Impact of higher-order aberrations on depth-of-field

Juan F. Zapata-Díaz
Grupo de Investigación en Ciencias de la Visión, Universidad de Murcia, Murcia, Spain
Faculty of Biology, Medicine & Health, The University of Manchester, Manchester Academic Health Science Center, Manchester, UK

Iván Marín-Franch
Grupo de Investigación en Ciencias de la Visión, Universidad de Murcia, Murcia, Spain
Department of Ophthalmology and Vision Sciences, School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

Hema Radhakrishnan
Faculty of Biology, Medicine & Health, The University of Manchester, Manchester Academic Health Science Center, Manchester, UK

Norberto López-Gil
Grupo de Investigación en Ciencias de la Visión, Universidad de Murcia, Murcia, Spain

It is well known that depth-of-focus (DOF) is influenced by optical factors (such as pupil size and monochromatic aberrations). However, neural factors such as blur sensitivity and defocus adaptation may play an important role on the extent of DOF. A series of experiments were conducted to study if optical or neural factors are most pertinent in explaining the variability of DOF across subjects. An adaptive optics system with a black and white target, a 3.8-mm artificial pupil, and a subjective criterion (based on objectionable blur) were used to measure depth of field ([DOFi]; DOF computed in the object space) in 11 participants, after at least 6 min of adaptation. This was done under three conditions: (a) with their own higher order aberrations (HOA); (b) after correction of their monochromatic HOA; and (c) after altering the HOA pattern for some participants to reflect the HOA pattern measured for a different participant. Natural DOFi and DOFi after HOA correction were positively correlated ($R^2 = 0.461$), but a significant decrease in DOFi (21% on average) was found after HOA correction ($p = 0.042$). Effect of HOA on the intersubject variability of DOFi was 3.9 times smaller than the effect of the image neural processing. This study shows that DOFi depends on both optical and neural factors, but the latter seems to play a more important role than the former.

Introduction

The depth-of-focus (DOF) of the human eye has been widely studied due to its importance in obtaining a precise refractive correction (Tucker & Charman, 1975), and in determining the accommodation response (e.g., Bernal-Molina, Montés-Micó, Legras, & López-Gil, 2014). More recently, the extension of the DOF is being studied as a potential tool that may provide an improvement for multifocal corrections to ameliorate the consequences of presbyopia (Charman, 2014). Depth-of-field ([DOFi]; i.e., the counterpart of DOF in the object space) can be defined as the dioptric range in which an object can be placed without being perceived with an objectionable lack of sharpness. DOFi is influenced by a variety of factors such as luminance, contrast, target configuration (size and spatial frequency), wavelength, visual acuity (VA), pupil size, retinal eccentricity, age, and refraction (Wang & Ciuffreda, 2006). However, the majority of studies show an important variability of the DOF extent between subjects (Wang & Ciuffreda, 2006). The causes of this variability have not been investigated so far.

Zapata-Díaz, J. F., Marín-Franch, I., Radhakrishnan, H., & López-Gil, N. (2018). Impact of higher-order aberrations on depth-of-field. *Journal of Vision*, *18*(12):5, 1–11, https://doi.org/10.1167/18.12.5.

https://doi.org/10.1167/18.12.5 Received June 29, 2017; published November 6, 2018 ISSN 1534-7362

Recent studies have suggested that induced wavefront aberrations might modulate DOFi and be useful to design optical corrections for presbyopia. The addition of primary and secondary spherical aberrations, and certain combinations of both, has been found to be a good approach towards extending DOFi (Nio et al., 2002; Rocha, Vabre, Chateau, & Krueger, 2009; Benard, López-Gil, & Legras, 2010, 2011; Yi, Iskander, & Collins, 2011; Legras, Benard, & López-Gil, 2012). It has also been reported that nonrotationally symmetrical aberrations, such as coma-like aberrations and astigmatism, are able to modulate DOFi (Legras et al., 2012; de Gracia, Dorronsoro, & Marcos, 2013; Leube, Ohlendorf, & Wahl, 2016; de Gracia & Hartwig, 2017). Unfortunately, these induced aberrations produce some unwanted effects such as degradation in image quality and best focus shift. The addition of new aberrations was performed either over the natural higher order aberrations (HOAs) of the subjects (Rocha et al., 2009), or after correction of these natural HOAs (Benard et al., 2010, 2011; Legras et al., 2012). None of these studies investigated how much of the DOFi is explained by natural HOAs or the potential effects of neural factors on DOFi.

The impact of the eye optics on the visual performance can be investigated using adaptive optics (AO) systems to correct or induce wavefront aberrations. Several studies have investigated the eye's visual performance after correcting the monochromatic HOA (Liang, Williams, & Miller, 1997; Yoon & Williams, 2002; Guo, Atchison, & Birt, 2008; Marcos, Sawides, Gambra, & Dorronsoro, 2008; Rossi & Roorda, 2010; Hickenbotham, Tiruveedhula, & Roorda, 2012; Marcos et al., 2015). Nevertheless, as far as we know, the only study that investigated DOFi before and after the correction of natural HOA was performed by Atchison, Guo, and Fisher (2009). In this study, they found a decrease in DOFi by 8% (not significant) after correcting monochromatic HOA, and by 20% (significant) after correcting chromatic aberration. The study showed a considerable variation in sensitivity between subjects. The authors suggest that using a continuous procedure to correct HOA (they used an open-loop AO system) could have led to a significant change in DOFi when monochromatic HOA were corrected.

None of the previous studies that modulated DOFi by correcting or inducing HOA took into account the effect of blur adaptation or other potential neural processes influencing DOFi. The visual system can rapidly adapt to blur produced by filtering the spatial resolution of the target (Webster, Georgeson, & Webster, 2002) or by new amounts or patterns of HOA (Sawides, de Gracia, Dorronsoro, Webster, & Marcos, 2011). This adaptation to artificial blur influences subjective DOFi (Cufflin, Mankowska, & Mallen, 2007). The time course of short-term blur adaptation (tested every 2 min for 30 min) was found to be critical within the first 4 min of adaptation, and the adaptation was very limited after the first 6 min (Khan et al., 2013). As this adaptation process affects the blur perception over time, it is likely to also affect DOFi measurements when changing the wavefront aberrations of subjects.

HOAs vary widely in magnitude and distribution among the population (Porter, Guirao, Cox, & Williams, 2001; Thibos, Hong, Bradley, & Cheng, 2002; Castejón-Mochón, López-Gil, Benito, & Artal, 2002). It is therefore expected that this variability makes people have different DOFi. However, the extent of the influence of natural HOA on DOFi remains unclear. The human vision is also affected by the neural processing of the electrical signals sent by the retina (Campbell & Green, 1965), which may influence DOFi (Marcos, Moreno, & Navarro, 1999). To assess the potential benefit of inducing HOA to extend DOFi, it is important to understand the role that natural aberrations alone would have on DOFi and how they interact with neural factors influencing DOFi. Furthermore, it would be important to know whether the variability in DOFi between subjects is due to optical or neural factors (or both). The purpose of this study was to assess how much natural HOA affect the DOFi and if natural HOA alone or potential neural factors can explain the variability of DOFi between subjects.

Methods

Eleven Caucasian subjects (from 21 to 54 years of age, $M \pm SD = 34 \pm 12$ years) participated in the study (Table 1). All subjects were screened at the Clínica de la Visión Integral of the Universidad de Murcia (Spain). The inclusion criteria were: no ocular pathology, refractive error within the range of correction of the AO system (from +3.50 to –3.50 D of spherical equivalent), best corrected VA of at least 1 (decimal VA). Nonemmetropic (defined as having more than ±0.50 D of spherical equivalent refractive error or more than 0.50 D of astigmatism) subjects were included only if they usually wore their optical correction, in order to avoid the potentially complicating factor of a long-term adaptation to blur. All subjects were informed of the protocol and possible consequences of the experiment and informed consent was obtained. The study followed the tenets of the Declaration of Helsinki.

Figure 1 shows the diagram of the custom AO system used in this study. A superluminiscent diode ([SLD]; Hamamatsu L-8414-41) with a wavelength of 830 nm produced the measurement beam. The radiant flux received by the eye corresponded to a collimated emission of the SLD with a diameter of 1 mm and 102.5

			Refraction				Image quality	
Subject	Age	Eye	Sphere (D)	Cylinder (D)	Axis (°)	M (D)	HOA RMS (μm)	Strehl ratio
S1	29	Right	−0.50	−0.75	110	−0.88	0.073	0.539
S2	29	Right	+0.50	—		+0.50	0.037	0.845
S3	21	Right	−0.25	—		−0.25	0.054	0.740
S4	27	Right	+0.75	−0.75	105	+0.38	0.048	0.794
S5	47	Right	−3.25	−0.50	80	−3.50	0.072	0.610
S6	54	Left	−0.25	−1.50	140	−1.00	0.104	0.380
S7	49	Right	—	−1.25	75	−0.63	0.082	0.533
S8	24	Right	−1.00	−1.00	100	−1.50	0.042	0.840
S9	24	Right	+0.50	−0.50	180	+0.25	0.048	0.784
S10	38	Right	+0.25	—		+0.25	0.085	0.470
S11	27	Left	+2.50	—		+2.50	0.071	0.593

Table 1. Age, eye used for measurements, refraction, higher order aberration root mean square (HOA RMS), and Strehl ratio of participants for a 3.8-mm pupil. *Note*: Legend: M = Spherical equivalent refractive error.

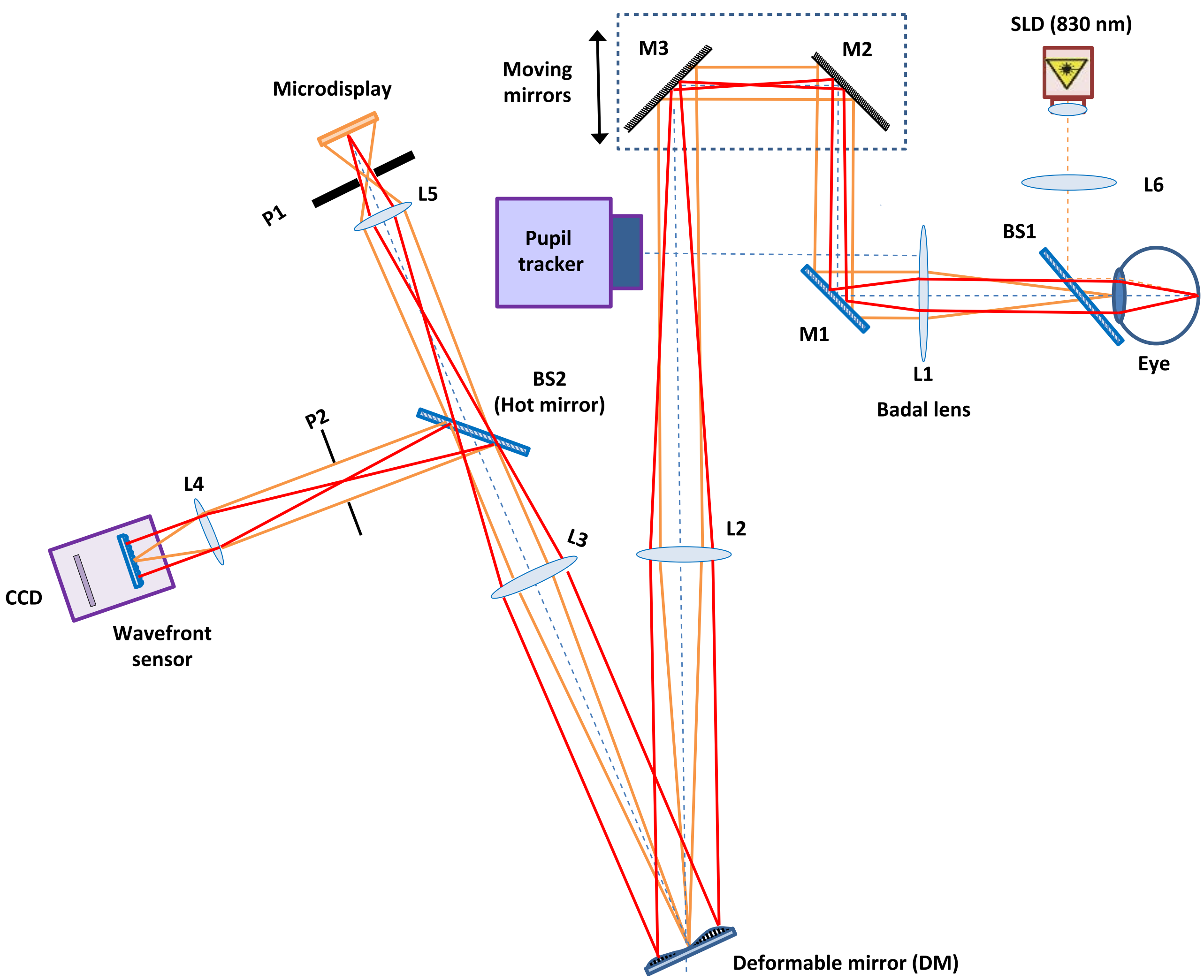

Figure 1. Schematic adaptive optics system setup. Legend: L1, L2, L3, L4, L5, and L6, lenses; M1, M2, and M3, mirrors; BS1 and BS2, beam splitters; P1 and P2, artificial pupils; SLD, superluminiscent diode; CCD, charge-coupled device camera; DM, deformable mirror. Red path shows retina-conjugated planes, and orange path shows pupil-conjugated planes.

μW, which is lower than the maximum permitted for a continuous exposition up to 3 hr (Delori, Webb, & Sliney, 2007). The beam splitter (BS1) placed in front of the eye reflected the beam produced by the SLD into the eye. The reflected light from the retina was transmitted through the rest of the optical system.

In order to correct the spherical equivalent refractive error of the subject and measure DOFi, we used a Badal system consisting of two lenses (L1 and L2) followed by two mirrors (M2 and M3) mounted on a stepper motor. There were three conjugated planes with subject's entrance pupil. The first plane is the one in which the deformable mirror (DM) was placed, which is the element that modifies the wavefront. This element is a membrane mirror with 52 actuators (model Mirao52e, Imaging Eyes, Orsay, France). The second plane conjugated with the subject's pupil corresponded with the plane of the microlenses of the Hartmann-Shack wavefront sensor (model HASO32, Imagine Eyes, Orsay, France), in which light was focused from the L4 lens. Finally, the last plane conjugated with the subject's pupil fell on half the distance between L5 lens and the microdisplay (EMA-100503, eMagin, Hopewell Junction, NY). On this plane, we placed an artificial pupil (P1) that determined the size of the subject's pupil to watch the microdisplay. The magnification between this plane and the subject's entrance pupil plane was 1.9. More details of the optical system and its calibration can be found in Bernal-Molina (2017).

The subjects received training in detecting blur following the criterion for "objectionable blur," defined as "the level of blur at which you would refuse to tolerate on a full time basis. You may or may not be able to read the chart" (Atchison, Fisher, Pedersen, & Ridall, 2005). However, the criterion used in this study differs from the one used by Atchison et al. (2005) in the use of a visual presentation along with the verbal explanation of the criterion. This visual presentation, consisting of a near vision optotype with different levels of Gaussian blur (with standard deviations from 0 to 5 pixels in steps of 0.5 pixels, each pixel subtending 2.6 minutes of arc), was presented to them to visually support the definition of this criterion. After verbal explanation of the definition, they were told that the images that met the objectionable blur criterion were the ones with Gaussian standard deviations from 2.5 to 3. The authors chose these images subjectively, following the already mentioned criterion. It was explained to the subjects that blur can be presented in multiple varieties and shapes, which might be different from the ones included in the presentation. Although it is difficult to follow the same criterion to detect it, they were asked to make an effort to be consistent with the criterion.

After this training, two drops (5 min apart) of cyclopentolate 1% (Colircusí, Alcon Cusí SA, Barcelona, Spain) were instilled in one eye (nine right and two left eyes), in order to paralyze accommodation. The eye with less astigmatism was chosen in order not to stress the DM when correcting low-order aberrations. A period of at least 30 min was allowed prior to the measurements. The contralateral eye was occluded with an eye patch.

All external factors (luminance, contrast, target configuration) influencing DOFi were controlled to be the same for all measurements and all subjects. The experiment was performed under dim light condition and background luminance was stable and controlled with room lights. Target luminance was constant at 32 cd/m^2. Target contrast and configuration was controlled by using the same target in the whole experiment.

The microdisplay subtended nearly 2 degrees of visual angle, and the target used to obtain the subjective DOFi measurements and the wavefront measurements was a customized black-and-white optotype consisting of a line with five Sloan letters (N D V K O) calculated to subtend 6.25 minutes of arc each, with the same spacing between them (decimal VA = 0.8).

A physical 2-mm pupil was placed at position P1 (Figure 1) that corresponded to a subject's 3.8-mm entrance pupil. Subjects' heads were stabilized using a bite bar. Pupil alignment with the system's optical axis was monitored during the whole experiment using a pupil-tracking camera and a monitor. The optical aberrations of the AO system were corrected using the DM in a closed loop operation before taking any measurement. Measurements were taken monocularly on each subject. An average over three wavefront measurements was obtained for each set of measurements.

Before any DOFi measurements, the subjects were asked to find the best focus using a motorized Badal system controlled by the subjects using a conventional three-button computer mouse. The best focus search was averaged from three measurements using a custom routine written in MATLAB (MathWorks, Natick, MA). This way the subjects' spherical equivalent was corrected with the Badal system in order to avoid the strain on the DM. After the best focus search, primary astigmatism coefficients (C_2^{-2} and C_2^{2}), and tilts (C_1^{-1} and C_1^{1}) were corrected using the DM. This correction was based on the aberrometer measurements, not the subjects' prescription.

Subjective DOFi was measured for three different conditions: (a) with eye's natural HOA (natural condition, $DOFi_N$), (b) with corrected HOA (AO-corrected condition, $DOFi_C$), and (c) with HOA from other subjects as simulated with the AO system (simulated condition, $DOFi_S$), in this order. The $DOFi_S$ condition is explained in more detail below.

Just before any subjective measurement, and after simulating each aberration condition, a 6-min video (a fragment of Charlie Chaplin's classic black and white film, *Modern Times*, from 1936) was displayed in order to allow the subject to get adapted to the simulated wavefront aberrations. After 6 min of adaptation, the target was displayed.

The subjects were then asked to mark both limits of DOFi following the objectionable blur criterion and using the motorized Badal system three times on each condition, alternating both limits and starting at the best focus position.

The simulated HOA patterns (corrected HOA and another subject's HOA conditions) were achieved using a closed-loop operation of the AO system during the adaptation period, but a static correction and simulation of HOA was used during subjective DOFi measurements. The frequency of the closed-loop operation fluctuated around 20 Hz with minimums above 15 Hz. Any subject pupil misalignment during the experiment was detected with the pupil tracker and corrected by the operator with two micropositioners connected to the bite bar. Wavefront simulations up to the 20th Wyant-order Zernike expansion were induced with the CASAO software (Imagine Optic SA, Orsay, France). Several HOA patterns from other subjects (between one and four patterns) were simulated to most of the subjects randomly in the third condition. However, these simulations were only performed when they were available and, as the experiment was performed in one session for each subject, no simulation was available for the first subject, only one simulation for the second subject, and so on.

Wavefront measurements in the subject's natural pupil size were averaged and rescaled for a 3.8-mm pupil (Schwiegerling, 2002) and reordered to American National Standards Institute convention (Thibos, Applegate, Schwiergerling, & Webb, 2002; American National Standards Institute, 2004). Strehl Ratio was used as image quality metric, and it was defined as the ratio between the maximum of the subjects' point spread function (PSF) and the maximum of the diffraction-limited PSF. The PSF was obtained from the averaged and rescaled wavefront measurements using standard Fourier optics procedures (Goodman, 1996).

Subjective DOFi measurements were averaged and mean and standard deviation calculated. Differences in DOFi between conditions were analyzed. A Wilcoxon matched-pairs signed-rank test was performed to check if differences in $DOFi_N$ and $DOFi_C$ were significant and orthogonal regression of these two variables was obtained.

We studied the linear relationship between DOFi and the root mean square (RMS) of HOAs, and between DOFi and Strehl Ratio. Standardized major-axis fits and Spearman correlations were obtained for both pairs. Bonferroni correction was applied. Thus, the level set to determine statistical significance was 0.025 (= 0.05 / 2 correlations). A two-way analysis of variance (ANOVA) was performed in order to see the effects on DOFi of subjects (interindividual differences) and of changing the pattern of wavefront aberrations. The null hypothesis of homogeneity of variances among subjects and among patterns of aberrations could not be rejected using Levene tests at a significance level of 0.05. Nevertheless, the null hypothesis that the residuals follow a normal distribution was rejected with the Shapiro–Wilk test for normality. We used the ANOVA even though the data was not normally distributed because there is no established alternative to the two-way ANOVA and because its key outcomes are the signal-to-noise ratios (*F* statistics), which are a good way to quantify the relative effects of subjects and patterns of wavefront aberrations on DOFi, regardless of the distributions of the data.

Results

Subjective DOFi with and without natural HOA: $DOFi_N$ and $DOFi_C$

Average $DOFi_N$ over all subjects was 1.27 ± 0.38 D ($M \pm SD$) for a 3.8-mm pupil, varying from 0.62 to 1.83 D. Correlation was not statistically significant for $DOFi_N$ with HOA RMS (Spearman $r = 0.146$, $p = 0.673$), or with Strehl ratio (Spearman $r = -0.136$, $p = 0.694$). Figure 2 shows the $DOFi_N$ as a function of HOA RMS (left) and as a function of Strehl ratio (right) with the corresponding standardized major-axis fits.

Average $DOFi_C$ over all subjects was 1.01 ± 0.32 D ($M \pm SD$), varying from 0.51 to 1.43 D. The analysis of correlation between $DOFi_C$ and the previously corrected HOA RMS (Spearman $r = -0.346$, $p = 0.300$), and Strehl ratio (Spearman $r = 0.346$, $p = 0.300$) did not achieve statistically significant correlation (Figure 3).

$DOFi_C$ was positively correlated with $DOFi_N$, showing the relation: $DOFi_C = 0.760 \times DOFi_N + 0.045$ (major-axis fit) with $R^2 = 0.461$. Figure 4 shows the subjective $DOFi_N$ and $DOFi_C$ ordered as increasing value of $DOFi_N$. As can be seen, the change in subjective DOFi after HOA correction is different in every subject, but statistical significant difference ($p = 0.042$) between both conditions was achieved. Although seven of the 11 subjects show $DOFi_C < DOFi_N$, this was not the case for the rest of subjects.

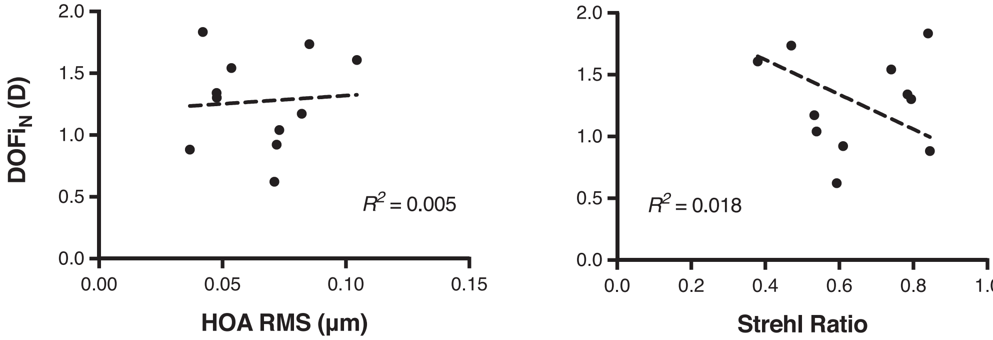

Figure 2. Correlation between subjective DOFi in the natural condition ($DOFi_N$) and HOA RMS (left), and Strehl ratio (right). Dashed lines were obtained using standardized major-axis fit.

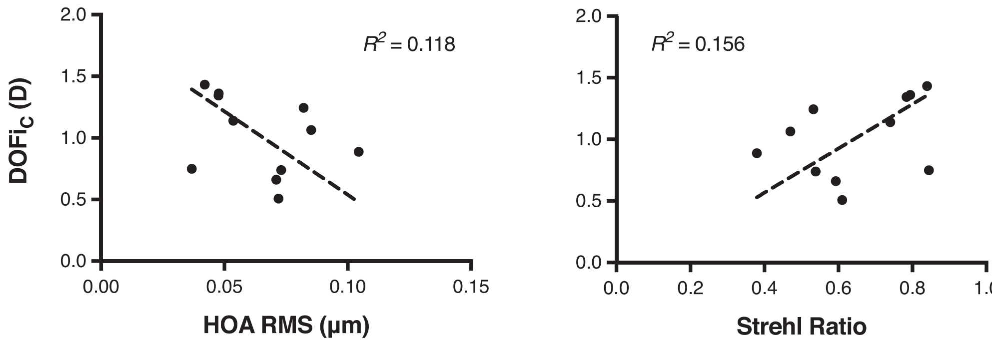

Figure 3. Correlation between subjective DOFi after HOA correction ($DOFi_C$) and the previously corrected HOA RMS (left), and Strehl ratio (right). Dashed lines were obtained using standardized major axis.

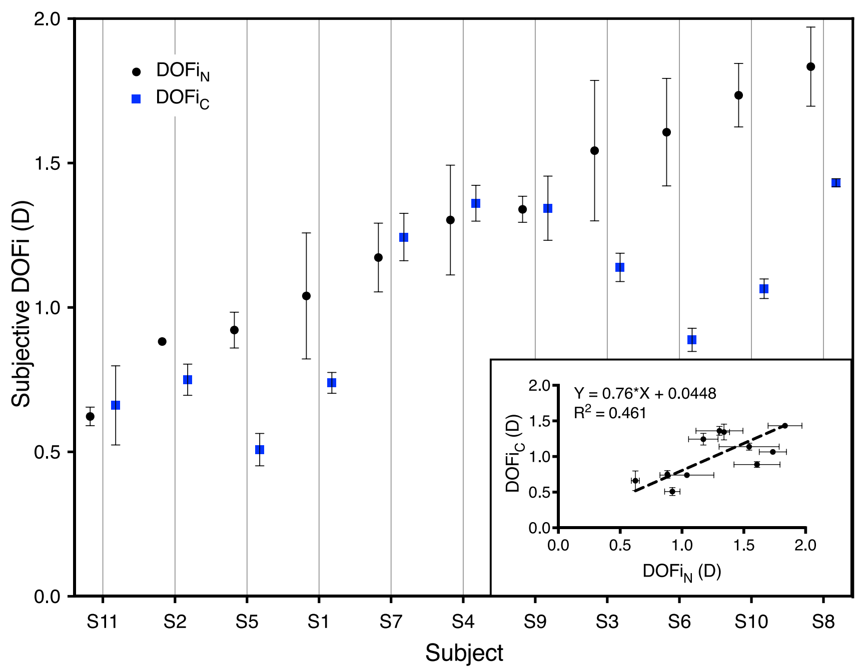

Figure 4. Subjective DOFi of every subject before ($DOFi_N$, black dots) and after ($DOFi_C$, blue squares) correcting their HOAs. Correlation of $DOFi_N$ with $DOFi_C$ is shown in additional lower right graph. Dashed line represents orthogonal regression (equation and R^2 are shown). Error intervals represent $\pm SEM$.

Summary of DOFi measurements in Diopters

Subject	Corrected HOA	S1 HOA	S2 HOA	S3 HOA	S4 HOA	S5 HOA	S6 HOA	S7 HOA	S8 HOA	S9 HOA	S10 HOA	S11 HOA
S1	0.74	**1.04**										
S2	0.75	0.43	**0.88**									
S3	1.14	—	1.20	**1.54**								
S4	1.36	1.73	1.69	1.45	**1.30**							
S5	0.51	0.25	0.31	0.39	0.43	**0.92**						
S6	0.89	0.58	1.16	—	0.65	0.92	**1.61**					
S7	1.24	0.79	1.23	—	—	1.25	—	**1.17**				
S8	1.43	1.29	1.36	—	—	1.66	1.39	—	**1.83**			
S9	1.34	1.24	1.42	—	—	0.97	1.26	—	1.01	**1.34**		
S10	1.07	0.71	0.76	0.77	0.53	0.66	—	—	—	—	**1.74**	
S11	0.66	—	1.26	—	0.72	1.24	—	—	—	—	1.24	**0.62**

Table 2. Summary of depth of field measurements in all conditions. *Note*: Columns represent each simulation and rows represent the subject in which DOFi was measured. Data are averages of three measurements. Bold values represent $DOFi_N$. HOA = higher order aberration.

Subjective DOFi after HOA simulations: $DOFi_S$

Table 2 shows DOFi values measured under all conditions. The DOFi values after simulations of other subjects' natural HOA patterns ($DOFi_S$) are shown from the third column to the last column. As can be seen in Table 2, each HOA pattern has a different effect on $DOFi_S$ when induced for different subjects. New HOA patterns tend to decrease $DOFi_S$ in most of the subjects, but in a few subjects, $DOFi_S$ increased when new HOA patterns were simulated (e.g., S4 and S11). Both subject, $F(10, 34) = 9.487$, $p < 0.001$, and HOA, $F(11, 34) = 2.423$, $p = 0.024$, had a significant effect on subjective DOFi. The variance in DOFi explained by interindividual differences was, thus 3.9 times (9.487 / 2.423) greater than the variance explained by changes in optical wavefront. Figure 5 shows an example of the variability in DOFi between two subjects.

Discussion

The present study tackles two main questions: (a) to what extent natural HOAs influence the DOFi of the eye? and (b) is the variability in DOFi between subjects explained by HOAs, by neural factors, or both? To this effect, we measured the DOFi with and without HOAs to answer the first question, while the DOFi obtained after an exchange of aberrations between subjects will shed light to the second question.

Our $DOFi_N$ results agreed well with the ones shown by Atchison et al. (2009) under similar conditions. They

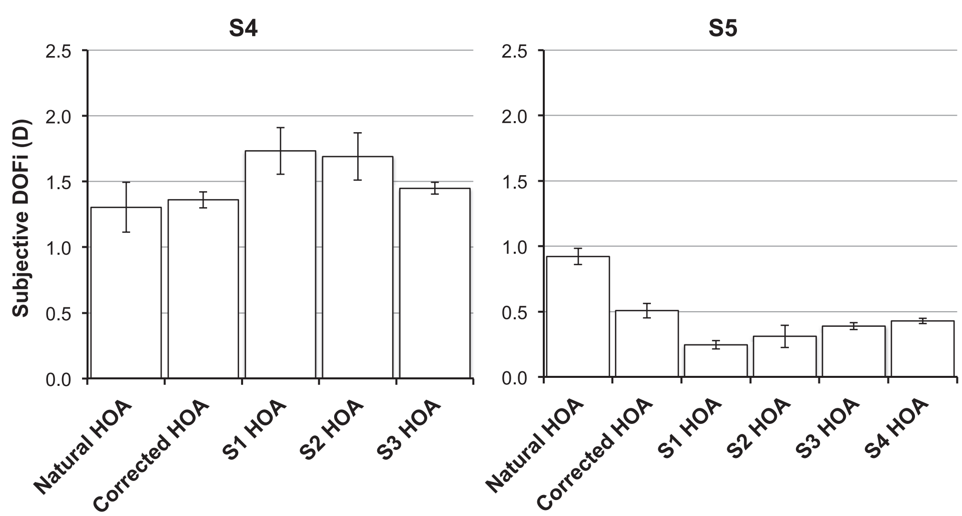

Figure 5. Example of the change in $DOFi_S$ of two subjects. S4 (left) and S5 (right), when different HOA patterns were simulated. Bars represent the average subjective DOFi in each case. Error intervals represent ±*SEM*.

found a mean subjective $DOFi_N$ of approximately 1.30 D (seven subjects, 4-mm pupil diameter, objectionable blur), while in the present study the average subjective $DOFi_N$ was 1.27 D (11 subjects, 3.8-mm pupil diameter, objectionable blur). Nevertheless, DOFi after HOA correction was substantially smaller in the present study (1.01 D) than in Atchison et al. (2009) study (approximately 1.20 D). The main difference between both studies was the 6-min period of adaptation to the corrected condition in the present study. This adaptation to a sharper image might have increased subjects' perceptual blur thresholds (Webster et al., 2002) and thus decreased subjective DOFi compared to a nonadapted corrected condition.

An important finding of this research is that DOFi changed significantly after HOA correction, which demonstrates the influence of natural HOA on DOFi. Assuming that long-term blur adaptation is playing a small role, it is worth noting that the difference in DOFi between the two conditions (natural and after HOA correction) might be considered as the impact of natural HOA on subjective DOFi. On average, subjective DOFi decreased by 21% when HOAs were corrected for a 3.8-mm pupil size, although this difference is clearly dependent on the subject (Figure 4). These results answer our first question about the extent of the influence of HOAs on DOFi. Nevertheless, image quality metrics (HOA RMS and Strehl ratio) measured at best focus, were not correlated with $DOFi_N$ or $DOFi_C$ in our study (Figures 2 and 3), which suggests that nonoptical factors may have a more important role on the differences observed in DOFi. This finding concurs with Atchison et al. (2009) who found a small and nonsignificant decrease of 8% on DOFi after HOA correction for several pupil diameters (3, 4, and 6 mm) and several blur criteria (just noticeable, troublesome, and objectionable blur). It is worth noting that in the natural condition, the natural HOAs of the eye were not corrected and then induced. The subjects were corrected for low-order aberrations only. Thus, it is likely that measurement errors and noise were not of the same magnitude in the natural condition than those in the rest of conditions.

$DOFi_C$ was positively correlated with $DOFi_N$—that is, subjects who presented larger DOFi in the natural condition showed a similar trend after HOA correction (Figure 4). Thus, differences in $DOFi_N$ between subjects are not only due to different HOA patterns, as these differences remain after HOA correction. Moreover, the correlation between $DOFi_C$ and the amount of corrected HOA (expressed in terms of HOA RMS and Strehl ratio) did not achieve statistical significance (Figure 3). This suggests that the aftereffect of a long-term neural adaptation to the previously corrected HOA was not responsible for the DOFi extent after correcting these HOA.

The variability of subjects' $DOFi_C$ (Figure 4) suggests that the neural processing associated to the detection of blur may be somewhat different between subjects. These results agree with those from Atchison et al. (2009) who also found a considerable range of blur sensitivity between subjects. They found up to 3.1 times different DOFi between the most and the least sensitive subjects. Coppens and van den Berg (2004) also found a considerable variability in the resolving ability of the subjects for different blurred stimuli even when the contribution of the PSF on the retinal image was negligible. Indeed, those researchers suggested that these differences in neural processing of the retinal image between subjects might form part of the explanation of the large differences in VA among the population. In the present study, we asked if variance in DOFi among subjects is influenced more by optical or neural factors. We investigated the effect of these factors on the variance in DOFi when the same HOA pattern was induced for different subjects (including the corrected condition), and when different HOA patterns were induced to the same subject—that is, different neural factors (subjects) with same optics (HOA pattern)—and the same neural factors (subject) with different optics (HOA patterns). In the hypothetical case that only optical factors are influencing subjective DOFi, two subjects looking through the same HOA pattern should present a similar DOFi. Table 2 clearly shows that this is not the case. The example in Figure 5 shows that S5 did not present the same DOFi extent as S4 when looking through S4's HOA pattern. It is expected that S4's long-term adaptation to his own HOA must have yielded a higher DOFi extent than S5's short-term adaptation to the same HOA pattern. However, both subjects were at the same stage of adaptation when the S1, S2, and S3's HOA patterns were simulated, and they did not present similar DOFi in any case. These results show that the subjects' individual perceptual processing has an impact on DOFi and its difference between subjects, even when looking through the same HOA pattern at the same stage of adaptation. Thus, the modulation of DOFi by inducing new HOA patterns does not produce the same visual perception in all subjects. The results of the two-way ANOVA showed that the effect of neural factors (others than neural adaptation to defocus) accounted for 3.9 times more than the effect of HOA, although both factors had a significant effect on DOFi.

These results suggest that new approaches that try to extend DOFi of the eye by inducing aberrations to mitigate the effects of presbyopia (Benard et al., 2011; Yi et al., 2011; Villegas et al., 2014) might achieve unpredicted results depending on the subject due to the potential influence of the individual neural processing of the retinal image. Thus, the suitability of every subject to these approaches should be studied in advance by using psychophysical techniques. Further investigation is needed to study which approaches are effective to measure such suitability. Adaptive optics systems have been proved to be a good option to bypass the optical factors influencing the visual function and study its neural factors (Artal et al., 2004), but they are still complicated and expensive to be used in everyday clinical practice. Some other approaches, such as contrast detection in noise methods (Legge, Kersten, & Burgess, 1987; Pardhan, Gilchrist, & Khar, 1993; Pardhan, 2004; Radhakrishnan & Pardhan, 2006; Goris, Zaenen, & Wagemans, 2008), could be effective to achieve this goal, as they have been used to isolate the sampling efficiency of the visual system from the internal noise produced by optical factors. If the measurement of the sampling efficiency is able to predict the suitability of the subject to the induction of aberrations, this could avoid the possible disappointment following surgical methods.

In conclusion, the main findings of this study are that the eye's natural HOAs influence subjective DOFi. The HOAs are not solely responsible for between-subjects differences, and the manipulation of HOAs might have a different effect on subjective DOFi depending on the subject. These conclusions suggest that inducing HOAs to extend DOFi and mitigate the effects of presbyopia might benefit some individuals more than others. Hence, this approach will be beneficial if done on a case-by-case basis.

Keywords: wavefront aberrations, *depth of field*, *depth of focus*, *visual optics*, *physiological optics*

Acknowledgments

This work has been funded by the European Marie Sklodowska-Curie Grant AGEYE 608049-FP7-People to JZD, HR, and NLG, and by the Fundación Séneca Grant, Región de Murcia 15312/PI/10 to NLG. The authors declare that there is no conflict of interest regarding the publication of this paper.

Commercial relationships: none.
Corresponding author: Hema Radhakrishnan.
Email: hema.radhakrishnan@manchester.ac.uk.
Address: Faculty of Biology, Medicine & Health, The University of Manchester, Manchester Academic Health Science Center, Manchester, UK.

References

American National Standards Institute. (2004). *American National Standard for Ophthalmics: Methods for reporting optical aberrations of the eye* (ANSI Z80.28-2004), Washington, DC: Author.

Artal, P., Chen, L., Fernández, E. J., Singer, B., Manzanera, S., & Williams, D. R. (2004). Neural compensation for the eye's optical aberrations. *Journal of Vision*, *4*(4):4, 281–287, https://doi.org/10.1167/4.4.4. [PubMed] [Article]

Atchison, D. A., Fisher, S. W., Pedersen, C. A., & Ridall, P. G. (2005). Noticeable, troublesome and objectionable limits of blur. *Vision Research*, *45*(15), 1967–1974.

Atchison, D. A., Guo, H., & Fisher, S. W. (2009). Limits of spherical blur determined with an adaptive optics mirror. *Ophthalmic and Physiological Optics*, *29*(3), 300–311.

Benard, Y., López-Gil, N., & Legras, R. (2010). Subjective depth of field in presence of 4th-order and 6th-order Zernike spherical aberration using adaptive optics technology. *Journal of Cataract & Refractive Surgery*, *36*(12), 2129–2138.

Benard, Y., López-Gil, N., & Legras, R. (2011). Optimizing the subjective depth-of-focus with combinations of fourth- and sixth-order spherical aberration. *Vision Research*, *51*(23–24), 2471–2477.

Bernal-Molina, P. (2017). Estudios teóricos y experimentales del efecto de las aberraciones en la profundidad de campo, la refracción y la acomodación ocular [Theoretical and experimental studies of the effect of aberrations in depth-of-field, refraction and ocular accommodation]. València: Universitat de València.

Bernal-Molina, P., Montés-Micó, R., Legras, R., & López-Gil, N. (2014). Depth-of-field of the accommodating eye. *Optometry and Vision Science*, *91*(10), 1208–1214.

Campbell, F. W., & Green, D. G. (1965). Optical and retinal factors affecting visual resolution. *The Journal of Physiology*, *181*(3), 576–593.

Castejón-Mochón, J. F., López-Gil, N., Benito, A., & Artal, P. (2002). Ocular wave-front aberration statistics in a normal young population. *Vision Research*, *42*(13), 1611–1617.

Charman, W. N. (2014). Developments in the correction of presbyopia II: surgical approaches. *Ophthalmic and Physiological Optics*, *34*(4), 397–426.

Coppens, J. E., & van den Berg, T. J. T. P. (2004). A new source of variance in visual acuity. *Vision Research*, *44*(9), 951–958.

Cufflin, M. P., Mankowska, A., & Mallen, E. A. H. (2007). Effect of blur adaptation on blur sensitivity and discrimination in emmetropes and myopes.

Investigative Ophthalmology & Visual Science, *48*(6), 2932–2939.

de Gracia, P., Dorronsoro, C., & Marcos, S. (2013). Multiple zone multifocal phase designs. *Optics Letters*, *38*(18), 3526–3529.

de Gracia, P., & Hartwig, A. (2017). Optimal orientation for angularly segmented multifocal corrections. *Ophthalmic and Physiological Optics*, *37*(5), 610–623.

Delori, F. C., Webb, R. H., & Sliney, D. H. (2007). Maximum permissible exposures for ocular safety (ANSI 2000), with emphasis on ophthalmic devices. *Journal of the Optical Society of America A*, *24*(5), 1250–1265.

Goodman, J. W. (1996). *Introduction to Fourier optics* (2nd ed.). New York: McGraw-Hill.

Goris, R. L. T., Zaenen, P., & Wagemans, J. (2008). Some observations on contrast detection in noise. *Journal of Vision*, *8*(9):4, 1–15, https://doi.org/10.1167/8.9.4. [PubMed] [Article]

Guo, H., Atchison, D. A., & Birt, B. J. (2008). Changes in through-focus spatial visual performance with adaptive optics correction of monochromatic aberrations. *Vision Research*, *48*(17), 1804–1811.

Hickenbotham, A., Tiruveedhula, P., & Roorda, A. (2012). Comparison of spherical aberration and small-pupil profiles in improving depth of focus for presbyopic corrections. *Journal of Cataract & Refractive Surgery*, *38*(12), 2071–2079.

Khan, K. A., Dawson, K., Mankowska, A., Cufflin, M. P., & Mallen, E. A. H. (2013). The time course of blur adaptation in emmetropes and myopes. *Ophthalmic and Physiological Optics*, *33*(3), 305–310.

Legge, G. E., Kersten, D., & Burgess, A. E. (1987). Contrast discrimination in noise. *Journal of the Optical Society of America A*, *4*(2), 391–404.

Legras, R., Benard, Y., & López-Gil, N. (2012). Effect of coma and spherical aberration on depth-of-focus measured using adaptive optics and computationally blurred images. *Journal of Cataract & Refractive Surgery*, *38*(3), 458–469.

Leube, A., Ohlendorf, A., & Wahl, S. (2016). The influence of induced astigmatism on the depth of focus. *Optometry and Vision Science*, *93*(10), 1228–1234.

Liang, J., Williams, D. R., & Miller, D. T. (1997). Supernormal vision and high-resolution retinal imaging through adaptive optics. *Journal of the Optical Society of America A*, *14*(11), 2884–2892.

Marcos, S., Moreno, E., & Navarro, R. (1999). The depth-of-field of the human eye from objective and subjective measurements. *Vision Research*, *39*(12), 2039–2049.

Marcos, S., Sawides, L., Gambra, E., & Dorronsoro, C. (2008). Influence of adaptive-optics ocular aberration correction on visual acuity at different luminances and contrast polarities. *Journal of Vision*, *8*(13):1, 1–12, https://doi.org/10.1167/8.13.1. [PubMed] [Article]

Marcos, S., Velasco-Ocana, M., Dorronsoro, C., Sawides, L., Hernandez, M., & Marin, G. (2015). Impact of astigmatism and high-order aberrations on subjective best focus. *Journal of Vision*, *15*(11):4, 1–12, https://doi.org/10.1167/15.11.4. [PubMed] [Article]

Nio, Y. K., Jansonius, N. M., Fidler, V., Geraghty, E., Norrby, S., & Kooijman, A. C. (2002). Spherical and irregular aberrations are important for the optimal performance of the human eye. *Ophthalmic and Physiological Optics*, *22*(2), 103–112.

Pardhan, S. (2004). Contrast sensitivity loss with aging: sampling efficiency and equivalent noise at different spatial frequencies. *Journal of the Optical Society of America A*, *21*(2), 169–175.

Pardhan, S., Gilchrist, J., & Khar, G. (1993). Contrast detection in noise: A new method for assessing the visual function in cataract. *Optometry and Vision Science*, *70*(11), 914–922.

Porter, J., Guirao, A., Cox, I. G., & Williams, D. R. (2001). Monochromatic aberrations of the human eye in a large population. *Journal of the Optical Society of America A*, *18*(8), 1793–1803.

Radhakrishnan, H., & Pardhan, S. (2006). Contrast detection in noise with positive and negative defocus in myopes. *Vision Research*, *46*(18), 2949–2955.

Rocha, M. R., Vabre, L., Chateau, N., & Krueger, R. R. (2009). Expanding depth of focus by modifying higher-order aberrations induced by an adaptive optics visual simulator. *Journal of Cataract & Refractive Surgery*, *35*(11), 1885–1892.

Rossi, E. A., & Roorda, A. (2010). Is visual resolution after adaptive optics correction susceptible to perceptual learning? *Journal of Vision*, *10*(12):11, 1–14, https://doi.org/10.1167/10.12.11. [PubMed] [Article]

Sawides, L., de Gracia, P., Dorronsoro, C., Webster, M., & Marcos, S. (2011). Adapting to blur produced by ocular high-order aberrations. *Journal of Vision*, *11*(7):21, 1–11, https://doi.org/10.1167/11.7.21. [PubMed] [Article]

Schwiegerling, J. (2002). Scaling Zernike expansion coefficients to different pupil sizes. *Journal of the Optical Society of America A*, *19*(10), 1937–1945.

Thibos, L. N., Applegate, R. A., Schwiergerling, J. T., & Webb, R. (2002). Standards for reporting the optical aberrations of eyes. *Journal of Refractive Surgery*, *18*(5), S652–S660.

Thibos, L. N., Hong, X., Bradley, A. & Cheng, X. (2002). Statistical variation of aberration structure and image quality in a normal population of healthy eyes. *Journal of the Optical Society of America A*, *19*(12), 2329–2348.

Tucker, J., & Charman, W. N. (1975). The depth-of-focus of the human eye for Snellen letters. *American Journal of Optometry and Physiological Optics*, *52*(1), 3–21.

Villegas, E. A., Alcón, E., Mirabet, S., Yago, I., Marín, J. M., & Artal, P. (2014). Extended depth of focus with induced spherical aberration in light-adjustable intraocular lenses. *American Journal of Ophthalmology*, *157*(1), 142–149.

Wang, B., & Ciuffreda, K. J. (2006). Depth-of-focus of the human eye: theory and clinical implications. *Survey of Ophthalmology*, *51*(1), 75–85.

Webster, M. A., Georgeson, M. A., & Webster, S. M. (2002). Neural adjustments to image blur. *Nature Neuroscience*, *5*, 839–840.

Yi, F., Iskander, R., & Collins, M. J. (2011). Depth of focus and visual acuity with primary and secondary spherical aberration. *Vision Research*, *51*(14), 1648–1658.

Yoon, G.-Y., & Williams, D. R. (2002). Visual performance after correcting the monochromatic and chromatic aberrations of the eye. *Journal of the Optical Society of America A*, *19*(2), 266–275.