Review Article

Ocular Shape and Myopia†

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Abstract

Introduction: To learn if eye shape might be a useful parameter in refractive research. Materials and Methods: Laboratory research on eye growth mechanisms is summarised. The available clinical literature relating refraction to eye shape and peripheral refraction is critically assessed in the context of the laboratory research on refractive development. Results: Almost all refraction research assesses optical and length parameters exclusively along the visual axis. Contemporary laboratory research demonstrates a remarkable phylogenic conservation of the neural mechanisms regulating refractive development. On-axis image quality regulates central refractive development in animals and probably, to some extent, in humans. Off-axis image quality at the retina depends on anterior segment geometry and optics, and on the 3-dimensional conformation of the retina. In chicks, eye shape is a predictable parameter linked to the underlying neural mechanisms modulating eye development. Based on the sparse clinical literature in human adults and children, the eye shapes induced in chicks are also seen in human subjects in patterns suggesting that eye shape may be a useful parameter in clinical studies. Conclusion: The diverse findings suggest that incorporating the 3-dimensional conformation of the eye into future clinical studies may help resolve many of the ambiguities in contemporary refractive research.

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Key words: Eye growth, Eye shape, Hyperopia, Myopia, Peripheral refraction, Refractive errors

Introduction

Myopia develops from a mismatch of the eye's anatomical axial length and its focal length, as determined by the combined optical powers of the cornea and lens. For higher degrees of myopia and myopic progression, this mismatch develops primarily as a consequence of disproportionate ocular growth, chiefly of the vitreous chamber.[1] It is not known why myopia develops or why its prevalence is increasing.[2-7] The literature on myopia pathogenesis tends to revolve around long-held, hypothesised classical risk factors.[1,8] Unfortunately, the research addressing these classical risk factors has so far failed to provide the biological insights needed to introduce effective measures to prevent myopia onset or to significantly retard its progression.[9] The reasons for these disappointments are not clear. As commonly hypothesised, myopia may comprise a "multifactorial" disorder, caused by environmental and/or genetic mechanisms. Yet, our knowledge is quite fragmentary about how these multiple factors act singly or together to induce myopia. Perhaps, as implied in many contemporary reports, improved methodology for assessing these risk factors or identification of an essential, yet presently unrecognised, risk factor is needed for the conceptual breakthrough. Alternatively, the ambiguities about myopia pathogenesis might be explainable by confounding factors, unknowingly introduced by combining subjects from subgroups of distinct but non-interacting, or only partly interacting, aetiologic mechanisms. For instance, many clinical studies have seemingly implicated visual near work in myopia pathogenesis, but it still remains unclear whether near work comprises an independent risk factor or is confounded by other parameters such as socioeconomic status or education.[10]

Conceptualising the Eye in 3-Dimensional Terms

Almost all refractive research assesses ocular parameters

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exclusively along the visual axis, specifically on-axis refraction, central corneal curvature and the components from A-scan ultrasound. This emphasis is understandable given the impact of axial parameters on refractive error and the functional success of correcting refractive errors along the optical axis of the eye. The patterns of eye development in laboratory animals and a longstanding, but largely overlooked, clinical literature suggest that conceptualising the eye exclusively in the axial dimension may be an oversimplification, at least for understanding aetiologic mechanisms of myopia. Many categorisations of myopia have been proposed under the widely held and clinically justified hypothesis that myopia comprises a group of disorders,[1,11] but none have included 3-dimensional shape of the eye as a biologic parameter. Hence, we pose the questions: is eye shape a regulated variable, intrinsically coupled to the mechanisms modulating refractive development, and could stratifying eyes by shape provide a basis for an improved mechanistic understanding of the pathophysiology of ametropias in human populations?

Visual Image Quality and Refractive Development

Findings in monkey and chick demonstrated that postnatal eye growth and refractive development depend largely on the quality of visual input to the eye.[12,13] Depriving the retina of a clear visual image through such means as an eyelid suture or an image diffusing goggle induces ipsilateral myopia in many species, so-called form deprivation myopia.[14-25] Stimulated by the findings in experimental animals, the same phenomenon subsequently was observed in children with disorders such as ptosis or corneal opacities that obscure the visual input.[26-37] In chicks, tree shrews, marmosets and other monkeys,[38-41] the wearing of either concave or convex spectacle lenses to induce image defocus causes adjustments in eye growth to maintain the retina in a position conjugate with the image. The eyes of chicks or tree shrews beneath goggles that obscured only part of the visual field grew asymmetrically, with greatest scleral beneath retinal regions receiving a blurred image.[42-45] These findings suggest a local influence on scleral growth by the image quality of the subjacent retina region. Along with the impaired emmetropisation seen in many childhood visual disorders,[46] these observations have led to the widely accepted view that vision-dependent feedback mechanisms modulate eye growth, and that image blur influences refractive development.[47,48] Reviewed elsewhere, the vision-dependent mechanism that regulates eye growth localises largely to the retina itself.[43,45,48,49]

Refractive Development: Phylogenetic Conservation

Due to rapid eye growth, excellent optics and good central visual acuity, much research in refractive development is conducted in chick, and many laboratory groups have contributed to the identification of visual and neural mechanisms that regulate refractive development in this species. So far, the major visual and neural mechanisms reported to act in chick have been identified in identical or in modified form in mammals (including monkeys) and, when practical, in man (Table 1). Besides specific details, the length of this list demonstrates the remarkable phylogenetic conservation of mechanisms that control refractive development. Whether all future findings in chick will be extendable to mammals is not known, but the results of refractive research in chicks must be considered as plausible hypotheses for future investigation in mammals and humans.

Table 1. Refractive Development: Some Parallels between Chicks and Mammals

Precise emmetropization[1,22,50-52]
Vitreous chamber enlargement in myopia[1,14,22,53,54]
Form deprivation myopia: juvenile and adolescent ages[55-57]
Vision mediated changes in choroidal thickness[55,58-60]
Recovery from experimentally induced refractive errors[39,40,45,53]
Eye growth response to lens-induced defocus[38-41,45]
Asymmetric vitreous chamber growth following partial goggle wear[42-45]
Diurnal fluctuations in intraocular dimensions[61-64]
Light: dark cycle effects on eye growth[65-69]
Retinal regulatory site[14,47,49]
Pharmacologic influences on myopia: dopaminergic and muscarinic[9,14,70-76]

Human Refractive Development

The insight that normal refractive development is regulated by image quality has diminished the likelihood that accommodation comprises a primary mechanism for the cause of myopia.[48,49,77] It has also led to the hypothesis that visual blur might provide a mechanism for clinical myopia (the so-called "blur" hypothesis). The blur hypothesis has stimulated new investigations of optical corrections to retard myopia progression. Bifocal and varifocal lens treatments, at least with the protocols adapted to date, have revealed either no reduction of myopia progression or a statistically significant reduction that is too small in magnitude for clinical import.[78-81] While not providing clinical treatments, the limited effects in some studies substantiate the hypothesis that visual input may modulate refractive development in humans.

The Geometry and Image-Forming Properties of the Eye

The anterior segment and vitreous chamber geometry each impact on the image-forming properties of the eye. Although the gradient index properties of the lens affect the eye's optics to some degree, the image projected onto the retina is largely dictated by the 4 principal refracting surfaces (anterior and posterior surfaces of the cornea and lens) and the distance between these 2 refracting components (the anterior chamber depth). The geometric features of the supportive choroid and sclera determine the retina's position and curvature, that is, the "image plane" for the eye's optics. The optical properties of vertebrate eyes are well-studied in relation to paraxial or on-axis imaging, and spherical surface schematic eye models provide a good fit with experimental data. Off-axis imaging is less comprehensively studied and is more dependent on the asphericity of the ocular surfaces in determining optical performance.[82,83]

Retinal Image Quality and Image Processing

The overall quality of the retinal image depends on the optical properties of the anterior segment and the relative alignment of the retina with the optical image. Due to interactions of the retinal contour with off-axis astigmatism, spherical and other aberrations, and the reduction of aberrations by corneal and lenticular asphericity, the off-axis focal length and other off-axis image properties of the eye differ from those in the axial and paraxial regions.[84] Because of the potential importance of local image quality across the retina in eye development,[43-45] the designation of axial refractive properties alone is likely insufficient to describe the image quality in off-axis regions.

Eye Growth Control and Growth Patterns

The final component of optical regulation of eye growth is the interaction between the retina, now thought to guide the process, and the sclera, where growth and remodelling must take place if the eye is to change size and/or shape. Experimental evidence in chicks and tree shrews for local control of scleral growth with partial (or local) image degradation suggests spatial resolution at the anatomical level for the optical pathway modulating overall eye growth.[42-45] Based on regional image quality and local scleral growth perturbations, varying patterns of scleral geometry could accompany identical changes in axial length, such as by uniform enlargement with maintenance of the same overall shape or by local elongation at the posterior pole with a change in eye shape. While such different growth patterns may induce the same change in refraction, significant differences in local patterns of image quality across the retina will likely accompany different 3-dimensional retinal profiles.

Animal Studies: Altering Vitreous Chamber Shape

In chick, visual and neural mechanisms influence not only eye size and refraction but also affect the overall shape and conformation of the eye (Fig. 1). Experimentally altered geometric forms of the vitreous chamber in chick include diffuse enlargement,[43,44,85,86] selective elongation along the optic axis to produce a prolate (or long) eye[41,42] or selective expansion in the equatorial dimension to produce an oblate (or wide) eye.[70,73,87-90] Asymmetric or local expansions of the vitreous chamber also can be induced along either the nasal-temporal[43,44] or superior-inferior[91,92] orientations. These altered geometries of the vitreous chamber predictably follow experimental manipulations of visual input,[42-44,85,86,91,92] photoperiod,[66] or administration of neurotoxins[87-89] or drugs that bind to neurotransmitter receptors (Table 2).[42,44,47] For each of these experimental conditions, a specific alteration of vitreous chamber shape is induced.

Biochemical and modelling studies in myopia of experimental animals show regional patterns that is consistent with the hypothesis of eye shape regulation.[94-98] Biochemical approaches also may be able to provide more direct evidence for different regional patterns in eye growth from other interventions, but such data are not yet available.

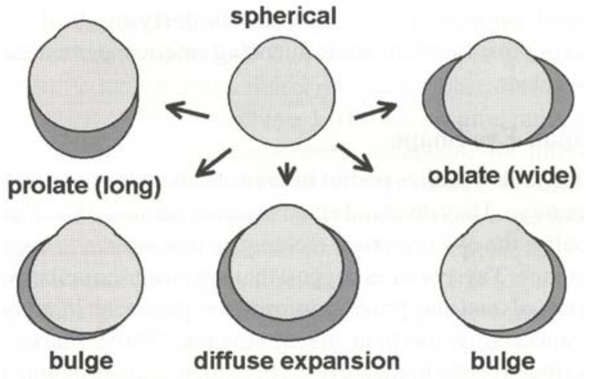

Fig. 1. Shapes of the vitreous chamber forms in chick. The vitreous chamber shape can be predictably modified in chick by altering visual input, changing photoperiod or administering pharmaceutical agents. The vitreous chamber can become diffusely enlarged, selectively elongated along the visual axis or selectively widened in the equatorial dimension. Asymmetries or local bulges can be induced in the posterior eye wall by altering the visual experience in part of the visual field. Each pattern is illustrated, superimposed on a spherical representation of the eye.

Table 2. Mechanisms of Altered Vitreous Chamber Shape in Chick

Resultant vitreous chamber shape	Experimental condition
Diffuse enlargement	Full goggles[43,44] Minus spectacle lenses[85,86]
Selective elongation (i.e., prolate eye)	Initial response to constant light rearing[66] Drugs interacting with GABA receptors[93]
Selective widening (i.e., oblate eye)	Retinal toxins[87-89] Treatment of form deprivation myopia with muscarinic antagonists or dopamine agonists[70,73]
Asymmetric deformation	Partial goggles[42-44] Adjustments to the ground or sky[91,92]

The vitreous cavity shapes correspond to those shown in Fig. 1.

Animal Studies: Altering Anterior Chamber Conformation

Research also suggests that neural mechanisms modulate not only the vitreous chamber shape but also the conformation of the anterior chamber. The clearest indication is the induction of corneal astigmatism with the wearing of toric spectacle lenses in both chicks[85,86,99] and monkeys.[100] Alterations in the photoperiod in chick influence anterior chamber depth and corneal curvature[65,66] and area.[101] Toxins that lesion specific retinal neurons also affect anterior segment depth.[87,88,102]

Melatonin seems to contribute partly to the corneal effects of altered photoperiod,[103] but the underlying biological basis of other mechanisms influencing anterior segment depth is not clear.

Human Eye Shape

Only a few studies permit inferences about the shape of the human eye. They involved either imaging methods that directly visualise the eye or optical techniques that indirectly suggest eye shape. These studies suggest that eye shape varies between individuals and may prove an informative parameter in studying the underlying mechanisms of myopia. Three shapes are described for the human eye: spherical, prolate (or elongated along the visual axis) and oblate (or widened in the equatorial dimensions). On balance, the literature suggests that emmetropic eyes tend to be spherical, myopic eyes tend to be prolate and hyperopic eyes tend to be oblate. Current laboratory investigations, however, suggest a need to re-examine the relationship of human eye shape and refraction.

Direct Measures of Human Eye Shape

Only a few studies have used imaging techniques to compare directly the geometry of the eye to refraction, and they do not permit unambiguous conclusions on the relationship between of refraction and human eye shape. A radiographic study of 45 eyes of mostly adult British subjects[104] found the longest dimension of 15 myopic eyes was the axial length, consistent with a prolate or long eye; emmetropic and hyperopic eyes in this series were spherical, prolate or oblate in shape. In a magnetic resonance (MR) imaging of the eyes of 21 adult subjects in the United States,[105] most eyes had spherical or oblate shapes, including most of the 7 myopic eyes in this series. In another study that used MR imaging to examine the retinal contour of 15 teenagers and young adults in the United States,[106] the retinal contour of the 5 myopic eyes deviated more from sphericity than that of emmetropic or hyperopic eyes. In a study of 255 eyes of 131 adult Chinese subjects using computed tomography (CT) scans,[107] most (95.7%) myopic eyes had a prolate or long shape, hyperopic eyes were mostly (89.5%) oblate or wide and most emmetropic eyes were either oblate (43.4%) or spherical (51.3%) in shape.

Besides the disparate results, these investigations did not provide direct measures of the vitreous chamber length or adjust axial lengths for either corneal vault or anterior chamber depth. Hence, each study offers limited information on the conformation of the posterior segment *per se*. It is also not clear if the differences among these studies can be attributed to demographic differences in their subjects, such as race or age, the small sample sizes or to methodologic limitations in adapting radiography, MR imaging or CT scans to identify eye shape.

Inferring Eye Shape from Peripheral Refraction

As the axis of refraction progressively deviates from the visual axis, particularly beyond ~20º, oblique astigmatism and other optical aberrations become more pronounced.[108] In many clinical writings, the peripheral refraction is simplified by representing it as the spherical equivalent refraction (sphere + 0.5 cylinder) that corresponds to the "circle of least confusion" or the average of the astigmatism in the sagittal and tangential meridians.[109-111] To infer the shape of the vitreous chamber with the on-axis and off-axis refractions, it is assumed that the image shell is spherical in form (Fig. 2). A spherical image shell will parallel the retinal contour of an eye with a spherical posterior eye wall contour. In this case, the off-axis refractions across the retina remain constant compared to the refraction at the fovea as the geometric shape of the image and retina is identical but of constant offset determined by the on-axis refraction. In a prolate or elongated eye, the eye wall is steeper than a spherical image shell, the image shell in the periphery becomes displaced progressively more posterior relative to the retinal position, and the peripheral refraction becomes progressively more hyperopic than the central refraction with increasing distance from the fovea. In an oblate or wide eye, the eye wall curvature is flatter than that of the spherical image shell, the image shell in the periphery becomes displaced anteriorly relative to the retina, and the refraction becomes progressively more myopic in the periphery relative to that at the fovea.

The simplifying assumption of a spherically-shaped image shell has not been validated systematically in human eyes and is likely an oversimplification.[109,112] While this assumption may be valid in eyes with spherical refracting surfaces, off-axis optical modelling requires incorporating the asphericity of the principal refracting surfaces of both cornea and lens.[83,113-115] Since the anterior segment optics and retinal contour determine peripheral refraction, assigning eye shape based on peripheral refraction requires establishing the image-forming properties of each eye. This has yet to be examined adequately in human ametropic eyes. Despite these qualifications, the assumption of a spherically-shaped image shell underlies

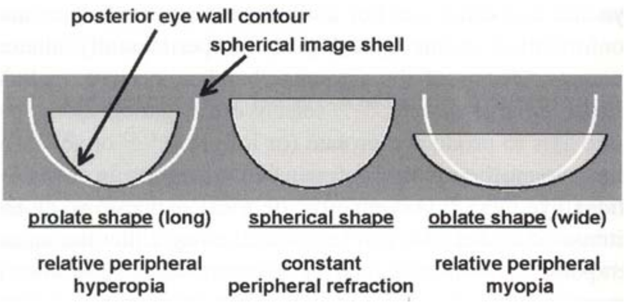

Fig. 2. Relative peripheral refraction and posterior eye shape. The relationship between the posterior eye wall contour (black curve) and a spherical image shell (white curve) is illustrated for an *emmetropic* eye. The posterior eye wall and the image shell coincide for each eye shape at the posterior pole, but their relationship in the periphery varies with eye shape. For myopic eyes, the eye wall is displaced posteriorly from the image shell; for hyperopic eyes, it is displaced anteriorly.

the clinical reports that use peripheral refraction to infer human eye shape.

Peripheral Refraction and Adult Human Eye Shape

Previous investigations in adult humans of peripheral refraction and eye shape vary considerably in sample size and methodology; most results are at best preliminary.[108,110,112,116-120] Nevertheless, these reports tend to suggest a relationship of central refraction to relative peripheral refraction and, by implication, to eye shape. Myopic eyes tend to have less myopia in peripheral than central refractions, suggesting a prolate (or long) vitreous chamber shape. Hyperopic eyes tend to have less hyperopia in peripheral than central refractions, suggesting an oblate (or wide) vitreous chamber shape. Emmetropic eyes tend to have comparable central and peripheral refractions, suggesting a spherical eye shape. A nasal/temporal asymmetry in peripheral refraction may be a regular feature of peripheral refractions of human eyes.[109] Nasal/temporal asymmetry may characterise some 3% to 14% of adult human eyes,[117,119,120] perhaps a greater percentage based on asymmetric patterns to the Stiles-Crawford effect in 10 myopic subjects.[121] Notably, the vitreous chamber shapes suggested in human eyes from off-axis refractions correspond to those identified in chick (Fig. 1).

Eye Shape and Peripheral Refraction in Children

There is only 1 study that has used peripheral refraction to assess eye shape in children.[111] This study evaluated 822 children in the United States. Some 7% of subjects were myopes (at least – 0.75 D in each meridian), 9% were hyperopes (at least + 1.0 D in each meridian) and most were emmetropes. Cycloplegic autorefraction was used to provide 2 spherical equivalent refraction values in the right eye, one along the visual axis and the other oriented 30° off the visual axis in the temporal periphery of the retina. As only a single off-axis refraction reading was obtained, the results overlook the possibility of nasal/temporal asymmetry in peripheral refraction. The off-axis refractions were obtained by requesting subjects to shift their gaze. This is a reasonable protocol unless eye rotation in the orbit influences the vitreous chamber shape.[108,116] Relative peripheral refraction was defined as the difference between the off-axis and central spherical equivalent refractions. The mean (± S.D.) relative peripheral refractions in myopic, emmetropic and hyperopic eyes were + 0.80 ± 1.29 D, –0.41 ± 0.75 D and –1.09 ± 1.02 D, respectively. The authors concluded that the eye shape in children corresponds to the trends in adults. In children, that is, myopic eyes are prolate (or long), hyperopic eyes are oblate (or wide), and emmetropic eyes are almost spherical, perhaps slightly oblate.

While these conclusions are informative, the large magnitude of the standard deviations relative to the mean values suggests broader interpretations, particularly in the context of the relationship between ocular growth mechanisms and eye shape seen in chick. In an attempt to relate these clinical data to laboratory results, we re-analysed the data to learn the distribution of eye shapes within refractive categories. For this purpose, we chose 2 different arbitrary definitions (termed “models”) of a “spherical” eye shape in children, using the criteria of peripheral refraction of relative peripheral refractions either within ± 0.5 D or within ± 1.0 D of the central refraction. While arbitrary, either range seems acceptable for inferring a spherical eye shape, given the accuracy of clinical refractions and the caveats in relating relative peripheral refraction to vitreous chamber form. Thus, depending on the model, a relative peripheral refraction >+ 0.5 D (or + 1.0 D) suggests a prolate (or long) eye, and a relative peripheral refraction <–0.5 D (or –1.0 D) suggests a oblate (or wide) eye. The number of subjects in this study with spherical, prolate or oblate eyes can be estimated, assuming a normal distribution, for each refractive category from the mean and standard deviation (Table 3).

The eye shapes in children inferred from relative peripheral refractions show not only different patterns between myopia, emmetropia and hyperopia but also striking *within-group* shape distributions that depend on the “model” of spherical eye shape (Table 3). Prolate, spherical and oblate eyes are found for myopic, emmetropic and hyperopic eyes using either models (Table 3a). Significant proportions of the myopic eyes, for instance, have prolate, spherical or oblate shapes with each model. Myopic eyes do seem to differ from emmetropic and hyperopic eyes in the proportion of prolate, spherical or oblate eyes, but in a relative and not an absolute sense. Similar statements can be for the emmetropic and hyperopic eyes (Table 3). When the same data are tabulated according to eye shape (Table 3b), emmetropic eyes comprise 67% (or 44%) of the prolate eyes and 83% (or 76%) of oblate eyes in this population, depending on the model. In contrast to the conclusion drawn from the distribution means,[111] these stratifications suggest that a prolate shape is not a specific characteristic of myopia and that an oblate eye shape is not a specific characteristic of hyperopia, at least for children.

Potential Implications of Peripheral Refraction Data

From the perspective of the broad phylogenetic conservation of the mechanisms regulating refractive development (Table 1), these complexities between refractive error and eye shape raise the question of whether eye shape in children could identify underlying developmental mechanisms, as in chick (Table 2). For instance, is eye shape genetically programmed and constant, or does it change as the eye grows under diverse environmental influences? Are the mechanisms responsible for myopia identical or different in prolate, spherical or oblate eyes? In chick, diffuse vitreous chamber enlargement follow defocus and blur. Does a spherical shape in human eyes identify susceptibility to myopia from blur? In chick, vitreous chamber elongation follows certain GABA drugs[93] or comprises the initial response to disrupting the light:dark cycle.[66] Does an interference in retinal signaling or a susceptibility to light:dark disruptions contribute to myopia in prolate human eyes? Are

Table 3. Central Refractions and Apparent Eye Shape in US Children

3a. Central refraction versus apparent eye shape

	Central refraction – Number and percentage of eyes		
Apparent eye shape	Myopia	Emmetropia	Hyperopia
Prolate (long)	34; 59% (25; 43%)	78; 11% (21; 3%)	5; 6% (2; 3%)
Spherical	15; 26% (28; 48%)	299; 44% (518; 75%)	17; 22% (34; 44%)
Oblate (wide)	9; 16% (5; 9%)	310; 45% (148; 22%)	55; 71% (41; 53%)
Total number of eyes	58 (58)	687 (687)	77 (77)

3b. Apparent eye shape versus central refraction

	Apparent eye shape – Number and percentage of eyes		
Central refraction	Prolate (long)	Spherical	Oblate (wide)
Myopia	34; 29% (25; 52%)	15; 5% (28; 5%)	9; 2% (5; 3%)
Emmetropia	78; 67% (21; 44%)	299; 90% (518; 89%)	310; 83% (148; 76%)
Hyperopia	5; 4% (2; 4%)	17; 5% (34; 6%)	55; 15% (41; 21%)
*Total number of eyes	117 (48)	331 (580)	374 (194)

* The number of eyes classified into each shape varies according to the peripheral refraction criterion used to define a spherical eye.

The relationship of central refraction and apparent eye shape in a study of United States children, calculated from relative peripheral refractions (peripheral minus central refraction). Two models were assumed to define an apparent spherical eye shape: 1) the peripheral and central refractions corresponded to within ± 0.5 D; or 2) in parentheses, the peripheral and central refractions corresponded to within or ± 1.0 D. The estimated numbers of eyes and percentages in each category were calculated from data for the right eyes on 822 children in Mutti, et al., using the authors' definitions for axial myopia, emmetropia and hyperopia and assuming a normal distribution to the published data.[111]

prolate but emmetropic eyes at higher risk of developing myopia in the future? Are oblate but emmetropic and hyperopic eyes relatively protected from myopia? If so, under all environmental influences, or only some? These questions, and analogous questions suggested by the relations in Table 3, are presently unanswerable.

Off-axis Image Quality and Refractive Development

The ability of the retina to detect image quality away from the visual axis depends largely on photoreceptor and neural sampling density in the para-foveal and peripheral retina. While most species show a decline in photoreceptor and neural sampling with increasing eccentricity, this is less marked in chick than in primates.[122,123] In humans, spatial acuity declines with eccentricity.[124] That animals with a far lower behavioural acuity than primates can accurately regulate eye growth to compensate for lenses[38,125,126] implies that high neural sampling is not a prerequisite for optical regulation of eye growth, although lower acuity would be expected to restrict the ability to detect higher spatial frequencies that are most sensitive to defocus. The variation in spatial tuning in eccentricity would be expected to have the greatest impact on defocus-driven growth, rather than with form-deprivation or altered lighting, which seemingly would be less affected by eccentric resolving ability.

Involvement of the extra-foveal retina in the regulation of eye growth in humans could be conceptually important if peripheral image quality and/or the subjacent retina locally controls scleral growth, as seeming occurs in some laboratory animals. Variations in peripheral image quality that result from different eye shapes and corresponding off-axis refractive differences could lead to different patterns of image-dependent eye growth and refractive errors. As off-axis refraction is also affected by corneal asphericity, anterior segment geometry and optics may be important determinants of refractive development. Only 1 study has addressed the potential clinical utility of off-axis refraction in humans. In a prospective study of Dutch trainee pilots,[127] a refractive shift towards myopia occurred in 25% of subjects, half of whom actually became myopic. The presence of peripheral hyperopic astigmatism at the initial examination was the refractive pattern most predictive for a myopic shift during the course of training. Based on the above considerations, this peripheral astigmatism pattern is consistent with a prolate eye shape. This study suggests that eye shape may be an important determinant of future refractive errors and a useful parameter in the research on human refractive development.

Myopia Mechanisms and Eye Shape

The literature on myopia causality is vast, with many hypotheses and few unambiguous conclusions on pathogenesis. Despite much research, a clinically acceptable, effective therapy is still lacking to prevent myopia onset or slow its progression. A possible explanation is that the clinical study on refractive development may be confounded by classification bias, by grouping together eyes that experienced distinct growth regulatory mechanisms. We hypothesise here that eye shape may comprise a physiologically regulated variable to incorporate into clinical research on refractive development and myopia pathogenesis. Of course, the extent to which eye geometry is related to the underlying growth mechanisms in man is not known; certainly, eye shape is not now an accepted parameter for classifying human subjects in refractive studies. In chick, eye shape characterises discrete mechanisms that modulate eye development. So far, the major mechanisms regulating eye growth are broadly conserved across species, and the altered forms in vitreous cavity shape that occur in chick also seem to develop in humans. As best can be ascertained from available literature, differences in human eye shape occur both *between* refractive categories and *within* refractive categories, possibly suggesting distinctive developmental mechanisms. To address these concepts, the 3-dimensional conformation of the eye would need to be incorporated with optical, physiological and biochemical information in future myopia research, including epidemiology, genetics and perhaps therapeutic trials.

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