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Effects of color-enhancing glasses on color vision in congenital red-green color deficiencies

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Abstract: As commercially available glasses for color vision deficiency (CVD) are classified as low risk, they are not subject to stringent marketing regulations. We investigate how EnChroma and VINO glasses affect performance on the Colour Assessment and Diagnosis (CAD) test in individuals with CVD. Data were obtained from 51 individuals with red-green CVD. Blood or saliva samples were collected to examine the structure of the *OPN1LW/OPN1MW* array. Individuals completed the CAD test twice without glasses and once with each pair of glasses. Although there was a statistically significant effect of both glasses, only that of VINO could be considered functionally meaningful.

1. Introduction

Human trichromatic color vision is mediated by the function of three classes of cone photoreceptor, which are maximally sensitive to either short (S), middle (M) or long (L) wavelengths within the visible portion of the electromagnetic spectrum [1]. The L and M cones are encoded by the *OPN1LW* and *OPN1MW* genes respectively, which are positioned on the Xq28 chromosome in a head-to-tail tandem array [2]. The arrangement in trichromatic individuals is *OPN1LW* followed by one or more *OPN1MW* genes. These genes are highly homologous, with around 96% similarity at the amino acid level [3], making them susceptible to unequal recombination and/or mutation during meiosis [1], which can lead to alternate gene arrangements that result in congenital red-green (RG) color vision deficiency (CVD) [3], affecting approximately 1 in 12 males.

CVD can be categorized by both type and severity. The type of deficiency is determined by which class of cone is non-functional or missing. A lack of L-cone function is associated with a protan deficiency whereas a lack of M-cone function leads to a deutan deficiency. The severity ranges from minimal anomalous trichromacy to dichromacy. Dichromacy (protanopia or deuteranopia) can arise when there is only a single opsin gene in the array or when all the genes in the array encode the same opsin – as a result, color vision is mediated by only two cone types (S and either L or M). Anomalous trichromacy (protanomaly or deuteranomaly) arises when both genes encode opsins from the same class but the spectral sensitivity of either the first or second opsin is shifted by just a few nanometers – in this case, color vision is mediated by three cone types (S, and either L and L´ or M and M´). Anomalous trichromacy is therefore less severe than dichromacy [3,4].

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Although gene therapy has shown success in restoring trichromatic color vision in mouse and squirrel monkey models of dichromacy [5,6], there is currently no treatment for CVD in humans. There has, however, been a long history of using optical aids to assist individuals with CVD [7–10]. Most optical aids work by selectively filtering certain wavelengths, either digitally [11], for example, by modifying display settings on one's computer, or through use of wearable lenses [8,12,13]. Both approaches alter the spectral composition of the light reaching the retina, and thereby the chromatic or achromatic contrast between colored stimuli.

Recently there has been renewed interest in the use of wavelength-filtering lenses, owing to the increased media attention that commercially available color-enhancing glasses have received. As these products are classified as not posing a significant risk to the health of the user, they are not subject to the stringent regulations imposed by the U.S. Food and Drug Administration (FDA) on marketing of medical devices [14]. However, therapeutic claims that are misleading or unsubstantiated could put the consumer at a financial disadvantage, as well as compromising user safety, for example if the product was relied upon to improve performance during visual and/or color-related tasks, such as driving a car or other vessel.

EnChroma and VINO are just two examples of companies that produce commercially-available glasses claiming to enhance color perception in CVD individuals. Prices for a new pair of glasses range upwards from $299 for EnChroma (outdoor use glasses) and $304 for VINO (color blindness glasses). Literature assessing the quantitative effects of EnChroma glasses is limited, and show mixed reports of color-related performance in CVD individuals, ranging from minimal effect [15–19], to improvement [18,20]. Scientific studies investigating the effects of VINO glasses are even fewer [15,21]. Furthermore, to the best of the authors' knowledge, no studies to date have confirmed the genotype of their CVD participants, other than our pilot study [15].

The distinction between dichromats and anomalous trichromats is particularly important for EnChroma, as the premise behind their technology is that it "selectively filters out wavelengths" at the point of overlap in spectral sensitivity between the L/M photopigments – they are therefore not intended to be used by or expected to assist dichromats. Indeed, neither product could theoretically be expected to improve chromatic discrimination per se in dichromatic individuals: any apparent filter-induced improvement in performance by dichromats would be expected to be due entirely to changes in achromatic contrast. However, given that VINO do not make distinction between dichromats and anomalous trichromats in their marketing efforts and, moreover, specialized color vision and/or genetic testing (that is not routinely available) is required to provide a differential diagnosis between anomalous trichromacy and dichromacy, we deemed it pertinent to assess the effects of the glasses in both CVD groups.

Here we used the Colour Assessment and Diagnosis (CAD) test [22,23] to isolate the use of color signals, and to identify the participants' type and severity of color vision loss when viewing a fully calibrated, LCD display. Phenotypes were confirmed using the Rayleigh match and all participants had their type of color vision defect confirmed molecularly. We aimed to investigate whether the use of 'color-enhancing' lenses in anomalous trichromats and in dichromats had the benefit of lowering the participants' chromatic discrimination thresholds when viewing the same LCD display. The glasses assessed were the EnChroma Cx-65 (designed for indoor use, "such as cooking, or viewing computers and TV") and VINO Optics Oxy-Iso. Although this particular EnChroma Cx-65 lens was discontinued in 2016, its spectral transmittance is comparable to the Cx-1 lens that (at the time of writing) is currently available [19]. The NEC display employed in the CAD test uses broadband primaries (CCFL backlights), which provide good coverage of the visible spectrum (See Supplement 1, Fig. S1, which shows the spectral radiance data for the D65 background employed in the CAD test). The results are relevant to work on visual displays, but they may also be of interest when viewing natural scenes under broadband illumination through the same glasses.

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2. Methods

Fifty-four individuals (53M, 1F; aged 18 to 74 years) with self-reported CVD were recruited. Each individual provided a blood or saliva sample, from which DNA was isolated. The opsin genes (*OPN1LW* and *OPN1MW*) were amplified and sequenced using previously described methods in order to genetically characterize their CVD [24].

Individuals were screened, and had their phenotype characterized, using the Rayleigh anomaloscope. The CAD test was completed binocularly under photopic CIE Standard Illuminant D-65 lighting conditions. The emission spectra of the LCD display is shown in Fig. S1. All testing took place in a small room with neutral colored walls and dark carpet, as well as a selection of magazines. After baseline testing, the participant adapted for 30 minutes in the same room while wearing either EnChroma Cx-65 or VINO Optics Oxy-Iso. Participants were allowed to leave the room as long as they did not remove the glasses at any time, and they were not restricted in their use of phones or other devices. The adaptation was followed by CAD testing with the glasses remaining on. This process was then repeated (i.e. baseline CAD; adaptation with glasses; CAD with glasses) for the other type of glasses. Testing with the first type of glasses and the second baseline run was conducted at least one hour apart and, whenever possible, on separate days. The period between follow-up visits did not exceed 5 months. CAD units are normalized to 1 for the standard normal observer. The Shapiro-Wilk test was used to assess the data for normality and to guide choice of statistical methods.

We used a Konica Minolta CS-2000 Spectroradiometer to measure the transmittance of each pair of glasses (Fig. 1). In an attempt to further understand the effect of the glasses on color vision, we used the measured transmittance to compute theoretical chromatic contrast of the stimulus at threshold when wearing glasses.

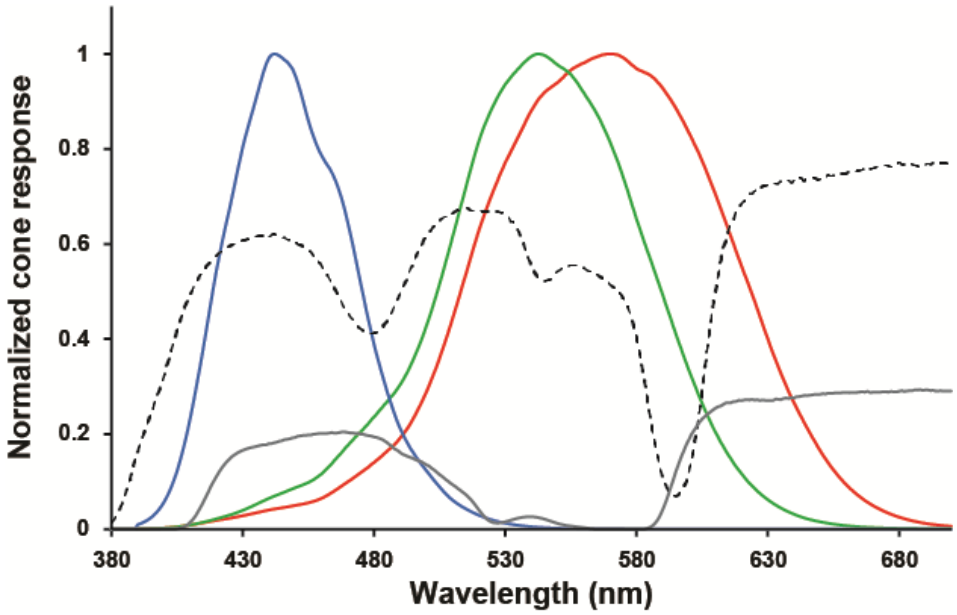

Fig. 1. Measured transmittance of each pair of glasses in relation to cone sensitivity. The EnChroma glasses (black dashed line) transmit a greater amount of light overall, with a sharp cut-out at around 595 nm. VINO glasses (gray solid line) transmit less light, with a broader cut-of between around 530 and 580 nm.

The Baylor et al. (1987) [25] template was used to create photopigment absorbance spectra for an anomalous deutan with 6 nm separation between L and L´ and an anomalous protan with 3 nm

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spectral separation between M and M´. These absorbance spectra were corrected for the effects of self-screening, using Baylor et al.'s (1987) values for photoreceptor axial optical density (0.27 for all three cone types) [25]. They were also corrected for preceptoral filtering; lens and macular pigment density spectra were obtained from Stockman et al. (1999) [26] and scaled using Baylor et al.'s (1987) factors for the lens and macular pigment spectra [25]. The chromatic contrast was then calculated from measured baseline thresholds (i.e. the relative cone response elicited by the stimulus with respect to that of the neutral background) and the difference in response between the two available opsins (L and L´ or M and M´) was assessed.

This study followed the tenets of the Declaration of Helsinki and was approved by MCW's institutional review board (PRO: 24510). Informed consent was obtained from all individuals, after the nature and possible consequences of the study were explained. No data from our pilot study was used in this study [15].

3. Results

3.1. Participants

Fifty-four individuals took part; one participant was excluded due to uncooperativeness and, upon inspection of the data, two additional participants were excluded due to highly variable CAD results (i.e. > 20 units difference between run 1 and 2 or a YB threshold of > 6 units). Of the remaining 51 participants, shown in Table 1, two did not complete both scheduled visits; these individuals could not be included in assessment of repeatability, but were included in assessment of the effect of the glasses tested (i.e. run 1 vs glasses). The genotype and clinical phenotype (based on Rayleigh matches) of each individual is shown in Table 1. Three individuals demonstrated a genotype-phenotype discrepancy, most notably JC_11359, whose matching range was smaller than that expected for someone with two identical M opsins. Of particular interest was JC_11356's gene array, whose phenotype was that of a protanope, as indicated consistently by Rayleigh match and CAD (Fig. S2), as well as AO-HRR. This individual had a Y309 mutation in exon 5, which is usually found in L genes [27,28]. However, amplification of the first gene revealed that it was M, which was consistent with his phenotype.

3.2. Chromatic discrimination in CVD without glasses

CAD thresholds are shown in Table 2. Without glasses, color discrimination on the CAD test ranged from 2.81 to 31.27 units for the RG axis and 0.87 to 5.13 on the yellow-blue (YB) axis across all CVD participants. For RG thresholds, the within-subject standard deviation (Sw) across both baseline visits was 1.40 units. The repeatability is defined as 2.77*Sw, or 3.87 units. This means that the difference between two measurements for the same individual is expected to be less than this value for 95% of pairs of observations. In other words, we considered changes *greater* than this to be clinically meaningful. For YB thresholds, the repeatability was 0.66 units. The average of both baseline runs (where possible) was used for subsequent comparisons with the data obtained using the glasses.

3.3. Effect of glasses on CAD thresholds in CVD

Firstly, we sought to establish whether either of the two glasses were effective at reducing RG CAD thresholds in individuals with CVD. Although neither product was expected to affect chromatic (as opposed to achromatic) contrast for dichromats, many potential customers are unlikely to have a clinical diagnosis of CVD type and/or severity; we therefore considered the effect of glasses on performance of the CVD group, as a whole, to be of general interest. There was a statistically significant effect of both EnChroma ($p < 0.001$) and VINO ($p < 0.001$), with an average reduction of 1.16 (± 1.69) and 8.03 (± 9.07) units respectively, across all CVD participants. For context, the standard deviation of differences was 1.91 between baselines, 1.69

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Table 1. Genotype and clinical phenotype for all color vision deficient individuals[a]

ID	Age	Phenotype	Rayleigh	L/M array	SS (nm)
JC_10830[b]	54	Deuteranomalous	10 - 21	LLM	6.5
JC_10736	44	Deuteranomalous	13 - 33	LLM	6.5
JC_11420	36	Deuteranomalous	4 - 33	LLM	6.5
JC_11421	50	Deuteranomalous	0 - 40	LL	6.5
JC_1005	29	Deuteranomalous	16 - 22	LLM	6
JC_10730	64	Deuteranomalous	0 - 28	LLLLM	6
JC_10627	68	Deuteranomalous	3 - 32	LLM	6
JC_10795	66	Deuteranomalous	0 - 33	LLLM	6
JC_11261	25	Deuteranomalous	11 - 23	LLM	2.5
JC_11454	22	Deuteranomalous	13 - 29	LLM	2.5
JC_11922	29	Deuteranomalous	28 - 60	LL	2.5
JC_11431	33	Deuteranomalous	0 - 37	LLM	2.5
JC_11435	22	Deuteranomalous	0 - 39	LLM	2.5
JC_11283	21	Deuteranomalous	0 - 63	LLLM	2.5
JC_11873[c]	22	Deuteranope	0 - 73	LL	2.5
JC_11892[c]	33	Deuteranope	0 - 73	LLMM	2.5
JC_11606	56	Protanomalous	58 - 70	MMMM	3
JC_11340	25	Protanomalous	34 - 68	MMM	3
JC_11906	29	Protanomalous	14 - 69	MMM	3
JC_11526	65	Protanomalous	0 - 72	MMM	3
JC_11259	23	Deuteranope	0 - 73	L	N/A
JC_11258	23	Deuteranope	0 - 73	L	N/A
JC_11436	23	Deuteranope	0 - 73	L	N/A
JC_11667	24	Deuteranope	0 - 73	$LM_{Cys203Arg}$	0
JC_11270	25	Deuteranope	0 - 73	L	N/A
JC_11272	25	Deuteranope	0 - 73	L	N/A
JC_11455	25	Deuteranope	0 - 73	L	N/A
JC_11588	27	Deuteranope	0 - 73	L	N/A
JC_11422	29	Deuteranope	0 - 73	L	N/A
JC_11361	30	Deuteranope	0 - 73	L	N/A
JC_11349	31	Deuteranope	0 - 73	L	N/A
JC_11843[b]	35	Deuteranope	0 - 73	L	N/A
JC_11279	40	Deuteranope	0 - 73	L	N/A
JC_11260[d]	42	Deuteranope	0 - 73	L	N/A
JC_11594	44	Deuteranope	0 - 73	L	N/A
JC_11587	44	Deuteranope	0 - 73	L	N/A
JC_11274	52	Deuteranope	0 - 73	LLM	0
JC_11325	53	Deuteranope	0 - 73	L	N/A
JC_10836	61	Deuteranope	0 - 73	L	N/A
JC_11546	68	Deuteranope	0 - 73	L	N/A
JC_11359[c]	18	Protanomalous	20 - 57	MMM	0
JC_11278	60	Protanope	0 - 73	MM	0
JC_11795	23	Protanope	0 - 73	MMM	0
JC_11312	24	Protanope	0 - 73	M	N/A
JC_11452	28	Protanope	0 - 73	MM	0
JC_11662	32	Protanope	0 - 73	MM	0
JC_11668	36	Protanope	0 - 73	MMMM	0
JC_11356	37	Protanope	0 - 73	MML	0
JC_0434	49	Protanope	0 - 73	MMMM	0
JC_11308	54	Protanope	0 - 73	MMM	0
JC_11365	58	Protanope	0 - 73	MMM	0

[a] SS = spectral separation; N/A = not applicable, i.e. only one *OPN1LW/OPN1MW* gene present in the array
[b] Did not complete both runs
[c] Discrepancy between phenotype (Rayleigh match) and genotype (SS = spectral separation)
[d] Female

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Table 2. Colour assessment and diagnosis thresholds for all individuals

	Baseline (no glasses)				EnChroma Cx-65		VINO Optics Oxy-Iso	
ID	RG 1	YB 1	RG 2	YB 2	RG	YB	RG	YB
JC_10830	9.15	2.59	–	–	–	–	7.55	3.01
JC_10736	6.90	2.05	5.77	1.66	5.41	1.58	4.42	1.88
JC_11420	3.58	1.04	3.36	0.95	2.50	0.92	3.13	0.84
JC_11421	5.76	2.01	5.83	1.86	5.13	2.15	4.98	2.02
JC_1005	2.81	1.15	2.83	1.15	2.26	1.06	2.74	1.20
JC_10730	5.24	2.09	4.65	1.95	4.30	2.44	5.24	2.09
JC_10627	20.02	4.49	20.77	5.13	20.20	4.22	8.22	4.47
JC_10795	8.13	2.89	7.50	2.86	8.47	2.99	5.18	2.72
JC_11261	14.76	1.02	15.20	1.51	11.44	1.15	6.04	1.42
JC_11454	10.87	1.27	12.63	1.76	10.44	1.50	5.65	1.45
JC_11922	9.36	1.59	9.21	1.50	8.76	1.68	5.17	1.87
JC_11431	10.87	1.40	11.20	1.41	9.92	1.21	5.32	1.57
JC_11435	7.98	1.35	7.33	1.48	5.64	1.18	4.55	1.56
JC_11283	9.07	1.21	8.03	1.20	6.51	1.13	4.90	1.16
JC_11873	16.93	1.50	17.53	1.56	15.25	1.24	6.12	1.60
JC_11892	15.88	1.76	14.66	1.07	11.93	1.05	5.37	1.34
Deuteranomalous mean	**9.83**	**1.84**	**9.77**	**1.80**	**8.54**	**1.70**	**5.29**	**1.89**
JC_11606	17.63	1.73	15.93	1.67	14.59	1.48	11.35	1.87
JC_11340	6.61	1.06	6.27	1.22	6.61	0.83	5.16	1.92
JC_11906	4.76	0.97	4.63	0.94	4.44	0.83	3.00	1.39
JC_11526	27.08	3.54	25.27	3.16	26.06	2.98	26.53	3.48
Protanomalous mean	**14.02**	**1.83**	**13.03**	**1.75**	**12.93**	**1.53**	**11.51**	**2.17**
Anomalous mean	**10.67**	**1.84**	**10.45**	**1.79**	**9.47**	**1.66**	**6.53**	**1.94**
JC_11259	18.86	1.16	17.24	1.32	20.31	1.19	5.76	1.40
JC_11258	27.99	1.19	25.94	1.02	23.87	0.98	5.94	1.24
JC_11436	27.20	2.00	23.12	1.34	20.67	1.31	4.82	1.27
JC_11667	21.79	1.22	16.56	1.14	18.17	1.08	4.14	1.20
JC_11270	20.94	1.09	19.28	0.87	21.22	0.81	3.53	0.67
JC_11272	11.98	1.95	11.02	2.09	11.82	2.31	5.29	2.30
JC_11455	25.95	1.12	23.41	1.10	25.60	1.17	5.09	1.06
JC_11588	20.00	0.99	23.07	1.16	21.32	1.12	4.76	1.09
JC_11422	18.14	0.95	15.71	0.91	17.05	0.80	3.97	0.95
JC_11361	24.96	1.37	17.65	1.21	23.02	1.10	3.36	1.07
JC_11349	22.89	1.53	22.18	1.29	23.46	1.20	4.34	1.19
JC_11843	22.30	1.46	-	-	23.01	1.16	-	-
JC_11279	14.43	1.75	18.42	1.71	15.24	1.40	5.03	1.93
JC_11260	23.19	1.05	23.11	1.08	20.79	0.89	5.24	1.06
JC_11594	23.51	1.75	21.46	1.59	18.32	1.38	4.59	1.49
JC_11587	20.78	1.11	19.69	1.19	18.24	1.21	4.35	1.04
JC_11274	27.51	1.60	25.36	1.66	23.87	1.40	4.50	1.47
JC_11325	28.35	1.06	29.40	1.04	28.41	1.24	3.69	0.81
JC_10836	30.70	1.93	30.79	1.98	29.87	2.05	6.01	2.26
JC_11546	30.97	1.19	31.27	1.38	28.39	1.39	4.83	1.45
Deuteranopia mean	**23.12**	**1.37**	**21.83**	**1.32**	**21.63**	**1.26**	**4.70**	**1.31**
JC_11359	24.80	1.20	25.87	1.03	21.13	0.93	24.35	1.09
JC_11278	23.73	1.61	24.56	2.29	24.32	3.16	30.79	1.86
JC_11795	24.87	1.00	26.23	1.20	26.32	1.10	26.37	1.54
JC_11312	23.97	1.27	24.74	1.13	19.48	1.03	27.95	1.66
JC_11452	23.67	0.97	20.60	0.98	19.67	0.88	22.60	1.10
JC_11662	25.22	1.26	24.79	1.38	24.92	1.11	20.53	1.25
JC_11668	24.49	1.27	24.07	1.33	24.91	1.33	27.47	1.83
JC_11356	23.79	1.76	25.73	2.08	21.13	0.93	24.35	1.09
JC_0434	28.65	1.94	29.28	2.06	28.08	1.83	25.85	1.90
JC_11308	24.99	2.83	24.56	1.55	22.80	1.45	27.33	1.96
JC_11365	26.77	1.78	27.27	2.65	24.44	2.52	35.37	2.34
Protanopia mean	**25.00**	**1.54**	**25.25**	**1.61**	**23.38**	**1.48**	**26.63**	**1.60**
Dichromacy mean	**23.79**	**1.43**	**23.08**	**1.43**	**22.25**	**1.34**	**12.74**	**1.42**
Total mean	**18.64**	**1.59**	**18.18**	**1.57**	**17.39**	**1.46**	**10.26**	**1.63**

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for mean baseline vs. EnChroma, and 9.07 for baseline vs. VINO. The difference in threshold made by each pair of glasses is shown in Fig. 2. Only four individuals showed a reduction in RG threshold with EnChroma (i.e. an improvement) greater than the repeatability, and which could therefore be considered clinically meaningful: all four of them were deuteranopes. In contrast, 28 individuals (7 deuteranomalous, 1 protanomalous, 19 deuteranopic, 1 protanopic,) showed a reduction with VINO that exceeded repeatability limits.

3.4. Differences in effect of glasses between dichromats and anomalous trichromats

Of greater scientific interest was whether there was a difference in the effect of either type of glasses in relation to spectral separation between the L/M opsins, as only anomalous trichromats have a realistic chance of achieving true improvements in chromatic discrimination at the confusion locus (as opposed to changes in achromatic contrast). As such, a significantly greater reduction in anomalous trichromats would indicate that the glasses (particularly EnChroma, which use notch filters) work as intended, i.e. improve chromatic discrimination; any other finding would indicate that the effect on performance is due to induced changes in achromatic contrast. In spite of these arguments, the possibility of the color-enhancing glasses affecting YB chromatic sensitivity and in particular the contribution to either the L- or M-cone signals to the YB chromatic channel, cannot be ignored. One outcome of such contributions would be a shift in the orientation of the deutan or protan colour confusion axes. Mann-Whitney testing was used for comparing differences made by the glasses (i.e. mean baseline – run with glasses). There was no statistically significant difference in the effect of EnChroma between those who had spectral separation between the L/M opsins and those who did not ($p = 0.952$), in contrast to the information given on the manufacturer's website. There was a significant difference in the effect of VINO, however, with the glasses being associated with a greater reduction in thresholds for genotypically-dichromatic individuals ($p = 0.032$). For genotypically-anomalous individuals, the mean reduction in RG threshold was 1.14 (± 1.13) units for EnChroma and 4.00 (± 3.89) for VINO. Again, only changes above 3.87 units would be considered functionally meaningful. For further context, the maximum allowable CAD threshold for pilots in the UK (where the CAD is used to determine eligibility of applicants) [29] is 6 units for deutan and 12 units for protan deficiencies. Given that the mean thresholds were 9.78 and 13.52 units for deuteranomalous and protanomalous participants respectively, only the VINO glasses would result in a sufficient reduction in threshold to make a practically meaningful difference to the average anomalous trichromat's color vision.

Spearman correlations were used to assess the relationship between the effects of the two types of glasses. As might be expected, there was no correlation between the differences (i.e. mean baseline – run with glasses) made by the two types of glasses for dichromats ($p = 0.947$). There was however, a significant correlation for anomalous trichromats (Spearman $r = 0.500$, $p = 0.029$), suggesting that an individual who finds one pair to be effective is more likely to find the other pair effective as well.

3.5. Differences in effect of glasses between protans and deutans

Interestingly, for VINO glasses there was a rotation in the angle of confusion for protans, effectively transforming their deficiency to that of a deutan (Fig. 3). This observation is consistent with a change in the orientation of the tritan axis. There was also a statistically significant difference between protans and deutans, with a greater reduction in thresholds for deutans ($p < 0.001$). There was no difference in the effect of EnChroma between protans and deutans ($p = 0.663$).

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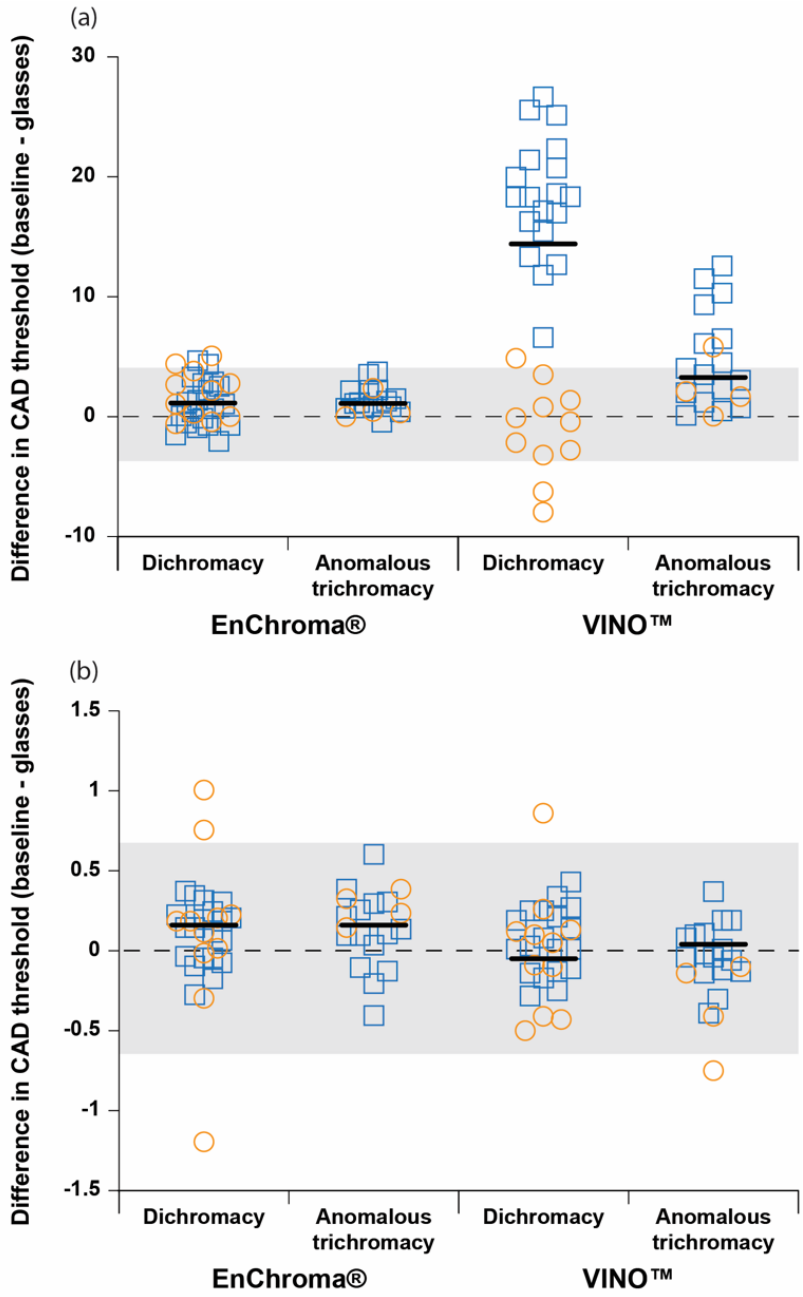

Fig. 2. Scatter plot showing differences between both (a) red-green (RG) and (b) yellow-blue Colour Assessment and Diagnosis (CAD) thresholds at baseline and with each type of glasses for each participant. Values above y = 0 represent an improvement in chromatic discrimination. The grey shaded regions indicate baseline repeatability, outside which differences could be considered to be functionally meaningful. VINO were associated with a larger improvement in RG discrimination than EnChroma. Yellow circles = protan; blue squares = deutan; solid horizontal lines = median.

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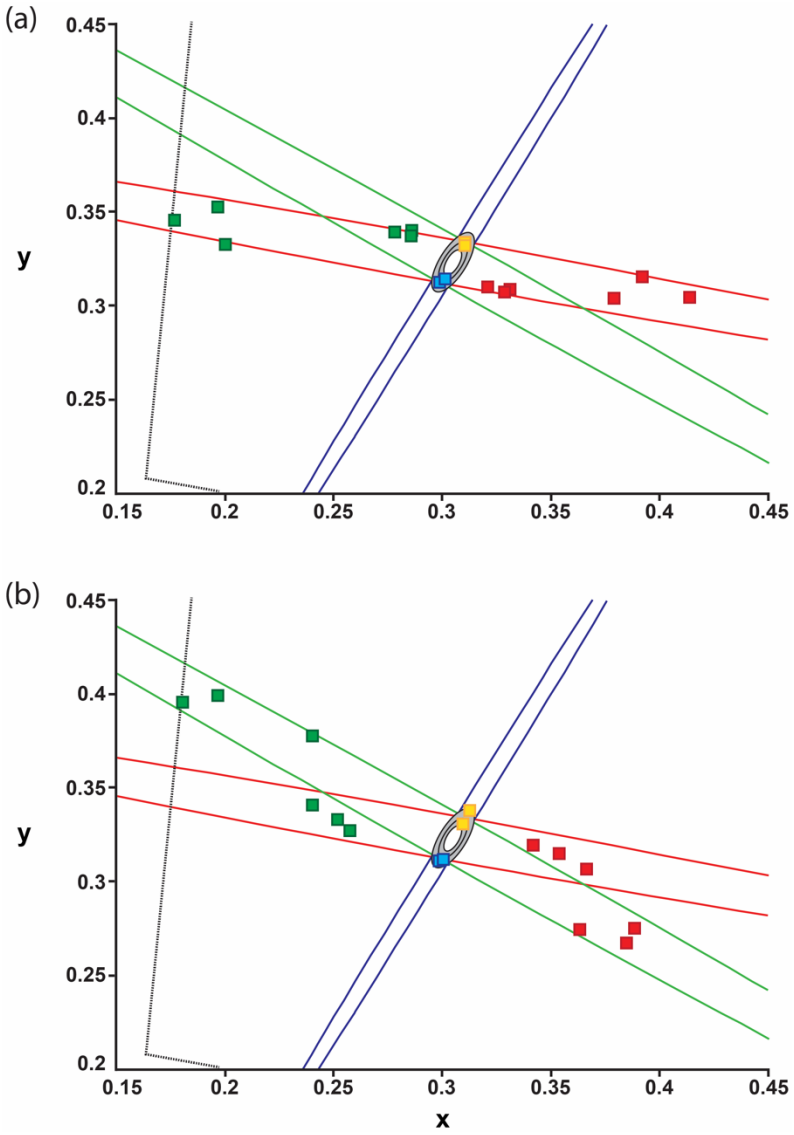

Fig. 3. Colour Assessment and Diagnosis thresholds plotted in CIE (x,y) 1931 chromaticity space for a representative protanopic individual (JC_11452) for (a) Run 1 baseline and (b) with VINO glasses. The shallower red lines represent the axis of confusion for protans and the steeper green lines represent that for deutans. Normal trichromatic thresholds would be expected to fall within the central gray ellipse. Although the glasses made little difference to the overall threshold, there was a rotation in the axis of confusion to mimic that of a deutan.

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3.6. Modeling of chromatic contrast with glasses

Using measured baseline CAD thresholds (average of two runs), we calculated the change in chromatic contrast in the presence of both types of glasses for two individuals who were representative of their group: a deuteranomalous individual with 6 nm separation (JC_1005) and a protanomalous individual with 3 nm separation (JC_11340). Chromatic contrast was calculated for each of the twelve directions (CIE 1931 color space) corresponding to the red and green stimuli, and the difference in response between the two available L/M opsins was averaged to find the overall percentage change in chromatic contrast. For the deuteranomalous individual, EnChroma would be expected to increase RG contrast by 10%, while VINO glasses would be expected to increase the RG contrast by 4%. For the protanomalous individual, EnChroma had an expected increase of only 1% whereas VINO had an expected increase of 182%. Despite nearly a two-fold expected increase in RG contrast for the protanomalous individual with VINO glasses, the measured thresholds showed a reduction of only 1.28 units (6.44 at baseline – 5.16 units with glasses), which was within repeatability.

4. Discussion

In this study, we measured performance on an objective psychophysical test of chromatic discrimination to quantify the effects of two types of commercially-available glasses, which are targeted at those with CVD. After presenting the results from our initial pilot study using EnChroma outdoor glasses [15], we were advised by EnChroma to use their indoor glasses, although it should be noted that since data collection, their website has been updated to specify that indoor glasses are "not recommended for strong protans or strong deutans". They also state that "EnChroma does not endorse or recommend attempting to use our products to pass [. . .] any [. . .] color blindness test" and that they are "required per FDA labelling regulations to warn users that our glasses are not for use while driving".

The VINO and EnChroma glasses differentially modulate the intensities of certain wavelengths of light reaching the eye. Color vision is, by definition, the ability to discriminate wavelength independently of intensity, thus it is not possible for either type of glasses to improve wavelength discrimination for dichromats beyond about 550 nm, unless 1) there were rod-cone interactions, which would not be expected at the photopic light levels used here, or 2) there were optical density differences between cones with the same photopigment. The latter is unlikely to be relevant to the vast majority of deuteranopes who have only one (L) gene within the gene array. Indeed all but two of the 20 deuteranopic individuals tested here had a single L gene. In the case of multigene dichromats (i.e. the majority of protanopes) however, it is possible that differences in photopigment optical density between cones of the same class could give rise to limited trichromacy [30]; the extent of which could possibly be affected by filters. As this study did not assess optical density, it is not possible to determine whether there was any such effect.

Colored filters can introduce sufficient luminance cues to pseudoisochromatic stimuli to allow individuals with CVD to "cheat" on standard color vision tests, as the VINO glasses did for deutans. The CAD test assesses discrimination along twelve red-green directions in colour space, which are not evenly distributed, i.e. they are clustered within the confusion axes of protans/deutans. This enabled us to detect a consistent rotation in the confusion axis for protans with VINO, as we show in Fig. 3. Although we did not observe a rotation for deutans with VINO, we cannot rule out the possibility that the effect also exists for deutans, and may have been detectable if we tested along additional directions [31]. Theoretically, colored filters could sharpen color discrimination for anomalous trichromats for certain spectral distributions within the RG region. An example of this is to use an inverse-designed aid lens, the transmittance of which is customized based on the wavelength shift of each CVD patient [32].

The aim of this study was not to draw generic conclusions about the effectiveness of the two types of color-enhancing glasses based on the findings from this study, simply because the

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overall effectiveness of the glasses, as well as any test outcome, can be affected by the spectral composition of the illuminant and, in the case of visual displays, by the spectral power distribution of the primary colors. It is possible that different results would have been obtained had we used real (pigmented) colored patches, such as Munsell chips, with smoothly changing reflectances when illuminated with true natural daylight. However, there are currently no color vision tests that use such broadband stimuli while offering the same level of precision in measuring small changes in chromatic discrimination and simultaneously minimizing rod input.

It is also possible that extended adaptation with the glasses could have led to a greater shift in the weighting of L/M inputs due to the neural plasticity of the nervous system [33]. This was demonstrated in anomalous trichromats with extended use of EnChroma glasses; participants showed improved performance on a color discrimination task using suprathreshold Gabor patches *when tested without the glasses*, demonstrating plasticity in the chromatic response [34]. One explanation for the disparity between the results of Werner et al. [34] and our own is that, threshold measurements are thought to reflect the signal-to-noise ratio within the system, whereas suprathreshold contrast is thought to reflect the signal [35,36]. It is possible that the glasses simultaneously increase the L/M signal as well as the noise and, in the case of discrimination thresholds measured here, cancel each other out. If the glasses do indeed induce a postreceptoral gain adjustment, its effect on luminance perception [37,38], and its potential to manifest in improvement for some color combinations at the expense of others, is unknown. Another likely source of differences between studies is the use of different models. In this study, we used the EnChroma Cx-65 (designed for indoor use), which is no longer available (at the time of writing). In the study by Werner et al. [34], participants were asked to wear both indoor and outdoor versions of EnChroma glasses and, although the specific models are not reported, the spectral profiles appear very different to that of the Cx-65. Differences in models and study procedures can complicate comparisons between studies, highlighting the importance of disclosing the specific model and spectral properties of the lenses used in such studies, as well as providing details about the viewing conditions.

In this study, we used a simple model of chromatic contrast, which accounted for the predicted shift in peak cone sensitivity, as indicated by genetically-confirmed amino acid positions, as well as measured chromatic discrimination thresholds. Our modeling showed that EnChroma would be expected to have minimal effect on chromatic contrast of CAD stimuli for both representative deuteranomalous and protanomalous individuals, whereas VINO should have minimal effect on contrast for deutan but a sizeable effect for protanomalous individuals, although this was not borne out in the measured thresholds. Interestingly, our contrast modelling showed that, although CAD thresholds are higher for those with CVD than for those with normal trichromatic vision, their performance is better than would be predicted, given the spectral separation between their opsins. It is therefore possible for them to detect a smaller difference in the relative L:L´ or M:M´ response than the difference in L:M response required for normal patients at threshold. This is in agreement with previous work, which suggests that there is a compensatory shift in the weighting of L/M inputs, which allows anomalous trichromats to maximize their chromatic discrimination [33,36,38,39]. It must be noted that a number of factors may have an impact on color discrimination and thereby contribute to individual differences in performance among those with the same genotype, such as optical density of the photopigment within the cone cells [40,41], macular pigment [42–44], and the lens [42,45]. Our model did not adjust for individual differences in these preretinal factors and, as such, should be treated as an approximation only.

Finally, we characterized individuals' color deficiency for analysis based on whether there was spectral separation between the first two opsins in the *OPN1LW/OPN1MW* array. Three individuals demonstrated discrepancies between genotype as determined by spectral separation and phenotype determined by Rayleigh match (though the CAD results were consistent with the genotype). At first pass, this might suggest that using spectral separation as the defining

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characteristic in our analysis is not valid. However, given the premise behind EnChroma's filter technology, it was our opinion that spectral separation was the most pertinent factor in this analysis.

Despite the limitations of this study, we provide important repeatability data for dichromats and anomalous trichromats; such data may be useful for future studies that use the CAD test to assess changes in chromatic discrimination among individuals with CVD and to determine whether they are functionally meaningful. We are also able to posit with confidence that color signal strength does not improve with the use of glasses under the conditions of our experiments. Other factors that have not been explored in this study, such as changes in effective luminance contrast or YB chromatic sensitivity, may also have contributed to the smaller chromatic displacement needed to detect RG stimuli when wearing VINO glasses.

5. Conclusion

VINO and EnChroma glasses differentially modulate the intensities of certain wavelengths of light reaching the eye, resulting in a reduction of RG CAD thresholds in some patients. However, we did not find any functionally meaningful changes induced by EnChroma and, although VINO did induce a functionally meaningful reduction in thresholds, their claim that the technology "corrects red-green color deficiency" is not supported by our data.

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Data availability. Data underlying the results presented in this paper are presented in Tables 1 and 2.

Supplemental document. See Supplement 1 for supporting content.

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