Failure to preserve cortical binocularity in strabismic monkeys raised in a unidirectional visual environment

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

It has been claimed that cortical binocularity can be preserved by raising exotropic kittens in a visual environment consisting of spatially periodic contours. We raised visually immature monkeys (Macaca mulatta) with prismatic or surgically induced horizontal and vertical strabismus in a visual environment consisting exclusively of vertical stripes. Electrophysiologic studies of the striate cortex yielded results that are comparable to those obtained in strabismic monkeys raised in an unrestricted visual environment. Thus we cannot confirm in strabismic monkeys that binocularly responding cortical neurons can be preserved by exposing the animals to a nonconflicting repetitive visual environment.

Key words: monkeys, strabismus, cortical dominance, lateral geniculate nucleus, receptive fields, spatial orientation, electrophysiology, amblyopia

Surgically and primitively induced experimental strabismus depletes the population of binocular neurons in the striate cortex of infant monkeys and kittens, and the loss of binocular cortical neurons is proportional to the duration of the strabismus. It has been reported that cortical binocularity can be preserved by raising strabismic kittens in a repetitive visual environment, providing each eye with similar visual input in spite of the ocular misalignment. This observation, if confirmed in monkeys, could have far-reaching implications with regard to therapy of acquired strabismus in human infants. It is the purpose of this article to report on the cortical electrophysiology of esotropic and exotropic monkeys (Macaca mulatta) that were raised partially or exclusively in a visual environment providing approximately equal and simultaneous stimulation to each eye.

Material and methods

During the first months of life three macaque monkeys (61479, 71979, and 92079) were fitted with lightweight fiberglass and aluminum helmets in which thin optical prisms (25 mm diameter) were mounted before each eye (Fig. 1). The prisms were placed at a vertex distance of about 8 mm, with an interpupillary distance of 20 mm, resulting in monocular fields of 106°, a binocular field of 82°, and a total field of vision of 135°. A total of 27 prism diopters base-in were divided between the two eyes, and the base of one prism (10° or 17°) before the right eye was rotated 20° downward to introduce a vertical deviation in addition to the large horizontal retinal image disparity. With this amount of combined horizontal and vertical prismatic dissociation it was reasonable to assume that fusion was disrupted and that a com-

From the Cullen Eye Institute, Baylor College of Medicine, and the University of Texas Health Science Center at Houston, Sensory Sciences Center and Department of Ophthalmology, Houston, Texas.

This work was supported by research grants EY 01120 and EY 02530 from the National Eye Institute, National Institutes of Health, Department of Health, Education, and Welfare.

Submitted for publication Sept. 12, 1980.

Reprint requests: Dr. G. K. von Noorden, Department of Ophthalmology, Texas Children's Hospital, P. O. Box 20269, Houston, Texas 77025.

© 1981 Assoc. for Res. in Vis. and Ophthal., Inc.
von Noorden and Crawford

May 1981

Fig. 1. Monkey wearing helmet with prisms before each eye.

Table I. Summary of experimental treatment data

<table>
<thead>
<tr>
<th>Monkey</th>
<th>Birth date</th>
<th>Prisms on</th>
<th>Prisms off and sacrificed</th>
</tr>
</thead>
<tbody>
<tr>
<td>61479</td>
<td>5/29/79</td>
<td>6/21/79</td>
<td>7/19/79</td>
</tr>
<tr>
<td>92079</td>
<td>9/2/79</td>
<td>10/11/79</td>
<td>11/15/79</td>
</tr>
<tr>
<td>12890</td>
<td>1/15/80</td>
<td>2/8/80*</td>
<td>3/12/80</td>
</tr>
<tr>
<td>12600</td>
<td>7/25/78</td>
<td>8/24/78</td>
<td>9/29/78</td>
</tr>
<tr>
<td>12601</td>
<td>7/31/78</td>
<td>8/24/78</td>
<td>10/23/78</td>
</tr>
<tr>
<td>1-3199</td>
<td>6/4/80</td>
<td>from 7/4/80 to 7/31/80 (sacrificed)</td>
<td></td>
</tr>
</tbody>
</table>

*Date of surgery.
†Animal raised in cylinder between dates indicated.

Combined esotropia and right hypertropia had been induced. Previous experiments in infant monkeys had shown this form of prismatic dissociation to be effective in causing deterioration of cortical binocularity. A fourth monkey (12980) was made exotropic during the first month of life by tenotomy of both medial rectus muscles. He developed an exotropia of about 30°.

The monkeys were raised in a restricted visual environment by placement for various periods of time in an acrylic cylindrical chamber in which they were exposed to high-contrast vertical grating patterns. The stripe pattern (1/4 inch wide black and white stripes) was painted on the inside walls of the cylinder (Fig. 2). The floor and the ceiling were painted uniformly white or black, except in one experiment (with monkey 61479) in which the ceiling and floor had additional black and white stripes radiating from the center to the wall of the drum. This environment created redundant exposure of both eyes to black and white stripes, the purpose of which was to reduce to a large extent the conflicting visual input caused by ocular misalignment present in a normal, visually enriched environment and to provide cortical binocular neurons with edges and borders of a wide variety of disparities. Moreover, to expand the range of spatial frequencies, one area of the cylinder wall at eye level of the monkey served as a rear projection screen on which additional vertical gratings of various spatial frequencies were randomly and continuously projected by a slide projector from outside the drum.

One monkey (61479) spent 8 to 9 hr per day (a total of 135 hr) in the chamber but otherwise had visual exposures to the normal primate nursery environment during 12 hr of daylight. One monkey (71979) spent 8 to 9 hr per day (a total of 264 hr) in the chamber. When outside the chamber this monkey’s prism goggles were covered with translucent masking tape so that no form stimulation occurred. One monkey (92079) spent 385 consecutive hr in the training chamber, except for brief daily cleaning periods during which the prisms were taped. Whenever the helmet had to be removed for cleaning, all monkeys were placed in a light-proof box. The monkey with surgically induced exotropia (12980) spent 33 consecutive days in the chamber until the day of the neurophysiologic experiment. Thus, with the exception of 61479, the monkeys used in this study had no visual experience other than that supplied by the striped cylinder from the day strabismus was induced prismatically or surgically until the day recordings were made from the striate cortex 4 to 5 weeks after the onset of strabismus.

As control experiments, one 4-week-old monkey without strabismus (1-3199) was raised in the cylinder for 1 month with no other visual experience, and two monkeys (12600 and 12601) were raised in an unrestricted visual environment for one and two months, respectively, while wearing prisms identical to those worn by the experimental monkeys.

Because strabismus was not induced experimentally until the third and fourth week of life, all monkeys had brief periods of normal binocular visual exposure to the primate nursery environment prior to the onset of strabismus. The experimental data are summarized in Table I.

After periods of 4 to 5 weeks the prism goggles were removed and video recordings of the eyes failed to show any misalignment of the visual axes. The animals then were temporarily anesthetized.
Fig. 2. Experimental chamber. For explanation, see Material and methods.

Fig. 3. Eye dominance histograms of 30 cells recorded from the striate cortex of each of four monkeys. Categories 1 and 7 contain neurons that were driven only through the left or right eye. The remaining categories represent graded degrees of binocular influence, with neurons in 4 being equally influenced by both eyes.

with ketamine hydrochloride, paralyzed with pancuronium bromide, and prepared for microelectrode recording of single striate neurons as described previously. Refractive errors, if present, were corrected with contact lenses. Multiple oblique tungsten microelectrode penetrations were made, distributed over an 8 mm² area of the foveal striate cortex. We attempted to penetrate and detect as many eye-dominance columns as possible. Stimulus specificities from 30 neurons were described for each monkey and the orientation specificity of each neuron was especially noted.

The monkeys were perfused with a solution prepared of equal parts of 2% glutaraldehyde and 2% paraformaldehyde in cacodylate buffer at a pH of 7.3. Celloidin embedded coronal sections through the lateral geniculate nuclei (LGN) were stained with thionin, and the cells were photographed and measured planimetrically, as described in earlier publications. Matched samples of 50 cells were measured in the rostrocaudal posterior half of each LGN layer, except in monkeys 12600 and 92079, the LGNs of which were used for other studies.

Results

The results of the neurophysiologic experiments are shown in Fig. 3 and are presented in histograms according to cortical eye dominance categories. The data show a significant reduction of binocularly driven cortical neurons in all experimental monkeys. Although the population of binocularly driven cells in normal M. mulatta is approximately 80% of all cells recorded, only 3% to 31% such cells were found in esotropic or exotropic monkeys raised in a restricted environment.
These results are identical to those obtained from the three control monkeys (Fig. 4) and to those reported by us in earlier publications from strabismic monkeys raised in an unrestricted visual environment. The preferred orientation of each recorded striate neuron failed to show a bias toward vertical orientation specificity in any of the monkeys, including the controls, but rather showed a full complement of receptive field orientations. Receptive field orientations (30 cells each) from the experimental (12980 and 71979) and control group (1-3199 and 12601) are shown in Fig. 5.

Histologic comparisons between corresponding layers of the right and left LGN showed no significant differences between cell sizes in the experimental and control groups by multiple t tests (p < 0.05).

Discussion

Our results show that infant monkeys with prismatically induced esotropia, surgically induced exotropia, and controlled exposure to a visual environment consisting of vertical stripes lose a significant number of binocularly innervated striate neurons and are not different in this respect from strabismic monkeys exposed to visually unrestricted surroundings. Thus we were unable to confirm in the monkey the observation of Blakemore and Van Sluyters and Blakemore in strabismic kittens that cortical binocularity can be preserved by a redundant visual environment. It must be noted, however, that Blakemore found some variability in his results and reported that "in a few strabismic kittens there has been a definite decrease in the proportion of binocularly driven neurons despite exposure to a striped environment." Our results also show that, unlike that in kittens, the distribution of receptive field orientation in monkeys cannot be biased in a particular direction by restriction to a visual environment consisting of spatially periodic contours. It is difficult to explain the failure to main-
tain cortical binocularity in the monkey in view of results reported with the kitten. On theoretical grounds we had expected to be able to repeat Blakemore's work in the monkey, accepting the premise that the cause for disruption of cortical binocularity in strabismus is the conflicting visual input received by corresponding retinal points of each eye or, conversely, the absence of concordant binocular input. What then are some of the possible reasons for the loss of binocularly responding cortical cells in our monkeys?

First, one must consider that species differences alone may account for these discrepancies in results even though many of the effects of abnormal visual stimulation during infancy on function and structure of the visual system have been reported in recent years to be similar in cats and monkeys. Second, it is possible that the monkeys, while in the training cage, may have experienced brief periods of double vision as they viewed parts of their body (hands, feet, tail) or as they fed from the formula bottle that was visible to them with both eyes. The dissimilarity of visual input received by each eye during these brief periods may have been sufficient to disrupt cortical binocularity. Blakemore and Cooper prevented their nonstrabismic stripe-raised kittens from seeing their own body by attaching a wide black collar around their neck, but Blakemore did not mention whether similar precautions were taken during his experiments with strabismic kittens. It is unlikely that the visually restricted environment per se may have altered the normal predominance of binocularly driven cells in the striate cortex, if one considers the normalcy of data obtained from the nonstrabismic monkey raised in the drum (I-3199).

An incidental finding of this study was the normal distribution of spatial orientation of cortical neurons. This is in contrast with data from stripe-reared kittens in which an orientation bias according to the direction of the stripes has been described. Species differences and duration of exposure to the stripes may account for this discrepancy. Moreover, whatever the role of a restricted visual environment on orientation tuning of cortical neurons may be in monkeys, it probably can be effective only if the monkey's head is stabilized with respect to the orientation of the stripes. This factor was not controlled in our experiments, since the monkeys were moving freely about in the cylinder and the head movements were unrestricted. However, a certain preferential exposure to vertical stripe orientations did exist, since the monkeys were observed to be sitting on the cylinder floor for most of the time with their heads erect.

The absence of cell size differences between LGN portions innervated by the right and left eye found in this study can be expected if we assume that all experimental monkeys developed an alternating fixation pattern. This assumption could be confirmed by direct observation only in monkey 12980, since it is difficult to assess the fixation pattern reliably in monkeys wearing prism goggles. In view of the strong right eye dominance shown in the cortical histogram of monkey 71979, we suspect that this animal may have developed a mild strabismic amblyopia of the left eye, since the cortical histogram is similar to those previously reported by us in monkeys with esotropia of long duration and behaviorally proven strabismic amblyopia. Amblyopia in monkeys has also been shown to be associated with a decrease of LGN cell sizes connected with the amblyopic eye. We have previously reported that cortical neurophysiologic changes in visually deprived monkeys precede the development of histologic anomalies in the LGN, which explains the normalcy of the LGN in this monkey on the basis that esotropia was present for only one month.

We thank James Miears, Michael Crawford, David Fagan, and Adrian Heston for their technical assistance.

REFERENCES