RESEARCH

Change in monochromatic aberrations with accommodation in a large adult population

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Abstract

Background During accommodation, the eye undergoes significant structural changes, altering wavefront aberrations. So, this study aimed to evaluate changes in Zernike coefficients up to the 6th order with different accommodation demands and ages in a large cohort of young adults, considering the decrease in pupil size with the accommodation.

Methods Aberrometric measurements for 210 healthy subjects aged 18–40 were performed with the irx3 (Imagine Eyes, Orsay, France), stimulating accommodation with the Badal system of the instrument, from 0 to 5 D. Each wavefront was rescaled to a standardized pupil size for each accommodative vergence. Variations of Zernike coefficients were analyzed for each accommodative demand, and the change of Zernike coefficients with age.

Results The most notable changes observed during accommodation was the increase in C(2,0). Both C(2, \pm 2) astigmatism showed a reduction in magnitude during accommodation. C(4,0) became less positive, or more negative, as accommodation increased. C(3,-1) remained constant as the accommodation demand increased, while C(3,1) showed an increase. Changes were observed with accommodation and age, where C(2,0) had a negative linear relationship. The C(4,0) changed gradually with age only for accommodative demands below 3 D. C(3, \pm 1) decreased with age.

Conclusions Wavefront aberration coefficients presented changes during accommodation in people aged 20–40 years. C(2,0) underwent the most pronounced changes and C(4,0) changed more with accommodation than other higher-order aberrations. Zernike coefficients C(2,0), C(4,0) and C(3, \pm 1) decreased with age, and C(2, \pm 2) astigmatisms showed an increase in magnitude with age. These findings were made considering the decrease in pupil size with accommodation, highlighting the importance of accounting for pupil diameter variations when evaluating wavefront aberrations.

Keywords Monochromatic aberrations, Wavefront aberrations, Zernike coefficients, Accommodation, Pupil size

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Background

Accommodation is the natural adaptive optics mechanism of the eye that enhances the quality of the retinal image for objects located at various distances [1]. This physiological process involves adjusting the eye's refractive power to bring objects into clear focus [2]. Thomas Young, in the early 19th century, notably demonstrated that this dynamic change in refractive power is facilitated by the crystalline lens [3].

In the context of ocular accommodation, noticeable alterations in wavefront aberrations are expected due to, the large structural changes within the eye. These alterations involve modifications in the shape, position and gradient refractive index of the lens during accommodation [4]. The characterization of wavefront changes during accommodation has been the subject of previous research [1, 5-7].

Wavefront changes during accommodation extend far beyond the defocus Zernike coefficient [8] with several coefficients changing in different levels of magnitude. This is especially the case for spherical aberration, the higher-order Zernike coefficient that undergoes the most pronounced changes. Numerous authors [5, 6, 9–12], described how this coefficient shifts from positive to negative during accommodation, while other high-order coefficients, such as vertical and horizontal coma, either show no systematic changes [10, 13] or remain stable [5, 9, 14]. Studying how the wavefront changes with accommodation could aid in the development of technologies for presbyopia correction and myopia control treatment [15].

Although several studies described the behavior of the Zernike coefficients during accommodation [1, 5–7, 9, 13, 16–20], most of them differ in the pupil size analyzed and do not account for the decrease in pupil size typically associated with accommodation [21, 22]. Additionally, the methods used to stimulate accommodation, the measuring principles of the aberrometer, or a narrow age range vary considerably between studies, hindering a direct comparison. Hence, this study's main objective was to determine and evaluate the consistency in the behavior of the variations in Zernike coefficients (from 2nd to 6th order) for different accommodative demands, considering in decrease pupil size with the accommodation, in a large sample.

Methods

Participants

The monocular aberrometric data from 210 healthy volunteers were included (76 males, 134 females), with a mean age of 26.2 ± 5.6 years (range 18 to 40 years), and average subjective refraction of sphere -1.35 ± 2.22 D and cylinder -0.53 ± 0.47 D. These volunteers were students from the University of Minho (Portugal), University of Zaragoza (Spain) and from the University of Murcia (Spain). Measurements across the three centers were conducted over a one-year period, spanning 2022 to 2023.

Subjective accommodation amplitude (AA) measurements with the minus lens method and with the pushup method were measured. Participants were excluded if they had any accommodative problems (accommodation amplitude below the standard, accommodative sufficiency, excess of accommodation or accommodative infacility) or a corrected visual acuity more than 0.0 Log-MAR as measured with an EDTRS LogMAR chart. Participants were excluded if they had a refraction outside the range of the sphere \pm 10 D and cylinder higher than -1 D. Other exclusion criteria were the wearing of hard contact lenses less than one month prior to testing, having undergone cataract or refractive surgery, pregnancy, and taking drugs that affect the accommodative state.

The study adhered to the tenets of the Declaration of Helsinki and received approval from the Ethics Subcommittee for Life and Health Sciences of the University of Minho (Ref. 081/2022), the Clinical Research Ethics Committee of Aragón (CEICA) (Ref. PI21-074) and the Ethics Committee of the University of Murcia. All participants signed informed consent forms after receiving an explanation of the purpose of the study.

Materials

The irx3 aberrometer (Imagine Eyes, Orsay, France) was used to measure ocular aberrations based on the Hartmann-Shack principle. The Hartmann-Shack [23, 24] is an objective, parallel, double-pass aberrometric technique, it measures ray deviations at different pupil positions of the wave reflected by the retina from a point light source. The irx3 has been widely used by various authors to measure wavefront aberrations, particularly during accommodation [1, 5, 10, 25–29], with its repeatability and measurement variability thoroughly evaluated [30, 31].

This instrument features a built-in fixation target designed for central measurements, comprising a black 6/12 Snellen letter "E" on a retro-illuminated white background. The entire target occupies a field of view of approximately 0.7° x 1.0° and has a luminance of 85 cd/m². Aberration measurements are made in infrared light (780 nm) and the results are corrected for longitudinal chromatic aberration. The irx3 aberrometer includes an external lens that acts as a Badal lens and an internal mechanism that moves the entire optical system, including the stimulus and its collimating lens, to modify the vergence of the stimulus and over a range of 35 D in which the angle subtended by the stimulus from the observer's view does not change.

During the examination, the participant focuses on the target. The beam is then reflected on the retina and travels back across the ocular surfaces, exits the eye, and is projected directly onto a Hartmann-Shack wavefront sensor with a 32×32 lens array. The deviations of these points from the reference points are analyzed by the software to calculate the wavefront.

Procedures

The aberrometry measurements were all performed in a dark room, an illumination level of 0 cd/m2. The measured eyes were fixated on the target, while the contralateral eye was occluded. In all three sites, participants underwent measurements without prior cycloplegia or dilation, aiming to maintain a state closely resembling the everyday physiological condition of the eye.

Aberrometric measures were taken for each eye by stimulating accommodation from 0 D to 5 D in eleven 0.5 D steps, using the internal Badal system of the instrument. A brief 2 s pause in the movement of the target was introduced between measurements to allow the subject to modify his/her accommodative state. The measurement sequence spanned a total of 22 s, and participants had the opportunity to blink as needed to minimize optical aberrations linked to changes at the air-tear film interface [32, 33]. The participant was given clear instructions to focus on a small and distinguishable feature of the target stimulus to improve fixation stability. A single measure was performed for each subject due to the repeatability obtain by the irx3 in the repeated measurements [30].

Refractive corrections were not worn during the aberrometric measurement sessions to derive the spherical equivalent (SE) based on each individual's natural refraction to capture the eye's least accommodated state. To ensure ocular relaxation, the irx3 employed a fogging technique [5, 10], positioning the stimulus 1 D beyond the remote point (measured via Zernike refraction) while continuously monitoring the eye's refractive state. This approach allowed for the assessment of aberration when the eye was in its most positively refracted state, a value referred to as the unaccommodated eye. Starting from this SE value, the aberrometer automatically determined the wavefront aberration for accommodation levels in 0.5 D increments, ranging from 0 to -5 D.

To avoid the influence of the strong correlation between the left and right eyes, a random selection was made between the left and right eyes for each subject using a discrete uniform distribution in the interval [1, 2].

Zernike coefficients and pupil size

Aberrations were originally determined at the pupil plane and exported for the maximum round pupil size, in the form of Zernike coefficients C(n, m), where *n* is the radial order of the polynomials and *m* the azimuthal frequency according to the ANSI standards [34, 35].

As the dataset included both the right eye and left eye, the signs of the Zernike coefficients with negative, even meridional indices and positive, odd meridional indices were reversed for all left eye data before the analysis to account for the mirror symmetries along the vertical meridian between right and left eyes [34].

Since accommodation affects the pupil diameter [21, 22, 36, 37] a standardized pupil diameter was used for each accommodative level for an accurate comparison of measurements. This value was chosen so that the pupil size of 95% of the eyes would be larger for that accommodative state (5th percentile). The wavefront data of that 95% of eyes were then rescaled according to the selected pupil size, using the method described by Schwiegerling [38] and corrected by Visser et al. [25]. The remaining 5% of eyes with smaller pupils were disregarded for that level of accommodation, reducing the sample size to 198 eyes in the cases of 0 D, 1 D, 3 D, and 4 D, and to 199 eyes in the cases of 2 D and 5 D.

Statistics

The data analysis consisted of 4 parts.

Firstly, a descriptive analysis was performed of the main Zernike coefficients that typically show major changes with accommodation, consisting of histograms and descriptive statistics (mean, standard deviation, and normality with the Kolmogorov-Smirnov test). Zernike coefficients for each accommodative demand were then compared using an ANOVA or a non-parametric ANOVA if the distribution was not normal, followed by post-hoc Bonferroni tests to determine significant differences between accommodative demands. Spearman's correlation coefficients were then calculated for each Zernike coefficient in the accommodative states, followed by linear regressions to determine the relationship between the Zernike coefficients in each state and the non-accommodative state.

Finally, the behavior of the Zernike coefficients for each accommodative demand was explored through linear regression as a function of age.

Significance levels of *p*-value = 0.05 including Bonferroni correction were used throughout the analysis. All calculations were performed using Matlab R2022b (The MathWorks, MA, USA), Excel 365 (version 2310, Microsoft Corp, WA, USA) and SPSS (version 29.0, IBM Corp, Armonk, NY).

Results

Subjective AA with the minus lens method was 8.10 ± 2.15 D and with the push-up method was 8.95 ± 2.31 D.

The pupil diameter decreased from 6.47 ± 0.82 mm at 0 D to 5.77 ± 0.96 mm at 5 D (Table 1). To avoid having

Table 1 Mean and standard deviations (in mm) for the pupil size in each accommodative state

	0 D	0.5 D	1 D	1.5 D	2 D	2.5 D	3 D	3.5 D	4 D	4.5 D	5 D
Mean	6.47	6.42	6.39	6.33	6.32	6.21	6.16	6.05	5.97	5.87	5.77
Standard deviation (±)	0.82	0.87	0.87	0.87	0.88	0.89	0.92	0.93	0.92	0.98	0.96
5th percentile	4.66	4.63	4.76	4.44	4.47	4.40	4.09	3.96	4.07	3.82	3.68

 Table 2
 Mean, standard deviations (SD), 95% range,

Kolmogorov-Smirnov test (KS) for the normality of the data AND non-parametric ANOVA test

Parame	eters	MEAN (SD) (μm)	CONFIDENCE INTERVAL 95% (µm)	KS	ANOVA		
C (2,-2)	0 D	0.017 (0.213)	[-0.013, 0.047]	< 0.001*	0.951		
	1 D	0.021 (0.226)	[-0.011, 0.053]	< 0.001*			
	2 D	0.015 (0.192)	[-0.012, 0.042]	< 0.001*			
	3 D	0.014 (0.157)	[-0.009, 0.036]	< 0.001*			
	4 D	0.007 (0.158)	[-0.016, 0.029]	< 0.001*			
	5 D	0.005 (0.135)	[-0.014, 0.024]	< 0.001*			
C (2,0)	0 D	1.249 (1.747)	[1.004, 1.493]	< 0.001*	< 0.001*		
	1 D	1.544 (1.902)	[1.278, 1.811]	< 0.001*			
	2 D	1.826 (1.757)	[1.580, 2.071]	< 0.001*			
	3 D	1.948 (1.390)	[1.753, 2.143]	< 0.001*			
	4 D	2.335 (1.493)	[2.126, 2.544]	< 0.001*			
	5 D	2.278 (1.312)	[2.095, 2.462]	< 0.001*			
C (2,2)	0 D	-0.159 (0.362)	[-0.209, -0.108]	0.005*	< 0.001*		
	1 D	-0.129 (0.366)	[-0.180, -0.078]	< 0.001*			
	2 D	-0.090 (0.318)	[-0.135, -0.046]	< 0.001*			
	3 D	-0.066 (0.271)	[-0.104, -0.028]	< 0.001*			
	4 D	-0.035 (0.271)	[-0.073, 0.003]	< 0.001*			
	5 D	-0.020 (0.227)	[-0.052, 0.011]	0.033*			
C (3,-1)	0 D	0.024 (0.082)	[0.013, 0.036]	0.094	0.988		
	1 D	0.026 (0.091)	[0.013, 0.039]	0.200			
	2 D	0.026 (0.074)	[0.016, 0.037]	0.200			
	3 D	0.023 (0.063)	[0.014, 0.032]	0.028*			
	4 D	0.025 (0.067)	[0.015, 0.034]	0.200			
	5 D	0.022 (0.052)	[0.015, 0.029]	0.098			
C (3,1)	0 D	< 0.001 (0.060)	[-0,008, 0.009]	0.200	< 0.001*		
	1 D	-0.005 (0.067)	[-0.014, 0.005]	0.057			
	2 D	0.002 (0.059)	[-0.007, 0.010]	0.200			
	3 D	0.007 (0.057)	[-0.001, 0.015]	0.200			
	4 D	0.011 (0.066)	[0.001, 0.020]	0.055			
	5 D	0.011 (0.060)	[0.002, 0.019]	0.018*			
C (4,0)	0 D	0.039 (0.050)	[0.032, 0.462]	0.020*	< 0.001*		
	1 D	0.036 (0.056)	[0.029, 0.044]	0.061			
	2 D	0.016 (0.049)	[0.010, 0.023]	0.023*			
	3 D	0.002 (0.041)	[-0.004, 0.007]	0.038*			
	4 D	-0.004 (0.048)	[-0.011, 0.002]	0.028*			
	5 D	-0.008 (0.041)	[-0.013, -0.002]	0.002*			
C (6,0)	0 D	-0.001 (0.013)	[-0.003, 0.001]	0.015*	0.714		
	1 D	-0.001 (0.014)	[-0.003, 0.001]	< 0.001*			
	2 D	-0.001 (0.013)	[-0.003, 0.001]	< 0.001*			
	3 D	-0.001 (0.009)	[-0.002, 0.000]	0.008*			
	4 D	-0.002 (0.009)	[-0.004, -0.001]	< 0.001*			
	5 D	-0.001 (0.006)	[-0.002, -0.001]	0.030*			

Denote statistically significant values (p-value < 0.05), mark with an asterisk *

to reduce all the pupils to the smallest diameter available, the 5th percentile value was used as a cutoff for each vergence.

Descriptive statistics

The accommodative measurements were conducted within the diopter range of 0 D to 5 D, with intervals of 0.5 D. However, only increments of one diopter were systematically examined to discern the most prominent variations.

Among the Zernike coefficients, as expected, defocus C(2,0) exhibits the greatest change with increasing accommodative demand (Table 2; Fig. 1). Astigmatism coefficients C(2,-2) and C(2,2) exhibit an average decrease of approximately 0.001 μ m and 0.139 μ m, respectively, in response to a change in accommodative demand from unaccommodated to 5 D. The distributions of these Zernike coefficients across different accommodative states exhibit no apparent differences between them (Fig. 1).

Furthermore, the 2nd order Zernike coefficients show larger standard deviations, for higher accommodative demands, indicating greater variability between participants at those accommodation levels (Table 2).

The mean vertical coma coefficient C(3,-1) does not change with increasing accommodation. In contrast, horizontal coma coefficient C(3,1) increases its coefficient by 0.011 μ m from the unaccommodated state to 5 D of the accommodation state (Table 2; Fig. 1).

The subsequent non-parametric ANOVA shows a significant difference between the accommodative demands of C(2,0), C(2,2), C(3,1), and C(4,0) (*p*-*v*alue < 0.001), and the post-hoc Bonferroni test, indicate that significant differences occur between accommodative demands 0 D and >2 D. No significant differences are observed between the accommodative demands of the coefficients C(2,-2), C(3,-1) and C(6,0).

C(4, 0) is the dominant higher-order aberration in the unaccommodated state with an average of $0.039 \pm 0.050 \ \mu m$ for a 4.66 mm pupil size. It changes more than the other terms in response to accommodation, with a shift in the negative direction for increasing accommodative demands (*p*-value < 0.001, ANOVA, Table 2). The transition from a positive to a negative value is observed at an accommodative demand of approximately 3 D. The change in average spherical aberration is -0.047 μm from the unaccommodated state to 5 D of accommodation. Such a shift is not seen for the



Fig. 1 Histogram of the Zernike coefficients up to 4th order, for each accommodative state

secondary spherical aberration C(6,0) (Table 2). In most cases, a decrease in standard deviation is associated with increased accommodative demands.

Supplements 1 and 2 show the results obtained for the missing Zernike coefficients up to 6th in Table 2; Fig. 1, respectively.

Correlation coefficients matrix between accommodative stages

A robust correlation is observed between the defocus coefficients of successive accommodative demands (r > 0.918; Fig. 2, above the diagonal). However, this correlation decreases for larger differences between accommodative demands, such as between 0 D and 5 D (r = 0.722). Similarly, strong, albeit lower correlations are observed between consecutive accommodative demands for the astigmatism coefficients C(2,-2) and C(2,2)(r > 0.905). Lower correlation coefficients are observed for the higher-order Zernike coefficients for coma C(3,-1), C(3,1), and spherical aberrations C(4,0). Nevertheless, the correlation pattern resembles that the second-order Zernike coefficients, exhibiting higher correlations for consecutive accommodative demands and lower correlations for demands that are more separated.

All correlations were statistically significant (Fig. 2, below the diagonal) for all accommodative vergences and

all Zernike coefficients. Supplement 3 shows the results of the correlation coefficients obtained for the missing Zernike coefficients up to the 6th order in Fig. 2.

Changes in Zernike coefficients with accommodation

The linear regressions of the Zernike coefficients of the five different accommodative stages compared to those of the unaccommodated eye are presented in Fig. 3, and mathematical values are presented in Supplement 4. In each instance, the slopes associated with the variables become flatter with increasing accommodative demand.

Some differences between the linear regression profiles can be discerned for Zernike coefficients C(2,2), C(3,-1), and C(6,0) (Fig. 3). While the 2 D, 3 D, and 4 D accommodative demands show comparable regression trajectories, more pronounced changes are observed between accommodative demands of 1 D and 5 D. The Zernike coefficient C(4,0) also changes substantially for various accommodative demands, with regression slopes tapering to near-flat levels at the 5 D accommodative demand.

Change in Zernike coefficients with age

Figure 4 shows the linear regressions for each Zernike coefficient with different accommodative demands as a function of age.

		Corre	lation M	Aatrix -	C(2,0)		1			Correl	ation N	latrix -	C(2,-2)		1	1			Correl	ation M	atrix - 0	C(3,-1)		_	1
0.0D	-	0.99	0.97	0.95	0.91	0.87	0.98	0.0D	-	0.98	0.97	0.95	0.95	0.93 -	- 0	0.99	0.0D		0.88	0.88	0.83	0.81	0.75	-	0.95
1.0D	<0.01		0.99	0.97	0.94	0.90	0.96	1.0D	<0.01		0.98	0.96	0.95	0.94 -	- 0	0.98	1.0D	<0.01		0.89	0.82	0.77	0.71 -	-	0.00
2.0D	- <0.01	<0.01		0.98	0.95	0.92	- 0.94	2.0D	<0.01	<0.01		0.96	0.96	0.93 -	- 0	0.97	2.0D	<0.01	<0.01		0.90	0.85	0.81 -		0.95
3.0D	<0.01	<0.01	<0.01		0.97	0.94	- 0.92	3.0D	<0.01	<0.01	<0.01		0.96	0.95 -	- 0	0.96	3.0D	<0.01	<0.01	<0.01		0.90	0.85		0.00
4.0D	- <0.01	<0.01	<0.01	<0.01		0.97	0.9	4.0D	<0.01	<0.01	<0.01	<0.01		0.95 -	- C	0.95	4.0D	<0.01	<0.01	<0.01	<0.01		0.85 -	-	0.8
5.0D	<0.01	<0.01	<0.01	<0.01	<0.01	-	- 0.88	5.0D	<0.01	<0.01	<0.01	<0.01	<0.01	-		0.94	5.0D	<0.01	<0.01	<0.01	<0.01	<0.01	-	-	0.75
	0.0D	1.0D	2.0D	3.0D	4.0D	5.0D			0.0D	1.0D	2.0D	3.0D	4.0D	5.0D				0.0D	1.0D	2.0D	3.0D	4.0D	5.0D		
		Corre	lation N	latrix -	C(4,0)		_1			Corre	lation N	latrix -	C(2,2)		_ 1				Corre	lation N	latrix -	C(3,1)		_	4
0.0D		Corre 0.89	lation N 0.86	Aatrix - 0.80	C(4,0) 0.68	0.59 -	1	0.0D	-	Corre 0.98	lation N 0.97	Aatrix - 0.95	C(2,2) 0.92	0.86 -	1	1).98	0.0D		Corre 0.91	0.83	1atrix - 0.75	C(3,1) 0.73	0.57 -		1 0.95
0.0D 1.0D	<0.01	Corre 0.89	0.86 0.90	1atrix - 0.80 0.82	C(4,0) 0.68 0.72	0.59 - 0.64 -	- 0.95 - 0.9	0.0D 1.0D	- <0.01	Corre 0.98	0.97 0.98	Matrix - 0.95 0.96	C(2,2) 0.92 0.92	0.86 -	- 0 - 0	1).98).96	0.0D 1.0D	<0.01	0.91	0.83 0.86	0.75 0.79	C(3,1) 0.73 0.76	0.57 -		1 0.95 0.9
0.0D 1.0D 2.0D	<0.01	0.89	lation N 0.86 0.90	Aatrix - 0.80 0.82 0.88	C(4,0) 0.68 0.72 0.79	0.59 - 0.64 - 0.73 -	1 - 0.95 - 0.9 - 0.85 - 0.8	0.0D 1.0D 2.0D	- <0.01	0.98	0.97 0.98	Aatrix - 0.95 0.96 0.97	C(2,2) 0.92 0.92 0.94	0.86 - 0.87 - 0.89 -	- 0 - 0 - 0	1).98).96).94	0.0D 1.0D 2.0D	<0.01	0.91	lation N 0.83 0.86	0.75 0.79 0.86	C(3,1) 0.73 0.76 0.85	0.57 - 0.60 - 0.72 -		1 0.95 0.9 0.85 0.8
0.0D 1.0D 2.0D 3.0D	<0.01 <0.01 <0.01	0.89 <0.01 <0.01	lation N 0.86 0.90 <0.01	Aatrix - 0.80 0.82 0.88	C(4,0) 0.68 0.72 0.79 0.87	0.59 - 0.64 - 0.73 - 0.82 -	1 - 0.95 - 0.9 - 0.85 - 0.8 - 0.8	0.0D 1.0D 2.0D 3.0D	- <0.01 - <0.01 - <0.01	0.98 <0.01 <0.01	lation N 0.97 0.98	Aatrix - 0.95 0.96 0.97	C(2,2) 0.92 0.92 0.94 0.96	0.86 - 0.87 - 0.89 - 0.92 -	- 0 - 0 - 0	1).98).96).94).92	0.0D 1.0D 2.0D 3.0D	<0.01 <0.01 <0.01	Corre 0.91 <0.01 <0.01	lation N 0.83 0.86	1atrix - 0.75 0.79 0.86	C(3,1) 0.73 0.76 0.85 0.91	0.57 - 0.60 - 0.72 - 0.82 -	-	1 0.95 0.9 0.85 0.8 0.8
0.0D 1.0D 2.0D 3.0D 4.0D	 <0.01 <0.01 <0.01 <0.01 	Corre 0.89 <0.01 <0.01 <0.01	lation N 0.86 0.90 <0.01 <0.01	Alatrix - 0.80 0.82 0.88 <0.01	C(4,0) 0.68 0.72 0.79 0.87	0.59 - 0.64 - 0.73 - 0.82 - 0.88 -	1 - 0.95 - 0.9 - 0.85 - 0.8 - 0.8 - 0.7 - 0.7	0.0D 1.0D 2.0D 3.0D 4.0D	- <0.01 - <0.01 - <0.01 - <0.01	Corre 0.98 <0.01 <0.01	lation N 0.97 0.98 <0.01 <0.01	Aatrix - 0.95 0.96 0.97	C(2,2) 0.92 0.92 0.94 0.96	0.86 - 0.87 - 0.89 - 0.92 -	- 0 - 0 - 0 - 0	1 0.98 0.96 0.94 0.92	0.0D - 1.0D - 2.0D - 3.0D - 4.0D -	<0.01 <0.01 <0.01 <0.01	Correl 0.91 <0.01 <0.01 <0.01	lation N 0.83 0.86 <0.01	1atrix - 0.75 0.79 0.86 <0.01	C(3,1) 0.73 0.76 0.85 0.91	0.57 - 0.60 - 0.72 - 0.82 - 0.88 -		1 0.95 0.85 0.86 0.75 0.77 0.65
0.0D 1.0D 2.0D 3.0D 4.0D 5.0D	 <0.01 <0.01 <0.01 <0.01 <0.01 	Corre 0.89 <0.01 <0.01 <0.01	lation N 0.86 0.90 <0.01 <0.01	Matrix - 0.80 0.82 0.88 <0.01	C(4,0) 0.68 0.72 0.79 0.87 <0.01	0.59 - 0.64 - 0.73 - 0.82 - 0.88 -	1 - 0.95 - 0.9 - 0.85 - 0.8 - 0.8 - 0.7 - 0.65 - 0.65	0.0D 1.0D 2.0D 3.0D 4.0D 5.0D	- <0.01 - <0.01 - <0.01 - <0.01 - <0.01	Corre 0.98 <0.01 <0.01 <0.01 <0.01	lation N 0.97 0.98 <0.01 <0.01	Aatrix - 0.95 0.96 0.97 <0.01	C(2,2) 0.92 0.92 0.94 0.96	0.86 - 0.87 - 0.89 - 0.92 - 0.95 -		1).98).96).94).92).92).88	0.0D - 1.0D - 2.0D - 3.0D - 4.0D - 5.0D	<0.01 <0.01 <0.01 <0.01 <0.01	Corret 0.91 <0.01 <0.01 <0.01	lation N 0.83 0.86 <0.01 <0.01	1atrix - 0.75 0.79 0.86 <0.01	C(3,1) 0.73 0.76 0.85 0.91 <0.01	0.57 - 0.60 - 0.72 - 0.82 - 0.88 -		1 0.95 0.85 0.8 0.75 0.7 0.65 0.6

Fig. 2 Above the diagonal: Spearman's correlation for each Zernike coefficient between each accommodative demand. Lighter colors indicate stronger correlations between parameters, while blue shades indicate lower correlations. Below the diagonal: p-values with Bonferroni correction were applied (p-value < 0.05/36 = 0.00139)



Fig. 3 Zernike coefficients of the different accommodative stages compared to those of the unaccommodated eye (1 D in blue, 2 D in green, 3 D in red, 4 D in orange, and 5 D in brown)

The defocus coefficient C(2,0) decreases with age with a slope that does not appear to be influenced by the accommodative state highlighting the age-associated decline in accommodative capacity.

Next, the primary spherical aberration C(4,0) consistently increase in magnitude with age up to accommodative demand, but its range gradually decreases with age.

Conversely, the astigmatism coefficient C(2,-2) increases with age transitioning from negative to positive values at 23–25 years of age, with a slope that increases with the degree of accommodation. The other astigmatism coefficient C(2,2) increases in magnitude with accommodative demand, and this increase becomes more pronounced with age. This is particularly evident in accommodative demands of 1 D, 2 D, and 3 D.



Fig. 4 Zernike coefficients of the different accommodative stages as a function of age

Vertical coma and horizontal coma $C(3,\pm 1)$ both decrease with age. Vertical shows minimal variation between accommodative demands, but horizontal coma shows a gradual increase.

Discussion

The primary point of distinction between the present investigation and comparable studies lies in the larger sample size, and the consideration of the decrease in pupil size with accommodation. Although there are several large population studies on non-accommodative wavefront error [9, 39-42], no larger study reports wavefronts under different levels of accommodation. Other studies on wavefront accommodation, include the work by Ninomiya et al. [18] who examined 33 eyes of young participants aged between 24 and 32 years and reported similar findings as the current study for accommodative demands up to 3 D. Furthermore, Radhakrishnam and Charman [16] explored 47 eyes across a broader age range (17-56 years) and concluded that age significant affects the magnitude and direction of the change in spherical aberration with accommodation. Cheng et al. [13] analyzed 91 right eyes of individuals aged 21-40 years, but, their measurements were conducted under 2.5% phenylephrine, as was also done in another study [27], which would have affected the accommodative response. As such, with around 200 eyes, this work provides the basis for more robust conclusions.

The initial step established a common pupil diameter for data analysis. Given the decrease in pupil diameter size with increasing accommodative demand, this ensured a representation closest to natural conditions and with the largest possible pupil [43]. Consequently, each wavefront was rescaled to a standardized pupil size for each accommodative vergence (Table 1). This analysis showed a reduction of 0.70 mm in the pupil diameter from the unaccommodated to the accommodated status (Table 1). Tarrant et al. [44] reported a pupil reduction of 2.00 mm at 5 D accommodation in emmetropes and 1.75 mm in myopes, although the age range was between 19 and 31 years, and it is well known that younger eyes present larger pupil dynamics [45]. Lara et al. [10] measured the pupil diameter change in low-light conditions and observed a 2.00 mm decrease for a sample of 15 eyes aged between 22 and 40 years. The reduction in pupil diameter of only 0.98 mm in the present work is the result of choosing of the 5th percentile to ensure that 95% of cases can be included in the analysis. As the pupil size for the highest accommodation demands would be very small, using this pupil diameter for all demands would result in the loss of peripheral wavefront information at the lowest demands [46, 47]. Moreover, the rescaling of pupils based on accommodative vergence aligns more closely with the natural proximal miosis condition for nearer targets [10, 22]. The figure in Supplement 5 illustrates the distributions of Zernike coefficients for each accommodative demand for a uniform pupil size of 3.68 mm corresponding to the 5th percentile pupil value at maximum accommodative demand of 5 D. Comparative analysis with Fig. 1 reveals no discernible alterations in the distributions of Zernike coefficients, except for defocus, C(2,0), and primary spherical aberration, C(4,0). Overall, Supplement 5 exhibits change along the trends observed in Fig. 1, albeit of a lesser magnitude.

The next step was to identify the most important Zernike coefficients that change during accommodation. A comprehensive review of existing literature [1, 5-7, 9, 13, 16-20] reveals that Zernike coefficients C(2,2), C(2,0), C(2,-2), C(3,-1), C(3,1) and C(4,0) show the greatest changes with accommodation. But there are discrepancies between different studies that may be associated with sample size [6, 11, 37, 48-50], age range [51, 52], stimulus range [17, 18, 49, 53-55], the method to provide the accommodative stimulus (e.g., Badal system [50], variation of target distance [5, 11, 13, 18, 37, 48, 52, 54, 55], negative spherical lenses [51, 53], or the measurement principles of the aberrometer used (e.g. aberroscope [17], spatially resolved refractometer [6] and Hartmann-Shack aberrometer [5, 50]).

In the literature [1, 7, 27, 48, 54], defocus C(2,0) undergoes the most significant changes during accommodation, similar to this study, (Fig. 1), which is related to the lens' pivotal role to alter its refractive power to focus on objects at a near and far distance. If each of the values obtained for each vergence is subtracted from the value of the vergence of the stimulus, the subject's accommodative lag is obtained, which represents the diopters of accommodative lag that the subject has for the vergence of the accommodative stimulus, in Fig. 5, in average lag in the first measurement is evident, contrary to expectations and assuming participants had normal subjective accommodative values. Individually observed during measurements, participants experiencing this delay typically had astigmatism > 0.75 D. Given that the irx3 Badal system only corrects SE, it is plausible that this initial lag in some participants stems from this reason. The trend in accommodative lag is distinctly evident, progressively increasing with accommodative demand. In the unaccommodated eye, the mean magnitude of lag was not zero probably due to the wavefront refraction metric used and the presence of uncorrected astigmatism. Defocus shows a negative linear correlation with age for each accommodative demand (Fig. 4) during the first 50 years of life [2, 56, 57], due to the decline in the eye's accommodative capacity.

Both cylinder Zernike coefficients C(2,-2) and C(2,2) decrease in magnitude with accommodation (Table 2), with C(2,2) showing the greatest decrease. Some studies



Fig. 5 Representation of the mean accommodative lag obtained in diopters for each target vergence

reported small changes in magnitude [58], however, others reported higher changes in both magnitude and axis [59]. The cylinder calculated from the values of the coefficients C(2,-2) and C(2,2) shows a value of -0.07 D in the accommodative state and a decrease to -0.01 D with increasing maximal accommodative demand. Changes in the amount of astigmatism can be explained by the vertical displacement due to the gravity of the crystalline lens and the weak zonular tension at the highest accommodative in cylinder axis and magnitude are closely tied to the degree of astigmatism, and the sample present in this study consist of individuals with low levels of astigmatism.

The average spherical aberration C(4,0) for a 4.5 mm pupil obtained in the actual study was $0.039 \pm 0.050 \mu$ m, which was similar to the $0.034 \pm 0.050 \mu$ m reported by Radhakrishnan and Charman for 47 subjects between 17 and 56 years old for the unaccommodated state [16].

Primary spherical aberration coefficient C(4,0) shifts towards less positive values during accommodation (Fig. 1), inverting to negative signs for higher demands in line with previous results [5]. In our results, this occurs at 3 D of accommodation, which agrees with Radhakrishnan and Charman [16], who reported it between 2 D -3 D, while other studies reported this at 3 D [6, 37, 48, 49, 51]. This phenomenon is associated with the hyperbolic shape of the lens surfaces [50]. Large variations can exist between individuals, however, as Atchison et al. [17] reported that not everyone has a negative trend and Cheng et al. [13] found that spherical aberration always decreases proportionally to the change in accommodative response, matching our observations (Fig. 3). Spherical aberration at accommodative demands below 3 D increase gradually with age while spherical aberration above 4 D show no change with age (Fig. 4). Some authors [11, 13] observe no discernible pattern in C(6,0), others report positive changes for higher accommodative demands, as opposed to primary spherical aberration [13, 50], although one study reported negative changes [61].

Vertical coma C(3,-1) remains constant on average with increasing accommodative demand, but the standard deviation decreases (Table 2), suggesting greater variability at lower accommodative states. The slope of the line for the accommodative state of 5 D is 0.168, approximately 0.4 times less than that observed at the accommodative demand of 1 D (Fig. 3). This may be because upon accommodation, the lens zonules relax, causing a slightly lower decentration of the lens [62].

For horizontal coma C(3,1), the change between accommodative demands is more substantial increasing by 0.011 μ m from unaccommodated to 5 D of accommodation state (Fig. 1). With aging, this coefficient becomes less positive, which is in line with the findings by Marthur et. al. [63] and by Hartwig and Atchison [9]. Nevertheless, various authors have described both coma Zernike coefficients as exhibiting no systematic changes [5, 17] or are relatively stable [6, 14, 16] during accommodation.

In the present study, the main limitation was that the pupil values used were not integer or typical values to compare with other studies. Moreover, the gender of the participants was not balanced with 67% female participants and 33% male, but there is no study reporting differences in wavefronts or accommodative responses between men and women [42]. There are, however, studies reporting differences in accommodative amplitude depending on the individual's refractive error [64-66], concluding that hyperopes (SE > + 0.75 D) and emmetropes $(-0.50 \le SE \le +0.75 \text{ D})$ have, on average, significantly higher amplitudes of accommodation than myopes (SE < -0.50 D) [67]. In this study 52.5% of participants were myopic, 36.5% emmetropic, and 11% hypermetropic, a distribution similar to that reported in population studies [68–71]. Othe potential limitation of the study is the exclusive measurement of whole-eye aberrations. While the evaluation of higherorder aberrations revealed subtle changes, it would be valuable to employ a combined topographer/tomographer wavefront sensor to specifically assess the accommodative changes in the internal aberrometric profile, particularly the lenticular component [72, 73]. Given the known inter-subject variability in corneal aberrations, the current approach effectively captures the combined effects of lenticular and corneal wavefront changes without isolating the corneal contribution. This limitation may obscure how specific aberrations, such as astigmatic Zernikes, are influenced by corneal factors, potentially missing critical information on the distinct roles of the cornea and lens in overall wavefront alterations.

The study introduces a reduction in pupil diameter during accommodation, distinguishing it from previous research on Zernike coefficients distribution with accommodation [1, 5, 13, 16, 18, 51] This addition aims to elucidate the anatomical and physiological effects of accommodation and pupillary constriction in the eye when focusing on nearby objects.

Conclusion

Wavefront aberration coefficients change considerably during accommodation in people aged between 18 and 40 years. This has been previously reported, however, the present study extends beyond previous research by measuring a larger sample population and considering the decrease in pupil size with the accommodation. Defocus undergoes more pronounced changes in lower-order aberrations. The primary spherical aberration changes more with accommodation than other higher-order aberrations and changes signs in the process. The horizontal coma changes in the positive direction. Furthermore, with each accommodative demand coefficients C(2,0)and $C(3,\pm1)$ consistently decrease with age, while C (4,0) and $C(2,\pm2)$ astigmatisms increase in magnitude with age.

Abbreviations

D	Diopters
SE	Spherical equivalent
AA	Accommodation amplitude
CEICA	Clinical Research Ethics Committee of Aragón
SD	Standard deviation

Supplementary Information

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Supplementary Material 1

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Author contributions

All authors read and approved the final manuscript. Authors MMG, JR, and JMGM contributed to the study conception, design of the study, data conception, data interpretation, drafting of the manuscript and revising the manuscript. Authors ASC, EOH, MAC, PF, RJMDA, and VFS contributed to data acquisition, analysis of data, and revising of the manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study adhered to the tenets of the Declaration of Helsinki and received approval from the Ethics Subcommittee for Life and Health Sciences of the University of Minho (Ref. 081/2022), the Clinical Research Ethics Committee of Aragón (CEICA) (Ref. PI21-074) and the Ethics Committee of the University of Murcia. All participants signed informed consent forms after receiving an explanation of the purpose of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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