Impact of astigmatism and high-order aberrations on subjective best focus

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We studied the role of native astigmatism and ocular aberrations on best-focus setting and its shift upon induction of astigmatism in 42 subjects (emmetropes, myopes, hyperopes, with-the-rule [WTR] and against-the-rule [ATR] myopic astigmats). Stimuli were presented in a custom-developed adaptive optics simulator, allowing correction for native aberrations and astigmatism induction (+1 D; 6-mm pupil). Best-focus search consisted on randomized-step interleaved staircase method. Each subject searched best focus for four different images, and four different conditions (with/without aberration correction, with/without astigmatism induction). The presence of aberrations induced a significant shift in subjective best focus (0.4 D; $p < 0.01$), significantly correlated ($p = 0.005$) with the best-focus shift predicted from optical simulations. The induction of astigmatism produced a statistically significant shift of the best-focus setting in all groups under natural aberrations ($p = 0.001$), and in emmetropes and in WTR astigmats under corrected aberrations ($p < 0.0001$). Best-focus shift upon induced astigmatism was significantly different across groups, both for natural aberrations and AO-correction ($p < 0.0001$). Best focus shifted in opposite directions in WTR and ATR astigmats upon induction of astigmatism, symmetrically with respect to the best-focus shift in nonastigmatic myopes. The shifts are consistent with a bias towards vertical and horizontal retinal blur in WTR and ATR astigmats, respectively, indicating adaptation to native astigmatism.

Introduction

Understanding the focus setting at which a subject judges an image to appear optimally focused is of critical importance in everyday tasks (adjusting focus in optical devices such as binoculars, microscopes, or projectors), as well as in clinical management of refractive errors. Achieving best focus is the goal in correction of ocular refractive errors by spectacles, contact lenses, intraocular lenses, or refractive surgery. While spherical refractive errors arise from a physical

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mismatch between the power of the optics of the eye and eye length, there is an increasing awareness that the fine tuning of this correction is critically affected by interactive effects between defocus, astigmatism, and high-order aberrations (HOAs) (Bradley, Xu, Thibos, Marin, & Hernandez, 2014; Cheng, Bradley, Ravikumar, & Thibos, 2010; Iseli, Bueeler, Hafezi, Seiler, & Mrochen, 2005; Marcos, Sawides, Gambra, & Dorronsoro, 2008; McLellan, Prieto, Marcos, & Burns, 2006; Xu, Bradley, & Thibos, 2013), and that neural adaptation plays a role in the adjustment of best focus (Sawides, de Gracia, Dorronsoro, Webster, & Marcos, 2011b; Sawides et al., 2010b; Vinas, Sawides, de Gracia, & Marcos, 2012).

Several studies have demonstrated the interactions between defocus and spherical aberration (Applegate, Ballentine, Gross, Sarver, & Sarver, 2003; Thibos, Hong, Bradley, & Applegate, 2004) and the need to take into account the contribution of spherical aberration to the spherical refraction (Cheng, Bradley, Hong, & Thibos, 2003; Guirao & Williams, 2003). Also, the specific interaction of the signs of the Zernike coefficients in real eyes appears to be critical in achieving a high modulation transfer function (McLellan et al., 2006). In addition, chromatic and monochromatic aberrations also tend to produce a positive balance in optical quality. In a previous study, we showed possible favorable interactions of astigmatism and coma (de Gracia et al., 2010). Using adaptive optics (AO), Marcos et al. (2008) showed shifts in subjective best focus when HOAs were corrected. These interactive effects across aberrations and their impact on spherical error need to be considered when the correcting alternatives (i.e., customized refractive surgery, toric, or aspheric intraocular lenses) correct or induce astigmatism and/or HOAs at the same time that they correct spherical error.

Besides the shifts in the plane of focus predictable by the use of retinal image quality metrics, subjective best focus is likely to be highly influenced by the subject's long-term adaptation. Recent studies show that the best perceived image from a series of degraded images presented to different subjects (using an AO system that corrects for the subject's aberrations, thereby guaranteeing identical images projected in all subjects) is highly correlated to the subject's own optical quality (Sawides et al., 2011b). Also, images degraded by blur with similar orientation to the blur orientation produced by the subject's aberration are perceived as sharper than images degraded by similar blur level with a different orientation (Artal et al., 2004; Sawides, de Gracia, Dorronsoro, Webster, & Marcos, 2011a; Sawides, Dorronsoro, Haun, Peli, & Marcos, 2013).

In particular, the presence of astigmatism has been shown to produce strong blur orientation bias. The isotropic perceived focus following short-term adaptation to simulated astigmatic images (Sawides et al., 2010b), as well as in real astigmatic subjects (Vinas et al., 2012), is significantly shifted from isotropy, with these subjects perceiving images blurred along their axis of astigmatism as isotropic. In fact longer adaptation times (four hours) in an orientation-specific deprived environment produced increased sensitivity to the deprived orientation (Zhang et al., 2009). In addition, visual acuity in astigmatic subjects appears relatively unchanged upon induction of astigmatism (de Gracia et al., 2011) and, in particular, when astigmatism is induced along the axis of their natural astigmatism (Vinas et al., 2013). Perceived visual quality in astigmats should be considered when handling correction of astigmatic patients. Debate whether low amounts of astigmatism should be corrected is common among practitioners facing correction of patients with toric intraocular or contact lenses (Villegas, Alcon, & Artal, 2014). Beyond potential interactive effects of astigmatism and HOAs (de Gracia et al., 2010; Villegas et al., 2014), potential bias caused by prior astigmatism may be critical.

In this study, we evaluated how the subjective best-focus setting by a patient is affected when astigmatism is induced in groups of patients with different refractive error profiles, in particular, with-the-rule (WTR) and against-the-rule (ATR) astigmats. Measurements were performed under natural aberrations, and also with their natural aberrations corrected with AO. As expected, the presence of ocular aberrations shifted the subjective best-focus setting. In addition, the shifts in best focus when astigmatism was induced depended on both types (WTR or ATR) of the native astigmatism.

Methods

Best-focus search, adjusting the sphere power using a Badal optometer, was performed on five groups of subjects, with different refractive profiles (emmetropes, myopes, hyperopes, WTR myopic astigmats, and ATR myopic astigmats), in different conditions (natural aberrations, corrected aberrations with AO, and upon induction, or not, of astigmatism). Differences in the best-focus setting across conditions and upon induction of astigmatism were evaluated.

Subjects

A total of 42 White subjects (ages ranging from 20 to 45 years, mean 28.02 ± 6.44) participated in the study. Subjects were screened and followed an optometric and ophthalmological examination at the School of Optometry Clinic of the Universidad Complutense de Madrid (UCM), to ensure good eye health, and

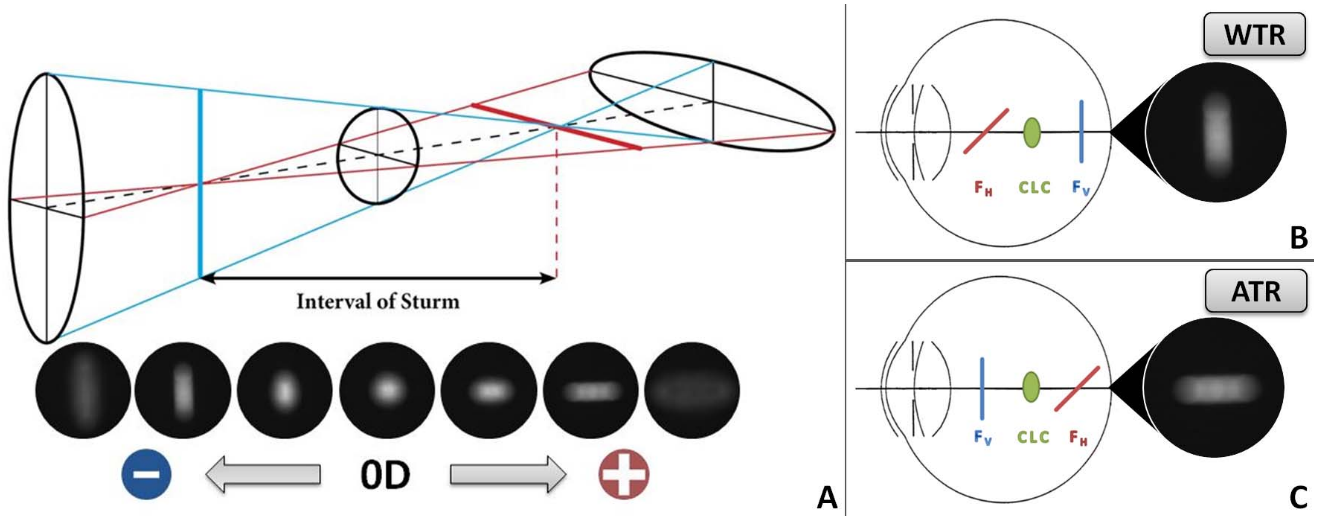

Figure 1. (A) Series of "retinal" images of a circular spot captured in the CCD camera at the focal plane of a lens acting as an artificial eye, when astigmatism—Z(2,2) = 0.92 μm for 6 mm pupil diameter—is induced by the electromagnetic deformable mirror. (B) Illustration of the astigmatic foci in a myopic with-the-rule astigmat. (C) Illustration of the astigmatic foci in a myopic against the rule astigmat. FV = vertical focus; CLC = circle of least confusion; FH = horizontal focus.

compliance with the inclusion criteria. Clinical refraction was performed by standard subjective refraction technique in natural conditions and under cyclopegia. If the magnitude/axis of astigmatism between both conditions differed by more than 0.25 D/10°, the subject was not invited to participate. Subjects were classified in five groups: G1, emmetropic group (spherical error between –0.25 D and +0.5 D, astigmatism ≤0.25 D); G2, myopic group (spherical error between –4.00 D and –1.00 D, astigmatism ≤0.25 D); G3, hyperopic group (spherical error between +0.75 D and +3.00 D, astigmatism ≤0.25 D); G4, WTR myopic astigmats (spherical error between –4.25 D and +0.25 D, astigmatism ≥0.75 D, axis: 10°–170°); and G5, ATR myopic astigmats (spherical error between –4.75 D and 0.00 D, astigmatism ≥0.75 D, axis: 90°–105°). All astigmatic subjects were chosen to be myopes to guarantee that, in uncorrected normal viewing conditions, the entire Sturm interval falls in front of the retina (see Figure 1; Vilaseca et al., 2012). Table 1 summarizes the refractive profile of the subjects. All myopic subjects, and astigmatic subjects except for two subjects (G4-S7 and G5-S6) were habitually corrected with spectacles.

All subjects had an eye examination before enrollment in the study, and signed an informed consent form. Experimental protocols were approved by the Institutional Review Board (CSIC).

Experimental set-up

A custom-made AO system, described in detail in previous publications (Marcos et al., 2008; Sawides, Gambra, Pascual, Dorronsoro, & Marcos, 2010a; Sawides et al., 2010b), was used to measure and correct the aberrations of the subject, as well as to induce astigmatism. The main components of the system are: A Hartmann-Shack wavefront sensor (32 × 32 microlenses; 503 lenses in a 5.73-mm pupil diameter; HASO 32 OEM, Imagine Eyes, Paris, France); a superluminescent diode (827 nm); an electromagnetic deformable mirror (52 actuators and a 50-μm stroke; MIRAO, Imagine Eyes, Paris, France); a motorized Badal system; a natural pupil monitoring system; and a stimulus display (CRT monitor, Mitsubishi Diamond Pro 2070). The state of the mirror that compensates the aberrations of the subject was set in a closed-loop operation. Focus correction was achieved by means of a Badal system mounted on a linear motor stage. The system was automatically operated by custom-developed software written in C++, which controlled the operation of the wavefront sensor and electromagnetic mirror, the visual stimulus generator (Visage; Cambridge Instruments, Somerville, MA), and the Badal system.

Best-focus search method

A best-focus search algorithm, based on interleaved staircases, was specifically developed for the study. The best-focus search is performed using a motorized Badal optometer, that allows adding positive or negative sphere power (in 0.125 D) until the optimum appearance is reached, according to the subject's responses. The algorithm is based on a randomized-step efficient method, where the subject reports (using a two buttons

			OD					OS				
		Age	Sph	Cil	Axis	VA (Dec)	VA (LogMAR)	Sph	Cil	Axis	VA (Dec)	VA (LogMAR)
Emmetropes	S1	31	+1.25	−0.75	117°	1.0	0.00	**0.00**	**−0.25**	**8°**	**1.2**	**−0.08**
	S2	31	+5.00	−0.75	90°	0.75	0.12	**0.00**			**1.1**	**−0.04**
	S3	30	**+0.50**			**1.5**	**−0.18**	+0.50	−0.50	30°	1.5	−0.18
	S4	22	**0.00**			**1.5**	**−0.18**	0.00			1.5	−0.18
	S5	20	**0.00**	**−0.25**	**180°**	**1.5**	**−0.18**	0.00			1.5	−0.18
	S6	31	+0.50	−0.50	170°	1.2	−0.08	**+0.50**			**1.3**	**−0.11**
	S7	27	−0.50			1.5	−0.18	**−0.25**			**1.5**	**−0.18**
	S8	20	**0.00**			**1.5**	**−0.18**	+0.25			1.5	−0.18
Myopes	S1	20	**−3.50**			**1.2**	**−0.08**	−4.25			1.2	−0.08
	S2	26	**−4.00**			**1.3**	**−0.11**	−4.00			1.1	−0.04
	S3	23	−1.00			1.2	−0.08	**−1.00**			**1.2**	**−0.08**
	S4	22	**−3.25**			**1.5**	**−0.18**	−2.75			1.5	−0.18
	S5	31	**−3.25**			**1.2**	**−0.08**	−3.25			1.2	−0.08
	S6	21	**−2.25**			**1.3**	**−0.11**	−1.25			1.3	−0.11
	S7	21	**−1.00**			**1.2**	**−0.08**	−1.00			1.2	−0.08
	S8	26	−3.00			1.3	−0.11	**−2.75**			**1.3**	**−0.11**
	S9	20	**−2.25**			**1.5**	**−0.18**	−1.75	−0.25	120°	1.5	−0.18
Hyperopes	S1	40	+0.75	−0.50	74°	1.2	−0.08	**+0.75**	**−0.25**	**105°**	**1.2**	**−0.08**
	S2	24	**+1.25**			**1.2**	**−0.08**	+1.25			1.2	−0.08
	S3	34	**+1.00**			**1.5**	**−0.18**	+1.00			1.5	−0.18
	S4	35	+0.75	−0.25	86°	1.2	−0.08	**+1.25**			**1.2**	**−0.08**
	S5	35	+1.25	−0.50	165°	0.9	0.05	**+1.00**			**0.9**	**0.05**
	S6	25	+1.25	−0.50	10°	1.5	−0.18	**+1.00**			**1.5**	**−0.18**
	S7	35	+3.25			1.5	−0.18	**+3.00**			**1.5**	**−0.18**
	S8	30	**+2.00**			**1.5**	**−0.18**	+2.25	−0.50	180°	1.5	−0.18
Myopes + WTR Ast	S1	36	−4.50	−1.25	165°	1.2	−0.08	**−4.25**	**−1.25**	**180°**	**1.2**	**−0.08**
	S2	30	**−1.75**	**−1.50**	**180°**	**1.1**	**−0.04**	−2.25	−1.25	20°	1.1	−0.04
	S3	28	**+0.25**	**−0.75**	**180°**	**1.2**	**−0.08**	+0.25	−0.75	20°	1.2	−0.08
	S4	31	−4.25	−1.25	175°	1.3	−0.11	**−4.25**	**−1.25**	**180°**	**1.3**	**−0.11**
	S5	35	**−3.50**	**−1.00**	**12°**	**1.5**	**−0.18**	−4.00	−1.25	168°	1.4	−0.16
	S6	21	**−2.75**	**−1.25**	**180°**	**1.3**	**−0.11**	−2.50	−1.25	180°	1.3	−0.11
	S7	33	**0.00**	**−0.75**	**170°**	**1.3**	**−0.11**	0.00	−0.75	10°	1.5	−0.18
	S8	21	**+0.50**	**−1.00**	**2°**	**1.2**	**−0.08**	+0.50	+0.50	165°	1.2	−0.18
	S9	28	0.00	−0.50	180°	1.3	−0.11	**−1.00**	**−0.75**	**10°**	**1.3**	**−0.11**
Myopes + ATR Ast	S1	27	**−2.00**	**−1.00**	**100°**	**1.2**	**−0.08**	−2.25	−1.00	80°	1.2	−0.08
	S2	21	−2.00			1.2	−0.08	**−2.75**	**−1.00**	**90°**	**1.2**	**−0.08**
	S3	41	**−4.75**	**−1.00**	**100°**	**1.0**	**0.00**	−5.25	−1.00	70°	1.0	0.00
	S4	45	−0.25	−0.75	70°	1.0	0.00	**−0.00**	**−1.00**	**105°**	**1.0**	**0.00**
	S5	30	**−0.50**	**−2.00**	**93°**	**1.0**	**0.00**	−0.50	−1.50	84°	0.85	0.07
	S6	21	**−1.00**	**−0.75**	**95°**	**1.3**	**−0.11**	−0.75	−0.75	55°	1.5	−0.18
	S7	29	**−2.75**	**−0.75**	**90°**	**1.5**	**−0.18**	−3.25	−0.50	90°	1.5	−0.18
	S8	22	**−0.75**	**−1.25**	**90**	**1.3**	**−0.11**	−0.75	−0.75	70°	1.25	−0.10

Table 1. Summary of the refractive profile and visual acuities (decimal and LogMAR) in all subjects. The measured eye is shown in red and empty cells represents cases in which no astigmatism was found.

in a keyboard) whether a gray-scale image presented in the display appears more blurred or sharper than the precedent image. The maximum number of trials in each staircase was 30, and best focus was selected after a maximum number of 11 reversals. Four staircases are interleaved with different initial values (–0.75 D, –0.50 D, +0.50 D, +0.75 D) from an initial focus setting. The subject's responses may be beyond the interval given by the initial settings. A typical focus setting was completed in 60 s. We found the interleaved staircase method to be more rapid (by 58.3%) and more repeatable (0.0961 vs. 0.1222 D repeated measurement standard deviations) than a standard manual best-focus search using the same Badal system. For each experimental condition, best-focus search was performed using four different image types (Bradley et al., 2014): oblique black E letter on a white background, an image of a face, an urban landscape, and an image of fruits). A power spectrum analysis revealed that the "fruits" and "face" images power spectrum was described by 1/f function, and the "E" and "urban landscape" images showed some preferred frequencies, and had signal until at least 120 c/°. The field of view of the images was 2°.

Experimental protocol

Best focus setting was performed in the AO instrument in four different conditions: (a) natural HOAs and astigmatism; (b) natural HOAs and astigmatism + induced astigmatism; (c) AO correction of all aberrations; and (d) AO correction of all aberrations + induced astigmatism. Astigmatism was always induced by the same amount (+1 D) and was induced in such a way that the circle of least confusion fell at the initial best correction, or equivalently Zernike coefficients Z(2,–2) = 0, Z(2,2) = +0.92 μm, for a 6-mm pupil.

The induction of the astigmatism, Z(2,2) = +0.92 um, by the electromagnetic deformable mirror was tested in an artificial eye provided with a camera lens and a CCD (charge-coupled device) in place of the retina. Figure 1 illustrates retinal images in the artificial eye and the relative orientation of the retinal images as the Badal is moved to induce positive and negative spherical defocus (A), and sketches the relative position of horizontal and vertical blur in the WTR (B) and ATR (C) astigmats, as well as the effect of induced astigmatism.

Subjects were dilated with tropicamide 1% (Hofmeister, Kaupp, & Schallhorn, 2005), two drops 10 min apart at the beginning of the experiment and then every 45 min to ensure paralyzed accommodation during the measurements, which was demonstrated by high repeatability (<0.15 D) in the focus setting. Following dilation, the eye's natural pupil was aligned to the optical axis of the instrument, with eye translations reduced by the use of a dental impression. The subject performed an initial manual subjective focus setting (by means of a Badal system), using a Maltese cross as a stimulus. The automatic staircase-based best-focus search was then performed for the natural aberration condition as well as the natural aberration + induced astigmatism condition. A closed-loop operation in the AO system was then performed to compensate for the natural aberrations of the subject. The subject performed a subsequent manual subjective focus setting for the AO-corrected aberrations. In general, this setting differed from that in the natural condition; therefore, the tested intervals differed across conditions. This setting was used as a baseline for the staircase-based best-focus search under AO-corrected aberrations and AO-corrected aberrations + induced astigmatism. The same procedure was repeated for the four different images used in the experiment.

All measurements were performed in a single experimental session, which lasted approximately 2.5 hours.

Data analysis

Optical aberrations were described by a Zernike polynomial expansion using the OSA (Optical Society of America) Standards for the report of ocular aberrations (Thibos, Applegate, Schwiegerling, Webb, & VSIA Standards Taskforce, 2002). Root mean square (RMS) wavefront error and Strehl ratio (normalized volume under the modulation transfer function, truncated at 60 c/°) were used as optical quality metrics.

Statistical analysis was conducted to study significant dependencies of the best-focus setting with image type, correction of aberration, induction of astigmatism, and refractive group.

Two-way ANOVA with an interaction model was used to test factors "image type" and "refractive group" (and their interactions) on the potential differences in the relative focus setting upon AO correction and upon astigmatism induction.

One-way ANOVA was used to test the null hypothesis that all refractive groups are drawn from the same population in the amount of aberrations, relative focus setting upon AO correction, and upon astigmatism induction. Statistical significance was set at $p < 0.05$. Student's t tests were used to test statistical shifts of best focus upon AO correction or astigmatism induction, for each group (one-sample t tests), and statistical differences across groups (two-sample unpaired t tests).

Results

Measured, induced, and corrected aberrations

The average RMS following AO correction was 0.11 ± 0.03 μm (5.73-mm pupil). There was no statistically significant difference across groups in the performance of the correction. Astigmatism was induced with an average accuracy of 0.09 D (attempted induced astigmatism: 1 D; achieved average astigmatism: 1.09

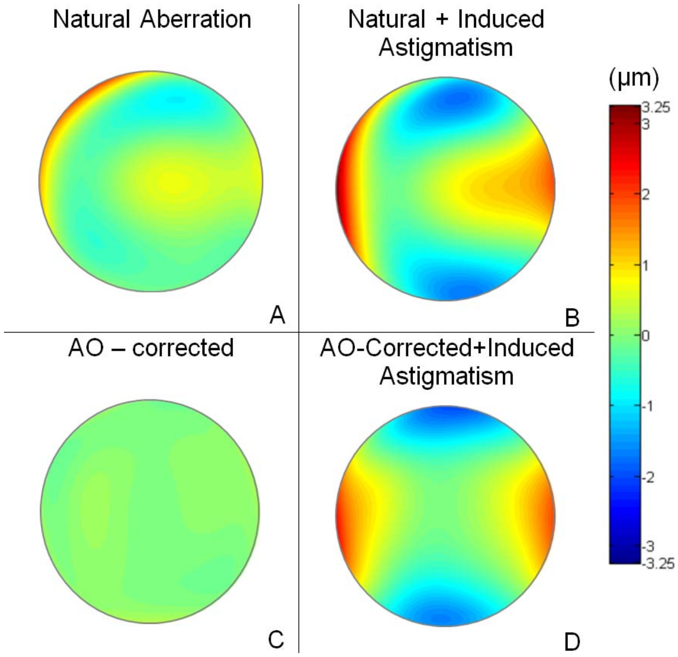

Figure 2. Example of wave aberration patterns (high-order aberrations + astigmatism) for one subject (S1 from G3), and for the four conditions of the study. (A) Natural aberrations, (B) Natural aberrations + induced astigmatism, (C) AO-corrected aberrations, (D) AO-corrected aberrations + induced astigmatism. Data are for 5.73 mm pupil diameter.

± 0.1 D). Figure 2 shows examples of the wave aberration pattern measured in a hyperopic subject (G3-S1) in different conditions: natural aberrations (A), natural aberrations + induced astigmatism (B), after AO correction (C), and AO corrected + induced astigmatism (D).

Figure 3 shows the average higher-order RMS (including astigmatism) for the five groups and four testing conditions.

Figure 4 shows the spherical aberration in all individuals of each group. Some groups showed statistically significant differences in specific aberrations. Figure 5 shows average and statistical significances for spherical aberration, horizontal and vertical coma, and third- and higher-order aberrations.

Best focus settings

The average variability in best-focus setting was 0.15 ± 0.11 D, on average across images, conditions, and refractive groups. There was no relationship between accuracy of best focus and image type (Bradley et al., 2014), although a one-way ANOVA revealed statistical differences in accuracy across groups ($p = 0.0027$) and conditions ($p < 0.0001$). Figure 6 shows the focus settings with natural aberrations and natural aberrations + induced astigmatism (A) and AO-corrected aberrations and AO-corrected aberrations + induced astigmatism (B), for all subjects in each group. Data are the averages of the best-focus setting across the four image stimuli. Error bars represent the average standard deviation in the focus setting across the four images. The standard deviations were obtained from the four interleaved staircases in the test. Data are referred to initial manual focus settings with a Maltese cross target with natural aberrations (A) and AO-corrected aberrations (B). As previously explained, when astigmatism is induced, the circle of least confusion (Figure 1) falls on the initial manual best correction (corresponding to best focus = 0 in the graphs). There are consistent shifts upon induction of astigmatism in all groups, although the amount and direction of the shift varies across groups.

Effect of image type on best-focus setting

A two-way ANOVA showed statistically significant differences across refractive groups in the relative focus setting upon correction of aberrations ($p = 0.0247$) and induction of astigmatism ($p = 0.0015$ for natural

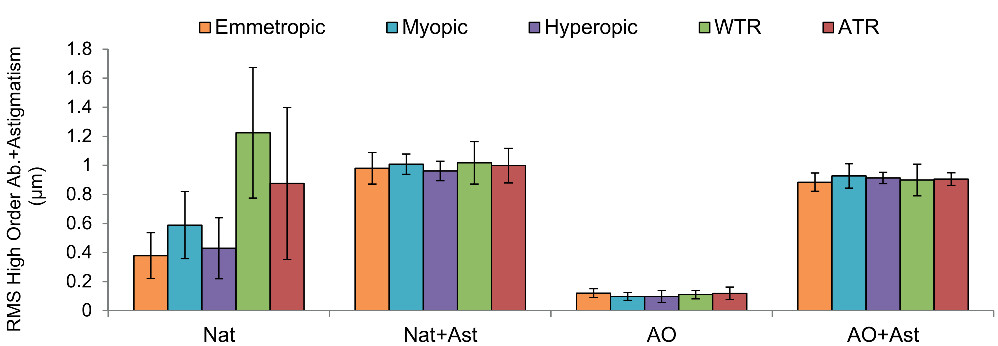

Figure 3. Average root mean square for high-order aberrations and astigmatism for the different conditions of the study (Natural, Natural + induced astigmatism, AO-corrected, and AO-corrected + induced astigmatism), for the five groups of the study. WTR and ATR stand for myopic with-the-rule astigmats and myopic against-the-rule astigmats. Data are for 5.73-mm pupil diameters.

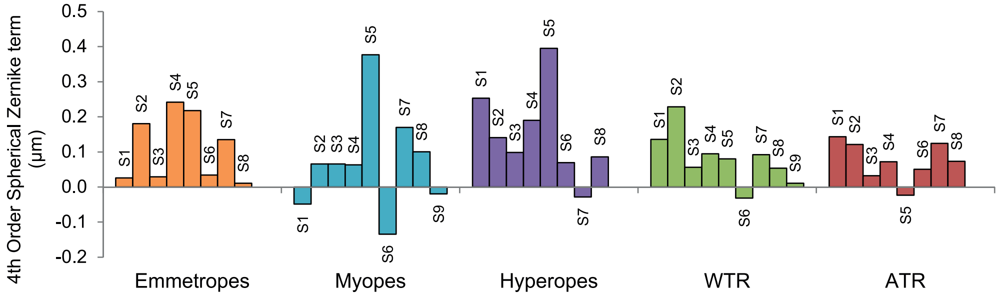

Figure 4. Fourth order spherical aberration Z(4,0) in all subjects of the study, divided by group. WTR and ATR stand for myopic with-the-rule astigmats and myopic against-the-rule astigmats. Data are for 5.73-mm diameter.

aberrations and $p = 0.0006$ for AO-corrected aberrations), but not across image types (p ranging between 0.2354 and 0.9950). The interaction parameter ranged between 0.995 and 1, indicating that best-focus shifts with astigmatism were similar across image types in all groups. Figure 7 shows the average best-focus settings (averaged across groups and conditions, for the four different images). While the best-focus shift is, on average, independent of image type (one-way ANOVA; natural condition, $p = 0.2659$; AO condition, $p =$

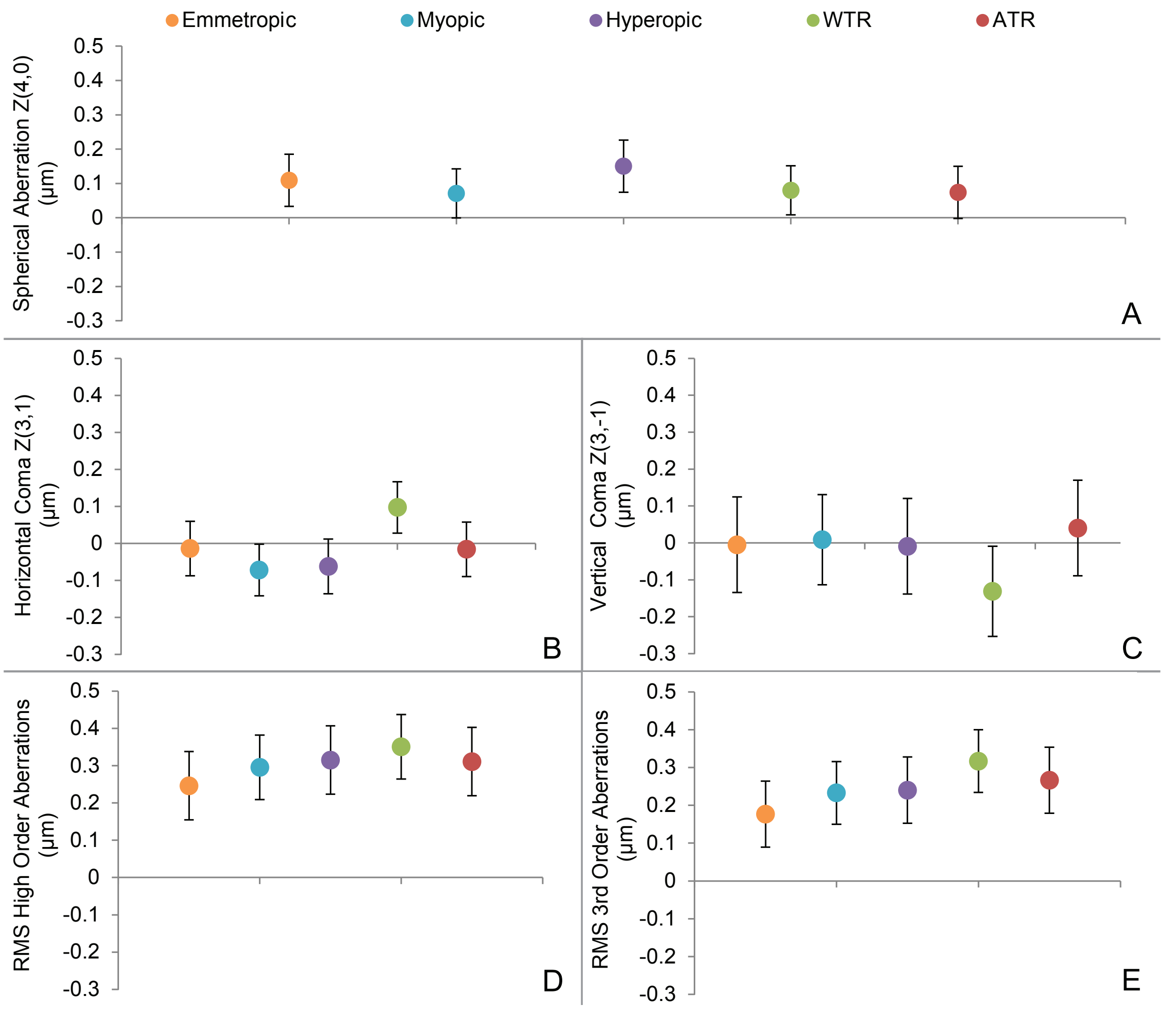

Figure 5. Selected Zernike terms, and RMS averaged across subjects in each group. Data are for 5.73 mm-pupils. (A) Fourth order spherical aberration, (B) Horizontal coma, (C) Vertical coma, (D) High-order aberration RMS, (E) Third order RMS. WTR and ATR stand for myopic with-the-rule astigmats and myopic against-the-rule astigmats. Error bars represent the Tukey-Kramer critical value for one-way ANOVA comparison (Hochberg & Tamhane, 1987). Statistically significant differences ($p < 0.05$) exist across groups if the bars do not overlap. Values are statistically different from zero ($p < 0.05$) if the error bars do not cross zero.

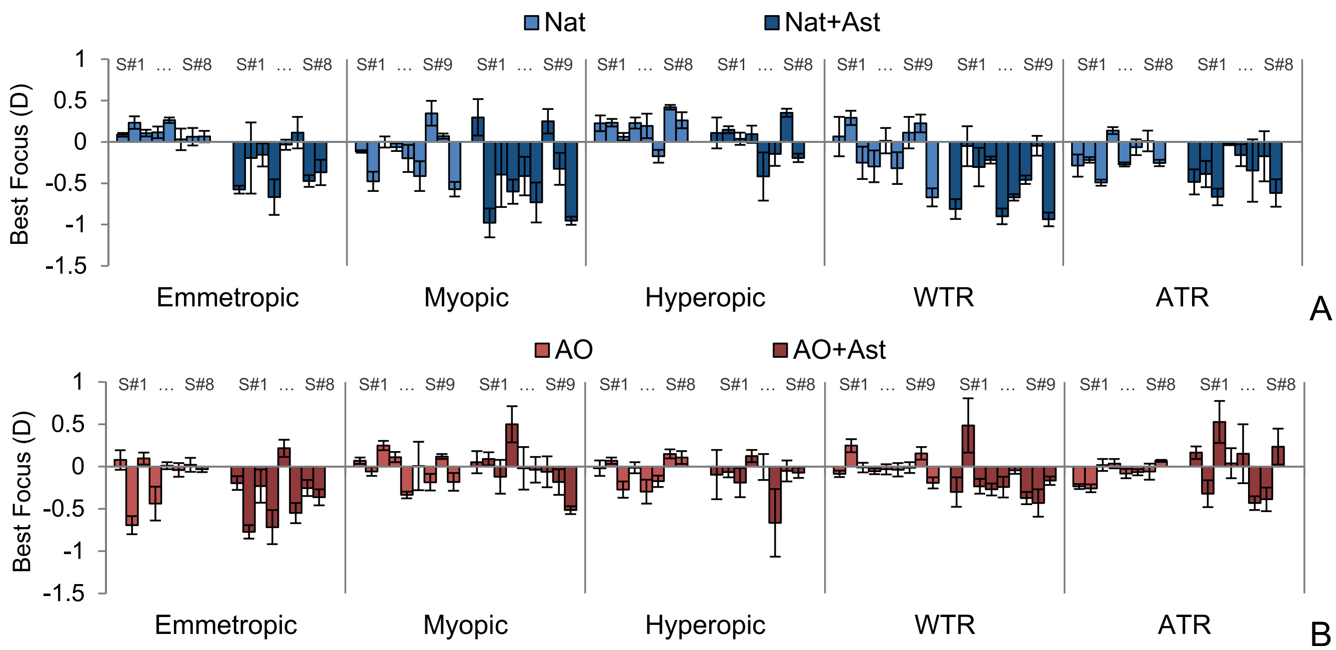

Figure 6. Magnitude of spherical defocus setting for all patients in each group, for different conditions. (A) Focus setting under natural aberrations and under natural aberrations + induced astigmatism. (B) Focus setting under AO-corrected aberrations, and under AO-corrected aberrations + induced astigmatism. Data are the average focus settings obtained for the four different images. WTR and ATR stand for myopic with-the-rule astigmats and myopic against-the-rule astigmats. Error bars represent standard deviations, obtained from the last four trials in the staircase procedure (averaged across images).

0.26378), there was a trend for the best-focus setting using the fruits image to be the most shifted from zero (t test; natural condition, $p < 0.0001$; AO condition, $p = 0.0014$).

Effect of aberration correction on best-focus setting

In general, correction of HOAs produced a shift of the best-focus setting with respect to the focus settings under natural aberrations (–0.4 D, on average across groups), which was statistically significant ($p < 0.01$) in all groups (Figure 8). Differences were not statistically significant (one-way ANOVA, $p = 0.1956$) across groups.

There was no apparent correlation between the average shift in best focus with AO corrections of aberrations, and the average magnitude of spherical aberration or high-order aberrations in each group. However, an analysis across individual subjects (and taking into account the individual aberrations) shows significant correlations between the shift of the subjective best focus upon correction of the aberrations and the shift in best focus producing highest optical quality (in through-focus optical Strehl ratio curves with and without correction of optical aberrations) in nonastigmatic groups ($p < 0.0001$).

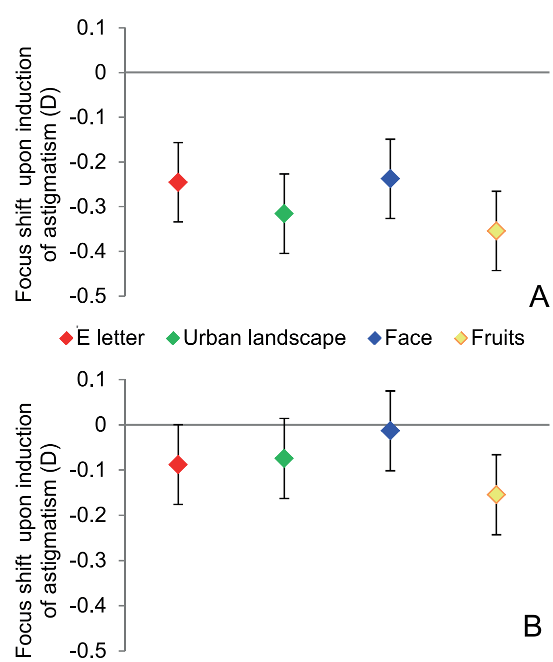

Figure 7. Shift of the best-focus setting upon induction of astigmatism under natural aberrations (A) and AO-corrected aberrations (B) averaged across groups and conditions for the four different images. Error bars as in Figure 5.

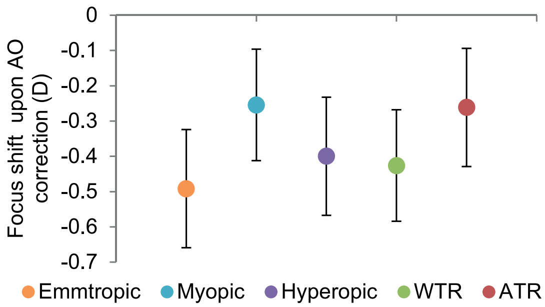

Figure 8. Average shift between best-focus setting with AO-corrected aberrations and best-focus setting under natural aberrations, averaged across images and all subjects in each group. WTR and ATR stand for myopic with-the-rule astigmats and myopic against-the-rule astigmats. Error bars as in Figure 5.

Effect of astigmatism induction on best-focus setting

For several groups, induction of astigmatism produced a shift of the best-focus setting with respect to the focus settings without induction of astigmatism, both under natural aberrations (Figure 9A) and under AO-corrected conditions (Figure 9B).

The shift in best focus upon induction of astigmatism was statistically significant in all groups ($p < 0.001$) under natural aberrations, and in emmetropes ($p < 0.00001$) and WTR astigmats under corrected aberrations ($p < 0.0001$). Best-focus shift upon induction of astigmatism was significantly different across groups, both for natural aberrations (one-way ANOVA, $p =$ 9.98E-04) and AO correction (one-way ANOVA, $p =$ 3.99E-04). Trends in the shifts across groups tended to be similar in both conditions. In particular, the best focus shifted in opposite directions in WTR and ATR astigmats upon induction of astigmatism, symmetrically with respect to the best-focus shift of non-astigmatic myopes. Also, a statistical analysis taking age (23.3 ± 3.67 in myopes, 29.2 ± 5.43 in WTR, 29.5 ± 9.1 in ATR) as a correction factor did not find any relationship between age and best focus shift.

Discussion

Optical aberrations and refractive errors

Several studies report differences in ocular aberrations across refractive errors (Collins, Carroll, Black, & Walsh, 1979; Llorente, Marcos, Dorronsoro, & Burns, 2007; Martinez, Sankaridurg, Naduvilath, & Mitchell, 2009). To our knowledge, no previous study had investigated ocular aberrations in astigmats. Given geometrical differences (corneal shape, angle k, corneal asphericity, corneal curvature, axial length, and vitreous chamber depth) across myopic, emmetropes, hyperopes, and astigmats (Budak, Khater, Friedman, Holladay, & Koch, 1999; Carney, Mainstone, & Henderson, 1997; Davis, Raasch, Mitchell, Mutti, & Zadnik, 2005; Llorente, Barbero, Cano, Dorronsoro, & Marcos, 2004; Mainstone et al., 1998; Sheridan & Douthwaite, 1989; Strang, Schmid, & Carney, 1998), differences in ocular aberrations are not unexpected. As previously reported by Llorente et al. (2004), we found higher amounts of positive spherical aberration in hyperopes than in any other group. Interestingly, horizontal and vertical coma shift in opposite directions (i.e., shift sign) in WTR and ATR astigmats, suggesting some interactions between astigmatism and coma. We did not find statistically significant differences in other HOAs in myopes, emmetropes, and hyperopes (typically associated to differences in angle k), very likely due to the relatively small amounts of ametropias in our sample.

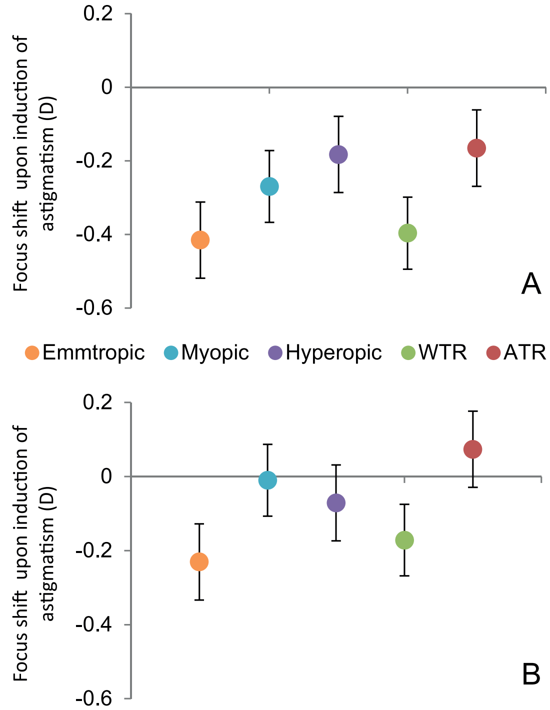

Figure 9. Average shift between best-focus setting upon induction of astigmatism: (A) for natural aberrations, (B) for AO-corrected aberrations. Data are averaged across subjects in a group and images. WTR and ATR stand for myopic with-the-rule astigmats and myopic against-the-rule astigmats. Error bars as in Figure 5.

Influence of aberrations on best focus

Interactions of low- and HOAs are well known to cause an impact on optical quality. In particular, the position of best focus is highly influenced by the presence of HOAs. Earlier studies (Marcos et al., 2008) found that correction of HOAs produced shifts in subjective best focus that mirrored those observed in computational through focus plots of image quality. An analysis of the through-focus optical quality (Strehl) in all eyes, obtained from the natural aberrations and AO-corrected aberrations measured in each eye revealed focus shifts in the peaks of the through-focus curves (–0.146 D) consistent in general with the subjective focus shifts (–0.339 D). The hyperopic shift when natural aberrations are present is consistent with the overall positive spherical aberrations found in most eyes. Considering all eyes, there was a statistically significant correlation between the subjective focus shift and objective focus shift ($r = 0.429$; $p = 0.0046$). The correlation was highly statistically significant in the nonastigmatic groups ($r = 0.685$; $p < 0.0001$), and it did not reach significance in the astigmatic groups ($r = 0.4037$; $p = 0.108$) (Cheng et al., 2003). The presence of double peaks in the through-focus curves in astigmats, and likely orientation bias in the focus setting are likely playing a role in the higher discrepancy between the subjective focus and the optical predictions. Interestingly, the larger differences in coma between ATR and WTR appear to result also in differences in the shift of best focus when aberrations are corrected (Figures 5 and 8).

Influence of induced astigmatism on best focus

Astigmatism was initially induced in such a way that the circle of least confusion (i.e., isotropic blur) fall at the initial best correction. However in many cases, subjects shifted the best-focus setting towards oriented blur when astigmatism was induced. For positive Z(2,2), a positive shift is consistent with horizontally oriented blur in the retina, and a negative shift with vertically oriented blur in the retina (see Figure 1). In the absence of aberrations, the lowest shifts upon induction of astigmatism (i.e., isotropic setting) occurred in myopes and hyperopes, which may be associated to the fact that ametropic eyes may be more adapted to symmetric blur. On the other hand, emmetropes shifted focus towards vertical retinal blur. The reasons for this consistent shift are not clear, but may be connected to recent findings that visual acuity in emmetropes is in fact significantly less reduced upon induction of vertical than upon induction of horizontal blur (Vinas et al., 2013) Myopic WTR astigmats and myopic ATR astigmats shifted focus in different directions upon induction of astigmatism when natural aberrations were corrected (see Figure 9). Previous studies have shown a bias towards their astigmatic axes in habitually corrected myopic astigmats (Vinas et al., 2012), as well as a small impact on visual acuity when astigmatism is induced along their astigmatic axes, as opposed to other axes (Vinas et al., 2013). The fact that these effects occur even in astigmatic subjects that are habitually corrected for their astigmatism may be explained by evidence showing that adaptation can be actually transferred to a long-term storage that can be instantly engaged when blur is reapplied (Yehezkel, Sagi, Sterkin, Belkin, & Polat, 2010). These results are consistent with our finding that WTR astigmats shift the position of best focus towards vertical retinal blur and ATR astigmats shift the position of best focus towards horizontal retinal blur, as they would be naturally adapted to vertical and horizontal retinal blur, respectively. While the absolute shifts are changed in the presence of aberrations, as expected from interactions of HOAs (particularly coma) and astigmatism (de Gracia et al., 2010; de Gracia et al., 2011), the relative trends of best focus shifts with induced astigmatism remain when subjects performed the experiment with their natural aberrations corrected. In particular, the opposite shift in best-focus setting when astigmatism is induced in myopic WTR or ATR astigmats with respect to nonastigmatic myopes appears independent on the presence of HOAs, and consistent with the bias of astigmats towards the blur orientation produced by their own axis of astigmatism (even if they are normally corrected).

Conclusions

1. Subjective best focus shifts when ocular HOAs are corrected. This shift is well predicted optically from through-focus optical Strehl curves.
2. The induction of astigmatism produces a statistically significant shift of the best-focus setting in all groups under natural aberrations. The shift in best focus upon induction of astigmatism varied significantly across the different refractive profiles of patients. The best-focus setting in WTR and in ATR astigmats shifts in opposite directions upon induction of astigmatism, and symmetrically with respect to the best-focus shift in nonastigmatic myopes.
3. The shifts in best focus in presence of induced astigmatism are consistent with a bias towards vertical retinal blur in WTR astigmats, and horizontal retinal blur in ATR astigmats.
4. These findings indicate that the best-focus setting in presence of astigmatism is biased by prior adaptational effect.

Keywords: astigmatism, refraction, aberration, best focus

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