Ocular Measurements throughout the Adult Life Span of Rhesus Monkeys

Alcides Fernandes,1,2 Dolores V. Bradley,1,3 Margarete Tigges,1 Johannes Tigges,1 and James G. Herndon1

**Purpose.** To examine the relationship of ocular components to refractive error throughout the adult life span of the rhesus monkey (Macaca mulatta).

**Methods.** Cycloplegic retinoscopy, A-scan ultrasonography, slit lamp examination, indirect ophthalmoscopy, and keratometry were performed in a cross-sectional study of 111 monkeys, aged 5 to 31 years. Lens thickness and anterior and vitreous chamber depths were measured from the echograms. The intercorrelations of these variables were analyzed, as well as their association with age and sex.

**Results.** In monkeys aged 5 to 15 years, the mean refractive value of +1.5 D with an SD of 1.7 D was maintained near the previously established developmental asymptote of +2 D. In monkeys older than 15 years, there was greater interindividual variation (SD = 4.5 D), including extreme myopia and hyperopia. The cornea became steeper with age. The axial length of the eyes increased up to 12 years of age and began to shorten after 20 years. Changes also occurred in the other individual components that constitute eye length. These age-related changes were decreed vitreous chamber depth, decreased anterior chamber depth, and increased lens thickness. In general, males had longer eyes than females. The eyes of old monkeys were more likely to exhibit cataract and drusen, but generally had shorter eyes than females. The eyes of old monkeys were more likely to exhibit cataract and drusen, but generally had shorter eyes than females.

**Conclusions.** The components of the monkey eye change with age in a pattern similar to that reported in humans. Age-related changes in individual ocular components that could be detrimental to refraction appear to be compensated for by changes in other components. (Invest Ophthalmol Vis Sci. 2003;44:2373–2380) DOI:10.1167/iovs.02-04944

Greater life expectancy in most of the world’s populations has led to an increased prevalence of visual impairments associated with aging. In particular, cataract and age-related macular degeneration account for the majority of visual deficits in patients aged 75 years or more.1 Obviously, age-related changes in ocular structures in the elderly could result in impairment of such functions as visual acuity and contrast sensitivity and therefore could have an adverse impact on activities of daily living and impede the ability to perform some cognitive tasks.2 To minimize the detrimental effects of decline in vision on the quality of human life, a complete understanding of the mechanisms involved in aging of the visual system is essential.

The rhesus monkey has been used extensively in the investigation of the structure and function of the visual system, including the effects of the manipulation of visual experience on the refractive development of the eye.3–5 An area of particular interest is the study of the mechanisms that regulate ocular growth and emmetropization. In a previous analysis of ocular growth data from a large number of normal monkeys at ages ranging from birth to 5 years, we established that the postnatal process of eye growth in monkeys shares similarities with that of humans, including axial eye elongation, flattening of the cornea, and a reduction of the hyperopia present at birth.6 We also found one important difference between the two species: the end point of emmetropization in adolescent monkeys is hyperopic, with an average refractive value of approximately +2 D, whereas that of the adolescent human is in the range of plano refraction.

The present study extends this work to monkeys ranging in age from young adults to old adults, thus covering the entire adult life span of this species.7,8 Specifically, we addressed the question of whether the hyperopic refraction observed throughout adolescence declines with age and investigated the relationships among the ocular components during aging. Finally, we evaluated the appropriateness of the rhesus monkey eye as a model for the aging human eye by comparing our results with established findings in humans.

On the basis of a survival rate and life span study of our rhesus monkey colony,9 we use a ratio of 1:3 when comparing ages of adult monkeys and humans—that is, 20 monkey years are equivalent to 60 human years. In studies on the developing visual system, a ratio of 1:4 may be more appropriate (for a review of the literature, see Ref. 24).

The present data should be of interest to those who study the visual system and the effects of aging on this system. In addition, our results have relevance for studies of cognitive function and visually guided or modulated behavior in monkeys, because the physical status of the eye has obvious implications for the performance of such tasks.

**Materials and Methods**

**Animals**

In a cross-sectional study, we examined 111 rhesus monkeys (Macaca mulatta), aged 5 to 31 years. Because monkeys reach sexual maturity at approximately 5 years of age and have a maximum life span of approximately 35 years, this sample includes nearly the entire adult life span. All monkeys were in good health and had not been used previously in studies of the visual system. There were 55 females and 56 males; 93 monkeys had been born in captivity, one was born in the wild, and 17 were of unknown origin. The birth dates of the captive-born monkeys were known; the ages of the other monkeys were estimated on their arrival at the Yerkes National Primate Research Center, based on such criteria as weight, general appearance, dentition, and the records provided by the suppliers. When possible, we
also examined our animal records database to determine the length of time that each monkey had lived indoors or outdoors. All procedures were in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and were approved by the Institutional Animal Care and Use Committee of Emory University.

Ophthalmic Examinations

The same ophthalmologist (AF) examined eyes of all monkeys during routine health assessments. Anesthesia was induced in the monkeys with an intramuscular injection of ketamine hydrochloride (10 mg/kg) and maintained with a mixture of tiletamine, zolazepam, and mannitol (4 mg/kg). The monkeys were placed supine in a headrest apparatus to stabilize the head. Cyclopentolate was induced by the instillation of 1 drop of 1% cyclopentolate hydrochloride and 1 drop of 2% phenylephrine hydrochloride; this procedure was repeated two more times at 5-minute intervals. A lid speculum was used to hold the eyelids open. Corneas were kept moist with saline drops to preserve the integrity of the corneal epithelium and to avoid distortions of the measurements, which may be caused by dry eyes.

Refractive measurements in diopeters (D) were obtained by streak retinoscopy between 25 and 30 minutes after application of the last set of drops. Care was taken to perform retinoscopy on axis. Refractions were reported as spherical values. For monkeys with astigmatism, these values included spherical equivalents of the cylindrical errors. The corneal refractive powers (in diopeters) of the vertical and horizontal meridians were measured with a handheld autokeratometer (Renaissance; Alcon Surgical, Irvine, CA). The mean of three sets of measurements of each eye was recorded as the corneal power. Axial length was measured with an ultrasound A-Scan system (Sonomed, Lake Success, NY). At each examination session, the A-Scan was calibrated for accuracy against a standard of known length. Tissue velocities were set at 1548 m/s for cataractous eyes and 1550 m/s for all others. Care was taken to ensure that the measurements were on axis and that the ultrasound transducer did not compress the cornea. The mean of 10 measurements of each eye defined that eye’s axial length. For each eye, three echograms were printed. Echograms included spikes corresponding to the surface of the cornea, the front and back surfaces of the lens, and the surface of the retina, thus permitting measurement of lens thickness and vitreous chamber depth. These measures were obtained with a digital caliper (Brown and Sharpe, Renens, Switzerland). The anterior chamber depth, which included the thickness of the cornea, was calculated automatically by the A-Scan. Slit lamp examinations were performed with a portable slit lamp (model SL2; Kowa Co., Tokyo, Japan). Lenses were examined by retroillumination or direct visualization with a slit lamp. Subtle as well as pronounced changes were recorded as cataract. No attempt was made to photograph the cataracts or to classify them according to density or type. The fundi were inspected with an indirect ophthalmoscope (Keeler, Windsor, UK) and a 20-D lens (Nikon Vision Corp., Tokyo, Japan). The presence of one or more drusen and one or more areas of focal atrophy of the retinal pigment epithelium were recorded. The intraocular pressure was measured with a Perkins applanation tonometer (Kowa).

Data Analysis

We prepared scatterplots of the continuous variables (refractive value, corneal power, axial length, vitreous chamber depth, anterior chamber depth, lens thickness) for both eyes. Table 1 lists the ranges of these variables and their means, for females and males, in age groups of 5 to 15 years, 15 to 25 years, and 25 years and older. The table also reports the number of monkeys for which each datum was obtained. The distributions of the variables were examined to determine whether a parametric statistical analysis was appropriate. For each variable, we computed stepwise linear regression models to check for the effect of sex (coded as 0 for female and 1 for male) and for a linear effect of age. We also tested a quadratic, or curvilinear, term for age (age²) in each model. Interocular differences were also calculated for each continuous variable. A similar modeling technique was applied to determine whether these differences vary according to age or sex.

We used multiple linear regression (MLR) to characterize the correlation of the physical eye measures (corneal power, axial length, vitreous chamber depth, anterior chamber depth, and lens thickness) with refractive value, as well as the correlation of age with this collection of measures. We used a stepwise procedure, as implemented in the S-plus statistical programming language to produce the initial linear model. Next, to determine whether chronological age had effects on refraction, not accounted for by physical measurements of the eye, we recomputed the MLR model, adding age as a predictor variable.

For the discrete variables (cataract, drusen, and focal atrophy of retinal pigment epithelium), we examined frequency tables of the variables by age range and sex. We also investigated whether the length of time lived outdoors predicted the occurrence of cataract. To determine whether any such relationship exists independent of age, we calculated a logistic regression in which the presence of cataract (yes/no) was the dependent variable, and the potential independent variables were age and length of time housed outdoors. Stated differently, this analysis allowed us to determine whether any increase in frequency of cataract with increased time outdoors was accounted for by the greater age of animals that had lived outdoors the longest.

RESULTS

The corneas of all the eyes were clear, intraocular pressures were in the normal range, and no abnormalities of the optic nerve head were observed. Some pathologic changes were noted, and their frequencies are reported herein.

Scatterplots (not shown) comparing the left with the right eye for the continuous variables (refractive value, corneal power, axial length, vitreous chamber depth, anterior chamber depth, and lens thickness) revealed very similar patterns in the two eyes, as confirmed by high Pearson’s correlation coefficients (0.92–0.99). Therefore, only the right eyes were considered in all remaining statistical analyses.

Refractive Value

Table 1 lists, for 90 monkeys, the range of refractive values with mean and standard deviation, according to sex and age groups. In the 20 females aged 5 to 15 years, the refractive values ranged from −7.00 to +3.75 D. The mean refractive value was −1.29 ± 2.14 D. In the 20 females aged 15 to 25 years, the values ranged from −11.00 to +5.50 D (mean, +0.39 ± 3.60 D). In the eight females older than 25 years, the values ranged from −1.00 to +11.50 D (mean, +3.14 ± 3.78 D).

In the 24 males aged 5 to 15 years, refractive values ranged from 0.00 to +4.25 D (mean, +1.61 ± 1.15 D). The values in the 12 males aged 15 to 25 years ranged from −8.00 to +2.50 D (mean, −0.77 ± 3.35 D). In the six males older than 25 years, the values ranged from −17.00 to +3.00 D (mean, −2.75 ± 7.42 D).

Figure 1 shows the measurement of refraction for each of the 90 monkeys, and the best-fitting lines for females and males. To determine a range representative of the 5- to 15-year-old monkeys, we plotted dashed lines at 2 SD above and below the mean for this age group, after a single individual with high myopia was removed. The mean of this 5- to 15-year-old group (+1.66 D) was close to the +2.1 D obtained previously in monkeys aged 1.5 to 5 years. The majority (74%) of the monkeys aged 15 years and older fell within 2 SD (SD = 1.04 D) of this mean. In monkeys that deviated from this range, the trend of the dispersion was toward myopia in the older monkeys. This shift may be accounted for, at least in part, by the presence of cataract in most of the monkeys aged more than 20 years.
Atrophy of RPE*  
Drusen*  
Cataracts  

Vitreous chamber depth (mm)  

<table>
<thead>
<tr>
<th>Variable</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>5–15</td>
<td>15–25</td>
</tr>
<tr>
<td>Mean Age (y)</td>
<td>8.5</td>
<td>20.5</td>
</tr>
<tr>
<td>SD</td>
<td>2.93</td>
<td>2.71</td>
</tr>
<tr>
<td>Refractive value (D)</td>
<td>n</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>−7.00–3.75</td>
<td>−11.00–3.50</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.29 ± 2.14</td>
<td>0.39 ± 3.36</td>
</tr>
</tbody>
</table>

**Corneal Power**

Table 1 lists, for 79 monkeys, the range of measurements of corneal power with mean and SD according to sex and age group. For example, in the monkeys aged 5 to 15 years, the measurements for the 18 females ranged from 48.10 to 53.80 D (mean, 51.83 ± 1.65 D) and for the 8 males from 47.75 to 54.40 D (mean, 51.58 ± 2.15 D).

Figure 2 shows the measurement of corneal power for each of the 79 monkeys. The values were widely distributed at all ages. Furthermore, corneal power increased throughout the adult life span of the rhesus monkey. The best-fitting line for these data (described parametrically in Table 2) also demonstrated an upward linear increase of corneal curvature with age, but the sexes did not differ. In other words, the cornea became steeper as monkeys of either sex progressed from young adult to old adult.

**FIGURE 1.** Refractive values of the right eyes of rhesus monkeys as a function of age. The two parallel *horizontal lines* indicate an interval of two standard deviations from the mean refractive value in the 5- to 15-year-old group. Thus indicating the limits of normal refractive value for the adult rhesus monkey. The other two *lines* represent the best-fitting linear estimates of the relationship of this variable with age for females and males.

---

*May have been undercounted in older groups because of presence of cataracts.
†Percentage of total.

---

years. The best-fitting lines illustrate this shift toward myopia and also show a slight difference between females and males.

The model for refractive value as a function of age and sex did not account for a significant proportion of the variance ($R^2 = 0.05; P = 0.10$), and terms for sex, age, and age$^2$ were not statistically significant (Table 2).

---

Ocular Measurements in Adult Monkeys 2375

**TABLE 1.** Measurements of Ocular Components and Characteristics of Rhesus Monkeys

<table>
<thead>
<tr>
<th>Variable</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>5–15</td>
<td>15–25</td>
</tr>
<tr>
<td>Mean Age (y)</td>
<td>8.5</td>
<td>20.5</td>
</tr>
<tr>
<td>SD</td>
<td>2.93</td>
<td>2.71</td>
</tr>
</tbody>
</table>

---

For the adult rhesus monkey. The best-fitting lines illustrate this shift toward myopia and show a slight difference between females and males.

---

The model for refractive value as a function of age and sex did not account for a significant proportion of the variance ($R^2 = 0.05; P = 0.10$), and terms for sex, age, and age$^2$ were not statistically significant (Table 2).

---

**Corneal Power**

Table 1 lists, for 79 monkeys, the range of measurements of corneal power with mean and SD according to sex and age group. For example, in the monkeys aged 5 to 15 years, the measurements for the 18 females ranged from 48.10 to 53.80 D (mean, 51.83 ± 1.65 D) and for the 8 males from 47.75 to 54.40 D (mean, 51.58 ± 2.15 D).

Figure 2 shows the measurement of corneal power for each of the 79 monkeys. The values were widely distributed at all ages. Furthermore, corneal power increased throughout the adult life span of the rhesus monkey. The best-fitting line for these data (described parametrically in Table 2) also demonstrated an upward linear increase of corneal curvature with age, but the sexes did not differ. In other words, the cornea became steeper as monkeys of either sex progressed from young adult to old adult.

---

**FIGURE 1.** Refractive values of the right eyes of rhesus monkeys as a function of age. The two parallel *horizontal lines* indicate an interval of two standard deviations from the mean refractive value in the 5- to 15-year-old group. Thus indicating the limits of normal refractive value for the adult rhesus monkey. The other two *lines* represent the best-fitting linear estimates of the relationship of this variable with age for females and males.
Axial Length

Table 1 lists, for 98 monkeys, the range of measurements of axial length with mean and SD, according to sex and age group. In all 3 age groups, the eyes of females were shorter than those of males. For example, in the 19 females aged 5 to 15 years, the range was 18.3 to 21.5 mm (mean, 19.31 ± 0.84 mm). In the 30 males of the same age group, axial lengths ranged from 18.6 to 22.5 mm (mean, 19.93 ± 0.91 mm).

Figure 3 illustrates the axial length in each of the 98 monkeys. The globe size varied widely at all ages and in both sexes. It is also obvious that axial eye elongation continued, by a small amount, to approximately 20 years of age, when maximum axial length was achieved. Thereafter, axial length gradually shortened. The two lines illustrate the best-fitting curves for the two sexes, demonstrating both the initial increase and the subsequent decline after 20 years, as well as an overall sex difference.

Table 2 presents the magnitude of these effects and the fit of the linear model. The fitted model accounts for a significant proportion of the variance (12%, $P = 0.0080$); furthermore, the average eye length of males was approximately 0.26 (0.2586) mm greater than that of females. The magnitude of the sex-adjusted linear increase with age is approximately 0.15 mm/year, and the curvature of the line describing axial length as a function of age is $-0.0039$ mm/year$^2$.

Vitreous Chamber Depth

Table 1 lists, for 71 monkeys, the range of measurements of vitreous chamber depth with mean and SD, according to sex and age groups. For example, in the 17 females aged 5 to 15 years, vitreous chamber depth ranged from 10.9 to 14.4 mm (mean, 12.22 ± 0.89 mm). In the 16 males of the same age group, vitreous chamber depth ranged from 11.3 to 14.2 mm (mean, 12.24 ± 0.78 mm).

Figure 4 illustrates the measurement of vitreous chamber depth for each of the 71 monkeys. Because there were no significant sex differences in this measure (Table 2), the males and females are represented by a single curve. Vitreous chamber depth varied widely at all ages. It increased until approximately 20 years of age, when maximum depth was achieved; thereafter, the depth gradually decreased. The curvilinear increase and decrease across the life span is very similar to that displayed for axial length in Figure 3, with coefficients for age and age$^2$ being nearly identical with those for axial length. This was expected because vitreous chamber depth is a major component of axial length.

Anterior Chamber Depth

Table 1 lists, for 76 monkeys, the range of measurements of anterior chamber depth with mean and SD, according to sex and age group. There were only small differences between females and males in each age group. For example,
in monkeys aged 5 to 15 years, the range in the 18 females was from 3.30 to 3.90 mm (mean, 3.64 ± 0.18 mm) and in the 16 males was from 3.40 to 4.10 mm (mean, 3.71 ± 0.24 mm).

Figure 5 shows the anterior chamber measurement in each of the 76 monkeys. The best-fitting curves for the two sexes are identical and are, therefore, indicated by a single line. The values were widely scattered for both sexes at all ages; however, they clearly declined from the youngest to the oldest monkeys in both sexes, resulting in a shallower anterior chamber. Table 2 confirms that the anterior chamber measurements were the same for males and females and documents a significant decline with age.

**Lens Thickness**

Table 1 lists, for 76 monkeys, the range of measurements of lens thickness with mean and SD, according to sex and age groups. In all age groups, males had slightly thicker lenses than females. For example, in monkeys aged 5 to 15 years, thickness in the 18 females ranged from 3.00 to 4.20 mm (mean, 3.73 ± 0.36 mm) and in the 16 males from 3.20 to 4.40 mm (mean, 3.89 ± 0.35 mm).

Figure 6 shows the measurement of lens thickness for each of the 76 monkeys. The thicknesses varied in both sexes at all ages. Also, it increased throughout the adult life span of the rhesus monkeys. The best-fitting lines for these data (described parametrically in Table 2) demonstrated a curvilinear increase of lens thickness with age. Overall, the lenses of males were 0.1017 mm thicker than those of females ($P = 0.0329$). The magnitude of the upward curvature of the best-fitting line describing lens thickness was +0.0006 mm/year$^2$, an amount that is statistically significant ($P < 0.0027$).

**Pathologic Changes**

In the process of obtaining the ocular measurements described, we opportunistically scored the presence or absence of cataract, drusen, and focal atrophy of the retinal pigment epithelium. We recorded the presence or absence of disease; we did not grade them formally. The most prevalent pathologic condition was cataract. Its presence or absence is recorded in Table 1. Among the 19 females aged 5 to 15 years, only a single individual (7 years old) displayed a cataract. Likewise, among the 32 males of the same age group, only a single 13-year-old monkey had a cataract. The prevalence of cataract increased with age, from 5% in females and 3% in males aged 5 to 15 years, to 14% in females and 7% in males aged 15 to 25 years, and finally to 22% in females and 13% in males older than 25 years.

Logistic regression analysis indicated that increasing age was significantly associated with a higher probability of cataracts ($P = 0.01$). The length of time spent outdoors correlated highly with age ($r = 0.99$), reflecting the fact that the older monkeys had spent more of their lifetimes outdoors. Because of this high correlation, time spent outdoors did not improve the predictive power of the logistic model—that is, time spent outdoors was not an independent predictor of the likelihood of cataracts.

Another pathologic sign was the presence of drusen, which we recorded as present or absent (Table 1). Most drusen identified were located in the macula and perimacular region. Although we used the method of indirect ophthalmoscopy, we concentrated the examination on the posterior pole. The prevalence of drusen increased with age, from 5% in females and 3% in males aged 5 to 15 years, to 14% in females and 7% in males aged 15 to 25 years, and finally to 22% in females and 13% in males older than 25 years.
years. The drusen may have been undercounted in older monkeys, where more advanced cataracts may have prevented their detection. Nevertheless, the age-related increase of drusen was statistically significant.

The third pathologic condition recorded was focal atrophy of the retinal pigment epithelium (Table 1). This defect was observed mostly in or around the macula. There was no significant age-related increase in the prevalence of retinal pigment epithelium defect in either sex. However, this defect may have been undercounted in older monkeys with more advanced cataracts, due to the difficulty in clearly visualizing the fundus.

Finally, a few monkeys aged 12 years and older had pathologic refraction. The most extreme cases were a 26-year-old female that had +11.50 D of hyperopia and a 28-year-old male that had −17.00 D of myopia. The axial lengths and vitreous chamber depths of these monkeys were also the most extreme observed. The hyperopic female had the shortest eye (Fig. 2; 16.5 mm axial length), whereas the myopic male had the longest eye (23.8 mm axial length). In the hyperopic female, vitreous chamber depth was 9.0 mm and that of the myopic male was 15.7 mm.

Multivariable Analysis

We analyzed how individual parameters were related to one another across the adult life span in the 64 monkeys for which all measures were available. Table 3 shows the intercorrelation matrix of the ocular measurements and the age at the time of the eye examination. A strong pattern of intercorrelations among the variables is present. For example, there is a very high correlation \( r = 0.91 \) between axial length and vitreous chamber depth. An MLR model, such as the one presented in Table 4, descriptively summarizes the strong pattern of relationships among the variables. Three variables (corneal power, vitreous chamber depth, and lens thickness) account for 76% of the variance in refractive value, as indicated by the multiple \( R^2 \). Each of these variables accounted for a significant proportion of the variance in refractive value. Addition of axial length or anterior chamber depth to this model did not significantly improve its predictive ability. The addition of age to the model in Table 4 increased the percentage of variance accounted for only slightly (to 80%). All the individual coefficients in this augmented model (not shown) were highly significant. This indicates that age has an effect on refraction beyond that accounted for by age-induced changes in the other eye measures.

TABLE 4. Multiple Linear Regression that Best Accounts for Refractive Value in Terms of Other Eye Measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>SE</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>88.1219</td>
<td>8.791</td>
<td>10.0241</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vitreous chamber depth</td>
<td>−5.2789</td>
<td>0.2411</td>
<td>−15.6012</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lens thickness</td>
<td>−3.4899</td>
<td>0.5542</td>
<td>−6.4571</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Corneal power</td>
<td>−0.6560</td>
<td>0.1241</td>
<td>−4.0716</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multiple ( R^2 )</td>
<td>0.76</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values in bold are greater than 0.37 or less than −0.37 and are significant at \( P < 0.05 \), after correction for multiple tests.

DISCUSSION

In this report, we describe the refraction in the eyes of 111 adult rhesus monkeys. None of these monkeys had ever been subjected to any ocular manipulation. We also report measurements of the individual ocular components and their interrelationships from young adulthood through senescence and identify pathologic changes associated with aging in this group of monkeys. These cross-sectional results establish norms for this species and provide a solid basis for future studies to evaluate the ocular changes resulting from environmental and experimental manipulations.

FIGURE 7. Residuals of estimation of refractive value as a function of age. Residuals are the deviations of each monkey's actual refractive value from that predicted by the MLR model in Table 4. The line represents the best-fitting linear estimate of the relationship of this variable with age; because the measurements did not differ between the sexes, only one line is shown.
One goal of the study was to determine whether the aging monkey eye could serve as a model for the aging human eye. A comparison of the human and monkey literature, including the present report, shows that both species display increased dispersion of refractive values with age, including an increase in the number of extreme myopes and hyperopes. Nevertheless, the average refractive value remains remarkably stable in both species. In addition, both humans and monkeys exhibit a decrease in axial length and in vitreous chamber depth in the second half of the adult life span. In both species, there is also a reduction in anterior chamber depth, an increase in lens thickness, and a steepening of the cornea. The pathologic ocular changes reported herein are also similar to those in humans. These include age-related development of cataract, of drusen, and of focal atrophy of the retinal pigment epithelium. Thus, individual ocular components undergo similar changes during the life span of both species, firmly establishing that the eyes of aging and old monkeys are useful as a model for the aging process of human eyes.

An additional goal of this study was to determine whether the average hyperopia of approximately +2.0 D, typically observed in juvenile and young adult monkeys up to 5 years of age, declines as a function of age. With the exception of some outliers, the monkeys retained refractive values in this species-typical range. This prevalence of hyperopia may be the result of an adaptation to visual requirements as the species evolved and could represent an example of functional emmetropia.

The decrease in axial length and the steepening of the cornea are suggestive of an overall reduction in the size of the aging eye. The changes in lens thickness and anterior chamber depth are in opposite directions: the lens grows thicker, whereas the anterior chamber becomes shallower. The coordination during aging of these two opposing changes can be seen by comparing Figures 5 and 6. This close temporal relationship strongly suggests that the decrease in anterior chamber depth is due to the increase in lens thickness. As in humans, lens power in monkeys may also increase with lens thickening during aging, but our methods did not address this question.

In view of the marked alterations in the multiple structures that determine refraction, the question arises as to how so many of the aging monkey eyes retain a stable refractive value, as indicated by the absence of a significant bivariate correlation between age and refractive value. A MLR model underscored the relative stability of refraction in all age groups. This model accounted for 76% of the variance in refraction in terms of only three variables exclusive of age: corneal power, vitreous chamber depth, and lens thickness. Age was, however, a significant predictor of the deviation, or residuals, of refraction from the value predicted by this model, which suggests that the increased dispersion of refractive values with age may result from an age-related decrease in the eye's ability to control refraction by means of the physical properties of corneal power, vitreous chamber depth, and lens thickness.

Our data establish that the observed overall stability in refraction is the result of the coordination of changes in several ocular elements during aging. We have reported previously that postnatal developmental changes in individual ocular components are also coordinated. During the most rapid phase of postnatal development in neonatal hyperopia, for example, there is very strong correlations between the measurements of refraction, axial length, and corneal power. Once refractive value achieves asymptote at 1.5 years of age, however, there is a shift in the strength of the relationship between these three components. Refractive values remain stable through adolescence, despite axial elongation and corneal flattening that continue until adulthood. Thus, the stability of refractive values throughout adolescence and young adulthood appears to be coordinated by the changes in the axial length and corneal power of the eye. Our data from adult monkeys confirm that there is a close linkage of several ocular elements. Although an increase in corneal and lens power and a decrease in anterior chamber depth would lead the eye toward less hyperopia or more myopia, a decrease in axial length of the eye would have the opposite effect. It appears, therefore, that a coordination operates both during emmetropization and ocular aging in the rhesus monkey. Although this coordination appears to be an active process serving to maintain refractive value near the normal range, general age-related phenomena (such as shrinkage of connective tissue or hardening of the sclera) may also play a role. In addition, the present data also suggest that this coordination may be vulnerable to the effects of aging, as seen by the increased dispersion in refraction as a function of age, including cases of extreme hyperopia and myopia.

Based on their work in humans, Ooi and Grosvenor have proposed the term “adult emmetropization” to describe the coordination of changes in ocular elements that occur during aging. They noted, however, that the coordinating mechanism operating in the mature eye is unlikely to be identical with the mechanism that operates in the developing eye. Because emmetropization is an established term associated with the postnatal development of the eye, we propose the term “adult ocular compensation” to define these changes in the adult eye. Understanding the mechanism that underlies this process in a monkey model may lead to the identification of possible modes of clinical intervention to preserve optimal vision in aging humans.

The apparent existence of an adult ocular compensation raises the question of whether visual experience may influence its course. Because such experience can determine or alter the course of emmetropization in young animals (for extensive review, see Refs. 21, 49), and possibly humans, visual experience is a potential modifer of adult ocular compensation as well. Thus, modulation of the visual environment holds potential as a treatment for some forms of geriatric visual impairment.

Acknowledgments

The authors thank the veterinary staff of the Yerkes National Primate Research Center of Emory University for expert assistance during the ophthalmic examinations and the animal care staff for animal husbandry and Jean Torbit, Sarah Hix, and Rita Thomas for assistance in the maintenance of the monkey eye database.

References


