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Lag of accommodation does not predict changes in eye growth in chickens

Andrea Aleman, Frank Schaeffel*

Section of Neurobiology of the Eye, Ophthalmic Research Institute, University of Tuebingen, Elfriede Aulhorn Strasse 7, 72076 Tuebingen, Germany

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ABSTRACT

Emmetropization is controlled by the defocus in the retinal image. It is a classical problem how changes in focus, introduced by accommodation, are taken into account. We have quantified accommodation errors in chickens wearing negative lenses to find out whether they can predict subsequent eye growth. Two groups of chicks, aged 10 to 13 days, wore lenses (−7D) monocularly for 4–7 days. Fellow eyes remained untreated. Vitreous chamber depth (VCD) was measured in alert hand-held chickens with high resolution, using the Lenstar LS 900 (Haag-Streit, Koeniz, Switzerland). Non-cycloplegic refractive state was measured by automated infrared photoretinoscopy with and without the lenses in place. In group 1 ($n = 6$), measurements were done 5 times a day to obtain detailed VCD growth curves. In group 2 ($n = 10$), measurements were only taken twice, at 9 am and 4 pm, to reduce the risk of recovery from induced myopia due to the frequent removal of the lenses. As expected from the negative power of the lenses, refractions measured through the lenses were more hyperopic although not as much as predicted by the lens powers, indicating that chickens partially refocused their eyes by accommodation. Among different animals, accommodation errors varied from 1.1 ± 0.9 to 3.6 ± 1.1D (group 1, mean ± 1 standard deviation) and 0.22 ± 1.25 to 1.72 ± 1.23D (group 2). No correlations were found between the magnitude of the accommodation errors in individual animals and subsequent changes in VCD. With negative lenses, VCD grew both during day and night while fellow eyes grew only during the day but shrank during the night. In conclusion, accommodation errors did not predict future eye growth. This raises the question as to why brief periods of clear vision, when lenses are taken off, have a strong inhibitory effect on myopia development while periods of clear vision due to accommodation have apparently no effect. A possible explanation is that, in addition to retina-driven control of eye growth, there is a second neural pathway for the control of eye growth that carries the signal of accommodation – although it is striking that no neuronal and structural correlate has been identified to date.

1. Introduction

There is considerable experimental evidence from animal models (review: Wallman & Winawer, 2004) that axial eye growth is controlled by defocus in the retinal image. If refractive errors are experimentally induced by placing spectacle lenses in front of the eye, axial eye growth changes until refractive errors imposed by the lenses were eliminated over time. Also in humans, emmetropization can be demonstrated since the wide scatter of refractive errors at birth is minimized during development such that the refractive states are optimal at the age of around 5 years (i.e. Schaeffel, Mathis, & Bruggemann, 2007).

In the initial experiments with spectacle lenses in chickens, it was assumed that chicks with negative lenses would accommodate more and that the increase in accommodation tonus would be the signal to stimulate eye growth. Conversely, chicks with positive lenses were assumed to accommodate less which should reduce axial eye growth (Schaeffel, Glasser, & Howland, 1988). However, later it was found that neither eliminating accommodation by lesions in the Edinger-Westphal nucleus (Schaeffel, Troilo, Wallman, & Howland, 1990) nor by lesions of the ciliary nerve (Schmid & Wildsoet, 1996), or optic nerve section prevented compensation of lens-induced refractive errors (Wildsoet & Wallman, 1995). Furthermore, eye growth was found to be controlled by local retinal vision-dependent mechanisms (Diether & Schaeffel, 1997; Norton & Siegwart, 1995; Smith, Huang et al., 2009). Since accommodation changes the focus in the retinal image uniformly across the whole visual field (Tabernero & Schaeffel, 2009), local changes in eye growth cannot be explained by accommodation. There is now general agreement that the visual control of eye growth occurs largely by image processing and defocus detection in the retina.

But even if the retina can determine the amount and sign of defocus (Schaeffel & Diether, 1999; Wallman & Winawer, 2004), it remains a "classical" problem how static refractive errors can be distinguished from defocus generated by insufficient accommodation. In the first paper on chickens with lenses it was stated that "It was verified by

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* Corresponding author.
E-mail address: frank.schaeffel@uni-tuebingen.de (F. Schaeffel).

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infrared photoretinoscopy that the chickens could keep their retinal images in focus" (Schaeffel et al., 1988). However, there was no statistics on how often the chickens were actually in focus. Therefore, the question was not fully answered. Later, Schaeffel and Howland (1988b) simulated refractive development in chickens with and without accommodation and concluded that accommodation must somehow be taken into account to explain the experimental results. Diether, Gekeler, and Schaeffel (2001) found an increase in contrast sensitivity in chicks after one hour when they were wearing spectacles lenses of either sign. They concluded that accommodation must have been incomplete, leaving the retinal image temporarily out of focus and triggering compensatory elevation of contrast sensitivity.

Several studies tackled the problem of potential effects of accommodation errors on emmetropization also in humans. To explain the link between reading and myopia, it was assumed that the "lag of accommodation" might impose hyperopic defocus to the retina which, in turn, should stimulate axial eye growth (Charman, 1999; Goss & Rainey, 1999; Goss, Hampton, & Wickham, 1988; Gwiazda, Thorn, Bauer, & Held, 1993). It was also proposed that higher levels of hyperopic defocus from greater accommodative lag should result in faster myopia progression (Irving, Callender, & Sivak, 1991). There is evidence that myopic children have larger lags of accommodation than emmetropes (Abbott, Schmid, & Strang, 1998; Gilmartin, Bullimore, Rosenfield, Winn, & Owens, 1992; Gwiazda et al., 1993; McBrien & Millodot, 1986) but Mutti et al. (2006) found that the accommodative lags do not precede the development of myopia but rather develop concomitantly. Based on these findings, it became less likely that the lag of accommodation was a reason for myopia onset. In summary, the role of the lag of accommodation in myopia remained controversial: either no association between accommodative lag and myopia progression in children (Berntsen, Sinnott, Mutti, Zadnik, & Group, 2011; Weizhong, Zhikuan, Wen, Xiang, & Jian, 2008), or an association between elevated accommodative lag and myopia progression in adults (Allen & O'Leary, 2006), or even the reversed – lower accommodative lag associated with more myopia progression in adults (Rosenfield, Desai, & Portello, 2002).

Obviously, the role of accommodation in the emmetropization process is not fully understood and also not sufficiently explored. Therefore, we have studied this question in more detail in the chicken model.

2. Methods

2.1. Animals

Experiments were conducted in agreement with the ARVO statement for the use of Animals in Ophthalmic and Vision Research and approved by the Commission for Animal Welfare of the Medical Faculty of the University of Tuebingen. White Leghorn W36 and White Leghorn H&N chicks (Gallus domesticus) were obtained from a local hatchery (Weiss, Kirchberg, Germany) one day after hatching and were raised in groups in large cages in the animal facilities of the institute in a temperature controlled environment at a light cycle of 12L/12D. Water and food were supplied *ad libitum*. The experiments were approved by the University committee for animal welfare. The work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). To keep the number of animals low, individual chicks were studied in great detail, rather than considering only average data from groups. To this end, we discontinued using A-scan ultrasonography because it requires repeated corneal anesthesia. Instead, low coherence interferometry was used which can be done many times a day in alert animals.

2.2. Lenses

PMMA plastic lenses of −7D power were used. The lenses were glued to Velcro rings and attached the chicken heads by mating Velcro rings that were glued to the feathers around the chickens' eyes. Lenses were cleaned at least twice a day. Lenses were attached to one eye (treated eye), leaving the fellow eye untouched (control eye).

2.3. Measurements

Sixteen chicks, aged 10–13 days, were studied. They wore the lenses monocularly for 4–5 days (group 1; n = 6) and for 5–7 days (group 2; n = 10). Refractive states were measured by automated infrared photoretinoscopy (Seidemann & Schaeffel, 2002) with and without lenses in place. The software tracked the eye based on the first Purkinje image. Different from mice and humans, the pupil margins were not automatically detected due to the low contrast between iris and pupil and had to be pre-adjusted by the user via keyboard (Seidemann & Schaeffel, 2002). All data were written to a file but the averages of 10 subsequent measurements were also continuously displayed on the screen. Before attaching the lenses, the most hyperopic readings were determined for each eye and taken as the baseline refractions. The first measurements with the lens in place were taken after one hour. Three

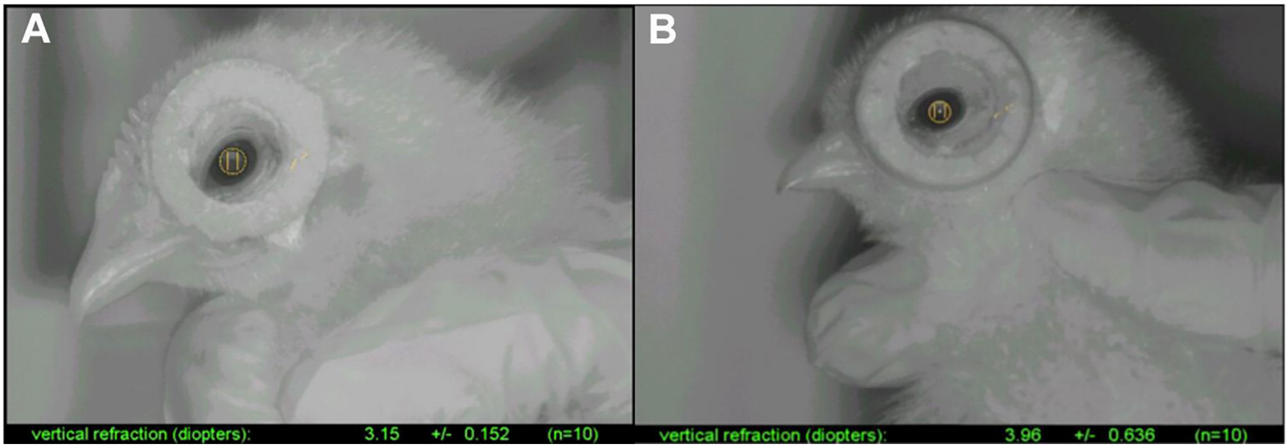

Fig. 1. (A) Appearance of the computer screen when a chicken was refracted by automated infrared photoretinoscopy without lens (only the velcro ring is visible). (B) Refraction with the lens in place. In the case shown here, the chicken became only little more hyperopic with the −7D lens, indicating almost 7 D of accommodation.