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Binocular facilitation of cone-specific visual evoked potentials in colour deficiency

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Background: Neural compensatory mechanisms have been proposed, which preserve the binocular visual field in glaucoma, as well as cognition in Alzheimer's disease and motor function in Parkinson's disease. It is conceivable that comparable mechanisms operate to preserve function in congenital and/or dystrophic disease. In hereditary colour vision deficiency (CVD), we observed significant facilitation in the amplitude of the binocular cone-specific visual evoked potential (VEP) compared to the monocular amplitude for the cone type corresponding to the CVD. We propose that this finding may reflect preservation of function in hereditary colour vision deficiency.
Methods: Binocular and monocular L, M and S cone-specific VEPs were recorded from 12 colour vision deficient subjects and 17 with normal colour vision, confirmed to be CVD or normal on a battery of colour vision tests. Binocular VEP amplitudes were compared to monocular amplitudes within subjects and between subject groups.
Results: Subjects with CVDs showed binocular facilitation of VEP amplitude (enhancement more than 2.0 times; mean: 2.8 times, p = 0.0003) for the cone type corresponding to their CVD. Mean facilitation of 2.8 times exceeded binocular enhancement for other cone types within CVDs (2.8 times versus 1.2 times) and compared to colour vision normals (2.8 times versus 1.2 times).
Conclusions: Hereditary CVDs show binocular facilitation of cone VEP signals for the cone type corresponding to their CVD. As CVD is typically assessed with foveal stimuli, our findings using wider-field binocular stimulation suggest that enhanced colour perception may occur in CVD across a more extensive area of visual field. These results may relate to binocular visual field enhancement in glaucoma and improved colour vision in CVD at supra-threshold levels of stimulation.

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Neural compensatory mechanisms have been proposed which preserve visual function in glaucoma,[1,2] as well as cognition and motor function in Alzheimer's, Parkinson's and Huntington's diseases.[3–5] In moderate to severe glaucoma, a visual field defect in one eye can be compensated for by visual field retention in the corresponding area seen by the fellow eye, thus preserving the binocular field; an intriguing phenomenon attributed to central nervous system (CNS) control.[1,2] It is conceivable that during development, compensation for dysfunction may occur in hereditary and/or dystrophic conditions affecting vision and other modalities which, in response to environmental demands, serve to enhance sensory and/or motor function. Compensation for red-green hereditary colour vision deficiency (CVD) can occur at supra-threshold levels of stimulation.[6,7] While developing a cone-specific visual evoked potential (VEP) to objectively assess CVD,[8] we observed that binocular VEP signals from CVD anomalous trichromats were nearly three times larger than their monocular VEPs for the cone type corresponding to their CVD. It is proposed that this VEP finding may relate to the binocular visual field enhancement in glaucoma[1,2] and supra-threshold enhancement of colour vision observed in CVD.[6,7]

METHODS

A Diagnosys (diagnosysllc.com) system was used to record L, M and S cone-specific VEPs presented on a fully calibrated, high-resolution LCD monitor in pattern-onset mode with coloured checkerboards presented as increments against a grey background (127 cd/m^2; x, y = 0.303, 0.323).[8] The coloured checks were presented for 100 msec, twice per second each followed by the grey field lasting 400 msec. VEP signals were recorded for 300 msec. At the onset of each checkerboard presentation, amplified eight times, band-pass filtered (1–30 Hz) and averaged across 75 pattern onsets recorded twice from right, left and both eyes (mean of the two recordings were used for analysis). Display size was 30 degrees at 57 cm in a dark room. Subjects wore habitual corrections with added power for those 40 years and older. L and M cone check sizes were one degree and S cone two degrees to compensate for lower resolution of the S-cone pathway. The active electrode was 1.0 cm above the inion with reference and ground

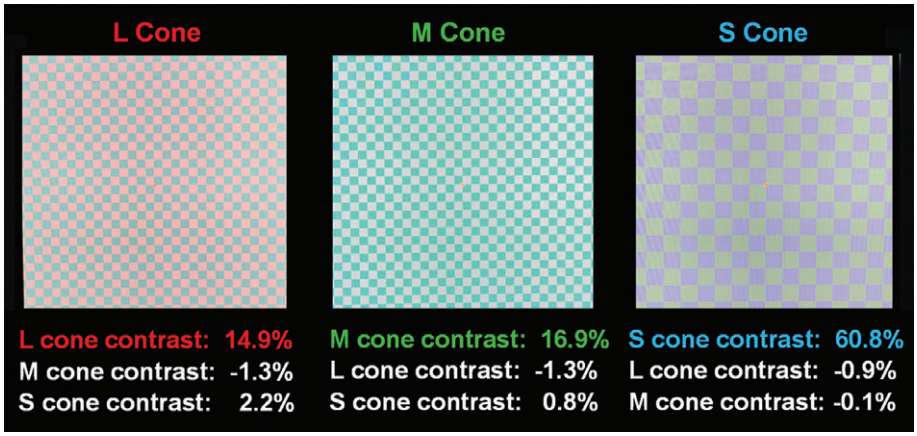

Figure 1. L, M and S cone checkerboards patterns used for pattern-onset visual evoked potentials. The checks appeared as increments to the grey background. Weber contrast values are colour-coded for each cone type, while white text is in contrast to other cones near or below threshold for detection.

affixed to earlobes. Subjects adapted to the grey background for six minutes prior to testing.

Figure 1 shows cone VEP displays, which isolate L, M and S cone stimulation based on silent substitution, for example, the reddish L cone checks stimulate L cones at a significantly higher level than the grey background but stimulate M and S cones at the same level as the grey background, thus limiting stimulation to L cones with each checkerboard onset. The same approach is used for M and S cones. This approach does create a small amount of luminance contrast (two to four per cent) for L and M stimuli, while the S cone stimulus is isoluminant. The stimulus is based on the Cone Contrast Test (CCT, Innova Systems, Inc.) which presents letters of decreasing cone contrast to determine L, M and S cone contrast thresholds for CVD diagnosis.[9] The cone contrasts chosen for this study were approximately 10 times higher than L, M and S CCT thresholds to elicit robust VEPs, which would readily separate CVDs and colour vision normal (CVN) subjects. In the present study binocular and monocular cone-specific VEPs were recorded from 12 CVD subjects (mean age: 29 ± 12 years) and 17 CVN subjects (mean age: 32 ± 11 years) confirmed to be CVD or CVN on a battery of colour vision tests including the Ishihara pseudo-isochromatic plates, Oculus HMC Anomaloscope (Oculus, Inc) and CCT. All CVD subjects were confirmed to be protanomalous (n = 4) or deuteranonomalous (n = 8) by anomaloscope testing (mean and standard deviation from normal midpoint: 17 ± 3; mean matching range: 14 ± 12) and by CCT (39 ± 14; normal 75 or more on scale of 100; Table 1). All subjects were recruited from university patients, students, faculty and staff, had 6/6 visual acuity, no history of ocular, systemic or neurologic disease and provided written informed consent to participate in our Institutional Review Board approved protocol. Two-way analysis of variance (ANOVA) and post-hoc t-tests were used to compare binocular to monocular VEP amplitudes and post-hoc paired and unpaired t-tests were used to identify specific differences. Binocular enhancement of VEPs was quantified by computing the binocular/monocular VEP amplitude ratios.

Number	Gender/ Age	CVD type	Anomaloscope matching midpoint*	Anomaloscope matching range*	CCT score (CVD cone)*
1	M/52	Deuteranomalous	16.4	10.9	50
2	M/31	Deuteranomalous	18.6	12.3	37.5
3	M/37	Deuteranomalous	17.2	9.3	60
4	M/27	Deuteranomalous	20.7	37.1	32.5
5	F/25	Deuteranomalous	23.3	33.8	30
6	M/25	Deuteranomalous	25.4	26.6	40
7	M/20	Deuteranomalous	20.7	22.6	55
8	M/42	Deuteranomalous	17.6	5.3	45
9	M/22	Protanomalous	56.9	2.3	12.5
10	M/52	Protanomalous	53.1	6.5	30
11	M/27	Protanomalous	55.7	7.7	25
12	F/28	Protanomalous	57.1	1.5	55

*Normal anomaloscope midpoint: 36–44, range: <5; normal CCT score: ≥75.
CCT: Cone Contrast Test, CVD: colour vision deficiency.

Table 1. Characteristics of colour vision deficient subjects (mean of right and left eyes)

RESULTS

Figure 2A shows monocular and binocular VEPs from CVN, protanomalous (red deficient) and deuteranomalous (green deficient) subjects. Protanomalous and deuteranomalous CVDs show significantly decreased monocular amplitudes and delayed latencies for the cone corresponding to their CVD as reported recently;[8] however, CVDs show increased binocular/monocular amplitude ratios for the VEP corresponding to their CVD: the protan shows binocular facilitation (enhancement greater than twice) for the L cone VEP; the deutan shows binocular facilitation for the M cone VEP.

In CVNs two-way repeated-measures ANOVA across viewing condition (binocular versus monocular) and cone type (L, M, S) showed no significant differences in VEP amplitude for viewing ($F = 2.51$, $p = 0.09$) or cone type ($F = 1.81$, $p = 0.18$). CVDs showed significant differences between monocular and binocular viewing

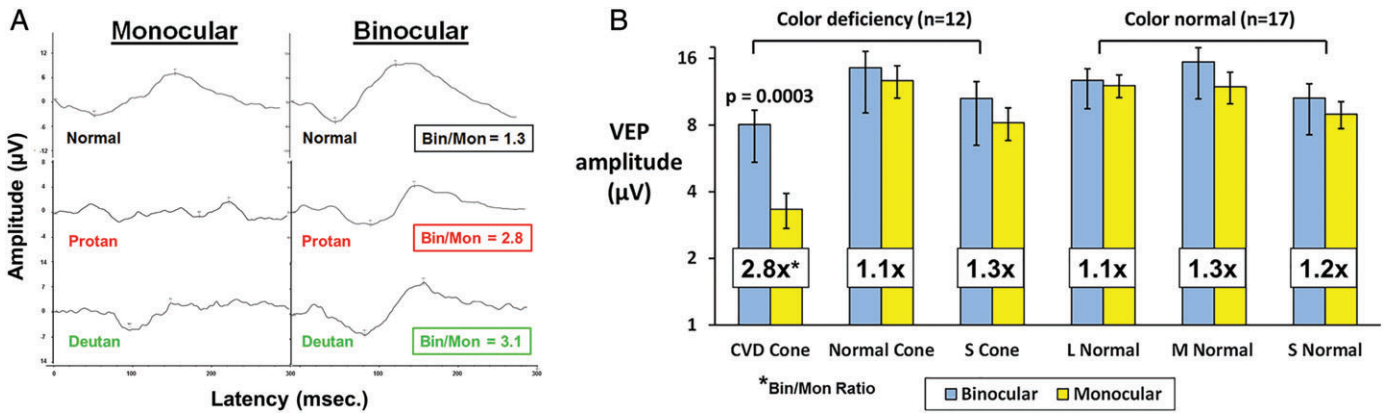

Figure 2. (A) Monocular and binocular visual evoked potentials (VEPs) are shown for normal, protanomalous and deuteranomalous subjects. Binocular/monocular amplitude ratios are indicated with colour vision deficiencies (CVDs) showing binocular facilitation (bin/mon two or more). VEP amplitudes were measured from the first prominent negative trough to the subsequent positive peak. (B) Mean (± 1 SE) binocular and monocular VEP amplitudes (μV) for CVD and colour vision normal (CVN). CVD means include the anomalous cone (L cone for protans, M cone for deutans), the normal cone type and S cones. Means for CVN include L, M and S cones. Boxes show the ratio of binocular/monocular amplitudes. The only significant difference is between CVD binocular and monocular amplitudes.

(F = 3.94, p = 0.05) and cone type (CVD cone, normal cone, S cone; F = 9.44, p = 0.0002). Post-hoc two-tailed paired t-tests showed that the only significant difference in CVDs was between binocular and monocular VEP amplitudes for the cone type of their CVD (t = 2.59, p = 0.0003). These findings are illustrated in Figure 2B showing mean (±1 SE) binocular and monocular VEP amplitudes (μV) for CVD and CVN subjects. Means for CVD include the anomalous cone (L cone for protans, M cone for deutans), the normal cone type and S cones. Means for CVN include L, M and S cone amplitudes. The boxes show the ratio of binocular/monocular amplitudes. Substantial binocular facilitation (2.8 times) occurs in CVDs for the cone type of their deficiency.

DISCUSSION

We found that anomalous trichromats show binocular facilitation of the VEP signal for the cone type corresponding to their CVD. By comparison, much less VEP signal enhancement was observed in CVD and CVN subjects for normal cone types. As CVD is typically assessed with smaller, foveal stimuli, our findings using wider-field binocular stimulation raise the possibility that enhanced colour perception may occur in CVD for stimuli across a more extensive area of the visual field. This finding may relate to binocular visual field enhancement in glaucoma,[1,2] as well as improved colour vision in anomalous trichromacy at supra-threshold levels of stimulation, which has been attributed to post-receptoral processing.[6,7] The present results, showing very diminished monocular CVD VEP signals but binocular signals nearly three times larger suggest that binocularity may also enhance colour vision in anomalous trichromacy. Potential mechanisms could include field-specific increases in anomalous cone numbers and/or photopigment density and/or central processing driven by impoverished cone signals during development. Alternatively, it is conceivable that monocular VEP signals arising from normal cones approach amplitude saturation and thus, show much less enhancement binocularly, while the weak signals from impoverished cones, which receive less cone contrast add to yield large-signal VEPs; however, it seems unlikely that a three times increase in signal would eventuate from simple addition of weak signals unless stimulus contrast was effectively amplified as well, as proposed for anomalous trichromacy, based on psychophysical measurements and modelling.[6,7]

Additionally, parvocellular chromatic signals show less saturation than magnocellular luminance signals with increasing contrast.

While it is conceivable that the enhanced VEP binocular signals from CVDs represent luminance artefacts adding to weak signals from the CVD cones, this is unlikely given the small amount of luminance contrast in the L and M cone stimuli (two to four per cent), while the S cone stimulus was isoluminant. It is also possible that the large field introduced peripheral luminance artefacts, which enhanced the signal in VEPs but such intrusions minimally impact chromatic VEP signals.[10]

Limitations of this study include the relatively small number of subjects coupled with the speculative relationship between VEP signal enhancement and evidence of CVD compensation,[6,7] as well as field retention in glaucoma.[1,2] Additional research including cone-specific measures of visual field sensitivity in CVD and comparisons between binocular and monocular VEPs in glaucoma is warranted.

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