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The relationship between perifoveal achromatic, L- and M-cone acuity and retinal structure as assessed with multimodal high resolution imaging

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ABSTRACT

The relationships between perifoveal measures of achromatic-, L- and M-cone acuity and retinal structure were investigated in healthy young males. Thirty-two males, aged 20–39 years, with normal foveal logMAR letter acuity and no observed ocular abnormalities participated in the study. Achromatic and isolated L- and M-cone spatial acuity was measured in the dominant eye with a Sloan E letter of 90% achromatic decrement contrast or 23% increment cone contrast, respectively. Separately, the central part of the same eye was imaged with high-resolution spectral-domain optical coherence tomography (SD-OCT) and adaptive optics ophthalmoscopy (AOO). Thickness measures and cone density in the fovea and parafoveal region were not correlated with perifoveal structural measures. A significant correlation was observed between thicker retinal pigment epithelium (RPE) complex, higher cone density and better L-cone logMAR at 5 deg eccentricity, but not for achromatic or M-cone logMAR. The results imply that single letter perifoveal L-cone acuity, rather than achromatic acuity, may provide a useful measure for assessing the structure-function relationship and detecting early changes in the perifoveal cone mosaic.

1. Introduction

The cone photoreceptors in the central retina are essential for normal visual function such as spatial and color vision. The standard clinical measures for optimizing correction of refractive errors as well as detection of central retinal changes is measurement of foveal high-contrast achromatic letter acuity, usually referred to as visual acuity. Visual acuity is typically measured using rows of equally spaced black letters on a white background (decrement contrast), where the smallest resolvable letter represents the individual's visual acuity. But, foveal visual acuity is not a reliable measure in terms of detecting mild to moderate structural changes in the central retina (Klein, Wang, Klein, Moss, & Meuer, 1995; Neelam, Nolan, Chakravarthy, & Beatty, 2009)

In some normal healthy individuals, it has been shown that, when bypassing or compensating for refractive errors and optical aberrations, foveal spatial acuity can be predicted by the cone density, whereas parafoveal spatial acuity can be predicted by the midget ganglion cell density (Enoch & Hope, 1973; Rossi & Roorda, 2010; Thibos, Cheney, & Walsh, 1987; Williams & Coletta, 1987). Clinically measured foveal or near-foveal visual acuity, however, remains within normal limits even in observers with degenerative retinal conditions who have less than half the normal cone density (Carroll et al., 2009; Michaelides et al., 2011; Ratnam, Carroll, Porco, Duncan, & Roorda, 2013). Spatial resolution in the fovea also depends on neural contrast sensitivity and spatial resolution improves with increasing contrast within the central 5 deg (Green, 1970). Uncompensated aberrations will not only cause blur, but also reduce contrast. It is therefore likely that individuals with relatively high foveal cone density may oversample a spatial acuity task, if refractive errors and/or higher-order aberrations are not compensated for in full, due to a redundancy of cones. Thus, a large fraction of cones may need to be lost before it can be

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measured functionally (Choi et al., 2006, Ratnam et al., 2013). In addition, it appears as if foveal cones somehow are protected to a larger degree than para- and peri-foveal cones, both with regards to ageing (Curcio, 2001; Song, Chui, Zhong, Elsner, & Burns, 2011) and disease (Sandberg & Berson, 1983). The question is: will changes in visual acuity beyond the fovea be more telling of early structural changes?

Until now, there have been no studies on the relationship between retinal structure and spatial acuity in the perifovea. The hypothesis is that there is less redundancy of cones in the perifovea and less oversampling, even if refractive errors and/or higher-order aberrations are not compensated for in full. A correlation may therefore exist between a psychophysical measure of single letter acuity and retinal structure at this location, even in normal healthy individuals. Another attractive feature about measuring in the perifovea and particularly around 5 deg of eccentricity, is the assumed 1:1 relationship between cones and midget ganglion cells (Dacey, 1993). In this study, the relationship between achromatic and cone-type isolating measures of single letter acuity and the characteristics of retinal layers and cone mosaic in the temporal perifovea were examined in normal healthy individuals. Single letter achromatic and cone isolated acuity were measured with a Sloan E at 5 deg eccentricity. Multimodal high-resolution imaging was employed to examine the outer retina in healthy males with normal or defective color vision.

2. Participants and methods

The study was designed as an observational study, and men aged 18–40 years who were available for participation at the University College in Kongsberg between January 2014 and January 2015 were invited to participate. To identify suitable participants, an initial assessment included history and symptoms, habitual visual acuity measured with a digital high-contrast logMAR chart at 2.3 m (TestChart 2000, Thomson Software Solutions, London, UK), stereoacuity measured at 40 cm with the TNO test for stereoscopic vision (16th edition: Lameris Ootech B.V., Nieuwegein, Netherlands), objective monocular refraction measured with the Nidek AR-1000 autorefractor (Nidek Co., Ltd., Aichi, Japan), axial length, corneal curvature and anterior chamber depth measured with the IOLMaster (Carl Zeiss Meditec AG, Jena, Germany). Each observer's color vision was examined with the Ishihara (24 pl. ed., Kanehara Trading INC, Tokyo, Japan, printed 2005) and the Hardy-Rand-Rittler 4th edition (HRR: Richmond Products, Albuquerque, NM) pseudoisochromatic plates under controlled illumination in a dark room with the lamp "True Daylight Illuminator with Easel" (correlated color temperature 6200 K, model number 1339R, Richmond Products, Albuquerque, NM). The level of illumination was measured at the surface of the test plates with a digital lux meter (Hagner Model EC1, Hagner AB, Solna, Sweden), and averaged about 800 lx. The initial assessment took about 20 min for each participant. Men with corrected-to-normal visual acuity ($\leqslant$0.1 logMAR), normal stereo acuity ($\leqslant$120 arc seconds), without any known ocular pathology, former intraocular or refractive surgery and/or systemic diseases were invited to participate in the rest of the study. Fifty-six of 71 men who participated in the initial assessment met the inclusion criteria; 32 volunteered to participate in the main study. The L and M pigment genes are located on the X chromosome. Only men, who have a single X chromosome, were included in this study to avoid the confounding effects of polymorphisms commonly found in females (Dees, Gilson, Neitz, & Baraas, 2015).

The main study consisted of four sets of approximately 1-h examinations carried out on separate days in random order: color vision testing, perifoveal measures of visual acuity, fundus photography, spectral-domain optical coherence tomography (SD-OCT) and adaptive optics ophthalmoscopy (AOO) retinal imaging.

2.1. Color vision testing

Each individual's color vision was examined with Rayleigh anomaloscopy (Oculus HMC Anomaloscope MR (Typ 47700), Oculus Optikergäte GmhB, Wetzlar, Germany) and the Cambridge Color Test (CCT) trivector test was performed twice (Cambridge Research Systems Ltd, Cambridge, United Kingdom) following standard procedures.

2.2. Perifoveal measures of single letter visual acuity

Achromatic and isolated L- and M-cone spatial acuity was measured in the dominant eye with a Sloan E letter of 23% increment cone contrast and 90% achromatic decrement contrast, the latter as a control. The background was always 10 cd/m^2 with chromaticity metameric to CIE illuminant D65 (0.313, 0.329; appears grey for the luminance level used). The CIE (x, y, Y)-coordinates of the L- and M-cone isolating Sloan E stimulus at 23% was (0.385, 0.316, 11.5) and (0.234, 0.382, 10.8), respectively. Cone excitations were calculated from the CIE (1931) (x, y, Y) coordinates using Smith & Pokorny (1975) cone fundamentals based on transformations from Cole and Hine (1992) and Judd (1951) color matching functions. Relative (Weber) cone contrasts between the Sloan E and the background were calculated for each cone type (Cole & Hine, 1992). The stimuli were displayed on a calibrated 22-inch CRT monitor (ViewSonic P227f, ViewSonic Corporation, Walnut CA, USA) via an nVidia Quadro FX2000 graphics card (NVIDIA Corporation, Santa Clara, CA, USA) at resolutions of: 30 bits per pixel spectral; 1600 $\times$ 1200 pixels spatial; 100 Hz temporal. To ensure the chromatic stability of the monitor, colorimetric values were measured with a spectrophotometer (SpectraScan PR650, Photo Research Inc., Chatsworth, CA, USA) before any experiments were carried out. Errors in the displayed CIE (x, y, Y) coordinates of test patches were <0.005 in (x, y) and <5% in Y (within the range of light levels of the stimuli). Observers were corrected to best logMAR letter acuity and viewed the stimuli monocularly (using their preferred eye with natural pupils) from a distance of 229.2 cm. Refractive error was calculated as spherical equivalent refraction (SER) which equals spherical power + 0.5 $\times$ cylinder power in diopters [D]. The size of the stimulus was calculated as the minimum angle of resolution MAR [in minutes of arc (arcmin)] (Weymouth, 1958). The smallest stimulus possible was MAR = 1.2 (just slightly larger than the minimum resolvable Sloan E size of 5 pixels) and the largest was about MAR = 80 (limited by the height of the monitor). The experiment was carried out in an otherwise darkened room. Prior to each experiment, the participants were dark adapted for three minutes, then light adapted for one minute by viewing a neutral grey screen with the same color and luminance as the background of the stimuli. The Sloan E was presented at 5 deg temporal eccentricity. Correct fixation was verified with an eye tracker, which monitored direction of gaze 120 times per second (ASL Eye Tracking System Model 5000, Applied Science Laboratories, Bedford, MA, USA). A trial was repeated (with a different orientation of the Sloan E) if the participant's gaze deviated more than 1.5 deg from the fixation point for more than 80 ms. A four-alternative forced-choice procedure was implemented, and the size of the Sloan E was altered using a double staircase employing a two-down/two-up and three-down/one-up rule (Wetherill & Levitt, 1965). The staircase step size was N/24, where N was the range of initial testing contrasts, except the first 5 reversals which used step sizes of 6N/24, 3N/24, 2N/24, 1.5N/24 and 1.2N/24 respectively. This strategy quickly localized the participant's threshold and still retained a sufficiently small step size for

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