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ORIGINAL ARTICLE

Early Versus Delayed Correction of Infantile Strabismus in Macaque Monkeys: Effects on Long-Term Eye Alignment

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ABSTRACT *Purpose*: To determine how the duration of infantile strabismus influences the eventual eye alignment. *Methods*: Six infant macaques were fitted with prisms, which were removed after 3 weeks (wks.), 3 months (mos.), or 6 mos. Two control monkeys wore plano lenses. Eye alignment was measured using search coils. *Results*: Longer duration of infantile strabismus is correlated with a more severe misalignment. The strabismus in the 6-mos. group was 96% greater than that in the 3-mos. group, which, in turn, was 25 times greater than that in the 3-wks group ($p < 0.05$). *Conclusions*: Longer duration of infantile strabismus causes larger-angle esotropia. Early correction of infantile strabismus is supported.

KEYWORDS Infantile strabismus; eye alignment; macaque; optical strabismus; prisms

INTRODUCTION

Infantile esotropia is a nasal misalignment of the eyes with an onset by six months of age. While most agree that surgical correction for infantile esotropia is essential, the appropriate age for surgery is controversial. Some clinicians advocate surgery before age six months to improve binocular fusion and stereopsis outcome,[1,2] while others recommend observation and surgery at older ages to prevent overcorrection–especially in cases which might spontaneously resolve with time.[3]

Behavioral studies have shown that infant macaques are an appropriate model to test the efficacy of early strabismus correction.[4–6] The purpose of this study was to determine how early versus delayed correction of an optical strabismus induced in early infancy in macaque monkeys influences the eventual eye alignment outcome, and to investigate whether the duration of image decorrelation correlates systematically to the magnitude of the resultant strabismus.

MATERIALS AND METHODS

Animals Rearing and Experimental Protocol

Rhesus monkeys (Macaca mulatta) were fitted with goggles on first day of life.[7,8] The goggles consisted of two lens holders so that Fresnel plastic prisms could be inserted. All experimental animals wore prism goggles to induce binocular image deccorelation of at least 11.4° (20 PD) in each eye. Five experimental animals wore 11.4° base-down prism in one eye, and 11.4° base-in prism in the other eye, causing a combined horizontal and vertical image decorrelation. A sixth experimental animal, wore 11.4° base-in prism in each eye, causing a 22.8° (40 PD) horizontal image decorrelation. Two normal control animals wore plano lenses.

Among the experimental monkeys, the goggles were removed after 3 weeks (n = 2), 3 months (n = 2), or 6 months (n = 3), emulating surgical repair of strabismus in humans at 3, 12, and 24 months of age, respectively.[9] At 4 to 6 months of age, the monkeys were transported to Washington University in St. Louis, Missouri, USA, where they were trained to perform visual fixation and tracking tasks. Cycloplegic refractions showed a refractive error <+3.00 spherical equivalent, and spatial sweep VEPs showed equal visual acuity in both eyes in each animal. All procedures were performed in compliance with the Association for Research in Vision and Ophthalmology resolution on the use of animals in research and were approved by the Washington University Animal Care and Use Committee.

Eye Movement Recordings

Eye movements were recorded using the magnetic search coil technique.[10] During each recording session, the monkey sat in a primate chair in the middle of field coils and viewed a small laser spot (subtending approximately 0.05°) projected onto the back of a translucent screen located 50 cm in front of the animal. The head restraint was locked to preclude head movement, and the room was lit with dim background illumination. Eye position was calibrated by the use of a calibration coil and by having the animal perform a lever-response task in which it had to detect 50% dimming of the target within 300 milliseconds while the target remained stationary at known horizontal and vertical positions.

The experiments were performed during automated single and alternate-cover testing. During each session, the laser spot appeared in center gaze and four other cardinal positions of gaze (10° up, left, down, and right). Voltages proportional to eye position were digitized at 500 Hz. Angular resolution of the system was approximately 0.05°.

Data Analysis

Data were acquired and analyzed with the aid of a computer and interactive signal processing software (Spike2 for Macintosh, Cambridge Electronic Design, UK, and Igor Graphics, Wave Metrics, Lake Oswego, Oregon, USA). Data points were excluded from analysis when it was obvious that the monkey was not concentrating on the task. Horizontal eye misalignments were analyzed and compared using ANOVA, with significance set at $p < 0.05$ level.

RESULTS

The magnitude of eye misalignments for each animal, averaged across five cardinal positions of gaze are shown in Figure 1. A small physiological (<2 deg or 4 prism diopter [PD]) heterophoria was present in the control (WE and AY) and 3-wks.-duration (TE and SY) animals. The 3-mos.-duration monkey (GO) exhibited a moderate angle esotropia of 4.6 deg (9 PD). In the 6-mos. group, each of the three monkeys (HA, QN and EY) exhibited a large angle esotropia (8.4–9.6 deg or 17–19 PD).

The longer the duration of image decorrelation, the greater the magnitude of the resultant concomitant

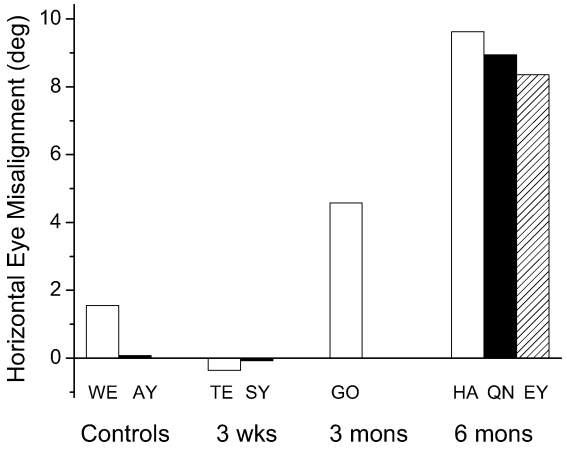

FIGURE 1 **The magnitude of horizontal eye misalignments for each animal, averaged across five cardinal positions of gaze, during left or right eye viewing.**

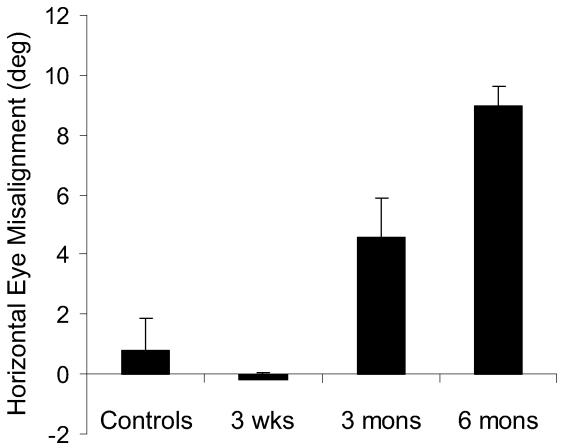

FIGURE 2 **The mean group magnitude of horizontal eye misalignments, averaged across five cardinal positions of gaze, during left or right eye viewing.**

esotropia (Fig. 2). The magnitude of esotropia in the 6-mos. duration group was 96% greater than that in the 3-mos. duration group, which, in turn, was 25 times greater than the heterophoria found in the 3-wks. duration group ($p < 0.05$). There was no significant interaction between duration of image decorrelation and gaze directions.

DISCUSSION

The major finding from this study is that binocular image decorrelation imposed early in life for a sufficient duration causes permanent eye misalignment. The findings of the current report and previous reports from our laboratory[5,6] also reinforce the utility of the macaque monkey as a model for exploring the critical period that dictates successful and unsuccessful correction of infantile strabismus in humans.

Each of the monkeys with the shortest duration (3 wks.) of prism rearing exhibited physiological heterophorias. The critical factor in development of normal eye alignment is therefore timely restoration of binocular image correlation for the development of fusion. In monkeys who had intermediate (3 mos.) and long (6 mos.) duration of prism rearing, a "dose-dependent" response was evident: the longer the duration of binocular image decorrelation, the greater the maldevelopment of the (tonic) vergence system, manifested as larger-angle esotropia. These results reinforce the importance of restoring normal eye alignment in infancy within a short period of time.

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