Optically induced concomitant strabismus in monkeys

M. L. J. Crawford and G. K. von Noorden

In infant monkeys that view the world through dissociating prisms the binocular neurons of the striate cortex cease to function. The loss of binocular cortical neurons is proportional to the duration of prism wear. Virtually all binocular neurons will disappear from the striate cortex within 60 days, and the remaining monocular neurons will become equally divided between the two eyes. Although the cortical neuron population is dramatically altered, this form of experimental strabismus failed to affect the size of principal cells of the lateral geniculate nucleus.

Key words: esotropia, monkeys, lateral geniculate nucleus, electrophysiology, binocular vision

Misalignment of the optical axes from surgery of the extraocular muscles in young animals produces dramatic changes in the responsiveness of striate cortical neurons (refs. 1 to 6 and R. C. Van Sluyters, personal communication), reducing the visual acuity of the deviated eye (amblyopia)7-9 and altering the size of neurons of the lateral geniculate nucleus (LGN).2, 8, 10 Surgery, however, may create incomitant strabismus, an accompaniment of restricted ocular motility. Maffei and Bisti11 have even suggested that asymmetric input from the extraocular muscles alone may be sufficient to produce many or all of these effects. Moreover, in studying the reversibility of the changes in the visual system caused by strabismus, we have found that corrective realignment is technically difficult and cannot always be accomplished.2

Shlear12 used prisms to create vertical retinal disparity in kittens, and Smith et al.3 found that optical misalignment of the visual axes will decrease the number of binocular neurons in the striate cortex in kittens which have had a limited, exclusive view of the world through dissociating prisms. The purpose of this paper is to describe similar experiments in infant rhesus monkeys in which helmets fitted with prisms were worn continuously.

Material and methods

Infant rhesus monkeys (Macaca mulatta) were hand-fed with an infant liquid diet (Similac) supplemented by laboratory Monkey Chow and reared individually in small cages. They were received from the supplier at about 3 weeks of age, and the experiment was begun when they were 30 days of age.

Each monkey was fitted with a lightweight fiberglass and aluminum helmet (Fig. 1) in which thin optical prisms of 25 mm diameter were held before the eyes. The prisms were placed at a vertex distance of about 8 mm, resulting in monocular fields of 106°, a binocular field of 82°, and a total

From the University of Texas Health Science Center; the Cullen Eye Institute, Baylor College of Medicine; and the Department of Ophthalmology, Texas Children's Hospital, Houston, Texas.

Supported by Research grant EY 01120 from the National Institutes of Health.


Submitted for publication June 15, 1979.

Reprint requests: M. L. J. Crawford, University of Texas Health Science Center, Sensory Sciences Center, Medical School, Box 20708, Rm 7238B, Houston, Texas 77025.
Fig. 1. A monkey and the helmets as used in this study to hold the optical prisms.

field of view of 135° (interpupillary distance = 20 mm). The power of the prisms ranged from 10 to 27 prism diopters. The prisms were placed base-in before each eye, and one prism was rotated base-down 15° to 20° to introduce a vertical as well as a nasal image disparity. With this amount of combined horizontal and vertical prismatic dissociation, the assumption could be made safely that fusion was interrupted at any fixation distance and that combined esotropia and hypertropia had been produced experimentally. Once the mask was fitted, the monkeys viewed the laboratory environment exclusively through the prisms. Their eyes were covered by a dark drape when the helmet was removed for cleaning and repadding (about 5 min). When longer periods (30 min to 1 hr) were needed for servicing the helmet, the monkey was placed in a light-tight box. The prisms were inspected and cleaned daily. Therefore the visual experience of these monkeys was normal during the treatment period, except that fusion was interrupted by the prisms at all times.

At the end of the treatment period, the animals were temporarily anesthetized with ketamine hydrochloride, paralyzed with pancuronium bromide, and prepared for microelectrode recording of the eye dominance of single neurons of the striate cortex, as described by Crawford et al. Any refractive errors present were corrected with contact lenses. Anisometropia was not found in any of these monkeys. Multiple, oblique, and disparate tungsten microelectrode penetrations were made through the foveal and parafoveal striate cortex, and a special effort was made to penetrate and detect as many eye dominance columns as possible. Thirty or more neurons were described for each monkey. The monkeys were then perfused with a solution prepared of equal parts of 2% glu-
Optically induced concomitant strabismus

Taraldehyde and 2% paraformaldehyde in cacodylate buffer at a pH of 7.3. Frozen coronal sections through the lateral geniculate nuclei (LGNs) were stained with thionin, and the cells were photographed and measured with planometric techniques described in our earlier publications. 

Results

The changes in the eye dominance histogram of the striate cortex of the infant monkey following periods of prismatically induced binocular dissociation are shown in Fig. 2. The individual histograms of 4 monkeys (B to E) were compared with a composite histogram from normal infant and adult monkeys (A) in which binocular neurons make up approximately 70% of a striate cortex sample. This figure shows that as the period of wearing prisms was increased, there was a progressive decrease in the binocular neurons and the remaining neurons were controlled by the left or the right eye. Within 25 days after onset of binocular dissociation, the normal proportion of binocular neurons was reduced by one half, and within 60 days binocular neurons were virtually absent (Fig. 2, F). The receptive fields of the cortical neurons of these monkeys appeared normal in every respect, except for the degree of binocular influence.

LGN cell size was not affected in any of the optically dissociated monkeys, as illustrated in Fig. 3 and compared there with a monkey made esotropic by surgical means. Even with the longest duration of 56 days, optical dissociation had no measurable effect upon the size of LGN parvocellular cells, whereas only 7 days of surgically induced esotropia resulted in significantly smaller LGN cells connected with the eye.

Discussion

Optical misalignment of the visual axes in infant monkeys dramatically decreases the population of binocular striate cortical neurons, an observation comparable to findings in kittens (refs. 3 to 6 and R. C. Van Sluyters, personal communication). Therefore prismatic disruption of fusion in infancy is sufficient to decimate the binocular neurons of the striate cortex in the absence of any extraocular muscle impediment. The monkey is born with some binocular connection to neurons of the cortex, and binocular visual experience early in life is essential for the maintenance and further development of this binocular neuron population. However, misalignment of the optical axes will cause a functional loss of these innate connections and thwart additional development of binocularity. It will be interesting in further experiments to determine whether any binocular connections can be restored by a posttreatment period of normal binocular viewing experience.

The loss of binocular neurons from the striate cortex and the preservation of a relative balance in the cortical monocular eye control are consonant with the idea that opti-
Fig. 3. Two pairs of curves showing the size difference of LGN parvocellular cells of an optically strabismic monkey and a surgical strabismic monkey. Each curve is the cumulative proportion of 200 measured cell sizes from LGN layers 3 to 6 which had input from one eye paired with a comparison curve of parvocellular neurons with input from the opposite eye. Filled arrows, Average LGN principal cell size; open arrows, maximum difference ($d_{\text{max}}$) between curves. The Kolmogorov-Smirnov nonparametric statistic was used to test for significant differences between curve pairs.

cal dissociation did not create a competitive advantage of one eye over the other during the period of prism wear. Even though we were unable to reliably perform the cover test in these behaviorally untrained monkeys, we assume they developed alternating fixation similar to that observed in monkeys with surgically induced exotropia.10 However, the balance between the input received by each eye may be a delicate one, since factors such as brief periods of visual deprivation of one eye may cause a profound cortical dominance change in favor of the eye in which the image is clearest.17–19

The current thinking is that during the first weeks of life the LGN neurons which have their input from one eye continue to compete with neuron terminals with input from the opposite eye for synaptic space upon cortical neurons of layer IVc, a process begun in the fetal brain.15 Failing to gain such synaptic space in this competition, the LGN neurons subsequently decrease in size, presumably as a result of reduced metabolic demand.20 Within the context of such a model, our results suggest that whenever it is impossible for the monocular images to be fused, the number of binocular neurons continues to decrease by some unknown process as the time of dissociation is extended. When the two monocular images are of comparable quality, the competition between LGN neurons for cortical space apparently is balanced, and the metabolic activity of all LGN cells is normal. Hence there is no reduction in LGN size.

As an experimental technique, prismatically induced strabismus has an obvious advantage over surgical strabismus. It is concomitant, at least in the horizontal gaze positions, and therefore is more comparable to human strabismus occurring in early infancy. Since prismatically induced strabismus is reversible, the extent of recovery of the electrophysiologic and morphologic consequences of loss of binocular vision can now be studied more precisely.

Adrian Heston made the helmets, cared for the monkeys, and together with Dave Fagan helped with the recordings. Mark Borchert did the histology and cell photography, and Mike Crawford helped with animal care on weekends.

REFERENCES