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A functional MRI case study of acquired cerebral dyschromatopsia

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Abstract

Evidence from imaging studies suggests that primary visual cortex and multiple areas in ventral occipitotemporal cortex subserve color perception in humans. To learn more about the organization of these areas, we used structural and functional MRI (fMRI) to examine a patient with damage to ventral cortex. An art professor, KG, suffered a cerebrovascular accident during heart surgery that impaired his ability to perceive color. The Farnsworth–Munsell 100-Hue test was used to assess the extent of his deficit. When tested 12 months after the lesion, KG performed worse than 95% of age-matched normals on the 100-Hue test, but well above chance. Structural and functional MRI studies were conducted 3 years after the lesion to investigate the neuroanatomical correlates of KG'ss remaining color ability. Structural MRI revealed bilateral damage to ventral occipitotemporal cortex. In young and age-matched normal controls, an fMRI version of the 100-Hue reliably activated bilateral, color-selective regions in primary visual cortex and anterior and posterior ventral cortex. In subject KG, color-selective cortex was found in bilateral primary visual cortex. In ventral cortex, no color-selective activity was observed in right ventral cortex, and only a small area of activity was observed in left anterior ventral cortex. However, significant color-selective activity was observed in posterior left ventral cortex spared by the lesion. This posterior left ventral activation was similar in extent, position, and degree of color-selectivity to the posterior left posterior activation observed in normal controls, suggesting that this focus may be the cortical substrate underlying KG's remaining color perception. Published by Elsevier Science Ltd.

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1. Introduction

Over a century ago, a link between ventral occipitotemporal cortex and color perception was proposed ([38] reviewed in [45]). Evidence from many studies of patients with lesions in this region, including post-mortem anatomical analysis [10,28] and anatomical imaging [18,24] support the conclusion that ventral cortex is crucial for human color perception.

However, questions remain about the organization of the ventral cortex underlying color perception. Is color processing subserved by one or multiple ventral areas? Are these areas widely distributed in ventral cortex? Do different regions of ventral cortex perform different color processing functions?

Anatomical studies of patients are poorly suited to answering these questions, because lesions are often extensive, not focal, and differentiation of normal from damaged tissue does not allow determination of the regions of cortex actually involved in processing color information.

Functional imaging studies in normal human subjects have provided information complementary to the

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findings from lesion studies, such as establishing that ventral sites are important for color perception in normals [7,47]. More recently, imaging data has suggested that multiple sites in ventral cortex are important for processing color [5]. However, imaging studies have limited deductive power because of their inferential nature. In an imaging study, areas may be active because they are involved in a task component unrelated to color processing.

We hoped to combine these two breeds of studies, reducing the flaws inherent in each type, by performing an imaging study on a patient with impaired color perception. Functional imaging should allow the specification of exactly which regions of damaged cortex are functional in the lesioned subject. Conversely, determining how damage to ventral areas affects color perception should provide an important clue to their role in normal subjects.

Patients with deficits in cerebral color perception are relatively rare, because damage to ventral areas often also damages its anatomical neighbor, primary visual cortex, resulting in cortically blind subjects unaware of any specific color deficit. We were fortunate to obtain a referral for KG, a painter and art teacher, who suffered bilateral ventral occipital damage from vascular accident during heart surgery. KG found that his perception of colors was sharply changed by his injury. Before the infarcts, KG's sense of color was acute (he had even worked matching colors in a paint factory) but after the lesion he complained that even brightly colored objects appeared sepia-toned. To assess the extent of KG's color impairment, the Farnsworth–Munsell 100-Hue test was administered. To study how damage to his ventral areas had impaired his color ability, and understand the neuronal correlates of KG's remaining color abilities, a functional MRI (fMRI) version of the 100-hue test was administered. We describe the damage to ventral cortex, and functional activation in these regions when KG performed the 100-Hue fMRI test. Then, we consider the implications for our understanding of cortical color processing.

2. Methods

The primary subject in this experiment was KG. Other subjects included a control subject matched for sex, age, and education level (subject LS) and 12 young controls (five males, seven females, average age 27.7 years). Informed consent was obtained from all subjects according to the declaration of Helsinki [43] and was approved by the Human Research Review Committee of the Medical College of Wisconsin and the NIMH human subjects committee.

2.1. Case description

KG is a right-handed male (born 2/1/1938) who worked as a painter and art professor at a local university. On 3/3/1995, he suffered a right occipital stroke during coronary artery surgery. A second, left-lateralized occipital stroke occurred 1 week later. A comprehensive neuropsychological evaluation was performed on 3/25/1996; a follow-up examination was performed on 9/1/1998.

2.1.1. Neuropsychological assessment: overview

The patient's clinical examination revealed a relatively focal color deficit and memory problems; however, the patient also complained of topographic disorientation. Significant deficits were observed in hue discrimination on formal testing. He was able to name most colors he viewed as well as the colors of objects he imagined (e.g. the color of his toothbrush). Formal neuropsychological testing revealed memory problems, inconsistent visuospatial deficits, and intact object and face discrimination and identification abilities.

2.1.2. Formal intellectual and neuropsychological testing

Intellect was in the superior range with no significant difference between verbal and performance IQ (verbal IQ = 124; performance IQ = 111; full scale IQ = 122). Some neuropsychological deficits were observed in memory and visuospatial and perceptual abilities. Performance was borderline impaired on a visuospatial test that involved mentally rotating and assembling fragmented line drawings of objects. Scores on all other visuospatial/perceptual tests, including discrimination of unfamiliar and naming of famous faces, and line orientation discrimination were average or above average. There was no evidence of neglect. Memory deficits were characterized by relatively intact immediate verbal recall and borderline recall after a 30 min delay. The patient's scores were borderline to impaired on tests involving immediate recall of nonverbal material (line drawings and spatial dot patterns). All other tests, including verbal, motor, and sensory (other than visual) functions were consistent with IQ. Despite his visual field defects, his score on a test involving negotiating mazes (Porteus Mazes) was within the normal range for age-matched controls. The patient was able to draw a map of the room layout of his house and place objects into it. He was able to image walking through his house with no evidence of neglect of his scotomatous visual field. Perception of illusions related to monocular depth, such as the Ponzo illusion, were intact. Performance on a test of binocular depth perception using a red-green anaglyph random dot test was normal. The patient did not have any difficulty with visual saccades on gross testing. The follow-up examination found no major changes in

his cognitive abilities, but changes in his color perception were noted.

2.1.3. Color sensitivity testing

The Farnsworth–Munsell 100-Hue test, a clinical test of color discrimination and color sequencing [12] was administered on several occasions during the 3 years following the strokes. In each session, scores from one to three repetitions of the test were averaged to provide the best possible estimate of KG's color sensitivity.

2.2. Anatomical magnetic resonance imaging

In September 1998, KG was examined using anatomical and functional MRI. To determine the extent of the lesion, anatomical images were collected using a 3D Fast Spoiled Grass sequence with TR = 14.4 ms, TE = 5.4 ms, flip angle = 20° for optimal gray–white segregation. Several repetitions of this scan with voxel size $0.9375 \times 0.9375 \times 1.2$ mm were collected. The entire anatomical dataset can be inspected online at "http://hippo.nimh.nih.gov/people/mikeb/KG/KGanat.html".

2.3. The fMRI version of the Farnsworth–Munsell 100-Hue test

To investigate the organization of color-selective visual cortex, fMRI studies were conducted using an adaptation of the 100-Hue test suited for the scanner environment. In the fMRI version of the 100-Hue test, subjects order the entire set of Munsell hues as they are presented, five at a time, as colored wedges arrayed around a central fixation bar (Fig. 2A).

The test consists of alternating experimental periods. In the chromatic period, subjects make an ordered/disordered decision on the colored wedges, pressing the right response button if the hues form a regular sequence from the 11 o'clock position to the 1 o'clock position and the left response button if they do not. In the achromatic period, subjects view a set of grayscale wedges and make an analogous ordered/disordered response based on luminance. In Fig. 2A, both chromatic and achromatic wedges are shown out of order.

In the chromatic condition, the hue difference between wedges is twice the distance in color-space between consecutive Farnsworth–Munsell test caps. For instance, if the test caps are numbered 1, 2, 3, ... a sample ordered wedge set would be 1, 3, 5, 7, 9 and a sample disordered wedge set would be 1, 3, 7, 5, 9. In the achromatic condition, the average luminance difference between adjacent wedges is 2.7 cd/m^2. The average luminance of the achromatic wedges and chromatic wedges is 53 cd/m^2. All wedges are brighter than the background luminance of 10 cd/m^2 (all luminances measured with an S370 optometer; United Detector Technologies, Baltimore, MD).

Each sequencing period lasts for 21 s, with a new set of randomly-selected wedges presented every 3 s. The sequencing periods are interspersed with 21-s fixation control periods. Each run contains 12 periods (three chromatic, three achromatic and six fixation) with ordering (chromatic or achromatic first) counterbalanced across runs. Typically, six runs are acquired for each subject, resulting in 126 trials of each type.

2.3.1. Luminance matching across hues

In the clinical 100-Hue test, the systematic difference in hue across the test caps is superimposed on small, random variations in chroma (color saturation) and value (luminance) [12]. This prevents color sequencing judgments based on the apparent luminance of the caps by subjects with abnormal color vision. The video projection system used for our fMRI adaptation of the test did not allow for the fine control of saturation and luminance achievable with caps viewed under a controlled illuminant. However, as a coarse method of equating luminances across nearby hues (preventing judgments based on luminance alone) each subject performed flicker photometry on every hue in the test set. The adjusted luminance value for each hue was then used when that hue was presented in the fMRI test.

To perform flicker photometry, subjects viewed a colored annulus presented at the same eccentricity as the test wedges that flickered at 15 Hz between the test hue and a uniform gray of luminance 53 cd/m^2 [32]. Subjects adjusted the luminance of the colored annulus to minimize the perceived flicker. The minimal degree of perceived flicker was greater for shorter wavelength stimuli because of the lack of short-wavelength input into the luminance (magnocellular) pathway [22].

2.3.2. Difficulty matching

Differences in task difficulty can lead to changes in brain activation patterns [2,34]. We wished to assure that activation differences in the comparison between chromatic and achromatic tasks were due to differences in the visual stimulus and not due to differences in task difficulty. Therefore, for each subject, the difficulty of the achromatic sequencing task was matched to the difficulty of the chromatic sequencing task by slightly increasing or decreasing the luminance difference between the achromatic wedges.

2.4. KG's ability to perform the fMRI 100-Hue test

2.4.1. Tests of fixation

Because the fMRI 100-Hue test requires subjects to maintain fixation, we tested KG's ability to fixate during visual tasks outside the scanner using an infrared-illuminated pupillary eye-tracking system (ISCAN,

Inc., Burlington, MA). KG's ability to fixate over the course of a two-minute visual sensitivity test did not significantly differ from that of two control subjects.

2.4.2. Visual field defects

We wished to determine whether KG was able to accurately view the fMRI 100-Hue test wedges, which were presented from 1° to 4° eccentricity. Corrected Snellen acuity was 20/20. Visual field analysis with Goldmann and Humphrey (program 24-2; Humphrey Instruments, San Leandro, CA) tests revealed visual field defects in the left hemifield and upper right quadrant, with macular sparing. Tangent screen perimetry (done at the same time and using the same stimulus apparatus as was used to project the 100-Hue stimuli) revealed that KG's upper left quadrant defect completely obscured one of the colored wedges and portions of another.

2.4.3. Quarterfield version of the 100-Hue fMRI test

The dense upper left visual field defect that rendered KG unable to see one of the test wedges could be expected to reduce his ability to perform the fMRI 100-Hue test, quite apart from any deficits in color perception. Therefore, a modified version of the fMRI test was also administered in which all of the wedges were visible to KG. In this quarterfield version of the test, the five chromatic or achromatic wedges were reduced in size and arranged in a circular array in KG's lower right quadrant (spared by the lesion) instead of being arrayed around the fixation bar.

2.4.4. Achromatic contrast sensitivity

We were concerned that KG's color perception difficulties might be due to a more general deficit in contrast sensitivity. Therefore, we tested achromatic contrast sensitivity using psychophysical software that allowed 15-bit absolute luminance control [6]. KG's foveal contrast sensitivity was not significantly different from controls at spatial frequencies of 0 cycles per degree (cpd), 1 cpd, 1.9 cpd and 7.8 cpd. In the periphery, KG's contrast sensitivity was not significantly different from controls at spatial frequencies of 0 cpd, 2 cpd or 7.9 cpd, except in the upper left quadrant, the location of his densest visual field defect.

2.4.5. Differences in color sensitivity between quadrants

To determine whether KG's color perception differed across the visual field, his color sensitivity in different quadrants was measured in two different ways. In the first test, KG's ability to detect isoluminant red/green gratings with counterphase flicker at 2 hz was measured at spatial frequencies of 0 cpd, 1 cpd and 3.9 cpd using the method of adjustment [13]. Color sensitivity was not significantly different across the relatively spared right hemifield and lower left quadrant. The upper left quadrant, shown by perimetry to have the densest field defect, had color contrast sensitivity that was significantly less than the spared quadrants at low spatial frequency ($1.3\% \pm 0.2\%$ SD vs $22.1\% \pm 5.9\%$ at 0 cpd; $1.0\% \pm 0.1\%$ vs $14.8\% \pm 5.0\%$ at 1 cpd).

For a second measure of color sensitivity, we attempted to have KG perform the quarterfield 100-Hue test in each quadrant. KG was able to perform the test with similar accuracy in the upper right, lower right, and lower left quadrants (83, 77 and 90% correct, respectively). KG's dense upper left field defect prevented him for performing the test in this quadrant.

Neither measure suggested systematic differences in color-sensitivity across the intact regions of KG's visual field.

2.5. Analysis of the fMRI datasets

Gradient-echo echo-planar functional images were collected using a 1.5 T scanner (General Electric, Milwaukee, WI) with a repetition time (TR) of 3000 ms, an echo time (TE) of 40 ms, and in-plane resolution of 3.75×3.75 mm. Depending on the geometry of each subject's brain, from 21 to 25 axial slices with a thickness of 4 or 5 mm were collected. Subjects KG and LS were scanned at the Medical College of Wisconsin; the 12 young controls were scanned, using identical parameters, at the National Institutes of Health. A detailed account of the results from the young controls has been published elsewhere [5].

Comparison of the blood oxygen level dependent response in chromatic and achromatic stimulation periods with fixation allowed detection of brain regions responsive to visual stimulation, while comparison of the chromatic and achromatic responses revealed visual regions selective for color. Functional images were registered and multiple regression was performed on each voxel's time series using AFNI v2.21 [8,9]. Two mutually orthogonal regressors with zero mean were used in the regression. The first regressor, consisting of value '0.5' during stimulation periods and '−0.5' during fixation periods, measured response to stimulation vs fixation. The second regressor, consisting of value '1' during chromatic stimulation, '0' during fixation, and '−1' during achromatic stimulation, measured the response difference between chromatic and achromatic stimulation. Both regressors were smoothed with a gaussian function (lag of 4.8 s, dispersion of 1.8 s) approximating the cerebral hemodynamic impulse response function [14,44]. All brain voxels were examined to find those showing an experimental effect (significant proportion of variance accounted for by the best-fit combination of the two regressors) using a rigorous threshold of $z > 4.416$ ($p < 10^{-5}$ per voxel) to correct for multiple compari-

sons. Those few voxels showing an experimental effect were classified by the second regressor, which measured color-selectivity. Visually responsive voxels with a $z > 1.6$ ($p < 0.05$) for the second regressor were termed 'color-selective'. The locations of active regions are reported in Talaraich coordinates as the distance in mm from the anterior commissure in the form (x, y, z) where the x-axis is left-to-right, the y-axis is posterior-to-anterior, and the z-axis is inferior-to-superior. 'Ventral areas' were defined as those lying below the commissural plane ($z < 0$) and outside the calcarine fissure, and were subdivided into anterior ($y > -60$) and posterior ($y < -60$) regions.

3. Results

3.1. Color sequencing ability

Following the lesion, KG complained that his color vision was impaired: even brightly colored objects appeared sepia-toned. KG's subjective report of impairment was confirmed by the 100-Hue test. In the first administration of the test, 1 year after the stroke, KG's 100-Hue score was 179, worse than 95% of age-matched control subjects [39].

A gradual improvement was noted in the 3 years following the stroke. At the time of his fMRI exam, KG scored 75, near normal levels. Subjectively, KG reported that his color vision had recovered somewhat but remained less acute than before the lesion.

3.2. Anatomical magnetic resonance imaging of the lesion

Three years after the lesion, anatomical MRI revealed extensive damage to bilateral ventral occipito-temporal cortex (Fig. 1). Damaged areas were visible in the T1-weighted images as regions of low signal intensity. In the right hemisphere, the most severe damage extended from the inferior surface of the occipital lobe ($z = -23$) superiorly into the inferior bank of the calcarine sulcus ($z = -5$). The bulk of the lesion extended from the occipital pole ($y = -98$ mm) to the

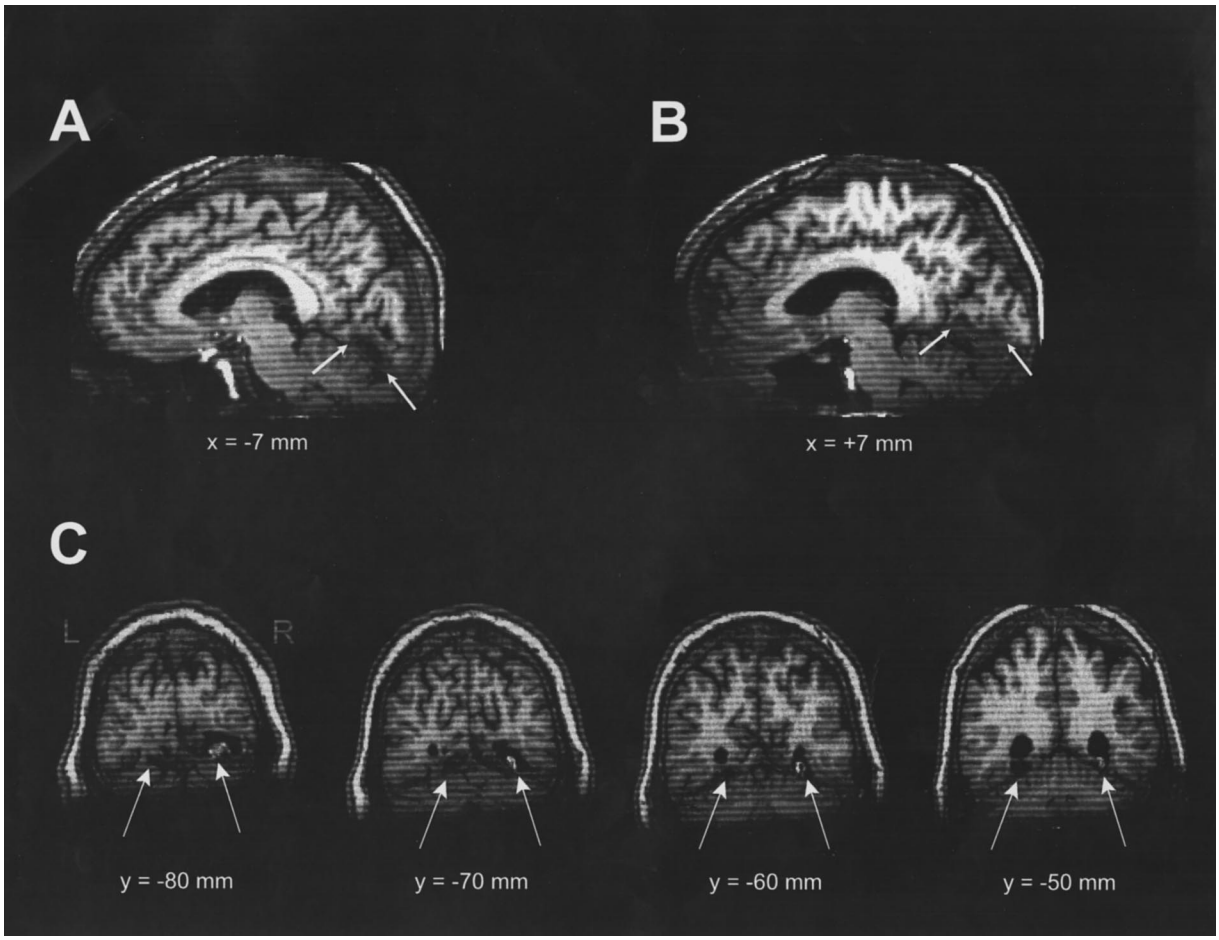

Fig. 1. T1-weighted anatomical MR images of subject KG. Sagittal sections through the left hemisphere (A) and right hemisphere (B) 7 mm from the midline illustrate the anterior to posterior extent of the lesion. (C) Coronal sections at four successively more anterior locations in the occipital lobe illustrate the medial to lateral extent of damaged cortex. (L: left; R: right). White arrows indicate the areas of heaviest damage.

occipital/temporal border ($y = -51$ mm) and from the midline laterally to the occipitotemporal sulcus. Large blood vessels appeared as bright inclusions in the center of the otherwise dark lesion (e.g. Fig. 1C, $y = -80$ mm). In the left hemisphere, the damage was less severe and was restricted to ventral cortex, extending from $z = -15$ to $z = -23$ mm. In the anterior-posterior axis, the most severe cortical damage extended from $y = -62$ mm to $y = -32$ mm, and included medial regions of ventral cortex, especially the lingual gyrus, but did not extend laterally beyond the collateral sulcus.

3.3. fMRI 100-Hue test: behavioral data

During performance of the fMRI 100-Hue test, KG's accuracy and RT were similar for the chromatic and achromatic sequencing tasks (chromatic: 66% correct; RT 1640 ms; achromatic: 68% correct, RT 1750 ms). His performance improved during the quarterfield version of the test, but remained matched for the chromatic and achromatic tasks (chromatic: 82% correct; RT 1400 ms; achromatic: 77% correct, RT 1530 ms). The average performance of the young controls on the fMRI test was also equivalent for the chromatic and achromatic versions of the task (chromatic: 82% correct $\pm$ 8% SD, RT 1640 ms $\pm$ 170 ms; achromatic: 85% correct $\pm$ 8% SD, RT 1650 ms $\pm$ 160 ms). The age-matched control (subject LS) had similar results (chromatic: 86% correct; RT 1100 ms; achromatic: 83% correct, RT 1110 ms).

3.4. fMRI 100-Hue test: active brain areas

When KG performed the chromatic and achromatic sequencing tests of the fMRI 100-Hue test, a number of brain areas responded with increased MR signal relative to fixation control. Regions in frontal, parietal, and occipital cortex all responded more strongly to chromatic and achromatic sequencing than fixation control.

Most active areas showed equal MR responses to chromatic and achromatic stimuli. However, three brain areas preferred chromatic to achromatic stimuli, including a region of frontal cortex with center of mass (33, −19, 66) and bilateral regions of calcarine cortex. The area with the strongest preference for chromatic to achromatic stimuli was found in left ventral occipitotemporal cortex, with center of mass (−35, −66, −21).

As shown in Fig. 2B, ventral color-selective activity was observed in the left collateral sulcus and posterior fusiform gyrus. An average MR time series from this cortex (Fig. 2A) illustrates an average response in left ventral cortex to chromatic stimuli of 2.7%, and an average response to achromatic stimuli of 1.8%. No functional activity (color-selective or otherwise) was observed in right ventral cortex.

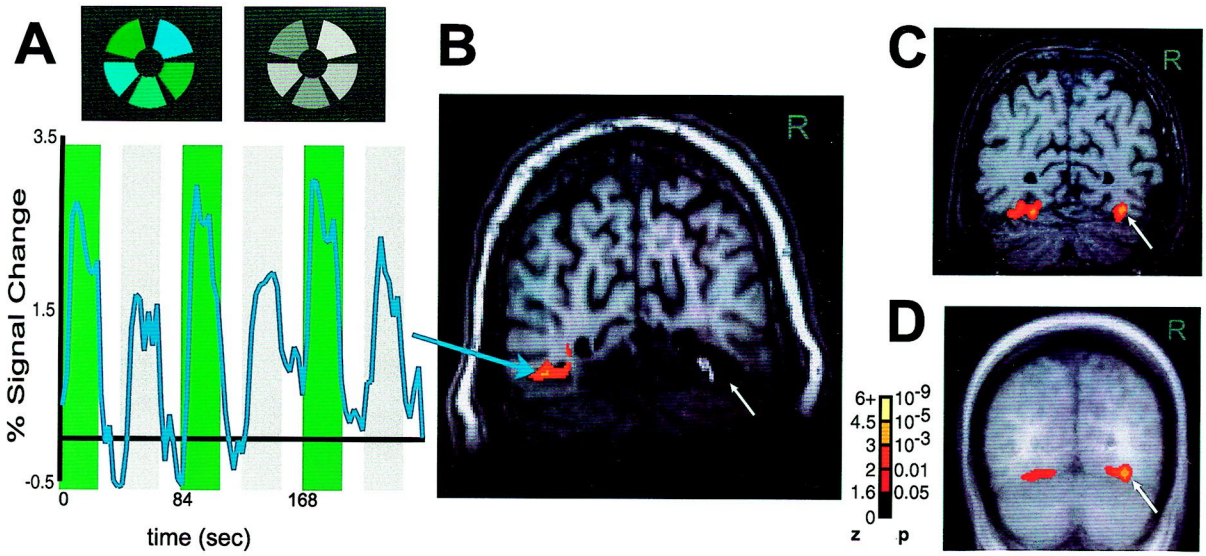

Fig. 2. Ventral Color-Selective Activity in Case KG and controls during performance of the fMRI 100-Hue test. During the fMRI test, subjects alternately viewed chromatic and achromatic stimuli (A, top) interspersed with fixation only. An average time series (A, blue graph line) from color-selective voxels in KG's left ventral cortex illustrates greater MR signal increase during chromatic stimulation (green bars) than during achromatic stimulation (gray bars). B shows KG's color-selective cortex (colored voxels) overlaid on coronal section of anatomical dataset (gray scale) with location $y = -72$ mm. C illustrates ventral color-selective activity in age-matched control subject LS at $y = -67$ mm, D illustrates average color-selective activity in 12 young control subjects at $y = -69$ mm. Color scale illustrates degree of color-selectivity for B, C, D. White arrows indicate location of right ventral color-selective region in normal controls and damaged cortex in KG.

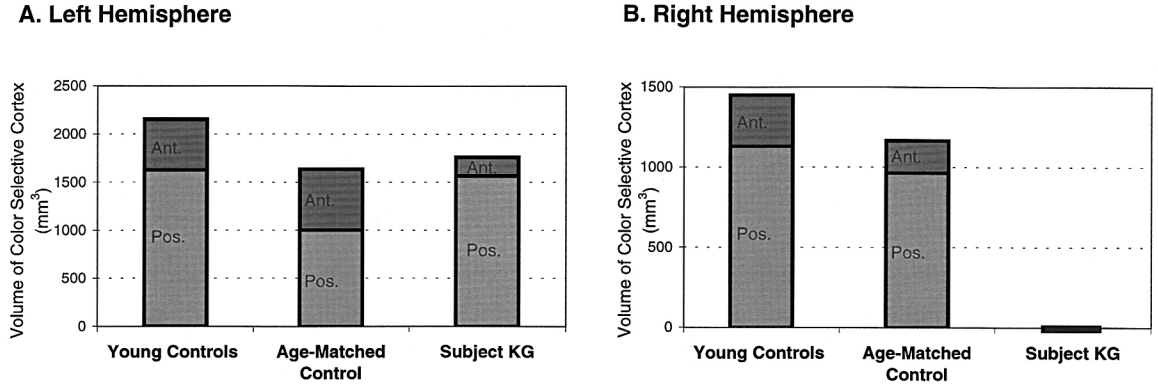

Fig. 3. Histogram portraying volume of ventral color-selective activity in young controls ($n = 12$); age-matched control subject LS; and subject KG in left (A) and right (B) hemispheres. Active cortex below the commisural plane ($z < 0$) was assigned to anterior ($y > -60$) and posterior ($y < -60$) divisions (labeled as Ant. and Pos.) SEM for young controls: 130 mm^3 (anterior left hemisphere), 280 mm^3 (posterior left), 170 mm^3 (anterior right hemisphere), 180 mm^3 (posterior right).

3.5. Quarterfield 100-Hue test

Because of KG's upper left visual field defect, the upper left wedge in the standard 100-Hue stimulus was not visible to him. Therefore, a version of the test in which a smaller version of the stimulus was presented entirely within KG's lower right quadrant was administered. The same brain areas were active in the quarterfield and full-field 100-Hue tests, but some differences in the activation were noted. The calcarine cortex activity changed from bilateral in the full-field test to unilateral left in the quarterfield test, reflecting the different retinotopic organization of the visual stimulus (bilateral vs. right visual field only). The location of the left ventral activity was shifted slightly medially relative to the full-field test, with center of mass (−31, −68, −22). Consistent with the smaller size of the visual stimulus in the quarterfield test, the volume of active cortex in left ventral cortex decreased by 57% relative to the full-field test; the amplitude of activity decreased by 45% (the average response was 1.5% during the chromatic condition vs 1.1% in the achromatic condition).

3.6. Comparison with control subjects

KG's pattern of activation (Fig. 2B) was compared with the activation maps from 12 young controls (average shown in Fig. 2D) and an age and sex-matched control (Fig. 2C). Both normals and subject KG showed bilateral, color-selective activation in primary visual cortex. Like KG, every control subject also showed a large volume of color-selective activity in left ventral cortex (Fig. 3A). However, in contrast to normal subjects, KG showed no color-selectivity in right ventral cortex (Fig. 3B). No visually responsive voxels were found in this region, consistent with the heavy damage observed with anatomical MRI. KG's lack of right ventral activation in comparison with controls is highlighted in Fig. 2 (white arrows).

In controls, left ventral activity was found in two distinct locations: a posterior fusiform region extending from $y = -60$ to $y = -80$ and an anterior, mid-fusiform region with center of mass at $y = -46$. Compared with controls, KG showed a normal volume of color-selective cortex in posterior left ventral cortex (Fig. 3A). The degree of color-selectivity in this region was also similar to that of controls (subject LS: MR signal change of 2.3% for chromatic stimulation, 1.6% for achromatic stimulation; average of 12 young controls: 2.3% ± 0.6% SD chromatic, 1.0% ± 0.5% achromatic; compared with 2.7%/1.8% for KG). However, there were differences between KG and controls in anterior left ventral cortex. Anatomical imaging showed damage to KG's left mid-fusiform cortex, location of the more anterior color-selective focus in controls. As shown in Fig. 3A, KG had significantly less anterior color-selective cortex than controls ($p < 0.001$).

4. Discussion

Anatomical MRI revealed bilateral damage to KG's ventral occipitotemporal cortex. Previous imaging [7,47] and case studies [28] have determined that this region is an important locus of cerebral color perception. Consistent with this finding, KG's color perception was impaired following the damage to ventral cortex, with a 100-Hue test score worse than 95% of age-matched controls.

However, KG's color impairment was less severe than the total achromatopsia observed in some patients (e.g. [21]). Anatomical MRI suggested that spared tissue was present in ventral cortex. Functional MRI was used to determine if any of the undamaged

cortex was active during a task that required the active use of color information.

When KG performed the fMRI 100-Hue test, two regions in occipital lobe showed strong color-selective activity: bilateral primary visual cortex and left posterior ventral cortex.

4.1. Primary visual cortex (V1)

Normal subjects show color-selective activity in V1 [5,17,23,27]. In KG, anatomical damage to V1 was most severe in the inferior bank of the right calcarine sulcus (corresponding to KG's upper left visual field defect) and no functional activity was seen in this region. However, color-selective activity was observed in undamaged portions of superior and inferior left calcarine and superior right calcarine cortex, corresponding to the spared portions of KG's visual field (right hemifield and lower left quadrant).

4.2. Ventral occipitotemporal cortex

In normal controls, the fMRI 100-Hue test activates ventral cortex bilaterally, in anterior and posterior subdivisions [5,46]. Anatomical imaging revealed extensive damage in KG's right ventral cortex, and no functional activity was observed there. In KG's left hemisphere, anatomical images showed damage to anterior ventral cortex, with a corresponding reduced volume of active cortex compared to controls. However, in KG's posterior left ventral cortex (relatively undamaged on anatomical images) a strong color-selective focus was observed. This cortex was similar in color-selectivity, extent, and location to that observed in normals.

4.3. Cortical color processing

A simplified description of cortical color processing suggests that initial processing for each hemifield is performed by V1 in the contralateral hemisphere, using input from the color-opponent parvocellular pathway [25,26]. Next, ventral extrastriate areas are assumed to complete a second stage of processing required for more complex color tasks, such as the sequencing required by the 100-Hue test. Indeed, damage to ventral cortex leads to severe impairment on the 100-Hue test [19].

Given this model, we were surprised to find that KG showed no visual field asymmetry in his color deficit: he was able to sequence hues equally well in his lower-left or lower-right quadrants. While KG's first stage of color processing was intact in both hemispheres (as shown by bilateral functional activity in V1) one might assume that the loss of KG's right ventral color-selective areas would cause impaired color perception in the contralateral (left) hemifield. This was not the case.

One possible explanation for this unexpected finding is that spared right ventral cortex, not visible in our anatomical or functional scans, performed the color processing computation for the lower left quadrant. This seems unlikely given the severity of damage in the region that would normally contain color-selective cortex (Fig. 2). Even at very low statistical threshold, little functional activity was observed in right ventral cortex. Yet we cannot rule out the possibility that vascular changes that occurred after the stroke modified the metabolic coupling between neuronal activity and vascular response (or the anatomical organization of the vasculature) rendering neuronal activity invisible to our blood oxygenation level dependent measure.

A more interesting possibility is that KG's left ventral focus is processing color information for the entire visual field. In general, each hemisphere processes information about the contralateral visual field. V1 is characterized by strict retinotopic organization, with each visual hemifield represented almost exclusively by the contralateral hemisphere [11,36]. Areas later in the processing hierarchy, such as inferotemporal cortex, can show less precise retinotopy, with receptive fields spanning both hemifields [16]. If KG's left ventral focus is processing color in both hemifields, it could receive color information about the ipsilateral field from color-selective neurons in right V1 via transcallosal connections [37]. How could this have occurred? It could be that in normal controls, ventral color-selective areas represent the entire visual field, so that damage to one hemisphere would not impair perception in the contralateral hemifield. Mapping studies from independent groups reported that the more posterior color-selective area (termed V8 or V4) forms a continuous representation of the *contralateral* visual field [17,27]. Yet some evidence suggests that there may be ipsilateral inputs into ventral areas, though weaker than the input from contralateral hemifield [35]. If color processing in KG's left visual field is occurring in left ventral cortex, it seems likely that weak connections between right V1 and left ventral cortex were strengthened following KG's lesion, resulting in a representation of both left and right hemifields in left ventral cortex and allowing similar color processing performance across the visual field.

It should be noted that KG's color sequencing ability improved during the 3 years following his lesion. An attractive hypothesis is that some of the improvement in KG's color skills occurred as the ensemble of color processing areas reorganized, perhaps spurred on by KG's acute awareness of his color deficit. However, with only a single fMRI data point, we can only speculate about the neuronal substrates of KG's recovery.

4.4. Comparison with other case studies: achromatopsia vs dyschromatopsia

There are a substantial number of case reports of subjects with acquired deficits in cerebral color perception (e.g. [10,15,20,28,30,45]). The evidence suggests that in most of these cases, the ability to perceive colors was impaired but not abolished. For instance, in case 1 of Mendola and Corkin [29] a patient described as having achromatopsia scored 150 on the 100-Hue test. While this is above the normal range, it is well below the score of 1200 expected for random guessing on the test [40]. Other patients with impaired color perception were also able to name the colors of very bright objects or score above chance on the 100-Hue test [1,3,4,15,28,31,33,41,42]. In contrast, there are relatively few patients with complete achromatopsia, like patient MS of Heywood and colleagues [19] who score at chance levels on the 100-Hue test.

Our results suggest a possible explanation for the preponderance of partial over complete impairments in color perception. Because the ensemble of areas underlying color perception is distributed in multiple areas in ventral cortex, most patients suffer damage to only a subset of these ventral areas, resulting in only partial deficits (V1 is also a crucial component of the network, but damage to V1 typically leaves subjects cortically blind and unaware of specific color deficits.)

Our study emphasizes that the ensemble of areas for processing color is complex. Rather than a single area underlying color perception in each hemisphere [27] these findings suggest that there is a flexible network of areas for processing color. More work is needed to address the processing role of these different areas in subserving normal color perception and to understand how damage to these areas impairs perception.

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