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Rotated prism-wear disrupts emmetropization but does not reliably induce hyperopia in the New World monkey

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Abstract

To determine whether a disruption of binocular vision that has been previously shown to be amblyogenic disturbs visually guided growth, and in particular to follow-up the observation by Kiorpes and Wallman [Kiorpes, L., & Wallman, J. (1995). Does experimentally-induced amblyopia cause hyperopia in monkeys? *Vision Research, 35*(9), 1289–1297] that monkeys in whom strabismus had been induced some years earlier were hyperopic in eyes that had become amblyopic, we induced unilateral fixation in five infant New World monkeys (marmosets) through the wearing of a Fresnel prism (of 15 or 30 prism dioptres power) in front of one eye for four weeks. The prism was rotated every three hours during the prism-wear period to encourage a preference for fixating with the contralateral eye. Refractive error and intraocular axial dimensions were measured before, and at intervals after the prism-wearing period. Fixation preference was measured behaviourally, during and after the prism-wear period. Cortical visual function was subsequently assessed through recording of pattern-reversal VEPs in each marmoset between 11 and 14 months of age to assess whether amblyopia had developed in the non-fixing eye. All marmosets used the untreated eye almost exclusively for a monocular visual task by the end of the prism-rearing period. This preference was still present up to at least 7 months after prism-wear had ceased. VEP measures showed a loss of sensitivity at low spatial frequencies (the only ones we were able to test), compatible with amblyopia having developed in the non-fixating eyes of the prism-reared marmosets. Eyes that wore prisms were not significantly different from their fellow eyes in mean refractive error or mean vitreous chamber depth (repeated measures ANOVA; $P > 0.05$) before or at any time after prism-wear had ceased. Two marmosets developed 2–3 D of anisometropia (one hyperopic and one myopic) at the end of prism-wear, that was attributable to interocular differences in vitreous chamber depth, and which decreased towards isometropia in the period following prism-wear removal. Disruption of binocular vision with rotating prisms can influence emmetropization and ocular growth, although it does not appear to do so in a consistent way.

Keywords: Emmetropization; Amblyopia; Eye growth; Hyperopia; Monkey

1. Introduction

Evidence has been accumulating that the development or maintenance of emmetropia during infant eye growth is a visually guided process in both humans and animals (Crewther, 2000; Edwards, 1996; Norton & Siegwart, 1995; Wallman, 1993; Wildsoet, 1997). It is clear from animal models that growth and refractive status of the infant eye can be altered in response to changes in optical demand early in life (Graham & Judge, 1999b; Hung, Crawford, & Smith, 1995; Irving, Sivak, & Callender, 1992; Schaeffel, Glasser, & Howland, 1988; Shaikh, Siegwart, & Norton, 1999; Smith & Hung, 1999; Wildsoet & Wallman, 1995). Eyes that wear positive lenses develop shorter axial lengths than usual and (more) hyperopic refractions, while eyes that wear negative lenses develop longer axial lengths and (more) myopic refractions compared to untreated eyes (Irving, Callender, & Sivak, 1991; Schaeffel et al., 1988; Smith & Hung, 1999; Whatham & Judge, 2001a; Wildsoet

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& Wallman, 1995). There is evidence for such a selective and differential effect of altered optical demand in the chick (Irving et al., 1992; Schaeffel et al., 1988; Wildsoet & Wallman, 1995), Old World monkey (macaque) (Hung et al., 1995; Smith & Hung, 1999) and New World monkey (marmoset) (Whatham & Judge, 2001a), and to some extent in the tree shrew (Siegwart & Norton, 1993).

There is evidence (largely from studies in the chick) that visually guided growth is under retinal control (Bitzer & Schaeffel, 2002; Wildsoet & Wallman, 1995). Yet disruption of compensation for imposed optical defocus by optic nerve section has been reported, suggesting an influence of post-retinal visual pathways on ocular growth (Wildsoet & Wallman, 1995). In particular, evidence for a post-retinal influence on ocular growth and refraction has also come from observations on adult macaque monkeys in whom the amblyopigenic conditions of strabismus or anisometropia had been imposed early in life (Kiorpes & Wallman, 1995). Many years later these monkeys were found to have developed hyperopic refractions associated with the presence of amblyopia (Kiorpes & Wallman, 1995). The potential involvement of amblyopia in eye growth and refraction is interesting as both strabismic and anisometropic amblyopia are believed, from both human and animal studies, to be primarily, if not exclusively, cortical in origin (Barnes, Hess, & Dumoulin, 2001; Crewther & Crewther, 1990; Gillard-Crewther & Crewther, 1988; Hess, Baker, & Verhoeve, 1985; Imamura, Richter, & Fischer, 1997; Kiorpes, Kiper, & O'Keefe, 1998; Sharma, Levi, & Klein, 2000; Yin, Li, & Pei, 1994). An association between the presence of amblyopia and the development or maintenance of hyperopia had also been noted in older longitudinal observational studies in children (Abrahamsson, Fabian, & Sjostrand, 1992; Lepard, 1975; Nastri, Perugini, & Savastano, 1984). These studies suggested either a development or increase in hyperopic refractive state, or at least preservation of infantile hyperopia, in the amblyopic eye. The presence of strabismus in human infants has also been reported to inhibit emmetropization (Ingram, Gill, & Lambert, 2003).

It is possible that the association between amblyopia and eye growth may, in fact, reflect an association between one of the factors predisposing towards amblyopia and eye growth. In the case of strabismus, it may be the ocular misalignment *per se* that disrupts ocular growth rather than the amblyopia that develops as a result of the unilateral ocular deviation. For example, because a strabismic eye does not maintain fixation on the object of interest, its fovea may be pointing towards some other visual stimulus at a plane that is not conjugate with the retina, resulting in defocus. If such stimuli are predominantly located further than the object of interest, which may frequently occur for small hand-held objects in particular, then the fovea of the deviated eye would receive myopic defocus which could act as a stimulus for a hyperopic shift through an active emmetropization process. Thus the hyperopic shift associated with strabismic amblyopia might be a compensatory response to myopic defocus secondary to the deviation of a strabismic eye.

The aim of the current study was to follow up the observations of Kiorpes and Wallman described above by investigating whether a disruption of binocular viewing, that in the long run is likely to cause amblyopia, induces hyperopia in the non-fixating eye. To do this, we fitted infant New World monkeys (marmosets) with a prism in front of one eye for one month early in life, with the intention of preventing binocular fusion and creating an initial diplopia—thus optically simulating strabismus. Studies from macaque monkeys indicate that this form of treatment rapidly reduces the population of binocularly excitable cells in primary visual cortex as well as producing marked deficiencies in stereoacuity (Crawford, Harwerth, Smith, & von Noorden, 1996; Crawford, Smith, Harwerth, & von Noorden, 1984; Crawford, von Noorden, & Meharg, 1983). Reductions in stereoacuity as well as binocular summation are commonly reported in human strabismic and amblyopic populations (Cooper & Feldman, 1978; Giuseppe & Andrea, 1983; Harwerth & Levi, 1983; Henson & Williams, 1980; Levi, Harwerth, & Smith, 1980; O'Keefe, Abdulla, Bowell, & Lanigan, 1996). To induce amblyopia in macaque monkeys, it is not sufficient to fit a prism with a fixed orientation (Crawford, 1996; Crawford & von Noorden, 1979; Crawford, Harwerth, Chino, & Smith, 1996; Crawford, Pesch, & von Noorden, 1996; Crawford et al., 1996, 1984; Harwerth, Smith, & Boltz, 1983; Smith, Chino, & Ni, 1997), and we therefore rotated the prism regularly in front of one eye in order to encourage fixation with the contralateral eye—as fixating with the prism-rotated eye would require frequent oculomotor adaptation after each prism rotation, whereas fixation with the contralateral eye would not. The method of frequent unilateral prism rotation has previously been used successfully to produce unilateral fixation and amblyopia in cats (Mower, Burchfiel, & Duffy, 1982).

2. Methods

2.1. Subjects

Five infant marmosets (*Callithrix jacchus*) were fitted unilaterally with a 'Fresnel' ophthalmic prism at 4 weeks of age. All marmosets were reared with their natural family groups. All experimental procedures were conducted in accordance with the ARVO statement for the Use of Animals in Ophthalmic and Vision Research and were licensed under the UK Animals (Scientific Procedures) Act of 1986.

2.2. Prism-wear

Fresnel prisms were fitted to a monocle system attached to a skull pedestal, fitted to the infant marmosets under anaesthesia. The procedure for implantation and removal of skull pedestals has been described in detail in a previous publication (Graham & Judge, 1999b). Each infant marmoset was fitted with a skull pedestal at 4 weeks of age. Prisms were worn for 28 days until 8 weeks of age, at which time both prism-wear was discontinued and the pedestal supporting the prism was removed under anaesthesia. Each marmoset was monitored after prism-wear had ceased until 273 days (39 weeks) of age. Three animals wore a 15 PD prism and two