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Normal development of refractive state and ocular dimensions in guinea pigs ☆

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Abstract

Purpose: This study investigated changes in refraction, corneal curvature, axial components and weight of posterior sclera in guinea pig eyes during the normal development from birth.

Methods: Sixty-four guinea pigs were assigned to eight groups ($n = 8$ each). Each group underwent a series of ocular measurements at one of the eight time-points (0, 1, 2, 3, 5, 7, 9 and 11 weeks), including refraction (streak retinoscopy), corneal radius of curvature (CRC; keratometry), anterior segment length (AS: corneal thickness and depth of the anterior chamber), thickness of the crystalline lens (CL), vitreous chamber length (VC; all A-scan ultrasonography) and dry weight of a circular 6 mm diameter punch in the posterior sclera (electronic balance). Results of all the measurements were statistically compared between right eye and left eye, male and female and among different age groups. Artifacts of retinoscopy due to small eye artifact were also estimated at different ages.

Results: The refraction in guinea pig eyes was $+5.22 \pm 0.23$ D (Mean, SE) at birth. This value decreased rapidly during the first 3 weeks followed by a slow decline. The overall decrease in refraction was highly significant from birth to 11 weeks ($p < 0.001$ one way ANOVA). The small eye artifact was approximately 4.00 D at birth, which reduced to 2.76 D at 11 weeks. The guinea pig eyes were emmetropic by 3 weeks of age when the small eye artifact was taken into account. The CRC (3.24 ± 0.01 mm at birth), AS (1.20 ± 0.01 mm at birth), CL (2.72 ± 0.03 mm at birth) and VC (3.28 ± 0.01 mm at birth) increased within the first 3 weeks despite a transient decrease in the CRC within the first week. The increase in CRC, CL and VC continued after 3 weeks, however, the AS remained constant after this age. The increase in VC was better correlated to the decline of hyperopia ($R^2 = 0.70$) than the other components ($R^2 = 0.33$–0.39). Dry weight of the posterior sclera increased linearly from birth ($p < 0.001$ between any two close time-points from 3 to 9 weeks) and had a moderately linear correlation with the VC ($R^2 = 0.60$). There were no significant differences between the right eye and left eye or between male and female in all the measurements.

Conclusions: In guinea pigs, the hyperopia present at birth rapidly reduces to emmetropia within the first 3 weeks of age. The emmetropization process in guinea pigs is mainly related to the increase in the vitreous chamber length. This relationship in guinea pigs is similar to that in chickens, tree shrews, primates and humans. The axial development of the vitreous chamber in guinea pigs appears to be associated with tissue growth of the posterior sclera.

Keywords: Emmetropization; Guinea pig; Refraction; Ocular axis; Corneal curvature

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1. Introduction

Guinea pigs are small mammals that have been used as an animal model to study pathogenesis and genetics for cataracts, retinal diseases, visual impairment in neonates and other ocular complications of systemic disorders (Bantseev et al., 2004; Han, Little, David, Giblin, & Schey, 2004; Lei, 2003; Lo, Zhou, & Reddan, 2004; Loeliger et al., 2004; Rosolen et al., 2004). Like most mammals, except some monkeys, the guinea pigs is a dichromate, with the rods and short- and middle-wavelength sensitive cones that have a maximal wavelength absorbance similar to that of corresponding human photoreceptors (Jacobs & Deegan, 1994; Lei, 2003). Guinea pigs also demonstrate electroretinogram patterns similar to humans and primates (Rosolen et al., 2004; Racine et al., 2004) and therefore appear to be an appropriate model for the study of visual electrophysiology of human eyes.

Furthermore, guinea pigs have been used to study refractive changes associated with defocus of the eye and have shown responses similar to chickens, tree shrews and primates in dimensional and refractive development of the eye (Howlett & McFadden, 2002; McFadden, 2002). Recently, guinea pigs were also used for the study of form-deprivation myopia where a moderate myopia (−5.8 D) could be induced after 2 weeks of form-deprivation since birth (McFadden, Howlett, & Mertz, 2004). Additionally, guinea pigs have advantages over tree shrews, rabbits, cats and primates as experimental animals because they are bred easily, grow quickly (developmentally mature at the age of 5 months), readily available, very cooperative and cost-effective (Woerpel & Rosskopf, 1988).

There are marked inter-subject differences in results of biometric and refractive measurements of the eye in normal and experimental conditions in either tree shrews, guinea pigs or primates (McBrien & Norton, 1992; McFadden et al., 2004; Norton & McBrien, 1992; Troilo & Judge, 1993; Wiesel & Raviola, 1977). Therefore, it is important to have data on the normal development of the eye for these animal models. Results on the normal development of ocular components and refractive state have been available for chickens, tree shrews and primates (Graham & Judge, 1999; Norton & McBrien, 1992; Wallman & Adams, 1987; Wallman, Adams, & Trachtman, 1981). However, little is known about the normal growth of various ocular components and the associated refractive development in guinea pigs. This study investigated changes in refraction, corneal curvature, axial components and weight of posterior sclera in guinea pig eyes during the normal development of the animals from birth. Data from similar studies in other animal models were discussed to facilitate comparisons.

Materials and methods

1.1. Animals and experimental design

The animal research in this study was approved by the Animal Care and Ethics Committee at Wenzhou Medical College, Wenzhou, China. The treatment and care of animals was conducted according to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Sixty-four guinea pigs were collected from the Animal Experimental Centre at the College and were assigned to eight groups ($n = 8$ with four males and four females in each group). Each group underwent a series of ocular measurements at one of the eight time-points (0, 1, 2, 3, 5, 7, 9 and 11 weeks) after birth. The measurements included refraction, corneal radius of curvature, axial length including anterior segment length, thickness of crystalline lens and vitreous chamber length and dry weight of a tissue sample of defined area from the posterior sclera. Prior to the measurement, the guinea pig body was held in a cloth capsule (same external size for different ages) that only exposed the head of the animal. The measurements were performed by two researchers who were masked with regard to the age and gender of the animals although the head size may have provided some cues. All animals were raised at a 12/12 h light/dark cycle.

1.2. Refraction

Refractive status of the eye was examined using a streak retinoscope and trial lenses in a dark room. One hour prior to retinoscopy, one drop of 1% cyclopentolate hydrochloride (ALCON, Belgium) was topically administered every 5 min for four times to achieve a completely dilated pupil. Refractive states were recorded as the mean refractions of the horizontal and vertical meridians (McBrien & Norton, 1992; McFadden et al., 2004). The artifact of retinoscopy (Glickstein & Millodot, 1970) was estimated at different time-points using a formula (Norton & McBrien, 1992) as follows:

Small eye artifact $= N_V \times T_{ret}/P' \times AL \times (AL - T_{ret})$, where N_V = refractive index of vitreous chamber; T_{ret} = thickness of retina; P' = posterior focal length/AL and AL = axial length (from cornea to photoreceptors). The values of N_V and P' were 1.336 and 0.75, respectively, from results of tree shrews (Norton & McBrien, 1992). The value of T_{ret} was 0.115×10^{-3} m from guinea pigs at 1 week of age (McFadden et al., 2004) and the AL was based on the results from the current study.

1.3. Corneal radius of curvature

Corneal radius of curvature was measured with keratometry. A + 8.0 D lens was attached onto the anterior surface of the keratometer so that the keratometry could be performed on the steep cornea of the guinea pig. A group of stainless-steel ball bearings with diameters ranging from 5.5 to 11.0 mm were used for calibration. Corneal radius of curvature measured in the guinea pigs was then deduced from the mean of three readings on the balls with known radii (Norton & McBrien, 1992).

1.4. Axial length

An A-scan ultrasonagraphy (Cinescan A/B with a focal length of 25 mm) was used to measure the axial length of the eye, which consists of anterior segment length (depth of the anterior chamber and the corneal thickness), thickness of the crystalline lens and vitreous chamber length. The ultrasound frequency was 11 MHz which has also been used for measurements of axial length in eyes of adolescent rhesus monkeys (Zhong et al., 2004a, Zhong, Ge, Nie, & Smith, 2004b). The conducting velocity was 1540 m/s for measurement of both the anterior segment and vitreous chamber and 1645 m/s for measurement of the crystalline lens. These velocities were previously used in tree shrews (Marsh-Tootle & Norton, 1989). The velocity used for measurement of the anterior segment in the present study (1540 m/s) was close to that (1557 m/s) used for the corresponding measurement in tree shrews (Marsh-Tootle & Norton, 1989).

Corneal anesthesia was achieved by topical application of 0.5% proparacaine hydrochloride (Alcon, Belgium) prior to the ultrasound measurement. The ultrasound probe had direct contact with the cornea during the axial measurement (Zhong et al., 2004a, 2004b). The tip of the probe had a red light that was used to align the probe perpendicular to the corneal surface at the corneal apex. Repeated measurements showed a standard deviation of less than 10 μm. Slight indentations of the cornea caused