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Age-related changes in centripetal ciliary body movement relative to centripetal lens movement in monkeys☆

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ABSTRACT

The goal was to determine the age-related changes in accommodative movements of the lens and ciliary body in rhesus monkeys. Varying levels of accommodation were stimulated via the Edinger-Westphal (E-W) nucleus in 26 rhesus monkeys, aged 6–27 years, and the refractive changes were measured by coincidence refractometry. Centripetal ciliary process (CP) and lens movements were measured by computerized image analysis of goniovideographic images. Ultrasound biomicroscopy (UBM) at 50 MHz was used to visualize and measure accommodative forward movements of the ciliary body in relation to age, accommodative amplitude, and centripetal CP and lens movements. At ∼3 diopters of accommodation, the amount of centripetal lens movement required did not significantly change with age ($p = 0.10$; $n = 18$ monkeys); however, the amount of centripetal CP movement required significantly increased with age ($p = 0.01$; $n = 18$ monkeys), while the amount of forward ciliary body movement significantly decreased with age ($p = 0.007$; $n = 11$ monkeys). In the middle-aged animals (12–16.5 years), a greater amount of centripetal CP movement was required to induce a given level of lens movement and thereby a given level of accommodation ($p = 0.01$), compared to the young animals (6–10 yrs). Collectively, the data suggests that, with age, the accommodative system may be attempting to compensate for the loss of forward ciliary body movement by increasing the amount of centripetal CP movement. This, in turn, would allow enough zonular relaxation to achieve the magnitude of centripetal lens movement necessary for a given amplitude of accommodation.

1. Introduction

Accommodation in the human eye occurs with the forward and centripetal movement of the ciliary muscle during its contraction, releasing tension on the zonula that are attached to the lens and allowing the lens to thicken and increase in curvature. Presbyopia is the loss of the eye's ability to accommodate as it ages and has been attributed to increased hardening of the lens with age (Fisher, 1971, 1977; Pau and Krantz, 1991; Glasser and Campbell, 1998, 1999), or to the inability of the ciliary muscle to undergo configurational changes with age (Tamm et al., 1991, 1992a).

Existing evidence supports the theory that the lens plays a role in presbyopia (Fisher, 1969, 1971, 1977; Bito and Miranda, 1989; Koretz et al., 1989; Pau and Krantz, 1991; Glasser and Campbell, 1998, 1999; Heys et al., 2004; Croft et al., 2006a). Indeed, age-related loss of deformability in the older excised human lens (i.e., above ∼40 years of age) can account entirely for presbyopia (Glasser and Campbell, 1998, 1999). However, lens hardening may occur as a result of reduced accommodative effect on the lens due to reduced ciliary muscle configurational change during accommodation. Decreased centripetal lens movement could be consequent to decreased ciliary body forward movement, given that there is a significant correlation between them (Croft et al., 2006a).

The ciliary muscle does not lose the ability to contract with age, but it does lose the ability to move forward and centripetally with age, perhaps due to an increasingly inelastic posterior attachment (Tamm et al., 1992a,b; Croft et al., 2006a). The loss of muscle movement with age is sufficient to explain losses in centripetal lens movement and in accommodative amplitude (Croft et al., 2006a) and may be involved in the pathophysiology of presbyopia.

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The rhesus monkey provides an excellent model with which to study human accommodation and presbyopia. Although there are some differences between the species, the accommodative mechanism in the rhesus is virtually identical to that in humans, and both species develop presbyopia on the same relative timescale.

In rhesus monkeys, we studied accommodation and the magnitude of the movements made by the components of the accommodative apparatus, to determine if any early differential age-related changes occurred between components that could provide clues to the presbyopia puzzle.

2. Materials and methods

Details of all experimental preparations, equipment, iridectomy, goniovideography and ultrasound biomicroscopic (UBM) imaging, electrode implantation, central stimulation, measurement of accommodation, image calibration, etc., have been thoroughly described previously (Kaufman and Lütjen-Drecoll, 1975; Crawford et al., 1989; Vilupuru and Glasser, 2002; Croft et al., 2006a,b). Brief descriptions and illustrations are provided below.

2.1. Monkeys

Twenty-six rhesus monkeys (*Macaca mulatta*), of either sex, aged 6–27 years and weighing 5.5–15.1 kg, were used for this study. Prior to the start of the study, all animals included had normal ocular biomicroscopic slit-lamp examinations, with no signs of ocular pathology (other than age-related lenticular opacification).

Details of all animal handling procedures and anesthesia, surgical and experimental preparations, iridectomy, etc., have been described previously (Kaufman and Lütjen-Drecoll, 1975; Crawford et al., 1989; Vilupuru and Glasser, 2002; Croft et al., 2006a,b). All procedures conformed to the ARVO Statement for the Use of Animals in Research and were in accordance with institutionally approved animal protocols.

2.2. Measurement procedures

2.2.1. Edinger-Westphal (E-W) stimulation and accommodation

Accommodation was stimulated via the E-W nucleus (Crawford et al., 1989; Croft et al., 2006a). A Hartinger coincidence refractometer (aus Jena, Jena, Germany) was used to measure resting refractive error and accommodation in response to stimulation of the E-W nucleus.

2.2.2. Definitions–Accommodative stimulus

Maximal Stimulus: the level of E-W stimulus current necessary to induce maximum accommodative change. Supramaximal Stimulus: any level of E-W stimulus current above the maximal stimulus. Submaximal Stimulus: any level of E-W stimulus current below the maximal stimulus.

2.2.3. Goniovideography

Various stimulus levels were given to induce accommodation from zero diopters up to and beyond that necessary to induce maximum accommodation. Centripetal lens movement and centripetal ciliary process (CP) movement (reflects centripetal ciliary body movement) were measured by computerized image analysis of goniovideographic images (Fig. 1) (Croft et al., 2006a). The amount of accommodation was tabulated along with the corresponding amount of CP and lens movement at each stimulus level (Croft et al., 2006a).

2.2.4. Ultrasound biomicroscopy (UBM)

Ultrasound biomicroscopy (UBM) at 50 MHz was used to visualize accommodative movements of the ciliary body (Fig. 2). Using these images, the angle between the anterior aspect of the ciliary body and the inner aspect of the cornea (CB-Cornea angle) was measured in the unaccommodated (resting) eye and during supramaximal stimulation to induce accommodation (Croft et al., 2006a). The extent that the CB-Cornea angle narrowed in the accommodated versus the unaccommodated state (defined as the accommodative CB-Cornea angle change) was used as a surrogate indicator of forward ciliary body movement (Fig. 2) (Croft et al., 2006a) and is referred to as such hereafter. Forward ciliary body movement was examined in relation to age, accommodative amplitude, and centripetal lens and centripetal CP movement.

2.3. Statistical analysis

Simple linear regression (i.e., centripetal lens or forward ciliary body movement versus age, and centripetal lens versus centripetal CP movement) and multiple regression analysis (i.e., accommodation versus lens and centripetal CP movement) were undertaken.

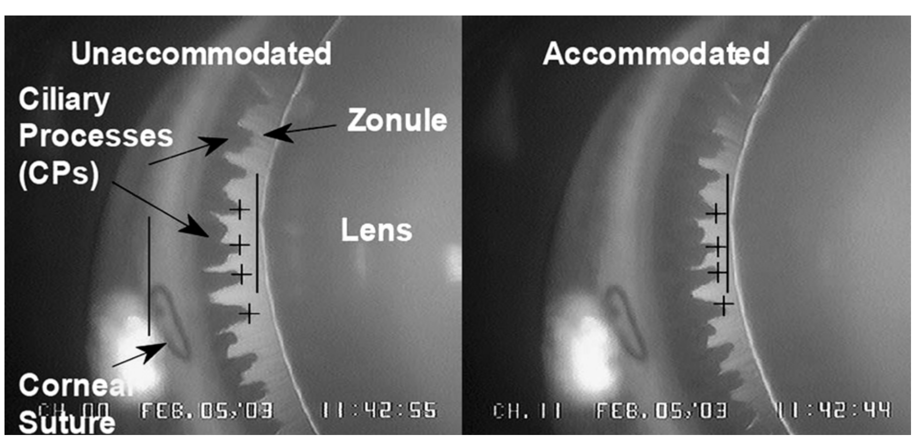

Fig. 1. Goniovideography images of normal lens and ciliary process (CP) configuration in the accommodated and unaccommodated states. To obtain quantitative measurements, a 9-0 nylon suture placed at the corneoscleral limbus served as a reference point (left solid vertical line) from which to measure distances to the lens equator (right solid vertical line) and the CPs (cross-hairs) for each image during a 2.2-sec stimulus period. Reprinted with permission from: Croft et al. Accommodative Ciliary Body and Lens Function in Rhesus Monkeys I. Normal lens, zonule and ciliary process configuration in the iridectomized eye. *Invest Ophthalmol Vis Sci* 2006; 47:1076–1086; copyright Association for Research in Vision and Ophthalmology (ARVO).