of both K and W retinal ganglion cells are to small-celled layers that are either next to the optic tract or intercalated between the main layers. Neurochemically, these small-celled layers have been identified using antibodies to the calcium-binding protein calbindin. In prosimian bush babies, and both New World and Old World simians including owl monkeys, marmosets, and macaque monkeys, calbindin is found in K layers, but not in M or P layers of the LGN (Johnson and Casagrande, 1995; Hendry and Reid, 2000; White *et al.*, 2001; Xu *et al.*, 2001). Calbindin also labels cells in the tree shrew LGN exclusively in the layers that contain W-like cells, layers 3 and 6 (Diamond *et al.*, 1993). In the cat, although W-cell layers in the LGN contain calbindin, many GABAergic (γ-aminobutryric acid, GABA) interneurons in the LGN also contain calbindin (Demeulemeester *et al.*, 1991), obscuring a possible relationship between the W-cell pathway and calbindin content.

K cells in the LGN differ in their relative laminar development in different primate lines (Hendry and Casagrande, 1996). The K pathway also appears to be physiologically and anatomically more heterogeneous than either the P or M pathways (for review, see Casagrande and Xu, 2004). For example, K cells lying ventral to the M layers in K layer 1 project mainly to layers IIIA and I of primate V1, and can be distinguished physiologically from K cells that lie close to the P layers and send axons to the CO blobs located in layer IIIBα of V1. Some K cells carry S-cone input although most K cells do not, at least in marmosets (White *et al.*, 2001). Some K cells defined by calbindin antibody labeling appear to project exclusively to the middle temporal visual area (MT) in macaque monkeys (Stepniewska *et al.*, 1999; Sincich *et al.*, 2004). This means that subdivisions of the K pathway could have been lost or added in different primate lines (Ding and Casagrande, 1998; Shostak *et al.*, 2002). In cats, W cells have similar projections: to layer 1 and to the CO blobs in layer III of V1 (Boyd and Matsubara, 1996), and to extrastriate cortex (Kawano, 1998). It is not yet clear if these different structures are targeted by different classes of W cells, or by collaterals of the same cells.

The K-cell pathway and the W-cell pathway are also similar in that they have close interconnections with the superior colliculus. Some retinal ganglion cells of the K and W classes project to the colliculus, and the colliculus makes projections to the K- and W-cell layers of primate and cat LGN. In tree shrews as well, there is a projection from the colliculus to LGN layers 3 and 6. Because the colliculus is considered by some to be phylogenically older than the LGN, being homologous with the main target of retinal axons in nonmammalian vertebrates, the optic tectum, it has been suggested that the K/W pathway is phylogenetically older than the M/X and P/Y pathways (Bishop, 1959). Other features of the K/W pathway, such as finer axons with more diffuse projections, have also been suggested to be primitive conditions. Ultimately, the question of pathway evolutionary age is extremely difficult to answer since we have no good biological markers of relative age specific for visual pathways. If anything, the K pathway in primates shows more morphological and physiological variation than the P or M pathways, so could be considered biologically (perhaps evolutionarily) less stable.

In summary, there is strong evidence from anatomy to support the conclusion that K cells in all primates are homologous and that at least some K cells have homologues in other mammals: (1) both K and W cells receive midbrain input from the parabigeminal nucleus and superior colliculus; (2) some W-like and K cells always lie adjacent to the optic tract in a large variety of mammals (Harting *et al.*, 1991); (3) K and W LGN cells send axons that terminate above layer IV in V1; (4) K cells are more likely than other LGN cell classes to project to extrastriate areas outside of V1; (5) K and W cells tend to be slowly conducting and have smaller cell bodies on average; and (6) K LGN cells in all primates and tree shrews (and perhaps W cells in cats) contain calbindin. There is also a variety of physiologically defined similarities between these cell classes, although the overlap in response properties between all relay cell classes in the LGNs of mammals and the influence of lifestyle on spatial and temporal thresholds make it difficult to make useful comparisons.

4.05.5 Color Vision in Primates and the Evolution of P and K Pathways

The ability to see color derives from the ability to compare wavelengths. Such color opponency is constructed at the retina from cones sensitive to short (S; e.g., blue), medium (M; e.g., green), and long (L; e.g., red) wavelengths by creating receptive fields with ON responses to one wavelength and OFF responses to an opposing wavelength or wavelengths. Thus, S cones oppose the M plus L cones to create a blue/yellow color axis, M opposes L to create a green/red axis and all three cones oppose each other to create an achromatic OFF/ON black/white axis. This simple view is complicated by the facts that some primates have only a single cone type and are therefore presumably color blind, most primates are dichromatic possessing two cone types, and some primates (such as humans) are trichomatic (Jacobs, 1996, 1998). Trichromacy, however, appears to have evolved separately in different primate lines (Jacobs, 1996; see The Comparative Biology of Photopigments and Color Vision in Primates). A number of articles have been written about the evolution of color vision in primates as well as the genetics of color vision (Jacobs, 1996, 1998; Nathans, 1999; Tan and Li, 1999; Dacey and Packer, 2003). A commonly held belief is that primates evolved from a nocturnal ancestor. Support for this argument has been recently reviewed (Ross, 2000) and will not be considered in detail here except where relevant to parallel pathway evolution. Relevant to the current article are proposals concerning which parallel pathways carry chromatic signals and what this might tell us about the evolution of parallel pathways in primates. At least four types of ganglion cells carrying cone signals have been identified in macaque monkeys. Of these, three carry signals from S cones, small and large bistratified ganglion cells carrying blue ON signals and large monostratified ganglion cells carrying blue OFF signals. It has been proposed that these blue pathways project to LGN K cells given that some K cells have been identified at the level of the LGN to carry S cone signals in macaque monkeys and marmosets (White *et al.*, 1998). In marmosets, approximately 20% of K cells carry S cone signals based upon studies in which immunocytochemistry for calbindin was used to directly identify K cells at the level of the LGN after single unit recording (White *et al.*, 1998). In addition, it has been argued by many that midget ganglion cells in several primates carry L/M opponent signals to the P LGN layers (see Dacey and Packer, 2003; but see, however, Calkins and Sterling, 1996). At present, it is unclear if some P cells also carry S cone signals, as was originally proposed by Wiesel and Hubel (1966), given that K cells, defined by either calbindin or CamKII immunocytochemistry, can lie below each P and M layer, can be found scattered within these layers, or can even form bridges of cells that pass directly through the P layers (Johnson and Casagrande, 1995; Hendry and Casagrande, 1996; Hendry and Calkins, 1998). Definitive data linking particular ganglion cell classes whose chromatic signature is well defined to particular visual pathways that project through the LGN to cortex is still lacking.

Evidence that does exist suggests the following. In all primates examined it has been demonstrated that K cells in the LGN defined by immunocytochemistry or laminar location send axons above layer IV (IVC of Brodmann) of V1 (Lachica and Casagrande, 1992; Ding and Casagrande, 1998). These K axons terminate in the CO blobs of V1, in cortical layer I and probably also in cortical layer IIIBβ (IVA of Brodmann) (Yazar *et al.*, 2004). With the exception of projections to layer IIIBβ this pattern of axonal projections can be demonstrated in prosimians as well as in New World and Old World simians, apes, and humans. Since, as discussed earlier, some prosimians such as the bush baby and at least one simian, the owl monkey, have only a single cone type and lack S cones entirely (Jacobs, 2002), it could be argued that the K pathway evolved before the evolution of color vision in primates. This would have to be the case if the prosimian bush baby represents the ancestral original nocturnal condition of primates.

An alternative proposal is that ancestral primates were actually dichromatic (Tan and Li, 1999). The evidence to support this view is as follows. First, S cones are considered to be of ancient origin genetically and are present in many mammalian groups, including carnivores, ungulates, and primates (Calkins, 2001). More important is the fact that both prosimian bush babies and simian owl monkeys appear to have the gene for S cones but this gene is not expressed in either species due to defects in the gene (Jacobs, 2002). The presence of the gene strongly suggests that functional S cones existed in their ancestors. Support for this view comes from studies that have examined for the S opsin gene in a relative of the bush baby, the slow loris (*Nycticebus coucang*) (Kawamura and Kubotera, 2004) and found evidence to support the view that this gene was disrupted in the common ancestor of galagiods (e.g., bush babies) and lorisids. Second, S and M cones are both present in at least one nocturnal prosimian, the mouse lemur (*M. murinus*), as well as in several diurnal lemurs and in the tarsier (Dkhissi-Benyahya *et al.*, 2001). Third, S and M

cones have been identified in cat W cells (Wilson *et al.*, 1976). Cat W cells also project to the CO blobs in V1 (area 17) just as K cells do in primates. Cat W cells also share many other characteristics in common with primate K cells as reviewed above and earlier (Casagrande and Norton, 1991). Taken together, these data support the view that the common ancestor of primates may actually have been diurnal with S and M cone signals passing to a population of K cells. Since all LGN cells receive input from cones, this does not inform us about the evolution of color vision relative to the parallel pathways. If this hypothesis is correct, it does predict that, as in cats, S cone signals should be confined to K cells in those prosimians that have functional S cones, a hypothesis that could be tested directly by examining for S cone input to LGN K cells in the mouse lemur. It also predicts that in dichromatic lemurs (perhaps all dichromatic primates) wavelength discrimination would depend upon K cells since P and M cells would only receive from a single M cone.

The issue of whether some primate ancestors were trichromatic is more complicated given the different ways prosimians, Old World primates, and New World primates construct color vision. All Old World primates have two separate opsin genes (M and L) on the X chromosome in addition to the single S autosomal gene. New World simians, and prosimian lorises, and lemurs have only one opsin gene on the X chromosome, but polymorphism of this gene allows females with different versions of the opsin gene on each of their two X chromosomes to achieve trichromacy. Males, with only one X chromosome, can never be trichromats in species that rely on polymorphism. Tan and Li (1999) have argued that the phylogenetic distribution of the M and L opsins across strepsirhine primates (lemurs, lorisids, and tarsiers) supports the idea that the X-linked polymorphism and primate trichromacy arose early in primate evolution. It is interesting that, regardless of whether trichromacy is achieved via polymorphism of a single gene on the X chromosome as in New World simians or on two separate genes on the same chromosome as in Old World simians, it would appear that the M/L (green/red) opponency can be identified electrophysiologically in some P cells in both cases but not so far in K cells (White *et al.*, 1998). This would support the view that M cone input to P cells via midget ganglion cells was the default condition in dichromatic primates with L cone opponency added later. Whether the P pathway further specializes when trichromacy is the norm as in Old World simians, one branch of New World primates, as well as apes and humans, remains unclear (Jacobs, 2002).

One aspect of the chromatic pathway to V1 that appears to show species-specific differences concerns the S cone input to V1 layer IIIBβ (IVA of Brodmann). Callaway and colleagues (Chatterjee and Callaway, 2003) have shown that, in macaque monkeys, cells in layer IIIBβ respond to S cone input in the form of blue ON- and blue OFF-center cells. Since thalamic axons project to layer IIIBβ in many diurnal simians but not in the nocturnal owl monkey, the prosimian bush baby, or in some apes (chimpanzee), or in humans, this pathway appears to be a specialization of some primates and not others (Preuss and Coleman, 2002). These findings indicate that apes and humans may have diverged from a primate ancestor in which the K pathway carrying S cone input did not innervate layer IIIBβ. In macaque monkeys, there is no physiological evidence for a direct S cone input via the thalamus to the CO blobs based upon recording from LGN axons in V1 where cell responses were silenced with the $GABA_A$-receptor agonist muscimol (Chatterjee and Callaway, 2003). Presumably, S cone input reaches cortex via another pathway in apes and humans. Taken together, these observations support the hypothesis that components of the K pathway may either have been lost in the evolution of apes and humans or that their common ancestor showed a parallel pathway organization more like that of present-day prosimians where the thalamus does not project to layer IIIBβ.

4.05.6 Ocular Dominance and Other Properties

At the level of the LGN in primates, retinal ganglion cells within the left and right eyes send input to separate layers. Additionally, ganglion cells with either ON-center or OFF-center responses innervate separate sets of cells at the level of the LGN. These parallel pathway features from retina to LGN appear to generalize across placental mammals. At the level of V1, however, the degree to which these properties remain segregated at the first synapse varies widely among mammals (see Casagrande and Norton, 1991, for review). For example, although close relatives of primates (e.g., tree shrews) show both ocular segregation and segregation of ON- and OFF-center responses to separate cortical layers, primates do not. Instead ON- and OFF-center responses appear combined at the first synapse in all primates examined to date, even

Table 2 Ocular dominance columns in striate cortex

Columns present	*Columns present*	*Columns absent*
Macaque (Hubel and Wiesel, 1969)	Talapoin monkey (Florence and Kaas, 1992)	Rat (Hubel and Wiesel, 1977)
Human (Hitchcock and Hickey, 1980; Horton and Hedley-Whyte, 1984)	Capuchin monkey (Hess and Edwards, 1987; Rosa *et al.*, 1988)	Mouse (Drager, 1974)
Owl monkey (Rowe *et al.*, 1978; Diamond *et al.*, 1985)	White-faced saki (Florence and Kaas, 1992)	Tree shrew (Casagrande and Harting, 1975; Hubel, 1975)
Marmoset (DeBruyn and Casagrande, 1981; Spatz, 1989)	Chimpanzee (Tigges and Tigges, 1979)	Gray squirrel (Weber *et al.*, 1977)
Green vervet (Hendrickson *et al.*, 1978)	Cat (Shatz *et al.*, 1977)	Brushtailed possum (Sanderson *et al.*, 1980)
Red monkey (Hendrickson *et al.*, 1978)	Ferret (Law *et al.*, 1988)	Rabbit (Hollander and Halbig, 1980)
Baboon (Hendrickson *et al.*, 1978)	Mink (McConnell and LeVay, 1986)	Sheep (Pettigrew *et al.*, 1984)
Spider monkey (Florence *et al.*, 1986)	Bush baby (Glendenning *et al.*, 1976; Hubel and Wiesel, 1977; Diamond *et al.*, 1985)	Goat (Pettigrew *et al.*, 1984)

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though ON- and OFF-center cells have been reported by some to be segregated to separate layers in the macaque LGN (Schiller and Colby, 1983). The finding that ferrets, but not cats, show segregation of ON and OFF pathways through the LGN to V1, suggests that parallel ON and OFF pathways that extend to cortex evolved several times in different mammalian lines of descent (Zahs and Stryker, 1988). The advantage of maintaining separability of ON and OFF pathways to cortex in diurnal tree shrews and nocturnal ferrets remains unclear given that these species have very different lifestyles and evolutionary histories.

Similarly, although eye input remains segregated at the first cortical synapse in cortex in tree shrews and many other mammals including some primates, the variability in both the pattern and degree of segregation of ocular inputs suggests that the organization of ocular dominance pathways from LGN to cortex evolved independently in primates and other mammalian species. In tree shrews, left and right eye input to cortex is segregated into sublayers within layer IV of V1 (Casagrande and Harting, 1975), whereas in all primates ocular input segregation (if present) occurs in the form of columns not layers. Among primates, examples of well-developed cortical ocular dominance columns can be found in some members of a number of distantly related groups including prosimian bush babies, New World simian spider monkeys, and all Old World simians and apes thus far examined, including humans (Florence *et al.*, 1986; Florence and Kaas, 1992; Preuss and Coleman, 2002; see Table 2). Even in primates in which ocular dominance columns show high interindividual variability, such as New World squirrel monkeys, or show very weak segregation, as in New World owl monkeys and marmosets, segregation occurs in the form of columns and not in the form of layers as in tree shrews (Florence *et al.*, 1986). These findings suggest that the tendency to segregate ocular information into columnar dominance columns in V1 was present already in the common ancestor of primates but not in the ancestor of tree shrews and primates.

Examination of the different patterns of ocular dominance columns in different primate species, however, indicates that well-developed ocular dominance columns either evolved several times in different lines of descent or regressed in different lines of descent from a well-developed pattern (Florence *et al.*, 1986; Florence and Kaas, 1992). Distinguishing between these different scenarios is difficult given that we do not understand the functional significance of ocular dominance columns since they appear to occur in both small nocturnal primates with no color vision and in large diurnal primates with good color vision, and appear variable across simians (Florence *et al.*, 1986). It may also be the case that such segregation is simply a byproduct of the degree of synchrony between active ganglion cells in the two eyes during a critical phase of development, especially since the expression pattern shows such a high degree of interindividual variation in squirrel monkeys (Horton and Hocking, 1996).

4.05.7 The Evolution of Dorsal and Ventral Cortical Streams

It has been proposed that there are basically two cortical streams for processing visual information

in primates – a ventral stream to the temporal lobe and a dorsal stream to the parietal lobe – the first being involved with object vision and the second with spatial vision or vision for action (Mishkin *et al.*, 1983). The dorsal and ventral streams both start with the intracortical circuitry in V1, which processes the three main classes of LGN inputs described earlier (M, P, and K) to create multiple distinct outputs originating from separate classes of projection neurons in cortical layer III and projecting to several different extrastriate areas. Two hierarchical chains of connections, one to the temporal lobe and one to the parietal lobe (albeit with some connections between areas and compartments belonging to the different streams), can be traced through the multiple (more than 30) extrastriate areas found in primates (DeYoe *et al.*, 1994).

The ventral stream, in order, consists of layer IIIBα blobs and layer IIIBα interblobs in V1, thin stripes and interstripes in the secondary visual cortex (V2), DL/V4, and various inferotemporal areas. The temporal areas at the top of this hierarchy are physically close to and interconnected with perirhinal cortex and hippocampus, structures involved with object recognition and encoding visual memories. The dorsal stream consists of layer IIIC and layer IIIBα interblobs, which give rise, respectively, to a direct and an indirect pathway via V2 to V5/MT, CO thick strips in V2, MT/V5, and surrounding superior temporal areas, and, finally, parietal cortex. These parietal areas are close to, and interconnected with, premotor cortical areas involved with programming eye movements and other visually guided behaviors. In this section, we examine the evolution of these processing streams. We will first consider the early stages of processing through V1 and V2, and then the later stages through specialized extrastriate areas.

To review, in primates, M LGN afferents terminate in upper layer IV, P afferents in lower layer IV, and K afferents in the blobs in layer IIIBα and in layer I. As mentioned in previous sections, these pathways likely have homologues in other mammals, so the building blocks for the two streams will at least be homologous structures. Immediately above the M input layer is found a population of projection neurons that are an important early part of the dorsal pathway, receiving M input and projecting directly to V5/MT. These cells are found in all primates, where they may be pyramidal (prosimians) or stellate (Old World monkeys) or both (New World monkeys). In cats, large pyramidal cells at the base of layer III receive Y-cell input and project to lateral suprasylvian cortex (Matsubara and Boyd, 2002), which is, like V5/MT, an area that processes motion (see below). These projections are probably homologous. In cats, prosimians, and New World primates, these projections are robust, and are concentrated directly below CO blobs. In macaque monkeys, there are far fewer MT-projecting cells in V1 and it has been debated as to whether or not these are concentrated beneath CO blobs (Boyd and Casagrande, 1999; Boyd and Matsubara, 1999; Sincich and Horton, 2003). This could represent a gradual evolutionary reduction of the fast direct pathway to V5/MT in primate evolution, and perhaps of the entire dorsal stream, as increased emphasis is placed on slower indirect pathways passing through upper layer III, which is proportionately thicker and more differentiated in primates (especially simians) then in other mammals. This scenerio suggests a change in visual processing, with more emphasis on analysis of visual form and less emphasis on reaction to movement.

The indirect dorsal stream through V2 originates from neurons in layer IIIBα interblobs that probably receive both M and P input via intralaminar projections from layer IV. The neurons of the ventral stream to V2 are in layer IIIBα blobs and interblobs, and so receive K input in addition to M and P. In species with color vision, the K input may carry color information (see previous sections), an important cue for object recognition but not for visuomotor tasks. Within V2, recent evidence points to the existence of four stripe compartments, two which stain darkly for CO (the CO thick and thin stripes) and receive input from dorsal and ventral stream neurons in V1, and two interstripe compartments that may also receive from both streams but definitely get input from ventral stream neurons in V1 (Xu *et al.*, 2004). In some prosimians, CO stripes are faint or absent in V2, but there still is evidence that projections from blobs and interblobs are segregated into different compartments within V2, so the striped architecture likely is homologous across all primates. There is no clear example yet of a similar striped architecture (with or without accompanying CO staining) in nonprimates. There is some evidence for segregation of blob and interblob projections to extrastriate areas in the cat, but this occurs not in V2, but in area 19. The cortical hierarchy in primates continues through V2 into V5/MT for the dorsal stream, and into V4/DL for the ventral stream. Again, although the prosimian galago does not have distinct CO stripes or functional compartments with low orientation selectivity as in simians (Xu *et al.*, 2005), neurons projecting from V2 to V5/MT and to V4/DL form interdigitated stripes (Krubitzer and Kaas, 1986), showing that the underlying architecture (albeit perhaps less complex) is the same in prosimian V2 as for other primates.

Thus, the earliest levels of the dorsal and ventral streams can be recognized in all primates. Can the same be said of the higher levels? This is an important question because an increase in neocortex size and an increase in the number of sulci and gyri have occurred independently in the evolution of different mammalian lines, and even in the evolution of different primate lines. Both Old World primates and sheep, for example, have large, gyrencephalic brains, but examination of fossil endocasts suggests that their last common ancestor had a small lissencephalic brain (Radinsky, 1967, 1975, 1981). Not surprisingly, sheep and primate neocortex, while superficially similar, show important differences, as, for example, the relative development of the temporal lobe, which is proportionately less prominent in sheep brains than in primate brains, and the olfactory cortex, which in sheep is proportionately enormous by primate standards. Also, the obvious occipital development and landmarks that characterize the primate visual cortex such as the calcarine fissue are not obvious in sheep (nor in other nonprimate mammals) in spite of the fact that other fissures are well developed and the sheep brain is larger and more fissured than many primate brains. In summary, primitive mammals had small brains and likely possessed only a few cortical areas for each sensory modality, perhaps only V1 and V2 for vision (Northcutt and Kaas, 1995). The number of extrastriate visual areas has increased independently in different mammalian lines, so it might be impossible to define homologies across mammalian groups for many extrastriate areas.

Even within the primate lineage, the patterns of sulci and gyri vary between New World and Old World monkeys, apes, and prosimians, and brain size has increased independently in these lines. It is therefore important to determine which of the multitude of visual areas can be unambiguously identified in all primates and are thus likely to be homologous. Homologies among visual areas in different primate lines are recognized on the criteria of size, shape, and position in the cortex with respect to other cortical areas, layout of the visual field map, physiological response properties, patterns of connections with other cortical areas and subcortical structures, and cortical architecture. For example, the V1 can be recognized, not just in primates but also in all mammals, by its position in the occipital lobe, by receiving strong projections from the LGN, by the complete map of the visual field it contains, and by its distinctive histological architecture.

In all primates (and likely all mammals), V2 forms a narrow strip immediately lateral to V1. In addition to its position, it can be recognized by its visual field organization, sharing a representation of the vertical meridian with V1, and by its distinctive mosaic pattern of connections with V1, which are related to the CO architecture (Casagrande and Kaas, 1994). In all primates, an important dorsal stream area, called MT (sometimes referred to as V5) in Old World primates, New World primates and prosimians, occupies a densely myelinated oval-shaped area in the dorsal temporal lobe. This area contains many motion-sensitive neurons, most selective for the direction of stimulus motion. MT/V5 is also identified by its distinctive patterns of projections from V1 and V2, and by its projections to parietal cortex. In all primates, an important ventral stream area, called V4 in Old World primates and DL in New World primates and prosimians, occupies cortex caudal to V5/MT and receives inputs from compartments in V2 not projecting to V5/MT. The homology, however, of this region is less well established, perhaps due to uncertainties in the extent and possible subdivisions of this region of cortex, as it does not have a distinctive architecture, and its visual field map is not as regular as that of MT. Proposed homologies of primate cortical areas higher in the hierarchy are even more tenuous, for similar reasons. It is possible that more homologies will become apparent when the cortical organization of different primates becomes better understood. (This presupposes that regions of cortex outside of primary areas and certain easily identifiable areas such as V5/MT are, in fact, best described as collections of discrete areas with sharply defined borders, and not as larger fields of loosely graded response properties and connections.) With presently available information, then, only areas on the lower levels of the visual-processing hierarchy can be homologized across different primate species, suggesting that areas higher in the hierarchy were added independently in different primate lines. Even so, the dorsal and ventral streams in different primate lineages can be identified without concomitantly identifying homologues for all of the visual areas involved.

Is it possible to identify dorsal and ventral streams in other mammals, given that so few extrastriate areas are likely to be homologous between primates and other mammals? As suggested above, processing in the dorsal and ventral streams prepares visual information for the ultimate use by motor cortex and limbic cortex, respectively, structures that are likely homologous in all mammals. Even if the primitive mammalian visual system consisted of a single area, V1 (although V2 at least was likely also present in the earliest mammals), separate

dorsal and ventral streams could still exist, consisting of separate populations of V1 neurons projecting directly to motor and limbic cortex, respectively. As was suggested to be the case for different primate groups, extra areas could be inserted to form processing hierarchies independently in different mammalian lineages. Inserting areas between V1 and limbic cortex will route the ventral stream through the temporal lobe based on simple proximity to the hippocampus. Similarly, inserting areas between V1 and motor cortex will result in a dorsal stream through parietal cortex.

There is evidence for dorsal and ventral streams in mammalian lineages as different as carnivores and rodents, both of which have multiple extrastriate visual areas that are unlikely to be homologous with any primate areas. The cat has about 15 different extrastriate areas and, as a model species, has the rare advantage that many of these areas have been extensively investigated (Payne, 1993). Evidence for dorsal and ventral streams in cats comes from studies of connections, physiological response properties, and behavioral deficits. Similar to V5/MT in primates, an area in the lateral suprasylvian (LS) sulcus of the cat receives a direct input from V1, projects to parietal and visuomotor areas, and displays motion selectivity. Inactivating this area leads to visual orienting and motion processing deficits (Lomber, 2001), as would be expected from a dorsal stream area. The cat also possesses a temporal visual stream consisting of multiple areas progressing through the temporal lobe to the hippocampus. As would be expected for the ventral stream, inactivation of the temporal lobe areas does not impair visual orienting behavior (Lomber, 2001).

The similarities between V5/MT and LS cortex are strong enough that it has been proposed that these areas are homologous (Payne, 1993). If V5/MT was present in the last common ancestor of cats and primates (more than 65 Mya), one would expect it to also be present in all mammalian lines that share a common ancestor with either cats or primates that is more recent than their last common ancestor (Northcutt and Kaas, 1995). Current mammalian classifications place primates in the superorder Euarchontoglires along with Glires (rodents and rabbits), flying lemurs, and tree shrews. As carnivores, cats are members of the superorder Laurasiatheria, which also includes insectivores, bats, ungulates, and whales (Madsen *et al.*, 2001; Murphy *et al.*, 2001; Waddell *et al.*, 2001; Amrine-Madsen *et al.*, 2003). Thus, if V5/MT and LS are homologous, a similar area should be identifiable in other members of these two superorders; such identifications are currently hampered by lack of data from relevant species.

For Euarchontoglires, at least partial data on extrastriate cortical organization are available from tree shrews and some rodents. Tree shrews have a series of visual areas adjoining V2, one of which, the temporal dorsal area (TD), has been proposed as a possible homologue for MT. Like MT, TD contains a complete representation of the visual field (Sesma *et al.*, 1984), stains more strongly than surrounding cortex for myelin and the Cat-301 antibody (Jain *et al.*, 1994), and receives inputs from V1 (Lyon *et al.*, 1998). However, TD in tree shrews is adjacent to V2, unlike MT, which is separated from V2 by DL/V4, and TD appears to lack connections with visuomotor areas of frontal cortex (Lyon *et al.*, 1998), which is part of the connectional signature of MT in at least some primates (Krubitzer and Kaas, 1990). No data on the detailed response properties in TD are currently available, so it is not yet known if this area contains direction-selective neurons.

The organization of extrastriate visual cortex in rodents is not completely clear, and appears to show substantial species variability (Rosa and Krubitzer, 1999). Germane to the present discussion is that rodents are thought to be monophyletic, and that mice and rats share a more recent common ancestor than either do with squirrels (Reyes *et al.*, 2004). In squirrels, V2 forms the lateral border of V1, with at least two tiers of multiple extrastriate areas lateral to it (Kaas *et al.*, 1972, 1989). In the rat, microelectrode mapping studies suggest that V1 is bordered laterally, not by a single area V2, but by multiple small retinotopically defined extrastriate visual areas named topographically (rostromedial, anterolateral, lateromedial, posterolateral, etc.) and corresponding to regions free of callosal connections (Espinoza *et al.*, 1992; Montero, 1993). Injections of tracers in different retinotopic locations in V1 lead to changes in the location of patches of label within these extrastriate areas that is consistent with the electrophysiological maps (Coogan and Burkhalter, 1993; Montero, 1993), mitigating against the argument that these projections correspond to multiple modules within a traditional retinotopically mapped V2 which, similar to other mammalian groups, extends along the entire lateral border of V1 (Malach, 1989). In mouse, microelectrode mapping shows a single V2 bordering V1 laterally, with at least one other area lateral to that. However, corticocortical projections from mouse V1 had a similar pattern as in the rat (Olavarria and Montero, 1989), suggesting that multiple visual areas adjacent to V1 were common at least to mice and rats. In order to resolve the

differences in cortical organization between different rodent species, it has been assumed that the largest of the areas bordering V1 laterally in rats (the lateromedial area, LM) is homologous to V2 in other species (Rosa and Krubitzer, 1999). According to this hypothesis, either new areas adjoining V1 were added in the mouse/rat lineage, or regressive events caused more lateral visual areas (perhaps homologous to the lateral visual areas in squirrels) to be shifted toward V1, at the expense of V2. A recent optical imaging study of mouse visual cortex (Kalatsky and Stryker, 2003), however, not only found evidence for multiple retinotopically defined extrastriate areas, but also suggested a narrow V2 with only a central visual field representation; detailed optical imaging maps of rat extrastriate cortex have not yet been published. The many patches following a V1 injection, and the tendency of visual fields to be congruent across borders, means that V1 projections to a narrow V2 could be continuous with a patch of labeling in an adjacent area, and thus overlooked in the anatomical mapping studies. The coarse sampling of microelectrode mapping, combined with the large receptive fields, may also have made it possible to have missed a narrow V2. Projections from V1 need to be combined with functional mapping and histological verification of the extent of V1 to determine if there really is a narrow V2 interposed between V1 and the lateral extrastriate areas in rats and mice.

Returning to the original question of functional streams, areas responding preferentially to moving stimuli can be found in both squirrels and mice/rats. In rats, the anterolateral area (AL) appears to have cells selective for movement (Montero and Jian, 1995), while, in mice, AL and another area (LM) bordering V1 laterally give rise to different connectional streams, AL preferentially connecting with dorsal and medial regions of cortex, LM with ventral regions of cortex (Wang and Burkhalter, 2004). In ground squirrels, an area (ML) with large receptive fields and direction-selective cells was found lateral to V2 (Paolini and Sereno, 1998), and thus in the right position to be homologous with MT. Both AL in rats and mice and LM in squirrels receive direct projections from V1, which is another similarity with V5/MT, although neither area appears to have the extensive myelination, an anatomical signature of V5/MT.

On the cat (Laurasiatheria) side, there is even less evidence from which to draw conclusions. It does appear that LS cortex, at least, has homologues in fellow carnivores, the mustelid ferrets (Manger *et al.*, 2002). Another laurasiatherian animal whose extrastriate cortex has been mapped is the megachirpopteran flying fox (*Pteropus*). Although once thought to be more closely related to primates than to michrochipoteran bats, all bats are now thought to comprise a single group within the Laurasiatheria (Van Den Bussche *et al.*, 2002). The occipitotemporal visual area (OT) was proposed as a possible megachiropteran homologue to LS/V5/MT based on its location lateral from V2, and its receptive field organization (Rosa, 1999). Microbats, relying on echolocation for navigation, have an enlarged auditory cortex, and very little extrastriate visual cortex. If this is a primitive condition for bats, it would mitigate against any proposed homologies of megachiropteran visual areas, given that bats are likely monophyletic. It is also possible that extrastriate cortex may have been reduced during microbat evolution.

In conclusion, specialized extrastriate areas belonging to dorsal and ventral cortical streams can be recognized in a wide range of mammals. Only the earliest stages of these streams and the last stages in motor and limbic cortex are likely to be homologous across mammalian lines, however. Even within primates, only a few areas can be unequivocally identified as homologues. Different lineages have added areas to the middle levels of these cortical streams independently. The constraint of proximity of the inserted areas to limbic cortex or motor cortex keeps the temporal stream temporal and the dorsal stream dorsal.

4.05.8 Conclusions, Questions, and Future Strategies

What can we usefully conclude about the evolution of parallel pathways in primates? We need to constantly remind ourselves that without specific definitions of what we are comparing and at what level (genes, molecules, cells, or pathways), we cannot develop definite or testable hypotheses. In this article we have focused on pathways originating with distinct classes of retinal ganglion cells and asked whether homologues of these visual pathways can be found across different primate species or between primates and nonprimates. We hypothesized that examining for similarities across distantly related species is the most important initial step in arguing for homology given the lack of genetic and fossil signatures of visual pathways. Nevertheless, we remain cognizant of the fact that different regions of the nervous system (e.g., retina, thalamus, and cortex) have different patterns of gene expression controlling their cellular composition and distribution. Therefore, we cannot simultaneously address the issue of homology at different levels of comparison (i.e., proteins, cells,

pathways, or brain regions). It is even more difficult to determine if similarities result from homology or homoplasy given that the developmental programs that establish visual cells and pathways are conservative and presumably have a restricted set of viable functional solutions for species to survive using the visible portion of the energy spectrum here on earth. Therefore, a useful future approach would be to compare the ontogeny (both early and late) of distantly related primates (e.g., a prosimian with a New World simian and an Old World simian) and primates and nonprimates (e.g., macaque monkey with rodent) examining for similarities at both the genetic and systems levels. A fuller understanding of commonalities in the ontogeny of different species would aid enormously in examining for homology in visual pathways.

Our examination of P, M, and K pathways leads to the hypothesis that these pathways are homologous across primates in spite of vast differences in the lifestyles and retinal organization in different primate species. It is also likely that what we call the P, M, and K pathways have general counterparts in other mammals since cats certainly appear to have pathways that specialize in spatial versus temporal resolution (i.e., X vs. Y cells) in a similar way to P and M cells in primates; W cells also resemble K cells anatomically and physiologically. Nevertheless, details of these pathways in nonprimates (even close relatives like the tree shrew) differ significantly; so significant changes have occurred independently in the P, M, and K pathways of different lineages.

We have also argued that the K pathway may be made up of more than one pathway so its evolutionary history is more difficult to try to define. Nevertheless, it does appear that cells in this pathway across a range of species can be recognized by the presence of calbindin. Other similarities to W cells in cats and other mammals suggest that a K-like pathway may have originated early in mammalian evolution. This does not necessarily make the primate K-cell pathway phylogenically older or newer than the P and M pathways since the K pathway shows enormous variability in the relative numbers of cells present in different LGN layers (identified neurochemically) across different primate species. What would be useful to know is which ganglion cells actually project to K layers in different primates and in close primate relatives such as tree shrews. For example, do bistratified ganglion cells project uniquely to K layers in tree shrews as would be predicted from work in macaque monkeys? This easily tested question would reinforce the view that some K cells evolved prior to the split between tree shrews and primates. Examining the same issue in cat W cells would extend the evolution of this component of the K pathway to other mammals.

A closely related issue concerns the evolution of chromatic pathways in different primates. Since some K cells receive input from S cones in some New World (marmosets) and Old World (macaque monkeys) primates, and K cells carrying S cone signals project to cortical layer IIIBβ in macaque monkeys, it will be important to understand how S cone signals are transmitted to V1 in primates such as apes and humans that lack an LGN projection to cortical layer IIIBβ. Such information could potentially inform us about the evolutionary split between monkeys and apes. Similarly, it would be informative to know if tarsiers or any diurnal lemurs that have functional S cones send these signals via K cells to cortical layer IIIBβ.

We have argued that, since nocturnal prosimians, such as bush babies, have the S cone gene (even though it is not functional) in addition to functional M cones, and that other prosimians (and tarsiers) also have both M and S cones, it is likely that earliest ancestors of primates were dichromatic like present-day tree shrews. If all nocturnal prosimians, however, show the same defect in the S cone gene, this would argue in favor of a nocturnal bottleneck. Alternatively, if distantly related nocturnal primates, such as galagos and owl monkeys, show that S cone genes were disabled in different ways, this would argue that the lack of functional S cones evolved secondarily when species moved from a diurnal to a nocturnal niche.

We reviewed also the evidence that segregation of ON and OFF pathways and segregation of left and right eye inputs (ocular dominance columns) evolved independently in different lines. ON and OFF pathways are combined at the first level in all primates examined, and the tendency to segregate ocular inputs into columns, although variable across primate species, exists in distantly related primates. These observations support the presence of at least weak ocular dominance segregation into columns in the common ancestor of primates and support the view that the ON and OFF pathways were not segregated to columns or layers in a primate ancestor. Why ocular dominance columns exist in primates remains a mystery. Given the high inter-animal variability of ocular dominance columns in squirrel monkeys, it might be useful to examine both the genetics and visual experience of animals that do with those that do not appear to show clear columns. It would also be useful to examine for ocular segregation in a wider range of primates.

Finally, we examined the most difficult issue, namely the evolution of dorsal and ventral cortical pathways originating in V1. Given that there is

disagreement even about the definitions of cortical areas that receive input from V1, we cannot provide solid conclusions about the homologies of dorsal and ventral streams beyond the statement that there is evidence for sets of projections to similar hierarchies of areas in all primates thus far examined. There is also evidence that the general cortical design for such streams may exist in nonprimate mammals even if specific cortical areas within each hierarchy are not homologous. Clearly, much more evidence concerning the number of visual areas in a range of primates and other mammals will need to be examined before more definitive statements can be made. Perhaps with the advent of high-resolution functional magnetic resonance imaging we will be in a position to more rapidly map visual areas in a variety of species.

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