Neurol Clin N Am
21 (2003) 483–500

NEUROLOGIC CLINICS OF NORTH AMERICA

Achromatopsia, color vision, and cortex

Charles A. Heywood, DPhil[a,*],
Robert W. Kentridge, PhD[b]

[a]*Department of Psychology and Wolfson Research Institute, University of Durham, Durham DH1 3LE, United Kingdom*
[b]*Department of Psychology, University of Durham, Durham DH1 3LE, United Kingdom*

Few researchers would deny the advantages that color vision confers on those who possess it. In low-level vision, color assists in segmenting the visual scene on the basis of chromatic boundaries, when fluctuating shadows create spurious luminance borders that camouflage the contour of an object, thereby rendering it invisible to a monochromatic observer. In higher-level vision, color enhances identification and recognition. It can provide information about the state of objects, for example its oft-cited role in indicating the ripeness of dietary fruit. In this respect, it is notable that the spectral tuning of retinal photoreceptors in African Old World monkeys and chimpanzees are exquisitely matched to maximize the discriminability of young green shoots concealed among less succulent foliage [1]. In frugivorous platyrrhine monkeys, such tuning is optimal for the detection of dietary fruits concealed against variegated foliage [2,3]. In addition, color may be used in the identification of conspecifics or to signal sexual receptivity. Color also improves visual recognition memory for natural scenes by facilitating the encoding and retrieval of images, particularly when they are endowed in their natural and characteristic colors [4–6].

The ubiquity of color is reflected in the considerable amount of neural tissue devoted to the analysis of color information. Neuroanatomic and neurophysiologic studies have described the functional properties of visual pathways in the primate. On the basis of many criteria, such as response properties of individual neurones, the presence of a topographic map, or a characteristic histochemical or immunocytochemical architecture, more

This work has been supported by grants from the MRC, Medical Research Council, London, UK.

* Corresponding author. Department of Psychology, Science Laboratories, South Road, Durham DH1 3LE, UK.

E-mail address: C.A. Heywood@durham.ac.uk (C.A. Heywood).

doi:10.1016/S0733-8619(02)00102-0

than thirty visual areas have been identified in the primate brain [7]. Establishing their individual contributions to the processing of the visual scene, however, has not been straightforward. An early proposal, which has not been sustained, was that a single area contained a preponderance of neurones that responded to a single visual attribute, such as color or motion, which might readily denote its perceptual role. The view that a single area might underlie the perception of a single visual attribute was encouraged by the existence of apparently selective perceptual losses after brain damage. One such striking example is the clinical syndrome of cerebral achromatopsia, or cortical color blindness, where, in its extreme form, brain damage results in a complete loss of color vision. The selective abolition of a single attribute was interpreted as suggesting the deletion of a region specialized for the processing of color. More recently, neuropsychologic studies have revealed some further dissociations in color processing where brain damage selectively can impair the ability to categorize, memorize, or name colors. These studies have been complemented with functional neuroimaging of human observers using positron emission tomography (PET) or, more recently, magnetic resonance imaging (MRI), which have charted brain regions involved in several aspects of spectral vision.

The computational feat achieved by our nervous system in endowing us with a richly colored world is not evident from the apparent simplicity of our color sensations. Objects themselves are not colored, nor are the wavelengths they reflect. Color is a product of our nervous system where lights of different wavelengths evoke different sensations. Before examining deficits in color processing caused by cerebral lesions and their anatomic substrates, it is helpful to understand the problems faced by the nervous system in assigning colors to surfaces.

Color vision

Colors can be classified readily in terms of relatively few parameters, namely hue, saturation, and brightness. Whereas approximately fifteen hundred steps can be discriminated in luminance, systematic variation of hue and saturation results in closer to a million discriminable colors.

The human visual system is sensitive to a narrow spectrum of electromagnetic radiation, ranging from wavelengths between approximately 380 nm and 730 nm. The photopigments in the three retinal cone classes differ in their efficiency in absorbing light of different wavelengths. This is reflected in overlapping cone sensitivities to light, which peak at wavelengths of 420 nm, 530 nm, and 560 nm. The three types of cones are therefore commonly referred to as short (S)-, medium (M)-, and long (L)-wavelength cones, respectively. Visible light of a single wavelength, or indeed a mixture of wavelengths, produces a triplet of responses differing in magnitude in the different cone types.

It is straightforward to illustrate that color appearance cannot be determined simply by the triplet representing the relative quantal absorption rates of the three cone classes. The upper pair of patches in Fig. 1 physically is identical to the lower pair and produces identical responses in the S, M, and L cones, yet they appear perceptually quite different. The brightness of each patch is not determined by absolute cone excitations, but instead by the contrast of the patch with its background (ie, the ratio of cone activations elicited by the patch and background for each cone type).

In the natural world, there can be considerable variation in the wavelength distribution that illuminates the scene. This includes diurnal variation in the composition of sunlight from dawn to dusk and more rapid changes as objects fall into shadow when the sun is obscured. The light reflected from a surface is a function of the wavelength distribution of the light illuminating it and the surface's spectral reflectance function.

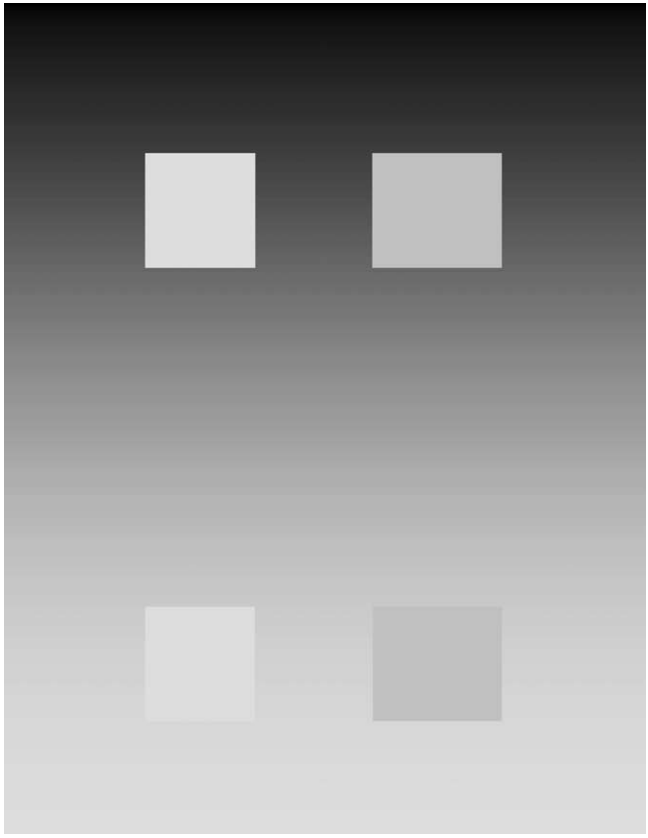

Fig. 1. The patches on the left (*top* and *bottom*) are of identical luminance. The same is true for the patches on the right. They appear different because their brightness is determined by their local contrast with their immediate background.

The spectral reflectance function of an illuminated surface describes the percentage of each wavelength reflected from that surface and is continuous across all wavelengths of the visible spectrum. One of the challenges the visual system faces is to disentangle the wavelength composition of the illuminant and the reflectance properties of a surface. How does the visual system extract an unvarying property of a surface, its spectral reflectance, in the presence of spectral and spatial variation of the illuminant? One potentially useful approach is to concentrate on the relative reflectances of adjoining surfaces rather than the absolute reflectance of each surface. A surface that is a more effective reflector of L-wavelength light than its neighbor always reflects relatively more L-wavelength light than its neighbor, no matter what the spectral content of the illuminant. The triplet of ratios of L-, M- and S-wavelength light reflected from a surface and its surround provides stable descriptors that remain unchanged with variations in ambient illumination. This can account for the tendency of surface colors to appear unaltered despite changes in the spectral composition of the illuminant and has been termed ''Type I constancy.'' As is apparent in Fig. 1, there are circumstances in which local cone contrast between adjacent surfaces contributes greatly to perceived color. Indeed, human observers perceive changes in a visual scene, which preserve cone ratios as a change in the illuminant. Changes in which cone ratios are altered are perceived as a change in the constituent surfaces.

When two surfaces with identical spectral reflectance, however, are part of a complex scene and viewed against different backgrounds (but under the same illumination), their perceived color remains largely the same despite large differences in the cone ratios across their local borders (Type II constancy). An influential proposal by Edwin Land (termed the ''retinex'' algorithm of color constancy) is that achieving type II constancy entails edge integration across the visual scene whereby cone ratios between widely separated surfaces can be compared. Thus, the visual system first extracts local contrast in L-, M-, and S-cones to derive relative reflectances of adjacent surfaces and then combines the increases and decreases in L-, M-, and S-reflectances across the borders falling between the two widely separated surfaces being compared. The result is a triplet of L-, M-, and S-reflectance ratios between the two separated surfaces. In Fig. 1, the paucity of edges and the gradual variation in reflectance lead the visual system to erroneously treat the patches as if they are displayed against a background of uniform reflectance with an illumination gradient. The reduced cone contrast in the lower patches is then consistent with their having a lower surface reflectance than their upper counterparts and consequently they appear darker.

In summary, color appearance results from a series of computations, which originate in the trichromatic signals from retinal cones. Extraction of local and global cone contrasts contribute significantly to mechanisms that assign color on the basis of the spectral reflectance of a surface.

Color disorders

Once colors are assigned to surfaces, observers are adept at classifying, naming, memorizing, and imaging them. Each of these abilities can be lost selectively as a result of brain damage, suggesting that each might be functionally independent. The ability to name a colored sample or point to a named color may be disrupted, as in color anomia [7]. Naming may be impaired, but the ability to select a named color may be spared, as in disorders of short-term color memory [8]. Cases of color agnosia [9,10], in which patients cannot sort colors (ie, the Holgrem test, in which nonidentical skeins of wool are sorted in their color categories), are distinct from losses in color naming or memory for object color. Impairments in memory for object color are not accompanied by difficulties in naming color samples or pointing to named colors. Apart from its low-level role in segmenting an object from its background, color plays a supporting role in recognition. Color can facilitate recognition of an object or scene, particularly when the object or scene possesses characteristic colors and is high in color "diagnosticity" [5]. Thus, a strawberry is recognized more rapidly when it is vested in its natural color, red, suggesting that color is tied closely to the internal representation of object shape. Impairments in retrieving the colors of familiar objects from pictorial or verbal cues in the presence of spared knowledge of object form were reported first in the classic studies of Lewandowsky [11–13]. The patient could neither name, nor indicate from a set of colored wool samples, the color of objects familiar to him, when presented with either the object name or an uncolored drawing. Deficits in the knowledge of stored object color, however, were accompanied by impairments in sorting colored skeins of wool by type and a failure to name, or point to, a skein of the color named by the examiner. Luzzatti and Davidoff [14] reported two patients who could name colors, but could not associate a color with an object (ie, they demonstrated an impairment in knowledge of object color). Both patients, however, appeared to have lost information about other attributes of objects, as was evident in drawing from memory, where important detail was overlooked, and performance on an object decision task requiring them to distinguish between real and unreal, invented objects. A patient in a more recent case [15] arranged colored patches by hue, recognized and named color samples, and had spared access to object form, size, and function. Nevertheless, she was severely impaired in accessing color knowledge. Together, these indicate a functional independence between color knowledge ("the colored sample is green") and object color knowledge ("a banana is yellow").

Little is known about the neural mechanisms underpinning the higher-order color disturbances described previously. In each, however, patients have no difficulty telling colors apart and color vision remains undisturbed. In contrast, in patients with cerebral achromatopsia, brain damage has stripped their visual world of color. A great deal is known about the early

stages of visual processing in primates. Information about the wavelength distribution of light is present in a plethora of visual areas of the primate brain. What, then, can the studies of neurologic patients tell us about the cortical construction of color?

Cerebral achromatopsia

Cerebral achromatopsia refers to the condition in which brain damage results in a loss of color vision [16–22]. Color imperceptions produced by cerebral lesions can be of varied nature and differ in their degree of recovery [23]. The loss rarely is complete and its incomplete form is referred to as dyschromatopsia.

Patients with achromatopsia are unable to name, sort, or match colors. The hallmark of the syndrome is poor performance on the Farnsworth-Munsell 100-Hue test, which requires the spectral ordering of equiluminant colored chips. In cases of complete achromatopsia, performance is uniformly poor in all regions of color space, but in its incomplete form there is frequently a greater loss of blues and greens and a relative sparing of reds [24]. Color disorders of retinal origin can be revealed using the Ishihara pseudoisochromatic plates. Patients with achromatopsa are able to read some or all of the plates [17,21] or can only do so under particular testing conditions, notably increased viewing distance [18–20]. (Increasing the viewing distance reduces the extent to which the optics of the eye and the visual system can resolve fine detail in an image. In an Ishihara plate, the scale of gaps between individual blobs of color is much finer than that of the figures they compose, so an increased viewing distance effectively eliminates the gaps between patches of color and transforms the image into one in which there are direct chromatic boundaries between figure and background.) Also, by using an increment threshold technique, where threshold detection of monochromatic test flashes are measured against a monochromatic background of a different wavelength at increasing intensities, it was shown that a patient with achromatopsia retained three functional cone mechanisms [25].

In an extensive review of 14 cases, Meadows [18] drew attention to several consistent features of the disorder. The impairment frequently, but not always [26], is accompanied by impairments in the recognition and identification of faces (ie, prosopagnosia [12 of 14 cases]) and the presence of altitudinal field defects (7 of 12 cases). There is widespread agreement that achromatopsia is associated with damage to ventromedial occipitotemporal cortex. The proximity of the crucial region of damage to the lower lip and bank of the calcarine fissure, which contains the topographic representation in primary visual cortex (area V1), accounts for common co-occurrence field defects confined to upper quadrants. Moreover, this may account for the rarity of the complete form of the disorder. If damage is extensive enough to abolish color vision in its entirety, it is likely to encroach more posteriorly

and result in cortical blindness. Similarly, prosopagnosia may be accounted for by evidence from neuroimaging normal observers, which suggests that regions crucial for face processing lie adjacent to those involved in color processes. Nevertheless, cases of achromatopsia have been reported without accompanying impairments [27–30].

Confirmatory evidence that ventromedial cerebral regions play a role in the processing of color has come from functional neuroimaging in normal observers. The first demonstration [31], using PET, compared regions activated when observers passively viewed a pattern of rectilinear colored patches, called ''Mondrians,'' with activations elicited by viewing an identical arrangement of achromatic patches of the same luminance. A focus of activity in the region of the lingual and fusiform gyri suggested the existence of a ''color center'' specialized for the processing of chromatic signals. The finding has since been confirmed many times using functional magnetic resonance imaging (fMRI) [32,33].

The brain regions implicated in achromatopsia invariably include the ''color center,'' although the damage always is more extensive. The discovery of the ''color center'' led to the plausible supposition, championed by Zeki [34,35], that it could be identified as the human homologue of one of the multiple visual areas in the primate brain that had been identified by other means. The suspect was cortical area V4, located on the prelunate gyrus of the macaque monkey brain. Electrophysiologic recordings from 77 single neurones sampled in V4 [36] indicated that every one showed selectivity to the wavelength of light falling in their receptive fields. Moreover, a decade later it was reported that the area contains cells that respond to the perceived color of a surface despite wide variation in the wavelength composition of reflected light [37]. Area V4 thus was implicated in color constancy and, by extension, the ''color center'' was proposed as the site engaged in the cortical construction of color. Additionally, cerebral achromatopsia could be interpreted as the loss of constancy mechanisms indispensable for assigning colors to surfaces in the visual scene. Results from studies with monkeys and achromatopsic observers, along with functional imaging of people, have modified this view.

Visual pathways in the primate brain

The primate brain contains an elaborate patchwork of visual areas, and their organization, functional specialization, and connectivity have been extensively reviewed elsewhere [34,37–39]. The parietal lobe is the destination of the so-called dorsal stream of processing, which is believed engaged in the visual control of action. Areas in the parietal lobe can be distinguished functionally from ventral stream areas that convey information about color and form to the temporal lobe [40]. Electrophysiologic studies have identified three channels of visual processing, commonly

referred to as the parvocellular (P)-, magnocellular (M)-, and koniocellular (K)-channels. Each channel originates in morphologically distinct retinal ganglion cells: Pα cells, Pβ cells, and small bistratified ganglion cells, respectively. The names of the channels derive from the relative sizes of the cells in segregated layers of the dorsal lateral geniculate nucleus (dLGN) to which they project. The segregation continues up to primary and secondary visual cortical areas. These channels are not confined exclusively to either dorsal or ventral stream areas, however. Thus, area V4, associated with the ventral stream, receives its predominant input from the P-channel; it also receives input from the M-channel [41]. Similarly, area MT (V5), which is normally assigned to the M-channel, receives a small P-channel input [42].

Labelling for cytochrome oxidase (CO), a metabolic marker, reveals a striking pattern of CO-rich "blobs" and CO-deficient "interblob" regions in area V1 and a pattern of thick, thin, and pale interstripes in area V2. The cells of the parvocellular layers of the dLGN project to layer 4Cβ of the visual striate cortex (V1) and thence to the blobs and interblobs in V1. The cells in the CO blobs are selective for wavelength, but not orientation. In contradistinction, orientation, but not wavelength selectivity, is common in cells in the interblobs. The CO thin stripes and interstripes in area V2 respectively receive input from the blobs and interblobs of V1 and in turn project to area V4. The magnocellular channel in dLGN projects primarily to layer 4Cα of area V1 and from there to Layer 4B. Layer 4B projects directly and via the CO-rich thick stripes in V2 to cortical area MT. K-cells are more numerous than previously believed and may be as common as M-cells. They project to the CO blobs of V1, where wavelength selective cells are particularly common, and perhaps also to early extrastriate areas, such as V2 and V4.

The three channels convey very different chromatic information. The P-channel conveys high spatial, and low temporal, frequency information; vice versa for the M-channel, consistent with the latter's contribution to motion processing. Cells in the P-channel signal color-opponent information, receiving antagonistic inputs from M- and L-wavelength cones (L − M) and respond best to red-green color modulation. Cells in the M-channel receive additive cone inputs [L + M], and therefore signal luminance, and are highly contrast sensitive. Whereas relatively little is known about the K-pathway [43–45], the bistratified ganglion cells receive an excitatory S-wavelength input and inhibitory projections from L and M cones (S − [L + M]). They therefore signal modulation in the blue-yellow color direction.

Cortical area V4

The status of monkey V4 as a "color area" and its proposed homology with the human "color center" were brought into question by the results of lesion studies. Bilateral ablation of area V4 in the monkey does not abolish

color vision; instead, it severely disrupts form vision [46,47]. The degree to which V4 is specialized for color has been questioned in recent years. The percentage of color selective cells in V4 now appears little different from that in adjacent areas [48], and other investigators have emphasized its role in spatial vision [49]. Furthermore, lesions anterior and ventral to V4 in the monkey inferior temporal lobe do result in color impairments [50,51], consistent with the increased activation shown in these regions when monkeys perform color discriminations during neuroimaging [52]. Some features of the neuronal population in area V4 are consistent with a role in some aspects of color processing, notably color constancy. The receptive fields contain a spectrally selective excitatory center with a large inhibitory surround with the same wavelength selectivity. Thus, the response of the cell signals spectral contrast, but is nulled when the receptive field is illuminated diffusely by light of the appropriate waveband [53]. This is just the property required for the ratio-taking process, which underlies rapid retinex-like constancy mechanisms. The large receptive fields of cells in V4 and their extensive callosal connections [54,55] also make them plausible candidates for undertaking the long-range interactions required for such computations. Some investigators, however, contest such an exclusive role for V4 by noting that responses of cells in V1 also show color constancy when stimuli are scaled to match the smaller receptive field [56]. The results of lesion studies [57,58] have been inconclusive and open to other interpretations, including the possibility that impairments were secondary effects on more anterior areas to which V4 projects.

Wavelength processing in cerebral achromatopsia

Leaving aside the issue of the identity of the ''color center,'' can cerebral achromatopsia best be characterized as a loss of color constancy? Further, if color constancy is lost, what is retained? It is likely that achromatopsia constitutes a family of disorders [23], whereas the varied nature of color impairments may be a consequence of the pattern of damage to a cluster of visual cortical regions or the extent of damage to the ''color center'' itself. It has become apparent that the processing of wavelength differences, apart from resulting in the phenomenal experience of color, contributes to other visual attributes. Clear dissociations in perceptual abilities are seen best in patients with complete achromatopsia. One such patient, M.S., has been studied extensively and reviewed elsewhere [59]. Patient M.S. performs randomly on tasks of color ordering and is unable to select an oddly colored patch embedded in an array of differently colored equiluminant hues. Yet, importantly, he has no difficulty in locating each of the targets and distractors presented against an equiluminant background. Edges defined by pure color differences remain visible to him. An early supposition was that the color-opponent P-channel was deleted in M.S., whose vision was now

mediated by the broad-band M-channel, which sums the outputs of the L- and M-wavelength cones. Two pieces of evidence show this is not true. First, it is known that cells in the M-channel respond to an equiluminant chromatic border falling in its receptive field [60] but cannot signal the sign of the color (ie, they do not distinguish between a red-green and a green-red border). Also, the M-channel is sensitive to rapid luminance fluctuations to which the P-channel is blind. The introduction of spatial and temporal flicker into chromatic displays, which render the M-channel incapable of distinguishing between chromatic and luminance contrast, did not prevent M.S. from detecting the chromatically defined shape concealed therein [61]. A similar dissociation has been reported in cases of incomplete achromatopsia [62]. Second, the amount of chromatic contrast required for M.S. to detect sinusoidally modulated equiluminant chromatic gratings is the same as in a normal observer [63]. Thus, M.S. is able to perceive form defined by pure color difference, even when the colors themselves are indistinguishable. Chromatic contrast sensitivity is not preserved invariably in achromatopsia [64], suggesting considerable variability in the severity of impairments of wavelength processing. Third, measurements of sensitivity to light of different wavelengths shows three peaks, rather than the single peak at ~550 nm, which characterizes the M-channel [60]. This is strongly indicative of color-opponent processing [65]. A color-opponent (eg, red^{+}-$green^{-}$) receptive field is maximally excited by L-, and inhibited by M-, wavelength light. The reverse occurs for cells showing opposite opponency ($green^{+}$-red^{-}). A red-green (ie, yellow) mixture places excitatory and inhibitory receptive field mechanisms in equilibrium. As a consequence, yellow appears as perceptually dimmer than expected on the basis of the summed red and green luminances. The same is true for M.S. and confirms residual color-opponent processes. Again, not all achromatopsic observers show evidence of preserved opponent P-channel or K-channel mechanisms [66], illustrating the heterogeneity of the condition.

Until recently, it was widely held that color and motion undergo independent processing, consistent with the segregation of the P- and M-channels, respectively. A color-opponent input into motion mechanisms now has been demonstrated [67–69], which has a high sensitivity to color, responds to slow speeds, and is sensitive to direction of motion, but does not code velocity veridically. This mechanism is distinct from a second that encodes rapid motion, is highly sensitive to luminance contrast, and treats color signals, such as low contrast luminance variation. Functional imaging has implicated visual area MT in the latter mechanism [70]. Cells in MT, an area firmly assigned to the dorsal stream, respond to equiluminant red-green chromatic gratings, which are phase-shifted by 90° from moment to moment. Each shift results in the replacement of a red-green, by a green-red, border. Its direction of apparent motion is ambiguous to an observer who has no access to the sign of the border contrast. M.S., who could not distinguish red from green, could nevertheless rapidly discern the direction of apparent motion [61].

There is a further report [69] of patients with achromatopsia in whom a robust motion response was demonstrated to high-contrast equiluminant chromatic gratings. By measuring the amount of luminance-defined counter-motion required to null it, the response was shown equivalent to that in normal observers.

Finally, there is indirect evidence for an intact parvocellular contribution to motion in achromatopsia [71]. The phenomenon of "motion slowing," where drifting, sinusoidal chromatic gratings are perceived as moving considerably more slowly than an achromatic grating drifting at the same speed, reflects the nonveridical velocity coding of the slow motion pathway. This pathway receives a color-opponent input and therefore is susceptible to the type of subadditive brightness responses described previously. Unintended brightness differences result from the construction of equiluminant, sinusoidally modulated red-green gratings. When red and green are added in equal proportion at the midpoint of each cycle, the yellow is perceptually dimmer. Such brightness variation influences perceived speed. When the brightness variation was corrected, by adding frequency doubled luminance, there was a further reduction in the apparent speed of the grating in normal observers and patient M.S [71]. Thus, P-channel processes, which lead to a brightness response, also contribute to motion perception.

In summary, there have been no circumstances in which patient M.S. can perform even the most rudimentary discrimination of equiluminant hues. Nevertheless, when these same hues, which lead to no phenomenal experience of color, are used to define form or motion, the latter attributes are readily accessible to MS.

Color constancy

Achromatopsia may be a failure of constancy mechanisms essential for the "synthesis" or "construction" of color [34,72]. The system, which compares surface reflectances for different wavebands across the scene and the system that generates the eventual color percept are deemed one and the same [73]. Alternatively, it is possible that the system that implements computations that underlie constancy (eg, the Retinex alorithm) is distinct from that which generates the percept of object color. The ratio of cone activation elicited by a surface, relative to that elicited by its background, is invariant with respect to shifts in the illuminant. An important contributor (reflected in many accounts of color constancy) to the means by which invariance is achieved is retinal adaptation to the prevailing illumination, for example during the course of the day. Slow adaptation, however, is unable to account for constancy under more rapid changes in the illuminant (eg, a cloud passes across the sun). The latter requires global comparisons among nonadjacent surfaces, a role assigned to V4. It is a comparison of these invariant descriptors of the scene, which ultimately specify the magnitude and direction of a vector in color space, that determines perceived color. Damage to this process of color synthesis could

result in achromatopsia, whereas a selective failure of color constancy with preserved color discrimination could occur at any number of earlier stages where invariances are derived. In this event, perceived color could be determined by comparisons of unscaled L-, M- and S-cone signals. Perceptual experience of an object's color would remain but would change with shifts in the wavelength composition of the illuminant. A patient, P.B., has been reported [74] who suffered a vascular insufficiency resulting in a total loss of form vision. Color vision was preserved but perceived surface color depended on the distribution of reflected wavelengths, and color constancy was lost. Neuroimaging revealed activity in areas V1 and V2 suggesting that early visual areas mediated this residual capacity. Similarly, in a case of incomplete achromatopsia, a patient has been described [75] in whom perceived surface color shifted predictably under systematic changes in the illuminant. In both cases, color elicited conscious color experience, which is inconsistent with the proposal that constancy and the generation of object color are subserved by a single mechanism. If activity in early visual areas can give rise to conscious color experience, moreover, then it is difficult to account for its absence in achromatopsic observers whose early visual areas remain intact.

Impairments in color constancy with intact color matching also have been reported in three patients with large ventral occipitotemporal lesions [76]. Similarly, in 27 patients with unilateral parietotemporal cortical lesions, five were reported to have lost color constancy but retained hue discrimination [77]. The region of common damage was in the superior and medial temporal gyri anterior to the "color center." Cases such as these are difficult to reconcile with the belief that achromatopsia is the loss of constancy mechanisms integral to the generation of object color.

Cone-contrast is a significant contributor to color appearance. Two isolated patches, eliciting different cone excitations and presented against different backgrounds, appear identical if the patches produce identical cone-contrasts with their backgrounds. Patient M.S. was tested under dichoptic viewing conditions, where targets and backgrounds were presented independently under different illuminants to each differentially adapted eye. As with normal observers, cone-contrast, rather than absolute cone excitation, determined his judgments of color appearance. M.S. was adept at discriminating local cone-contrast, albeit with raised thresholds. He was severely impaired, however, at making such judgments in complex scenes that contained multiple surfaces, which require global comparisons of cone-contrasts [78]. Type II constancy refers to the situation in which identical surfaces, viewed successively against different backgrounds, produce very different cone-contrasts yet appear relatively unchanged. A failure of Type II constancy in a patient with achromatopsia was reported by D'Zmura et al [79]. Judgments of surface appearance were influenced by the sign and magnitude of luminance contrast.

The surviving capacity to process local cone-contrast allows for rudimentary color constancy in cerebral achromatopsia. The accompanying

failure to make comparisons of widely separated surfaces in complex visual scenes is consistent the interpretation of achromatopsia as a loss of color constancy. The wavelength dependent and conscious color perceptions, however, of other neurologic patients cannot be readily explained if constancy and the generation of object color are one and the same. Functional imaging of normal observers, viewing a variety of chromatic displays, has now begun to reveal a greater complexity in the neural basis of chromatic vision.

Functional imaging of chromatic pathways

Many studies confirm the early demonstration of an extrastriate region implicated in color vision. A recent functional imaging study contends that the human "color center" indeed is distinct from area V4 [80]. Areas activated more by color than luminance variation were compared with boundaries of retinotopic areas. Foveal activation was present in cortical areas V1, V2, V3/VP, and a region previously suggested as the ventral subdivision of V4 (V4v). In addition, however, there was robust activation in the middle of the collateral sulcus. Notwithstanding that the location of this area corresponded to the cortical "color center" previously described as "human V4," the area has been renamed area V8. The debate chiefly centers on the identity of the region whose representation in each hemisphere is confined to the upper visual field, namely V4v. Whether or not the "color center" is dubbed V4 or V8, reifying it as the "color center" may serve to ignore other regions deserving of an equal status in their specialization for color processing. Functional imaging of normal observers performing a task of color ordering, as distinct from passive viewing of visual displays, exposed an additional region of activation more anterior and medial to the "color center" [81,82]. This region, V4α, is like putative V4 in that it contains a representation of the upper and lower quadrants of the contralateral visual field.It lacks the prominent retinotopic mapping, however, that is a feature of human V4. Together, V4 and V4α have been named the "V4 complex." In a direct test of brain regions engaged in color constancy, functional imaging was carried out while observers viewed chromatic and achromatic Mondrian patterns. In one condition, the wavelength composition and luminance of the patches remained unchanging during viewing. In two further conditions, the intensity or the wavelength composition of the illumination continuously changed. The latter, dynamic viewing conditions, was considered to make more demands on constancy mechanisms. Activations elicited by the two dynamic viewing modes were compared with the static condition. V4 and V4α showed robust activations in the chromatic and achromatic conditions. Only weak activation of the "V4 complex" resulted from changes in wavelength composition, compared with changes in intensity, for chromatic and achromatic displays. These results are interpreted as implicating the "V4 complex" in undertaking the required ratio-taking operations, which maintain color constancy.

Color impairments associated with color memory and color knowledge have been described previously. Simple, abstract Mondrian patterns were chosen for neuroimaging of color, as they were intended to minimize linguistic and mnemonic factors and were not readily endowed with meaning. In a study of brain regions involved with objects and their associated color [83], activity evoked by passive viewing of chromatic, compared with achromatic scenes, included the posterior two thirds of the fusiform gyrus. What was striking, however, was that this more extensive anterior activation only occurred if objects were presented in their natural colors. Abnormally colored scenes revealed activation strikingly similar to that obtained using Mondrian patterns. Furthermore, naturally and unnaturally colored scenes produced additional activation in dorsolateral and ventrolateral frontal cortex, respectively. Finally, additional analysis of a previous study [72] showed that V4 and V4α are co-active during the viewing of unnaturally colored scenes, whereas naturally colored scenes elicit activity in V4α and anterior regions implicated in face and object recognition. In summary, these studies probably allow one to distinguish between areas involved in the perception of color and those (more anterior) involved in the use of color as a specific object attribute in object recognition.

Summary

Brain damage can entirely abolish color vision in cases of complete achromatopsia. Other processes that depend on wavelength differences, however, can be retained. Form and motion defined by pure color differences can be perceived readily even when the colors themselves cannot be told apart. The loss of color vision in cerebral achromatopsia has been equated with the loss of a ''color center'' presumed indispensable for the phenomenal experience of hue. The ''color center'' has been assigned a role in the cortical construction of color, specifically in implementing the computations that underlie color constancy. Many features of the condition are consistent with this account. Other neurologic patients, however, retain conscious experience of hue, yet fail to disentangle the illuminant and the reflectance properties of surfaces. For them, color experience is determined by the wavelength composition of light reflected from a surface. If their wavelength-dependent vision is mediated by activity in early visual areas, then it is difficult to understand why these areas are unable to perform a similar role when they remain intact in achromatopsic observers. The prevalence of cells in the ventral visual areas of the monkey brain that code color and the further fractionation of color-related areas in human observers revealed by functional imaging suggest multiple color areas. Their different contributions are only just beginning to become apparent.

References

[1] Dominy NJ, Lucas PW. Ecological importance of trichromatic vision to primates. Nature 2001;410(6826):363–6.
[2] Regan BC, Julliot C, Simmen B, et al. Frugivory and colour vision in Alouatta seniculus, a trichromatic platyrrhine monkey. Vision Res 1998;38(21):3321–7.
[3] Sumner P, Mollon JD. Catarrhine photopigments are optimized for detecting targets against a foliage background. J Exp Biol 2000;203(13):1963–86.
[4] Tanaka JW, Presnell LM. Color diagnosticity in object recognition. Perc Psychophys 1999;61(6):1140–53.
[5] Tanaka J, Weiskopf D, Williams P. The role of color in high-level vision. Trends Cog Sci 2001;5(5):211–5.
[6] Gegenfurtner KR, Rieger J. Sensory and cognitive contributions to the recognition of natural scenes. Curr Biol 2000;10:805–8.
[7] Van Essen DC, Lewis JW, Drury HA, et al. Mapping visual cortex in monkeys and humans using surface-based atlases. Vision Res 2001;41:1359–78.
[8] Davidoff JB, Ostergaard AL. Colour anomia resulting from weakened short term memory. Brain 1984;107:415–31.
[9] Sittig O. Stoerungen im Verhalten gegenueber Farben bei Aphasischen. Monatsschr Psychiatr Neurolo 1921;49:63–68, 169–87.
[10] Beauvois M-F, Saillant B. Optic aphasia for colours and colour agnosia: a distinction between visual and visuo-verbal impairments in the processing of colours. Cognitive Neuropsychology 1985;2:1–48.
[11] Lewandowsky M. Abspaltung des Farbensinnes durch Herderkramgung des Gehirns. In: van Weyenberg GAM, editor. Compte rendu des travaux du 1er congrès international de psychiatrie, de neurologie, de psychologie et de l'assistance des aliénés. Amsterdam: J.H. de Bussy; 1908a.
[12] Lewandowsky M. Ueber abspaltung des farbensinnes. Monatsschr Psychiatr Neurolog 1908b;23:488–510.
[13] Davidoff JB, Fodor G. An annotated translation of Lewandowsky (1908). Cognitive Neuropsychology 1989;6:165–77.
[14] Luzzatti C, Davidoff J. Impaired retrieval of object-colour knowledge with preserved colour naming. Neuropsychologia 1994;32:933–50.
[15] Miceli G, Fouch E, Capasso R, et al. The dissociation of color from form and function knowledge. Nat Neurosci 2001;4(6):662–7.
[16] Brill NE. A case of destructive lesion in the cuneus, accompanied by color blindness. Am J Neurol Psychiatry 1882;1:356–68.
[17] Meadows JC. Disturbed perception of colours associated with localized cerebral lesions. Brain 1974;97:615–32.
[18] Albert ML, Reches A, Silverberg R. Hemianopic color blindness. J Neurol Neurosurg Psychiatry 1975;38:546–9.
[19] Green GJ, Lessell S. Acquired cerebral dyschromatopsia. Arch Ophthalmol 1977;95: 121–8.
[20] Heywood CA, Wilson B, Cowey A. A case study of cortical colour "blindness" with relatively intact achromatic discrimination. J Neurol Neurosurg Psychiatry 1987; 50:22–9.
[21] Victor JD, Maiese K, Shapley R, et al. Acquired central dyschromatopsia: analysis of a case with preservation of color discrimination. Clin Vision Sci 1989;4:183–96.
[22] Zeki S. A vision of the brain. Oxford (UK): Blackwell Scientific Publications; 1993.
[23] Rizzo M, Smith V, Pokorny J, et al. Color perception profiles in central achromatopsia. Neurology 1993;43:995–1001.
[24] Pearlman AL, Birch J, Meadows JC. Cerebral color blindness: an acquired defect in hue discrimination. Ann Neurol 1979;5:253–61.

[25] Mollon JD, Newcombe F, Polden PG, et al. On the presence of three cone mechanisms in a case of total achromatopsia. In: Colour vision deficiencies, vol V. Bristol (England): Hilger; 1980. p. 130–5.
[26] Duvelleroy Hommet C, Gillet P, Cottier J, et al. Achromatopsie cérébrale sans prosopagnosie ni alexie ni agnosie des objets. Rev Neurol (Paris) 1997;153:554–60.
[27] Mackay G, Dunlop JC. The cerebral lesions in a case of complete acquired colour-blindness. Scott Med Surg J 1899;5:503–12.
[28] Kölmel HW. Pure homonymous hemiachromatopsia: findings with neuro-ophthalmologic examination and imaging procedures. Eur Arch Psychiatry Neurol Sci 1988;237:237–42.
[29] Damasio A, Yamada T, Damasio H, et al. Central achromatopsia: behavioral, anatomic, and physiologic aspects. Neurology 1980;30:1064–71.
[30] Sacks O, Wasserman RL, Zeki S, et al. Sudden color-blindness of cerebral origin. Soc Neurosci Abstr 1988;14:1251.
[31] Zeki S, Watson JDG, Lueck CJ, et al. A direct demonstration of functional specialization in human visual cortex. J Neurosci 1991;11:641–9.
[32] Sakai K, Watanabe E, Onodera Y, et al. Functional mapping of the human colour centre with echo-planar magnetic resonance imaging. Proc R Soc Lond [Biol] 1995;261: 89–98.
[33] Kleinschmidt A, Lee BB, Requardt M, et al. Functional mapping of color processing by magnetic resonance imaging of responses to selective P- and M-pathway stimulation. Exp Brain Res 1996;110:279–88.
[34] Zeki S. A century of cerebral achromatopsia. Brain 1990;113:1721–77.
[35] Zeki S. Colour vision and functional specialisation in the visual cortex. Disc in Neurosc 1990;VI(2):11–64.
[36] Zeki SM. Colour coding in rhesus monkey prestriate cortex. Brain Res 1973;53:422–7.
[37] Zeki SM. Colour coding in the cerebral cortex: the reaction of cells in monkey visual cortex to wavelengths and colours. Neuroscience 1983;9(4):741–65.
[38] Merigan WH, Maunsell JHR. How parallel are the primate visual pathways? Annu Rev Neurosci 1993;16:369–402.
[39] Schiller PH, Logothetis NK, Charles ER. Functions of the colour-opponent and broad-band channels of the visual system. Nature 1990;343:16–7.
[40] Milner AD, Goodale MA. The visual brain in action. Oxford (UK): Oxford University Press; 1995.
[41] Ferrara VP, Nealey TA, Maunsell JHR. Mixed parvocellular and magnocellular geniculate signals in visual area V4. Nature 1992;358:756–58.
[42] Maunsell JHR, Nealy TA, DePriest DD. Magnocellular and parvocellular contributions to responses in the middle temporal visual area (MT) of the macaque monkey. J Neurosci 1990;10(10):3323–34.
[43] Dacey DM. Physiology, morphology and spatial densities of identified ganglion cell types in primate retina. In: Bock GR, Goodey JA, editors. CIBA Foundation Symposium 184: higher-order processing in the visual system. Chichester (UK): Wiley; 1994. p. 12–34.
[44] Dacey DM. Parallel pathways for spectral coding in primate retina. Annu Rev Neurosci 2000;23:743–75.
[45] Hendry SHC, Reid RC. The koniocellular pathway in primate vision. Annu Rev Neurosci 2000;23:127–53.
[46] Heywood CA, Cowey A. On the role of cortical area V4 in the discrimination of hue and pattern in macaque monkeys. J Neurosci 1987;7(9):2601–17.
[47] Heywood CA, Gadotti A, Cowey A. Cortical area V4 and its role in the perception of colour. J Neurosci 1992;12(10):4056–65.
[48] Schein SJ, Marrocco RT, De Monasterio FM. Is there a high concentration of colour-selective cells in area V4 of monkey visual cortex? J Neurophysiol 1982;47:193–213.
[49] McAdams CJ, Maunsell JHR. Attention to both space and feature modulates neuronal responses in macaque area V4. J Neurophysiol 2000;83(3):1751–5.

[50] Heywood CA, Gaffan D, Cowey A. Cerebral achromatopsia in monkeys. Eur J Neurosci 1995;7:1064–73.
[51] Cowey A, Heywood CA, Irving-Bell L. The regional cortical basis of achromatopsia: a study on macaque monkeys and an achromatopsic patient. Eur J Neurosci 2001;14(9):1555–66.
[52] Takechi H, Onoe H, Shizuno H, et al. Mapping of cortical areas involved in color vision in non-human primates. Neurosci Lett 1997;230:17–20.
[53] Schein SJ, Desimone R. Spectral properties of V4 neurons in the Macaque. J Neurosci 1990;10:3369–89.
[54] Van Essen DC, Zeki SM. The topographic organization of rhesus monkey prestriate cortex. J Physiol 1978;277:193–226.
[55] Desimone R, Moran J, Schein SJ, et al. A role for the corpus collosum in visual area V4 of the macaque. Vis Neurosci 1993;10:159–71.
[56] Wachtler T, Sejnowski TJ, Albright TD. Responses of cells in macaque V1 to chromatic stimuli are compatible with human color constancy. Soc Neurosci Abstr 1999;25:4.
[57] Walsh V, Butler SR, Carden D, et al. The effects of V4 lesions on the visual behaviour of macaques: Hue discrimination and colour constancy. Behav Brain Res 1993;53:51–62.
[58] Wild HM, Butler SR, Carden D, et al. Primate cortical area V4 important for colour constancy but not wavelength discrimination. Nature 1985;313:133–5.
[59] Heywood CA,, Cowey A. Cerebral achromatopsia. In: Humphreys GW, editor. Case studies in the neuropsychology of vision. Brighton (UK): Psychology Press; 1999. p. 17–39.
[60] Saito H, Tanaka K, Isono H, et al. Directionally selective response of cells in the middle temporal area (MT) of the macaque monkey to the movement of equiluminous opponent color stimuli. Exp Brain Res 1989;75:1–14.
[61] Heywood CA, Cowey A, Newcombe F. On the role of parvocellular (P) and magnocellular (M) pathways in cerebral achromatopsia. Brain 1994;117:245–54.
[62] Barbur JL, Harlow AJ, Plant G. Insights into the different exploits of colour in the visual cortex. Proc R Soc Lond [Biol] 1994;258(1353):327–34.
[63] Heywood CA, Nicholas JJ, Cowey A. Behavioural and electrophysiological chromatic and achromatic contrast sensitivity in an achromatopsic patient. J Neurol Neurosurg Psychiatry 1996;61:638–43.
[64] Cavanagh P, Hénaff M-A, Michel F, et al. Complete sparing of high-contrast color input to motion perception in cortical color blindness. Nat Neurosci 1998;1(3):242–7.
[65] Sperling HG, Harwerth RS. Red-green cone interactions in the increment-threshold spectral sensitivity of primates. Science 1971;172:180–4.
[66] Troscianko T, Davidoff J, Humphreys G, et al. Human colour discrimination based on a non-parvocellular pathway. Curr Biol 1996;6(2):200–10.
[67] Cropper SJ, Derrington AM. Rapid colour-specific detection of motion in human vision. Nature 1997;379:72–4.
[68] Derrington AM. Can colour contribute to motion? Curr Biol 2000;10:268–70.
[69] Gegenfurtner KR, Hawken MJ. Interaction of motion and color in the visual pathways. Trends Neurosci 1997;19(9):394–401.
[70] ffytche DH, Skidmore BD, Zeki S. Motion-from-hue activates area V5 of human visual cortex. Proc R Soc Lond [Biol] 1995;260(1359):353–8.
[71] Heywood CA, Kentridge RW, Cowey A. Form and motion from colour in cerebral achromatopsia. Exp Brain Res 1998;123:145–53.
[72] Bartels A, Zeki S. The architecture of the colour centre in the human visual brain: new results and a review. Eur J Neurosci 2000;12:172–93.
[73] Zeki S, Bartels A. Towards a theory of visual consciousness. Conscious Cogn 1999a;8:225–59.
[74] Zeki S, Aglioti S, McKeefry D, et al. The neurological basis of conscious color perception in a blind patient. Proc Natl Acad Sci USA 1999;96:14124–9.
[75] Kennard C, Lawden M, Morland AB, et al. Colour Identification and colour constancy are impaired in a patient with incomplete achromatopsia associated with prestriate cortical lesions. Proc R Soc Lond [Biol] 1995;260(1358):169–75.

[76] Clarke S, Walsh V, Schoppig A, et al. Colour constancy impairments in patients with lesions of the prestriate cortex. Exp Brain Res 1998;123:154–8.
[77] Rüttiger L, Braun DI, Gegenfurtner KR, et al. Selective color constancy deficits after circumscribed unilateral brain lesions. J Neurosci 1999;19(8):3094–106.
[78] Hurlbert AC, Bramwell DI, Heywood CA, et al. Discrimination of cone contrast changes as evidence for colour constancy in cerebral achromatopsia. Exp Brain Res 1998;123: 136–44.
[79] D'Zmura M, Knoblauch K, Henaff M-A, et al. Dependence of color on context ina case of cortical color deficiency. Vision Res 1998;38:3455–9.
[80] Hadjikhani N, Liu AK, Dale AM, et al. Retinotopy and color sensitivity in human visual cortical area V8. Nat Neurosci 1998;1(3):235–41.
[81] Beauchamp MS, Haxby JV, Jennings JE, et al. An fMRI version of the Farnsworth-Munsell 100-Hue test reveals multiple color-selective areas in human ventral occipito-temporal cortex. Cereb Cortex 1999;9(3):257–63.
[82] Zeki S, Bartels A. The clinical and functional measurement of cortical (in-) activity in the visual brain, with special reference to the ywo subdivisions (V4 and V4α) of the human colour centre. Philos Trans R Soc Lond [Biol] 1999;354:1371–82.
[83] Zeki S, Marini L. Three cortical stages of colour processing in the human brain. Brain 1998;121:1669–85.