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Adaptive Changes in Color Vision from Long-Term Filter Usage in Anomalous but Not Normal Trichromacy

Highlights

- Long-term use of color notch filters increases chromatic response in color anomals
- No such effects are observed in normal trichromats or a placebo condition
- Spontaneous comments of observers suggest that the effects may endure

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In Brief

Werner et al. report that extended usage of a spectral notch filter boosts chromatic response in individuals with the most common forms of red-green color deficiency (anomalous trichromacies). The measured effects are supported by spontaneous comments and persist even after removal of the filters.

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Adaptive Changes in Color Vision from Long-Term Filter Usage in Anomalous but Not Normal Trichromacy

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SUMMARY

For over 150 years, spectrally selective filters have been proposed to improve the vision of observers with color vision deficiencies [1]. About 6% of males and <1% of females have anomalies in their gene arrays coded on the X chromosome that result in significantly decreased spectral separation between their middle- (M-) and long- (L-) wave sensitive cone photoreceptors [2]. These shifts alter individuals' color-matching and chromatic discrimination such that they are classified as anomalous trichromats [3, 4]. Broad-band spectrally selective filters proposed to improve the vision of color-deficient observers principally modify the illuminant and are largely ineffective in enhancing discrimination or perception because they do not sufficiently change the relative activity of M- and L-photoreceptors [5, 6]. Properly tailored notch filters, by contrast, might increase the difference of anomalous M- and L-cone signals. Here, we evaluated the effects of long-term usage of a commercial filter designed for this purpose on luminance and chromatic contrast response, estimated with a signal detection-based scaling method. We found that sustained use over two weeks was accompanied by increased chromatic contrast response in anomalous trichromats. Importantly, these improvements were observed when tested *without* the filters, thereby demonstrating an adaptive visual response. Normal observers and a placebo control showed no such changes in contrast response. These findings demonstrate a boosted chromatic response from exposure to enhanced chromatic contrasts in observers with reduced spectral discrimination. They invite the suggestion that modifications of photoreceptor signals activate a plastic post-receptoral substrate that could potentially be exploited for visual rehabilitation.

RESULTS AND DISCUSSION

The method of maximum likelihood difference scaling (MLDS) was used to obtain suprathreshold contrast scales that have the property that equal ordinate differences are perceptually equal [7, 8]. The method is based on a paired comparison of perceptual intervals. When three Gabor patterns (Equation 1) are presented as in Figure 1A, observers can readily indicate which of the two bottom patterns appears more similar to the standard above. Triplets chosen from 9 suprathreshold contrast levels spanning a 30-fold range were used to test contrasts that were varied in luminance or chromaticity (M- and L-cone modulation). When over repeated trials the observer chooses the left or right stimulus with equal frequency, we assume that the standard bisects the perceptual interval between the two lower stimuli. Based on a signal-detection model (Equations 2, 3, and 4), perceptual scales (parameterized as d') were estimated for each of the 9 patterns by maximum likelihood that best predicted the observer's choices over the full set of 84 ordered triplets. The resulting difference scale varies nonlinearly as a function of contrast and was fitted by nonlinear least-squares with a Michaelis-Menten function (Equation 4) so that the two parameters controlling the maximum response and rate of increase, R_m and ς, respectively, could be estimated for each subject (example subject shown in Figure 1B). Figure 1C shows average curves obtained from 27 well-characterized participants (9 deuteranomalous, 9 protanomalous, and 9 normal trichromats) for contrasts modulated along each of two axes in color space [9]. The curves for luminance modulation (solid) are more similar for normal and anomalous trichromats than the curves for chromatic modulation (dashed), which show striking differences among the groups both in R_m (maximum contrast response or response gain) and ς (contrast at which the response attains half of the maximal asymptotic response or inverse of contrast gain). Effective contrast reduction at the input due to the decreased spectral separation of the photopigments (Figure 1D) does not suffice to explain either the smaller R_m or smaller ς of anomalous trichromats (Figure S1) [9].

Early-stage retinal processing involves a differencing operation between the M- and L-cone classes [13], illustrated by

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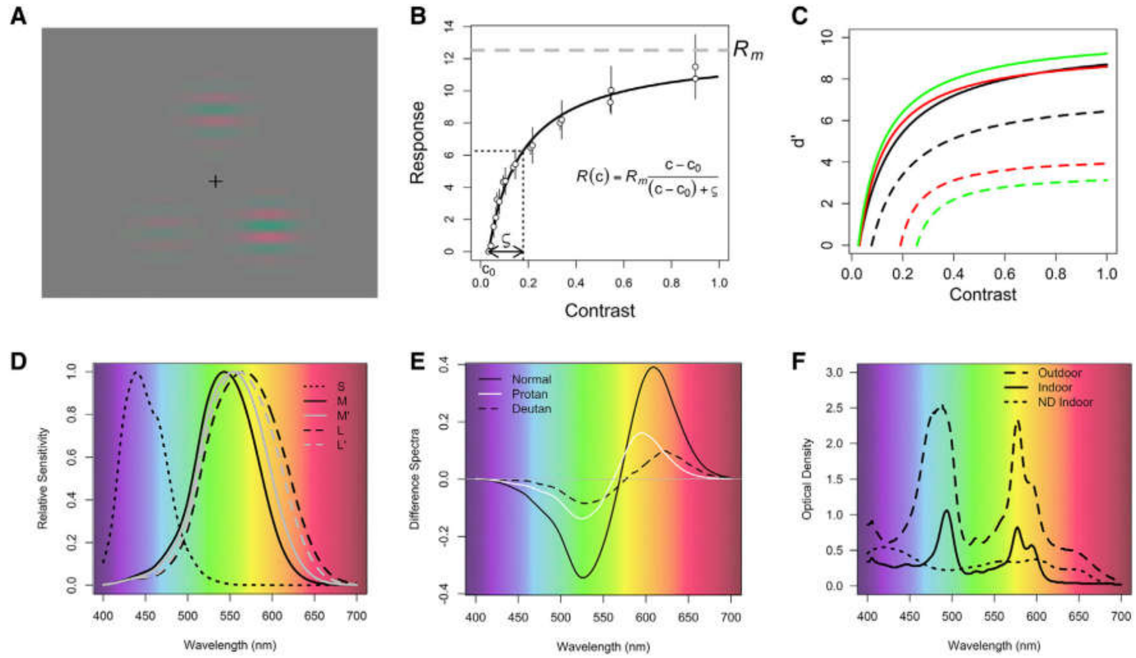

Figure 1. Experimental Design, Typical Results and Theoretical Analysis

(A) An ordered triplet of Gabor patterns varying in chromatic contrast from an MLDS trial. Observers fixated the cross and indicated which of the lower two stimuli was most similar to the standard on top. In separate sessions, the procedure was repeated using Gabor patterns varying in luminance contrast.

(B) Difference scale estimates from one normal trichromatic observer for luminance Gabor patterns. The results are means (±95% conf. int.) from 4 sessions, repeated on 2 separate days. The solid curve is the Michaelis-Menten model fit to the points by nonlinear least-squares; the parameters of the fit are shown by the inset.

(C) Average curves for normal (black), protanomalous (red), and deuteranomalous (green) trichromats. Solid curves denote response along a luminance (L+M) axis and dashed for chromatic (L−M) modulation (replotted from [9]) (also, see Figure S1). Contrast is specified, here and elsewhere in this article, as the nominal value with respect to the maximum attainable on the display.

(D) Spectral sensitivity of normal S, M, and L cones. M' and L' indicate sensitivity curves of anomalous observers (based on [4]). These estimates are for average observers, but polymorphisms result in individual differences in peak separation for both normal and anomalous trichromats [10–12].

(E) Difference spectra modeled for normal (L – M) and anomalous trichromats (Protan: M' – M; Deutan: L – L') with weights adjusted for a null response from an equal-energy light.

(F) Optical density (- $\log_{10}$ transmission) plotted against wavelength for commercial filters designed to increase the differential stimulation of M and L cones. The dotted curve shows the spectral density of the control neutral density filter.

Figure 1E. Compared to normal trichromats, the reduced spectral separation on average attenuates the peak-to-trough signal to 41% and 25% of the normal, respectively, in protanomalous and deuteranomalous individuals. It might be expected that this signal loss would reduce perceived color differences along a post-receptoral L-M axis [14–16]. Evidence that the perceptual compression along an L-M axis is less than predicted has been proposed to be due to neural recalibration that generates compensatory post-receptoral gain amplification [9, 16–18], a hypothesis that is also supported by the steeper rise of the anomalous chromatic response curves in Figure 1C.

The proposition that by modifying the spectral distribution of light reaching the photoreceptors, color filters could affect chromatic discrimination and color perception, has had a long history. Maxwell [1] proposed the possibility of improving color discrimination with red and green filters placed over the eyes of a dichromat who entirely lacked M or L cones, but this approach has been shown to be of limited efficacy [19]. Even though such methods cannot lead to normal color vision, it might be thought that anomalous trichromacy would be more amenable to improvements with filtering by spectral reshaping of the three present classes of cone sensitivities. Broad-band filters may, indeed, help individuals with M- or L-cone deficiencies to defeat standard color vision tests by modifying the test illuminant. However, this does not imply that they improve color vision [5, 6]. In theory, a notch filter can achieve this.

We tested the long-term effects of wearing a commercial notch filter (EnChroma®), henceforth referred to as the test filter, on contrast response. The absorption spectra for indoor and outdoor versions of the filter are shown in Figure 1F. Participants (classified as described in STAR Methods) were male volunteers (8 anomalous and 2 normal trichromats) invited to wear glasses with either of the two notch filters shown. One of the anomalous trichromats was given a neutral density filter having approximately the same overall light attenuation as the indoor test filter. Observers kept a diary and reported estimated daily usage of the glasses (mean = 7.7 h/day, SD = 3.61). The participants mostly preferred the indoor version because they worked indoors and because some of the testing occurred during the worst wildfire in California history (known as the Camp Fire). Although it was about 100 km from the lab, the air was smoke filled, and the

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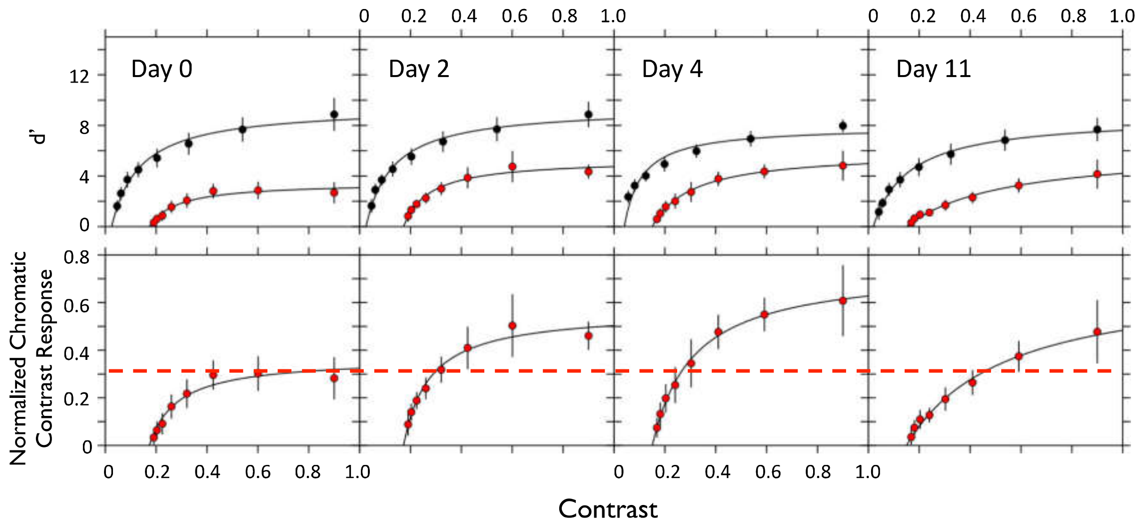

Figure 2. Results of Extended Filter Usage

The panels in the top row show mean MLDS values ± 1 SEM for achromatic (black symbols) and chromatic (red symbols) contrast response plotted against stimulus contrast for each day of testing. The curves are the least-squares best-fitting Michaelis-Menten functions. The lower panel shows the ratio of chromatic to estimated maximum achromatic response for each session. The dashed line shows the ratio from the baseline session in order to emphasize systematic changes in chromatic response over the period the glasses were worn (Additional results in Figure S2).

sun was hidden for several weeks, minimizing the time spent outdoors.

Figure 2 presents MLDS results from one protanomalous observer evaluated without the test glasses on day 0 and on 3 subsequent tests after wearing the glasses. All tests were performed without the glasses. The top panels show the contrast responses estimated for chromatic (red points) and achromatic (black points) stimuli for each session. The solid curves are individually fitted Michaelis-Menten functions. To control for day-to-day variation in the estimated R_m of the fitted functions, the chromatic (L-M) scale was normalized to the daily estimated R_m of the achromatic scale (luminance), shown in the lower panels. Note that the ratio at the maximum contrast tested increased on day 2 and was above the day 0 baseline (dashed red line) on all subsequent days of testing.

Spontaneous comments followed the changes in objective testing. On day 2, this participant said, "I wear the glasses very often… I am certain that I am seeing differences in everything that has red in it (flowers, leaves, cars)." On day 4, he reported that "Autumn foliage colors are what is most noticeably changed." On day 11, his relative chromatic response was lower than on day 4. Nevertheless, his relative chromatic response was still 72% above baseline. The small drop between days 4 and 11 may reflect his report that he only had worn the glasses once since the previous test date.

The pattern of results was consistent across subjects (Figure S2), although we did not identify differences between deuteranomalous and protanomalous observers (mean percentage change at day 11 for all subjects: 71%, 95% conf. int. = 45%–96%). Individual differences may reflect the amount of time observers wore the glasses as well as the recognized variability in anomalous cone spectral sensitivities [10, 11]. Six of the 7 anomalous observers who wore the test glasses made spontaneous comments indicating enhancement of the appearance of color with the glasses and when removed (Figure S2). Figure 3 shows average R_m ratios (black circles) from all anomalous observers fitted with an exponential function (black curve). The results cannot be attributed to practice because the protanomalous observer wearing neutral density filters showed no changes over days and reported no changes in his color vision (Figure 3, green points, and Figure S3). As the neutral density filter reduced the overall intensity similarly to that of the test filter, the effect cannot be attributed to sensitization due to an average reduction in retinal illuminance.

The filters were designed to enhance chromatic contrasts for observers with anomalous cone photopigments. Analysis of their effects on chromatic contrast indicates that the filters effectively sharpen the 2 lobes of the L-M function and increase the separation of their peaks for both normal and anomalous observers. Normal observers sometimes report an effect of the filters on color appearance, but the two normal trichromats who wore the filters displayed no change in their chromatic contrast response relative to their achromatic contrast response (Figure 3, blue points, and Figure S3). Despite the small sample, the percentage change of the anomalous who wore the test glasses differs significantly from the combined normal and placebo groups (permutation test: $n = 10{,}000$, $p = 0.008$). The data of the normal observers provide a reference for evaluating the improvement observed for anomalous observers. From the fitted function (Equation 5), the R_m of the average anomalous observer increased to 50% of its asymptotic value by 5.9 days.

For all anomalous subjects, there was no statistically significant change in response gain along the luminance axis (likelihood ratio test: $\chi^2(1) = 3.38$, $p = 0.07$). Along the L-M axis, anomalous observers showed a negative linear trend in the log contrast gain over days ($\chi^2(1) = 4.58$, $p = 0.03$), but the slope indicated that the change per day was quite modest (0.021, 95% confidence interval (−0.040, −0.002). Over 11 days, this

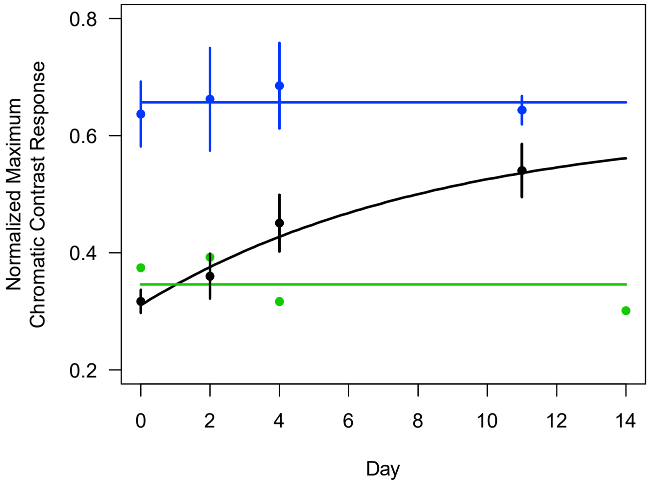

Figure 3. Change in Maximum Chromatic Response over Time

Average (±1 SEM) relative increase in maximum chromatic contrast response for all anomalous trichromats (black points) plotted against days wearing the test glasses. These data were fitted with an exponential function $f(d) = R_0 + \kappa(1 - exp(-d/\tau))$, where R_0 is the observer's response on day 0, and κ and τ are parameters estimated by a nonlinear mixed-effects model. The curve is the population response. The time constant, τ, indicates the day at which the change reached 63% of its maximum and was estimated at 8.5 days. Normal trichromats (blue, error bars indicate range) wearing the test glasses showed no evidence of change over time (linear regression: slope = 4e-4, $t(5) = -0.12$, $p = 0.92$), and their data are fitted with a horizontal line. A protanomalous control (green) wearing neutral density glasses showed no evidence of change over time (linear regression: slope = -0.008, $t(2)$, $p = 0.14$); the fitted function is a horizontal line at the mean value. Results for controls in Figure S3.

predicts a change of the log gain of 0.231. Given our previous demonstration of a linear relation between log gain and R_m [9], this predicts a change in response gain of 26%, which is about half of the change shown in Figure 3. Considering the uncertainty in these values, however, we cannot exclude the possibility that a small compensatory change in contrast gain drives an increase in response gain. Taken together, along with the fact that all testing was performed without the test filter, these findings demonstrate increases in L-M response over time for anomalous trichromats from extended wearing of the test glasses.

The results show an increase in the maximum response to chromatic contrast in anomalous trichromats following long-term usage of spectrally selective filters that effectively reduce the overlap in stimulation of their two long-wave cone sensitivities. This is a neural effect that may lend itself to adaptation in visual therapies, not just for color vision, but perhaps for other visual modalities as well. Given that MLDS yields a measure of the strength of appearance, the results suggest that the observers' experience of color intensity or saturation will have increased. This effect would not be possible with broadband filters. It is unclear how long the improvement lasts, but the evidence shows that the effect persists without the filters. Indeed, no participant arrived at the lab wearing the glasses, and we emphasize that all testing was performed without the glasses.

Previous proposals that the anomalous visual system adjusts its chromatic gain to match the range of chromaticities encountered in the world [18, 20] have received some empirical support [17, 19, 21]. While we recently reported higher chromatic contrast gain in anomalous observers [9], the results here demonstrate that the mechanism controlling chromatic response gain also displays plasticity when exposed to an enhanced chromatic environment. Thus, the current results align more closely with changes in luminance contrast discrimination obtained from long-term filtering of contrast [22] that could be described solely by a change in response gain. While the sensitivity improvements reported in this previous study resulted from extended exposure to contrast reduction, paradoxically, the increased response gain reported here is found subsequent to long-term exposure to contrast enhancement. This apparent contradiction suggests an alternate explanation based on a perceptual learning mechanism. In spite of evidence supporting gain amplification at low contrasts, anomalous trichromats display a lower maximum response to chromatic contrast [9], indicating an attenuated chromatic response system. The contrast response enhancements generated by the filters may have led the observers to become more aware of weak perceptual signals and, thus, to have learned to be more attentive to them. Under this hypothesis, the increased chromatic response gain might persist indefinitely. Indeed, intensive behavioral training methods have been reported to improve vision in amblyopia and stereoblindness via perceptual learning mechanisms [23, 24]. In the current study, however, the increases in contrast response remarkably resulted from only passive usage of the filters.

More than 160 years ago, James Clerk Maxwell tested whether red and green lenses could help a dichromat discriminate colors by binocular color mixtures. He was hoping that "the mental processes may become so familiar … as to act unconsciously like a new sense," ([1], p. 287) causing lasting improvement in color vision. This study tested anomalous trichromats who may indeed experience sustained improvements in their color vision. In this regard, the comment of a deuteranomalous observer is telling when he reported, "I now see that my girlfriend's brown hair has hints of red…; I now notice it even without wearing the glasses."

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- RESOURCE AVAILABILITY
  - Lead Contact
  - Materials Availability
  - Data and Code Availability
- EXPERIMENTAL MODEL AND SUBJECT DETAILS
- METHOD DETAILS
- QUANTIFICATION AND STATISTICAL ANALYSIS
  - Fitting Maximum Likelihood Difference Scales
  - Aggregate data analysis

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at https://doi.org/10.1016/j.cub.2020.05.054.

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AUTHOR CONTRIBUTIONS

Conceptualization, J.S.W. and K.K.; Methodology, J.S.W. and K.K.; Software, K.K and B.M.A.; Investigation, B.M.A.; Formal Analysis, J.S.W., K.K., and B.M.A.; Writing – Original Draft, J.S.W.; Writing – Review & Editing, J.S.W., K.K., and B.M.A.

DECLARATION OF INTERESTS

KK holds shares in EnChroma®. The authors declare no competing interests.

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REFERENCES

1. Maxwell, J.C. (1855). XVIII. – Experiments on colour, as perceived by the eye, with remarks on colour-blindness. Trans. R. Soc. Edinb. *21*, 275–298.
2. Nathans, J., Piantanida, T.P., Eddy, R.L., Shows, T.B., and Hogness, D.S. (1986). Molecular genetics of inherited variation in human color vision. Science *232*, 203–210.
3. J. Pokorny, V.C. Smith, G. Verriest, and A.J.L.G. Pinckers, eds. (1979). Congenital and Acquired Color Vision Defects (New York: Grune & Stratton).
4. DeMarco, P., Pokorny, J., and Smith, V.C. (1992). Full-spectrum cone sensitivity functions for X-chromosome-linked anomalous trichromats. J. Opt. Soc. Am. A *9*, 1465–1476.
5. Sharpe, L.T., and Jägle, H. (2001). I used to be color blind. Color Res. Appl. *26*, S269–S272.
6. Moreland, J.D., Westland, S., Cheung, V., and Dain, S.J. (2010). Quantitative assessment of commercial filter ‘aids’ for red-green colour defectives. Ophthalmic Physiol. Opt. *30*, 685–692.
7. Maloney, L.T., and Yang, J.N. (2003). Maximum likelihood difference scaling. J. Vis. *3*, 573–585.
8. Knoblauch, K., and Maloney, L.T. (2012). Modeling Psychophysical Data in R, *32* (New York: Springer).
9. Knoblauch, K., Marsh-Armstrong, B., and Werner, J.S. (2020). Suprathreshold contrast response in normal and anomalous trichromats. J. Opt. Soc. Am. A Opt. Image Sci. Vis. *37*, A133–A144.
10. Alpern, M., and Moeller, J. (1977). The red and green cone visual pigments of deuternomalous trichromacy. J. Physiol. *266*, 647–675.
11. Bosten, J. (2019). The known unknowns of anomalous trichromacy. Curr. Opin. Behav. Sci. *30*, 228–237.
12. Webster, M.A., and MacLeod, D.I.A. (1988). Factors underlying individual differences in the color matches of normal observers. J. Opt. Soc. Am. A *5*, 1722–1735.
13. Dacey, D.M. (2000). Parallel pathways for spectral coding in primate retina. Annu. Rev. Neurosci. *23*, 743–775.
14. Paramei, G., Izmailov, C.A., and Sokolov, E. (1991). Multidimensional scaling of large chromatic differences by normal and color-deficient subjects. Psychol. Sci. *2*, 244–249.
15. Bosten, J.M., Robinson, J.D., Jordan, G., and Mollon, J.D. (2005). Multidimensional scaling reveals a color dimension unique to ‘color-deficient’ observers. Curr. Biol. *15*, R950–R952.
16. Boehm, A.E., MacLeod, D.I.A., and Bosten, J.M. (2014). Compensation for red-green contrast loss in anomalous trichromats. J. Vis. *14*, 19, 1–17.
17. MacLeod, D.I.A. (2003). The Verriest Lecture: Colour discrimination, colour constancy and natural scene statistics. In Normal and Defective Colour Vision, J.D. Mollon, J. Pokorny, and K. Knoblauch, eds. (Oxford University Press), pp. 189–217.
18. Webster, M.A. (2020). The Verriest Lecture: Adventures in blue and yellow. J. Opt. Soc. Am. A Opt. Image Sci. Vis. *37*, V1–V14.
19. Knoblauch, K., and McMahon, M.J. (1995). Discrimination of binocular color mixtures in dichromacy: evaluation of the Maxwell-Cornsweet conjecture. J. Opt. Soc. Am. A Opt. Image Sci. Vis. *12*, 2219–2229.
20. Regan, B., and Mollon, J. (1997). The relative salience of the cardinal axes of colour space in normal and anomalous trichromats. In Colour Vision Deficiences XIII, C.R. Cavonius, ed. (Springer Kluwer Academic Publishers), pp. 261–270.
21. Tregillus, K.E., and Engel, S.A. (2019). Long-term adaptation to color. Curr. Opin. Behav. Sci. *30*, 116–121.
22. Kwon, M., Legge, G.E., Fang, F., Cheong, A.M., and He, S. (2009). Adaptive changes in visual cortex following prolonged contrast reduction. J. Vis. *9*, 1–16.
23. Ding, J., and Levi, D.M. (2011). Recovery of stereopsis through perceptual learning in human adults with abnormal binocular vision. Proc. Natl. Acad. Sci. USA *108*, E733–E741.
24. Li, J., Spiegel, D.P., Hess, R.F., Chen, Z., Chan, L.Y.L., Deng, D., Yu, M., and Thompson, B. (2015). Dichoptic training improves contrast sensitivity in adults with amblyopia. Vision Res. *114*, 161–172.
25. Peirce, J., Gray, J.R., Simpson, S., MacAskill, M., Höchenberger, R., Sogo, H., Kastman, E., and Lindeløv, J.K. (2019). PsychoPy2: Experiments in behavior made easy. Behav. Res. Methods *51*, 195–203.
26. R Core Team (2019). R: A Language and Environment for Statistical Computing (R Foundation for Statistical Computing). https://www.r-project.org.
27. Pinheiro, J., Bates, D., DebRoy, S., and Sarkar, D.; R Core Team (2019). nlme: Linear and Nonlinear Mixed Effects Models. R package version 3.1-141. https://CRAN.R-project.org/package=nlme.
28. Regan, B.C., Reffin, J.P., and Mollon, J.D. (1994). Luminance noise and the rapid determination of discrimination ellipses in colour deficiency. Vision Res. *34*, 1279–1299.
29. National Research Council (1981). Procedures for Testing Color Vision: Report of Working Group 41 (The National Academies Press). https://doi.org/10.17226/746.
30. Hardy, L.H., Rand, G., and Rittler, M.C. (1954). The H-R-R polychromatic plates. J. Opt. Soc. Am. *36*, 509–523.
31. Derrington, A.M., Krauskopf, J., and Lennie, P. (1984). Chromatic mechanisms in lateral geniculate nucleus of macaque. J. Physiol. *357*, 241–265.