Colour vision deficiency

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REVIEW

Abstract

Colour vision deficiency is one of the commonest disorders of vision and can be divided into congenital and acquired forms. Congenital colour vision deficiency affects as many as 8% of males and 0.5% of females—the difference in prevalence reflects the fact that the commonest forms of congenital colour vision deficiency are inherited in an X-linked recessive manner. Until relatively recently, our understanding of the pathophysiological basis of colour vision deficiency largely rested on behavioural data; however, modern molecular genetic techniques have helped to elucidate its mechanisms.

The current management of congenital colour vision deficiency lies chiefly in appropriate counselling (including career counselling). Although visual aids may be of benefit to those with colour vision deficiency when performing certain tasks, the evidence suggests that they do not enable wearers to obtain normal colour discrimination. In the future, gene therapy remains a possibility, with animal models demonstrating amelioration following treatment

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Introduction

Congenital colour vision deficiency is one of the commonest inherited disorders of vision: its prevalence may be as high as 8% in males and 0.5% in females. Those with colour vision deficiency are at a distinct disadvantage when performing certain visual tasks: for this reason, they have traditionally been barred from pursuing particular occupations. Furthermore, certain rare forms of congenital colour vision deficiency result in profound visual impairment. At this point in time, there is no

effective "treatment" of colour vision deficiency: whilst it has been suggested that tinted lenses could offer a means of enabling those with colour vision deficiency to make spectral discriminations that would normally elude them, clinical trials of such lenses have been largely disappointing. Recent developments in molecular genetics have enabled us to not only understand more completely the genetic basis of colour vision deficiency, they have opened the possibility of gene therapy. The application of gene therapy to animal models of colour vision deficiency has shown dramatic results; furthermore, it has provided interesting insights into the plasticity of the visual system with respect to extracting information about the spectral composition of the visual scene.

Materials and methods

This article was prepared by performing a primary search of Pubmed for articles on 'colo(u)r vision deficiency' and 'colo(u)r blindness'. In addition, the proceedings of the biannual meetings of the International Colour Vision Society (formerly known as the International Research Group on Colour Vision Deficiencies) were reviewed.

The physiological basis of colour vision

Normal human colour vision is trichromatic, meaning that any colour can be reproduced by a mixture of three judiciously chosen primary colours. The physiological substrate of colour vision is the cone photoreceptor, of which there are three classes—the blue, green, and red cones (also known as the short-, medium-, and long-wavelength sensitive cones, respectively). The different classes of cone contain different types of photopigment—molecules comprising two components: first, a heptahelical protein component (or 'opsin') and second, 11-cis retinal (a derivative of dietary vitamin A). It is the photopigments that are responsible for absorbing light—a process which forms the first

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stage of a signal transduction cascade on which vision is dependent. The blue cones are maximally responsive to light with a wavelength of 419 nm (violet), the green cones are maximally sensitive to light with a wavelength of 531 nm (green), and the red-cones are maximally sensitive to light with a wavelength of 558 nm (yellow-green).¹ The different classes of cone respond to light over a large range of wavelengths, and as a result they have overlapping sensitivity curves (Figure 1).

Each cone can only signal the rate at which light is absorbed and cannot alone convey information about wavelength (the so-called 'principle of univariance')—the visual system derives trichromatic colour vision by comparing the responses of the three different classes of cone. Such comparisons are thought to be made initially at the level of tertiary neurons: midget ganglion cells appear to be specialised for comparing red- and green-cone responses, whereas at least four distinct ganglion cell types appear to be specialised for comparing blue-cone responses to those of the red and green cones.^{2,3} Within the central retina, midget cells are thought to draw inputs into the centre of their receptive fields from single cones; there is still controversy as to whether the surround is normally drawn in a precise manner from cones of a different class or indiscriminately from adjacent cones.² The receptive fields of ganglion cells conveying blue-cone signals are larger than those of the midget cells and thus support an inferior level of spatial resolution.

Figure 1 Spectral sensitivity curves for the three classes of cone. Relative sensitivity is plotted against wavelength. The blue cones (inverted triangles) have a peak sensitivity at about 419nm, the green cones (upright triangles) have a peak sensitivity at about 531nm and the red cones (circles) have a peak sensitivity at about 558nm. Note that while the different types of cone have distinct sensitivities, there is a great degree of overlap.

The dichotomy between the red/green- and blue-cone systems is respected in the lateral geniculate nucleus (LGN); the midget ganglion cells transmit signals to the parvocellular layers of the LGN, whereas the ganglion cells subserving the blue cones transmit to a neurochemically distinct koniocellular pathway.⁴ The koniocellular layers in turn project to the lower echelons of layers 3 and 4A of the primary visual cortex, whereas the parvocellular layers project to layer 4C β .²

Congenital colour vision deficiency

Congenital colour vision deficiency results from genetic mutations that affect the expression of the full complement of normal cone photoreceptors. They are generally classified by severity (anomalous trichromacy, dichromacy, and monochromacy) and may be further classified by the type(s) of cone(s) affected.

Anomalous trichromacy

Anomalous trichromacy is the mildest form of colour vision deficiency. Like those with normal colour vision, the anomalous trichromat requires three primary colours to match any other colour. However, the way in which they mix the primary colours is aberrant, such that they will accept colour matches that a normal will not. In most instances, the converse is also true: this has led to the suggestion that anomalous trichromacy may be an advantage in breaking camouflage (see below).⁵ It is important to add that anomalous trichromats vary in their ability to discriminate between different colours, such that some anomalous trichromats may have normal—or near normal—colour discrimination, whereas others may have colour discrimination that approaches that of a dichromat (see below).^{6,7}

Anomalous trichromacy is subdivided into protanomaly (which affects the red cones), deuteranomaly (which affects the green cones), and tritanomaly (which affects the blue cones).

Dichromacy

The next severest form of colour vision deficiency is known as dichromacy. Dichromats have a reduced dimension of colour vision and require only two primaries to match any other colour.

Similar to anomalous trichromacy, dichromacy is subdivided into protanopia (in which there are no functional red cones), deuteranopia (in which there are no functional green cones), and tritanopia (in which there are no functional blue cones).

Until recently, the accepted doctrine was that dichromacy occurred through a 'replacement'

mechanism, whereby one class of cone was effectively replaced by another. This does seem to be the case in most dichromats. However, sophisticated optical imaging suggests that some forms of dichromacy may occur through a 'loss' mechanism, resulting from the loss of a cone class with a concomitant reduction in the cone population.^{8,9} Although the majority of dichromats are thought to enjoy otherwise normal visual function, there is some suggestion that a minority (with a presumed 'loss' mechanism) may perhaps have reduced visual function (see below).¹⁰

Monochromacy

The severest forms of congenital colour vision deficiency result in monochromacy, in which colour discrimination is absent. It is of note that a significant proportion of monochromats may—under special circumstances—display residual colour discrimination, which is thought to be supported by the interaction of cones and rods. Such monochromats are sometimes referred to as 'incomplete achromats'.

In rod monochromacy, the cones are severely dysfunctional or non-functional and visual function is dominated by the rods (which are chiefly used for night vision in the normal retina).¹¹ Autosomal recessive incomplete achromatopsia—considered by many to be a phenotypical variant of rod monochromacy—shares many features in common with the latter; however, psychophysical testing reveals residual cone function.¹² Blue cone monochromacy (also known as X-linked recessive incomplete achromatopsia) results from a

functional absence of both the green and red cones and vision is dependent on the blue cones and rods (a full complement of normal blue cones, which comprise only approximately 7% of the total cone population, is insufficient to support normal visual acuity).¹¹ It is worthy of note that a minority of blue cone monochromats appear to have some residual red cone function.¹³ Patients with these forms of monochromacy have similar signs and symptoms—profoundly impaired colour vision, poor visual acuity (about 6/60), nystagmus, photophobia, profoundly reduced sensitivity to long wavelength light and abnormal photopic electroretinographic responses.¹¹

There are reports in the literature of monochromats with normal visual acuity (so-called 'cone monochromacy').^{14–18} Such phenotypes are exceedingly rare and could theoretically arise from the dual inheritance of tritanopia with either deuteranopia (resulting in red cone monochromacy) or protanopia (resulting in green cone monochromacy); however, all individuals described with this form of deficiency have, by implication, some degree of post-receptoral defect.¹⁹

The different classes of congenital colour vision deficiency are summarised in Table 1.

The genetic basis of congenital colour vision deficiency

Red-green colour vision deficiency

'Red-green colour vision deficiency' is a term used to encompass protanomaly, deuteranomaly, protanopia, and deuteranopia, all of which are X-linked recessive traits. These colour vision deficiencies are the most

Table 1 A summary of the different forms of congenital colour vision deficiency

Deficiency	Cone(s) affected	Inheritance	Prevalence
<i>Anomalous trichromacy</i>			
Protanomaly	Red	XLR	1.08% ⁴¹
Deuteranomaly	Green	XLR	4.63% ⁴¹
Tritanomaly	Blue	AD	See tritanopia+
<i>Dichromacy</i>			
Protanopia	Red	XLR	1.01% ⁴¹
Deuteranopia	Green	XLR	1.27% ⁴¹
Tritanopia	Blue	AD	1 in 500 ³¹
<i>Monochromacy</i>			
Green-cone monochromacy	Red and blue	Dual XLR and AD ^a	≤1 in 1 000 000 ⁴¹
Red-cone monochromacy	Green and blue	Dual XLR and AD ^a	≤1 in 1 000 000 ⁴¹
Blue-cone monochromacy	Red and green	XLR	1 in 100 000 ⁴¹
Rod monochromacy and incomplete achromatopsia	Red, green, and blue	AR	1 in 33 000–50 000 ⁴²

AD, autosomal dominant; AR, autosomal recessive; XLR, X-linked recessive.

Prevalence refers to European populations and—in the case of X-linked recessive conditions—the prevalence in males. + Tritanomaly is considered to be a phenotypical variation of tritanopia—the combined prevalence may be as high as 1 in 500.

^aRed- and green-cone monochromacy may, in theory, arise from the combined inheritance of deuteranopia and tritanopia or protanopia and tritanopia, respectively. However, all published cases have had some degree of post-receptoral deficit.

prevalent, affecting between 2 and 8% of males and about 0.5% of females (the highest rates occur in Europeans and the lowest in Africans)²⁰ and arise from mutations to the genes coding for the red or green cone photopigments, or their promoter regions. The red and green photopigment genes lie in a tandem 'array' on the X-chromosome:²¹ the red gene is the first in the array and the green is the second. Whilst many subjects have arrays of three or more genes, only the first two genes are thought to be expressed at sufficient levels to influence colour vision:²¹ further discussions will, therefore, consider only the first two genes in the array. A number of genetic alterations have been implicated and the relationship between genotype and phenotype is not completely straightforward.

Owing to the close proximity of the red and green cone photopigment genes, and because of their high degree of similarity (96% in terms of their DNA sequence²¹), the gene array is subject to unequal recombination.²² This may result in the deletion of whole genes or in the generation of so-called red-green hybrid genes (see Figure 2). More rarely, the photopigment genes,^{23–25} or their promoter regions,²⁶ may contain point mutations. Deletions have been identified in the red cone pigment gene, though this leads to a progressive retinal degeneration.²⁷

An early assumption was that dichromacy occurs in those individuals in whom there is a single

Figure 2 A schematic diagram of recombination events in the X-chromosome-encoded photopigment genes. Normal arrays on the left consist of a red pigment gene (red cylinder) and a downstream green pigment gene (green cylinder). (a) Unequal intragenic recombination (left) leads to the generation of hybrid genes (right: red-green cylinder)—the upper right array consists of a red pigment gene, a red-green hybrid, and a green pigment gene, whereas the lower consists of a single hybrid gene. (b) Unequal intergenic recombination (left) leads to the generation of a normal array (right top) and a single red gene (right bottom). Single gene arrays are usually associated with dichromacy, whereas hybrid genes expressed in combination with normal genes may result in anomalous trichromacy (see text for detail). It is important to note that only the first two genes in an array containing three or more opsin genes are expressed at sufficient levels to influence colour vision.

X-chromosome photopigment gene, and this does indeed seem to be the case in some dichromats. However, dichromacy may also occur in those with arrays of two or more genes. This may be because the expressed X-linked photopigments have identical or near identical sensitivities,²³ because one of the genes codes for a non-functional photopigment^{8,23,25} (this is a proven genetic basis for the 'loss' mechanism described above) or because of a mutation in the cone photopigment promoter region.²⁶

Similarly, there is genotypic variation among those with the same forms of anomalous trichromacy. One early theory suggested that it occurs when cones with a sensitivity intermediate between the normal red and green cones is expressed together with either normal green cones (in the case of protanomaly) or red cones (in the case of deuteranomaly).⁶ The difference in peak sensitivity of the normal green and red cone photopigments can largely be accounted for by just three amino-acid residues at positions 180, 277, and 285 of the opsin molecule.^{28,29} Variations in residue 180 (serine or alanine) are considered to represent polymorphisms; a further four residues produce smaller (1 nm or less) shifts in peak sensitivity.²⁹ As recombination events are unlikely to uncouple the codons for positions 277 and 285, and because variations in the amino-acid residue at position 180 account for only about 4 nm shift in peak sensitivity there is a predilection for the peak sensitivities of the X-chromosome-coded photopigments (including so-called hybrid genes) to cluster around two peaks at about 531 and 558 nm, respectively.⁶ It has been suggested⁶ that most cases of anomalous trichromacy, therefore, result from the expression of two photopigments with similar, but non-identical sensitivities. Single X-chromosome opsin genes may sometimes be associated with a phenotype known as extreme anomalous trichromacy, in which there is residual red-green colour discrimination. Possible mechanisms for residual red-green discrimination include topological variations in cone photopigment optical density and rod participation in colour matching. It is worthy of note that some female carriers of red-green anomalous trichromacy—by virtue of random X-chromosome inactivation—may enjoy tetrachromatic colour vision.³⁰

Tritan colour vision deficiency

Colour vision deficiencies involving the blue cones (historically referred to as 'blue-yellow colour vision deficiencies, but now termed 'tritan deficiencies') are rare compared with those involving the green- and red-cones (the most recent estimated prevalence is 1 in 500,³¹ though an earlier estimate had suggested that it is far less

frequent, at somewhere between 1 in 13 000 and 1 in 65 000)³² and are inherited as autosomal dominant traits. These deficiencies are the result of missense mutations in the blue-cone photopigment gene on chromosome 7 and lead to amino-acid substitutions in the blue cone opsin sequence.^{33–35} There is phenotypic variation among those with the same type of blue cone opsin mutation, such that some subjects display residual blue cone function (ie they have tritanomaly), whereas others display tritanopia.

Monochromacy

Blue cone monochromacy is inherited as an X-linked recessive trait and results from three categories of mutation. In the first, mutations occur in a 'locus control region', which lies upstream of the red and green cone pigment genes and which is crucial for their expression.³⁶ In the second, unequal recombination results in a single X-chromosome-coded opsin gene: a point mutation^{36,37} or deletion³⁸ in this single gene renders its product non-functional. The third and final mechanism, described in the minority of blue cone monochromats, occurs in those with two X-chromosome opsin genes, both of which are affected by mutations that result in non-functional gene products.^{39,40} The exact prevalence of blue cone monochromacy is unknown, though some estimate it to affect 1 in 100 000 males.⁴¹

Rod monochromacy and incomplete achromatopsia are autosomal recessive conditions and affect between 1 in 33 000 and 1 in 50 000.⁴² These conditions result from genetic defects affecting either the cone ion channels (*CNGA3*⁴³ on chromosome 2 and *CNGB3*⁴⁴ on chromosome 8) or transducin (*GNAT2*⁴⁵ on chromosome 1)—all of which are crucial components of the signalling pathway within the cone photoreceptors.

There are no published reports of molecular genetic studies of cone monochromats with normal visual acuity; however, one unpublished investigation of a green cone monochromat cited by Sharpe *et al*⁴¹ found a mutation in the red cone photopigment gene, which was replaced by a red-green hybrid (presumably with a peak sensitivity approximating that of the normal green cone photopigment). No mutation of the blue cone photopigment was elucidated, leaving the possibility of either a hitherto unknown mutation affecting blue cone function or a post-receptor defect.⁴¹

Is congenital colour vision deficiency a form of retinal dystrophy?

There is evidence to suggest that a relatively common point mutation (cys203arg) associated with red-green colour vision deficiency,²³ which results in the disruption

of a disulphide bond in the opsin molecule,⁴⁶ causes retinal dystrophy. Some of this evidence is inferred: an analogous mutation in the rhodopsin gene causes retinitis pigmentosa⁴⁷ and blue cone monochromacy occurs in those who have a single X-chromosome photopigment gene containing the cys203arg mutation.⁴⁸ More direct evidence comes from candidate gene studies of patients with retinal dystrophy: those in which the first X-chromosome-coded opsin gene in the array contains this mutation display a phenotype consistent with a diagnosis of cone dystrophy.¹⁰ Furthermore, adaptive optics suggests that those in which the second photopigment gene in the X-chromosome-coded array contains the cys203arg mutation have a sub-population of optically empty cones.⁸

The collective evidence suggests that the spectrum of disease caused by the cys203arg mutation is a function of the position in which the mutated gene occurs in the X-chromosome opsin gene array. It is known that the first gene enjoys preferential expression,⁶ and as a result, mutation of this gene would be expected to cause—in addition to colour vision deficiency—a clinically detectable compromise of visual function. However, patients in which the mutation occurs to the second gene in the array may not display any additional abnormality unless special tests are used (eg retinal imaging using adaptive optics). A further possibility—implied from the analogous rhodopsin mutation and which has yet to be directly explored—is that those with red-green colour vision deficiency resulting from the cys203arg point mutation may display progressive disease.

Other point mutations, such as those described by Ueyama *et al*²⁵ appear to be less common. Two of these mutations, asn931lys and gly338glu, result in non-functional pigments when expressed *in vitro*. One of these mutations, arg330gln, shows weak light absorbance *in vitro*. These mutations, by inference, may also give rise to retinal dystrophy.

One pedigree has been described by Reichel *et al*²⁷ in which a major deletion in the red cone photopigment gene results in progressive and profound retinal degeneration.

It has also been argued that mutations in the blue-cone photopigment gene may lead to a progressive loss of cones with disruption of the photoreceptor matrix.⁹ As the blue cones represent only approximately 7% of the total cone population, the effects on visual function of blue cone photopigment mutations appear to be limited to colour vision deficiency.

Pedigrees with blue cone monochromacy^{37,40,49} and rod monochromacy^{48,50,51} may also show evidence of progressive deterioration in visual function.

Practical limitations of colour vision deficiency

Colour vision deficiency places the sufferer at a distinct disadvantage when performing certain visual tasks—in particular those tasks in which a coloured target is embedded in a variegated background of a different colour. One of the earliest descriptions of colour vision deficiency alludes specifically to this problem: Robert Boyle describes a case of ‘vitiating sight’ in a treatise from 1688.⁵² The subject in question—a young lady—was fond of picking flowers. Boyle writes that the maid sometimes ‘*had a mind to gather Violets, tho’ she kneel’d in that Place where they grew, she was not able to distinguish them by the colour from the neighbouring Grass, but only by the Shape, or by feeling them*’. As observed by Mollon,⁵³ this is a classic example of a task that exercises those with colour vision deficiency—the detection of fruit or flowers among foliage. As colour vision deficiency is maintained at a relatively high rate in the population—and because it results in a disadvantage in such visual search tasks—it has been proposed that it may confer a selective advantage in other visual tasks. One suggestion is that it confers an advantage under night-time viewing conditions. The first such suggestion dates to the 1818 case report of Nicholl,⁵⁴ and it has been claimed that the Japanese military deliberately selected pilots with colour vision deficiency for night-time missions in World War II.⁵⁵ However, the hypothesis that colour vision deficiency confers an advantage under night-time conditions does not bear up to closer scrutiny.⁵⁶ Another suggestion is that those with colour vision deficiency may break camouflage that confounds those with normal colour vision, and there is some evidence to support such an assertion.⁵

In the modern world, colour vision deficiency impairs the ability to recognise signal lights—for example those with protanopia and protanomaly (which both result in reduced sensitivity to long wavelength light) may be at increased risk of having rear-end collisions.⁵⁷ Colour vision deficiency may also have vocational implications: those with colour vision deficiency may be barred from certain professions—typically those in which the safety of the worker or others may be compromised, or when the quality of a product or service may be adversely affected because of the worker’s colour vision deficiency. For certain professions, specific vocational tests are used—these are designed to assess the subject’s ability to discriminate colours in a simulated environment. Vocational colour vision tests have been in existence since the late 19th century; however, their acceptance as a standard test for occupational purposes can be traced to the case of the tenacious merchant seaman, Trattles and his struggle with the Board of Trades (which has been sympathetically retold by Boltz⁵⁸). A recent report for the

Civil Aviation Authority has attempted to rationalise colour vision standards for flight crew.⁷

It would be remiss in such an article not to mention the implications of colour vision deficiency for the medical practitioner. There are certainly reports of doctors with colour vision deficiency misdiagnosing or missing clinical signs⁵⁹ (eg rashes, jaundice, confusing blood and pigment on ophthalmoscopic examination, misinterpreting histopathological stains). However, there is little evidence as to the impact of colour vision deficiency in terms of adverse outcomes. In the UK, there are no restrictions placed on medical practitioners with colour vision deficiency; this is not true, however, for the rest of the world (eg in Taiwan prospective medical school entrants are routinely screened for colour vision deficiency).⁵⁹

The management of colour vision deficiency

There are a number of putative methods of ‘correcting’ colour vision deficiency. In the late 19th and early 20th century, ‘training’ in colour naming was given to certain individuals who were deemed ‘colour ignorant’ or ‘colour stupid’. These latter concepts derived from the notion that certain individuals had not correctly learnt (or had never been taught) the correct names for colours. Such notions have little support today. A longer-lived means of ‘correcting’ colour vision deficiency is in the form of tinted spectacle or contact lenses. Typically, such lenses are worn monocularly, though they may be worn binocularly. Tinted lenses may also be used to provide a successive comparison by briefly viewing a visual scene through the lens. There are anecdotal claims that many of those with colour vision deficiency find that their colour vision is subjectively improved by tinted lenses and there are a number of means by which such filters might work.⁶⁰ Furthermore, there is empirical evidence based on laboratory experiments, which suggest that (in theory at least) monocular filters could improve colour discrimination in dichromats.⁶¹ A recent study by Formankiewicz and Mollon⁶² also suggests that interocular differences in contrast may be exploited to provide a surrogate for colour discrimination. They used data obtained in normal subjects to model the performance of deuteranopes at a clinical test of colour discrimination. They predict that a monocular long bandpass lens may enable a deuteranope to discriminate colours along a deutan axis (colours of equal luminance that lie along a deutan axis in colour space look indistinguishable to a deuteranopic observer), though discrimination is predicted to remain inferior to that of normal subjects. Another strategy—the use of so-called ‘notch filters’ to artificially separate the effective peak sensitivities of the expressed X-chromosome-coded

photopigments in red-green anomalous trichromats—has yet to be explored fully.

Clinical trials of bandpass filters have yielded generally disappointing results. Most studies imply that monocular long bandpass lenses have their main effect by either altering the colour confusions that those with colour vision deficiency make or by changing the relative brightness/lightness of different colours (ie by introducing luminance cues).⁶³ Moreover, long bandpass filters have been found to increase error scores at the FM 100 Hue and to induce tritan deficiency.⁶⁴ Interestingly, the most recent small clinical trial of a new lens design found a statistically significant improvement in confusion index scores at the FM-D15 test: this finding cannot easily be explained by the introduction of luminance cues.⁶⁵ Any alteration to colour discrimination afforded by monocular tinted lenses is offset by alterations to depth and motion perception. Furthermore, it is clear that such filters do not 'normalise' colour vision. Those with blue cone and rod monochromacy often find (binocular) tinted lenses helpful in the reduction of debilitating photophobia.¹¹

In theory at least, congenital colour vision deficiency could be amenable to gene therapy. Alexander *et al*⁶⁶ investigated the use of adeno-associated virus as a transfection vector in a mouse model of rod monochromacy. The rescue of cone function was observed both electrophysiologically and behaviourally in almost all animals treated. It remains unclear as to what stage of development rescue would need to be instituted in order to result in improved vision in humans, as rod monochromacy has been shown to result in alterations to inner retinal structure,⁶⁷ alterations in the photoreceptor mosaic,⁶⁸ and in reorganisation of the visual cortex.⁶⁹ It is likely that these changes alone would have an impact on visual function: even if successful targeting of cone photoreceptors with wild-type achromatopsia genes can be achieved via viral vectors, vision is unlikely to be returned to normal once such changes have occurred. A more recent study by Mancuso *et al*⁷⁰ has investigated the amelioration of red-green colour vision deficiency in an animal model of protanopia. They trained adult male squirrel monkeys—a species in which there is a single X-chromosome-coded photopigment gene—to detect coloured patches embedded in a background composed of greys. Two males expressing a single green cone photopigment gene were selected for transfection with a modified adeno-associated virus carrying a red cone photopigment gene together with the appropriate regulatory elements. Their results show that the red cone photopigment was expressed in a subset of cones. Furthermore, they show a clear and dramatic improvement in red-green colour discrimination in the

treated animals: this occurred despite the fact that expression of the red cone photopigment occurred in adulthood. It had previously been supposed that such therapy may fail in adult animals: other forms of visual deprivation have been shown to cause irreversible loss of visual function if not addressed during a 'critical' period of neural development. The authors themselves suggest that the phenomenon might be the result of hijacking and division of the neural pathways serving the blue cone subsystem. An alternative hypothesis is that the red-green system had already been primed to exploit the newly expressed red cone photopigment. Specifically, spectral comparisons could have been made via two mechanisms—(1) via topological variations in green-cone photopigment optical density and (2) via rod/green-cone interactions. Consistent with such a hypothesis is the observation that many human dichromats, including those with single X-chromosome-coded photopigments, display trichromatic vision under certain test conditions.⁴¹

The ethics of gene therapy in humans—especially in those with dichromacy and anomalous trichromacy—is open to debate.

Conflict of interest

The author declares no conflict of interest.

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