OPO OPHTHALMIC AND PHYSIOLOGICAL OPTICS
THE JOURNAL OF THE COLLEGE OF OPTOMETRISTS

Ophthal. Physiol. Opt. 2010 **30:** 717–723

Color vision impairment in type 2 diabetes assessed by the D-15d test and the Cambridge Colour Test

Claudia Feitosa-Santana[1,2,3], Galina V. Paramei[4], Mauro Nishi[5,6], Mirella Gualtieri[3], Marcelo F. Costa[3] and Dora F. Ventura[3]

[1]Department of Psychology, University of Chicago, Chicago, IL, USA, [2]Vision Science Laboratories & Institute of Mind and Biology, University of Chicago, Chicago, IL, USA, [3]Departamento de Psicologia Experimental, Instituto de Psicologia & Núcleo de Neurociências e Comportamento, Universidade de São Paulo, São Paulo, Brazil, [4]Department of Psychology, Liverpool Hope University, Liverpool, UK, [5]Hospital Universitário, Universidade de São Paulo, São Paulo, and [6]Deparment of Ophthalmology, Federal University of São Paulo, São Paulo, Brazil

Abstract

Color vision impairment emerges at early stages of diabetes mellitus type 2 (DM2) and may precede diabetic retinopathy or the appearance of vascular alterations in the retina. The aim of the present study was to compare the evaluation of the color vision with two different tests – the Lanthony desaturated D-15d test (a traditional color arrangement test), and the Cambridge Colour Test (CCT) (a computerized color discrimination test) – in patients diagnosed with DM2 without clinical signs of diabetic retinopathy (DR), and in sex- and age-matched control groups. Both color tests revealed statistically significant differences between the controls and the worst eyes of the DM2 patients. In addition, the degree of color vision impairment diagnosed by both tests correlated with the disease duration. The D-15d outcomes indicated solely tritan losses. In comparison, CCT outcomes revealed diffuse losses in color discrimination: 13.3% for best eyes and 29% for worst eyes. In addition, elevation of tritan thresholds in the DM2 patients, as detected by the Trivector subtest of the CCT, was found to correlate with the level of glycated hemoglobin. Outcomes of both tests confirm that subclinical losses of color vision are present in DM2 patients at an early stage of the disease, prior to signs of retinopathy. Considering the advantages of the CCT test compared to the D-15d test, further studies should attempt to verify and/or improve the efficiency of the CCT test.

Keywords: Cambridge Colour Test, color vision impairment, D-15d test, type 2 diabetes

Introduction

Color vision has been assessed in many studies of diabetes mellitus (DM) since the 1970s. Some studies focused predominantly on juvenile diabetes, or DM type 1 (e.g. Bronte-Stewart *et al*., 1970; Muntoni *et al*., 1982; Roy *et al*., 1984; Hardy *et al*., 1992). In several studies, color vision in both types of diabetes, type 1 (DM1) and type 2 (DM2), was examined (Bresnick *et al*., 1985; Trick *et al*., 1988; Greenstein *et al*., 1990; Doucet *et al*., 1991; Fong *et al*., 1999; Barton *et al*., 2004). In some studies the type of diabetes was not reported; however, from subject characteristics it can be inferred that patients with both types of diabetes were investigated (Lakowski *et al*., 1972; Aspinall *et al*., 1983; Tregear *et al*., 1997). Notably, very few studies have assessed color vision exclusively in DM2 (Ismail and Whitaker, 1998; Ventura *et al*., 2003b; Feitosa-Santana *et al*., 2006).

Assessment of color vision in DM of both types has demonstrated that color vision impairment emerges in the early stages of the disease and may precede diabetic

Received: 18 September 2009
Revised form: 29 January 2010
Accepted: 10 July 2010

Correspondence and reprint requests to: Claudia Feitosa-Santana.
Tel.: 1-773-702-9412; Fax: 1-773-702-0939.
E-mail address: claudia@feitosa-santana.com

 doi: 10.1111/j.1475-1313.2010.00776.x

retinopathy (DR), i.e., vascular alterations in the retina (Kurtenbach *et al*., 1994, 1999; Ismail and Whitaker, 1998; Ventura *et al*., 2003b; Feitosa-Santana *et al*., 2006). Further, when DR was present, color vision defects were shown to correlate with the duration of the disease and the severity of macular edema (Bresnick *et al*., 1985; Ismail and Whitaker, 1998).

In patients with DM2 in particular, early losses in blue-yellow (tritan) discrimination were predominantly found when the Farnsworth-Munsell 100-Hue Test was employed (Ismail and Whitaker, 1998). More recently, however, Ventura and colleagues (Ventura *et al*., 2003b; Feitosa-Santana *et al*., 2006) reported diffuse loss in DM2 patients, i.e., red–green in addition to blue–yellow losses. It is notable that the diffuse losses were detected using different diagnostic instruments and psychophysical methods: Ventura *et al*. (2003b) employed the Cambridge Colour Test (CCT) and examined a small sample (n = 13) of DM2 patients; Feitosa-Santana *et al*. (2006) studied a representative DM2 group (n = 32) using a composite assortment of 15 caps from the D-15 and D-15d and applied a triadic procedure for judgment of color dissimilarities.

In the present study, color vision of DM2 patients was assessed using the D-15d test and the CCT, and was compared to controls. The D-15d, a traditional color arrangement test, has been extensively used for the diagnosis of subclinical forms of acquired color vision deficiencies (e.g., Geller, 2001; Feitosa-Santana *et al*., 2006; Barboni *et al*., 2009). The CCT, a recently developed computerized color discrimination test (Mollon and Reffin, 1989, 2000) has been proven to be sensitive for detection and classification of color vision deficiencies (Regan *et al*., 1994, 1998; Ventura *et al*., 2003a,b; Costa *et al*., 2007; Feitosa-Santana *et al*., 2008; Moura *et al*., 2008).

In the present study, we address whether, for DM2 patients, the outcomes of the D-15d and CCT would converge in the diagnosis of early subclinical forms of color vision impairment.

Method

Subjects

Color vision was assessed in 31 patients with DM2 (16 males), of 30 to 76 years of age (mean = 52.8 ± 10.7 years), with no clinical signs of DR. Diabetes duration ranged from 1 to 27 years (mean = 9.0 ± 8.6 years) estimated from the date of the diagnosis. The patients were referred to the present study by the Ophthalmology Unit of the University Hospital of the University of Sao Paulo (Sao Paulo, Brazil).

Two control groups were formed. One was tested using the D-15d test (n = 31, 17 males; mean age 50.5 ± 11.5 years). The other was tested using the CCT (n = 36, 22 males; mean age 51.4 ± 12.5 years). Controls were selected from staff and students of the University of Sao Paulo or patients' spouses. Both control groups were matched to the DM2 patients by sex, age and education level.

Clinical history of both DM2 patients and controls was collected before the testing, to ensure no history of heavy metal exposure, alcoholism, or smoking, and absence of systemic diseases that could have affected the visual system.

For the screening of congenital color vision deficiencies, the D-15 test (Farnsworth, 1943) was applied, with quantitative and qualitative analyses of the color cap arrangement used to verify the color vision status. Subjects diagnosed with congenital color vision deficiency were not included.

All DM2 patients and controls underwent an ophthalmological examination, with the following inclusion criteria: best visual acuity of 0.2 log MAR; no ocular disease or surgery; a maximum of grade 1 of cortical opacity (C1), nuclear color (NC1), and nuclear opalescence (NO1) according to the Lens Opacity Classification System III, LOCS III (Chylack *et al*., 1993); no clinical signs of DR on fundus examination by indirect ophthalmoscopy, i.e., no hard exudates, microaneurysm, hemorrhage, or increased retinal thickness; no macular edema according to the ETDRS criteria (Fong *et al*., 1999; Barton *et al*., 2004). Fundus photography and fluorescein angiography were conducted in 62% of the patients (19/31). The interval between the ophthalmological examination and the color vision testing did not exceed 1 month.

Informed consent was obtained from all patients and controls, before the tests were performed. Testing procedures complied with the tenets of the Declaration of Helsinki and were approved by the Ethics Committees of the University of Sao Paulo.

Color vision tests, testing protocols, and raw data analysis

The D-15d is an arrangement color vision test (Luneau, Prunay-le-Gillon, France), consisting of 16 desaturated color caps (1.2 cm in diameter), each contained in a circular black plastic support. Their chromatic characteristics are defined by the Munsell System: varying only in hue, the color caps have the same lightness (Value = 5) and saturation (Chroma = 4).

For testing, the caps were placed on a desktop covered with a black cloth, under an illuminant source of 500 lux provided by two fluorescent lamps (Sylvania Octron 6500 K FO32W/65K Day-Light; Munich, Germany) in an otherwise dark room (cf. Lanthony, 1978).

Since many subjects, especially elderly individuals, had difficulty arranging these desaturated caps, the

D-15d test was repeated up to three times, and the best result was considered: this aimed to avoid false positives and separate the color vision outcome from a practice effect (Lanthony, 1995).

Errors in the D-15d tests were quantified in terms of the Total Color Distance Score, TCDS (Lanthony, 1986; Vingrys and King-Smith, 1988). The minimum TCDS value is equal to 56.4 and occurs when all the caps are in consecutive order (Geller, 2001). Values higher than this imply decrease in color discrimination.

The CCT was performed using the CCT version 2.0 software (Cambridge Research Systems Ltd., Rochester, Kent, UK). It was run on a microcomputer XTC-600 (Dell Dimension, Winston-Salem, NC, USA), equipped with a VSG5 graphics card (Cambridge Research Systems). A Trinitron color monitor GDMF500T9 (Sony Electronics Inc., Tokyo, Japan) had 100 Hz temporal resolution and 800×600 spatial resolution. Monitor luminance and chromatic calibrations were performed with a CS1000 photometer (Konica Minolta Sensing Inc., Osaka, Japan).

The CCT was performed in a dark room with illumination provided only by the monitor used to present visual stimuli. The visual stimuli consisted of a Landolt 'C' target, composed of small circles of a given chromaticity with variable size (0.5–2 cm in diameter, or 0.05–0.38° of visual angle) and variable luminance (six equal steps between 8 and 18 cd.m^{-2}), presented on a background of similar circles that differed in chromaticity. The design of the CCT stimuli is analogous to that of the Ishihara Pseudo-isochromatic Plates (for details, see Mollon and Reffin, 1989, 2000).

The subject was positioned 2.6 m away from the monitor, providing 1 deg visual angle for the gap in the Landolt 'C'. The gap appeared randomly in one of four orientations (up, down, left, or right), and the subject's task was to indicate its position by pressing a corresponding button on a response box.

The testing procedure started with a presentation of the Landolt 'C' target at a saturated chromaticity on a certain background and proceeded to a chromaticity closer to that of the background each time a subject responded correctly. Conversely, an incorrect response or no response was followed by the presentation of the target at a greater chromatic distance from the background, along the same vector. The response time limit was 6 s for each trial. After eleven reversals, the staircase was terminated, and a color discrimination threshold was computed as the mean of the last seven reversals.

The CCT offers two testing conditions: the Trivector and the Ellipses subtests. The Trivector measures color discrimination thresholds relative to the default background chromaticity (CIE 1976: $u' = 0.1977$, $v' = 0.4698$) as excursions in $u'v'$ units along the protan, deutan, and tritan confusion axes. The Ellipses subtest measures color discrimination thresholds along a number of color space vectors (between 8 and 20) for three ellipses, whose centers vary to allow capturing discrimination in the protan, deutan, and tritan chromatic systems. In the present study, the Ellipse 1 parameters were determined with the background CIE center coordinates as in the Trivector subtest, and using the eight vector protocol. The software compiled the responses, plotted the mean threshold for each vector, and fitted an ellipse through the thresholds centered on the given chromaticity. For further statistical analysis, two parameters were used: the ellipse area and the ratio of the major to minor ellipse axes (Mollon and Reffin, 1989, 2000; Regan *et al.*, 1994, 1998; Ventura *et al.*, 2003a).

In the DM2 patients, both eyes were tested monocularly. Scores obtained from the D-15d test, the Trivector and Ellipse 1 subtests of the CCT were used to determine the patients' best and worst eyes. In the controls, only one eye per subject was randomly tested.

Statistical analysis

The Statistica version 6.0 (StatSoft, Tulsa, OK, USA) was used for the analysis; the level of significance was set at $p < 0.05$. Since the data were not normally distributed, non-parametric tests were used: Mann–Whitney U test and Wilcoxon matched-pair test. For the DM2 patients' data, in addition, Spearman correlation was conducted to assess the relationship between the outcomes of the color vision tests and physiological indicators: diabetes duration, levels of glycated hemoglobin (HbA1c), fasting blood glucose, microalbuminuria, and total cholesterol.

Results

D-15d test

For the DM2 patients, the TCDS for the worst eyes was found to be significantly higher than that for the best eyes (Wilcoxon matched-pair test, $p < 0.001$). Also, the patients' worst-eye scores were significantly higher than those of the controls (Mann–Whitney U test, $p < 0.01$), but the patients' best-eye scores were not significantly different ($p > 0.05$) from those of the controls.

For further TCDS analysis, data of DM2 patients whose scores exceeded the normal range were considered. The latter was determined as the 95% boundary for the controls' scores, resulting in the TCDS = 67.32. This led to inclusion of data for 4/30 (13.3%) best eyes and 9/31 (29%) worst eyes. Importantly, the D-15d outcomes for all DM2 patients revealed tritan losses, except for one patient with diffuse losses in both eyes.

CCT

For the DM2 patients, the Trivector subtest revealed that there were significant differences in discrimination thresholds between the worst eyes and the best eyes along the protan ($p < 0.05$) and tritan ($p < 0.001$) axes. Compared to the controls, the worst-eye thresholds were elevated, but only the tritan thresholds were significantly different ($p = 0.007$). None of the best-eye thresholds were significantly different ($p > 0.05$) from those of the controls (*Figure 1*).

The Ellipse 1 subtest revealed significant differences between the two eyes of the DM2 patients with respect to the ellipse area ($p < 0.001$), its major axis ($p < 0.001$), and the major-to-minor axis ratio ($p < 0.01$). Compared to the controls, the DM2 patients' ellipses differed significantly for the worst eyes (but not for the best eyes): the ellipse area ($p < 0.001$), major axis ($p < 0.001$), minor axis ($p < 0.05$), and axis ratio ($p < 0.001$).

The normal ranges of the CCT thresholds (in *u'v'* units) were determined as the 95% boundary for the controls. In the Trivector subtest, the normal upper limits corresponded to the vector lengths of 108, 95, and 167 (in *u'v'* units) for protan, deutan, and tritan thresholds, respectively. For the Ellipse 1 subtest, the normal range for the ellipse area was 0.0018 and for the major axis was 0.0394. Data of the DM2 patients, exceeding these normal ranges, were considered as evidence of color vision impairment: 20% of the best eyes (6/30 eyes: 2/30 tritan and 4/30 diffuse) and 35.5% of the worst eyes (11/31 eyes: 2/31 tritan and 9/31 diffuse).

Despite the fact that congenital color vision deficiencies were screened only with the D-15 test which is not able to detect mild congenital deficiencies, the pattern of color vision impairment detected in the present study had no similarity with the pattern typical of color discrimination impairment associated with congenital protan or deutan abnormalities (cf. Regan *et al.*, 1994).

Comparing the results of the D-15d test and the CCT

The diagnostic outcomes of the two tests converged for four DM2 patients:

- One patient who had diffuse losses in both eyes in the D-15d also displayed the same losses in the CCT;
- Three eyes (from different patients) were classified by both tests as indicating tritan losses.

In several cases, the CCT appeared to better classify the type of impairment:

- Five eyes (from different patients), classified as tritan in the D-15d, showed diffuse losses in the CCT;
- Two eyes (from different patients), classified as normal in the D-15d, manifested tritan losses in the CCT;
- Five eyes (from three patients), classified as normal in the D-15d, revealed diffuse losses in the CCT.

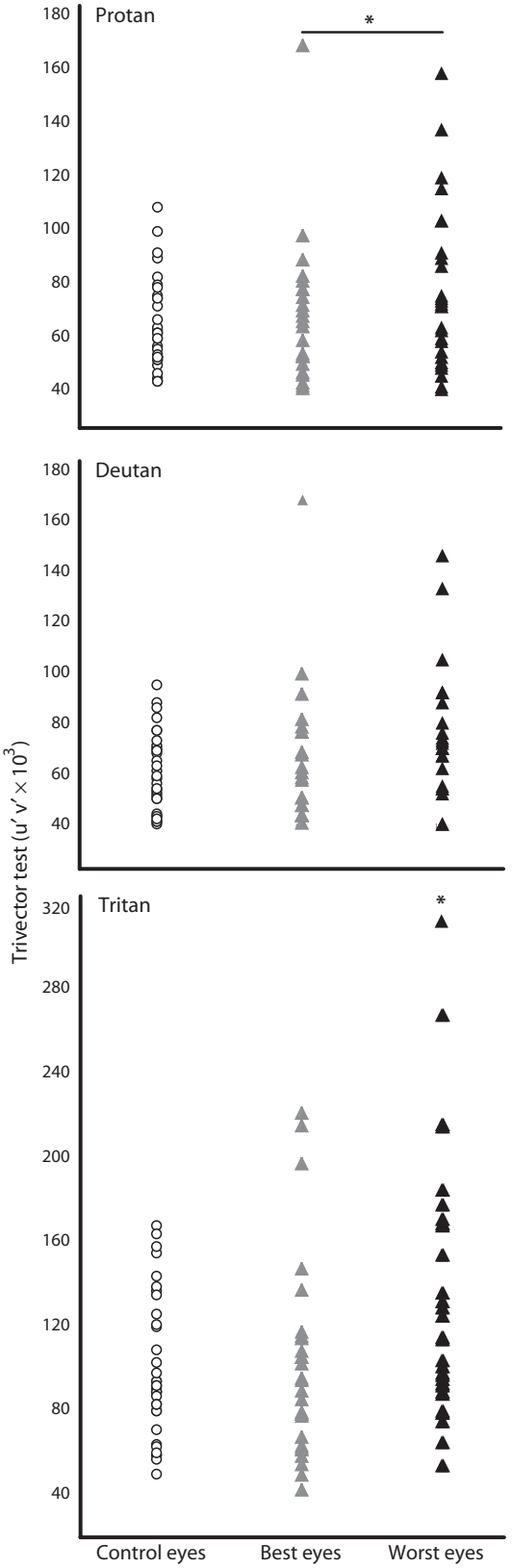

Figure 1. Chromatic thresholds (in *u'v'* units $\times 10^3$) measured by the CCT Trivector subtest. Individual data are presented for the controls, as well as the best and worst eyes of the DM2 patients. Asterisks indicate statistically significant differences.

Conversely, the D-15d test detected tritan losses in four eyes (from two patients) that displayed normal color vision on the CCT.

In summary, in 8.2% of the eyes (5/61) of the DM2 patients both D-15d and CCT revealed the same type of color vision loss; 19.7% eyes (12/61) were classified by the CCT with a more severe color vision loss; conversely, in 6.5% eyes (4/61) a more severe loss was revealed by the D-15d.

Correlations of color-vision test outcomes with diabetes clinical indices

Significant correlations were found between the outcomes of both tests for both eyes, and the duration of the disease (see *Table 1*). Further, significant positive correlation was found between the worst-eye tritan thresholds (Trivector subtest) and the level of glycated hemoglobin ($R = 0.45$, $p < 0.05$). No significant correlations were found between either the D-15d or the CCT outcomes, and the DM2 patients' clinical indices, such as fasting blood glucose, microalbuminuria, or total cholesterol.

Discussion

While the D15-d showed a predominance of tritan losses in the DM2 patients (except for one patient with diffuse losses in both eyes), the CCT revealed mostly diffuse color vision losses. Previously, diffuse losses have been reported at later DR stages of diabetes (Trick *et al.*, 1988). More recently, however, diffuse losses were found at initial stages of DM2 without retinopathy, when either the CCT was applied (Ventura *et al.*, 2003b) or a composite assortment of caps from the D-15 and D-15d was employed in combination with the triad procedure of color dissimilarity judgments (Feitosa-Santana *et al.*, 2006).

The results of the present study, that employed the CCT and examined a representative sample of DM2 patients, provide convincing evidence that at early stages of the disease, without clinical signs of DR, subclinical diffuse losses of color vision are emerging.

In the D-15d, color discrimination defects in DM2 patients were 67% more frequent among the worst eyes than the best eyes. In comparison, the CCT showed only 10% more frequent defects in the worst eyes, because color vision impairment was revealed also in the best eyes.

One possible explanation of the higher sensitivity of the CCT is that the test is composed of two subtests, which together contribute to detection of a minor deficiency in the best eye not revealed by the D-15d test. This explanation is supported by the present finding that both tests showed significant differences between the worst eyes of the DM2 patients and the controls' eyes, but not between the DM2 patients' best eyes and control eyes, suggesting that color discrimination defects detected by the CCT were minor.

Complementary reasons can be put forward to explain why the CCT revealed more losses (19.7%) compared to the D-15d (6.5%). One is related to the difference in what the two tests capture: the D-15d arrangement test registers errors in placement of equally saturated colors around the center of the CIE diagram, with the number of placement errors indicating the degree of color system malfunction. In comparison, the CCT estimates color discrimination thresholds, yielding a more precise measure of the performance of the system. Thus, one could consider that the two tests measure functioning at different levels of the color vision system, i.e., chromatic discrimination thresholds measured in the CCT may reflect a sensation-level function, whereas color arrangement in the D-15d test implies involvement, in addition, of a cognitive level.

In the present study, for DM2 patients without retinopathy, multiple correlations were found between the outcomes of both tests and the duration of diabetes. This finding extends those in previous studies for DM2 patients with DR, where color vision impairment was also shown to correlate with the duration of the disease and also with the severity of macular oedema (Bresnick *et al.*, 1985; Ismail and Whitaker, 1998).

Table 1. Spearman correlation coefficients between the DM2 patients' disease duration and the outcomes of the color vision tests. The following color vision outcomes were used as entries: TCDS (D-15d test; leftmost column); protan, deutan, and tritan threshold estimates (Trivector Test of the CCT); ellipse area and major-to-minor axis ratio (Ellipses 1 Test of the CCT)

	CCT test				
	Trivector test			**Ellipses 1 test**	
D-15d test	**Protan**	**Deutan**	**Tritan**	**Area**	**Axis Ratio**
Best Eye					
0.42 (<0.05)	0.36 ($p < 0.05$)	0.36 ($p < 0.05$)		0.57 ($p < 0.01$)	>0.50 ($p < 0.01$)
Worst Eye					
0.47 (<0.01)		0.40 ($p < 0.05$)	0.55 ($p < 0.01$)	0.50 ($p < 0.01$)	>0.45 ($p < 0.05$)

Since the majority of the examined subjects were aged 50+ years old, an aging effect could have contributed to the outcome. The aging effect, as has been reported in numerous studies, predominantly affects the tritan system (e.g., Smith *et al*., 1985; Regan *et al*., 1998). In this respect it is worth noting that for the DM2 patients, the tritan thresholds measured by the Trivector subtest were found to positively correlate with the diabetes duration, but not with the patients' age, this suggests that the detected tritan deficiency was related to the disease.

Except for a significant correlation for one parameter of the CCT test, between the tritan thresholds and the glycated hemoglobin level ($R = 0.45$, $p < 0.05$), no other correlations were found between the color vision test outcomes and metabolic parameters of DMZ patients. Future studies should scrutinize a possible association between metabolic control in DM2 patients and their color vision performance, to investigate the possibility of using sensitive color-vision tests for monitoring diabetes dynamics.

Conclusion

The present study provides evidence that in DM2 patients at early stages of the disease, and without clinical signs of DR, subclinical diffuse losses of color vision are present. Considering the advantages of the CCT test compared to the D-15d test, further studies should attempt to verify and/or improve the efficiency of CCT test.

Acknowledgements

Supported by FAPESP, CNPq, CAPES/PROCAD, FINEP IBN-Net. CFS is a fellow of the Institute of Mind and Biology, University of Chicago, and DFV is a CNPq fellow. CFS and MG were FAPESP fellows.

References

Aspinall, P. A., Kinnear, P. R., Duncan, L. J. and Clarke, B. F. (1983) Prediction of diabetic retinopathy from clinical variables and color vision data. *Diabetes Care* **6,** 144–148.

Barboni, M. T., Feitosa-Santana, C., Zachi, E. C., Lago, M., Teixeira, R. A., Taub, A., da Costa, M. F., Silveira, L. C. L. and Ventura, D. F. (2009) Preliminary findings on the effects of occupational exposure to mercury vapor below safety levels on visual and neuropsychological functions. *J. Occup. Environ. Med.* **51,** 1403–1412.

Barton, F. B., Fong, D. S. and Knatterud, G. L. (2004) Classification of Farnsworth-Munsell 100-Hue Test results in the Early Treatment Diabetic Retinopathy Study. *Am. J. Ophthalmol.* **138,** 119–124.

Bresnick, G. H., Condit, R. S., Palta, M., Korth, K., Groo, A. and Syrjala, S. (1985) Association of hue discrimination loss and diabetic retinopathy. *Arch. Ophthalmol.* **103,** 1317–1324.

Bronte-Stewart, J. M., Cant, J. S. and Craig, J. O. (1970) The detection of early visual loss in young diabetics. *Proc. R. Soc. Med.* **63,** 786–788.

Chylack, L. T. Jr, Wolfe, J. K., Singer, D. M., Leske, M. C., Bullimore, M. A., Bailey, I. L., Friend, J., McCarthy, D. and Wu, S. Y. (1993) The lens opacities classification system III. *Arch. Ophthalmol.* **111,** 831–836.

Costa, M. F., Oliveira, A. G. F., Feitosa-Santana, C., Zatz, M. and Ventura, D. F. (2007) Red-green color vision impairment in Duchenne muscular dystrophy. *Am. J. Hum. Genet.* **80,** 1064–1075.

Doucet, J., Retout, A., Poutrain, J. R., Ozenne, G., Leprince, M. P., Parain, D., Brasseur, G. and Schrub, J. C. (1991) Diabetic dyschromatopsia – a multifocal approach in 100 diabetic patients. *Diabetes Metab.* **17,** 31–37.

Farnsworth, D. (1943) The Farnsworth-Munsell 100-hue and dichotomous tests for color vision. *J. Opt. Soc. Am.* **33,** 568–578.

Feitosa-Santana, C., Oiwa, N., Paramei, G. V., Bimler, D., Costa, M. F., Lago, M., Nishi, M. and Ventura, D. F. (2006) Color space distortions in patients with type 2 diabetes mellitus. *Vis. Neurosci.* **23,** 663–668.

Feitosa-Santana, C., Barboni, M. T. S., Oiwa, N., Paramei, G. V., Simoes, A. L., Costa, M. F., Silveira, L. C. L. and Ventura, D. F. (2008) Irreversible color vision losses in patients with chronic mercury vapor intoxication. *Vis. Neurosci.* **25,** 487–491.

Fong, D. S., Barton, F. B. and Bresnick, G. H. (1999) Impaired color vision associated with diabetic retinopathy: Early Treatment Diabetic Retinopathy Study Report No.15. *Am. J. Ophthalmol.* **128,** 612–617.

Geller, A. (2001) A table of color distance scores for quantitative scoring of the Lanthony Desaturate color vision test. *Neurotoxicol. Teratol.* **23,** 265–267.

Greenstein, V. C., Sarter, B., Hood, D., Noble, K. and Carr, R. (1990) Hue discrimination and S cone pathway sensitivity in early diabetic retinopathy. *Invest. Ophthalmol. Vis. Sci.* **31,** 1008–1014.

Hardy, K. J., Lipton, J., Scase, M. O., Foster, D. H. and Scarpello, J. H. (1992) Detection of colour vision abnormalities in uncomplicated type 1 diabetic patients with angiographically normal retinas. *Br. J. Ophthalmol.* **76,** 461–464.

Ismail, G. M. and Whitaker, D. (1998) Early detection of changes in visual function in diabetes mellitus. *Ophthalmic Physiol. Opt.* **18,** 3–12.

Kurtenbach, A., Wagner, U., Neu, A., Schiefer, U., Ranke, M. B. and Zrenner, E. (1994) Brightness matching and colour discrimination in young diabetics without retinopathy. *Vision Res.* **34,** 115–122.

Kurtenbach, A., Schiefer, U., Neu, A. and Zrenner, E. (1999) Development of brightness matching and colour vision deficits in juvenile diabetics. *Vision Res.* **39,** 1221–1229.

Lakowski, R., Aspinall, P. A. and Kinnear, P. R. (1972) Association between colour vision losses and diabetes mellitus. *Ophthalmic Res.* **4,** 145–159.

Lanthony, P. (1978) The desaturated panel D-15. *Doc. Ophthalmol.* **46,** 185–189.

Lanthony, P. (1986) Evaluation du Panel D-15 désaturé. I. Méthode de quantification et scores normaux. *J. Fr. Ophtalmol.* **9,** 843–847.

Lanthony, P. (1995) Evaluation du panel D-15 désaturé. IV. Effet de la repetition du panel D-15 désaturé. *J. Fr. Ophtalmol.* **18,** 578–583.

Mollon, J. D. and Reffin, J. P. (1989) A computer-controlled colour vision test that combines the principles of Chibret and of Stilling. *J. Physiol.* **414,** 5.

Mollon, J. D. and Reffin, J. P. (2000) *Handbook of the Cambridge Colour Test*. Cambridge Research Systems, London.

Moura, A. L. A., Teixeira, R. A. A., Oiwa, N., Costa, M. F., Feitosa-Santana, C., Callegaro, D. and Ventura, D. F. (2008) Chromatic discrimination losses in multiple sclerosis patients with and without optic neuritis using the Cambridge Colour Test. *Vis. Neurosci.* **25,** 463–468.

Muntoni, S., Serra, A., Mascia, C. and Songini, M. (1982) Dyschromatopsia in diabetes mellitus and its relation to metabolic control. *Diabetes Care* **5,** 375–378.

Regan, B. C., Reffin, J. P. and Mollon, J. D. (1994) Luminance noise and the rapid determination of discrimination ellipses in colour deficiency. *Vision Res.* **34,** 1279–1299.

Regan, B. C., Freudenthaler, N., Kolle, R., Mollon, J. D. and Paulus, W. (1998) Colour discrimination thresholds in Parkinson's disease: results obtained with a rapid computer-controlled colour vision test. *Vision Res.* **38,** 3427–3431.

Roy, M. S., McCulloch, C., Hanna, A. K. and Mortimer, C. (1984) Colour vision in long-standing diabetes mellitus. *Br. J. Ophthalmol.* **68,** 215–217.

Smith, V., Pokorny, J. and Pass, A. S. (1985) Color axis determination on the Farnsworth-Munsell 100-hue test. *Am. J. Ophthalmol.* **100,** 176–182.

Tregear, S. J., Knowles, P. J., Ripley, L. G. and Casswell, A. G. (1997) Chromatic contrast threshold impairment in diabetes. *Eye* **11,** 537–546.

Trick, G. L., Burde, R. M., Gordon, M. O., Santiago, J. V. and Kilo, C. (1988) The relationship between hue discrimination and contrast sensitivity deficits in patients with diabetes mellitus. *Ophthalmology* **95,** 693–698.

Ventura, D. F., Silveira, L. C., Rodrigues, A. R., de Souza, J., Gualtieri, M., Bonci, D. M. and Costa, M. F. (2003a) Preliminary norms for the Cambridge Colour Test. In: *Normal and Defective Colour Vision* (eds J. D. Mollon, J. Pokorny and K. Knoblauch), Oxford University Press, Oxford, pp. 331–339.

Ventura, D. F., Costa, M. F., Gualtieri, M., Nishi, M., Bernick, M., Bonci, D. M. and de Souza, J. (2003b) Early vision loss in diabetic patients assessed by the Cambridge Colour Test. In: *Normal and Defective Colour Vision* (eds J. D. Mollon, J. Pokorny and K. Knoblauch), Oxford University Press, Oxford, pp. 395–403.

Vingrys, A. J. and King-Smith, P. E. (1988) Quantitative scoring technique for panel tests of color vision. *Invest. Ophthalmol. Vis. Sci.* **29,** 50–63.