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Directionality of individual cone photoreceptors in the parafoveal region

Hugh J. Morris [a,*], Leonardo Blanco [a,1], Johanan L. Codona [b], Simone L. Li [c], Stacey S. Choi [a], Nathan Doble [a]

[a] College of Optometry, The Ohio State University, 338 West Tenth Avenue, Columbus, OH 43210, USA
[b] Steward Observatory, University of Arizona, Tucson, AZ 85721, USA
[c] Laboratory of Visual and Ocular Motor Physiology, Akron Children's Hospital, Akron, OH 44224, USA

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ABSTRACT

The pointing direction of cone photoreceptors can be inferred from the Stiles–Crawford Effect of the First Kind (SCE-I) measurement. Healthy retinas have tightly packed cones with a SCE-I function peak either centered in the pupil or with a slight nasal bias. Various retinal pathologies can change the profile of the SCE-I function implying that the arrangement or the light capturing properties of the cone photoreceptors are affected. Measuring the SCE-I may reveal early signs of photoreceptor change before actual cell apoptosis occurs. In vivo retinal imaging with adaptive optics (AO) was used to measure the pointing direction of individual cones at eight retinal locations in four control human subjects. Retinal images were acquired by translating an aperture in the light delivery arm through 19 different locations across a subject's entrance pupil. Angular tuning properties of individual cones were calculated by fitting a Gaussian to the reflected intensity profile of each cone projected onto the pupil. Results were compared to those from an accepted psychophysical SCE-I measurement technique. The maximal difference in cone directionality of an ensemble of cones, $\bar{\rho}$, between the major and minor axes of the Gaussian fit was 0.05 versus 0.29 mm^{-2} in one subject. All four subjects were found to have a mean nasal bias of 0.81 mm with a standard deviation of ±0.30 mm in the peak position at all retinal locations with mean $\bar{\rho}$ value decreasing by 23% with increasing retinal eccentricity. Results show that cones in the parafoveal region converge towards the center of the pupillary aperture, confirming the anterior pointing alignment hypothesis.

1. Introduction

It is widely accepted that the human retina is directionally sensitive to incoming light, i.e., light entering the eye through the center of the pupil appears brighter to an observer than the same intensity light entering at the edge. This phenomenon is known as the Stiles–Crawford Effect of the First Kind (SCE-I) and was first discovered in 1933 (Stiles & Crawford, 1933). The effect is also apparent for light reflected from the retina (Di Francia & Ronchi, 1952) and this is sometimes termed the optical SCE (OSCE). The waveguide properties of the cone photoreceptors are thought to be responsible for the directional dependence (Enoch, 1963; Westheimer, 1967, 2008), although other models have been proposed (Vohnsen, 2014). Foveal cones were found to have a lower directionality to light than cones in adjacent retinal regions (Westheimer, 1967).

It has been demonstrated that various eye conditions and diseases have an altered SCE-I function. In myopic eyes, a systematic nasal shift in the peak position of the SCE-I function in the nasal retina with an increase in myopia has been reported (Choi, Enoch, & Kono, 2004; Choi, Garner, & Enoch, 2003). The alignment of cone photoreceptors in the nasal retina was tilted towards the optic nerve head due to the tractional forces associated with the axial elongation of the eye. Changes in the SCE-I function have also been found in a number of ocular diseases such as central serous choriodopathy (Smith, Pokorny, & Diddie, 1978), retinitis pigmentosa (Birch, Sandberg, & Berson, 1982), age related macular degeneration (Kanis, Wisse, Berendschot, van de Kraats, & van Norren, 2008) and a range of other retinal conditions (Bedell, Enoch, & Fitzgerald, 1981; Keunen, Smith, Pokorny, & Mets, 1991; Lakshminarayanan, Bailey, & Enoch, 1997; Lardenoye, Probst, DeLint, & Rothova, 2000; Smith, Pokorny, & Diddie, 1988).

Abbreviations: SCE-I, Stiles–Crawford Effect of the First Kind; OSCE, Optical Stiles–Crawford Effect; SLO, scanning laser ophthalmoscope; OCT, optical coherence tomography; AO, adaptive optics; SH-WFS, Shack–Hartmann wavefront sensor; DM, deformable mirror; SLD, superluminescent diode; MP, moving pupil.

* Corresponding author.
E-mail addresses: morris.1085@osu.edu (H.J. Morris), blanco.leonardo@gmail.com (L. Blanco), jlcodona@gmail.com (J.L. Codona), lli@chmca.org (S.L. Li), choi.1080@osu.edu (S.S. Choi), doble.2@osu.edu (N. Doble).
[1] Present address: Laboratoire d'Optique Appliquée, ENSTA ParisTech, CNRS, Ecole Polytechnique, Université Paris-Saclay, 828 bd des Maréchaux, 91762 Palaiseau Cedex, France.

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Bresnick, Smith, and Pokorny (1981) showed changes in the SCE-I function in diabetic retinopathy, however no changes were observed in diabetes mellitus (Zagers, Pot, & van Norren, 2005). It is well accepted that the SCE-I has its origin at the retina, hence measuring the SCE-I function in patients with retinal disease could potentially detect changes in the photoreceptors at a much earlier stage.

The SCE-I function was first measured psychophysically at various retinal locations to understand the arrangement of cones throughout the retina and their efficiency for capturing incoming light. Laties and Enoch performed extensive studies characterizing trans-retinal photoreceptor alignment using histological sections (Laties & Enoch, 1971) and determining the psychophysical implications for living human subjects (Enoch & Laties, 1971). They proposed 3 hypotheses for the trans-retinal alignment of the cones: (1) anterior pointing, (2) center pointing and (3) parallel pointing. The anterior pointing hypothesis predicts that if the photoreceptors are pointing towards the center of the pupillary aperture of the eye, the peak of the SCE-I function should not change with a change in the retinal location. If the center pointing hypothesis holds (i.e., photoreceptors are pointing towards the center of rotation of the eye), the peak of the SCE-I function would become progressively displaced from the center of the pupil as the retinal location is moved away from the posterior pole of the eye. The third hypothesis, parallel pointing, assumes that all the photoreceptors are parallel to each other, which would mean the peak of the SCE-I function moves out of pupillary aperture after a certain eccentricity of retinal locations in a direction exactly opposite to that would be predicted for the center pointing hypothesis. It has been shown that the anterior pointing alignment hypothesis holds true for human eyes, although there was one reported case where a non-amblyopic eye had a center pointing trans-retinal alignment whereas the fellow amblyopic eye had normal anterior pointing alignment; the implication of this finding was inconclusive (Bedell & Enoch, 1980) and contrary evidence has been offered since it was first reported (Delint, Weissenbruch, Berendschot, & van Norren, 1998). Although the SCE-I function in human eyes has been extensively studied through psychophysical measurements, it requires lengthy sessions and high level of concentration from the subjects, hence it is difficult to apply clinically (Applegate & Lakshminarayanan, 1993).

Reflectometric techniques can be used to measure the OSCE and are faster, objective and subject-friendlier while producing similar estimations for the peak position of the SCE-I function as in psychophysical measurements. However, the magnitude of cone directionality, ρ, within the sampled retina has consistently been twice as high compared to that of psychophysical measurements (He, Marcos, & Burns, 1999). Gorrand and Delori analyzed the distribution of reflected light at the pupil plane to determine photoreceptor alignment (Gorrand & Delori, 1995). This approach was further developed by Burns, Wu, Delori, and Elsner (1995) to image the full pupil plane distribution for a single entrance pupil position.

Another objective technique of measuring the OSCE function is through in vivo imaging of the retinal surface. Delint et al. used a custom-built scanning laser ophthalmoscope (SLO) to measure the fundus reflectance as a function of entrance pupil position (Delint, Berendschot, & vanNorren, 1997). Rativa and Vohnsen used the same imaging modality this time with adaptive optics (AO) to measure the angular tuning of individual cones (Rativa & Vohnsen, 2011). The OSCE can also be exploited to optimize the quality of cone images taken with a non-AO-SLO (Vohnsen, Iglesias, & Artal, 2004). An AO-OCT system has been used to measure the directional properties of various retinal layers (Gao, Cense, Zhang, Jonnal, & Miller, 2008).

In 2002, Roorda and Williams used an AO-flood illuminated fundus camera to measure individual cone pointing and angular tuning on two control subjects at 1° in the nasal retina (Roorda & Williams, 2002). Their results confirmed that the disarray in the pointing direction of individual cones was very small, as suggested by previous histological studies (Laties & Enoch, 1971) and showed that the angular tuning properties of an ensemble of cones is essentially the same as that of an individual cone.

In this study, the method of Roorda and Williams was employed to measure both cone pointing direction in the pupil and the degree of disarray in the alignment within the sampled retina on a single cone basis in 6 eyes of four control human subjects at eight retinal locations, so that the point of convergence could be investigated. The data was fitted with a generalized 2D elliptical Gaussian function. Psychophysical SCE-I measurements based on the method described by Choi et al. (2003) were also taken on two of the four subjects to validate the AO based OSCE measurements. The directionality of individual cones and cone ensembles are discussed and compared to published literature.

2. Methods

2.1. Subjects and imaging locations

Four control subjects (N1, N2, N3 and N4) with an age range of 21–42 years were recruited. All had a corrected Snellen acuity of 20/15, with refractive errors not exceeding ±2.75 D sphere and −0.75 D cylinder. Subject details are provided in Table 1. All four subjects were tested at 8 retinal locations in their right eye, namely 2° and 4° in the temporal retina (TR), nasal (NR), superior (SR) and inferior (IR). For subjects, N1 and N2, the same 8 retinal locations were also imaged in the left eye. The presence of abnormal ocular media and retinal disease was ruled out by a conventional eye exam, including slit lamp examination and ophthalmoscopy. Subjects were dilated with one drop of 1% tropicamide and one drop of 2.5% phenylephrine prior to AO imaging. A bitebar was used during imaging to minimize head motion. The tenets of the Declaration of Helsinki were observed and the protocol was approved by the Institutional Review Board of The Ohio State University (OSU). Written informed consent was obtained after all procedures were fully explained to the subjects and prior to any experimental measurements.

2.2. Adaptive optics fundus camera

The angular tuning properties of cones were measured using the AO-flood illuminated fundus camera at the OSU College of Optometry. Its primary characteristics have been reported previously (Headington, Choi, Nickla, & Doble, 2011), but several modifications were required for the work described here. Fig. 1 shows the layout with three primary changes: (i) an extra camera was added to the AO corrected path to constantly monitor the pupil position, (ii) the imaging light source was changed from a Hg–Xe arc-lamp to an SLD source (680 ± 20 nm) coupled into a multimode fiber (125 μm core diameter). The fiber output was collimated before being incident onto a motorized moving pupil (MP) aperture. The MP was used to control both the size and position of the incident imaging beam onto the entrance pupil of the eye. The collimated beam diameter at the MP plane was large enough to allow for testing anywhere within a 4 mm diameter entrance pupil at the eye. The beam diameter was 1.6 mm at the eye with a 0.5° field of view at the retina. The uniformity of the illumination profile was verified using a CCD camera mounted in the retinal plane of a model eye. The SLD light source allowed for faster imaging at ∼60 Hz. Finally, (iii) the Hg–Xe arc-lamp was repurposed as a bleaching source introduced into the system via a motorized flip mirror. This source also provided the 4° diameter background field