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## 8 Color vision changes in normal aging

John L. Barbur and Marisa Rodriguez-Carmona

### Introduction

The aging visual system undergoes myriad changes that affect physiological functions, with subsequent decline in visual performance as a result of either degraded retinal images or changes in the neural mechanisms in the retina and the visual pathways. The various attributes of vision, such as the ability to see fine spatial detail in objects of low contrast, to discriminate small color differences, and to detect motion and rapid flicker, decline gradually and in different ways (Haegerstrom-Portnoy *et al.*, 1999; Owsley, 2011; Werner *et al.*, 1990; Werner and Steele, 1988), but, as a result of adaptation processes, one often remains largely unaware of “normal” aging. We expect “good vision” throughout our lifetime (Enoch *et al.*, 1999), and as we grow older we only become aware of visual deficits when the retinal images are degraded heavily by refractive errors, increased scattered light, reduced retinal illuminance, or the presence of disease that affects the retina or the visual pathways. Separating the latter from the more gradual decline that can be attributed to normal aging is often difficult since during the early stages of disease many older subjects may not have normal vision but may exhibit no obvious clinical signs.

There are many vision attributes we can assess, but the eye is arguably most sensitive to color differences (Chaparro *et al.*, 1993), and, unlike achromatic contrast sensitivity, color thresholds under optimum conditions remain relatively unaffected by small changes in refraction, pupil size, and scattered light (Barbur *et al.*, 1997;

Barbur and Rodriguez-Carmona, 2012). Color assessment is therefore of interest in detecting early neural changes that cannot be attributed to normal, age-related decline. Under optimum conditions of light adaptation, color appearance is also independent of the optical density of the ocular media (Werner *et al.*, 2004), and, equally surprisingly, yellow/blue (YB) color thresholds remain relatively independent of both macular pigment optical density and absorption of short wavelength light by the lens (Rodriguez-Carmona *et al.*, 2006). Significant reduction in retinal illuminance and stimulus size can, however, cause large increases in color thresholds (Knoblauch *et al.*, 1987).

In order to establish adequate limits of normal color vision, it is useful to obtain reliable statistical data that describe the best chromatic sensitivity in young subjects under optimum conditions and then to establish how these parameters change as a function of age. The tests employed should ideally isolate red/green (RG) and YB chromatic mechanisms. They should also yield the most sensitive response and minimize the within-subject variability so that the variation in the measured thresholds can be attributed mostly to the inherent parameters that affect early-stage, color-vision signals. The latter reflect a number of parameters including small differences in peak spectral responsivity, optical densities, and the relative numbers of L- and M-cones in the retina. There are also other requirements in aging studies, such as the use of the same or similar tests for all age groups to ensure minimum change in response criteria, and, most important,

the need to define adequate filters to ensure that no subjects with increased thresholds as a result of congenital or acquired loss of chromatic sensitivity are included in the normal sample group. Since both RG and YB color thresholds remain relatively unaffected by moderate changes in the optics of the eye, it is also of interest to identify the most likely factors that cause the gradual loss of chromatic sensitivity with increasing age.

Rod photoreceptor density in central vision declines by as much as 30% over a lifetime, but the number of cones remains relatively constant in normal aging (Curcio *et al.*, 1993). Color vision relies on cone signals and the integrity of the retina and visual pathways. The number of retinal ganglion cell (RGC) axons decreases linearly by as much as 40% over a lifetime (Johnson *et al.*, 1989; Jonas *et al.*, 1992; Neufeld and Gachie, 2003). Although more difficult to count in older eyes, RGC cell body loss also increases gradually in normal aging.

The neuronal density and structural morphology of the primary visual cortex and extra-striate areas exhibit little or no detectable changes in normal aging (Calkins, 2013; Haug *et al.*, 1984; Vincent *et al.*, 1989). It is therefore of great interest to establish how the normal, gradual loss of RGC axons and the corresponding cell bodies in humans affects color vision and other aspects of visual performance. Equally important, the establishment of reliable, normal, upper threshold limits may make it possible to detect accelerated losses that cannot be attributed to normal aging. Such losses can reflect reduced inner retinal and choroidal blood circulation (Hirata and Nishiwaki, 2006), changes in the retinal pigment epithelium (Panda-Jonas *et al.*, 1996), damage to photoreceptors, and accelerated loss of RGC bodies and axons as reported in Alzheimer's disease (Curcio and Drucker, 1993) or glaucoma (Marvasti *et al.*, 2013; Tatham *et al.*, 2014). Less well-defined, neural and vascular changes can cause vision degradation and loss of chromatic sensitivity in patients with systemic disease

such as diabetes (Bronson-Castain *et al.*, 2012; Calkins, 2013; Feitosa-Santana *et al.* 2010; Harrison *et al.*, 2012; Tam *et al.*, 2012). Accurate measurements of RG and YB color thresholds coupled with reliable age-related, upper-threshold limits are of great clinical interest as the means to detect the earliest signs of disease.

### Methods employed to assess chromatic sensitivity –isolation of color signals

The majority of color vision tests were designed to discover congenital color deficiency, which almost exclusively results in a loss of RG chromatic sensitivity. Many of the tests minimize the detection of luminance-contrast (LC) signals that are often present in the colored stimulus by employing spatial features that vary randomly in luminance contrast. Some tests such as the Ishihara test plates also employ YB chromatic noise to provide better isolation of RG color signals. This makes the test extremely sensitive for detection of RG deficiency (Rodríguez-Carmona *et al.*, 2012). Lantern tests require the subject to name correctly the color of small signal lights that are usually presented against a dark background field (Birch, 2008). These conditions do not favor chromatic mechanisms; as a result, many subjects with normal color vision also fail and on other occasions subjects with mild congenital deficiency pass (Barbur and Rodríguez-Carmona, 2012; Squire *et al.*, 2005).

Other tests require the subject to differentiate spatially discrete stimuli on the basis of small color differences or to arrange colored samples according to minimum hue changes. The Farnsworth—Munsell (F–M) 100-hue test (which employs 85 color samples) and the smaller D15 test (based on only 15 samples) are examples of spatial arrangement tests. In the case of the F–M100-hue test, the severity of color vision loss is estimated by calculating the square root of the total “error score,” a parameter that follows an approximately normal

distribution (Kinnear, 1970; Kinnear and Sahraie, 2002). In the case of pseudo-isochromatic plate tests, the number of errors the subject makes is often taken as a measure of the severity of loss. Although, in general, subjects with severe loss of RG color vision tend to produce larger error scores, the total error scores correlate very poorly with the subject's loss of chromatic sensitivity (Rodriguez-Carmona, O'Neill-Biba, and Barbur, 2012). A number of new tests which emulate the Ishihara test plates on visual displays have been developed recently by generating static colored spots or patches that vary randomly in size and luminance so as to isolate the use of color signals (Birch *et al.*, 1992; Regan *et al.*, 1994; Wong *et al.*, 2008).

A new approach to isolating the use of color signals has emerged from studies on camouflage that employed moving, color-defined stimuli buried in dynamic LC noise. The results show that when using such stimuli, the selective loss of color signals (as in the case of dichromats) makes the color-defined stimulus invisible for modulations along the corresponding color confusion line, even for chromatic saturations that are limited only by the phosphors of the display (Rodriguez-Carmona *et al.*, 2005). Exposing the retina to time-varying LC noise reveals the loss of chromatic sensitivity since the subjects cannot make use of LC signals to see the moving stimulus (Barbur *et al.*, 2002).

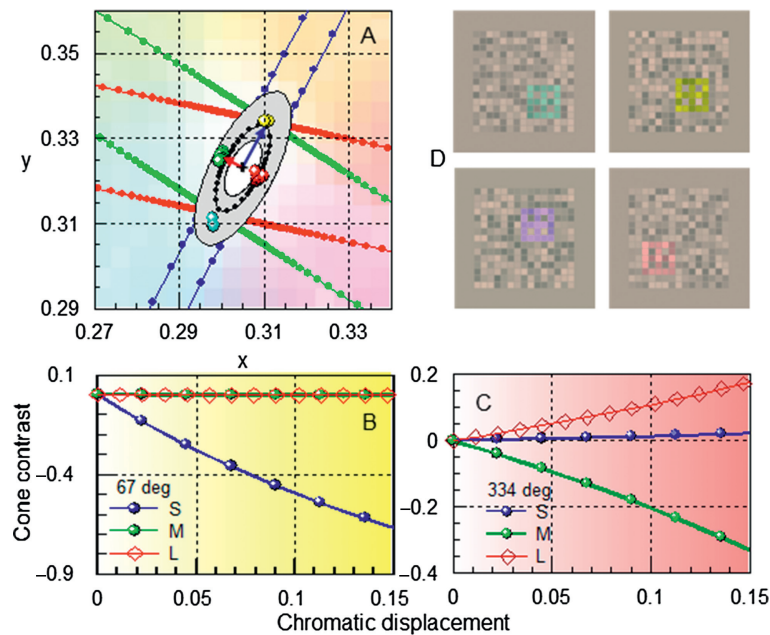
The following section describes briefly the Colour Assessment and Diagnosis (CAD) Test and in particular the standard normal (SN) CAD units which define the average thresholds for RG and YB color vision in young, normal trichromats. Many of the data that describe how normal aging affects color vision were obtained with the CAD test and are expressed in CAD units. Results from other important studies of aging that employed different tests have also been converted to CAD units and are shown and discussed for comparison.

## The standard normal CAD observer

The CAD units are based on the mean thresholds measured in 333 young, normal trichromats. The thresholds were measured in several color directions selected along the YB and RG axes (Figure 8.1A) and are shown normalized with respect to the median thresholds in Figure 8.2B and C. This sample is dominated by 20–30-year-old subjects, an age group that turned out to have the best chromatic sensitivity.

The median YB and RG thresholds are shown as blue and red arrows in Figure 8.1A. The colored symbols show CAD test results for a typical normal trichromat. The 16 directions measured make it possible to compute reliably the mean RG and YB thresholds and to diagnose accurately the subject's class of color vision (i.e., normal, deutan-, protan-, tritan-like congenital loss, or acquired color-vision deficiency) (Barbur and Rodriguez-Carmona, 2012). The amplitude of the measured thresholds relate almost linearly to the corresponding cone contrasts generated (Figure 8.1B and C). The stimuli employed (Figure 8.1D) yield high chromatic sensitivity with threshold cone contrasts for the median observer of less than 0.4% (L) and 0.8% (M). The median thresholds along the YB axis which isolates S-cone signals correspond to ~7% S-cone contrast (Rodriguez-Carmona, O'Neill-Biba, and Barbur, 2012).

When the thresholds are normalized and expressed in CAD units, normal trichromats exhibit ~2.2-fold range in their RG thresholds. The spread in YB thresholds is, however, similar and only marginally larger than that measured in RG thresholds (Figure 8.2B and C). This relatively large variability within normal trichromats is probably caused by neural noise, the presence of slightly variant M- and L-cone genes (Neitz and Neitz, 2011; Neitz *et al.*, 2004), and variation in the relative numbers of L- and M-cones in the retina and their optical densities (Hofer *et al.*, 2005; Roorda and Williams, 1999).



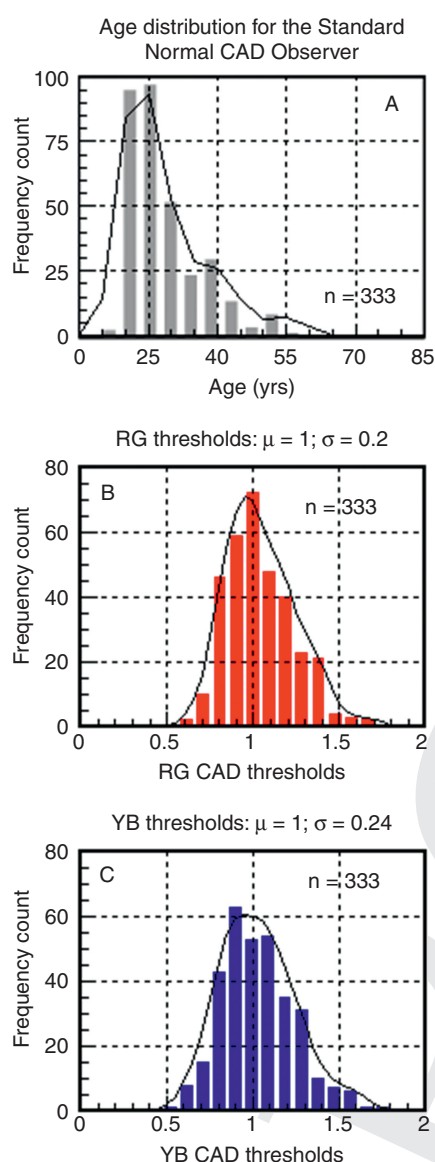
**Figure 8.1** The statistical limits for the standard normal (SN) CAD observer (Barbur *et al.*, 2006; Rodriguez-Carmona, Harlow, Walker, and Barbur, 2005) are plotted in the CIE (x,y) 1931 chromaticity chart (*panel A*). The black cross at the center of the diagram shows the chromaticity of the white background; that is, 0.305, 0.323. The dotted black ellipse represents the median values computed from the distribution of RG and YB thresholds in 333 normal trichromats. The red and blue arrows indicate the corresponding SN unit for RG and YB color vision, respectively. The gray-shaded area represents the statistical distribution of thresholds shown in Figure 8.2B and C. The inner and outer ellipses represent the 2.5% and the 97.5% limits of variability, respectively. The red, green, and blue dotted lines denote the "color confusion bands" based on data measured in protanopes, deuteranopes, and tritanopes, respectively. The large colored dots within the center gray area plot measured thresholds typical of a normal trichromat. The corresponding cone contrasts for chromatic displacement (CD) along the YB (67°) and RG (334°) directions are shown in panels B and C, respectively. The maximum CD distances shown correspond to ~14 SN thresholds units for YB discrimination and ~34 SN units for RG discrimination. The non-linearity increases with the size of CD involved, particularly for the YB axis, but the departure from linearity is small for both RG and YB thresholds, even for CD values that are well above threshold. The screen dumps in panel D show the RG and YB stimuli employed in the CAD test.

## The effects of retinal illuminance and stimulus size

Retinal illuminance and stimulus size are important parameters that affect chromatic sensitivity at

threshold (as shown in Figure 8.3). The background luminance and the stimulus size employed in the CAD test are indicated by vertical arrows. These values were selected in order to achieve





**Figure 8.2** The age distribution of the Standard Normal (SN) CAD observer,  $\mu = 28$  years,  $\sigma = 8$  (panel A) based on measurements in 333 normal trichromats. Panels B and C show the corresponding variability in RG and YB thresholds, respectively. The thresholds are expressed in SN CAD units with standard deviations of 0.2 for RG and 0.24 for YB. The results reveal ~2.3-fold change in threshold when comparing the most and the least sensitive normal subjects.

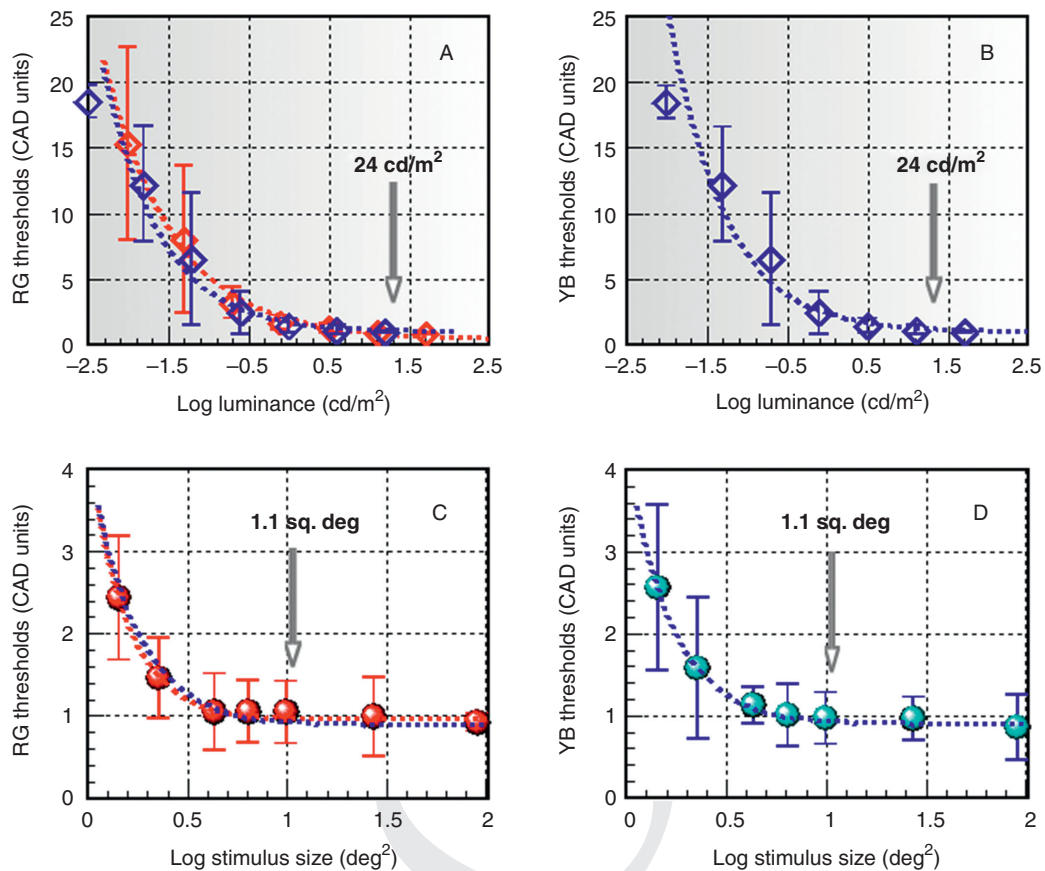
high chromatic sensitivity, to restrict the area tested to a small region of the visual field, and to allow for variation in pupil size and viewing distance.

The use of a higher luminance restricts the gamut of the visual display that can be achieved. Interestingly, the YB thresholds show a more rapid rise with decreased background luminance. Following adjustment for the expected decrease in retinal illuminance caused by the subject's lens and macular pigment absorption of short wavelength light, there is little or no difference between the YB and RG thresholds (see red and blue dashed traces in Figure 8.3A). Similarly, when the thresholds are expressed in SN CAD units, stimulus size affects equally both RG and YB thresholds (Figure 8.3C and D). The results suggest that a significant reduction in retinal illuminance, particularly for short wavelength light caused by selective absorption by the lens, the macular pigment, and a decrease in pupil size in older subjects, is likely to cause higher YB thresholds when the level of ambient illumination is low.

### Effect of normal aging – subject selection criteria

The large majority of subjects investigated were recruited from the Damme Optometri Practice (Kesteren, Netherlands), with some subjects (particularly in the younger age group) being recruited from and then tested at City University London.

A detailed medical history was taken from each subject followed by clinical assessment. The latter included examination of the anterior segment by a slit lamp and classification of lens opacity by the LOCS III system (Chylack *et al.*, 1993). Only subjects with grade 2 or less for nuclear-, cortical-, and posterior subcapsular opacities were included in the study. The fundus was assessed by undilated, indirect ophthalmoscopy and photographed with the Topcon non-mydratric fundus camera. The majority of subjects had RG and YB thresholds measured separately in each eye



**Figure 8.3** Effect of background luminance (*panels A and B*) and stimulus size (*panels C and D*) on RG and YB color thresholds. When expressed in SN units, both RG and YB thresholds increase equally rapidly as the stimulus size is decreased (see the blue, dashed line which shows the YB thresholds added to the RG thresholds (*panel C*) for comparison). The greater increase in YB thresholds with decreasing light level may reflect the increased prereceptor absorption of short wavelength light and hence the lower “effective” light adaptation level. The subject’s macular pigment optical density (averaged over the center  $2.8^\circ$ ) and the lens absorption of short wavelength light were estimated with the MAP test [(Barbur *et al.*, 2010) to be  $\sim 0.4$  and  $0.35$  optical density units, respectively. When the background luminance is lowered by  $0.75$  log units, the loss of YB sensitivity with decreasing luminance matches well the measured RG loss; see dashed, blue line in panel A). The vertical arrows indicate the background luminance and the stimulus size employed in the CAD test.

by the CAD test. Many of the very young subjects ( $<10$  years of age) examined at City University had congenital RG color deficiency, and their RG thresholds were not included in the study.

A number of “filters” were applied to all older subjects to ensure that those with potentially abnormal colour vision were not included in the analysis. The filters were defined as follows:

- (1) all subjects with congenital deficiency exhibiting elevated RG thresholds and normal YB thresholds
- (2) subjects with medical conditions such as diabetes, hypertension, and ocular abnormalities that may cause acquired loss of chromatic sensitivity



- (3) subjects with abnormal fundus appearance or drusen
- (4) subjects exhibiting a statistically significant difference in RG and/or YB chromatic sensitivity between the two eyes. The index employed to describe the asymmetry between the two eyes was the difference in monocular thresholds referenced to the best eye:  $\left| \frac{RE - LE}{\text{Smallest of } RE \text{ or } LE} \right|$ . Figure 8.5 shows the statistical distribution of this parameter for both RG and YB thresholds. All subjects outside the  $2\sigma$  limit were initially eliminated from the study. This filter is based on empirical observations which show that the two eyes are often affected differently in many cases of acquired loss of chromatic sensitivity.

### Monocular and binocular thresholds

Previous studies revealed significant differences between binocular and monocular measurements for both RG and YB thresholds. Conversion from monocular to binocular thresholds was carried out by using the mean monocular to binocular ratio measured in 57 subjects with normal color vision. Best eye monocular to binocular ratios were calculated with means and standard deviations of 1.29 and 0.16 for RG and 1.3 and 0.18 for YB color vision. The mean ratios of right and left eye thresholds and the corresponding standard deviations were 1.03 and 0.12 for RG and 1.02 and 0.09 for YB, neither being significantly different from unity. Since binocular threshold limits are also of interest, these ratios were used to convert monocular to binocular thresholds for the normal sample group. The corresponding best-fit equations that describe the age dependence of monocular and binocular thresholds for the final data set are given in the caption to Figure 8.7. Although the subject-specific monocular (R and L eye) thresholds are correlated, at least one element of the measured monocular variability can be attributed to random noise. Since no statistical comparison with other

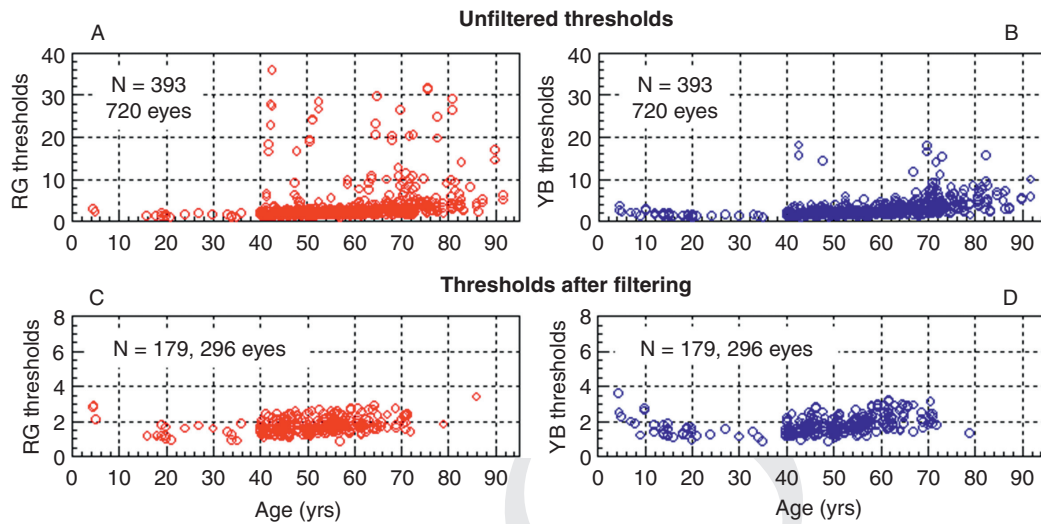
populations was carried out or intended, the thresholds for both eyes were included in the final sample whenever available in order to reduce random noise and hence improve the estimated variability.

### Effect of normal aging on RG and YB thresholds

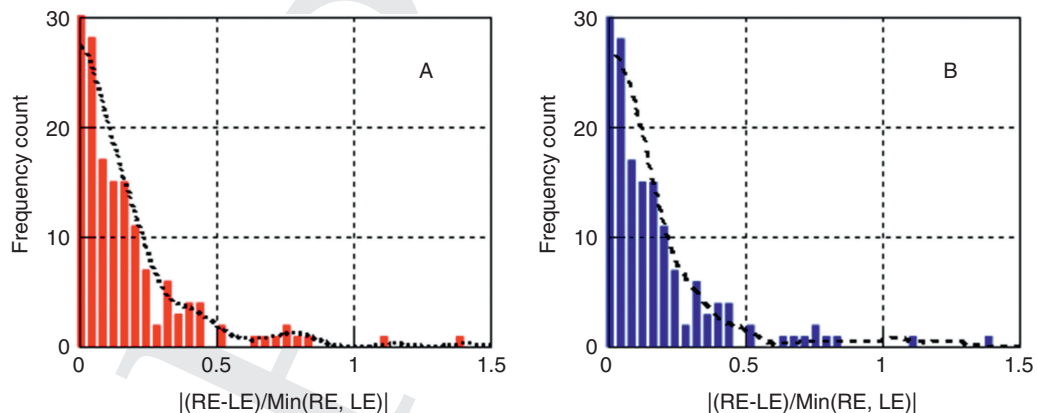
The filters described above were applied to the raw data, and the intermediate results after filtering are shown in Figure 8.4C and D. The exclusion of several eyes that are likely to be abnormal following the filtering applied to the raw data reveals more clearly the linear trend above 20 years age in both RG and YB thresholds. Equations of the form  $\text{mean threshold} = k_0 + k_1 * \text{age} + k_3 * \exp(k_4 * \text{age})$  were fitted to the data, and the differences between the measured points and the computed mean were then used to estimate  $\pm 2.5\sigma$  limits, as illustrated for the final data set in Figure 8.7.

It soon became apparent that some of the subjects eliminated as a result of filtering had color thresholds within the computed normal limits (see Figure 8.6C and D). Data for each of the subjects eliminated were re-examined, and those with thresholds within the normal limits are shown in Figure 8.6A and B as a function of age. Nine of the 197 male subjects diagnosed with congenital color deficiency had large RG thresholds and are not shown in Figure 8.6. Out of the 153 subjects with known medical conditions, 67 had thresholds within the normal limits, and, most importantly, these thresholds were distributed equally above and below the median values. Half of the 18 subjects diagnosed with unusual fundus appearance and four out of the 27 subjects that failed the asymmetry test also had normal thresholds (see Figure 8.6A and B).

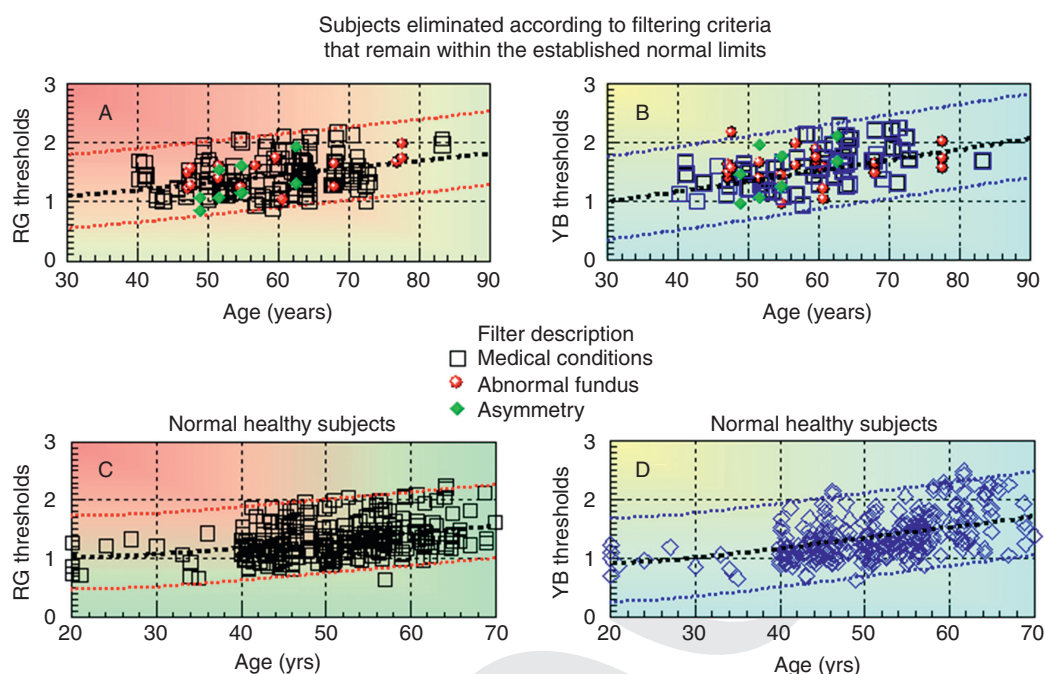
Based on this analysis all subjects with color thresholds within normal limits shown in Figure 8.6A and B were included in the final



**Figure 8.4** Comparison of thresholds before (*panels A and B*) and after filtering (*panels C and D*) the original monocular data measured at City University London and the Damme Optometrie Practice in the Netherlands (Kesteren). The age range of subjects was 4–90 years, and there were 215 females and 197 males. RG and YB CAD thresholds were measured separately for each eye. Exclusion criteria were applied to “filter” out subjects with congenital and acquired color-vision deficiencies. The filters were defined according to the following criteria: (1) congenital color-deficient subjects (which exhibit elevated RG and normal YB thresholds); (2) subjects with medical conditions (MC) such as diabetes, hypertension, and ocular abnormalities that may cause acquired loss of chromatic sensitivity; (3) subjects with abnormal fundus appearance or drusen; (4) subjects exhibiting a statistically significant difference in RG and/or YB chromatic sensitivity between the two eyes. The index employed to describe the asymmetry between the two eyes was the difference in monocular thresholds referenced to the best eye.



**Figure 8.5** Frequency histograms showing the distribution of RG (*panel A*) and YB (*panel B*) threshold differences between the two eyes (which formed the basis for the “asymmetry” test). The 97.5% limit was calculated with the best fit curve to each histogram (*dotted line*) – 27 subjects had thresholds above the  $2\sigma$  limit.



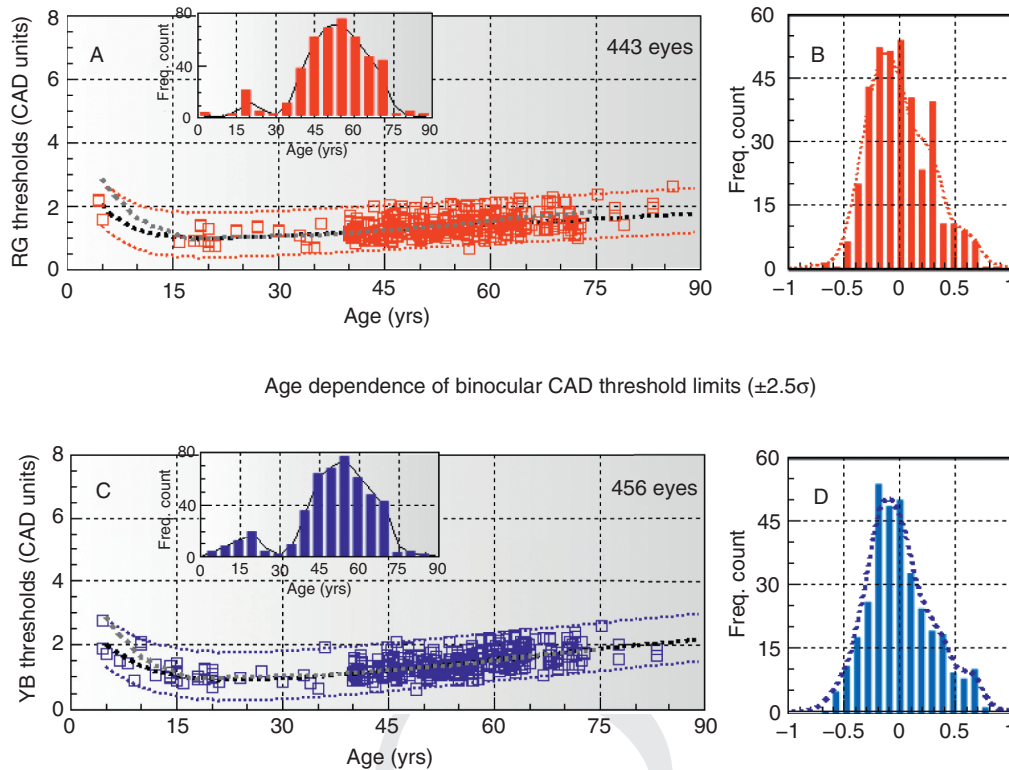
**Figure 8.6** The dotted lines in each section represent the statistical limits of normal variability as a function of age for the sample of normal subjects after applying each of the filters described above. The data points show the distribution of RG and YB thresholds for the subjects eliminated according to the filtering criteria, but with color thresholds within the established normal limits (*panels A and B*). Panels C and D plot the thresholds measured for the 179 subjects that passed all the filtering and were classed as normal. Nine of the 197 male subjects diagnosed with congenital color deficiency had large RG thresholds and are not shown in the graphs. Of the 153 subjects with known medical conditions, 67 had thresholds within the normal limits (and, most importantly, these thresholds were distributed equally above and below the median values). Half of the 18 subjects diagnosed with unusual fundus appearance and four of the 27 subjects that failed the asymmetry test also had normal thresholds (see *panels A and B*). Based on this analysis, subjects with color thresholds within normal limits were included in the final sample, even if they failed the specified, initial inclusion criteria.

sample, even if they failed the specified, initial inclusion criteria.

The revised data set based on 443 eyes for RG and 456 eyes for YB color vision was then used to calculate the mean thresholds and the corresponding  $\pm 2.5\sigma$  limits as a function of age. The results reveal the well-documented increase in thresholds below 10 years of age (Knoblauch *et al.*, 1995), the optimum age for best thresholds around 20 years, and the remarkably gradual and linear increase which almost doubles both the RG and the YB thresholds during the normal life

span. There are other interesting observations. The variability remains relatively unchanged within each decade. Although, on average, there is a 2.2-fold difference between the most and least sensitive normal subject, the filtered results show relatively uniform variability as a function of age (within the “normal” sample group).

A test for homoscedasticity (see caption to Figure 8.7) carried out for data points above 35 years of age reveals no significant difference in variability within this range.



**Figure 8.7** RG (panels A and B) and YB (panels C and D) binocular thresholds as a function of age for all the subjects examined in the study and deemed to have normal color vision. Conversion from monocular to binocular thresholds was carried out by using the mean monocular to binocular ratio measured in 57 subjects with normal color vision. Best eye monocular to binocular ratios were calculated with means ( $\mu$ ) and standard deviations ( $\sigma$ ) of 1.29 and 0.16 for RG and 1.3 and 0.18 for YB color vision, respectively. The ratios of right and left eye thresholds were 1.03 (RG) and 1.02 (YB), neither being significantly different from unity. The histograms (panels B and D) plot the differences between the measured RG and YB thresholds (in CAD units) and the corresponding mean values derived from the best-fit functions (black, dotted lines).

The filtered results show significant, but relatively uniform variability in color thresholds as a function of age within normal trichomats. Koenker's test for homoscedasticity (Koenker, 1981) carried out for data points within age range 35–75 years confirmed this observation ( $H_0$ -true,  $p = .224$ ,  $n = 270$ ).

The mean binocular thresholds as a function of age are given by:

$$RG_{\text{bin}} = 0.698 + 0.0121 * \text{age} + 3.373 * \exp(-0.19 * \text{age}) \text{ and}$$

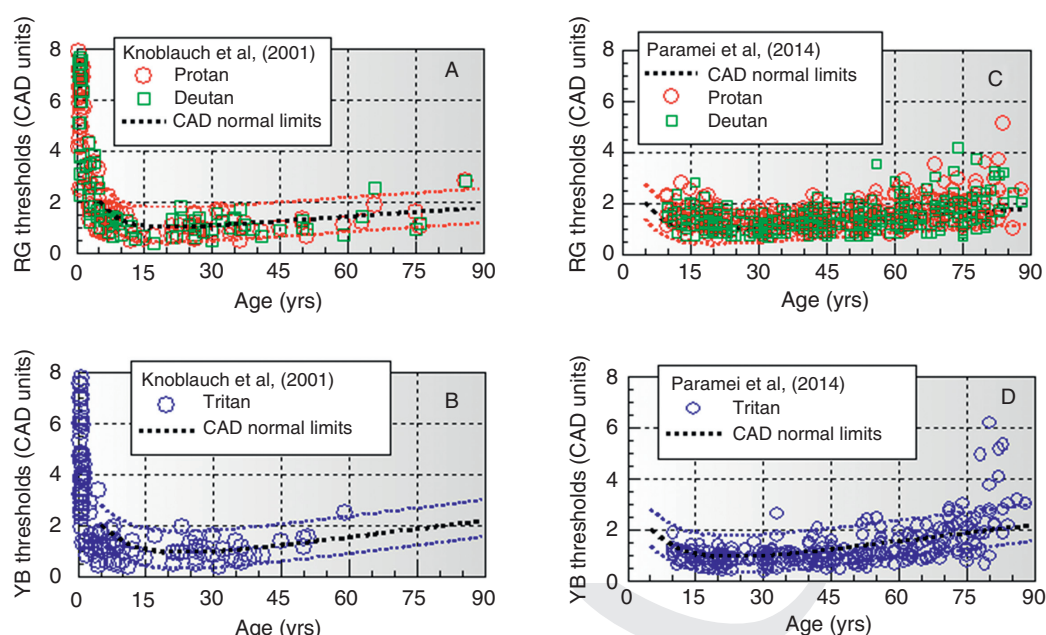
$$YB_{\text{bin}} = 0.24 + 0.0218 * \text{age} + 2.99 * \exp(-0.1136 * \text{age}).$$

The corresponding monocular thresholds are given by:

$$RG_{\text{mon}} = 0.901 + 0.0156 * \text{age} + 4.351 * \exp(-0.19 * \text{age}) \text{ and}$$

$$YB_{\text{mon}} = 0.306 + 0.0283 * \text{age} + 3.889 * \exp(-0.1136 * \text{age}).$$

The parameters above were fitted to the specified function using the JMP/SAS software nonlinear modeling algorithm (SAS Institute, Inc., V11). The black dashed lines in panels A and C describe how normal aging affects color vision, and the corresponding dotted lines above and below the mean represent the  $\pm 2.5\sigma$  limits. The age dependence of CAD thresholds is also in excellent agreement with the square root of the total error score ( $\sqrt{\text{TES}}$ ) as measured on the F–M 100-hue test (Kinnear and Sahraie, 2002). The gray dashed lines in panels A and B show Kinnear and Sahraie's  $\sqrt{\text{TES}}$  index normalized with respect to the best score.



**Figure 8.8** Color-detection thresholds measured by Knoblauch *et al.* (2001) and Paramei *et al.* (2014) converted to CAD units for comparison with the mean CAD thresholds and the corresponding  $\pm 2.5\sigma$  limits. The latter are taken from Figure 8.7 and shown as dashed lines in each figure.

## Comparison with other studies

The comparison is restricted to key studies that attempted to quantify color thresholds as a function of age in a way that can be traced back to the CIE (x,y) chromaticity chart.

One of the most extensive studies with emphasis on infant vision (Knoblauch *et al.*, 2001) measured thresholds along the deutan, protan, and tritan color confusion axes, using either the two-alternative or the forced-choice, preferential-looking techniques (Vital-Durand, 1996), depending on age. The “BabyCol” test used in this study also employed dynamic LC noise to isolate the use of color signals. Very young subjects show large thresholds with a rapid increase below 5 years. The thresholds measured along the deutan and protan directions were very similar and are shown together in Figure 8.8A. As age increases, all color directions show similar and gradual improvement until

adolescence, only to increase steadily afterwards over the remaining life span. The Knoblauch results shown in Figure 8.8A and B fit remarkably well within the new CAD limits reported here in spite of differences in visual stimuli and the use of the two-alternative and the preferential looking techniques. Unlike Knoblauch *et al.*’s study, which focused mostly on young subjects, the majority of subjects examined in this study were older subjects (above 40 years of age).

More recently, Paramei and Oakley also measured thresholds for displacement directions along the protan, deutan, and tritan lines, using the Cambridge Colour Test (CCT) (Paramei and Oakley, 2014). From a total of 423 subjects, 291 were selected for the study following a number of exclusion criteria which included self-reported congenital deficiency, known history of ocular/retinal disease, cataract, diabetes, and known neurological diseases. The measurements were



carried out binocularly with the CCT test, which employs static patterns of disks that vary randomly in size and luminance. The stimulus was a Landolt C defined by color with the gap position randomly placed at one of four locations on the ring: top, bottom, left, or right. Thresholds were measured in the CIE 1976 ( $u', v'$ ) space, unidirectionally along each of the three color confusion axes, using a four-alternative, forced-choice procedure. The data of Paramei and Oakley were converted to CAD units and are shown in Figure 8.8C and D. Given the large differences in stimulus conditions and measurement procedures, the results turned out to be very similar, with much of the data within the reported CAD limits. The results exhibited the features observed in previous studies with an initial improvement in thresholds with increasing age into adolescence, followed by a gradual increase over the remaining life span. One noticeable difference is the somewhat greater variability with increased scatter particularly for subjects above 60 years.

Combined normative data for RG and YB color vision have also been obtained in a number of different studies using the F–M 100-hue test (Kinnear and Sahraie, 2002; Knoblauch *et al.*, 1987; Verriest, 1963). Of particular interest is the study by Kinnear and Sahraie based on total error scores measured in 382 normal subjects. The age range covered was 5 to 79 years. The subjects selected for the study had normal color vision as assessed by the Ishihara test plates. Performance on this test is estimated by calculating the square root of the total “error score”,  $\sqrt{\text{TES}}$ , a parameter that follows approximately a normal distribution (Kinnear, 1970). The best performance on the F–M 100-hue test was for subjects ~20 years of age, in agreement with the CAD results and the remaining studies. In order to compare the reported F–M 100-hue test scores with mean CAD thresholds, the  $\sqrt{\text{TES}}$  index was normalized with respect to the average best scores measured for subjects between 18 and 22 years of age. The dashed, gray line in

Figure 8.7A and B plots the normalized  $\sqrt{\text{TES}}$  index for direct comparison with the mean CAD thresholds. Since the F–M 100-hue test measures the subject’s ability to discriminate small hue differences along a closed contour in the chromaticity chart (as a combined measure of the subject’s RG and YB sensitivity), we may be justified in expecting some correlation with the subject’s RG and YB thresholds.

The results are in remarkably good agreement, although some small differences remain, particularly for subjects below 10 years of age, who show a more rapid increase in the  $\sqrt{\text{TES}}$  index with decreasing age. Although CAD predictions for RG and YB thresholds extend down to 5 years of age, the predicted thresholds for young subjects may not be as reliable as for the older group, simply because of the small number of young subjects investigated. On the other hand, the mean CAD thresholds down to 5 years of age are in good agreement with the Knoblauch *et al.* (2001) findings, a study with many more subjects in this age group. Performance on the F–M 100-hue test may also be affected by other factors such as the subject’s non-verbal IQ (Hurlbert *et al.*, 2011). Further findings from Cranwell, Pearce, Loveridge, and Hurlbert (2013) (published abstract and paper presented at the 22nd Symposium of the International Colour Vision Society, Winchester, UK, 2013) suggest that in addition to chromatic discrimination sensitivity, performance on the F–M-100-hue test may also reflect intellectual and attentional ability (as captured by the subject’s non-verbal IQ); hence, measures of threshold discrimination that do not relate directly to IQ are likely to provide a more accurate estimate of chromatic sensitivity.

### Processes that may contribute to color vision changes in normal aging

Although there are significant differences among the studies reported here in terms of both the



stimulus parameters employed and the difficulties of the tasks designed to measure chromatic sensitivity, the results are in good agreement and confirm the rapid increase in sensitivity as one approaches adolescence and the gradual, linear trend that describes the loss of sensitivity over the remaining years. The improvement in visual sensitivity affects equally both RG and YB chromatic mechanisms, is rapid during the first year of life, and continues during the next few years into adolescence. The best chromatic detection sensitivity corresponds to ~20 years of age. This is somewhat late given the earlier maturation of the retina and that the neural connections between the visual cortex and related areas of the brain that are needed for optimum vision are usually established during the first 5 to 6 years of life (Graven, 2004; Tucker and Fitzpatrick, 2004)). The gradual improvement in sensitivity may well reflect small contributions that can be attributed to a number of factors including improvements in attentional ability and overall performance. The second phase must be linked to aging processes and is likely to involve physiological changes that also follow a gradual, linear trend. As discussed in the introduction, small changes in the optics of the eye that affect the quality of the retinal image, and even the absorption of short wavelength light by the lens and the macular pigment, seem to have little effect on chromatic sensitivity when the task is to measure color-detection thresholds with large stimuli against a background of high luminance. This is a great advantage since, unlike achromatic contrast sensitivity, which can be strongly affected by the optics of the eye, increased RG and YB color thresholds are more indicative of acquired retinal and/or systemic disease.

Color vision relies largely on normal cone signals and the integrity of the retina and visual pathways. Rod photoreceptor density in central vision declines by as much as 30% over a lifetime, but cone density is less affected (Curcio, Millican, Allen, and Kalina, 1993)), although phototransduction efficiency may not remain

constant over the life span. The number of RGC axons is known to decrease linearly by as much as 40% over the life span (Johnson, Miao, and Sadun, 1989; Jonas, Schmidt, Muller-Bergh, Schlotzer-Schrehardt, and Naumann, 1992; Neufeld and Gachie, 2003). Although more difficult to count in older eyes, RGC cell body loss also increases gradually in normal aging, although this obvious expectation remains somewhat equivocal (Calkins, 2013). The loss of RGC axons has been estimated in several studies to approach 0.5% per year (Jonas *et al.*, 1990), although lower rates have also been reported (Balazsi *et al.*, 1984; Repka and Quigley, 1989). Loss of myelinated axons and alterations or breakdown in the spatial distribution of myelin in nerve fibers in the deeper layers of the visual cortex have been linked to impairment in cognition, which, in turn, affects visual processing (Peters, Moss, and Sethares, 2000, 2001). Structural changes in the cortex caused by aging tend to affect other myelinated structures of the brain such as the axons of fibers in the fornix (Peters *et al.*, 2010) and are indicative of increased susceptibility to diminished metabolic resources with aging (Calkins, 2013).

In relation to color vision, it is of interest to compare the rate of loss of myelinated nerve fiber axons per year with the observed mean increase in RG and YB thresholds, which appears to be constant above ~20 years of age (Figure 8.7). These rates can be estimated by examining the mean thresholds in Figure 8.7 as ~1% for RG and ~1.6% for YB per year. Although, in principle, a large fraction of the measured loss of chromatic sensitivity can be attributed to the corresponding decrease in axon numbers, the results imply that other factors must also be involved. Interestingly, the more rapid loss of YB chromatic sensitivity suggests that some of these factors are specific to the YB system. The most obvious is the greater reduction in the contribution short-wavelength light makes to retinal illuminance with increasing age and hence the more rapid increase in YB

thresholds above 40 years of age. If the loss of RGC axons during the life span accounts for much of the increase in RG and YB thresholds observed in normal aging, accelerated loss of RGC axons and cell bodies as documented in glaucoma (Marvasti, Tatham, Zangwill, Girkin, Liebmann, Weinreb, and Medeiros, 2013]) may be directly linked to the corresponding increase in color thresholds that has also been shown to depend on retinal topography (Rauscher *et al.*, 2013). Further work is needed to establish whether the severity of localized RG and YB color loss in glaucoma can be used to estimate directly the percentage of ganglion cells lost or the rate of progression in glaucoma.

## Conclusions

Both RG and YB color thresholds decrease rapidly with increasing age during the first year of life with a more gradual decrease that continues into adolescence. The smallest thresholds correspond to ~20 years of age and define the SN CAD units. Above this age, thresholds increase linearly at a rate of ~1% per year for RG and ~1.6% for YB over the remaining life span. The loss of myelinated RGC axons and cell bodies with increasing age follows a similar trend and may account, at least in part, for the observed loss of chromatic sensitivity. The establishment of reliable upper threshold limits for RG and YB color vision may have important clinical applications by enabling the detection of the earliest signs of acquired loss of chromatic sensitivity and hence the presence of anatomical and physiological changes other than those attributable to normal aging. These limits also enable the development of optimized, rapid screening procedures for normal color vision.

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