Monochromatic Aberrations as a Function of Age, from Childhood to Advanced Age

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Purpose. To describe monochromatic optical aberrations of the eye as a function of age.

Methods. One hundred fourteen subjects with a spherical equivalent within ±3.50 D from emmetropia, corrected visual acuity of 20/40 or better, and normal findings in an ophthalmic examination were enrolled. The mean age was 43.2 ± 24.5 years (range, 5.7–82.3). Monochromatic optical aberrations were measured with a Hartmann-Shack wavefront sensor after pharmacological dilation and cycloplegia.

Results. For a 5-mm pupil and for third- to seventh-, third-, fourth-, and fifth- to seventh-order aberrations, as well as for coma and spherical aberrations, the root mean square (RMS) error as a function of age was modeled by a second-order polynomial regression. It decreased progressively through childhood, adolescence, and early adulthood; reached a minimum level during the fourth decade of life, then increased progressively with age, to age 82. For a 5-mm pupil, the mean modulation transfer function (MTF) was reduced in both the child- teenage (5–20 years; $n = 29$) and the elderly (61–82 years; $n = 37$) groups versus the middle-aged adult group (41–60 years; $n = 24$; $P < 0.05$). In young adults (21–40 years; $n = 23$) and elderly subjects, the MTF curves were very close and almost superimposed at spatial frequencies higher than 38 cyc/deg.

Conclusions. Aberrations of the whole eye were objectively measured from early childhood to an advanced age, and the relationship between monochromatic aberrations and age has been shown to fit a quadratic model. The results suggest that the definition of emmetropization should be broadened to include the reduction of higher order aberrations. (*Invest Ophthalmol Vis Sci.* 2003;44:5438–5446) DOI:10.1167/iovs.02-1042

Visual performance of the human eye has been found to be affected by aging.[1] Measurements of optical quality using objective double-pass techniques indicate that the average modulation transfer function (MTF) for the whole eye deteriorates with age, from 20 to 70 years.[2,3] Calver et al.[4] studied the effect of age on ocular monochromatic aberrations by using an objective method, the crossed-cylinder aberroscope. They found no statistically significant difference in root mean square (RMS) wavefront error between two groups of young (mean ± SD: 24.2 ± 3 years, $n = 15$) and older (68.0 ± 5 years, $n = 15$) subjects, for pupil sizes of 4 and 6 mm, presumably because of the small sample size. Older subjects, however, showed significantly larger absolute values with some of the third- and fourth-order coefficients when compared with young subjects for the same pupil size. McLellan et al.[5] analyzed the effect of age on monochromatic aberrations, using a subjective method, the spatially resolved refractometer. In a cross-sectional study involving 38 subjects aged 22.9 to 64.5 years, they showed a linear increase in RMS wavefront error as a function of age. Artal et al.[6] used an objective method, the Hartmann-Shack wavefront sensor, to study age dependence (26–69 years, $n = 17$) of the relative contribution of corneal and internal surface aberrations to the total ocular aberration.

He et al.[7] recently reported the first wavefront aberration (WA) measurements in preadolescents and adolescents. They compared 83 young emmetropes (10–17 years) with 54 young adult emmetropes (18–29 years) and found lower mean RMS values of the WA in the young adult group. However, accommodation was not paralyzed which implies that, despite precautions, accommodation, known to induce optical aberrations,[8] could not be totally ruled out in younger subjects. Carkeet et al.,[9] using an aberrometer (Zywave; Bausch and Lomb, Tampa, FL), have also recently reported monochromatic aberrations in 273 children (mean, 9.0 years; range, 7.9–12.7 years). No comparisons with adult data were made.

Although the optical properties of the eye have been documented in different age groups, a broad comparison of all these groups is still needed to gain better understanding of the effect of normal development and aging on the image optical quality of the human eye. Furthermore, all study groups involving ageing adults were small, and the description of ocular aberrations in subjects younger than 8 and older than 70 years is still not available. In the present study, we extended the investigation of the relationship between ocular monochromatic aberrations and age to a large population of normal subjects 5 to 82 years. We used a Hartmann-Shack wavefront sensor adapted to clinical needs. This simple, objective technique allowed rapid measurements and required little cooperation from the subject, both of these aspects being very important when working with inexperienced experimental subjects such as children and the elderly.

Methods

Experimental Setup

The ocular WA was calculated from images recorded with a Hartmann-Shack sensor. The theory and operating principle of this experimental system have been described in detail.[10,11] Additional changes and improvements to the original technique, made by Hamam and Campbell[12] to adapt the experimental setup to a clinical environment, have

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Presented at the annual meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, Florida, May 2002.

Supported by Grant MT-13385 from the Canadian Institutes of Health Research (CIHR), Fonds pour la Formation de Chercheurs et d'Aide à la Recherche Grant FCAR 97ER2702, and The Quebec Research in Vision Network.

Submitted for publication October 9, 2002; revised February 3 and June 23, 2003; accepted July 9, 2003.

Disclosure: **I. Brunette**, None; **J.M. Bueno**, None; **M. Parent**, None; **H. Hamam**, None; **P. Simonet**, None

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Investigative Ophthalmology & Visual Science, December 2003, Vol. 44, No. 12

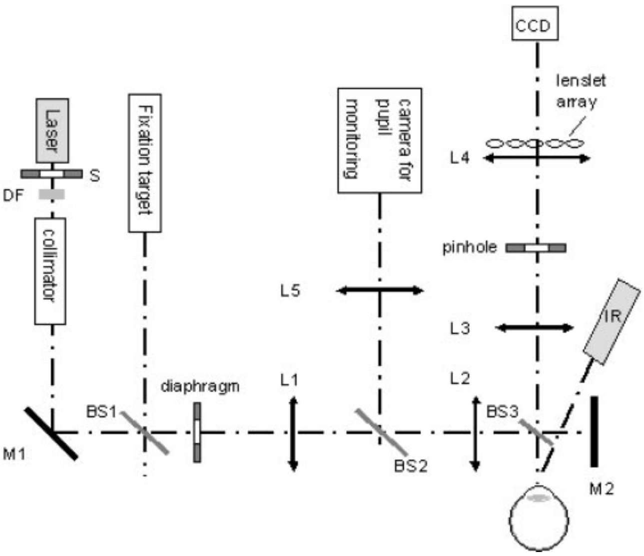

FIGURE 1. Schematic diagram of the experimental Hartmann-Shack sensor used for the measurement of the ocular aberrations: a laser, emitting light in the visible domain, is used for illumination and an infrared (IR) source is used for monitoring the pupil. BS, beam splitter; DF, density filter; L, lens; M, mirror; S, electronic shutter.

also been reported elsewhere. In the incoming pathway (Fig. 1), a collimated He-Ne ($\lambda = 633$ nm) laser source was used to illuminate the subject's eye.

A neutral density filter (Fig. 1, DF) was used to adjust the intensity of the light reaching the eye, and a shutter (Fig. 1, S) controlled the exposure time (0.8 second). The amount of light reaching the eye was in keeping with the American National Standard for the Safe Use of Lasers.[13] The beam was reflected by a mirror (Fig. 1, M1) and a beam splitter BS3 to obtain a diffraction-limited image projected on the retina. The size of the beam was controlled by a diaphragm (aperture, 1 mm) conjugated with the entrance pupil of the eye through lenses L1 and L2.

In the outcoming pathway, the wavefront generated by the light reflected from the retina and refracted by the optics of the eye was sampled by a microlenslet array and focused on the CCD plane of a camera (LV7500/AS, 768 × 492 pixels; Leutron Vision AG, Glattbrugg, Switzerland). The eye's pupil plane was conjugated with the lenslet array after lateral magnification by a modified telescope system composed of two achromatic doublets (Fig. 1, L3 and L4). Because of ocular aberrations, the magnified wavefront was transformed into an irregular matrix of spots by the lenslet array. The mirror M2 was used only for capturing a reference pattern.

The subject's head was stabilized by means of a chin rest mounted on an *x-y-z* positioning stage. Fixation targets in a Vernier pattern were used to ensure a measurement along the line of sight, according to the Optical Society of America (OSA) standards.[14] They were placed at infinity by means of achromatic doublets (Fig. 1, L1 and L2). A second camera and an infrared (Fig. 1, IR) source were used to monitor pupil alignment during measurements. The instrument was calibrated by measuring several known induced amounts of defocus and spherical aberration.[15,16] This calibration was then validated by comparing the eye measurements of two subjects (included in the study) with those obtained for the same subjects with a different experimental system. Similar results were obtained with both systems.

Procedure

Once the subject was aligned with respect to the incoming beam, Hartmann-Shack images were recorded. Subjects wore their glasses during measurements. Phenylephrine hydrochloride 5% and tropicamide 0.8% were instilled in all eyes, with a 45-minute delay between the instillation of drops and testing, to allow for full dilation and cycloplegia.

Numerical Reconstruction

When a planar WA reached the microlenses, the CCD recorded a regular two-dimensional pattern of spots. This pattern was registered with a planar mirror instead of the eye and was used as a reference for the numerical reconstruction of the ocular WA. Because the eye is not an aberration-free optical system, spots shifted from the reference pattern, and an irregular array of spots was registered. The lateral shifts of each spot relative to the optical axis of the corresponding microlens was proportional to the local slope of the WA and were used to reconstruct the WA numerically. The WA was expressed as a Zernike polynomial expansion up to the seventh order.[14] The method consisted of fitting the best possible expression of WA, the partial derivatives of which corresponded respectively to the lateral shifts along the *x*- and *y*-axes.[10,11]

The RMS wavefront error was used as a parameter of optical quality. It was computed from the obtained Zernike expansion, as the square root of the sum of the squares of the corresponding coefficients from the third to the seventh order. Because lower orders (i.e., 1 and 2, corresponding to tilt, regular astigmatism, and defocus) of the Zernike expansion can be corrected with conventional optics (spectacles or contact lenses), they were not taken into account for the RMS calculation. Aberrations were calculated for pupil diameters of 5 and 7 mm, using the matrix of spots obtained with the pharmacologically dilated pupil. A separate calculation was undertaken for each pupil size (5 and 7 mm), and in each case, the geometric center of the matrix of spots was used.

The WA for each pupil size was also used to compute the MTF, again excluding correctable refractive errors. The two-dimensional MTF was derived for 5- and 7-mm pupils. Estimates of one-dimensional MTFs were calculated as the radial average of the two-dimensional MTFs.

Corneal Topography

Subjects also underwent corneal topography (Orbscan II Anterior Segment Analysis System; Bausch & Lomb Surgical, Claremont, CA). Two parameters from this topography were used, the radius of curvature (R) of the best fit sphere (i.e., the sphere that best adjusts to the anterior surface of the cornea in the sense of the least mean square in an adjustment zone of 10.0 mm in diameter) and asphericity (Q) of the anterior corneal surface. Asphericity is the peripheral shape parameter

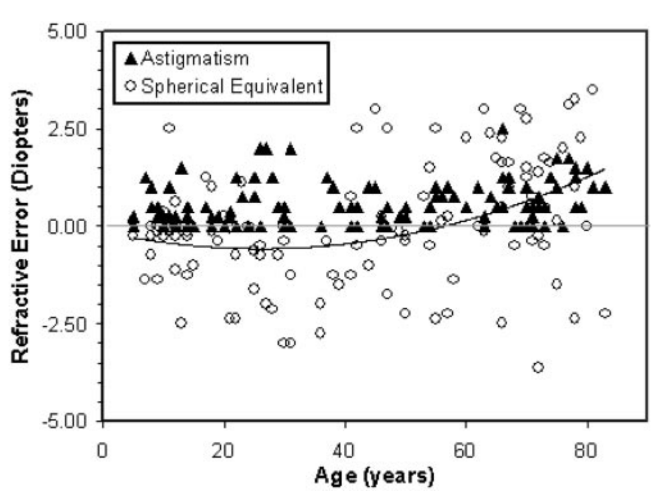

FIGURE 2. Distribution of the spherical equivalent and cylinder as a function of age. For the spherical equivalent, data fitted a second-order polynomial regression curve ($y = -0.107 - 3.59\text{E} - 2x + 6.733\text{E} - 4x^2$; $R^2 = 0.141$; $F_{2,111} = 9.11$; $P < 0.0001$). Refractive cylinder was not affected by age.

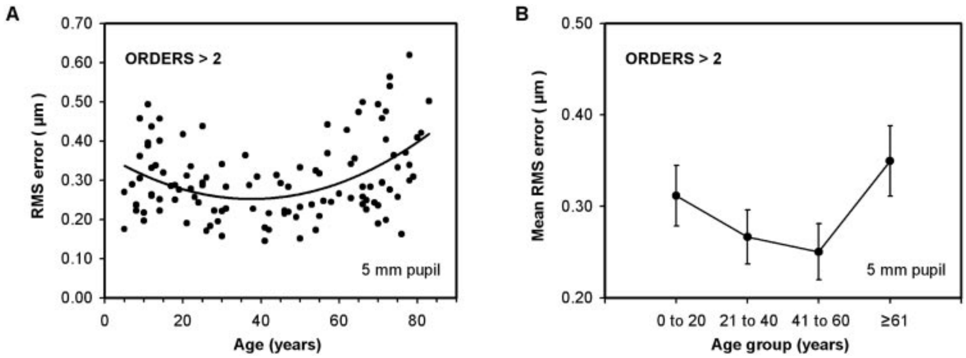

FIGURE 3. (**A**) RMS wavefront error for third- through seventh-order Zernike coefficients as a function of age for a 5-mm pupil. Data fitted a second-order polynomial regression curve ($y = 0.368 - 0.00617x + 8.224\text{E} - 5x^2$; $R^2 = 0.169$; $F_{2,110} = 11.158$; $P < 0.0001$). (**B**) Mean RMS for a 5-mm pupil in the four age groups, for third- through seventh-order aberrations. Error bars: minimum and maximum of the 95% confidence interval.

of a conoidal surface that quantifies its departure from a sphere (for a sphere: Q = 0). Both parameters, R and Q, are useful descriptors of the shape of the cornea.

Population

Subjects were recruited between June 2001 and December 2002 at the Department of Ophthalmology of Maisonneuve-Rosemont Hospital, affiliated with the University of Montreal. A maximum of three subjects of the same age (in years) were accepted. Only one eye per subject was tested: the one closer to emmetropia in the case of anisometropia or the right eye when refraction was identical in both eyes, except when there was a contraindication, in which case the left eye was chosen. A 20/40 or better best corrected visual acuity was required. Enrollment was preceded by a complete ophthalmic examination to rule out the presence of any factors likely to interfere with the transmission of light through the optics of the eye and its reflection on the retina. Subjects with opacification of the ocular media, including cornea, lens, and/or vitreous were excluded. Other exclusion criteria included corneal surface problems; abnormal pupil shape or size; retinal, RPE or choroidal detachment of any type; and a history of ocular surgery. The Lens Opacities Classification System III (LOCS III)[17] was used to assess transparency of the lens in all subjects. Scores superior to 1.75 for cortical opacification (0.1–5.9), nuclear opalescence (0.1–6.9), or color (0.1–6.9), and scores superior to 1 for posterior subcapsular opacification (0.1–5.9) were excluded. As ametropia within ±3.50 D from emmetropia was shown to have a minimal effect on the RMS wavefront error (Simonet P, et al. *IOVS* 1999;40:ARVO Abstract 2361), spherical equivalent refractions from −3.50 D to +3.50 D were accepted. The research protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Maisonneuve-Rosemont Hospital human experimentation committee. A signed informed consent was obtained from subjects after explanation of the nature and possible consequences of the study.

A total of 114 subjects were enrolled (age range, 5.7–82.3 years; mean ± SD, 43.2 ± 24.5). The mean (±SD) spherical equivalent refraction was −0.03 ± 1.58 D. Refractive cylinders ranged from 0 to 2.50 D (mean, 0.58 ± 0.55 D). As expected, there was no correlation between age and the refractive cylinder, but the spherical equivalent was found to vary with age according to the results of several epidemiologic studies (Fig. 2).[18,19]

Statistical Analysis

The relationship between the RMS wavefront error and age was modeled using a regression model (the best of the linear or polynomial models was used in each case) and the differences in RMS between age groups were established by analysis of variance with contrast analysis (polynomial[20] and Tukey-Kramer[21]). The differences in RMS due to pupil enlargement from 5 to 7 mm were studied using a Student's paired *t*-test. Each subject's MTF was modeled using a nonlinear model, and the parameters of the fitted model were compared across age groups by analysis of variance. Differences in area under the MTF curves between age groups were established by analysis of variance with contrast analysis (polynomial and Tukey-Kramer). A level of significance of $\alpha = 0.05$ was used in this study.

RESULTS

Results were first analyzed for the entire population, then subjects were divided into four age groups, and these were compared. Figures 3 to 6 show RMS errors for third- to seventh-order (Fig. 3A), third-order (Fig. 4A), fourth-order (Fig. 5A), and fifth- to seventh-order (Fig. 6A) aberrations as a function of age, for a 5-mm pupil. Coma and spherical aberrations are also plotted as a function of age for a 5-mm pupil in Figures 7A and 8A, respectively. Coma included horizontal and vertical primary, secondary, and tertiary comalike terms from the third, fifth, and seventh orders (i.e., two terms from each order). Spherical aberrations included the primary and secondary spherical aberration-like terms from the fourth and sixth orders (i.e., terms $Z_{4,0}$ and $Z_{6,0}$, respectively). We first attempted to model the relationship between RMS and age, to predict the RMS based on age. For all studied combinations of orders, with a 5-mm pupil, data fitted a second-order polynomial regression

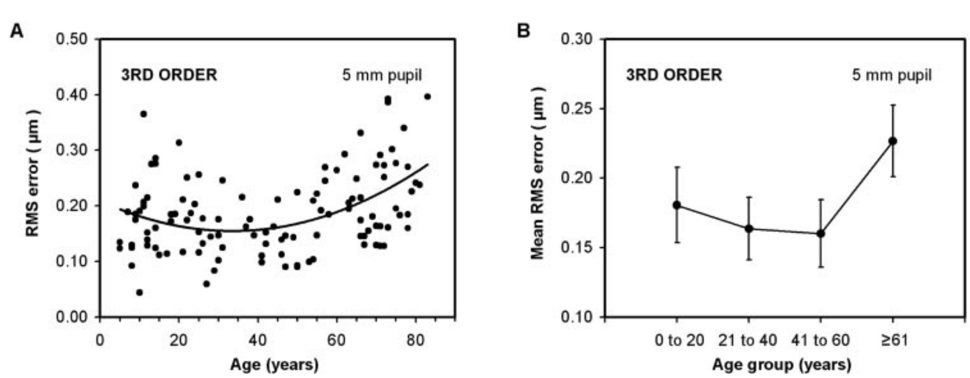

FIGURE 4. (**A**) RMS wavefront error for third-order Zernike coefficients as a function of age for a 5-mm pupil. Data fitted a second-order polynomial regression curve ($y = 0.210 - 0.0033x + 4.952\text{E} - 5x^2$; $R^2 = 0.182$; $F_{2,110} = 12.202$; $P < 0.0001$). (**B**) Mean RMS for a 5-mm pupil in the four age groups, for third-order aberrations. Error bars: minimum and maximum of the 95% confidence interval.

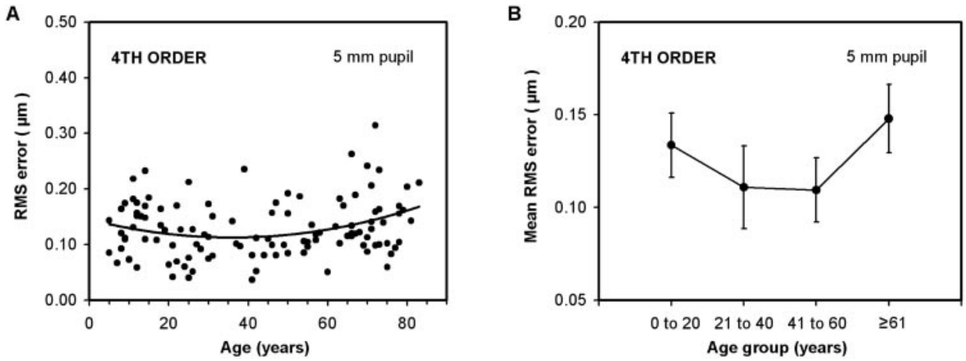

FIGURE 5. **(A)** RMS wavefront error for fourth-order Zernike coefficients as a function of age for a 5-mm pupil. Data fitted a second-order polynomial regression curve ($y = 0.145 - 0.00183x + 2.549\text{E} - 5x^2$; $R^2 = 0.071$; $F_{2,110} = 4.183$; $P = 0.018$). **(B)** Mean RMS for a 5-mm pupil in the four age groups, for fourth-order aberrations. Error bars: minimum and maximum of the 95% confidence interval.

curve (Figs. 3–8, panel A in each). In all cases, the polynomial model fitted better than the linear model, which means that the quadratic term was statistically significant and that the variance explained by this quadratic term was significantly superior to that of the linear term. The predicted RMS error was shown to be higher in children than in young adults. It decreased progressively during childhood and adolescence, stabilizing somewhat around age 30 to 50 years. It was only after that point that the progressive increase in RMS, known to occur with age, was observed. For third- through seventh-order aberrations and a 5-mm pupil, the predicted RMS was 0.339 μm at 5 years, it reached a minimum of 0.252 μm at age 37.5 years, and increased to a maximum of 0.415 μm at age 82 (Fig. 3A). Minimum predicted RMS values and corresponding ages are shown in Table 1 for each combination of orders studied, for a 5-mm pupil.

For a 7-mm pupil, the distribution of RMS as a function of age could not be adequately fitted, either with a polynomial or with a linear model, for any of the orders studied. However, as expected, for all orders studied, the RMS error increased significantly with pupil size, from 5 to 7 mm (two-tailed Student's paired *t*-test, $P < 0.0001$ in all cases).

Subjects were then arbitrarily divided into four age groups: Group 1 included children and teenagers (20 years of age or less; $n = 29$); group 2, young adults (21–40 years; $n = 24$); group 3, middle-aged adults (41–60 years; $n = 24$); and group 4, elderly subjects (61 years and older; $n = 37$). An analysis of variance with polynomial contrast approach was used to evaluate the change in RMS with age, from one group to the other, for each combination of order and pupil size. In Figures 3 to 8 (panel B in each), mean RMS and 95% confidence interval is reported for each group. For a 5-mm pupil, a statistically significant pattern, consisting of a decrease in RMS between children/adolescents (group 1) and young adults (group 2), followed by a further decrease between young adults and middle-aged adults (group 3), then followed by an increase between middle-aged adults and elderly subjects (group 4) was observed for the third to seventh, third, fourth, and fifth to seventh orders ($P = 0.00,002$, $P = 0.0209$, $P = 0.0004$ and $P = 0.0009$, respectively). The significance of this pattern was further reinforced by the Tukey-Kramer contrast analysis, which revealed that for third- to seventh-, third-, and fourth-order aberrations, the mean RMS for groups 2 and 3 were significantly lower than that of group 4, whereas no difference in mean RMS was found between groups 1 and 4. For the fifth to seventh orders, the only statistically significant difference was between groups 3 and 4 (the mean RMS for group 3 being lower than that of group 4). In the case of coma and spherical aberration, a slightly different pattern was observed, with a decrease between group 1 and group 2, followed by a progressive increase from groups 2 to 3, and from groups 3 to 4. For coma, this general pattern did not reach the level of statistical significance, whereas it did for spherical aberration ($P = 0.0281$). For a 7-mm pupil, no such V-pattern was observed when the studied population was divided into four groups.

In Figure 9, the mean MTF is illustrated for each age group, for 5-mm (Fig. 9A) and 7-mm (Fig. 9B) pupils. For a 5-mm pupil, the lowest MTF curve was that of children and adolescents, and the second lowest curve was that of elderly subjects. Middle-aged adults showed the highest MTF curve, whereas young adults showed the second highest curve. Curves in young adults and elderly subjects were very close and almost superimposed at spatial frequencies higher than 38 cyc/deg. In other words, the optical performances of children and elderly subjects were lower than that of middle-aged adults, and at spatial frequencies lower than 38 cyc/deg, they were also lower than that of young adults. With pupil enlargement from 5 to 7 mm, MTFs decreased in all four groups. However, the shift of the MTF curve for children and adolescents was less than that of the three other groups. With a 7-mm pupil (Fig. 9B), deterioration of the optical performance increased with age. Curves for children-adolescents and young adults were superimposed, and both were higher than that of middle-aged adults and elderly subjects.

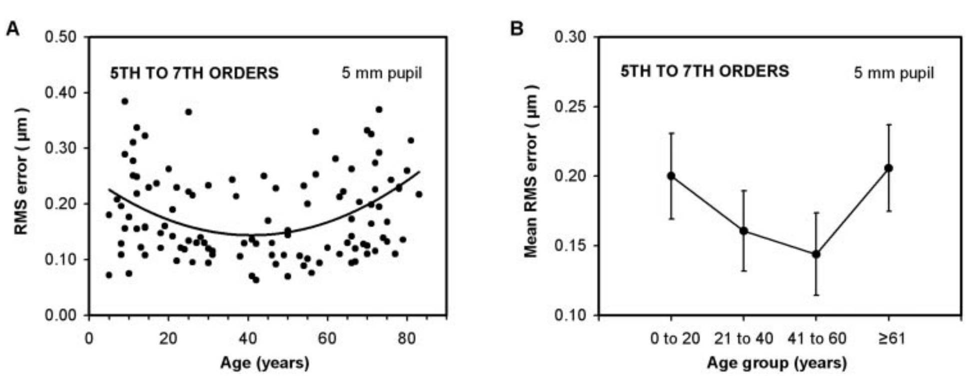

FIGURE 6. **(A)** RMS wavefront error for fifth- to seventh-order Zernike coefficients as a function of age for a 5-mm pupil. Data fitted a second-order polynomial regression curve ($y = 0.253 - 0.0054x + 6.636\text{E} - 5x^2$; $R^2 = 0.119$; $F_{2,110} = 7.448$; $P = 0.001$). **(B)** Mean RMS for a 5-mm pupil in the four age groups, for fifth- to seventh-order aberrations. Error bars: minimum and maximum of the 95% confidence interval.

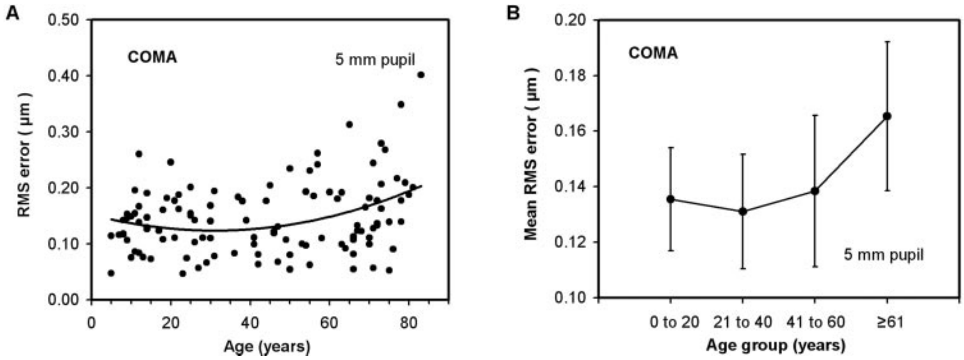

FIGURE 7. (**A**) RMS wavefront error for coma (i.e., third-, fifth-, and seventh-order Zernike coefficients) as a function of age for a 5-mm pupil. Data fitted a second-order polynomial regression curve ($y = 0.152 - 0.00182x + 2.958\text{E} - 5x^2$; $R^2 = 0.107$; $F_{2,110} = 6.563$; $P = 0.002$). (**B**) Mean RMS for a 5-mm pupil for the three age groups, for third-, fifth-, and seventh-order aberrations. Error bars: minimum and maximum of the 95% confidence interval.

To evaluate the statistical significance of these results, each MTF was modeled, based on a logistic model,[22] according to the equation

$$MTF = 1 - \frac{\alpha}{1 + e^{-\beta(f-\gamma)}}$$

where α, β, and γ were three parameters and f the spatial frequency (in cycles per degree). The parameter γ was the spatial frequency corresponding to the maximum negative slope of the function. This maximum negative slope was given by $\alpha \cdot \beta/4$. An analysis of variance was performed on the four age groups, for the three parameters α, β, and γ. For a 5-mm pupil, the β of group 3 ($\beta = 0.110$) was significantly lower than that of groups 1 ($\beta = 0.132$; $P = 0.014$) and 4 ($\beta = 0.133$; $P = 0.011$), which means that the MTF curve decreased at a slower rate in group 3 than in groups 1 and 4. Also with a 5-mm pupil, the γ of group 3 ($\gamma = 26.1$) was significantly higher than that of group 4 ($\gamma = 22.35$; $P = 0.014$), which means that the maximum negative slope occurred at a higher spatial frequency for group 3 than for group 4. Analysis of the area under the MTF curve also confirmed the statistically significant difference between groups ($P = 0.0145$) for a 5-mm pupil. The area under the MTF curve was significantly higher for group 3 (area = 32.073) than for groups 1 (area = 28.086; $P = 0.021$) and 4 (area = 28.528; $P = 0.035$). These analyses confirmed once more the lower optical performance of children-adolescents and elderly subjects in comparison with that of adults with a 5-mm pupil. With a 7-mm pupil, none of the observed differences between MTF curves was statistically significant (tested parameters: α, β, and γ and the area under the MTF curve).

Corneal topography was available for 93 of the subjects (Fig. 10). The corneal front surface radius of curvature varied as a function of age according to the quadratic model described in Figure 10A. The corneal front surface flattened somewhat during the childhood and teenaged years, until early adulthood, and steepened afterward with advancing age. The corneal front surface asphericity (Q) also varied as a function of age, and data fitted a second-order polynomial regression curve (Fig. 10B). Asphericity decreased during the childhood and teenaged years until adulthood and then increased again with advancing age. Q started more in the negative early in life and returned to the negative in the elderly.

DISCUSSION

In this study, we analyzed the image optical quality of the eye across nearly the entire span of human life, from early childhood to advanced age. To the best of our knowledge, this is the first time ocular aberrations of the whole eye have been objectively measured in persons as young as 5 years to as old as 82 years.

The interesting finding of this study is that for a 5-mm pupil, the effect of age on the monochromatic aberrations was best modeled with a second-order polynomial model, rather than a linear model, as reported up to now. The reasons for this are most probably the large sample size and the wide range of ages studied. For a 7-mm pupil, a regression model could not be adequately fitted, and the division in four age groups did not allow identification of the characteristic V-pattern observed with a 5-mm pupil. However, from a purely descriptive point of view, the hypothesis of a similar phenomenon cannot be rejected. The increased variance observed with a 7-mm pupil may in part have been responsible for this lack of significance. An increase in variance as a function of pupil size has also been documented by others.[16,23]

The general pattern described in this study with a 5-mm pupil indicates not only that the eye of the younger adult produces a retinal image of higher quality than the elderly eye, but also that, as far as RMS is concerned, the optical quality of a child's eye is suboptimal and could be compared with that of an elderly eye.

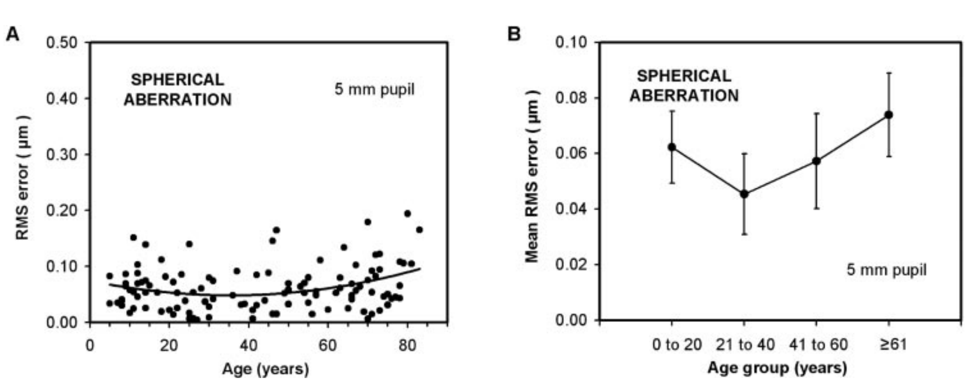

FIGURE 8. (**A**) RMS wavefront error for spherical aberrations (i.e., fourth- and sixth-order Zernike coefficients) as a function of age for a 5-mm pupil. Data fitted a second-order polynomial regression curve ($y = 0.07477 - 0.0015x + 2.125\text{E} - 5x^2$; $R^2 = 0.085$; $F_{2,110} = 5.116$; $P = 0.008$). (**B**) Mean RMS for a 5-mm pupil in the three age groups, for fourth- and sixth-order aberrations. Error bars: minimum and maximum of the 95% confidence interval.

TABLE 1. Minimum Predicted RMS Values and Corresponding Age for Each Combination of Orders Studied, for a 5-mm Pupil

Type of Aberration	Minimum RMS (μm)	Age (y)
Less than 2nd order	0.252	37.51
3rd order	0.155	33.32
4th order	0.111	36.29
5th to 7th order	0.143	40.69
Coma	0.124	30.76
Spherical aberration	0.048	35.29
Mean		35.64
Standard deviation		3.43
Minimum		30.76
Maximum		40.69

The same pattern was also found for MTF in a 5-mm pupil, the mean optical performance of children-adolescents and elderly subjects being similar and in both cases significantly lower than that of middle-aged adults.

Previous studies using different experimental setups have demonstrated an increase in ocular aberrations as a function of age among adults. Artal et al.,[6] using a Hartmann-Shack sensor, as well as McLellan et al.,[5] using a spatially resolved refractometer, showed a linear increase in RMS with age. It is interesting to note that we also found a linear increase in RMS with age when analyzing similar ranges of age and pupil size. These comparisons are illustrated in Figure 11. For young adults aged 25 to 35 years, our regression curves predicted RMS values of the same magnitude as those reported by Artal et al. and McLellan et al. The mean intersubject variability in RMS values was also comparable. Deterioration of the optical performance in elderly subjects, however, was more pronounced in the Artal and McLellan studies. The fact that we used the LOCS III for the slit lamp classification of lens opacities may in part explains this difference. Although cataract can easily be ruled out by a routine ophthalmic examination, the LOCS III requires the classification of more discrete cortical and posterior subcapsular irregularities, as well as subtle changes in color and density of the nucleus, which are known to affect the refractive index gradient of the crystalline lens. These early signs of lens senescence could induce a non-negligible increase in aberrations. This hypothesis is in agreement with the findings of Barbero et al. (Barbero S, et al. *IOVS* 2002;43:ARVO E-Abstract 388), who reported an increase in mean total RMS in cataractous eyes. Future comparisons between studies may become easier with the standardization of wavefront measurement techniques and a better knowledge of the various parameters that influence the WA.[23]

Many factors are involved in the deterioration over time of the optical image quality of the adult eye. The ageing process induces several physical and anatomic changes in the dioptric elements, all of which can alter the optical quality of the eye.

At the corneal level, reports, including our study (Fig. 10A), indicate that the mean radius of curvature of the central front surface decreases during late adult life,[24,25] with most of the change occurring along the horizontal meridian.[25,26] The asphericity of the adult corneal front surface was also found to be age-dependent, with a decrease in asphericity between ages 20 and 40 followed by a return of asphericity and accentuation of the prolate ellipsoidal contour between ages 40 and 80 years (Fig. 10B). Guirao et al.[24] observed a similar decrease in mean asphericity between young (20–30 years, $n = 27$) and middle-aged adults (40–50 years, $n = 14$), with minimal change between middle-aged and older subjects (60–70 years, $n = 17$). The discrepancy between their results and ours for older subjects may be due to sample size or to the absence in their data of subjects older than 70 years. Studies on front corneal WA derived from topographical measurements in adults indicate that spherical aberration[24] and coma[24,27] increase with age. However, this increase is too small to account for the degradation of the optical quality of the eye observed in the ageing process. This indicates that the effects of age on crystalline lens shape and structure are also involved in the modification of monochromatic aberrations in the elderly.

Owing to the continual production of new fibers, the aging lens becomes thicker. Its front surface and center of mass are translated anteriorly, whereas the volume of the lens nucleus remains unchanged.[28,29] Dubbelman and Van der Heijde,[30] using Scheimpflug slit images of the crystalline lens corrected for distortion, showed that the radii of curvature of the anterior and posterior lens 3-mm central surfaces decrease with age (16–65 years, $n = 102$ and $n = 65$, respectively for each surface). Koretz et al.[28] using a parabolic fit of Scheimpflug images also observed a linear decrease with age in the radius of curvature of both anterior and posterior lens surfaces ($n = 100$; 18–70 years). Millodot[31] measured peripheral refraction and derived the total oblique astigmatism of the eye as a function of retinal eccentricity. He found that this optical aberration increases with age in adults, whereas that of the cornea remains approximately constant, indicating that the increase with age in the total oblique astigmatism of the eye is accounted for mostly by the lens. Millodot[31] also noticed that the total oblique astigmatism of old eyes is very close to that of Le Grand's theoretical eye model, using spherical rather than aspherical surfaces. This suggests that, with age, the lens becomes more spherical.

Changes in lens surface profiles seem to be responsible for most of the increase in monochromatic aberrations that occur

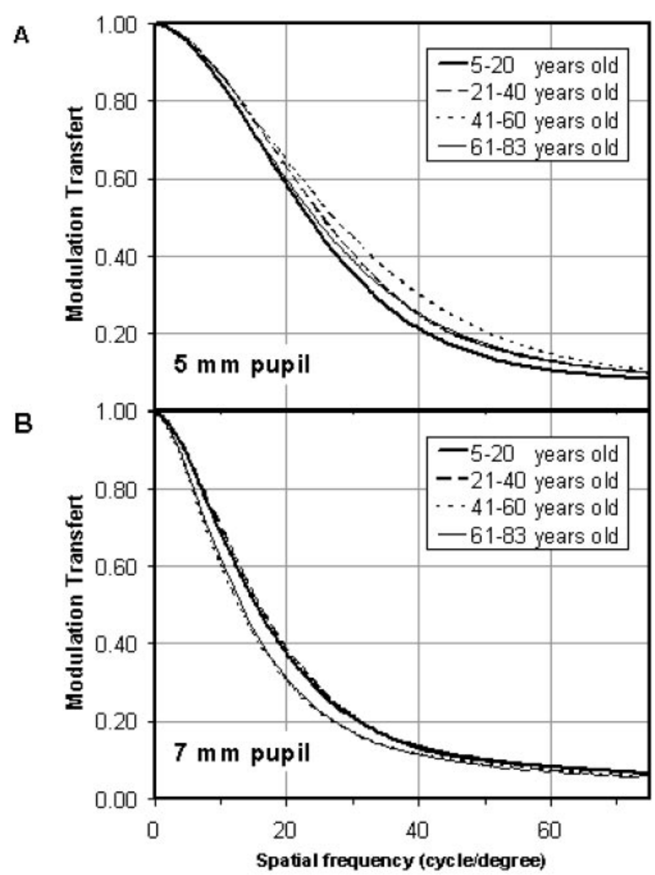

FIGURE 9. Mean MTF in the four age groups for 5-mm (**A**) and 7-mm (**B**) pupils.

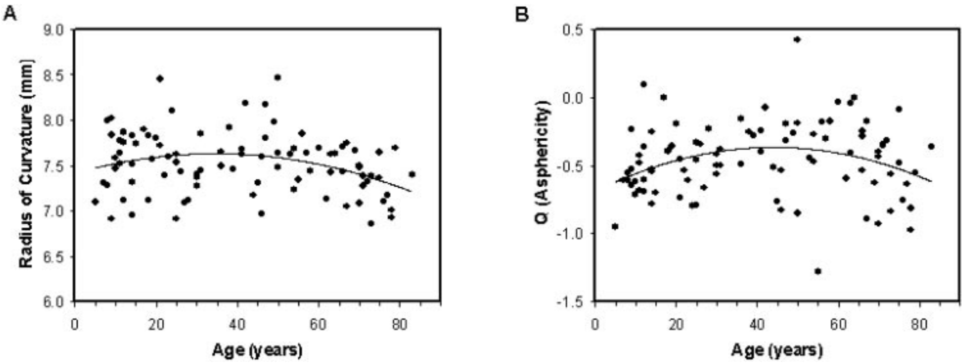

FIGURE 10. Corneal topography data (n = 93). (**A**) Corneal front surface radius of curvature as a function of age. Data fitted a second-order polynomial regression curve (y = 7.408 + 0.01301x − 1.88E − 4x^2; R^2 = 0.091; $F_{2,90}$ = 4.521, P = 0.013). (**B**) Corneal front surface asphericity (Q) as a function of age. Data fitted a second-order polynomial regression curve (y = −0.697 + 0.0152x − 1.73E − 4x^2; R^2 = 0.076; $F_{2,90}$ = 3.711; P = 0.028).

with age. However other optical elements, such as the lens refractive index, may also play a role. In isolated lenses, initial in vitro studies showed no significant age-dependent changes in equivalent refractive index[32] or refractive gradient index.[33] However, in more recent work involving magnetic resonance microimaging, age-related changes in refractive index distribution were documented.[34] For in vivo conditions, similar findings are reported. Dubbelman and Van der Heijde[30] reported a small but significant decrease in equivalent refractive index as a function of age. Hemenger et al.,[35] using their own gradient index model, concluded from biometric data obtained from the living eyes of young (19–31 years) and older (49–61 years) subjects that, with age, the refractive index gradient becomes flatter near the center of the lens and steeper near the surface.

These structural and anatomic changes of the aging lens are compatible with the variations in spherical aberration observed with age. Glasser and Campbell[32,36] reported that in vitro, the spherical aberration of the lens, expressed in diopters, increases linearly with age, with a low negative value in young adults; a null value within the range of 32 to 40 years, depending on whether the lens is stretched, and a positive

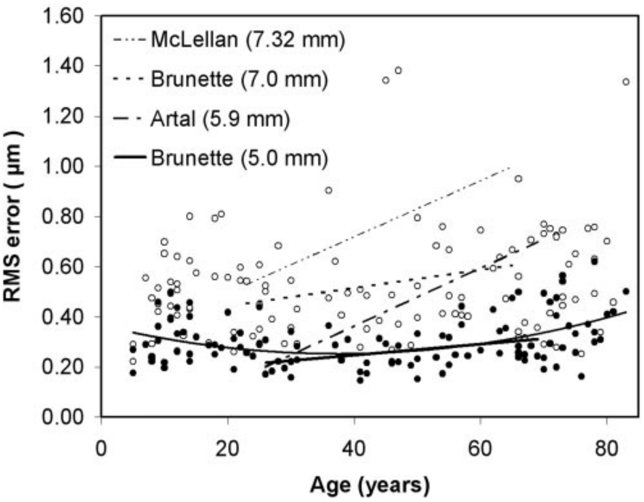

FIGURE 11. RMS as a function of age for third-through seventh-order Zernike coefficients. Comparison of the linear regressions obtained by Artal et al.[6] (age range, 26–69; from third to sixth order) and McLellan et al.[5] (age range, 23–65) with our results for similar pupil diameter and age ranges. For the 25- to 69-year interval and a 5-mm pupil, our data also fitted a linear model (y = 0.169 + 2.054E − 3x; R^2 = 0.121; $F_{1,50}$ = 6.914; P = 0.011). For the 25- to 69-year interval and a 7-mm pupil, the linear fit was not statistically significant. (●) All available RMS data (age range, 5–82 years) for a 5-mm pupil with the polynomial curve shown in Figure 3A; (○) all available RMS data (age range, 5–82 years) for a 7-mm pupil.

value after this age. Removal of the lens capsule did not change the trend of the data.[32] Smith et al.[37] measured, in vivo, the total aberration of the eye (crossed-cylinder aberroscope), the corneal front surface radius of curvature and corneal asphericity from young (n = 13; 20–29 years) and older subjects (n = 13; 56–72 years), and concluded that the spherical aberration of the lens becomes less negative with age.

In a young subject, contrary to an elderly person, the ocular media are clear, but the eye is still growing. Major anatomic and optical changes occur during childhood and adolescence, each being likely to affect the amount of eye aberrations. At birth, the cornea is steep. Central corneal flattening occurs mostly during the first year of life,[38] with moderate change in central corneal curvatures between ages 2 and 14.[39,40] Our data also show a decrease in corneal anterior surface asphericity from childhood to adulthood.

The axial length of the eye, anterior chamber depth, and vitreous chamber depth continue to increase until the teenage years.[41,42] As shown by Mutti et al.,[42] the crystalline lens also undergoes numerous structural changes during the growing process. Its axial thickness decreases until age 10 and remains relatively stable during adolescence.[43] Both the anterior and posterior lens surfaces flatten between ages 6 and 14 years.[42,44] The calculated power of the lens decreases during childhood.[45] Mutti et al.[42] reported an early decrease in calculated lens power between ages 6 and 10 years, followed by little change between ages 10 and 14 years. The lens equivalent refractive index is also reported to vary with age. Results from the Orinda Longitudinal Study of Myopia data display a decline of the equivalent refractive index with age in early childhood, followed by an increase between ages 10 and 14 years.[42] All these growth patterns are also dependent on the type and level of ametropia (Jones LA, et al. *IOVS* 2002;43:ARVO E-Abstract 2025).

During childhood, the concurrent thinning and flattening of the lens, axial elongation of the eye and the change in corneal profile are oriented toward emmetropization of the eye. The goal of this process, as far as ametropia is concerned, is the control of the second-order aberrations defocus and astigmatism. However, the results of the present study, as well as other recent findings, suggest that higher order aberrations may also be involved in this process. Our data show a decrease in RMS during childhood and adolescence, which means that higher order monochromatic aberrations, such as low-order aberrations corresponding to ametropia, decrease with the development of the optical structures of the eye. This suggests that the definition of emmetropization should be broadened to include the reduction of higher order aberrations.

Recently, He et al.[7] also reported higher mean RMS values among preadolescent and adolescent emmetropes (10–17 years; n = 83) than among young adult emmetropes (18–29 years; n = 54). Our results, obtained with an objective method, confirm their findings. They compared their data with those from two groups of myopes (10–17 years; $n = 87$ and 18 to 29 years; $n = 92$) and found that for both age intervals, myopes had a greater mean RMS than emmetropes. They proposed that high amounts of WAs, which degrade the retinal image quality, may play a role in the development of myopia. Carkeet et al.,[9] using an aberrometer (Zywave; Bausch and Lomb), also reported monochromatic aberrations in 273 children (mean, 9.0 years; range, 7.9–12.7 years). Subjects with low myopia (more than −3.00 to −0.50 D) showed slightly but significantly less positive levels of spherical aberration than either high myopes, emmetropes, or hyperopes. The anterior corneal spherical aberration (calculated from topography) did not vary significantly with refractive error, whereas the residual spherical aberration (i.e., of posterior cornea and crystalline lens) did. Carkeet et al. concluded that their results did not provide evidence for aberration-driven form deprivation as a major mechanism in the development of myopia.

In the present cross-sectional study, ametropia was voluntarily maintained within ±3.50 D of emmetropia. Consequently, our data do not provide any direct evidence that the development of myopia is driven by a form-deprivation mechanism involving monochromatic aberrations. However, higher order aberrations were shown to decrease during emmetropization. As monochromatic aberrations provide an odd-error cue to focus direction, as shown recently by Wilson et al.,[46] higher order aberrations may be at the origin of the control of the refractive state during ocular growth, in which case monochromatic aberrations would constitute an input signal for the emmetropization process. However, if optimization of second-order and higher order aberrations is the final goal of eye development, a low level of optical aberrations could also be the output result of the process. A prospective study is needed to determine whether optimization of second-order and higher order aberrations is simultaneous or sequential during eye development. Additional investigation is also needed to determine whether the role of optical aberrations in the ocular emmetropization process is active or passive.

It is interesting to notice that in the present study, the 30- to 40-year age interval also seemed to constitute a turning point. The minimum (or maximum) of most quadratic curves were documented around ages 30 to 40, including most RMS curves (panel A in Figs. 3–8; Table 1), radius of corneal curvature (Fig. 10A), and corneal asphericity (Fig. 10B). The prepresbiopia decade seems to be the period of life during which the eye has the best optical quality.

Before we conclude, it should be remembered that similar RMS values do not necessarily imply similar optical performance, as parameters other than RMS may affect performance. Scattering, for example, was not specifically measured in the present study. Ijspeert et al.[47] have demonstrated that stray light increases with the fourth power of age, doubling from age 20 to 70. Westheimer and Liang[48] have documented the influence of ocular light scatter on ocular optical performance, reporting no decrement in visual acuity, but difficulty with small, low-contrast targets; reports of glare in the presence of bright targets; and a reduction in some psychophysical thresholds at which contrast played a role. Also, the design of this study did not allow us to take into account the progressive miosis that occurs with age and that is believed to compensate, at least in part, for the deterioration in optical performance associated with aging.[4] Our measurements were made in eyes under cycloplegia and pharmacologic dilation to cancel accommodation in children and to allow the standard 5- and 7-mm pupil sizes to be reached in elderly subjects. Finally, it should be borne in mind, when comparing young and elderly subjects, that the image optical quality of the eye represents only one of the numerous aspects of visual perception, which is also governed by the complex functions of the central and peripheral neural visual systems.

Conclusions

The effect of age on the monochromatic aberrations of the eye was best modeled with a quadratic model rather than with the linear model that has been reported up to now. For a 5-mm pupil, there was a statistically significant decrease in RMS for most of the orders studied and also MTFs (both calculated from the WA) in young and elderly eyes versus adult eyes. Our results suggest that the definition of emmetropization should be broadened to include the reduction of higher order aberrations.

Acknowledgments

The authors thank Miguel Chagnon, MSc, Department of Mathematics and Statistics, University of Montreal, Montreal, Quebec, Canada, for statistical analysis of the results; Denise Descovich, MD, Brigitte Breault, MA, Brigitte I. Jaeger, MD, Benoît Bouliane, Lucie Bissonnette, MD, Michel Podtetenev, MD, FRCSC, Pierre Labelle, MD, FRCSC, and Jean Dumas, MD, FRSCS, for participation in the recruitment of study subjects and/or data collection.

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