Effect of dark-rearing on experimental myopia in monkeys

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When lids are surgically fused in rhesus monkeys before eye growth is completed, a high degree of myopia develops, which is caused by an elongation of the eye globe. The present study shows that in monkeys raised in the dark after monocular lid fusion, refraction and axial length were normal in both the closed and the open eye. Myopia, however, readily developed and the eye elongated when a monkey raised in the dark was transferred to illuminated quarters. These findings indicate that visual stimulation through the translucent lids was necessary for the development of this experimental ametropia.

Key words: myopia, eye elongation, neonatal lid fusion, dark-rearing, rhesus monkey

Unilateral lid fusion in neonatal macaque monkeys induces a high degree of myopia in the occluded eye, which is caused by increase in axial length. Myopia progresses with the duration of closure; it is less pronounced when lids are fused at the age of 12 months and cannot be produced in the mature monkey. Bilateral lid fusion induces myopia in both eyes; thus the appearance of the refractive error is not dependent on an interaction between the closed and the open eye. After neonatal lid suture, myopia also develops in the tree shrew (Tupaia glis), but in this species it is not clear whether the refractive error is caused by eye elongation.

The fused lids might influence the refractive state and size of the developing eye in several ways. They might stimulate growth by pressing on the eye globe, by causing an increase in orbital temperature, or by interfering with the drainage of the intraocular fluids. A more exciting possibility is that the nervous system plays a role in the genesis of this refractive error; in fact, the fused lids form a translucent barrier that prevents any real pattern vision and thereby presents an abnormal input to the visual centers. The present experiments were undertaken in an attempt to distinguish among these various alternatives.
EFFECT OF LID FUSION ON AXIAL LENGTH

Fig. 1. Neonatal lid fusion causes elongation of the eye globe in macaque monkeys when the animals are maintained in an illuminated environment. It has no effect on axial length when the monkeys are raised in the dark. In both diagrams the temporal halves of the right and left eye are juxtaposed. The axial length of the eyes is expressed in millimeters. (Diagram on right from Wiesel, T. H., and Raviola, E.: Nature 266:66, 1977.)

Methods

Two male rhesus monkeys (Macaca mulatta) were used in this study. They were removed from the mother at birth and bottle-fed on an infant formula until weaned; subsequently, they received Purina Monkey Chow (Purina Co., St. Louis, Mo.) and water ad libitum, supplemented daily with fresh fruits. In one animal, the lids of the right eye were sutured at the age of 9 days (for details of the surgical procedure see reference 2), and the animal was kept in total darkness for 12 months in a standard adult monkey cage. At the end of the period of confinement in the dark, the eye was reopened; pupillary reflexes were tested, and accommodation was paralyzed with 2 drops of a 1% solution of homatropine. Both eyes were refracted with a streak retinoscope and hand-held trial case lenses. The corneal curvature was measured with a keratometer, and the fundus was examined. The axial length of the eyes was determined by A-scan ultrasonography (Digital Biomeric Ruler DBR-300; Sonometrics Systems Inc., New York, N. Y.). The monkey was subsequently perfused through the aorta with 10% formalin, and the eyes were enucleated. An intracocular pressure of 20 mm Hg was restored by inserting into the vitreous body a needle connected to a water reservoir, and the distance between anterior and posterior poles of the eye globes was measured. The fixed eyes were transected with an equatorial incision; weight and dimensions of the lenses were determined, and the posterior hemispheres were prepared for microscopy.

In the second monkey, the lids of the right eye were fused at the age of 12 weeks, and the animal was maintained in the dark for 10 months. At the end of the period of dark exposure, the palpebral fissure was re-established, and the eyes were refracted. Subsequently, the lids of the right eye were resutured, the subject was exposed for 9 months to a 12 hr light/12 hr dark cycle in regular animal quarters; the luminance in the cage was about 1 log cd/m². Finally, the right eye was opened again, the animal was refracted, the corneal curvature of both eyes was measured, and the axial length was determined by ultrasonography. Measurements on enucleated eyes are not available, for the monkey is still alive. It is important to note that initially the monkey behaved as a blind animal, but after a few months in the light it was capable of pursuit movements when presented with a visual stimulus.

Results

The rhesus monkey raised for 12 months in the dark after neonatal fusion of the lids on the right was in good health. When the palpebral fissure was re-established, a normal conjunctival sac was found, and the appear-
ance of the exposed surface of the eye globe was identical on both sides. Direct and consensual pupillary reflexes were present bilaterally. The average keratometer reading was 53.00 D in both corneas, and retinoscopy showed that the refractive states were identical in the closed and open eyes, both of which were +2.00 D hypermetropic.* The dioptric media were transparent, and the fundus had a normal appearance. Axial length, as determined by ultrasonography, was 17.5 mm in both eyes. At autopsy, the distance between anterior and posterior poles of the eye globe was 18 mm on both sides. Since the thickness of the ocular tunics at the posterior pole was 1 mm, the axial length of the enucleated eyes was about 0.5 mm shorter than expected on the basis of the ultrasound measurements; this difference may be caused either by relief of the tension imposed by the extraocular muscles or by shrinkage of the eye globe during fixation. The lens had the same diameter, thickness, and weight in both eyes. Upon histological examination, the structure of both retina and optic nerve head appeared normal, but neither the numbers nor the morphology of the various types of retinal neurons was investigated.

Fig. 1 illustrates the effect of monocular lid fusion on axial length of the eye in two monkeys, one raised in the dark and the other maintained in an illuminated environment; the diagram on the right is reproduced from a previous study.2

Similar results were obtained in the second monkey. After 10 months in the dark the animal had a +2.00 D hypermetropia bilaterally. Subsequently, the lids on the right were resutured, and the monkey was transferred to an illuminated environment, in order to establish whether the closed eye would now develop myopia. Nine months later when the lids were opened, retinoscopy showed a −3.00 D myopia in the closed eye, whereas the open eye had remained +2.00 D hypermetropic. The axial length, as measured by ultrasonography, was 19.81 ± 0.18 (S.D.) mm in the closed eye and 18.77 ± 0.08 in the open eye. The thickness of the lens was the same in both eyes (3.34 ± 0.15 mm on the right and 3.36 ± 0.10 on the left), and the average refractive power of cornea was 52.00 D bilaterally. Thus ultrasonography showed that in the closed eye myopia was associated with an increase in axial length; however, the precise interrelationships between eye elongation and refractive error remain to be established. Similar interocular differences in refraction and axial length were previously reported for a 26-month-old monkey which was raised in the light and had the lids of one eye sutured at the age of 12 months.²

Discussion

These experiments demonstrate that neonatal lid fusion has no effect on the refractive state and axial length of the eye in monkeys raised in the dark; myopia, however, readily develops and the eye elongates when the animal is transferred to illuminated quarters. A crucial factor in the pathogenesis of this experimental myopia thus seems to be the distorted representation of the visual world that the fused lids present to the nervous system. Furthermore, the fact that neither the closed nor the open eye becomes myopic in the dark suggests that the attenuation of the incoming light per se is not the cause of myopia development. How the nervous system may affect the axial length of the closed eye remains to be elucidated. Accommodation or activity of the extrinsic ocular muscles is possibly involved, whereas pupillary dilation seems to be out of the question, for in the dark the pupil is most likely mydriatic.

The results of our experiments do not rule out mechanical or thermal effects of lid fusion on the appearance of the refractive error. Abnormal neural influences may in fact cause eye elongation because the intraocular pressure or the orbital temperature have increased as a consequence of lid fusion.

The fact that lid fusion causes myopia only when the monkeys are kept in the light may explain why this surgical procedure has little

* This hypermetropia may be due, at least in part, to an inherent error of the retinoscopic technique, as suggested by Glickstein and Milbot.¹
or no effect in the cat.\textsuperscript{5,6} In our monkeys, the fused lids attenuate light by about half a log unit and thus prevent pattern vision without blinding the animal. In the cat, the fused lids attenuate light by about 4 log units, so that if the animal were kept in poorly illuminated quarters, the retina of the occluded eye may not receive adequate stimulation.

Our finding that young monkeys develop myopia in response to an abnormal visual input has clinical interest, in view of reports that myopia is frequently associated with pathological conditions which affect the transparency of the dioptric media of the infant eye, such as retrolental fibroplasia,\textsuperscript{7–11} Wagner's disease,\textsuperscript{12} and Marfan's syndrome.\textsuperscript{13} Furthermore, it is well known that myopic subjects commonly show alterations of the vitreous body; it would be interesting to investigate whether these abnormalities precede the onset of myopia, for they might represent the cause rather than the consequence of the refractive error.

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**REFERENCES**


