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Report

Perception Matches Selectivity in the Human Anterior Color Center

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Summary

Human ventral cortex contains at least two visual areas selective for color [1]: a posterior center in the lingual gyrus labeled V4 [2–4], V8 [5], or VO-1 [6] and an anterior center in the medial fusiform that has been labeled V4α [3, 4]. We examined the properties of the anterior color center using electrical recording and electrical stimulation in a subject with an electrode implanted over the anterior color center, as determined with BOLD fMRI in the same subject. Presentation of visual stimuli evoked local field potentials from the electrode. Consistent with fMRI, the potentials were larger for chromatic than achromatic stimuli. The potentials differed depending on stimulus color, with blue-purple colors evoking the largest response. The spatial receptive field of the electrode was central/parafoveal with a contralateral bias. In the absence of a visual stimulus, electrical stimulation of the electrode produced an artificial visual percept of a blue-purple color near the center of gaze. These results provide direct evidence of a tight link between selectivity and perception in ventral temporal cortex. Electrical stimulation of the anterior color center is sufficient to produce the conscious percept of a color whose identity is determined by the selectivity of the stimulated neurons.

Results

Neuroimaging

Structural magnetic resonance imaging (MRI), blood-oxygenation-level dependent functional MRI (BOLD fMRI), and computed tomography were used to localize a subdural electrode implanted on the ventral temporal cortex of a human subject (Figure 1). The electrode was situated on the fusiform gyrus, mid-way between the temporal pole and the occipital pole, with standardized coordinates (26, −49, −20). The electrode was located just lateral to the collateral sulcus, in the anatomical location of the anterior color center observed in previous neuroimaging studies. BOLD fMRI showed significant color responses in the cortex proximal to the electrode (Figure 1B). Posterior to the electrode, phase-encoded retinotopic mapping revealed responses to the lower as well as the upper quadrant of the contralateral visual field, with a representation of the fovea distinct from that of V1/V2/V3, consistent with previous reports of V4 [4], V8 [5], and VO-1 [6] (Figure 1C).

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Electrical Stimulation

Pulses (300 ms) of stimulating current were passed through the electrode to evoke activity in nearby neurons, and the subject was interviewed about the resulting percept. The subject reported that stimulation of the electrode produced a percept of a "blue, purple color, like aluminum foil when it burns" and that the blue-purple percept was near the center of gaze but was not localizable to a small region of the visual field. Repeated stimulation of the electrode produced the same subjective percept. Increasing the stimulation duration to 1 s lengthened the duration of the evoked percept but did not change its quality.

To objectively confirm the patient's report of an evoked visual percept, the subject performed a two-alternative temporal forced-choice task as the stimulation current level was randomly varied from trial to trial (Figure 2A). At low current levels, the subject could not reliably detect the electrical stimulus, resulting in chance performance (Figure 2B). At high current levels, the subject was almost always able to correctly determine the stimulation epoch, demonstrating that the stimulation produced a reliable percept. The psychometric curve showed a detection threshold of 1.7 mA (1.4–1.9 mA, 95% confidence interval). Similar current levels delivered to electrodes implanted over primary visual cortex produce the small, discrete flashes of white light known as phosphenes, thought to indicate evoked activity in a small population of pyramidal neurons surrounding the electrode [7].

Electrical Recording

Local field potentials (LFPs) were recorded from the mid-fusiform gyrus to determine whether neurons producing the electrically evoked colored percept responded selectively to different colors. Because higher visual areas have large receptive fields, large color squares were presented that covered most of the left visual field, contralateral to the implanted electrode. Color squares evoked LFPs that began 100 ms after stimulus onset, peaked at 154 ms, and returned to baseline at 378 ms (Figure 3A). In order to calculate the amplitude of the response to each of the 26 colors, the root-mean-square (RMS) power of the LFPs was measured between 100 and 378 ms. The largest response, 102 μV, was evoked by a blue-purple color, and the weakest response, 21 μV, was evoked by a yellow-brown color.

The normalized cone contrast of each color square relative to the gray background was calculated using the equations $L = (L - L0)/L0$, $M = (M - M0)/M0$, and $S = (S - S0)/S$, where L is the long-wavelength cone response, M is the medium-wavelength cone response, and S is the short-wavelength cone response (see Table S1 available online). Two orthogonal color axes were created: (L − M) for long- to medium-wavelength color contrast and S − (L + M) for short-wavelength color contrast, with a third axis (L + M) for luminance [8]. Plotting response power versus color revealed that blue-purple colors evoked large responses and red-browns evoked weak responses (Figure 3B). The electrode responses were well fit ($F = 5.7$, $p = 0.005$) by a hyperplane with equation $P = 7.2 \times (S - (L + M)) - 16.2 \times (L - M) + 3.6 \times (L + M) + 55.1$, where P is response power (Figure S2 shows the iso-response plane).

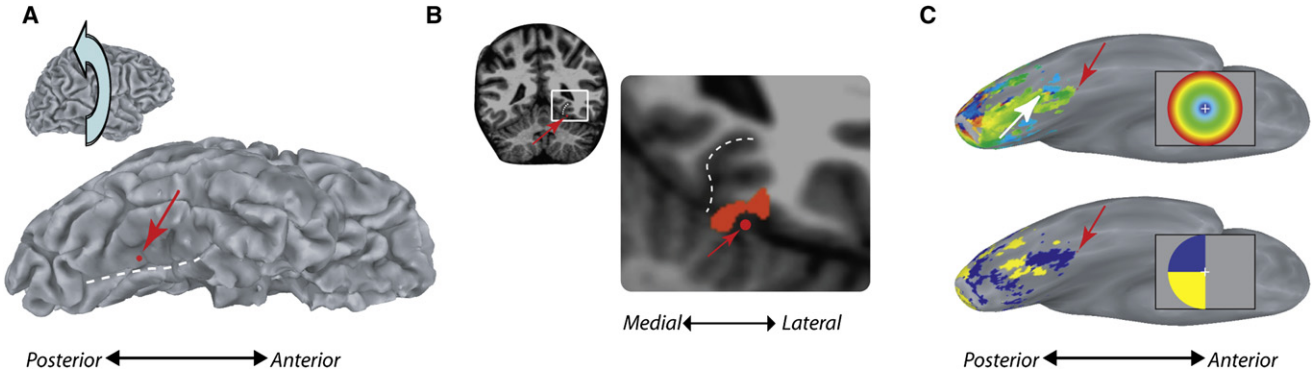

Figure 1. Location of the Implanted Electrode

(A) Lateral (top) and ventral (bottom) views of a cortical surface model of the subject's right hemisphere. The electrode, located on the fusiform gyrus, is shown as a red sphere (highlighted with a red arrow). The collateral sulcus is marked with a dashed white line.

(B) Coronal MR image in the plane of the electrode, shown as a red circle lateral to the collateral sulcus (dashed white line). Orange voxels showed a significant ($p < 0.01$) BOLD fMRI response to color stimuli.

(C) Ventral view of the subject's inflated right hemisphere. The top panel shows the results of eccentricity mapping (nodes are colored according to their preferred location in the visual field, inset). Blue nodes preferred foveal stimulation. The white arrow shows the location of the ventral foveal representation; the red colored nodes and red arrow indicate the location of the electrode. The bottom panel shows the results of polar angle mapping. Blue nodes responded to visual stimulation in the upper left quadrant, yellow nodes to visual stimulation in the lower left quadrant (inset).

To quantify the difference between preferred and nonpreferred colors, the actual response powers of the five colors predicted to evoke the strongest and weakest responses by the best-fit hyperplane were compared. Preferred colors had mean response 77 μV, and nonpreferred colors had mean response 45 μV ($p = 10^{-6}$).

Our color stimuli were not isoluminant with each other or with the background. The hyperplane fit showed a very weak positive correlation between luminance contrast and power of the electrode response (95% CI of the regression coefficient, −1.8 to +9.0). In agreement with this result, two colors that bracketed the luminance of the preferred blue-purple color (−1.01 and −0.46 versus −0.82) evoked responses with dissimilar powers (39 μV and 84 μV versus 102 μV). To directly test the relationship between luminance and response power, 8 blue stimuli and 16 achromatic squares of varying luminance were presented (Figures 3C and 3D). The blue stimuli evoked a uniformly large response (67 μV ± 8 uV SD) with no correlation between luminance and response power ($r = 0.12$, $p = 0.8$). There was a weak negative correlation between luminance and response power for achromatic squares ($r = -0.36$, $p = 0.2$). In sum, response power did not exhibit a consistent relationship with stimulus luminance.

The achromatic squares evoked a significantly weaker response than the blue squares (32 μV versus 67 μV, $p = 10^{-6}$). Although the achromatic responses were weak, even the weakest achromatic response was significantly greater than baseline ($p = 0.009$). These results are consistent with neuroimaging evidence showing that the anterior color center shows small but significant responses to achromatic stimuli [1, 9].

Previous neuroimaging studies have reported distributed responses to complex images in ventral temporal cortex. The response of the electrode to 17 chromatic images, including scenes, faces, and man-made objects that covered the same spatial extent as the uniform color squares, was measured. Many of the chromatic images that evoked large responses contained a great deal of blue, such as a picture of the Lone Ranger wearing a denim shirt against a blue sky (33 μV). The mean response to all chromatic images was 25 μV. Although it is difficult to compare responses across runs because of possible gain changes, this was weaker than the

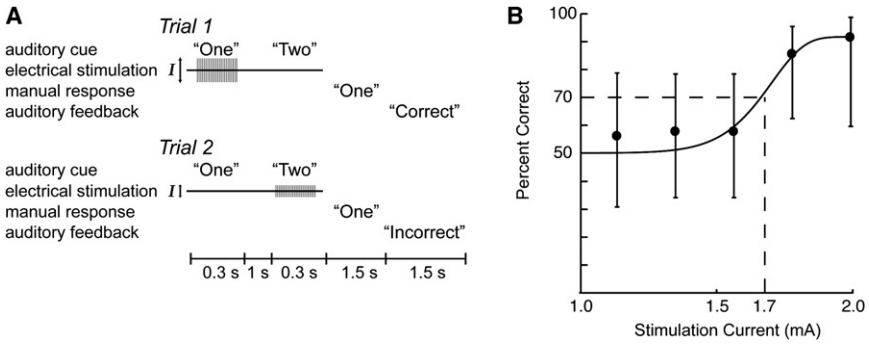

Figure 2. Stimulation of the Implanted Electrode

(A) The structure of each stimulation trial, shown for two sample trials. Each trial contained 200 Hz biphasic electrical stimulation delivered in one of two epochs. The subject attempted to detect the epoch in which the stimulation was delivered, responded with a button press after the completion of both epochs, and then received feedback. The amplitude of the stimulation current (I) varied from trial to trial. In these examples, the first trial contained high stimulation current, and the stimulation epoch was correctly detected. The second trial contained low stimulation current, and the stimulation epoch was not correctly detected.

(B) Psychometric function showing percent correct detection of stimulation epoch plotted against amplitude of stimulation current (I) for five different currents (error bars show 95% confidence intervals).

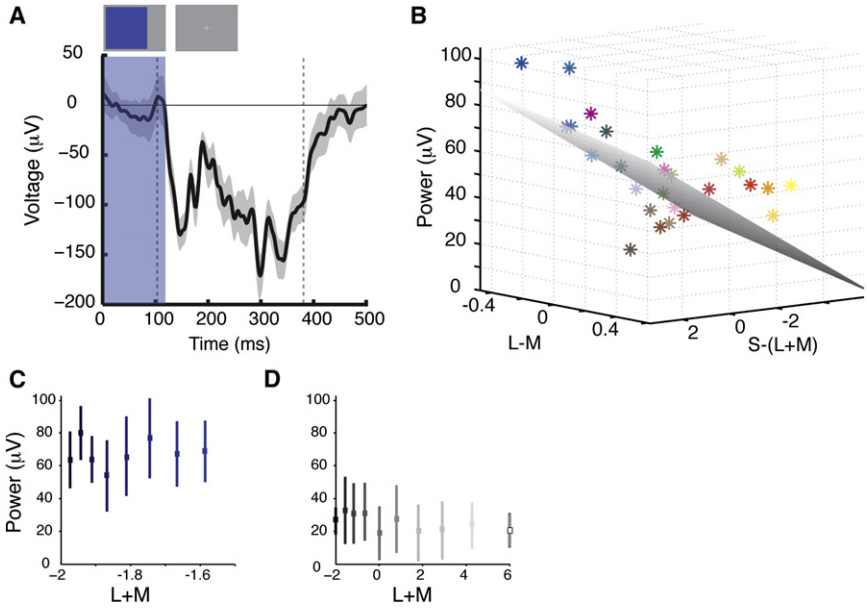

Figure 3. Response of the Implanted Electrode to Visual Stimulation

(A) Average evoked response to presentation of a blue stimulus. The stimulus is shown at the top of the plot: a blue square on a gray background was presented for 125 ms and was then replaced with a baseline display. In the plot, the heavy trace is the mean response; the gray-shaded area is the 95% confidence interval. The blue-shaded rectangle shows the stimulus duration. The dashed lines show the time interval used to calculate the response power.

(B) Power of the response to different colors. Each symbol represents the response to a color square of the same color as the symbol (stimulus configuration shown in [A]). The x axis is dimensionless L − M cone contrast, the y axis is S − (L + M) cone contrast, and the z axis is the root-mean-square response power. The best-fit plane is shown in gray.

(C) Power of the response to blue stimuli with increasing luminance contrast. Each symbol represents the average response (bars represent 95% confidence interval) to a stimulus of the same color as the symbol.

(D) Power of the response to achromatic stimuli with increasing luminance contrast. Each symbol shows the luminance of the stimulus, except for the rightmost (white) symbol, shown with a black outline for visibility.

mean response to color squares (68 μV). The maximum response to a chromatic image was only one-third as large as the maximum response to a color square, suggesting that simple, uniform colors are potent stimuli for this region of cortex.

Because implanted electrodes record from a small population of neurons, evoked LFPs can also be used to study spatial receptive fields. We have adapted mapping techniques similar to those used in electrophysiological studies in nonhuman primates for use in patients with implanted electrodes. These techniques allow the measurement of receptive fields in human V1 of less than a degree in size [10]. In order to measure the spatial receptive field of neurons in mid-fusiform gyrus, the preferred blue-purple stimulus was presented at different locations in the visual field, and the evoked response was measured (Figure 4). The receptive field was central/parafoveal, with a contralateral bias.

Discussion

Human functional neuroimaging studies of color processing have focused on V1 [11, 12] or on a color-selective region in lingual gyrus in ventral occipital lobe, alternately labeled V4 [2–4], V8 [5], or VO-1 [6]. However, a number of studies have identified an additional color-selective region in mid-fusiform gyrus in ventral temporal lobe. This anterior color center, which has been labeled V4α [3, 4], is active during tasks requiring color-ordering [1, 13], color imagery [14], knowledge about color [15–17], color illusions [18], and processing of object color [4, 19]. Because neuroimaging studies provide only correlational evidence about the relationship between neuronal activity and perception, it has been difficult to determine the role of the anterior color center. Electrical stimulation in the cortex of nonhuman primates allows examination of the causal relationship between activity and perception, but animals cannot report the quality of the percept evoked by stimulation [20, 21]. Electrical stimulation of human cortex can produce a variety of visual and nonvisual percepts [22]. Stimulation of visual cortex commonly produces the percept of a single, small spot of white light known as a phosphene [23], although colored percepts have also been reported [24–26].

Our study demonstrates a correspondence in human ventral temporal cortex between neuronal responses measured *indirectly* with BOLD fMRI and *directly* with electrical recording. Because human cortical anatomy is variable, anatomical landmarks or standard spaces cannot precisely identify the location of visual areas across subjects. Within a single subject, we demonstrate that the anterior color center, identified with BOLD fMRI, shows larger local field potentials to chromatic compared with achromatic stimuli.

A striking concordance was observed between the percept evoked by electrical stimulation and the selectivity for visual

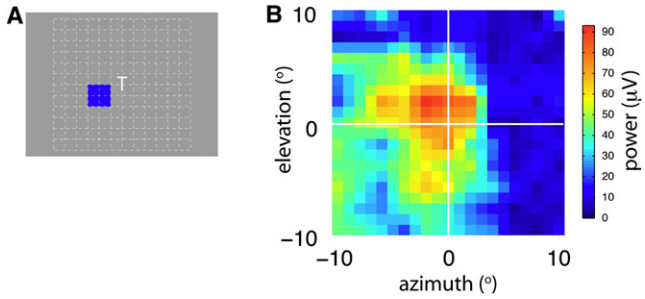

Figure 4. Receptive Field of the Implanted Electrode

(A) The visual stimulus used for receptive field mapping. Blue squares were presented in 121 visual field locations (white dashed lines, not present on actual display, show all possible locations). The subject performed a detection task on foveally presented letters to ensure fixation.

(B) The power of the evoked electrical response from the electrode for stimuli presented at each visual field location, interpolated to account for overlap between adjacent stimuli. Color indicates strength of the response. White crosshairs show the horizontal and vertical meridia for reference.

stimuli of neurons in mid-temporal lobe. In addition to evoking action potentials from nearby neurons, electrical stimulation can activate fibers of passage [7]. Because the local field potential from neurons near the electrode was color selective and matched the evoked percept, the color percept in our study could not have arisen from stimulation of unrelated fibers of passage. The minimum current level required to evoke a percept was several-fold lower than current levels reported in previous studies [25, 26], further suggesting that the subject's percept of "blue" was produced by activity in a small population of neurons surrounding the electrode. Studies in nonhuman primates have suggested that patchy domains in V1 [27] and V2 [28] are selective for individual colors; a recent report suggests that the same may be true in human visual cortex (I. Kuriki et al., 2007, Soc. Neurosci., abstract). In our study, electrical stimulation evoked only one chromatic sensation. This could be the result of an organization by color in the human anterior color center. Stimulation of a group of neurons near the electrode, all selective for a similar color, could create the percept of that color. Evidence for this idea comes from the observed color-selective local field potentials. If neighboring neurons were selective for completely different colors, the local field potential (the result of synaptic activity near the electrode) would not be expected to be strongly color selective.

Unlike earlier stages of color processing, in mid-fusiform gyrus the color selectivity extends over a large portion of visual space. Correspondingly, stimulation of this area resulted in a diffuse chromatic percept, unlike the small, discrete phosphenes produced by electrical stimulation of V1.

Neuroimaging studies in humans and monkeys have identified color responses in V1, V2, VP, V4/V8/VO-1, and the anterior color center [29–32]. While patients with lesions to occipitotemporal cortex can present with a variety of color vision disturbances [13, 33–37], it has been difficult to determine the relationship between activity in different identified visual areas and color perception. We demonstrate a close correspondence in one of these areas—the human anterior color center—between visually evoked activity, electrical stimulation, and the conscious percept of color.

Experimental Procedures

The subject was a 38-year-old right-handed male with a 5 year history of medically intractable complex partial seizures of unknown etiology. An array of subdural electrodes was implanted to determine the location of the seizure focus, guided solely by clinical criteria, and included a six-contact strip electrode implanted laterally-to-medially on the right ventral temporal cortex. One week before electrode implantation, BOLD fMRI was used to localize visual areas. MRI data were analyzed using AFNI [38]. Cortical surface models were constructed with FreeSurfer [39] and visualized in SUMA [40]. Following implantation, a whole-head computed tomography scan was obtained and aligned to the presurgical structural MRI. Analysis of clinical EEG recordings by the clinical neurophysiology team determined that the seizures did not originate from the region of cortex covered by the ventral temporal strip of electrodes. Electrical stimulation and recording for research purposes was performed on these electrodes. Informed consent was obtained from the subject, and all procedures were approved by the Baylor College of Medicine Institutional Review Board or the Committee for the Protection of Human Subjects at the University of Texas Health Science Center at Houston. For a complete description of the Experimental Procedures, please see the Supplemental Data.

Supplemental Data

The Supplemental Data for this article can be found online at http://www.current-biology.com/cgi/content/full/18/3/216/DC1/.

Acknowledgments

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References

1. Beauchamp, M.S., Haxby, J.V., Jennings, J.E., and DeYoe, E.A. (1999). An fMRI version of the Farnsworth-Munsell 100-Hue test reveals multiple color-selective areas in human ventral occipitotemporal cortex. Cereb. Cortex *9*, 257–263.
2. Zeki, S., Watson, J.D.G., Lueck, C.J., Friston, K.J., Kennard, C., and Frackowiak, R.S.J. (1991). A direct demonstration of functional specialization in human visual cortex. J. Neurosci. *11*, 641–649.
3. Lueck, C.J., Zeki, S., Friston, K.J., Deiber, M.P., Cope, P., Cunningham, V.J., Lammertsma, A.A., Kennard, C., and Frackowiak, R.S. (1989). The colour centre in the cerebral cortex of man. Nature *340*, 386–389.
4. Zeki, S., and Bartels, A. (1999). The clinical and functional measurement of cortical (in)activity in the visual brain, with special reference to the two subdivisions (V4 and V4 alpha) of the human colour centre. Philos. Trans. R. Soc. Lond. B Biol. Sci. *354*, 1371–1382.
5. Hadjikhani, N., Liu, A.K., Dale, A.M., Cavanagh, P., and Tootell, R.B.H. (1998). Retinotopy and color sensitivity in human visual cortical area V8. Nat. Neurosci. *1*, 235–241.
6. Brewer, A.A., Liu, J., Wade, A.R., and Wandell, B.A. (2005). Visual field maps and stimulus selectivity in human ventral occipital cortex. Nat. Neurosci. *8*, 1102–1109.
7. Tehovnik, E.J., Tolias, A.S., Sultan, F., Slocum, W.M., and Logothetis, N.K. (2006). Direct and indirect activation of cortical neurons by electrical microstimulation. J. Neurophysiol. *96*, 512–521.
8. Webster, M.A., and Mollon, J.D. (1997). Adaptation and the color statistics of natural images. Vision Res. *37*, 3283–3298.
9. McKeefry, D.J., and Zeki, S. (1997). The position and topography of the human colour centre as revealed by functional magnetic resonance imaging. Brain *120*, 2229–2242.
10. Yoshor, D., Bosking, W.H., Ghose, G.M., and Maunsell, J.H. (2007). Receptive fields in human visual cortex mapped with surface electrodes. Cereb. Cortex *17*, 2293–2302.
11. Engel, S.A. (2005). Adaptation of oriented and unoriented color-selective neurons in human visual areas. Neuron *45*, 613–623.
12. Engel, S., Zhang, X., and Wandell, B. (1997). Colour tuning in human visual cortex measured with functional magnetic resonance imaging. Nature *388*, 68–71.
13. Beauchamp, M.S., Haxby, J.V., Rosen, A.C., and DeYoe, E.A. (2000). A functional MRI case study of acquired cerebral dyschromatopsia. Neuropsychologia *38*, 1170–1179.
14. Howard, R.J., ffytche, D.H., Barnes, J., McKeefry, D., Ha, Y., Woodruff, P.W., Bullmore, E.T., Simmons, A., Williams, S.C., David, A.S., et al. (1998). The functional anatomy of imagining and perceiving colour. Neuroreport *9*, 1019–1023.
15. Martin, A., Haxby, J.V., Lalonde, F.M., Wiggs, C.L., and Ungerleider, L.G. (1995). Discrete cortical regions associated with knowledge of color and knowledge of action. Science *270*, 102–105.
16. Chao, L.L., and Martin, A. (1999). Cortical regions associated with perceiving, naming, and knowing about colors. J. Cogn. Neurosci. *11*, 25–35.
17. Simmons, W.K., Ramjee, V., Beauchamp, M.S., McRae, K., Martin, A., and Barsalou, L.W. (2007). A common neural substrate for perceiving and knowing about color. Neuropsychologia *45*, 2802–2810.

18. Morita, T., Kochiyama, T., Okada, T., Yonekura, Y., Matsumura, M., and Sadato, N. (2004). The neural substrates of conscious color perception demonstrated using fMRI. Neuroimage *21*, 1665–1673.
19. Zeki, S., and Marini, L. (1998). Three cortical stages of colour processing in the human brain. Brain *121*, 1669–1685.
20. Cohen, M.R., and Newsome, W.T. (2004). What electrical microstimulation has revealed about the neural basis of cognition. Curr. Opin. Neurobiol. *14*, 169–177.
21. Murphey, D.K., and Maunsell, J.H. (2007). Behavioral detection of electrical microstimulation in different cortical visual areas. Curr. Biol. *17*, 862–867.
22. Penfield, W., and Rasmussen, T. (1950). The Cerebral Cortex of Man. A Clinical Study of Localization of Function (New York: The Macmillan Company).
23. Brindley, G.S. (1982). Effects of electrical stimulation of the visual cortex. Hum. Neurobiol. *1*, 281–283.
24. Bak, M., Girvin, J.P., Hambrecht, F.T., Kufta, C.V., Loeb, G.E., and Schmidt, E.M. (1990). Visual sensations produced by intracortical microstimulation of the human occipital cortex. Med. Biol. Eng. Comput. *28*, 257–259.
25. Allison, T., Begleiter, A., McCarthy, G., Roessler, E., Nobre, A.C., and Spencer, D.D. (1993). Electrophysiological studies of color processing in human visual cortex. Electroencephalogr. Clin. Neurophysiol. *88*, 343–355.
26. Lee, H.W., Hong, S.B., Seo, D.W., Tae, W.S., and Hong, S.C. (2000). Mapping of functional organization in human visual cortex: electrical cortical stimulation. Neurology *54*, 849–854.
27. Xiao, Y., Casti, A., Xiao, J., and Kaplan, E. (2007). Hue maps in primate striate cortex. Neuroimage *35*, 771–786.
28. Xiao, Y., Wang, Y., and Felleman, D.J. (2003). A spatially organized representation of colour in macaque cortical area V2. Nature *421*, 535–539.
29. Conway, B.R., and Tsao, D.Y. (2006). Color architecture in alert macaque cortex revealed by FMRI. Cereb. Cortex *16*, 1604–1613.
30. Tootell, R.B., Nelissen, K., Vanduffel, W., and Orban, G.A. (2004). Search for color 'center(s)' in macaque visual cortex. Cereb. Cortex *14*, 353–363.
31. Mullen, K.T., Dumoulin, S.O., McMahon, K.L., de Zubicaray, G.I., and Hess, R.F. (2007). Selectivity of human retinotopic visual cortex to S-cone-opponent, L/M-cone-opponent and achromatic stimulation. Eur. J. Neurosci. *25*, 491–502.
32. Conway, B.R., Moeller, S., and Tsao, D.Y. (2007). Specialized color modules in macaque extrastriate cortex. Neuron *56*, 560–573.
33. Heywood, C.A., and Kentridge, R.W. (2003). Achromatopsia, color vision, and cortex. Neurol. Clin. *21*, 483–500.
34. Bouvier, S.E., and Engel, S.A. (2006). Behavioral deficits and cortical damage loci in cerebral achromatopsia. Cereb. Cortex *16*, 183–191.
35. Zeki, S. (1990). A century of cerebral achromatopsia. Brain *113*, 1721–1777.
36. Meadows, J.C. (1974). Disturbed perception of colours associated with localized cerebral lesions. Brain *97*, 615–632.
37. Miceli, G., Fouch, E., Capasso, R., Shelton, J.R., Tomaiuolo, F., and Caramazza, A. (2001). The dissociation of color from form and function knowledge. Nat. Neurosci. *4*, 662–667.
38. Cox, R.W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. Comput. Biomed. Res. *29*, 162–173.
39. Fischl, B., Sereno, M.I., and Dale, A.M. (1999). Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. Neuroimage *9*, 195–207.
40. Argall, B.D., Saad, Z.S., and Beauchamp, M.S. (2006). Simplified intersubject averaging on the cortical surface using SUMA. Hum. Brain Mapp. *27*, 14–27.