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Influence of higher order aberrations and retinal image quality in myopisation of emmetropic eyes

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ABSTRACT

Refractive error, higher order aberrations (HOA), axial length (AL), anterior chamber depth (ACD) and average corneal radius of curvature were measured after cycloplegia from 166 emmetropic participants at the Sydney Myopia Study (SMS, 2004–2005, age 12.63 ± 0.48 years). Measurements were repeated approximately 5 years later at the Sydney Adolescent Vascular and Eye Study (SAVES, 2009–2010, age 17.08 ± 0.67 years). The baseline spherical equivalent (*M*) did not differ significantly between the participants lost to follow-up (65%) and the participants enrolled in SAVES study ($p = 0.932$). Refractive error and HOA were measured using a Shack-Hartmann aberrometer for a pupil diameter of 5 mm and AL, ACD and average corneal curvature measured using IOL Master at both visits. Retinal image quality in terms of Visual Strehl ratio (VSOTF) for a 5 mm pupil diameter was determined using on-axis lower and HOA. General linear model was used to determine the association of HOA and retinal image quality with change in refraction. Of the 166 emmetropes, 41 (25%) had myopic change (change in $M > -0.50$ D) and 125 (75%) had no change in refraction (change in *M* between +0.49 D and −0.49 D). Change in C[4,0] ($p < 0.001$, $R^2 = 0.236$), fourth order RMS ($p = 0.003$, $R^2 = 0.097$) and coma RMS ($p = 0.004$, $R^2 = 0.056$) from baseline were significantly correlated with change in refraction. More positive change in C[4,0] was associated with lesser myopic change in refraction. The eyes with myopic change in refraction decreased in positive C[4,0] (at baseline = +0.049 ± 0.05 μm, at follow-up = +0.024 ± 0.05 μm, $p < 0.05$). In comparison, eyes with no change increased in positive C[4,0] (at baseline = +0.033 ± 0.04 μm, at follow-up = +0.047 ± 0.04 μm, $p < 0.05$). Thus in conclusion, no significant association was observed between HOA and retinal image quality at baseline and development and progression of myopia among emmetropic eyes. The change in spherical aberration (C[4,0]) with myopic change is possibly associated with changes occurring in crystalline lens during ocular growth.

1. Introduction

Abnormal or high levels of higher-order aberrations (HOA) or variations in specific individual aberrations and degraded retinal image quality due to HOA are considered to play an important but weak role in myopiagenesis (Charman, 2005). Specific individual aberrations such as spherical aberration have been hypothesised to have the potential to disrupt emmetropisation, with negative spherical aberration inducing myopic ocular growth and positive spherical aberration retarding ocular growth (Collins & Wildsoet, 2000).

Several studies have attempted to determine the role of HOA in 'myopisation' by investigating the mean levels of aberrations in different refractive error groups, but the results are equivocal (Collins, Wildsoet, & Atchison, 1995; Porter, Guirao, Cox, & Williams, 2001; Carkeet, Luo, Tong, Saw, & Tan, 2002; He et al., 2002; Marcos, 2002; Paquin, Hamam, & Simonet, 2002; Cheng, Bradley, Hong, & Thibos, 2003; Llorente, Barbero, Cano, Dorronsoro, & Marcos, 2004; Radhakrishnan, Pardhan, Calver, & O'Leary, 2004; Buehren & Collins, 2006; Kirwan, O'Keefe, & Soeldner, 2006; Atchison, Schmid, & Pritchard, 2006; Jinhua Bao, Wu, Shen, Lu, & He, 2009; Martinez, Sankaridurg, Naduvilath, & Mitchell, 2009; Thapa, Fleck, Lakshminarayanan, & Bobier, 2011; Zhang et al., 2013). Some of the aforementioned studies reported myopic eyes to have high levels of HOA in comparison to non-myopic eyes (Buehren & Collins,

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2006; Collins et al., 1995; He et al., 2002; Kirwan, O'Keefe, & Soeldner, 2006; Marcos, 2002; Paquin et al., 2002; Radhakrishnan et al., 2004). High myopic eyes were reported to have high SA (Kirwan, O'Keefe, & Soeldner, 2006), coma (Paquin et al., 2002), 3rd-order and higher-order aberrations (Kirwan, O'Keefe, & Soeldner, 2006; Marcos, 2002) compared to low myopic or non-myopic eyes. Radhakrishnan et al. reported high but non-significant ($p = 0.08$) 4th-order SA in myopic eyes compared to non-myopic eyes (Radhakrishnan et al., 2004). Buehren et al. reported that myopic eyes possess high 4th, 5th and higher-order aberrations compared to emmetropic eyes (Buehren & Collins, 2006). A recent study reported higher amount of total HOA, coma RMS and third order RMS in eyes with fast progressing myopia (myopia progression $\geqslant$ 0.50 D) compared to slow progressing myopia ($\leqslant$0.50 D) (Zhang et al., 2013). Interestingly few studies have reported less 4th order (Collins et al., 1995), less SA (Kwan, Yip, & Yap, 2009; Marcos, 2002), less positive C[4,0] (Carkeet et al., 2002), less 3rd and higher-order aberrations (Kwan et al., 2009) in myopic eyes compared to non-myopic eyes.

Hyperopic eyes were observed to have high 3rd order, SA, higher-order aberrations and C[4,0] compared to myopic (Llorente et al., 2004) or emmetropic eyes (Martinez et al., 2009; Thapa et al., 2011). Yet other studies found no difference in aberrations between various refractive error groups (Atchison et al., 2006; Cheng et al., 2003; Jinhua Bao et al., 2009; Porter et al., 2001).

In addition to the results being equivocal, the studies were cross-sectional in nature and hence were unable to establish a clear understanding on the role of HOA in the development or progression of myopia.

This study aims to determine the role of HOA and the associated retinal image quality in 'myopisation' of emmetropic eyes. To achieve this aim, children who were emmetropic at baseline visit (mean age 12 years) were followed up after 5 years to determine if HOA and the associated retinal image quality was associated with the development of myopia in these eyes.

2. Methods

On-axis aberrations of the eyes of 678 adolescents aged 16–19 years were measured as part of the Sydney Adolescent Vascular and Eye Study (SAVES, June 2009–August 2010) and previously as part of the Sydney Myopia Study (SMS, 2004–2005) (Ojaimi et al., 2005). Of the 678 adolescents, 176 were emmetropic, 95 were myopic and 375 were hyperopic at the baseline visit (Sydney Myopia Study, 2004–2005).

The SAVES study followed the tenets of the Declaration of Helsinki and was approved by the Human Research Ethics Committee, University of Sydney and the New South Wales State Department of Education and Training, Australia. Written informed consent was obtained from at least one parent of each participant who was below 18 years of age and directly from the participants aged 18 years or above. Aberration data from both eyes were obtained, however data from only one eye (right eyes only) were analyzed due to the correlation observed between both eyes (Thibos, Hong, Bradley, & Cheng, 2002). Participants wearing contact lenses, those with astigmatism $\geqslant -1.00$ DC and those with ocular pathology were excluded from the analysis.

All eyes were cyclopleged prior to measurements as per the protocol of the SMS and SAVES studies. Briefly, the procedure involved instilling a drop of topical anesthetic (1% amethocaine hydrochloride, MINIMS, Chauvin Pharmaceuticals Ltd., London, England) in both eyes to enhance absorption of the cycloplegic drops (Mordi, Lyle, & Mousa, 1986). This was followed by one drop of cyclopentolate 1% and one drop of tropicamide 1% (MINIMS, Chauvin Pharmaceuticals Ltd., London, England). Drugs were instilled in two cycles, with an interval of 5 min between the two cycles. An additional two drops of phenylephrine 2.5% were administered in subjects who had dark irides. Aberrometry and ocular biometric measurements were performed 25–30 min after the instillation of the last drop to ensure no residual accommodation was present.

Refractive error and total ocular aberrations were obtained using a Shack-Hartmann aberrometer (Complete Ophthalmic Analysis System™, COAS™, version 1.41.05, Wavefront Sciences Inc, Albuquerque, NM, USA) at both visits. The method used by the COAS to compute aberrations has been described elsewhere (Salmon & van de Pol, 2005; Thibos, 2000). The aberrations were calculated at a reference wavelength of 550 nm. The COAS aberrometer uses the line of sight as the reference axis and the pupil diameter was set at 5 mm for analysis. Zernike coefficients were fitted up to 6th order using the standards recommended by the Optical Society of America (OSA) (Thibos, Applegate, Schwiegerling, & Webb, 2000). Participants were asked to rest the forehead and chin against forehead band and chin rest respectively to minimize the pupil misalignment. Thereafter while recording aberrometry measurements, participants were asked to blink and the measurements were taken. Measurements were repeated till an acceptable measurement was obtained. Thus for all the participants a maximum of three readings were taken. Acceptable measurement was determined after rechecking each Shack-Hartmann grid pattern of these three measurements. The measurement in which the Shack-Hartman grid pattern was complete with no local irregularities or variations in shape was acceptable and was saved at the screening site for analysis.

Refractive errors were calculated using power vectors (M, J_0 and J_{45}) from 2nd and 4th-order Zernike coefficients (Atchison, 2005). The root mean square (RMS) of 3rd-order, 4th-order, HOA (3rd and 4th-orders), spherical aberration (C[4,0]) and coma (C[3,−1] and C[3,1]) was also calculated.

The Visual Strehl ratio computed in the frequency domain and based on the optical transfer function (VSOTF) was used as the metric for retinal image quality. This was computed from the measured wavefront aberrations for a pupil diameter of 5 mm (Iskander, 2006; Thibos, Hong, Bradley, & Applegate, 2004) according to the equation:

$$\mathrm{VSOTF} = \frac{\iint_{-\infty}^{\infty} \mathrm{CSFN}(fx, fy) * |\mathrm{Re}\{\mathrm{OTF}(fx, fy)\}| dfx * dfy}{\iint_{-\infty}^{\infty} \mathrm{CSNF}(fx, fy) * \mathrm{OTFDL}(fx, fy) dfx * dfy}$$

where Re{OTF(fx, fy)} is the real part of the scaled optical transfer function, CSFN(fx, fy) is the neural contrast sensitivity function, OTFDL(fx, fy) is the diffraction limited optical transfer function and (fx, fy) denotes the spatial frequency coordinates. The scale of VSOTF ranges from 0 to 1.

Software for computing VSOTF was written in MATLAB (R2009a, Mathworks, Natick, MA, US) and the coefficients of lower and higher-order aberrations (3rd–6th orders) from individual eyes obtained using the COAS aberrometer were used for the calculation of VSOTF. This metric is used to determine if the image quality attributable to higher-order aberrations (3rd–6th orders) at the baseline visit might predict myopic changes in refractive error. Normative values of photoreceptors directionality (ρ) and horizontal and vertical peak location (in mm) of the Stiles-Crawford effect (SCE) were also incorporated during the computation of VSOTF (Applegate & Lakshminarayanan, 1993).

Axial length (AL), anterior chamber depth (ACD) and corneal radius of curvature were measured using IOLMaster™ (Carl Zeiss, Meditec AG Jena, Germany) after cycloplegia at both visits. The procedure has been detailed elsewhere (Ojaimi et al., 2005). Briefly, IOLMaster™ uses partial coherent interferometry to measure axial length and image analysis to measure ACD and corneal