Available online at www.sciencedirect.com
ScienceDirect
Vision Research 47 (2007) 1178–1190
Vision Research
www.elsevier.com/locate/visres

Emmetropization and schematic eye models in developing pigmented guinea pigs

Marcus H.C. Howlett, Sally A. McFadden *

School of Psychology, Faculty of Science and Information Technology, The University of Newcastle, NSW 2308, Australia

Received 20 September 2006; received in revised form 9 December 2006

Abstract

A model of the axial change in ocular parameters of the guinea pig eye from 2 to 825 days of age was developed and a corresponding paraxial schematic eye model applicable from 2 to 100 days of age was constructed. Axial distances increased logarithmically over time except for the lens in which growth was more complex. Over the first 30 days, ocular elongation was approximately linear: ocular length increased by 37 μm/day, the majority due lens expansion. The choroid and sclera thickened with age, while the retina thinned in proportion to the increased ocular size, and the model suggests that there is no small eye artefact for white light retinoscopy. Refractive error just after birth was +4.8 D but halved within the first week. Emmetropization occurred within the first month of life similar to that in other species when aligned at the point of sexual maturity and scaled by the time taken to reach adulthood. The power of the eye was 227 D at 2 days of age and reduced by 19.7 D by 100 days due to a 22% decrease in the power of the cornea. The posterior nodal distance (PND) was 4.7 mm at 30 days of age, with a maximum rate of change of 13 μm/day during the first week. The ratio of PND to axial length declined until at least 100 days of age, well after emmetropia was reached. This suggests that the maintenance of emmetropia is not sustained through proportional axial growth, but involves some active mechanism beyond simple scaling. The model predicts that 1 D of myopia requires an elongation of between 23 and 32 μm, depending upon age, suggesting that a resolution of at least 50 μm is required in methods used to determine the significance of ocular length changes in guinea pig models of refractive development. Retinal magnification averaged 80 μm/degree, and the maximum potential brightness of the retinal image was high, which together with a ratio of lens power to corneal power of 1.7–2.0 suggests that the guinea pig eye is adapted for noctural conditions.

Keywords: Schematic eye; Refractive error; Axial length; Emmetropization; Growth; Guinea pig; Cornea; Lens; Retina; Power

1. Introduction

Emmetropia is characterised by a match between the power of the optics and the axial length of the eye so that in the absence of accommodation, distant images are focussed at the photoreceptor layer. Emmetropization is the process of achieving emmetropia and involves a reduction in the refractive error that is present at birth. The human newborn refractive state varies between individuals (Cook & Glasscock, 1951; Gwiazda, Thorn, Bauer, & Held, 1993; Sorsby & Sheridan, 1960) and some species are born myopic (kestrel: Andison, Sivak, & Bird, 1992; ostrich: Ofri et al., 2001) but in most species, the newborn eye is hyperopic and over time becomes emmetropic (chick: Wallman, Adams, & Trachtman, 1981; mouse: Schmucker & Schaeffel, 2004; tree shrew: Norton & McBrien, 1992; marmoset: Graham & Judge, 1999; Troilo & Judge, 1993; rhesus monkey: Bradley, Fernandes, Lynn, Tigges, & Boothe, 1999; human: Ehrlich, Atkinson, Braddick, Bobier, & Durden, 1995; Gwiazda et al., 1993; Mayer, Hansen, Moore, Kim, & Fulton, 2001; Saunders, Woodhouse, & Westall, 1995; Sorsby, Benjamin, & Sheridan, 1961; Wood, Hodi, & Morgan, 1995). In many species studied, ocular components of the eye, notably the lens, continue to change and eye growth occurs beyond the time that initial emmetropia is obtained. Thus the eye also needs to

* Corresponding author. Fax: +61 249 216980.
E-mail address: sally.mcfadden@newcastle.edu.au (S.A. McFadden).

0042-6989/$ - see front matter
doi:10.1016/j.visres.2006.12.019

maintain emmetropia. It is undisputed that emmetropization is in part actively achieved through visual feedback (for a recent review see Wallman & Winawer, 2004). Less is known about the processes underlying the maintenance of emmetropia.

Since the process of emmetropization and the maintenance of emmetropia is affected by the relative growth of the various ocular components, it is important to carefully characterise ocular growth in a variety of species. The guinea pig eye provides a useful model to study the regulation of ocular growth which is partially controlled by visual input and the associated retinal activity (Howlett & McFadden, 2006; Lu et al., 2006; McFadden, Howlett, & Mertz, 2004). Key aspects of retinal development in the guinea pig eye are similar to humans (Loeliger & Rees, 2005; Spira, 1975). The guinea pig eye has also been used as a model to study a variety of factors which are effected by ocular development, including the cornea (Castro, Lutz, & Edelman, 2004; Foster, Zelt, Mai-Phan, & Kenyon, 1982), crystalline lens (Simpanya, Ansari, Suh, Leverenz, & Giblin, 2005) and retinal development (Loeliger & Rees, 2005). The interpretation of many of these studies would be aided by the development of schematic eye applicable to any age. A first-order paraxial schematic eye can be used to understand refractive errors including astigmatism, chromatic aberration, the size of the image on the retina and the blur associated with defocus (Westheimer, 2006). A description of some aspects of the normal ocular development of the guinea pig eye is available up to 11 weeks of age (Zhou et al., 2006). In this paper, we sought to accurately describe the ocular development of axial parameters in guinea pigs, and measured animals aged from 2 to 825 days of age. Additionally, we determined key aspects of optical development which we used to construct a paraxial schematic eye model applicable from 2 to 100 days of age.

2. Methods

2.1. Animals

Pigmented guinea pigs (*Cavia porcellus*, $n = 183$) aged from birth to 825 days were maternally reared until they were weaned at three weeks of age. They were then housed in groups of 2–3, in opaque plastic boxes ($65 \times 45 \times 20$ cm) with wire mesh lids. Each box had a small hiding area under a stainless steel shelf ($32 \times 16 \times 14$ cm) and the floor was covered with wood shavings. Water (supplemented with Vitamin C), guinea pig food pellets, and hay were available *ad libitum*, and mixed vegetable pieces were occasionally provided. Ceiling lights (36 W daylight fluorescent tubes) were switched on a 12 h light/12 h dark cycle. The room temperature was 22 °C. All procedures were approved by The University of Newcastle in accordance with NSW Animal Research Act and were in accordance with NIH Guidelines.

2.2. Refractive error

Refractive error was measured by streak retinoscopy in hand-held, awake animals in which cycloplegia had been induced 15–20 min prior to measurement with 1% cyclopentolate. We found it was important to bathe the cornea with cyclopentolate for approximately 10 min by holding the animal so that the eye was horizontal. We have found this to be an effective method to rapidly induce cycloplegia since in a separate longitudinal study, we found that guinea pigs refracted in the same manner and time frame with and without cycloplegia were consistently more hyperopic with cycloplegia (average difference of $+3.0 \pm 0.9$ D over the first 30 days, $n = 7$, $p < 0.001$). Furthermore, no pupil response was observed once cycloplegia was induced, and no change in the refractive state was observed during its measurement or when measured 30 min later. Refractive errors are reported as the mean of the horizontal and vertical meridians (see Fig. 1a in Howlett & McFadden, 2006). Particular care was taken to assess only the direction of movement of the retinoscopic reflex in the centre of the pupil on the optical axis (Hughes, 1977a; Mutti, Zadnik, Johnson, Howland, & Murphy, 1992).

2.3. Ultrasound measurement of axial dimensions

Axial dimensions of the eye were measured using high frequency ultrasound (20 MHz) in anaesthetised guinea pigs (1–2% Halothane in oxygen) as previously described (Howlett & McFadden, 2006; McFadden et al., 2004). The echo latencies from the different ocular tissues were transformed to distances between the surfaces based on a sound velocity of 1.534 mm/μs for all ocular tissue except for the lens which was calibrated at 1.774 mm/μs (Howlett & McFadden, 2006; McFadden et al., 2004). Peaks were selected for the front of the cornea, the front of the crystalline lens, the back of the crystalline lens, the vitreal–retinal, retinal–choridal and choridal–scleral interfaces, and the back of the sclera as previously described (see Fig. 1 in Howlett & McFadden, 2006; McFadden et al., 2004). The axial distance from the anterior corneal surface to the back of the retina was defined as the "axial length" and to the back of the sclera as the "ocular length". The thickness of the cornea was measured in 24 eyes from animals of either 3, 11 or 21 days of age using traces in which the corneal peaks were particularly clear. There was no significant difference between these three ages ($F = 1.12$, $p = .34$), so the average value (253.3 ± 2.5 μm) was used to approximate corneal thickness in all ages. The "anterior chamber depth" was the distance from the anterior corneal surface to the anterior lens surface minus this average value of the thickness of the cornea. The "posterior chamber depth" was the distance from the back of the lens to the vitreal–retinal boundary.

2.4. Infrared videokeratometry

The radius of the anterior cornea was measured in awake guinea pigs with a custom-made infrared keratometer as previously described (Howlett & McFadden, 2006). Images covered approximately 40% of the cornea and only those in which the reflection of the LED rings were centred on the pupil were digitised. Three such centred images were analysed for each eye measured. The corneal radius was determined using custom-made software and linear extrapolation based on the LED image reflected from two calibration ball bearings of known radii (3 and 4 mm). The power of the cornea was derived from the average of the four radii for each ring using the formula: $F = (n - 1)/r$, where F = anterior corneal surface power in diopters (D), n = corneal refractive index (1.336), and r = corneal radius (m). The inner 40% of the guinea pig's anterior corneal surface was approximately spherical, thus the data shown are the average power of the three rings. The maximum diameter of the entrance pupil was also determined from the images. The measurements were taken in a dark room with only infrared illumination to which the pupil reflex is insensitive and are referred to as the dark entrance pupil diameter.

2.5. Frozen sections

The radius of the anterior and posterior surfaces of the cornea and crystalline lens were determined in frozen hemisections from 16 guinea pig eyes. Animals were first anaesthetised with 2–4% halothane in oxygen, then rapidly euthanized by cardiac puncture with an overdose of pentobarbitone (lethobarb®), and the eyes were enucleated. Each eye was embedded in tissue freezing medium (Triangle Biomedical Sciences) and