Accommodation Demand and Deprivation in Kitten Ocular Development

Phillip Hendrickson* and William Rosenblum†

The effects of accommodation demand and deprivation on the development of ocular optics was investigated in four groups of kittens (total n = 29). Group 1 consisted of five normal kittens; group 2 (nine kittens) had monocular radial keratotomy to induce relative hypermetropia and more accommodation demand as well as to impart interoculär refractive differences (anisometropia); group 3 (eight kittens) received daily monocular atropine; and group 4 (seven kittens) had binocular radial keratotomy combined with daily monocular atropine. Regular examination provided documentation of ocular development from the first through the sixth months of life. Subsequently, the focal lengths of the crystalline lenses were determined in vitro. An apparent tendency for kitten eye pairs to grow toward isometropia, even when anisometropia had been induced early in life, was seen in those eyes in which the accommodative mechanism had been left intact (groups 1 and 2), but without accommodation anisometropia resulted (groups 3 and 4). There was relatively more elongation of the globe (3.08 ± 0.22%) as well as shorter than normal focal lengths of the crystalline lens (−4.91 ± 1.62% anterior, −2.78 ± 1.54% posterior) in the eyes of the second group, and the eye pairs regained isometropia. In those eyes of the third and fourth groups that received atropine daily, there was relatively less elongation of the globe (−3.09 ± 0.59% and −3.22 ± 0.67%, respectively) and shorter crystalline lens focal lengths (−3.50 ± 1.18% and −4.62 ± 1.07% anterior, −2.64 ± 1.02% and −1.59 ± 0.62% posterior, respectively). Response of the eye to excess accommodation demand (group 2) as well as increased demand with deprivation (groups 3 and 4) was thus seen to be manifested not only in axial length differences but also in alteration of the focal lengths of the crystalline lens, and it is demonstrated that these two elements contribute significantly to normal ocular development toward isometropia. Invest Ophthalmol Vis Sci 26:343-349, 1985

Within a normal population there is a strong representation of emmetropic individuals, with the ametropic remainder disproportionately biased toward myopia. Socio-economic factors1 were long overlooked in favor of genetic ones.2-4

In 1969 Young5 examined the influence of mandatory schooling following attainment of statehood in Alaska and reported a relatively high rate of myopia in Eskimo schoolchildren, although their illiterate parents and grandparents were, moreover, emmetropic or even hypermetropic. On the other hand, Steiger6 studied the distribution of individual ocular optical components within a normal population (5,000 eyes) and suggested that the chance combination of randomly distributed optical elements leads to a relatively normal distribution of normally sighted individuals.

Chance occurrence, genetic predetermination, or environmental influence: which actually leads to myopia? The suggestion that accommodation extent plays a role7-9 was taken into consideration when the present experimental model was being developed. In an attempt to elicit increased accommodation demand, the refractive power of the cornea was reduced by means of radial keratotomy, leaving the accommodative system intact. In other kittens, the accommodative mechanism was eliminated by atropinization, and, in yet further kittens, these two perturbations were combined.

Materials and Methods

Since accommodation was to be the essential experimental feature of this investigation, the model had to incorporate an animal that is not only highly visual but also one that has an accommodative range similar to that of humans.10 Furthermore, the animal had to be one that can be bred easily and economically in colony, and, with these factors in mind, the developing, mixed-breed kitten was chosen. The treatment and handling of all animals included in

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this investigation conform to the ARVO Resolution on the Use of Animals in Research.

Kittens develop cortical organization by the end of the first postnatal month, and adult-like visual acuity and function have been reported to exist by the sixth month of life, at which time the axial length of the globe has reached adult-like proportions. Therefore, the experimental influence was exerted from the first through the sixth months of life of the kittens in this present investigation (n = 29). There were five normal controls.

Radial Keratotomy

Other investigators have attempted to induce myopia by means of high minus lenses, restrictive environment, lid-suturing, as well as opacification. For example, it is popularly assumed that myopia via lid suture occurs according to the following process: lid suture causes accommodation; accommodation causes increased intraocular pressure; intraocular pressure causes scleral stretch; and then, scleral stretch causes myopia. This of course is a sequence of a great many “ifs.” Interestingly, lid-sutured macaque monkey eyes do not always lengthen but sometimes shorten or show no change at all.

We chose to impart only a mild refractive error by means of moderate perturbation in one eye in order to render the experimental model as close to clinically occurring conditions as possible. To avoid the difficulties inherent in fitting and maintaining appropriate contact lenses in small animals, the relatively simple technique of radial keratotomy was selected. In each cornea to be so treated (nine kittens, monocular), between 16 and 20 incisions through about 50% of the corneal thickness were made radiating from the corneal cap (2.5-mm diameter) to 1 mm from the limbus, resulting in a uniform reduction of refractive power of the cornea of up to 3 D. Had the incisions been made deeper, more power could have been eliminated from the cornea, but a mild effect was desired. At the time of treatment the ages of the nine kittens were 32, 32, 30, 30, 28, 28, 28, 19, and 19 days, respectively (mean = 27.3 days). Postoperative Neosporin ointment in the operated eyes precluded keratometry for at least a week.

Those kittens in which the extent of anisometropia imparted by monocular radial keratotomy fell markedly below an arbitrarily defined criterion of 1.5 D had repeat surgery.

Atropinization

It has been proposed that the mechanical stresses involved in accommodation (coronally inward) are conducive to secondary stress generation (longitudinally outward) and elongation of the ocular globe. Excessive accommodation should lead to excessive stresses and, thus, to excessive elongation (myopia). Coleman suggested that accommodation causes an increase in pressure in the vitreous chamber and, therefore, an increase in stress on the chamber itself. Estimation of these stresses has shown them to be small, but their significance is yet undetermined. However, Young measured the vitreous pressure increase in monkeys to be fully 7 mmHg during accommodation, and Coleman found vitreous pressure increases of 2–4 mmHg in one human volunteer in spite of cycloplegia (directly measured prior to enucleation). An additional role played by stresses exerted by the extraocular muscles during convergence also has been considered, and it is entirely possible that both mechanisms combine to cause elongation. It should follow that the elimination of the accommodative mechanism would lead to less than normal elongation. The engineering concepts of stress and strain related to accommodation and ocular growth have been considered further by Barraquer and Friedman.

If radial keratotomy causes excessive accommodation and elongation, the elimination of accommodation in eyes having had radial keratotomy should prevent such excessive growth, as success in bifocal and atropine control of developing clinical myopia (optical or pharmacologic reduction of accommodation) implies.

Table 1. Comparative mean terminal data for all groups (axial lengths and focal lengths)

<table>
<thead>
<tr>
<th>Group</th>
<th>Type</th>
<th>Final diff* in retina</th>
<th>% Diff. (dAL)</th>
<th>Axial length</th>
<th>Anterior focal length</th>
<th>Posterior focal length</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>N</td>
<td>0.02 ± 0.05</td>
<td>0.08 ± 0.07</td>
<td>0.45 ± 0.30</td>
<td>0.06 ± 0.05</td>
<td>0.44 ± 0.36</td>
</tr>
<tr>
<td>2</td>
<td>RK</td>
<td>0.12 ± 0.08</td>
<td>0.62 ± 0.05</td>
<td>3.08 ± 0.22</td>
<td>-0.67 ± 0.21</td>
<td>-4.91 ± 1.62</td>
</tr>
<tr>
<td>3</td>
<td>AT</td>
<td>1.94 ± 0.94</td>
<td>-0.64 ± 0.11</td>
<td>-3.09 ± 0.59</td>
<td>-0.47 ± 0.16</td>
<td>-3.50 ± 1.18</td>
</tr>
<tr>
<td>4</td>
<td>RK + AT</td>
<td>1.50 ± 0.54</td>
<td>-0.66 ± 0.13</td>
<td>-3.22 ± 0.67</td>
<td>-0.62 ± 0.14</td>
<td>-4.62 ± 1.07</td>
</tr>
</tbody>
</table>

* Diff = difference.

Lengths in millimeters; retinoscopic values in diopters; means ± SD. For normals (N): difference = greater — lesser. For treated animals: difference = treated eye — untreated eye.
Beginning on about the thirtieth day of life and continuing every day thereafter, one drop of 1% atropine was instilled into one eye of each kitten in groups 3 (eight kittens) and 4 (seven kittens). In the case of the latter group, in which radial keratotomy was performed first, atropinization began on the third postoperative day and continued through the sixth month of life.

**In Vivo Ocular Examination**

Examination of all kitten eyes was made prior to treatment onset and thereafter on a regular weekly or biweekly basis. When necessitated by extremely high corneal powers in 1–2-month-old kittens, supplementary lenses of 1.25 or 2.25 D were employed on the keratometer with appropriate correction. During this and the other ocular examinations, the kittens were anesthetized with Ketamine HCl (0.2 mg/kg). The refractive state of the two eyes was determined by means of retinoscopy.

Axial lengths as well as the axial extents of the individual ocular components were determined by means of A-scan ultrasonography (10 MHz focused transducer). Propagation velocities for ultrasound in cornea, aqueous, lens, and vitreous in the kitten (1.639, 1.486, 1.585, and 1.534 mm/μsec, respectively) were determined using in vitro samples of known linear dimensions (measure “t”; v = d/t). These values were used to calculate individual in vivo ocular
component dimensions, the total of which was regarded to be the axial length of a particular eye. From five measurements made on each eye at each examination session, the longest was accepted as most closely representing the actual axial dimension.

In Vitro Ocular Examination

Following the sixth month and the last in vivo ocular measurements, each kitten was killed, and the eyes were enucleated and prepared for focal length determination of the crystalline lenses. Here, the anterior and posterior ends are removed, leaving the lens suspended within its capsule and the central coronal section (as in vivo). Described in detail elsewhere,\textsuperscript{34} this interferogrammetric technique permits maintenance of the lens to be examined in a saline solution through which the optical pathway passes. Repeated measurements demonstrated a precision of about 1/10 mm. Focal lengths were measured to both the anterior and posterior vertices of the lens.

Results

Comparative mean terminal data for all four groups of kittens is given in Table 1. From each group a typical animal has been chosen to demonstrate axial growth, development of corneal power, and the re-axial length difference (dAL for normals = greater — lesser; dAL for treated animals = treated eye — untreated eye or RK + AT — RK); All lengths in millimeters.

<table>
<thead>
<tr>
<th>Group</th>
<th>Type</th>
<th>Eye</th>
<th>Cornea</th>
<th>Aqueous</th>
<th>Lens</th>
<th>Vitreous</th>
<th>Axial length</th>
<th>dAL §</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 N</td>
<td>OD*</td>
<td>0.90 ± 0.06</td>
<td>3.45 ± 0.14</td>
<td>6.72 ± 0.23</td>
<td>8.27 ± 0.21</td>
<td>19.34 ± 0.41</td>
<td>0.07 ± 0.04</td>
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</tr>
<tr>
<td></td>
<td>OS†</td>
<td>0.90 ± 0.08</td>
<td>3.44 ± 0.17</td>
<td>6.72 ± 0.15</td>
<td>8.28 ± 0.22</td>
<td>19.33 ± 0.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 RK</td>
<td>RK</td>
<td>0.92 ± 0.03</td>
<td>3.67 ± 0.28</td>
<td>6.75 ± 0.21</td>
<td>8.56 ± 0.37</td>
<td>19.90 ± 0.63</td>
<td>0.56 ± 0.10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>UE‡</td>
<td>0.92 ± 0.03</td>
<td>3.59 ± 0.26</td>
<td>6.79 ± 0.14</td>
<td>8.04 ± 0.29</td>
<td>19.34 ± 0.46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 AT</td>
<td>AT</td>
<td>0.92 ± 0.03</td>
<td>3.70 ± 0.19</td>
<td>6.63 ± 0.20</td>
<td>8.00 ± 0.20</td>
<td>19.25 ± 0.38</td>
<td>0.59 ± 0.12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>UE</td>
<td>0.92 ± 0.03</td>
<td>3.78 ± 0.19</td>
<td>6.69 ± 0.15</td>
<td>8.44 ± 0.23</td>
<td>19.84 ± 0.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 RK + AT</td>
<td>RK + AT</td>
<td>0.93 ± 0.04</td>
<td>3.59 ± 0.13</td>
<td>6.59 ± 0.20</td>
<td>7.93 ± 0.33</td>
<td>19.04 ± 0.44</td>
<td>0.58 ± 0.17</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RK</td>
<td>0.93 ± 0.04</td>
<td>3.76 ± 0.19</td>
<td>6.61 ± 0.17</td>
<td>8.31 ± 0.27</td>
<td>19.62 ± 0.26</td>
<td></td>
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</table>

Discussion

Axial Length and Crystalline Lens

Focal Length Development

In normal developing kittens the ocular axial length at 1 month of life is about 13 mm, extending to about 20–22 mm by the sixth month. Interocular differences in axial length are only slight (about 1/10 mm) if present at all. In all three treatment groups the interocular growth differences in axial length and crystalline lens focal length were obvious when compared with those seen in the normal group (Table 1).

Essentially two types of refractive deficiency were imparted to the treated eyes. The first, imparted to the nine radial keratotomy kittens (group 2), consisted solely of reduced corneal power, while the accommodative mechanism was left undisturbed. Accommodation then could provide an immediate and almost constant correction of the resulting hypermetropia. The fact that all kittens subjected to monocular radial keratotomy exhibited large interocular differences in axial length provides strong support for the suggestion that excessive demand upon accommodation may lead to an increased axial length (group 2 mean interocular difference = 0.62 ± 0.25 mm). Monocular relative hypermetropia of, for example, 3 D in an eye of approximately 20-mm axial length should be only partially corrected by an axial length excess of about 6/10 mm (equivalent to approximately 2 D), but these eye pairs were seen to have regained isometropia during the growth period (group mean terminal extent of anisometropia = ½ D). The remainder of the adjustment might be found in the differences in crystalline lens focal lengths in the treated and untreated eyes of this group (Table 1). The lenses of these eyes were seen to have developed a shorter focal length, which would be the appropriate compensation.\textsuperscript{35} A possible contralateral response to monocular perturbation is considered below in the section, "Axial Component Composition."

The second type of refractive deficiency imparted
Fig. 2. Group mean ocular component composition of values gained by interpolation: C = cornea; A = aqueous; L = lens; V = vitreous; MSD = monocular axial length standard deviation; and CSD = component SD. The range of kitten weights interpolated for day 175 = 962-2,860.

(group 3) was that achieved by means of atropinization, eliminating accommodation. Absence of the accommodative mechanism in the kittens treated with atropine would go unnoticed if they had only to view distant objects at six meters or more. However, in the case of a kitten growing up in a birthing box approximately \( \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \) m, then with its mother and siblings in a cage approximately \( 1 \times \frac{1}{2} \times \frac{1}{2} \) m, and finally in a group colony approximately \( \frac{1}{2} \times 2 \times 3 \) m with other kittens of various ages and freedom of interaction, such loss of the ability to add power for near objects (accommodation deprivation) may be considered a refractive defect. Atropine treatment also dilates the pupil and, thereby, reduces depth of field, thus increasing the need for exact dioptric adjustment to focus on near objects of regard and enhancing the deprivation effect.

The kittens of group 3, following long-term monocular atropinization, showed less axial length development in those eyes receiving atropine than in the untreated fellow eyes, a finding interestingly similar to the clinical control of developing myopia (atropine reduces accommodation, less myopia develops). The same was seen in the kittens in group 4 (binocular radial keratotomy with monocular atropine) but to a slightly greater extent. Relative lengthening of the radial keratotomy-treated eye (with no atropine) and relative shortening of the atropine- and radial keratotomy-treated fellow eye could have led to this slightly greater interocular axial length difference.
Anisometropia imparted in the kittens of groups 3 and 4 (Table 1, Figures 1C, D) was not relieved during the course of development studied. Crystalline lens focal length differences in these eyes were approximately the same as those of the radial keratotomy group. In all three treated groups, the interocular differences were greater for the anterior focal length, especially in the fourth group in which the ratio of differences anterior to posterior was almost 3:1 (Table 1). This finding would seem reasonable since it is in the anterior surface curvature that most of the changes of the crystalline lens occur during accommodation.\(^7\)

These in vitro focal length measurements demonstrate only relative differences and do not necessarily represent actual in vivo values at any particular accommodative state. As such they cannot be used directly to model the kitten eye.

**Axial Component Composition**

Seen in Table 2 and in Figure 2, the linearly interpolated 175-day axial component lengths are similar to those of the terminal measurements at various ages (Table 1), the mean values for the former being only slightly less than those of the latter.

Normalization of growth data for one particular age permits two further considerations:

1. The ocular component compositions in Figure 2 indicate that the strongest contribution to induced interocular axial length differences in all groups in this investigation is made by differences in vitreous depth, the other dimensions being consistently similar in extent. This conforms to the increased vitreous chamber pressure aspect of Coleman's model.\(^7\)

2. In monocularly treated kittens, eyes receiving no treatment have been referred to as "untreated" since they no longer existed in an absolutely normal environment, consisting of two untreated, normally developing fellow eyes, which become isometropic and attain binocularity. Furthermore, the untreated eye in a monocularly atropine-treated kitten may not be isolated completely from systemic communication with the drug.

**Percent Ocular Component Growth**

For organizational reasons, uniformity of initial (31 ± 6 days) and terminal (199 ± 29 days) examination ages could not be maintained, but normalizing the data by linear interpolation to an initial age of 35 days and a terminal age of 184 days can provide a general insight into the percent component growth extents of all kitten eyes in this study.

In all groups (29 kittens), percent ocular component growth from 35 to 184 days was moreover uniform in extent except for that of the depth of the anterior chamber. Whereas the corneal thickness, lens thickness and the depth of the vitreous increased only 29 ± 11%, 30 ± 9%, and 20 ± 7%, respectively, the increase in the anterior chamber depth had a mean value of 183 ± 53%.

Since anterior chamber depth is thus by far the site of greatest percentage growth during the first 6 months of kitten ocular development, its growth, providing separation of the refractive elements of the eye, might be considered to be one possible means by which the total refractive power of the eye is adjusted during development.\(^38\) Recalling our own finding that only the developing vitreous depth contributes significantly to interocular axial length differences that occur following induced anisometropia, we even might suggest further that coarse developmental adjustment of the optics of the eye occurs in the anterior chamber depth while fine adjustment takes place in the depth of the vitreous.

The findings of this investigation are consistent with the idea\(^9\) that ocular growth may be a self-regulating process guided by visual experience and dependent upon intact accommodative function.

**Key words:** accommodation, anisometropia, deprivation, development of kitten ocular optics, radial keratotomy

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**References**