



Optical factors influencing the amplitude of accommodation

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ARTICLE INFO

Article history:

Received 12 April 2016

Received in revised form 7 September 2016

Accepted 9 September 2016

Available online xxxx

Keywords:

Amplitude of accommodation

Presbyopia

Depth of focus

Aberrometry

Spherical aberration

Statistical modeling

ABSTRACT

The purpose of this work was to find plausible predictors among optical parameters that may explain the inter-individual differences in subjective amplitude of accommodation not explained by age. An exploratory multivariable regression analysis was carried out retrospectively on a dataset with 180 eyes from 97 subjects (ages ranged from 20 to 58 years). Subjective amplitudes of accommodation were recorded with the use of a custom-made Badal system. A commercial aberrometer was used to obtain each eye's wavefront during the full range of accommodation. The plausible predictors under study were pupil diameter in the unaccommodated eye, its reduction with accommodation; fourth- and six-order Zernike spherical aberration, their reduction with accommodation, and subjective refraction. At a significance level of 0.05, only fourth- and sixth-order Zernike spherical aberration were found to be predictors of subjective amplitude of accommodation not explained by age, each explaining on their own less than 5% of the variance, and about 9% together. All other optical parameters explained less than 2%. Spherical aberration did not explain the greater variability for younger eyes than for older eyes. The remainder variability in amplitude of accommodation not explained by age or spherical aberration was about ± 2.6 D for 20 year-old subjects, ± 1.5 D for 40 year-old subjects, and about ± 0.6 D for 55 year-old subjects. Optical factors do not seem to account for much of the inter-individual differences in subjective amplitude of accommodation. Most of the variability not explained by age must be due to anatomical differences and physiological, psychological, or other factors.

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1. Introduction

Although the reduction in the ability to accommodate is an irreversible consequence of visual function senescence, there are very large inter-individual differences in the maximum accommodation capacity for subjects of the same age. Fig. 1 is a reprint of a figure from Duane (Duane, 1922; Duane, 1909; Duane, 1912) showing the decrease in subjective amplitude of accommodation (AA) with age. The inter-individual differences are evident. For instance, for subjects of age 20, there are some subjects who accommodate more than 6 D more than others. Even for presbyopes older than 52 years, differences in AA can be as large as 2 D.

Duane's AA data may have been considerably influenced by axial refraction (Bernal-Molina, Vargas-Martín, Thibos, & López-Gil, 2016), as it was measured to the spectacle plane (Duane, 1909). Although he did not report specific refraction values of the subjects, this may explain the large variability of AA for any given age as seen in Fig. 1. In contrast, mean values of the data

obtained by Jackson (solid blue curve superimposed on Duane's graph in Fig. 1), who used a more appropriate plane of reference placed 2 mm behind the corneal vertex (Xu, Bradley, Lopez Gil, & Thibos, 2015), show lower subjective AA values, especially for non-presbyopic eyes. Jackson's data also exhibited larger inter-individual differences, even for subjects with age beyond 52 years (Fig. 1). The large variability in the AA found by these two researchers has also been found in more recent studies using subjective and objective measurements (Ostrin & Glasser, 2004; Wold, Hu, Chen, & Glasser, 2003).

The different methodology used by these two researchers may explain their differences in the mean AA value and illustrates that, in general, special care should be taken when comparing values of subjective AA obtained in different studies. In addition to differences in calculations, instructions given to subjects (Stark & Atchison, 1994), stimulus (Stark & Atchison, 1994), object luminance (Johnson, 1976; Lara, Bernal-Molina, Fernandez-Sanchez, & Lopez-Gil, 2014), and object chromaticity (Drew, Borsting, Stark, & Chase, 2012); refractive errors, amblyopia and biometric parameters (Maheshwari et al., 2011), and letter size (Heath, 1956; Lopez-Gil et al., 2013) have been shown to play an important role in the outcome of subjective AA. However, none of those studies, or

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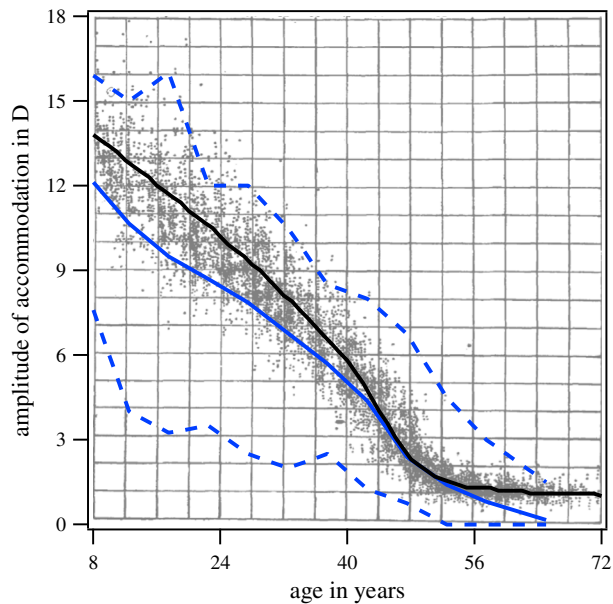


Fig. 1. Change in amplitude of accommodation with age. Original data from Duane (Duane, 1922), reprinted from American Journal of Ophthalmology, 5, Duane A, Studies in monocular and binocular accommodation with their clinical applications, 865–77, 1922, with permission from Elsevier. The solid black curve represents the mean AA and its change with age from Duane data. The solid blue curve represents the mean AA and its change with age from Jackson (Jackson, 1907) data. Maximum and minimum at each age (dashed blue curves) are also shown.

any other published so far, have provided an explanation of the large variability of the AA between subjects with similar biological parameters using similar methodological procedures (Duane, 1912; Jackson, 1907; Wold et al., 2003). Large variability in the AA may be due to inter-individual differences in ciliary muscle function or lens properties, optical factors other than physiological power change (ametropia, pupil size, HOA, ...), or psychological factors, such as variability in blur criterion among individuals (Woods, Colvin, Vera-Diaz, & Peli, 2010) or between different trials of the same individual. Other experimental errors also add to variability.

It is well known that high-order aberrations (HOA) differ considerably between subjects (Salmon & van de Pol, 2006; Thibos, Hong, Bradley, & Cheng, 2002) and that they affect the eye's depth of focus (DoF) (Benard, Lopez-Gil, & Legras, 2010; Rocha, Vabre, Chateau, & Krueger, 2009), as well as the accommodative response (Lopez-Gil & Fernandez-Sanchez, 2010). Nevertheless, since each eye of the same subject has slightly different HOA (Castejon-Mochon, Lopez-Gil, Benito, & Artal, 2002), their subjective AA should be different, which is not usually the case (Sabesan, Zheleznyak, & Yoon, 2012). One might argue that the reason they are not different is that the differences in HOA between eyes is not large enough to produce a measurable difference in DoF between eyes, or because DoF is mainly affected by those HOA that present similar magnitudes in most eyes (Castejon-Mochon et al., 2002; Porter, Guirao, Cox, & Williams, 2001). However, it has been shown that LASIK does not seem to change AA greatly, even though it does significantly change HOA.

Several studies have been performed so far regarding the variations of the aberration during accommodation (Duane, 1912; Jackson, 1907), its dependence with age (Castejon-Mochon et al., 2002; Ostrin & Glasser, 2004; Radhakrishnan & Charman, 2007; Sabesan et al., 2012), different ocular parameters (Abraham et al., 2010); and the variability of the AA measurements (Antona, Barra, Barrio, Gonzalez, & Sanchez, 2009). Nevertheless, no optical explanations have yet been given to the large variation found among the normal population.

The purpose of this work was to estimate how much optical factors such as pupil diameter, spherical aberrations (SA) and their variation with accommodation, and uncorrected spherical equivalent explain inter-individual differences in subjective AA not explained by aging. A non-linear model was fitted to the subjective AA and residuals, i.e., the part in AA not explained by age, extracted. In an exploratory analysis, simple and multiple linear regression fits were obtained for the residual AA over one or more covariates and the most statistically plausible model selected.

2. Methods

2.1. Subjects

This was a retrospective study with data extracted from a dataset of 180 eyes from 97 subjects (López-Gil, Fernández-Sánchez, Thibos, & Montés-Micó, 2009). All subjects in the study had a visual acuity of 20/20 or better in the eye analyzed. Exclusion criteria included eyes with glaucoma, conjunctivitis, keratitis, cataracts, dry eye syndrome, and amblyopia eyes. Eyes were discarded from young subjects that reported accommodative insufficiency or for which that insufficiency was evident during an initial clinical evaluation. After that evaluation none of the eyes involved in this study presented any factor that could interfere with general or ocular health, including accommodation and visual function. The study was conducted following the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant before testing and after explaining the procedure and goals of the experiment.

2.2. Subjective measurement of the amplitude of accommodation

The amplitude of accommodation was obtained subjectively with a custom-made Badal optometer. The stimulus used was a Bailey-Lovie chart (with a luminance of 100 cd/m²) located 6 m (20 feet) from the subject's eye. Optical details of the Badal optometer and measurement procedures have been described elsewhere (López-Gil et al., 2009). The origin of vergences used was the entrance pupil plane of the eye. The instrumental precision was ± 0.1 D. The subject's head was fixed using a chin rest and astigmatism corrected with a trial lens placed 12 mm in front of the eye. To avoid diplopia, the contralateral eye was covered. Changes in the equivalent sphere caused by astigmatism correction, as well as the distance between the target and the moving lens, were taken into account using Gaussian optics in the computation of the near and far point. The subject's task was to find the two extreme positions of the lens where the 20/25 line of letters was maintained clear without any perceptible blur. The same trained optometrist performed all subjective measurements. Mean and standard deviation of 5 repeated measurements for both subjective far and near points were obtained. When left and right eyes were measured, it was made randomly and without taking into account the potential difference between dominant and non-dominant eye. A high contrast letter chart with 20/25 letters was used as stimulus since it stimulus contains high spatial frequencies and so blur can be more easily detected when it is out of focus. The Badal system assured that the spatial frequency content in terms of cycles per degree stayed constant at any vergence.

2.3. Measurements of wavefront aberrations at different accommodative states

Wavefront aberrations of each eye were recorded during accommodation with a commercial aberrometer (irx3 Imagine Eyes, France). This device has a Shack-Hartmann wavefront sensor

with a 32×32 microlens array that measures the ocular wavefront with an exposure time of 33 ms. The built-in fixation target was polychromatic with multiple spatial frequencies (a balloon at the end of a road). Near infrared light (780 nm) was used for the wavefront measures. Subjects were instructed to carefully focus on the target and keep it as clear as possible during the experiment. Details can be found elsewhere (Lopez-Gil et al., 2008).

Measurements were taken as the target approached the eye by means of an internal Badal system in the aberrometer. The vergence was changed in steps of 0.5 D, starting from a point 0.5 D beyond the far point obtained with standard aberrometry and Zernike refraction (Thibos et al., 2004). The range of vergences used was at least one diopter larger than the subject's interval of clear vision. All measurements were taken monocularly (with the contralateral eye occluded), and the wavefront and pupil diameter recorded.

2.4. Statistical analysis

For the dataset of 180 eyes from 97 subjects, a linear model that explains part of the variability in subjective AA (mean of 5 repeated measures) not explained by age was derived from the list of candidate covariates in Table 1 as follows. First, a non-parametric local quadratic method, loess (Cleveland, 1979), was used to fit subjective AA as a function of age, with the smoothing parameter set to 1. Second, simple linear regression was performed between each candidate covariate in Table 1 and the residual amplitude, i.e., the part in subjective AA not explained by age. The covariates that explained less than 1% of the variability in residual AA through the fitted linear model were discarded and multiple linear regression analyses performed on all possible combinations of two and three of the remainder covariates. Models with interaction terms were also inspected. The final model selected was that for which slopes of covariates were significantly different from zero, at a significance level of 0.05. As a validation analysis, a stepwise procedure was carried out using all covariates in Table 1 with Akaike Information Criterion (Akaike, 1974) and both backward and forward directions. The results of the manual and automatic procedures were the same. Parameters used in Table 1 are the ones that can theoretically influence the accommodation response. Rotationally asymmetrical HOA should have no influence in the static or dynamic accommodation response of the eye, as has been demonstrated for coma and trefoil (Lopez-Gil et al., 2007).

Because some subjects had their two eyes included in the dataset, the standard error of the slopes in the multivariable linear model explaining subjective AA and, hence, the p -value are likely underestimated (Armstrong, 2013). As a further validation of the final model obtained, the analysis was replicated three times: after

averaging eye data for each of the 97 subjects, after selecting only the left eye of the subjects with two eyes in the study, and after selecting only their right eye.

All statistical analyses were carried out in the software environment for statistical computing R (R Core Team, 2016) and Igor Pro (version 6.34A; WaveMetrics, Portland, OR, USA).

3. Results

The left panel of Fig. 2 shows the subjective AA as a function of age for 180 eyes of 97 subjects. The age model obtained with a loess fit (Cleveland, 1979) shows that, on average, subjective AA decreases approximately linearly with age until about age 40 or 45 at about -0.3 D per year, in agreement with previous cross-sectional studies (Hofstetter, 1944; Turner, 1958) and Charman's model of linear decrease of subjective AA with age (Charman, 1989). The variability of residual amplitude shown in the right panel of Fig. 2 clearly decreases with age from about ± 2.9 D at age 20 to about ± 1.5 D at age 40 and to about ± 0.5 D at age 55.

The only covariates in Table 1 that alone explained more than 1% of the variability in residual amplitude shown in the right panel of Fig. 2 were pupil diameter ($R^2 = 1.3\%$), change in pupil diameter ($R^2 = 1.3\%$), fourth-order spherical aberration ($R^2 = 4.6\%$), and sixth-order spherical aberration ($R^2 = 4.1\%$). Out of the 7 simple linear regression fits, one for each candidate predictor in Table 1, only those for fourth- and sixth-order SA gave slopes significantly different from zero. The multivariable linear regression fit derived from both the manual exploratory analysis and the automatic stepwise method included only fourth- and sixth-order spherical aberration. Thus, the subjective AA not explained by age, or residual amplitude, a_r , is estimated from Zernike spherical aberrations as

$$a_r = 0.1 - 1.8C_4^0 - 7.4C_6^0, \quad (1)$$

where a_r is expressed in D and C_4^0 and C_6^0 in microns. For a particular subject, the subjective AA can be predicted as the sum of AA given her or his age obtained with the loess fit plus the subjective AA calculated from Eq. (1) given her or his fourth- and sixth-order spherical aberrations. The multivariable model explained about 8.7% of the subjective AA not explained by age (adjusted R^2 was 7.6%). The left panel of Fig. 3 shows the residuals of the model, i.e. the subjective AA not explained by age or spherical aberrations as a function of predicted amplitude. Because there is no visible trend in the residuals, a linear model seems reasonable for describing the association between spherical aberration and AA. In the right panel of Fig. 3, the same residuals are shown as a function of age. Variability still continues to decrease with age, this time from about ± 2.6 D at age 20 to about ± 1.5 D at age 40 and to about ± 0.6 D at age 55.

The decrease in variability of subjective AA with age seen in the right panel of Fig. 3 (and also of Fig. 2) follows a clear funnel-shaped pattern; that is, variance of residual amplitude is not constant with age. In fact, they seem to be roughly proportional to the magnitude of subjective AA as can be seen in Fig. 4.

As in any analysis that attempts at gathering statistical evidence, results are influenced by sampled data and the methods decided upon. The multivariable-regression analysis was, therefore, replicated after averaging eyes' results for subjects whose two eyes were included in the study, after selecting only the left eye of those subjects, and after selecting the right eye. Table 2 shows the results of multivariable regression for these three datasets.

At a level of significance of 0.05, tests with only the right eye did not identify any of the two slopes for Zernike SA as different from zero. Significance was found if data for the left eye were used. For the average data per subject, only the slope for the sixth-order aberration was found significantly different from zero.

Table 1

List of candidate covariates in linear regression models for amplitude of accommodation not explained by age.

Name	Brief description
Spherical equivalent (far point)	Spherical equivalent (M) of the relaxed eye measured with the Badal system
Pupil diameter	Pupil size when the eye is fixating at its far point measured with the aberrometer
Fourth-order spherical aberration	C_4^0 Zernike coefficient of the unaccommodated eye ^a measured with the aberrometer
Sixth-order spherical aberration	C_6^0 Zernike coefficient of the unaccommodated eye ^a measured with the aberrometer
Change in pupil diameter	Difference in pupil size between far point and near point
Change in fourth-order spherical aberration	Difference in C_4^0 between far and near point
Change in sixth-order spherical aberration	Difference in C_6^0 between far and near point

^a Zernikes are presented for the measured natural pupil.

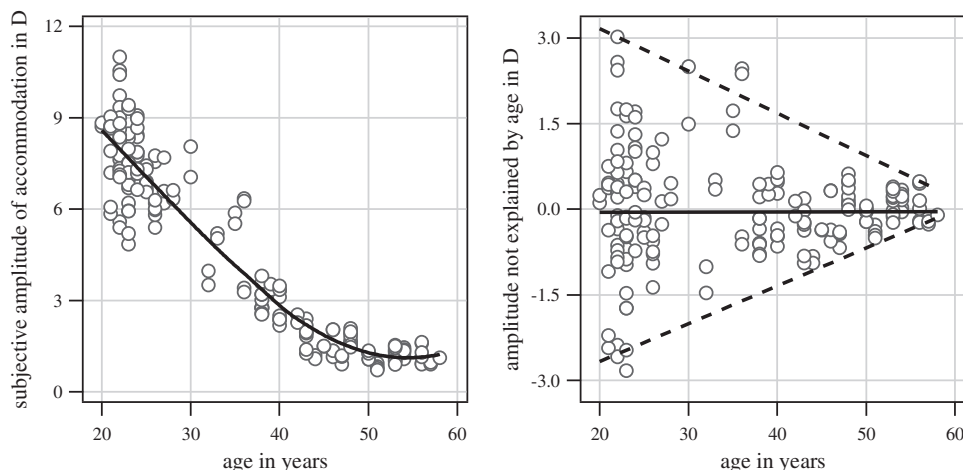


Fig. 2. Loess age model (solid line in left panel) and subjective amplitude of accommodation not explained by age, or residual amplitude (right panel), as a function of age. The open circles in left panel are the amplitude of accommodation for the 180 eyes of 97 subjects. The solid and dashed lines in the right panel are the median and 2.5% and 97.5% quantile functions on age obtained with quantile regression (Quantile Regression, 2005).

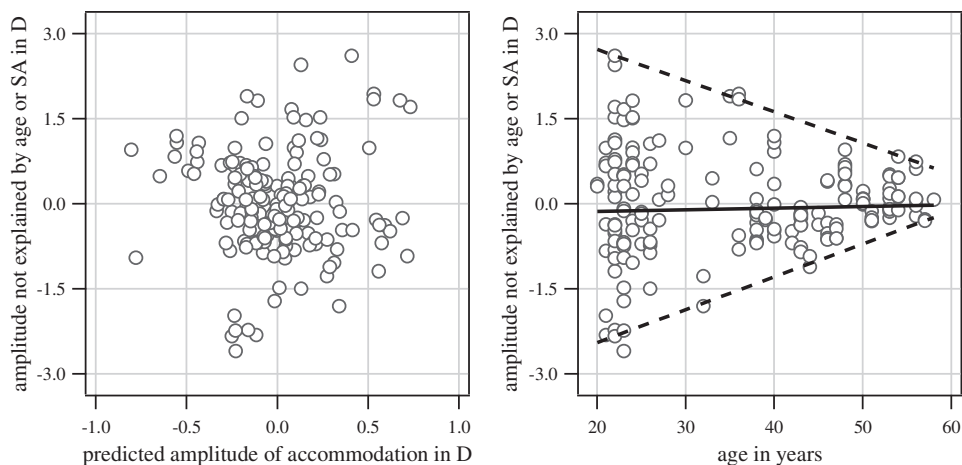


Fig. 3. Residuals of the model, i.e. subjective amplitude of accommodation not explained by age or fourth- and sixth-order spherical aberrations as a function of predicted amplitude (left panel) and as a function of age (right panel). Other details as in Fig. 2.

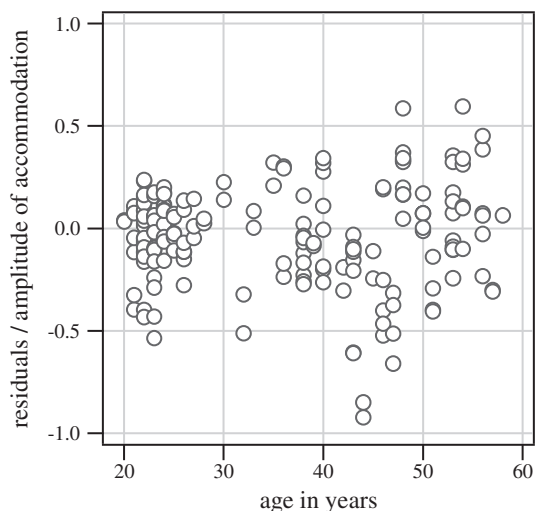


Fig. 4. Residuals divided by subjective amplitude of accommodation as a function of age.

4. Discussion

The main goal of this study was to identify optical factors explaining the inter-individual differences in subjective AA not explained by age in a large population of 180 eyes from 97 subjects. A statistical analysis was used for identification of predictors for subjective AA among plausible optical factors obtained from the measurement of the unaccommodated as well as the accommodated eye's wavefront (Table 1).

The first step was to remove the age effect on subjective AA. Left panel of Fig. 2 shows the relationship between monocular subjective AA and age. These AA values might increase a little for binocular vision (Duane, 1922). The solid curve was obtained with a local quadratic loess fit. Other models were tested, such as logarithm AA as a linear function of age, and for the same groups as in Table 2. The fits (not shown here) were remarkably similar to each other but did not seem to fit the data as well as the loess fit; the root-mean-squared error for the loess fit was 0.92 D, lower than for the logarithmic fit by 7.6%.

A weak, yet statistically significant association was found between subjective AA not explained by age; that is, not explained

Table 2

Intercept and slope estimates for different sub-datasets extracted from the 180 eyes from 97 subjects. The first column is the number of subjects included in the dataset. The second, third, and fifth columns are the estimates for intercept and slopes for the Zernike SA in each dataset. The fourth and sixth columns show the p -values for the slopes for fourth- and sixth-order SA.

	Sample size	Intercept	C_4^0 slope	p -value	C_6^0 slope	p -value
Only right eyes	83	0.0	−0.8	0.40	−6.3	0.10
Only left eyes	83	0.1	−1.7	0.04	−10.1	0.01
Average per subject	97	0.1	−1.3	0.12	−8.3	0.02

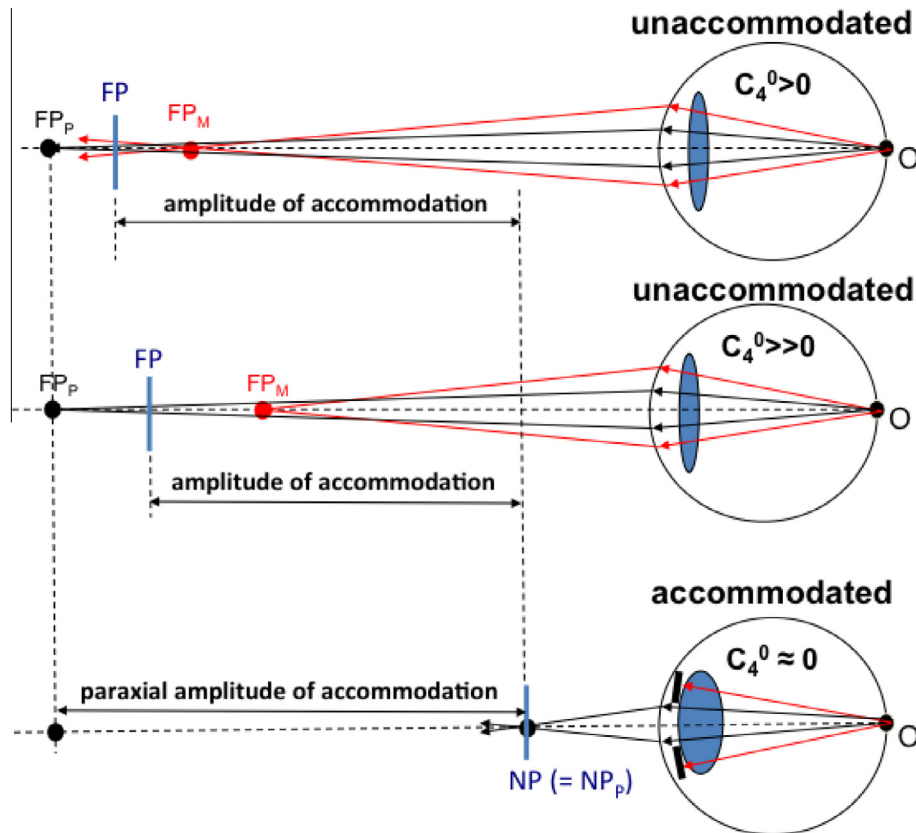


Fig. 5. Schematic ray tracing of the light coming out from a point source in the retina in a myopic eye. Top and middle panels show an unaccommodated myopic eye with low or high positive fourth-order spherical aberration, respectively. In the bottom panel a fully accommodated myopic eye is shown with a low value of fourth-order spherical aberration due to pupil accommodating. FP_P , FP_M , FP , NP_P , and NP indicate respectively the paraxial, marginal, and subjective far point, and the paraxial and subjective near point.

by the hardness process that the lens undergoes with time; and fourth- and sixth-order spherical aberration of the unaccommodated eye (Eq. (1)), which can change in a different way in subjects with the same age (López-Gil & Fernández-Sánchez, 2010; López-Gil et al., 2008; López-Gil et al., 2009). Spherical aberration explained only 8.7% of the variability in subjective AA not explained by age: 4.6% was explained by fourth-order SA and 4.1% by sixth-order SA. These results can be influenced, however, by the fact that this analysis was done with cross-sectional data leading to a non-linear average decrease of subjective AA, whereas decrease is possibly linear for each particular subject (Charman, 1989). A replication of the multivariable analysis for 112 eyes of the 62 subjects below 40 years of age, where average decrease is linear (see loess fit in the left panel of Fig 2), continued to find significant association of subjective AA with only fourth- and sixth-order SA, but with a greater R^2 ; variability explained by SA in subjective AA increased from 8.7% to 13.3%.

About 95% of pupils in the dataset had sizes from 3.6 mm to 7.3 mm for the unaccommodated eye, and the mean pupil change with accommodation was 1.7 mm. Yet, unexpectedly, pupil

diameter and its change during accommodation, which affects ocular DoF (Ripps, Chin, Siegel, & Breinin, 1962), were not found to affect subjective AA significantly (both with $R^2 = 1.3\%$, and p -value = 0.13), even though fourth- and mainly sixth-order SA strongly depends on the pupil size.

Negative slopes were found for fourth- and sixth-order SA. Subjects with negative values of fourth- and sixth-order spherical aberration in the unaccommodated eye tend to have larger subjective AA. The slight increase in accommodation related to negative fourth-order SA agrees with other studies showing that negative values of SA increase objective accommodation. For instance, Gamba and collaborators (Gamba, Sawides, Dorronsoro, & Marcos, 2009) showed that adding $-1 \mu\text{m}$ of fourth-order SA increases the slope of the accommodation response respect to the natural eye aberrations whereas adding $+1 \mu\text{m}$ of that aberration to the eye decrease the slope. López-Gil & Fernández-Sánchez (López-Gil & Fernández-Sánchez, 2010) also showed, theoretically as well as after numerical calculations based in experimental data, that the presence of a positive fourth-order SA and its reduction during accommodation, decreases the accommodation response when

Zernike refraction is used to compute the accommodation response (Thibos, Bradley, & Lopez-Gil, 2013).

The effects of the SA in subjective AA, can be also seen in the classical accommodation studies where accommodation is measured using a stigmascopes (Hamasaki, Ong, & Marg, 1956) or a laser speckle optometer (Mohon & Rodemann, 1973). In those systems, refractive state is biased towards a more peripheral region of the pupil. Fig. 5 shows a schematic explanation of the potential effect of the fourth-order spherical aberration in the AA by comparing the accommodative amplitude of two eyes with a different value of positive C_4^0 , but the same paraxial AA. Rays originating from a probe beam on the retina will converge to a far point (FP) in the unaccommodated eye and a near point (NP) in a fully accommodated eye (upper panel). In the presence of positive SA, the paraxial FP_p is farther from the eye than the marginal optics FP_M. The far point that generates best subjective image quality, FP, will be between these two extremes. If paraxial power does not change, but Seidel SA is increased (middle panel), the preferred, subjective FP will approach the eye. Thus, when compared the subjective AA with that of an accommodated eye without SA (lower panel), the subjective AA will be lower in the eye with greatest SA. This figure emphasizes the point made by Thibos et al. (2013) that it is the magnitude of the change in SA that will affect measured AA.

The increase in subjective AA with sixth-order spherical aberration of the relaxed eye (Eq. (1)) may be also explained by the presence of the negative ρ^4 term in the expression of the sixth-order Zernike polynomial (Thibos, Applegate, Schwiegerling, & Webb, 2000). While the mean value of C_4^0 in the population study was positive at 0.083 μm , the mean value of C_6^0 was negative, although very close to zero, at $-0.004 \mu\text{m}$. It has been shown recently that C_6^0 term may play a role in the final refraction of the eye and depth-of-focus (Xu et al., 2015; Yi, Robert Iskander, & Collins, 2011).

The results of this study indicate that only a small portion of variability in subjective AA not explained by age (about 8.7%) can be explained by the optics of the eye. Physiological, psychological, and other non-optical factors beside age must account for inter-individual differences in subjective AA. Apart from the aforementioned, other non-optical factors may also play a role: the level of ultraviolet (UV) radiation may influence the average age at which presbyopia appears (Jaggernath, Haslam, & Naidoo, 2013; Stevens & Bergmanson, 1989). The present study was performed in a population from the same geographic area (south east of Spain) from urban areas, but it was not controlled whether subjects usually wear UV protection, such as sunglasses, and for how long. Physiological differences in ciliary muscle or lens hardness may be modulated by genetic and environmental factors, such as diet, average lighting conditions, etc.

Understanding the modulation of subjective AA through optics can be used for the design of optical devices, such as ophthalmic, contact, or intraocular lenses that try to increase the subjective AA of the presbyopic eye. The effects of non-optical factors, which are estimated to account for more than 90% of inter-individual differences in subjective AA not explained by age, need to be studied further.

Conflict of interest

The authors have no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

Acknowledgments

Authors thank F. Lara for his help in the subjective and objective accommodation measurements. This work was funded by European grant ERC-2012-StG 309416-SACCO.

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