Pathways to colour in the retina

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ABSTRACT

The description of colour pathways in the primate retina has become clearer within the past decade. I summarize here current views as to the pathways subserving colour vision in the primate retina, beginning in the receptors and outer retina and leading to the mechanisms in inner retina which add and subtract the receptor signals. Although the main features of colour pathways are now well defined, there remains uncertainty as to some of the wiring details. In particular, the question as to how much connectional specificity is present is unresolved.

1. INTRODUCTION

Primates are the only mammals to possess trichromatic vision. All Old-World primates including human appear to possess similar colour vision, and the Old-World species serve as an animal model for our perception of colour and form. The New-World primates show a considerable variety of phenotypes and genotypes. The evolution of red-green colour vision in primates has its origin in the opsin genes on the X-chromosome, but the retina must also have evolved to accommodate this new dimension of visual experience. The retinal mechanisms which underlie our processing of chromatic information have become better understood in the past decade or so. This has come about by more sophisticated techniques for anatomical investigation of the retina and more sophisticated approaches to assessing the physiology of retinal neurons. A major advance has also been the development of a viable *in vitro* preparation of primate retina in which it is possible to record from neurons and then stain them for later identification[1]. It has become clear that the primate retina possesses some unique features. Some of these may be due to the superimposition of red-green colour vision onto a standard mammalian retinal plan. I discuss recent developments in retinal anatomy and physiology and attempt to highlight the features of retinal colour processing in the primate which are unique, unexpected or unexplained.

The cone photoreceptors and outer retina

Trichromacy begins in the short- (S) middle- (M) and long-wavelength (L) sensitive cones. It is possible to selectively stain the S cones to reveal their numerosity and distribution. In all primates they make up ~5-10% of cones, are absent or relatively sparse at the fovea and show a similar distribution as a function of retinal eccentricity. However, there are interesting differences in the local distribution of S cones; in some species they form a regular, hexagonal mosaic but in others their arrangement appears more random[2]. The reason for this difference is unknown. The middle (M) and long (L) wavelength sensitive cones cannot be distinguished by staining methods, but it has recently become possible to image the photoreceptor mosaic in the living eye and to identify the L and M cones[3]. These elegant studies have revealed that there is considerable variation among individuals in the relative proportions of L and M cones, as long posited based on individuals' different spectral sensitivities in photometric tasks. At the time of writing, it is thought that the arrangement of the L and M cones is random; early indications of a slight degree of order have been shown to be artifactual[4]. These issues are important for understanding of colour vision in the retina, since modelling of retinal cell behaviour often depends critically on assumptions as to cone distribution.

Following the receptors, in outer retina horizontal cells make specific contacts to the cones. There are now thought to be only two types of horizontal cell in primate, one (HI) making contacts with L and M cones and avoiding S cones and another (H2) making substantial contacts with S cones

but making some contact with the L and M cones[5]. This principle may be seen in the anatomical diagram of Fig. 1. All cone inputs hyperpolarize the horizontal cells, and so the situation in the primate differs fundamentally from that in non-mammalian vertebrates, in which the first stages of colour opponent processing are evident in the responses of the horizontal cell[6]. Other mammals possess two horizontal cell types, but it is not yet known if they show similar specificity of cone connectivity. The high degree of connectional specificity of horizontal cells is presumably important for chromatic processing, but how and why is unclear. It is often assumed that horizontal cells are involved in some way with gain controls or spatial processing in outer retina. It has been shown however that gain controls in primate outer retina are cone specific and spatially local[7], as found psychophysically[8]. This might be inconsistent with substantial feedback from horizontal cells onto cones (as occurs in the elaboration of opponency in non-mammalian vertebrates). Thus, the role of horizontal cells (if any) in the elaboration of cone opponency and receptive field structure remains controversial.

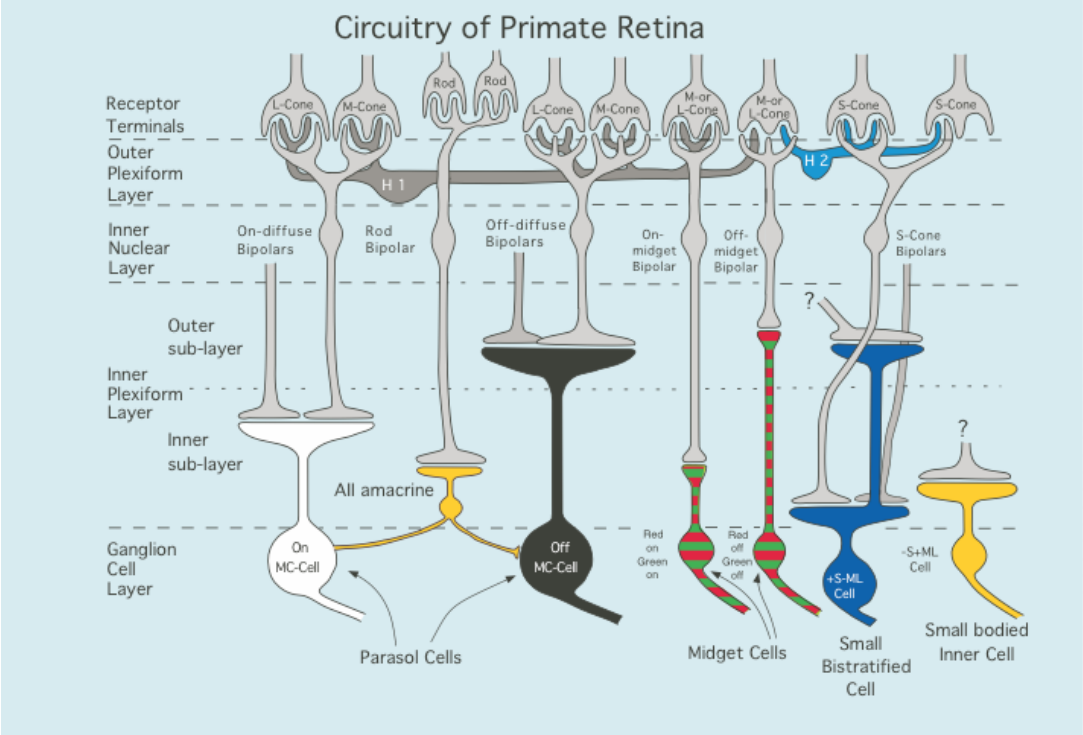

Fig. 1: A sketch of the current view of the wiring diagram of primate retina including the main cell classes which project to the thalamus.

The origins of colour opponency: the blue-yellow pathway

At the ganglion cell level, cone signals are added and subtracted to provide cell systems which form the basis of the luminance and chromatic channels of psychophysics. The main classes of ganglion cell which project to the lateral geniculate nucleus are sketched in Fig. 1. Parasol ganglion cells receive summed input from the M and L cones and there are on and off-center varieties, each receiving input from on or off diffuse bipolar cells. They project to the magnocellular (MC) layers of the lateral geniculate nucleus (LGN) and form the basis of a psychophysical luminance channel[9, 10].

Two systems elaborate chromatic signals in the primate retina. One of these involves differencing the S cone signal with the summed signals of the M and L cones. The +S-(L+M) cell has been identified as the small bistratified ganglion cell[11]. The inner layer of dendrites receives input from the (on) S cone bipolar, and the outer layer may receive input from off bipolars with L and M cone input, and so provide opponency. Most recently, an additional, sparse cell type with excitatory S-cone input has been identified following retrograde labeling from the LGN[12] but details are not yet available. The existence of a disputed –S+(L+M) cell type has long been established

physiologically[13], but this has now been tentatively identified by retrograde labeling as an inner stratifying neuron with a relatively large dendritic tree[12]. These sets of ganglion cells form the basis of a 'blue-yellow' system of colour vision. It has been argued that this system is phylogenetically ancient[14] and thus equivalent cell systems should be present in mammals other than primates. These ganglion cells are now considered to belong to the koniocellular pathway, a collection of LGN-projecting cell types which may predate the main parvocellular (PC) and MC systems.

The electrophysiology of these S cone cell types has only been studied extensively for the +S-(M+L) cell. The receptive fields of the excitatory and inhibitory cone inputs appear to be largely overlapping, i.e., Type II (D.M. Dacey and B.B. Lee, unpublished observations). Their temporal response is low-pass, i.e., they are sustained, and extends up to 20-30 Hz[15]. On the other hand, psychophysically the S cone pathway has long been considered to have a poor temporal response, not able to resolve frequencies greater than a few Hertz[16]. The brief impulse response of the S cone[17] and the fast response of +S-(M+L) cells indicates that this slow temporal response is a result of temporal filtering at a cortical site[15]. The S-cone system appears to share this filtering with the red-green system.

The red-green pathway; a primate novelty

The second chromatic system in the primate retina involves the differencing of signals from the M and L cones. Such differencing optimizes transmission of information leaving the retina. The development of this pathway in primates must have resulted in significant modification of the standard mammalian retinal plan, and development of cortical mechanisms to handle this information.

Midget ganglion cells, which project to the parvocellular (PC) layers of the LGN, are thought to form the basis of the psychophysical red-green channel; the suggestion that there may be an additional red-green chromatic system[18, 19] has not found experimental support. The textbook model for this system is that single M and L cones provide input to midget bipolar cells which in turn contact a single retinal ganglion cell, as sketched in Fig. 1. The chromatic specificity of the system arises partly because of the selective contacting of a single cone. Early physiological studies of these cells[20] revealed that they could be classified as either 'red on-center', with presumably input from a single L cone in the center, 'green on-center', with input from a single M cone, and corresponding off-center types, as in Fig. 1. Although early studies also reported achromatic cells within the parvocellular layers of the LGN[20], more sophisticated electrophysiological tests revealed almost all PC cells to be red-green opponent[21, 22]. Also, this pathway shows chromatic characteristics expected of a physiological substrate of a psychophysical red-green detection mechanism.

The simple plan of midget connectivity remains essentially valid, but a number of features of the pathway have become apparent which have made the picture more complex and underlined its unique nature. One of these is reflected in the fact that the midget ganglion cells in Fig. 1 are drawn in red-green zebra stripes. This is to emphasize that the red and green on-center midget cells are anatomically identical and form a *single* retinal matrix, and similarly for the off-center cells. Most classes of retinal neurons form a semi-regular array across the retinal surface (e.g.,[23]). With the exception of the cones themselves, cells within a given array have similar physiological properties. However, in the case of the midget system there is only one array each of midget on- and off-center ganglion cells so that, for example, red on-center and green on-center cells share the same array. This is a most unusual arrangement and presumably reflects the fact that, on the development of red-green colour vision in primates, a novel dimension of chromatic information had to be encoded by existing ganglion cell classes; presumably a precursor of the midget ganglion cell was taken over for this purpose. The price to be paid was a sharing of two diametrically opposite chromatic attributes within a cell class, which must have posed intriguing problems for central interpretation of the chromatic signal.

The question of how specific are cone inputs to midget ganglion cell centers and surrounds is not fully resolved. In the periphery many bipolar cells provide input to a midget, PC ganglion cell (these peripheral cells are usually called 'midget' despite their lack of midget morphology; all project to the PC layers of the LGN, and the transition from midget to peripheral morphology is gradual). Psychophysically, red-green chromatic sensitivity decreases substantially in the periphery and it was

proposed that this was due to a physiological loss of M,L cone opponency in peripheral PC cells due to mixed cone inputs to the center[24]. However direct measurement shows that peripheral PC cells are just as responsive to red-green modulation as central cells[25]. From a retinal viewpoint, the high chromatic responsivity of peripheral PC cells implies that connectivity to midget bipolars cannot be random; if so, calculations showed that little chromatic opponency would be expected[25].

The specificity of cone inputs to the surround has also been a matter of debate. Early studies (e.g.,[26]) assumed that the surround was cone specific but the differential adaptation techniques used to identify cone inputs begged the question. It was then shown that it was theoretically possible to achieve M,L cone opponency with random sampling of cones by the surround; a single cone center was enough to generate a chromatic response[27]. However, if the surround were mixed, then if, for example, a midget cell received input from a single L cone in the center and the L cone also provided input from the surround, then spatial antagonism should be detectable if just the L cone is modulated. Physiological studies have failed to show such antagonism[28-30]. On the other hand, anatomical investigations have failed to turn up any suggestion of cone-specific connectivity within the amacrine cells which could form the surround[19].

Physiological characteristics of red-green opponency

As mentioned above, L- and M-cone inputs to PC cells distribute close to a 1:1 ratio. The temporal response of PC cells extends to 30-40 Hz, as with +S-(M+L) cells. Flicker fusion of human observers to red-green chromatic modulation is 10-15 Hz, so central low-pass filtering of these cells' signals must take place[31]. There are two possible reasons why these high frequencies are not used psychophysically. Firstly, the chromatic information carried by the cell may become difficult to interpret. A center-surround latency difference of a few milliseconds[32] causes response amplitude to depend not only on the chromatic composition of the stimulus but also on frequency, so that at high frequencies the chromatic message is confounded. Secondly, the center-surround latency difference also makes response phase depend in a complex way on frequency and chromaticity. Since response phase is likely to be critical for localizing rapidly moving targets, it may be that positional information is also confounded.

The PC pathway also lacks the rapid saturation with phase advance characteristic of contrast gain controls[15, 33]. Again, this is consistent with a system designed to transmit a linear transformation of cone excitations to provide surface colour and brightness information.

What role does the PC pathway in transmitting information about the natural environment? We have recently examined this question by playing back natural scenes and taking a measure of information content within impulse trains[34]. Despite the fact that PC cells are much more responsive to the |M-L| than the |M+L| signal (Fig. 4), most of the information carried in this pathway has to do with achromatic brightness rather than colour, by a factor of ~3:1. This is because in the natural environment there is much greater variation (by more than a log unit) in luminance than chromaticity.

Retinal evolution and function: "*Nothing in biology makes sense except in the light of evolution*" - Dobzhansky

Knowledge of the evolution of colour vision in primates might help our understanding of human colour vision. Trichromacy in primates is unique among mammals. The evolution of trichromacy required not only multiple long-wavelength opsins, but also postreceptoral retinal machinery able to make use of their signals. The uniqueness of trichromacy to primates may have resulted from the presence of a retina able to elaborate an opponent signal when two opsins appeared. Wässle and Boycott[35] proposed that this was due to the presence of one or few cones per ganglion cell center; if much convergence were present, different opsins would be averaged out in the ganglion cell response. With just a few cones, some opponent signal would be likely to occur by chance. This is plausible, but it seems unlikely that the midget system *per se* predated trichromacy. A single cone input to a midget cell exceeds the resolution of the eye's optics, and it seems unlikely to have been

present in an ancestral system, but a refinement from a few to a single cone could then provide a more specific opponent signal. An additional factor may have been primate evolution from a nocturnal ancestor[36]; with a rod-dominated retina, the number of cones in a receptive field center is less, again improving the chance of an opponent signal arising by chance.

New-World primates throw interesting light on the evolution of retinal trichromacy. Male New-World primates of almost all species are dichromats but some females are trichromats. We have argued that the retinal anatomy and physiology of New-World primates are so similar to that in Old-World primates that parallel evolution of the PC pathway in these groups is unlikely[37]. If evolution of trichromacy and the PC pathway are closely linked, knowledge of how trichromacy evolved might help account for some of the unique features of this system.

Male New-World primates of most species are dichromats. In these individuals, the PC pathway retains properties characteristics of its trichromatic relatives; the cells are colour-blind versions of trichromat PC cells rather than modifying their properties to give, for example, greater achromatic contrast sensitivity. However, it has yet to be established if dichromatic New-World primates may provide a model for human dichromacy,

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