The neurological basis of conscious color perception in a blind patient

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We have studied patient PB, who, after an electric shock that led to vascular insufficiency, became virtually blind, although he retained a capacity to see colors consciously. For our psychophysical studies, we used a simplified version of the Land experiments [Land, E. (1974) *Proc. R. Inst. G. B.* 47, 23–58] to learn whether color constancy mechanisms are intact in him, which amounts to learning whether he can assign a constant color to a surface in spite of changes in the precise wavelength composition of the light reflected from that surface. We supplemented our psychophysical studies with imaging ones, using functional magnetic resonance, to learn something about the location of areas that are active in his brain when he perceives colors. The psychophysical results suggested that color constancy mechanisms are severely defective in PB and that his color vision is wavelength-based. The imaging results showed that, when he viewed and recognized colors, significant increases in activity were restricted mainly to V1-V2. We conclude that a partly defective color system operating on its own in a severely damaged brain is able to mediate a conscious experience of color in the virtually total absence of other visual abilities.

Different attributes of the visual input, such as form, motion, and color, are processed in parallel by spatially distributed and at least partly independent cortical systems of the primate brain, each of which is functionally specialized for handling a specific visual attribute (1–2). The concept of parallel processing in the primate brain is supported by experimental data (1, 3–5) and clinical evidence that circumscribed cortical lesions can cause partial and selective visual deficits (e.g., ref. 6). For example, color perception cannot only be selectively impaired by cortical lesions but also selectively spared by lesions that cause severe disturbances of some or most other visual abilities (7). The color of a surface depends on the wavelength composition of the light entering the eye, but the relation between wavelength composition and the subjective experience of color is far from simple. The apparent color of a surface depends as much on the wavelength composition of the light reflected from it as on that reflected from neighboring surfaces, such that its color tends to look the same regardless of the spectral content of the light in which it is viewed. This phenomenon of color constancy is the result of complex computations that enable the brain to compare the wavelength composition of the light coming from widely spaced regions of the field of view. The cortical color processing system in the monkey brain consists of several stages extending from V1 to V4, partly directly but mainly through V2 (1, 8–12), and beyond that to the inferior temporal cortex (13–15). A similarly organized system probably exists in the human brain, given the similarity in the topographic organization (16–18) and metabolic architecture (19, 20) between areas V1 and V2 in the two. Evidence suggests that a first stage of color processing in areas V1 and V2 is concerned mainly with registering the presence and intensity of different wavelengths and with wavelength differencing; a second stage, located in area V4, is concerned with automatic color constancy operations (21); and a third stage, based on the inferior temporal and frontal cortex, is more concerned with object colors (15). Lesions restricted to V4 lead to a specific loss of conscious color vision (cerebral achromatopsia). Although color blind, achromatopsic patients can discriminate between different wavelengths (22) but cannot attribute colors to them. Whether chromatic cues guide the behavior of cerebral achromatopsics in a covert fashion, without any conscious accompaniment, is still an open question (23).

Here we address the problem of the neural bases of color vision by considering a rare syndrome in which conscious color vision is largely preserved in an otherwise apparently blind subject. This condition has only been observed after episodes of vascular insufficiency or carbon monoxide poisoning. The first description was given by Wechsler (24), whose patient was rendered unconscious for 2 hours by a house fire. On recovery he was found to be virtually blind and incapable of recognizing objects, whether large or small; he could not guide himself visually, colliding with objects and persons when trying to do so. But his color vision was sufficiently well preserved to enable him to distinguish even the shades of colors. "He knew at once the colors of small objects which he could neither name nor tell the form of. He picked out colors on command" (ref. 24, p. 958). This led Wechsler to a remarkable conclusion, long since forgotten. He wrote, "The case herein presented warrants the statement that color vision and visual acuity can be dissociated in such a way that the former is preserved while the latter is impaired" (ref. 24, p. 965), a conclusion that, like the evidence of Verrey (25) for a color center in the brain, was universally ignored until the demonstration of a specialization for color in the primate brain (26). Wechsler's result has been confirmed (27–32), but whether color constancy mechanisms are intact in such patients is unknown.

Recently, another patient with a similar syndrome, but derived from a prolonged circulatory and respiratory arrest caused by a severe electric shock, has been described by Humphrey *et al.* (33). The episode left the patient virtually blind though with a relatively spared color vision. We thought it interesting to learn whether this patient's ability to discriminate color is wavelength-based or whether color constancy mechanisms in him are at least partly intact. If the former is true, then one would expect the necessary processing to be confined to areas V1/V2 (20, 34, 35), where there are heavy concentrations of wavelength selective cells, whereas in the latter case one would expect a participation of area V4 (35). This made it interesting to determine what parts of his brain became activated when he perceived color.

Methods

Patient PB and His History. PB has been briefly described elsewhere (33); here we add such information as is of relevance to this study. The major symptoms were caused by brain ischemia resulting from a severe electric shock sustained in April 1985 that led to cardiac and respiratory arrest. Resuscitated but in a comatose state, he was artificially ventilated and kept under barbiturate sedation for 12 days from admission. He regained

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consciousness and was able to communicate verbally 4 months and to walk 6 months after the episode. The first accurate neurological examination was done in July, 1986, when he was found to have normal muscle tone and force, symmetrical deep reflexes, and relatively normal pain and thermal sensitivities. On the other hand, his tactile, pressure, and kinesthetic sensibilities were severely impaired, and he exhibited dystonic gait and posture, possibly related to proprioceptive and kinesthetic deficits.

Neuropsychological examinations by one of the authors (S.A.) started in October, 1986. Because of his profound visual deficit, the patient's general cognitive status was difficult to test formally, although general intelligence appeared to be largely preserved. His speech was dysarthric, but naming on verbal description was intact, and there was no sign of syntactic impairment. Short and long term verbal memory were mildly impaired. Spatial memory was not testable in a formal way, although there was no apparent deficit in sound localization and recognition. A good ability to recognize sounds was indicated by his intact naming of sounds produced by animals (cat, dog, cow, cock) or musical instruments (guitar, piano, violin, drum). A study of his auditory-evoked potentials in 1987 (series of clicks of 100-μs duration, 60-dB intensity, and 20-Hz frequency) gave results within the normal range. Haptic recognition of objects was impaired: He was able to recognize by active touch only 11 of 20 common objects.

PB is virtually blind, so that most of the standardized tests for assessing visual functions cannot be used, although he can detect the presence or absence of light, his optokinetic nystagmus is intact, and pupillomotor and blink reflexes are evokable. Crude pursuit movements are present only with stimuli in the right hemifield; saccadic eye movements are erratic, and he displays an inability to maintain steady fixation, making a formal perimetric test impossible. Assessment of visual acuity (with both Snellen letters and Landoldt rings) were unsuccessful because he cannot recognize any element, although a P-100 wave of normal amplitude and latency could be recorded in 1987 in the potentials evoked by a reversing checkerboard visual stimulus. In spite of this severe visual disability, his capacity to name colors is intact, as is his capacity to name the typical color of imagined common objects (e.g., banana, snow, coal, sky, sea etc.). Although on occasions he can recognize a visually presented object by its color (e.g., an orange), he is consistently unable to recognize common objects by vision alone. Pointing to or reaching for visual targets is extremely deficient, either because he does not see the target or, in the case of colored targets, because of optic ataxia. The few successful attempts at reaching for visual targets occur when the target is in the right hemifield and he uses his right hand. When tested on a reduced version of the Efron task for the discrimination of shapes equated for total flux, correct responses occurred on 8 of 20 trials, chance being 10/20. His extremely poor visuomotor control made the Farnsworth-Munsell test difficult, but he was found to be consistently able to name the hues of two differently colored chips presented one above the other in the center of the visual field (33). On repeated tests of color and form perception, he was asked to name one of six colors (fuchsia, orange, blue, green, yellow, and white) presented randomly for either 10 or 40 s in two blocks of 18 presentations. Performance was correct on up to 90% of trials with both durations, even though he was given no previous knowledge of the stimulus set. But when asked to identify one of six large block letters subtending $10° \times 6°$, each presented three times for 40 s in a random order, he scored only $\approx$10%, even though he was given foreknowledge of the stimulus set. Training on form discrimination (15 sessions of 16 trials over 3 months in 1988) was totally unsuccessful. When required to discriminate between four colors (red, green, blue, and yellow) or four shapes (square, circle, triangle, and cross), all stimuli being grossly equated for luminance, he did well on color naming but extremely poorly on shape discrimination even after extensive training. Recent clinical assessments (1995–1998) suggest that his cognitive abilities are declining, although they have not been tested formally. This may be attributable to sensory (mostly visual and somatic) deprivation and the use of antidepressant and sedative drugs since 1987. But his receptive and expressive language skills are largely intact, although his speech tends to become more and more slurred.

Psychophysical Studies of Color Vision. Because of his severe visual impairment, we restricted ourselves exclusively to a study of PB's color vision and began by asking him to identify colors in simple two-color images presented on a TV monitor (Commodore 1084S, Commodore Business Machines U.K., Maidenhead, Berkshire, U.K.); each image consisted of a colored simple object (e.g., car, boat) displayed against a differently colored equiluminant background. On each trial, PB was asked to name the objects and the colors. The simplest way of learning whether color constancy mechanisms were still operating in his brain was to use the Land experiments (36, 9). The Land Mondrian is a multicolored display consisting of many patches forming an abstract scene with no recognizable objects. It is illuminated by three variable intensity projectors, each equipped with a filter allowing it to pass light of certain wavebands only. A telephotometer (Model 2000, Gamma Scientific, San Diego) allows the intensity of the light coming from a patch to be accurately specified in mW/steradian/m^2, which we shall refer to as units. When a given patch, say a green one, is made to reflect 60, 30, and 10 units of long-, middle-, and short-wave light, and is viewed in its context (normal mode), a normal observer reports the color to be green even though it is reflecting twice the amount of long- than of middle-wave light. When made to reflect this same triplet of energies, other patches will retain their color in the normal mode. Viewed on their own (void mode), they look white, but, if, without changing the energies reflected from them, the surround is now brought into view, each patch immediately regains its color. Any patch may thus be said to have two colors, a contextual (natural) color when it is part of the scene and a void color, when it is viewed in isolation.

The arrangement had to be simplified because of PB's poor visual capacity and his random gaze-shifts from one part of his field of view to another. We used one large Color Aid paper against a black velvet screen and surrounded this with four smaller Color Aid cut-outs to construct a rather simple Mondrian. The Commission Internationale de l'Éclairage coordinates of the nine patches used were taken with a telespectrophotometer (Photo Research Spectra-Colorimeter, Photo Research, Chatsworth, CA). PB sat $\approx$1 m from the screen but was allowed to move forward if he felt he needed to. He was first asked to identify the color of the large patch in room light, after which the telephotometer was used to set the three projectors so that a known composition of light was reflected; PB was then asked to report the color again. He often reported himself to be tired after a few sessions, and we did not continue once he had reached this state.

Imaging Studies. *Data acquisition.* PB and an age-matched normal male control were the subjects of this fMRI study, done with a 2 T Siemens Vision scanner (Siemens, Iselin, NJ) with a head radio-frequency resonator. The subject lay supine in the scanner, and the session began with the acquisition of a detailed structural MRI. This T1 weighted image was obtained by using a Multi-Planar Rapidly Acquired Gradient Echo (MPRAGE) sequence with Repeat Time = 9.7 ms, Echo Time = 4 ms. Images were acquired in transverse orientation, giving 108 slices with voxel size $1 \times 1 \times 1.5$ mm. A gradient echo Echoplanar imaging (EPI) sequence was used to acquire the functional, relatively T2 weighted images (Repeat Time = 6.084 s, Echo Time = 40 ms, delay time = 14 ms). The echoplanar imaging sequence was selected to reduce inflow effects and maximize Blood Oxygenation Level Dependent

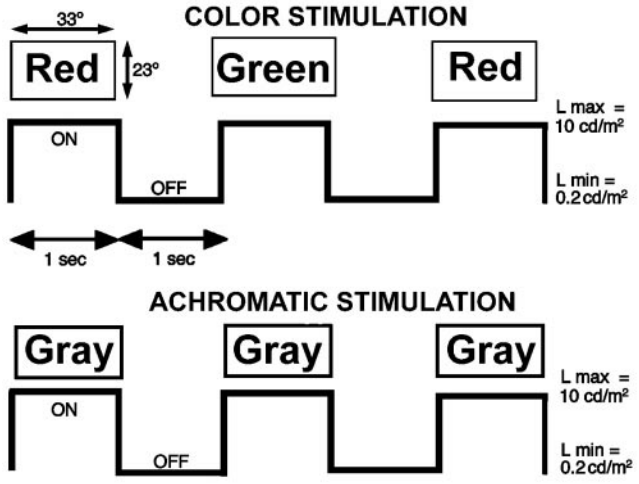

Fig. 1. A diagrammatic representation of the stimulus used in the fMRI study.

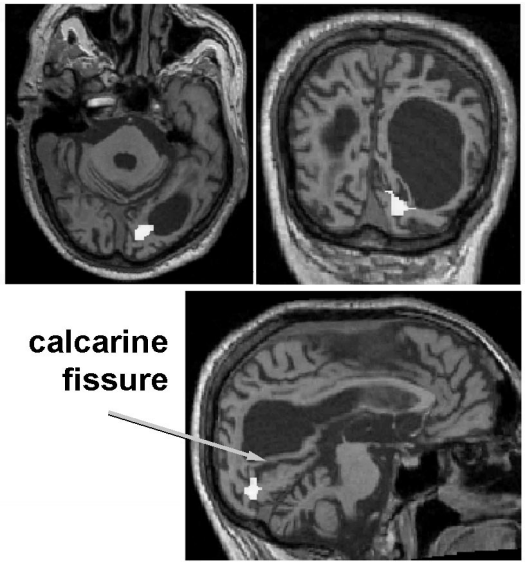

Fig. 2. Co-registered structural and functional MRI data from the patient PB showing, in coronal, sagittal, and transverse sections, the activation in the calcarine fissure (V1) during stimulation with a colored display. The white area shows the cluster of voxels exceeding an uncorrected significance level of <0.001.

(BOLD) contrast. The images consisted of 64 transverse slices, with each slice being 64×64 pixels (voxel size $3 \times 3 \times 3$ mm).

Visual stimulation. The light from a liquid crystal display projector driven by an Apple 7500/100 computer was projected onto a translucent screen, giving a field size of $30° \times 23°$, which the subjects viewed via a mirror angled at 45°. Because of the limited visual capacities of PB, large field, patternless color, and monochromatic stimuli were presented in an on–off mode, with a duty cycle of 2 Hz. The color stimuli (alternately red and green with a luminance of 10 cd/m^2 each) were presented for 1 s and then were replaced by a blank field of the same duration (Fig. 1). PB was able to detect the temporal changes and to correctly identify the constituent colors. A stimulus of similar spatial extent and temporal modulation was employed for achromatic stimulation, using a uniform gray field. This gray was of the same mean luminance as the color stimuli (Fig. 1). The stimuli were presented in a pseudorandom sequence in blocks lasting 30.42 s. In total, 320 whole brain volumes were acquired during the course of the 32-min fMRI experiment.

Statistical analysis. The fMRI data were analyzed by using the software package SPM96 (Wellcome Department of Cognitive Neurology, London); detailed descriptions are provided in previous publications (38, 39). In brief, the scans were first realigned and then smoothed with an 8-mm full-width half maximum Gaussian filter. Because this study is based, of necessity, on one subject only, the images were not normalized. The design matrix for SPM96 contained two columns, one for the blocks of colored stimuli and one for the blocks of achromatic stimuli, each modeled by a simple box-car, delayed by one scan to accommodate the latency of the BOLD response. The rest of the design matrix contained a series of discrete cosine functions modeling low frequency components (<0.5 cycles per minute) of the signal as effects of no interest. SPM96 determined the height and statistical significance of the parameter estimates for the colored and the achromatic blocks of stimuli, using an iterative least-squares fitting routine (see ref. 38 for a detailed explanation). Figs. 2 and 3 show statistical maps of the voxels where the parameter estimates exceeded an uncorrected significance of $P < 0.001$ (a relatively low threshold to show the extent of activation) superimposed onto the structural images. The statistical significance of the comparison of colored stimuli with achromatic stimuli in PB (Fig. 2) was adjusted by using a Bonferroni correction for multiple comparisons. Uncorrected statistical significance levels are given for the normal control subject because the results were expected *a priori* from previous studies (37, 39).

Results

Psychophysical Results. We confirm the earlier observations of Humphrey *et al.* (33) in showing that PB is visually severely defective but that his color vision is relatively intact and, indeed, surprisingly good, given his near-blind status. As Tables 1 and 2

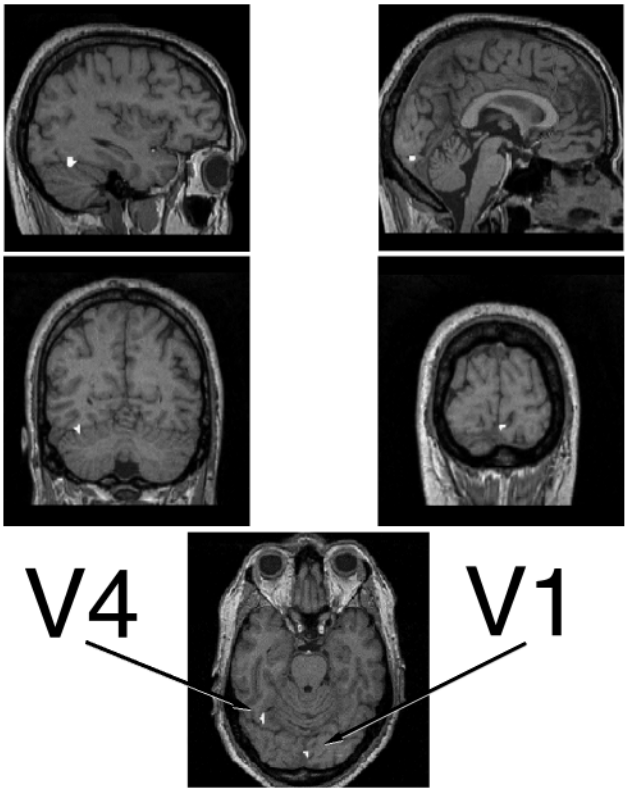

Fig. 3. Co-registered structural and functional MRI data from an age-matched normal control subject showing activation in the calcarine fissure (V1) on the left and in the fusiform gyrus (V4) on the right. Conventions are as in Fig. 2.

Table 1. The stimulus parameters used to test PB's form vision

Color	CIE 1931 co-ords (x, y, Y CD·m^{-2})
Red	0.600, 0.347, 3.75
Green	0.313, 0.584, 3.71
Blue	0.155, 0.069, 3.99
Yellow	0.422, 0.489, 4.53
Cyan	0.227, 0.294, 4.17
Magenta	0.299, 0.160, 3.89
White	0.302, 0.315, 27.5
Light gray	0.301, 0.314, 22.6
Mid gray	0.302, 0.312, 17.5
Dark gray	0.302, 0.309, 10.1
Black	0.305, 0.298, 3.51
Form	Width
Boat	14 × 17
Car	18 × 8
Chair	10 × 20
Cross	14 × 19
House	20 × 17
Key	19 × 9
Tree	23 × 21

show, he was mostly accurate in identifying the two colors in each image, although unable to distinguish between figure and background. He was invariably wrong in identifying the objects' shapes. The results of the color constancy tests (Tables 3 and 4) show that PB's color vision is very much wavelength-dominated, because he is correct in his identification when the color on the TV monitor was generated by a single phosphor or when the Color Aid papers were made to reflect a great excess of one wavelength over the others. Thus, he reported a green patch as green when it reflected a lot more middle wave (green) light. But when it was made to reflect more long-wave (red) light and still looked green to normal observers, because of the operation of the color constancy mechanism in them, PB usually reported it to be white (as would normals viewing it in the void mode) or red or brown. This is what would be expected if his color vision were wavelength-based and his color constancy mechanisms defective. Tables 3 and 4 give other examples and also show that there were 4 occasions of 52 when his color constancy mechanism was apparently operational, in that he was able to ascribe the correct

Table 3. Examples of typical responses given in PB when asked to identify a variety of color patches whose illumination could be varied

Target square	Ratio of LW:MW:SW, light reflected from target	Normal's response, natural	Normal's response, Void	PB's response, Natural
Light red	60:30:10	Red	White	Green
Dark red	60:30:10	Red	White	White
Dark red	150:30:10	Red	Red	Red
Dark green	60:30:10	Green	White	Dirty white
Dark green	50:60:10	Green	Green	Green
Yellow	60:30:10	Yellow	White	White
Dark blue	60:30:10	Blue	Gray	Pale brown
Dark blue	30:30:50	Blue	Blue	Light blue
Red-orange	120:30:10	Red	Red	Red
Red-orange	60:45:40	Red	White	White

color even in spite of changes in the wavelength composition. In summary, in spite of his ability to name colors correctly, our results show that his color constancy mechanisms are severely defective, although not absent, and that his color vision is very much wavelength-based.

Results of Imaging Studies. The comparison of color versus achromatic visual stimulation in subject PB revealed a single significant region of activation that was located in the posterior portion of the calcarine fissure ($z = 4.69$, $P < 0.04$ corrected; Fig. 2). This presumably corresponds to his area V1 (and perhaps V2, from which it is difficult to separate with certainty), even though the increase in the size of the lateral ventricle has resulted in considerable distortion of the sulcal and gyral anatomy of the occipital cortex. The same comparison for the control subject revealed a similar region of activation in the posterior calcarine cortex ($z = 3.79$, $P < 0.001$ uncorrected) and also an additional area located in the fusiform gyrus of the right hemisphere ($z = 3.88$, $P < 0.001$ uncorrected; Fig. 3). Previous studies (37, 40) have identified the latter as being the locus of the color center (the V4 complex) in the human brain (21). An activation located in the fusiform gyrus of PB, presumably in his V4, could only be detected if the threshold was set at a level of $P = 0.01$ uncorrected. This relaxation of the threshold did not reveal any other areas.

Table 2. The responses of PB when tested for color and form vision

Color	Color response	Form	Form response
White/medium gray	White	Boat	Triangle/fork
Green on red	Green/white Red and green	Boat	A drawing, a square
Dark Gray/white	White and black	Car	Cube
Blue on green	Purple/green White/yellow	Car	A rhombus
White/medium gray	White	Chair	A square
Cyan on red	Red and light blue	Chair	Stripes; given a list including a chair, said ''maybe a chair''
Light gray/medium gray	White	Cross	A hand tool
Green/magenta	Violet and green	Cross	Not a ball, a wheelbarrow
Black on white	Black and white	Key	A car/fork
Blue/yellow	Yellow on purple	Key	Motorbike
Mid gray/white	White and dark	House	Car
Red on cyan	Red and clear	House	Motorbike
Light gray/white	White Black on white	Tree	Tractor
Magenta/green	Violet and green	Tree	Flower

Table 4. χ^2 analysis of the responses of PB and normals when asked to identify the color of one of the test patches when illuminated in a variety of ways

Response given was	As if target was seen in void condition	As if target was in natural condition	Same for void and natural viewing	Incorrect for void and natural viewing	Total responses
PB	21	4	12	15	52
Normal	6	33	13	0	52

Six of the presentations were made in the void condition only; in thirteen of the presentations, the target had the same color when viewed in the natural and the void conditions. Difference is significant at $P < 0.0001$.

Discussion

PB is almost totally blind and does not even have that elementary visual reactivity that can apparently occur unaccompanied by consciousness in cortical blindness (41). Color naming tasks nevertheless testify to PB's nearly perfect identification of various surface and object colors through the use of a considerable range of color names, including less frequently used ones. This stands in contrast with the patient's complete inability to recognize the objects whose color he can correctly name. That the color vision is fully conscious is made clear by the patient's introspective reports, which consistently correspond to, and are felt to stem from, a phenomenal awareness of the visual input, rather than being mere guesses produced in reaction to "unseen" stimuli. Stated briefly, when PB says, "I see red, or blue, etc.," when presented with a colored stimulus, to all appearances he seems to be sharing a phenomenal experience of color with normal observers. A fair-to-good conscious color perception coupled to poor form vision has been reported in brain-damaged patients, but other visual abilities, including a fully preserved visual field and good visual acuity, are commonly quite normal in them. By contrast, PB not only systematically fails in tests of shape perception but is also perimetrically blind and lacks any visual acuity, thus qualifying as an indisputable case of long-standing cortical blindness.

Preservation of Color Vision in Cortically Blind Subjects. While successful wavelength discrimination and color naming in a forced-choice paradigm has been reported in cases of cortical blindness as an expression of "blindsight," which is in absence of a concomitant sensation of color (42, 43), conscious color perception in perimetrically blind fields is a much rarer occurrence. The selective preservation of color vision does not necessarily imply that the systems for conscious color vision are more widespread in the brain and therefore more immune to diffuse brain damage than those for other visual functions. Very few cases of a relative preservation of conscious color vision in the almost total absence of other visual abilities have been described after Wechsler's report (24). Two examples are Warrington's cases THR, who had bilateral occipital infarctions, and BRA, who suffered from hypoxic damage during a surgical operation (44). Both were severely impaired in all visual functions except color perception. Like PB, they could not be formally examined with the Farnsworth-Maunsell hue test because of their visuospatial disability, yet they could perform the Holmgren wools test with remarkable accuracy through their unfailing ability to name primary colors and respond to the full range of hues sampled by the test. Another case is that of Blythe *et al.* (45), who could correctly discriminate colors and report a sensation of color in an otherwise blind hemifield. Warrington (44) supposed that preservation of color vision in cortical blindness may represent the converse of acquired achromatopsia, but at least as far as PB is concerned, her assumption is untenable, because shape recognition and other achromatic visual abilities can be quite normal in achromatopsia, whereas PB's color perception, although quite efficient, can hardly be considered normal.

PB's Abnormal Color Vision. The abnormality of PB's chromatic vision was revealed when his color constancy mechanisms were assessed by the simplified Mondrian test. He behaved like normal controls in being able to name the colors of the target and the surrounding patches when the stimulus array was illuminated with white light. But when the spectral composition of the illuminant was changed, his responses usually varied with the reflected wavelength, unlike normals. This leads us to conclude that PB's conscious color vision is largely wavelength-based and does not use the mechanisms that subserve color constancy in normals. This conclusion may be debated, if only because color constancy mechanisms are far from being completely understood (46). For example, because eye movements have some role in color constancy in normal subjects (47), the apparent failure of color constancy in PB may be attributed to his abnormal oculomotor control and erratic fixation, leading to incomplete scanning of the Mondrian stimulus and disruption of the local adaptation processes that may play a major role in color constancy (48). PB, like other patients with occipitotemporal damage (49), could also be suffering from simultanagnosia, resulting in an incapacity to process different wavelengths from different locations at the same time. Although these may be contributing factors, the lack of a significant V4 activation in PB in the neuroimaging test provides a compelling argument for supposing that it is damage to a specific cortical area that is the root cause of his abnormal response to the Mondrian stimulus. Imaging experiments suggest that the ratio-taking operations that are at the heart of color constancy occur in the V4 complex (21). Humans with a damaged V4 either cannot see the world in color (7), or, if the damage is subtotal, are impaired in their color constancy mechanisms (50–52) as are monkeys with lesions in V4 (53–55), although with accompanying, nonchromatic visual deficits (54, 56, 57). This impairment relates well to the known physiology of the visual pathways. A characteristic of achromatopsic and dyschromatopsic patients is that, in spite of their severe color problems, they are able to distinguish wavelengths from one another, even though their thresholds are elevated and they cannot ascribe colors to what they are discriminating (58). This ability has been related to the responses of cells in V1 and V2 (7, 59). The cells in the former area are selective for wavelengths alone and are indifferent to the color of the stimulus (9). Their responses, in other words, are very much wavelength-based. The cells of area V2 have not been studied in as much detail, but the little we know suggests that their responses, too, are largely wavelength-based, although some at least may constitute the initial steps in the wavelength differencing mechanisms that are so critical for color constancy mechanisms (60). By contrast, at least some cells in V4 have responses that correlate with perceived color and are indifferent to the precise wavelength composition of the stimulus. This ability is presumably conferred on them by receptive field arrangements that allow them to collect information from large parts of the field of view (9, 61). One can suppose, therefore, that patients with a damaged V4 but an intact V1 and V2 will be able to distinguish between different wavelengths, but without being able to experience colors. They should thus be able to detect different surfaces if the light reflected from them is dominated by one waveband, as commonly happens. The difference between PB and such patients is that, unlike them, he is able to experience colors consciously, even though his color constancy mechanisms are severely defective. That chromatic stimulation can evoke activity in PB's V1 and probably V2 is clear from the imaging study, but the absence or severe impairment of color constancy

mechanisms in this patient naturally raise the question of whether activity in V1 and V2 can mediate a conscious perception of color, without involving V4.

Conscious Experience of Color Through V1 and V2. In the primate brain, the metabolically active blobs of V1, and possibly the thin stripes of V2, are much more richly vascularized than their metabolically less active neighbors (62). It is therefore reasonable to assume that, in the minority of cases in which reperfusion occurs before the color system has suffered irreparable damage, the richer vasculature and the high oxygen extraction of the system allow it to benefit from the circulation reinstatement at the expense of neighboring systems that may therefore be severely compromised. The activity in PB's calcarine cortex produced by chromatic stimulation was very restricted and appeared to be centered on V1 (and possibly V2); one could thus conclude that activity in these areas alone can mediate a conscious visual percept, although degraded and related directly to the color physiology of V1-V2, which, like the color perception of PB, appears to be wavelength-based. This suggestion has been made (53); its import would be in showing that a human subject can be conscious of activity in V1, which a current theory suggests is not possible (63). But this would leave other factors out of account. The first concerns the residual activity in V4, obtainable only by dropping the threshold below a statistically significant level. Although such residual activity could account for the conscious color experience of PB, it would remain at odds with an experiment on another blind subject, GY, and another visual subsystem, the motion one based on area V5. A recent study (39) has shown that activity in V5 must reach a certain threshold for GY to be able to experience motion consciously. Absolute levels of activity are obviously not measurable through imaging, and it may be that a lower level of activity in the color system, and specifically in V4, is enough to correlate with a conscious visual experience, although insufficient to sustain color constancy. Another factor concerns the activation of V2 and its possible contribution to color awareness, which is still largely unknown. What is certain is that, in PB and other patients like him, the color system can act more or less autonomously when the other systems are severely compromised or absent and that activity in the color system, without a detectable participation of the other systems, can lead to a conscious experience of color. But this is of a defective nature because it is mainly based on wavelengths, not on a comparison of the wavelength composition coming from many parts of the field of view, as in normals. A final issue that requires investigation is the possible participation of subcortical centers in the conscious experience of color, in analogy with the demonstrated involvement of the brain stem reticular formation in the conscious awareness of visual motion (39). Whatever the outcome of such studies, the results here add to the fact that form vision can be severely compromised, indeed absent, without compromising the color system to nearly the same degree, and hence supports the notion that the separate systems can act autonomously of one another (6, 39, 64).

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1. Zeki, S. M. (1978) *Nature (London)* **274,** 423–428.
2. Livingstone, M. S. & Hubel, D. H. (1988) *Science* **240,** 740–749.
3. Howard, R. J., Brammer, M., Wright, I., Woodruff, P. W., Bullmore, E. T. & Zeki, S. (1996) *Curr. Biol.* **6,** 1015–1019.
4. Wurtz, R. H., Yamasaki, D. S., Duffy, C. J. & Roy, J. P. (1990) *Cold Spring Harbor Symp. Quant. Biol.* **55,** 717–727.
5. Zeki, S. (1990) *Cold Spring Harbor Symp. Quant. Biol.* **55,** 651–661.
6. Merigan, W., Freeman, A. & Meyers, S. P. (1997) *NeuroReport* **8,** 3985–3991.
7. Zeki, S. (1990) *Brain* **113,** 1721–1777.
8. Zeki, S. M. (1971) *Brain Res.* **34,** 19–35.
9. Zeki, S. (1983) *Neuroscience* **9,** 767–781.
10. Zeki, S. & Shipp, S. (1989) *Eur. J. Neurosci.* **1,** 494–506.
11. Nakamura, M., Gattass, R., Desimone, R. & Ungerleider, L. G. (1993) *J. Neurosci.* **13,** 3681–3691.
12. DeYoe, E. A., Felleman, D. J., Van Essen, D. C. & McClendon, E. (1994) *Nature (London)* **371,** 151–154.
13. Desimone, R., Fleming, J. & Gross, C. G. (1980) *Brain Res.* **184,** 41–55.
14. Komatsu, H., Ideura, Y., Kaji, S. & Yamane, S. (1992) *J. Neurosci.* **12,** 408–424.
15. Zeki, S. & Marini, L. (1998) *Brain* **121,** 1669–1685.
16. Holmes, G. (1945) *Proc. R. Soc. London Ser. B* **132,** 348–361.
17. Daniel, P. M. & Whitteridge, D. (1961) *J. Physiol. (London)* **159,** 203–221.
18. Horton, J. C. & Hoyt, W. F. (1991) *Arch. Ophthalmol.* **109,** 816–824.
19. Horton, J. C. & Hedley Whyte, E. T. (1984) *Philos. Trans. R. Soc. London B* **304,** 255–272.
20. Livingstone, M. S. & Hubel, D. H. (1984) *Neuroscience* **4,** 309–356.
21. Zeki, S. & Bartels, A. (1999) *Philos. Trans. R. Soc. London B* **354,** 1371–1382.
22. Vaina, L. M. (1994) *Cereb. Cortex* **4,** 555–572.
23. Heywood, C. A., Kentridge, R. W. & Cowey, A. (1998) *Exp. Brain Res.* **123,** 145–153.
24. Wechsler, I. S. (1933) *Arch. Ophthalmol.* **9,** 957–965.
25. Verrey, D. (1888) *Arch. Ophthalmol.* **8,** 289–300.
26. Zeki, S. M. (1973) *Brain Res.* **53,** 422–427.
27. Adler, A. (1944) *Arch. Neurol. Psychol. (Chicago)* **51,** 243–259.
28. Adler, A. (1950) *J. Nerv. Ment. Dis.* **111,** 41–51.
29. Hécaen, H. & De Ajuriaguerra, J. (1956) *Rev. Neurol. (Paris)* **94,** 222–233.
30. Benson, D. F. & Greenberg, J. P. (1969) *Arch. Neurol. Psychol. (Chicago)* **20,** 82–89.
31. Milner, A. D. & Heywood, C. A. (1989) *Cortex* **25,** 489–494.
32. Milner, A. D., Perrett, D. I., Johnston, R. S., Benson, P. J., Jordan, T. R., Heeley, D. W., Bettucci, D., Mortara, F., Mutani, R., Terazzi, E. & Davidson, D. L. W. (1991) *Brain* **114,** 405–428.
33. Humphrey, G. K., Goodale, M. A., Corbetta, M. & Aglioti, S. (1995) *Curr. Biol.* **5,** 545–551.
34. Poggio, G. F., Baker, F. H., Mansfield, R. J. W., Sillito, A. & Grigg, P. (1975) *Brain Res.* **100,** 25–59.
35. Zeki, S. (1983) *Neuroscience* **9,** 741–765.
36. Land, E. (1974) *Proc. R. Inst. G. B.* **47,** 23–58.
37. McKeefry, D. & Zeki, S. (1997) *Brain* **120,** 2229–2242.
38. Frackowiak, R. S. J., Friston, K. J., Frith, C. D., Dolan, R. J. & Mazziota, J. C. (1997) *Human Brain Function* (Academic, London).
39. Zeki, S. & Ffytche, D. (1998) *Brain* **121,** 25–45.
40. Zeki, S., Watson, J. D. G., Lueck, C. J., Friston, K. J., Kennard, C. & Frackowiak, R. S. J. (1991) *J. Neurosci.* **11,** 641–649.
41. Stoerig, P. & Cowey, A. (1997) *Brain* **120,** 535–559.
42. Stoerig, P. (1987) *Brain* **110,** 869–886.
43. Stoerig, P., Barbur, J. L., Sahraie, A. & Weiskrantz, L. (1994) *Invest. Ophthalmol. Visual Sci.* **35,** 1813–1813.
44. Warrington, E. K. (1986) *Pontif. Acad. Sci. Scr. Varia* **54,** 247–261.
45. Blythe, I. M., Kennard, C. & Ruddock, K. H. (1987) *Brain* **110,** 887–905.
46. Kraft, J. M. & Brainard, D. H. (1999) *Proc. Natl. Acad. Sci. USA* **96,** 307–312.
47. Cornelissen, F. W. & Brenner, E. (1995) *Vision Res.* **35,** 2431–2448.
48. Walsh, V. (1995) *Curr. Biol.* **5,** 703–705.
49. Brazis, P. W., Graff-Radford, N. R, Newman, N. J. & Lee, A. G. (1998) *Am. J. Ophthalmol.* **126,** 850–851.
50. Kennard, C., Lawden, M., Morland, A. B. & Ruddock, K. H. (1995) *Proc. R. Soc. London Ser. B* **260,** 169–175.
51. Heywood, C. A., Cowey, A. & Newcombe, F. (1991) *Eur. J. Neurosci.* **3,** 802–812.
52. Clarke, S., Walsh, V., Schoppig, A., Assal, G. & Cowey, A. (1998) *Exp. Brain Res.* **123,** 154–158.
53. Walsh, V., Carden, D., Butler, S. R. & Kulikowski, J. J. (1993) *Behav. Brain Res.* **53,** 51–62.
54. Heywood, C. A., Gadotti, C. A. & Cowey, A. (1992) *J. Neurosci.* **12,** 4056–4065.
55. Schiller, P. H. (1993) *Visual Neurosci.* **10,** 717–746.
56. De Weerd, F., Desimone, R. & Ungerleider, L. G. (1996) *Neurosciences* **13,** 529–538.
57. Merigan, W. H. & Pham, H. A. (1998) *Visual Neurosci.* **15,** 359–367.
58. Heywood, C. A., Wilson, B. & Cowey, A. (1987) *J. Neurol. Neurosurg. Psychiatry* **50,** 22–29.
59. Zeki, S. (1993) *A Vision of the Brain* (Blackwell, Oxford).
60. Zeki, S. (1985) in *Color Pathways and Hierarchies in the Cerebral Cortex*, eds. Ottoson, D. & Zeki, S. (Macmillan, London), Vol. 43, pp. 19–44.
61. Desimone, R., Moran, J., Schein, S. J. & Mishkin, M. (1993) *Visual Neurosci.* **10,** 159–171.
62. Zheng, D., LaMantia, A. S. & Purves, D. (1991) *J. Neurosci.* **11,** 2622–2629.
63. Crick, F. & Koch, C. (1995) *Nature (London)* **375,** 121–123.
64. Zeki, S. (1997) in *The Color and Motion Systems as Guides to Conscious Visual Perception*, eds. Rockland, K. S., Kaas, J. H. & Peters, A. (Plenum, New York), pp. 777–809.