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Color space distortions in patients with type 2 diabetes mellitus

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Abstract

Color vision impairment was examined in patients with type 2 diabetes mellitus (DM2) without retinopathy. We assessed the type and degree of distortions of individual color spaces. DM2 patients ($n = 32$), and age-matched controls ($n = 20$) were tested using the Farnsworth D-15 and the Lanthony D-15d tests. In addition, subsets of caps from both tests were employed in a triadic procedure (Bimler & Kirkland, 2004). Matrices of inter-cap subjective dissimilarities were estimated from each subject's "odd-one-out" choices, and processed using non-metric multidimensional scaling. Two-dimensional color spaces, individual and group (DM2 patients; controls), were reconstructed, with the axes interpreted as the R/G and B/Y perceptual opponent systems. Compared to controls, patient results were not significant for the D-15 and D-15d. In contrast, in the triadic procedure the residual distances were significantly different compared to controls: right eye, $P = 0.021$, and left eye, $P = 0.022$. Color space configurations for the DM2 patients were compressed along the B/Y and R/G dimensions. The present findings agree with earlier studies demonstrating diffuse losses in early stages of DM2. The proposed method of testing uses color spaces to represent discrimination and provides more differentiated quantitative diagnosis, which may be interpreted as the perceptual color system affected. In addition, it enables the detection of very mild color vision impairment that is not captured by the D-15d test. Along with fundoscopy, individual color spaces may serve for monitoring early functional changes and thereby to support a treatment strategy.

Keywords: Color vision deficiency, Diabetes mellitus type 2, Lanthony D-15d, Multidimensional scaling, Color space

Introduction

Diabetes mellitus is accompanied by retinopathy, which may result in visual dysfunction, including color vision losses (Ismail & Whitaker, 1998). In patients with type 2 diabetes mellitus (DM2) who developed diabetic retinopathy (DR), losses in the B/Y confusion axis (tritan) have been reported and shown to increase with severity of DR (Barton et al., 2004; Fong et al., 1999; Ismail & Whitaker, 1998; Bresnick et al., 1985). Color vision impairment may precede DR and emerge at early stages of DM2, before the appearance of vascular alterations in the retina. At this stage, predominantly tritan losses were found (Ismail & Whitaker, 1998), but other authors reported diffuse losses as well (Trick et al., 1988; Ventura et al., 2003).

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In most of these studies color vision was examined with arrangement tests, such as the Farnsworth-Munsell 100-hue test (FM-100), or with the anomaloscope, to estimate Rayleigh (red-green) and Moreland (blue-green) matches (e.g., Kurtenbach et al., 2002). The outcome of the arrangement tests enables one, in the first place, to assess color vision loss (i.e. whether blue-yellow (B/Y) and/or red-green (R/G) discrimination is impaired). The FM-100 also provides an error score, which measures the overall loss of color discrimination. The anomaloscope matches give separate results for the two perceptual systems (B/Y and R/G), but the extrapolation from matching range to color impairment is far from direct.

In this study we investigated color vision in patients with DM2 without DR, in an attempt to assess impairment of color discrimination quantitatively, in terms of distortions of a color space. This study belongs to a tradition of color research, in which subjects assess the dissimilarities they perceive among color stimuli, as a way of probing the forms of variation among those subjects (Helm, 1964; Paramei et al., 1991; Shepard & Cooper, 1992).

A color space is a geometric representation of relations among colors, where the distance between a pair of colors reflects their perceptual difference (Helm & Tucker, 1962). As was first pointed out by Farnsworth (1943), color abnormalities can be represented as distortions of a normal color space. One parameter is interpreted as the axis along which the color space is compressed (the axis of color confusion). Another parameter is the extent of compression, which distinguishes normal trichromats from color-vision deficient; and among those, anomalous trichromats from dichromats. The arrangement tests, including the widely used FM-100, D-15 (Farnsworth, 1943) and D-15d (Lanthony, 1978) tests, are based on this concept. The two parameters can be assessed qualitatively by visual inspection of individual data plotted on a suitable diagram, and quantitatively by a vector-moment analysis (Vingrys & King-Smith, 1988).

Color spaces for individual observers can be reconstructed from estimates of color dissimilarity among the test caps, by applying multidimensional scaling (MDS) (Kruskal & Wish, 1978). Group (consensus) color spaces can also be computed. In a subsequent step, color vision impairment can be considered as a distortion of the color space obtained from controls. The distortion is characterized by both the axes (interpreted as R/G and B/Y) and the degree of compression of each axis. This paradigm has been used to model color discrimination for various types of congenital color vision deficiencies (Helm, 1964; Paramei et al., 1991; Shepard & Cooper, 1992; Bimler et al., 2000). Helm (1964) used a triadic procedure to elicit dissimilarities among a D-15-like array of 10 Munsell chips, and distinguished color-deficient from normal observers by analyzing the data with MDS.

The present study is an attempt to represent acquired color vision impairment in DM2 patients in terms of distortions of a color space. Estimates of color dissimilarity were obtained among D-15 and D-15d test caps, using a triadic procedure, from DM2 patients and control subjects. Previous applications of this non-traditional procedure have found it to be sensitive to quite subtle differences in color space (e.g. comparing smokers and non-smokers; Bimler & Kirkland, 2004). Thus the approach was expected to be capable of detection of subtle disease manifestations.

Materials and methods

Subjects

Thirty-two DM2 patients (18 males), aged from 30 to 76 years (mean = 50.5, SD = 10.7), with disease duration from 0.5 to 27 years (mean = 9, SD = 8.6), were examined. The absence of retinopathy was verified in fundoscopy (in 100% of the eyes) and by fundus photography and fluorescein angiography (62% of the eyes were examined; 100% of these lacked any sign of retinopathy). Twenty age-matched observers (15 males), aged from 35 to 80 years (mean = 51.17, SD = 11.5), served as controls.

Inclusion criteria for both groups were: best corrected Snellen visual acuity (VA) 20/30 or better; absence of retinopathy and known ophthalmologic pathologies; absence of posterior subcapsular cataract, and maximum of grade 1 for cortical opacity (C1), nuclear color (NC1), and nuclear opalescence (NO1) following chart for lens opacity classification system III (LOCS III).

Stimuli

For initial diagnosis, the D-15 and D-15d tests were used, each consisting of 16 color caps forming a color circle. In Munsell denotation, the D-15 caps have Value = 5 and Chroma = 4 (Farnsworth, 1943); the D-15d caps have the same hue but are lighter, with Value = 8, and less saturated, Chroma = 2 (Lanthony, 1978). The D-15 test was used for screening congenital color vision deficiencies, whereas the more sensitive D-15d test was employed to examine acquired color vision loss caused by diabetes.

For the experimental triadic procedure, a composite assortment of 15 caps was created by excluding the reference caps from the D-15 and the D-15d, and replacing the D-15 caps No. 3, 6, 9, 12, and 15 with their counterparts from the D-15d.

Procedure

D-15 and D-15d tests

The D-15 and D-15d tests were both used in the traditional way: starting with the reference cap, the subject arranged the stimuli in a color sequence, where each cap was followed by the cap most similar to it. This procedure was performed at the beginning of the session.

Triadic procedure

Next, the 15-cap composite assortment was shuffled into five randomized groups of three. The subject viewed each of these triads separately and chose the most dissimilar cap of each triad ('the odd-one-out'). No time limit was set. This procedure was repeated 14 times, eliciting 70 triad judgments (Bimler & Kirkland, 2004).

Illumination of 500 lux was provided by two fluorescent lamps (Sylvania Octron FO32W, with Coordinated Color Temperature = 6500 K, Color Rendering Index = 75).

Both procedures were administered monocularly, in a randomly chosen order, in the two eyes for DM2 patients and in one eye for controls.

Analysis

D-15 and D-15d tests

Outcomes of the D-15 and D-15d tests were individual diagrams and a *Total Color Distance Score* (TCDS) (D-15: Bowman, 1982; D-15d: Geller, 2001). Higher TCDS score values indicate deviation from the errorless cap arrangement.

Triadic procedure

The following algorithm was used to estimate the dissimilarity $D(i,j)$ between the i-th and j-th caps. The caps are represented as points $\mathbf{v}(i)$, where all pairs of points are initially equally distant. This involves a 15-dimensional space, where each $\mathbf{v}(i)$ has coordinates $v(i,j)$ initialized as 0 ($1 \le i,j \le 15$) except $v(i,i) = 1$. Then, each of the 70 triad judgments obtained from a subject was treated as a set of dissimilarity comparisons. If the caps $\{k,l,m\}$ comprise a triad, with k and l as the similar pair and m as the odd-one-out, then points $\mathbf{v}(k)$ and $\mathbf{v}(l)$ are moved closer together $[v'(k,k) = \cos(\alpha)v(k,k) - \sin(\alpha)v(k,l), v'(k,l) = \cos(\alpha)v(k,l) + \sin(\alpha)v(k,k), v'(l,k) = \cos(\alpha)v(l,k) + \sin(\alpha)v(l,l), v'(l,l) = \cos(\alpha)v(l,l) - \sin(\alpha)v(l,k)$, $\alpha = \pi/32 \cong 6°]$, while $\mathbf{v}(m)$ is moved further away from them $[v'(m,k) = \cos(\alpha)v(m,k) - \sin(\alpha)v(m,m), v'(m,l) = \cos(\alpha)v(m,l) - \sin(\alpha)v(m,m), v'(m,m) = (1 - v'(m,k)^2 - v'(m,l)^2)^{1/2}]$, providing new $\mathbf{v}'(k)$, $\mathbf{v}'(l)$, $\mathbf{v}'(m)$. After these 210 point rotations in 15-dimensional space, $D(i,j) = \|\mathbf{v}(i) - \mathbf{v}(j)\|$.

We apply non-metric MDS (Statistica, StatSoft, Inc.) for the dimensional reduction of $D(i,j)$ to $D'(i,j)$, where $D'(i,j)$ is the matrix of color dissimilarity in two dimensions. The outcome is a 2D MDS solution where each cap is represented by a point with coordinates (x_i, y_i) so that the spatial distances $D'(i,j)$ between the i-th and j-th points reflect $D(i,j)$ as closely as possible (Kruskal & Wish, 1978). The discrepancy between estimates and distances was quantified by a badness-of-fit function (*Stress*) and minimized by the method of steepest descent.

Individual color spaces for each eye were computed; in addition, group color spaces for the DM2 patients and controls were calculated as a consensus across eyes and subjects within each group.

The axes of these 2D solutions are interpreted as the R/G and B/Y perceptual opponent color systems. The data are too sparse to sustain 3D individual analyses, although this would provide a better approximation, since the stimuli varied in lightness (Value) and saturation (Chroma).

Although the relative distances D' between the coordinates (x_i, y_i) of the 15 caps are determined in the 2D color space, the axes of the MDS output are defined arbitrarily, without any absolute alignment (Kruskal & Wish, 1978). It is necessary to rotate and mirror the coordinates to a standard orientation. We choose that the cap 5Y should be at the top. If necessary, the solution is mirrored horizontally to ensure that the cap 2.5R is at the left and 10G at the right ($x_{10G} > x_{2.5R}$). Results are summarized in Fig. 1a for control group, and (c) and (d) for respectively right eye and left eye of DM2 patients' group.

The initial use of these group color spaces is a direct comparison between them. For more quantitative purposes, the 2D color space for control group is used as a standard for assessing the accuracy of individual color spaces in terms of the sum of residuals: comparing cap locations in the individual or group solutions against locations in the standard control group. It provides an index of impairment to the patient's color vision, and can be interpreted as B/Y and R/G dimensions. The question is whether the DM2 patients' color spaces are less accurate (as a population) than controls, and if so, whether their increased inaccuracy follows any particular form.

Results and discussion

For the traditional procedure of the D-15d, TCDS was calculated within each group of observers: controls: 60.25 ± 5.84; DM2 patients: 66.04 ± 13.61, right eye, and 67.29 ± 17.32, left eye. The difference between these results does not reach significance: right eye: $P = 0.08$; left eye: $P = 0.12$ (Mann-Whitney U Test).

Fig. 1a shows the MDS solutions for the controls. For comparison, Fig. 1b shows the D-15d caps arrangement in the traditional procedure, when these are arranged errorless. The DM2 patients' group solutions are shown in Fig. 1c for right eye and in Fig. 1d for left eye. Features correctly reconstructed in Fig. 1a include the arc composed by the caps, and the gap between caps 5B and 5P. In contrast, the correct sequence is not reproduced so well by the DM2 patient solutions (Fig. 1c and 1d). DM2 patients' errors are slightly greater along the B/Y axis. Across color spaces for right eye (R) and left eye (L) for the DM2 group, the average sum of residuals along the B/Y dimension were R = 0.20 and L = 0.32. Corresponding average residuals along the R/G dimension were R = 0.15 and L = 0.21.

A quantitative comparison of individual color spaces against the standard control group using the t-test showed that the residuals are statistically significant from those of the controls: for DM2 right eye, $P = 0.021$, and for DM2 left eye, $P = 0.022$ (t-test). This comparison provides an overall index of color vision loss.

Fig. 2a shows an example of individual solutions for a control and Fig. 2b, Fig. 2c, and Fig. 2d show examples of solutions from DM2 patients. Note that all these subjects performed the D-15d test without error (TCDS = 56.41), but the DM2 patient's color space is apparently more irregular. This visual impression is confirmed statistically: the standard color space (Fig. 1a) accounts for 98% of fitting in Fig. 2a, and for 42.2% in Fig. 2b and 0% in Fig. 2c and 2d.

This greater irregularity in cap locations for the DM2 patients can be interpreted as compression of their color spaces (so that random noise becomes proportionally greater). Compression can occur along the B/Y and R/G axes independently. We quantify axial compression—providing additional indices of color vision impairment—by separating the summed residual distances (based in the comparison with the control group adopted as the standard) interpreted as B/Y and R/G axis.

Individual color spaces obtained with the triadic procedure were reproducible within the same subject. Repetitions of the procedure revealed that the choice of the odd-one-out cap changed in an average 7% from the first to the second test, which should result in very similar compression indices. On the other hand, when individual color spaces were considered, these indices of compression appeared to vary dramatically among the subjects. Even among subjects who performed the D-15d test error-free, MDS of triadic data revealed a range of axial compression. In the examples of Fig. 2, the summed residuals for (Fig. 2a) control were 0.16 (R/G) and 0.26 (B/Y), as compared to DM2 patients: (Fig. 2b) 0.22 (R/G) and 0.30 (B/Y); (Fig. 2c) 0.37 (R/G) and 0.56 (B/Y); (Fig. 2d) 0.34 (R/G) and 0.66 (B/Y). This emphasizes a further advantage of presenting color discrimination as a color space: it allows one to reveal very mild color vision losses in DM2 patients without DR, and, in addition, to quantify the individual type and degree of the impairment—unlike the traditional use of the D-15 and D-15d tests.

The results obtained here pose a question of a possible locus (loci) and mechanism(s) of the visual system underlying our psychophysical findings.

It has been demonstrated (Birch, 2001; Lutze & Bresnick, 1991) that in DM2 patients lens yellowing develops at an accelerated rate, similar to that in older healthy subjects. One could, thus, argue that the B/Y compression found in the DM2 patients, in addition to the R/G compression, is a manifestation of lens yellowing. However, mean age of the controls in our study was comparable to that of the DM2 patients; besides, the latter showed no clinical signs of cataract. We therefore propose that the color vision losses in the DM2 patients, which are revealed by compression of the B/Y (and the R/G) axes result from reduced photoreceptor sensitivity. Indeed, in diabetic patients elevated thresholds of the photoreceptors were attributed to a reduction of the oxygen supply and, hence, the concentration of circulating glucose (Kurtenbach et al., 2006).

An alternative explanation for the obtained difference between the group color spaces for the controls and DM2 patients cannot be excluded. The set of caps used in the triadic procedure means that, as well as varying along the chromatic R/G and B/Y axes, they also vary in lightness and saturation, alternating between Value = 5/Chroma = 4 and Value = 8/Chroma = 2. This implies that a 3D solution (with an additional achromatic dimension) may be re-

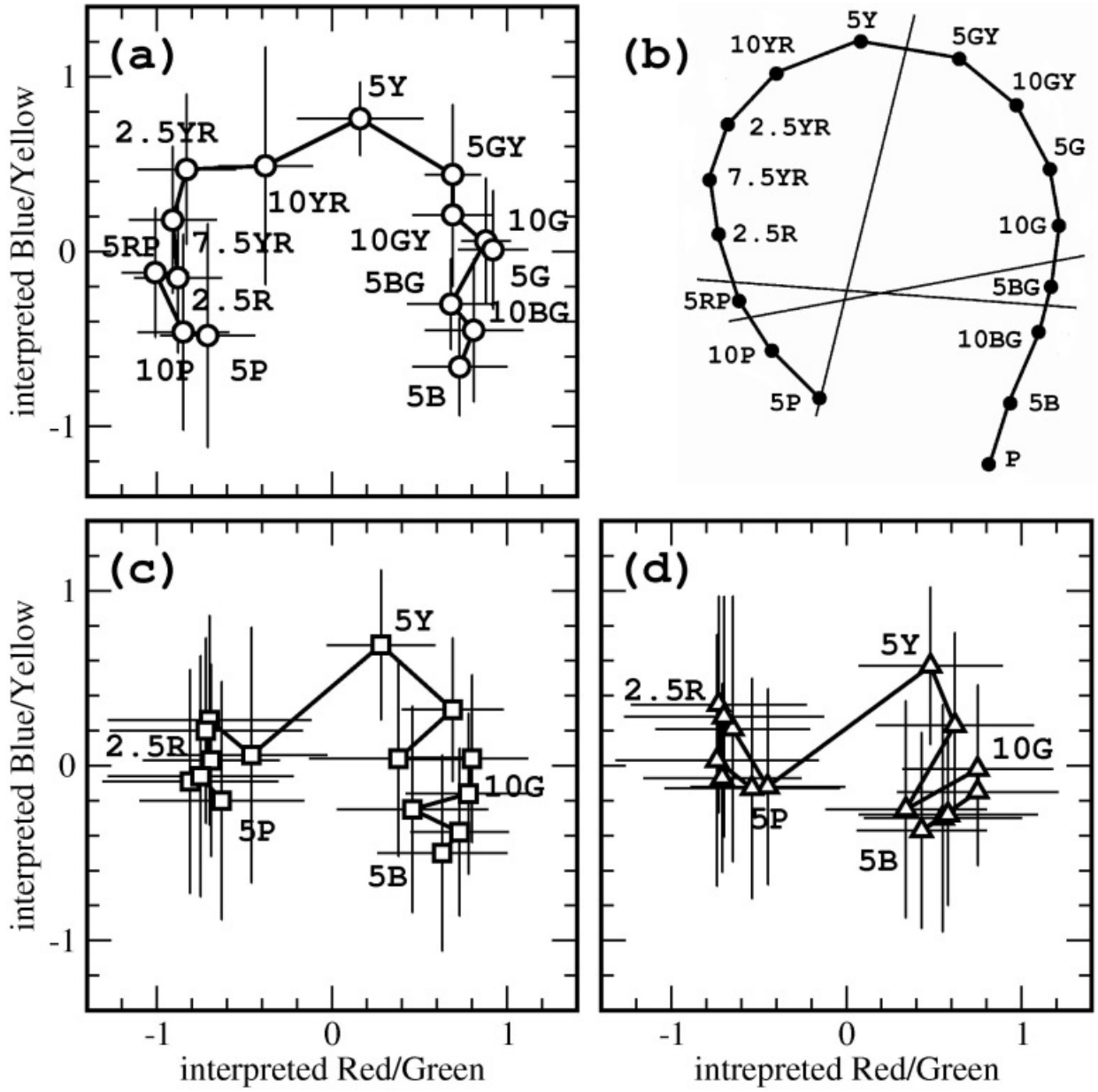

Fig. 1. (**a**) ○, Group color space for control group; (**b**) Diagram of D-15d test showing errorless cap arrangement (TCDS = 56.41); (**c**) □—Group color space for DM2 right eye; (**d**) △, Group color space for DM2 left eye. The *x*- and *y*-axes are in the same scale in (a), (c), and (d); they are interpreted as the B/Y and R/G perceptual opponent color systems. Error bars centered on each point *i* indicate the variance in x_i and y_i across individual solutions.

quired to fully account for the dissimilarity data. For controls, the lightness variation is empirically least salient—hence it is left out of the 2D solutions—whereas the R/G and B/Y variations are most significant (see Fig. 1a). It may be that the DM2 subjects tend to suffer a generalized loss of chromatic discrimination, which forces them instead to place more weight on the lightness/saturation variation when judging dissimilarity. Lightness would therefore replace the B/Y axis as the second dimension of their MDS solutions (with R/G remaining as the first dimension). In 2D solutions, the caps would zigzag up and down between the two values of Value/Chroma, departing from the expected angular sequence, as in Fig. 1c and 1d. To clear up whether this is indeed the case in DM2 patients, further study would be required using a set with no luminance differences or using a set with a substantially greater number of caps varying in Value and Chroma in order to reconstruct the 3D color space.

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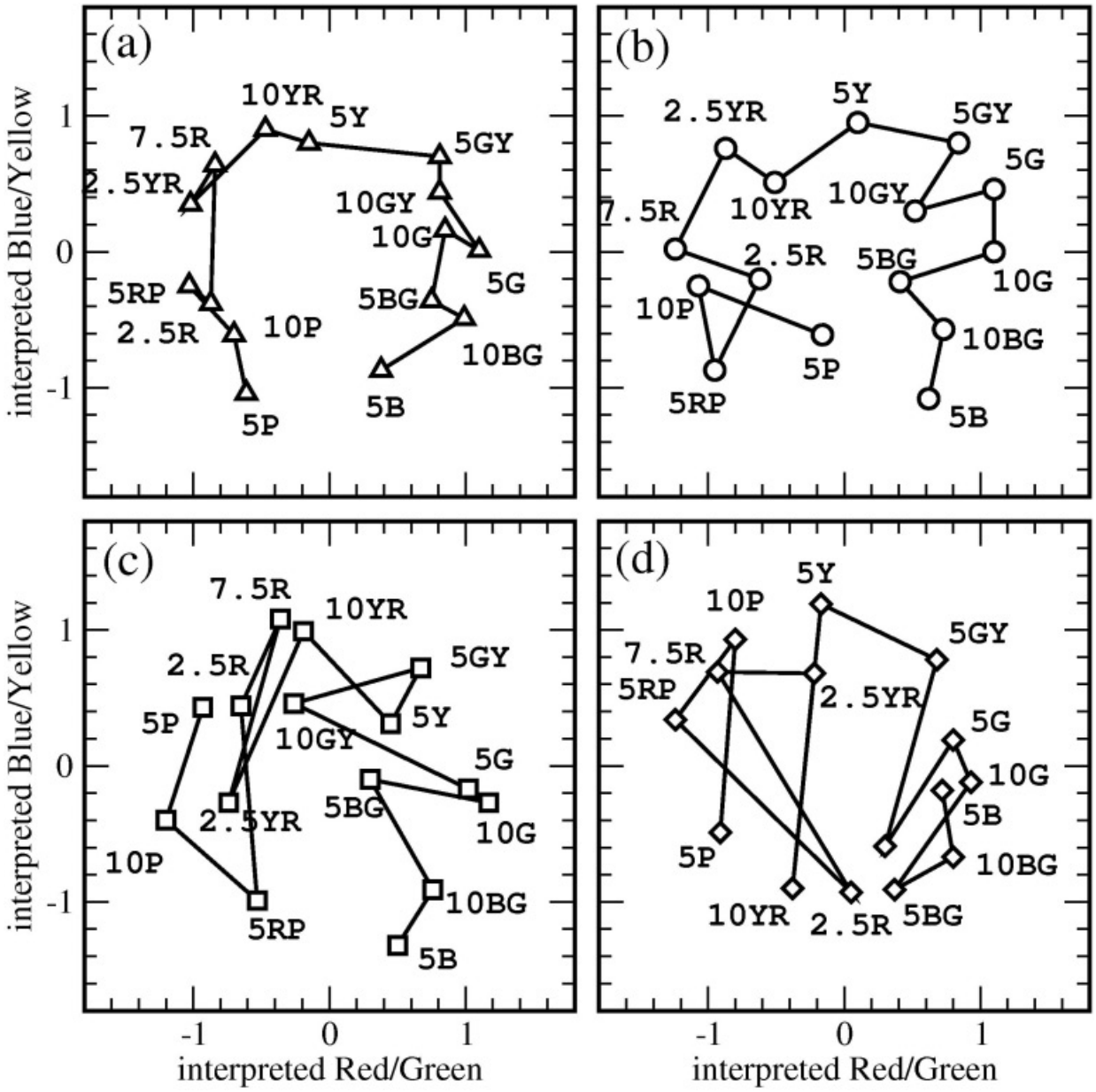

Fig. 2. Individual color spaces for a control (**a**) and DM2 patients (**b**), (**c**), and (**d**). Despite of the fact that the D-15d performance of all four observers was errorless, the color space of the DM2 patients indicate mild color discrimination impairment: (**a**) △—control subject: P(χ^2) = 98.2% and residuals = 0.16 (RG) and 0.26 (BY); (**b**) ○—DM2 patient: P(χ^2) = 42.2% and residuals = 0.22 (RG) and 0.30 (BY); (**c**) □—DM2 patient: P(χ^2) = 0.0% and residuals = 0.37 (RG) and 0.56 (BY); (d) ◇—DM2 patient: P(χ^2) = 0.0% and residuals = 0.34 (RG) e 0.66 (BY).

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