Functional Effects of Bilateral Form Deprivation in Monkeys

Ronald S. Harwerth,* Earl L. Smith, III,* Adele D. Paul,* M. L. J. Crawford,t and Gunter K. von Noorden, MD‡

Psychophysical methods were used to study the effects of binocular form deprivation, initiated at 1 month of age, on the visual sensitivities of young monkeys. All the monkeys reared with bilateral form deprivation for 7 weeks or longer had reduced spatial contrast sensitivity for both eyes. Although the contrast sensitivity deficits of the bilaterally form-deprived monkeys generally were larger for one eye than the other, the magnitudes of the deficits were small compared with those produced by similar periods of unilateral form deprivation. For other monocular vision functions investigated, temporal contrast sensitivity and increment-threshold spectral sensitivity, the data for the bilaterally form-deprived animals showed only minor variations from those of the control monkeys. However, none of the bilaterally form-deprived monkeys had binocular vision on either measures of binocular summation or stereodetection, even if the animal had normal monocular vision functions. Therefore, these results show that monocular sensory deficits caused by abnormal early visual experience as a result of bilateral form deprivation are much less severe than those caused by unilateral form deprivation. The differences in the severity of visual deficits may be attributed to the consequences of anomalous binocular competition associated with unilateral form deprivation that was minimized during bilateral form deprivation. Thus, these results illustrate that anomalous binocular competition is more detrimental to the developing visual system of infants than direct deprivation per se. Invest Ophthalmol Vis Sci 32:2311–2327, 1991

Discordant binocular vision during infancy causes amblyopia and/or suppression in adulthood.1 A clarification of the mechanisms by which abnormal visual experience affects the normal development of monocular and/or binocular capabilities is important for understanding visual development and for the clinical management of children with these visual disorders.

In most instances, visual deficits after early abnormal visual experience were believed to result, primarily, from anomalous binocular competitive interactions between the afferent inputs to the visual cortex from the two eyes.2-8 For example, with monocular form deprivation, inadequate pattern stimulation of the deprived eye gives the nondeprived eye a "competitive advantage," and as a result, the nondeprived eye gains control of visual cortical neurons at the expense of the deprived eye. However, in addition to competitive mechanisms, noncompetitive or direct deprivation effects also contribute to the total deficits resulting from unilateral form deprivation.1,6,9,10 Direct deprivation effects presumably occur because form deprivation prevents sufficient retinal stimulation to maintain the amount and/or the pattern of neural activity that is required for the maintenance of normal developmental processes.9

The results of previous physiologic investigations supported the binocular competition model by demonstrating that the induced alterations caused by bilateral form deprivation, in both monkeys4-6,8 and kittens,2,7,9 generally are less severe than those caused by unilateral form deprivation. The principal finding of these experiments was that, in bilaterally form-deprived animals, a substantial number of striate neurons could be driven by each eye; with unilaterally form-deprived animals, only a very small proportion of striate cells could be influenced by the deprived eye. However, in monkeys, relatively few neurons were driven binocularly in either bilaterally or unilaterally deprived animals. In addition, these studies also found a relatively higher proportion of visually unresponsive neurons in binocularly deprived animals than occurs in either monocularly deprived or control animals. Based on these physiologic studies, we would expect that the monocular visual capabilities of an
animal would be less severely affected by bilateral than unilateral form deprivation.

Of the strategies used to differentiate experimentally between the functional consequences of anomalous binocular competition and direct deprivation, the method most amenable to behavioral studies involves comparisons of the visual deficits produced by unilateral form deprivation with those produced by bilateral form deprivation. We would expect that unilateral form deprivation would produce more severe effects because both competitive and noncompetitive factors are operational. With balanced bilateral form deprivation, neither eye has a distinct competitive advantage, and consequently, only noncompetitive factors would be expected to influence visual development.9 This report presents the results of a test of this prediction. Specifically, behavioral data for a series of visual functions were compared in bilaterally and unilaterally form-deprived monkeys. Some of these results were reported briefly elsewhere.11,12 Investigations of the physiologic and anatomic effects of bilateral form deprivation are reported in our companion paper.13

Materials and Methods

Subjects

Fifteen rhesus monkeys, Macaca mulatta, (five bilaterally deprived, two unilaterally deprived, and eight normally reared controls) were used as subjects. All experimental and animal care procedures adhered to the ARVO Resolution on the Use of Animals in Research. The lids of the treated eyes of each of the experimental animals were fused surgically14 when they were about 1 month of age and then parted after various periods of deprivation (2, 6, 7, 13, or 16 weeks for the bilaterally deprived animals and 2 or 8 weeks for the unilaterally deprived animals). Throughout this report, the individual animals are coded by the type and the duration of deprivation, eg, BD-2 indicates the monkey who was deprived binocularly for 2 weeks, and MD-2 denotes the animal who was deprived monocularly for 2 weeks. Much of the data for the two unilaterally form-deprived animals (MD-2 and MD-8) were reported previously,15,16 but because these data are important for a comparison of the effects of monocular and binocular form deprivation, they are included in this report.

None of the monkeys developed eyelid infections or holes in the lids during the period of deprivation, but one animal (BD-2) had an eye irritation after the lids were parted. A small piece of suture material was left beneath the lid of the left eye and caused him to hold his eyelid shut voluntarily for about 1 week before the suture was found and removed.

By the time the behavioral experiments were started (12–18 months after the end of the deprivation period), all animals appeared visually competent, and they did not show permanent behavioral abnormalities similar to those reported for dark-reared monkeys7,18 or for monkeys bilaterally deprived for long periods.19 In addition, our observations of the monkeys at the beginning of the behavioral experiments indicated that they could make following eye movements in all fields of gaze and had normal binocular eye alignment (although the presence of a microtropia would not have been detected).

The refractive errors of three of the experimental monkeys (BD-6, BD-7, and BD-16) were determined by retinoscopy with cycloplegia at the beginning and end of the binocular deprivation. At both times, all three were bilaterally symmetric hyperopic animals. The refractive errors of all of the monkeys also were determined just before the behavioral experiments by retinoscopy with cycloplegia. The axial lengths were measured (A-scan ultrasonography), and an ophthalmoscopic examination of the eyes was done (Table 1). The refractive errors and axial lengths of the eyes of the bilaterally deprived animals were symmetric, and

| Table 1. Ocular characteristics of control (NC), bilaterally form-deprived (BD) and unilaterally form-deprived (MD) monkeys |
|---|---|---|
| Subject | Refractive errors | Axial lengths |
| NC-1 | OD: +1.00 × 045 | 18.5 mm |
| | OS: +1.00 × 040 | 18.5 mm |
| NC-2 | OD: +0.50-0.25 × 180 | 18.3 mm |
| | OS: +0.50-0.25 × 180 | 18.3 mm |
| NC-3 | OD: +0.50 ds | 19.2 mm |
| | OS: +0.50 ds | 19.2 mm |
| NC-4 | OD: -0.50 ds | 18.9 mm |
| | OS: -0.50 ds | 19.1 mm |
| NC-5 | OD: +1.25 ds | 17.8 mm |
| | OS: +1.25 ds | 17.9 mm |
| NC-6 | OD: +0.75 ds | 18.3 mm |
| | OS: +0.75 ds | 18.4 mm |
| NC-7 | OD: +0.50 ds | 19.2 mm |
| | OS: +0.50-0.50 × 180 | 19.3 mm |
| NC-8 | OD: +1.00 ds | 18.6 mm |
| | OS: +1.00 ds | 18.6 mm |
| BD-2 | OD: +0.50-2.00 × 135 | 19.0 mm |
| | OS: +1.50-0.50 × 090 | 19.0 mm |
| BD-6 | OD: +1.50 ds | 18.5 mm |
| | OS: +2.00-0.50 × 180 | 18.4 mm |
| BD-7 | OD: -1.00 ds | * |
| | OS: -1.00 ds | * |
| BD-13 | OD: -1.00-1.50 × 135 | 19.4 mm |
| | OS: +1.00 × 045 | 19.0 mm |
| BD-16 | OD: -0.50 ds | * |
| | OS: -0.50 ds | * |
| MD-2 | OD: -8.50 ds | 18.2 mm |
| | OS: +6.00-3.00 × 180 | 17.5 mm |
| MD-8 | OD: -8.50 ds | 20.1 mm |
| | OS: -2.00-1.75 × 045 | 19.0 mm |

* Data not available.
as with all control animals, there was less than a 1-
dioptrier difference in refractive error or a 0.4-mm dif-
ference in axial lengths between the two eyes of any of
the monkeys. By contrast, the refractive errors of the
two unilaterally form-deprived monkeys were asym-
metric with the form-deprived eyes being less hyper-
opic (MD-2) or more myopic (MD-8) than their non-
deprived eyes.20 Ophthalmoscopic examinations of
the monkeys' eyes did not reveal any abnormalities.

Apparatus

During the experiments, the monkeys were placed
in a standard primate chair inside a sound-attenuat-
ing room. The chair was fitted with a response lever
on the waist plate and a drink spout on the neck plate.
A device with two lens wells for correction of the
monkeys' eyes did not reveal any abnormalities.

The monkeys' refractive errors and the selection of monoc-
ular or binocular viewing was attached to the primate
chair.

The stimuli for the spatial and temporal modula-
tion sensitivity experiments were generated on the
cathode ray tube of a Tektronix 7603 oscilloscope
(Beaverton, OR) with a P4 (white) phosphor using
standard methods. The screen of the oscilloscope was
masked to subtend a 4° visual angle at the 114-cm
viewing distance and had a 40 cd/m² space-averaged
luminance. In the spatial contrast sensitivity experi-
ments, the detection stimuli were stationary, vertical
sinusoidal gratings presented for 500 msec with
square-wave temporal onset and offset properties. In
the temporal contrast sensitivity experiments, the lumi-
nance of the screen of the oscilloscope was modu-
lated sinusoidally in time to produce a uniform field
flicker. The flickering stimuli were presented for a 1-
sec viewing duration.

The optical system for the spectral sensitivity exper-
iments was a two-channel Maxwellian view system
with a 2.5-mm exit pupil. The light source for both the
10° background field and the 2° test field was a 1000-
W, heat-filtered xenon arc lamp. A Jarrel-Ash Mark
X monochromator (Fisher Scientific, Pittsburg, PA)
with a 10-nm half-band width produced the mono-
chromatic test stimuli presented for 50 msec by
means of an electronic shutter. The intensity of the
achromatic background for the increment-threshold
spectral sensitivity measurements was 3000 Td.

Dynamic random dot stereograms for the disparity-
grating detection task were produced on a color televi-
sion tube modified to gain control over the color guns.
Laboratory-designed signal generators permitted a
controlled horizontal spatial disparity between the red
and green signals. When viewed at 1 m, through
Wratten filters #29 and #58 (Kodak, Rochester, NY),
the disparity-controlled section of the screen sub-
tended a visual angle of 20° and appeared as a drifting
square-wave grating standing in front of (or behind) a
field of randomly moving noise. The disparity of the
bars of the grating could be varied from 3–30 min of
arc. The grating was made to disappear by de-
synchronizing the red and green signals for 100 msec.

To ensure stimulus control of the monkeys' behavior,
especially those who were possibly stereoblind, small
red and green light emitting diodes (LEDs) were cen-
tered on the face of the video display to produce con-
trolled monocular luminance cues. The LEDs were
matched to the two Wratten filters so that the mon-
keys could only see one of the colored LEDs with each
eye and the luminance change could be time locked to
the disappearance of the disparity grating.

The behavior required for the psychophysical para-
digm was developed through a series of successive ap-
proximations that required 1–2 months of training
time. The behavioral methods previously were de-
scribed in detail for increment thresholds,21 contrast
thresholds,22 and disparity-grating measurements.23

The response contingencies of the behavioral para-
digm were the same for each of the visual functions,
and only the stimulus characteristics were different
for each specific visual function investigated. The es-
setial features of the behavioral tasks were as follows.
The animals were trained to press and hold the re-
sponse lever in the presence of an auditory, "ready"
stimulus (an 8-Hz click tone). A sustained lever press
initiated a random-duration foreperiod that preceded
the test stimulus. Subsequently, if the monkey re-
leased the response lever within a criterion response
interval after the presentation of the stimulus (starting
150 msec after the stimulus onset and lasting 400
msec after the stimulus offset), it was assumed that
the monkey had detected the stimulus (a hit) and the re-
sponse was reinforced (a 1.6-kHz tone after each hit
and 0.5-ml orange on a 0.75 probability basis). To
maintain an acceptably low false-alarm rate of approx-
imately 5%, any lever releases during the foreperiod,
before the detection stimulus was presented, initiated
a mild punishment contingency in the form of a long
time out, i.e., an 8-sec intertrial interval after false-
alarm trials compared with a 1.5-sec interval after hit
or miss trials.

In the disparity-grating experiments, detection
rates were assessed for fixed retinal disparity values
(3–30 min of arc). However, for the increment-thre-
shold spectral sensitivity and contrast sensitivity ex-
eriments, psychophysical detection thresholds were
measured using a modified method-of-limits pro-
cedure. In the threshold experiments, the intensity or
contrast of the stimulus was decreased by 0.04 log
units in the spectral sensitivity experiments, or 0.1 log units in the contrast sensitivity experiments, after each hit trial. Alternatively, if the monkey did not release the lever during the criterion response interval, it was assumed that the stimulus had not been detected (a miss), the subject was not reinforced, and the stimulus intensity was not changed. After two consecutive misses, the intensity was reset to a suprathreshold level (0.7–1.0 log units above the threshold value) on a 0.5 probability basis. The stimulus intensity that resulted in resetting the stimulus to a suprathreshold level was defined operationally as the threshold value for that stimulus series. The final threshold estimates were derived from the geometric mean of 12 threshold measurements with resulting standard errors of approximately 0.05 log units for both the experimental and control eyes.

As an aid to describe the effects of form deprivation on the monkeys’ contrast sensitivity functions, the data were analyzed through a nonlinear-regression, curve-fitting routine. The algorithm optimized the fit with four independent parameters that described (1) the spatial or temporal frequency associated with the maximum contrast sensitivity; (2) the maximum contrast sensitivity value; (3) the slope of the low-frequency portion of the function; and (4) the slope of the high-frequency portion of the function. In all cases, the resulting fitted curves correlated highly with the empiric data and provided smoothed functions for comparison purposes.

Results

Spatial Contrast Sensitivity

To assess the effects of bilateral stimulus deprivation, the sensitivity functions from the bilaterally form-deprived monkeys were compared with sensitivity functions from a group of normally reared control animals. The average spatial contrast sensitivity data for the eight control animals are presented in Figure 1A. The data representing the mean monocular sensitivity values for the eight animals at each spatial frequency (filled circles) exhibit the band-pass shape that generally is characteristic of contrast sensitivity functions. The data were fitted well by the solid line which represents the contrast sensitivity function determined by the curve-fitting procedure. In addition, the variability of the contrast sensitivity data among the control subjects is illustrated by the dashed lines in Figure 1A which delineate the ±95% confidence limits. The confidence limits were approximately ±0.22 log units and nearly constant across spatial frequencies.

Spatial contrast sensitivity functions for the two animals who had undergone unilateral form deprivation are presented in Figures 1B and 1C. One of the monkeys was unilaterally form deprived for 2 weeks (MD-2, Fig. 1B) and the other monkey was deprived for 8 weeks (MD-8, Fig. 1C). Comparisons of the functions for the treated (filled symbols) and control (open symbols) eyes show that unilateral form deprivation of relatively short duration caused profound spatial contrast sensitivity deficits for the deprived eyes of these animals. The contrast sensitivity deficits were of such severity that the measurements included spatial frequencies where less than one stimulus cycle could be displayed on the stimulus screen. The contrast sensitivity functions, therefore, may not represent a spatial vision task in a traditional sense, but they demonstrate the degree of functional difference between the deprived and nondeprived eyes of these monkeys. They also illustrate that very large spatial contrast sensitivity losses occur as a result of the combination of anomalous binocular competition and direct deprivation that are created by early unilateral form deprivation.

The spatial contrast sensitivity functions for the bilaterally form-deprived animals are presented in Figure 2. Four of the five animals (BD-6 was the exception, Fig. 2B) had a deficit in spatial contrast sensitivity, for either one eye or both eyes, ie, the sensitivities fell outside of the 95% confidence limits for the normal animals. However, these deficits were less severe than those found for the monkeys reared for shorter periods of time with unilateral form deprivation (Figs. 1B–C). Although it is apparent that the monkeys reared with bilateral form deprivation have deficits in their spatial vision capabilities, a more quantitative assessment of these deficits requires comparison of their functions with those from the normally reared control monkeys. However, the comparison of functions from experimental and control animals was not straightforward because the spatial contrast sensitivity functions for most of the bilaterally form-deprived animals (Fig. 2) revealed interocular asymmetries in sensitivity. For each animal (except BD-6), the sensitivity of the right eye (open circles) was somewhat higher than the sensitivity of the left eye (filled circles). Most likely, this result was coincidental and was not an effect of our experimental-rearing or animal-testing procedures.

The interocular ratios in contrast sensitivity for the experimental and control animals are shown in Figure 3A. For these calculations on the control animals, the ratios were assigned positive values if the right eye had the higher sensitivity. The variability in the relative sensitivities between the two eyes of normally reared monkeys is delineated by dashed lines. Because the sensitivity ratios did not vary systematically across

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Fig. 1. Spatial contrast sensitivity functions for control and unilaterally form-deprived monkeys. Mean spatial contrast sensitivity data for eight control subjects with monocular viewing (●) and binocular viewing (□) (A). The dashed lines delineate ±95% confidence limits of the data for monocular viewing. Spatial contrast sensitivity functions for the nondeprived eye (○) and deprived eye (●) of a monkey unilaterally form-deprived for 2 weeks (B). Spatial contrast sensitivity functions for the nondeprived eye (○) and deprived eye (●) of a monkey unilaterally form-deprived for 8 weeks (C). Standard errors are shown for the unilaterally form-deprived subjects when they are larger than the symbol.

spatial frequencies, the ±95% confidence limits displayed in the graph represent the mean values for the 19 spatial frequencies used to determine the contrast sensitivity functions. The narrow confidence limits (mean, 0.12 log units) emphasize the close similarity of the contrast sensitivities of the two eyes of control monkeys. By comparison, the interocular contrast sensitivities for the experimental animals were more variable. To obtain positive ratios for most of the spatial frequency range, the ratios for these experimental animals were computed by comparing the eye with higher sensitivity with the eye with lower sensitivity (Fig. 2). These data demonstrate that the interocular sensitivity ratios of only one experimental animal, the monkey treated for 6 weeks (BD-6), were within the range of normal animals.

Although the sensitivity ratios of all other experimental animals were outside the normal range, the magnitudes of the deviations were not ordered with respect to the duration of bilateral form deprivation. For example, the interocular sensitivity ratios for BD-16 (open left-triangles), treated for 16 weeks, were closer to the normal range than those of the one treated for 13 weeks (BD-13, open diamonds). However, it is important to note that, in every case, the interocular sensitivity ratios for the bilaterally form-deprived monkeys were closer to those of the control group than the ratios for monkeys reared for equivalent periods with unilateral form deprivation (MD-2, filled circles; MD-8, filled triangles).

Of the bilaterally deprived subjects, the functions for BD-2 showed the largest differences between the two eyes, but the data for this animal required special consideration. This monkey was form deprived for 2 weeks, the shortest treatment period used in the study, and it might have been expected that he would be the subject most likely to have equal and normal sensitivities for the two eyes. However, at the end of the treatment period when the lids were parted, a piece of suture material caused an irritation of the left eye, and he voluntarily held his left eyelid closed for about 7 days until the irritant was removed. Therefore, in a sense, this subject was compromised for the bilateral form-deprivation experiment, but with respect to the analysis of direct-deprivation effects, it may be appropriate to include BD-2 in the study because any direct deprivation effects of the right eye would still be relevant for our purposes.

To evaluate direct deprivation effects in the presence of bilaterally asymmetric sensitivity deficits that were outside the range for normally reared control animals, we adopted a conservative approach and compared the sensitivities of the less-affected eyes of the experimental animals with the mean monocular sensitivities of the eight control animals. This approach may underestimate the effects of direct deprivation on the spatial contrast sensitivity of the eye because it assumes that (1) the additional deficit in the more-affected eye was caused by mechanisms other than direct deprivation and/or (2) interocular asymmetries were not the result of recovery of the function from one of the eyes subsequent to the period of deprivation. In any case, using the function from the less-affected eye for this analysis will indicate the min-
Fig. 2. Spatial contrast sensitivity functions for bilaterally form-deprived monkeys. The duration of deprivation for each monkey, in weeks, is indicated by the number in the subject identification code. Data are presented for right eye (○), left eye (●), and binocular (□) viewing conditions. Standard error bars are shown when they were larger than the symbol size.

The ratios of the contrast sensitivities of the control animals to those of the less-affected eyes of the experimental animals are presented, as a function of spatial frequency, in Figure 3B. To maintain a consistent convention, the dashed lines represent the 95% confidence limits for the control population variability (Fig. 1). Presentation of sensitivity ratios in this manner revealed that the spatial contrast sensitivity functions for the nondeprived eyes of both of the unilaterally deprived animals (MD-2 and MD-8) and the more sensitive eyes of the two animals bilaterally deprived for short durations (BD-2 and BD-6) fell within the range of normal variability at all spatial frequencies. It was also apparent that all of the other bilaterally deprived animals had losses in sensitivity, relative to the control group, that were outside the range of normal variability. For these animals, the differences between their data and the control group monotonically increased as a function of spatial frequency for stimuli above about 1 cy/deg, although the magnitude of the effect was not influenced strongly by the duration of bilateral form deprivation. Therefore, the comparison of spatial contrast sensitivity functions for the less-affected eyes of the experimental monkeys with monocular functions for control animals showed substantial direct deprivation effects on monocular spatial vision as a result of bilateral form deprivation. With short-term deprivation, these effects were not correlated highly with the duration of treatment.

Our previous behavioral investigations on the effects of early abnormal visual experience in monkeys showed that, in addition to spatial vision, unilateral form deprivation also affects other basic monocular visual capabilities. Therefore, to assess more completely the functional, direct deprivation effects on visual processes, temporal contrast sensitivity functions and photopic, increment-threshold spectral sensitiv-
Fig. 3. The logarithm of interocular spatial contrast sensitivity ratios as a function of spatial frequency for bilaterally (BD)– and unilaterally (MD) form–deprived monkeys. The symbol table indicates the type of treatment and duration (in weeks) for each of the subjects. Interocular contrast sensitivity ratios for the two eyes of each of the BD and MD animals (A). The dashed lines indicate the ±95% confidence for the interocular ratios of the control monkeys. Contrast sensitivity differences between the mean monocular sensitivities of the control subjects and the eye with higher sensitivity for each of the BD and MD subjects (B). The dashed lines show the ±95% confidence limits for the mean sensitivity of the control monkeys.

Temporal Contrast Sensitivity

Examples of temporal contrast sensitivity functions are presented in Figure 4. The first example (Fig. 4A) describes the mean monocular contrast sensitivities (filled circles) and the ±95% confidence limits (dashed lines) for the eight control animals. The band-pass shape, with a peak sensitivity at approximately 10 Hz, was typical of temporal contrast sensitivity functions of humans or monkeys when the stimulus viewing duration is limited to 1 sec. The confidence
Fig. 4. Temporal contrast sensitivity functions for control and form deprived monkeys. Mean temporal contrast sensitivity data for eight control subjects with monocular viewing (•) and binocular viewing (○) (A). The dashed lines delineate ±95% confidence limits on the data for monocular viewing. Temporal contrast sensitivity functions for the right eye (○), left eye (●), and binocular viewing (△) for a monkey bilaterally form-deprived for 16 weeks (B). Temporal contrast sensitivity functions for the nondeprived eye (○) and deprived eye (●) of a monkey unilaterally form-deprived for 8 weeks (C). Standard errors are shown when they are larger than the symbol size.

limits for these data (±0.18 log units) were similar to those for spatial contrast sensitivity measurements for the same animals (Fig. 1A). The other two contrast sensitivity functions in Figure 4 are presented as representative of the data for the bilaterally (BD-16; Fig. 4B) and unilaterally (MD-8; Fig. 4C) deprived subjects. These representative functions indicate that bilateral deprivation had little effect on the temporal contrast sensitivity of either eye (open and filled circles), whereas unilateral deprivation of shorter duration caused a substantial reduction in sensitivity, especially at higher temporal frequencies.

The temporal contrast sensitivity data for each of the experimental animals are summarized by the sensitivity ratio functions in Figure 5. The procedures for data analysis and the calculation of the ratios of monocular sensitivities for the temporal modulation sensitivity data were the same as those described for the spatial modulation sensitivity data (Fig. 3). The interocular contrast sensitivity ratios for each of the subjects are plotted in Figure 5A. These data showed that, compared with the interocular asymmetries in spatial contrast sensitivity, the temporal contrast sensitivities were very similar for both eyes of the bilaterally form-deprived subjects. The interocular sensitivity ratios for BD-13 and BD-16 were outside the 95% confidence limits at the higher temporal frequencies, but the deviations were relatively small, especially in comparison with the interocular sensitivity differences caused by unilateral form deprivation (filled symbols; Fig. 5A). In addition, although the interocular asymmetries for BD-2 were well outside the range of normal variability at all temporal frequencies, the temporal contrast sensitivity for his left eye was probably also affected by uncontrolled posttreatment factors. Consequently, the general trend of the data in Figure 5A indicated that any effects of short-term bilateral form deprivation, specifically on temporal vision, would usually be equal for the two eyes.

The evaluation of direct deprivation effects on temporal vision is presented in Figure 5B. This confirms that, compared with the monocular contrast sensitivities of the control group, temporal modulation sensitivity functions essentially were not affected by bilateral form deprivation. For the two animals subjected to the longest period of bilateral form deprivation (BD-13 and BD-16), there were ranges of temporal frequencies where the sensitivity ratios between the mean monocular sensitivity of the control animals and the sensitivity of the less-affected eye of these experimental animals exceeded the 95% confidence limits, but these deviations were not systematic for temporal frequency. These data suggest that periods of bilateral form deprivation that were longer than those used in our study may cause deficits in temporal and spatial vision.

Increment-Threshold Spectral Sensitivity

Our interpretation of the results of the investigations of photopic, increment-threshold spectral sensitivity functions were similar to those from the temporal modulation sensitivity investigations, i.e., the functions for all of the bilaterally form-deprived sub-
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Fig. 5. The logarithm of interocular temporal contrast sensitivity ratios as a function of temporal frequency for bilaterally (BD)- and unilaterally (MD) form-deprived monkeys. The symbol table indicates the type of treatment and duration (in weeks) for each of the subjects. Intercocular contrast sensitivity ratios for the two eyes of each of the BD and MD animals (A). The dashed lines indicate the ±95% confidence for the interocular ratios of the control monkeys. Contrast sensitivity differences between the mean of the monocular sensitivities of the control subjects and the eye with higher sensitivity for each of the BD subjects and each of the eyes of the MD subjects (B). The dashed lines show the ±95% confidence limits for the mean sensitivity of the control monkeys.

jects were virtually identical for the two eyes, and the spectral sensitivities were within the range of variability of the control monkeys for this function. By contrast, a substantial effect on the increment-threshold function resulted from unilateral form deprivation of 2 or 8 weeks' duration.

The data from the spectral sensitivity experiments are summarized in Figures 6 and 7. The functions presented in Figure 6 show the mean data and confidence limits for the control monkeys (Fig. 6A) along with the individual functions for a bilaterally-deprived (BD-7; Fig. 6B) and a monocularly-deprived (MD-8; Fig. 6C) experimental animal. The lines superimposed on the data to clarify the organization of the functions were determined by methods previously described to model increment-threshold spectral sensitivity data. The data for the control monkeys showed the typical three-peaked shape of the photopic, increment-threshold spectral sensitivity function with an achromatic adaptation field that generally was assumed to reflect the sensitivities of opponent-color channels. The control data also indicated that the intersubject variability of the spectral sensitivity measurement, as represented by the width of the ±95% confidence limits (±0.71 log units), was considerably larger than for either the spatial or temporal contrast sensitivity measurements.

The typical shape of the increment-threshold spectral sensitivity function also was apparent in the data of both eyes of the bilaterally form-deprived monkey (Fig. 6B) but not for the deprived eye of the unilaterally form-deprived monkey (Fig. 6C; filled symbols). A comparison of the spectral sensitivity functions for these two monkeys showed significant differences in

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the effects of bilateral compared with unilateral form deprivation. The sensitivity ratio functions from these measurements are presented in Figure 7. The functions display the ratios of the mean of the sensitivity values for the control monkeys to the sensitivities of the less-affected eye (Fig. 2) of individual experimen-

Fig. 6. Increment-threshold spectral sensitivity functions for control and form deprived monkeys. Mean spectral sensitivity data for eight control subjects (O) (A). The dashed lines delineate ±95% confidence limits on the data. Spectral sensitivity functions for the right eye (O) and left eye (●) for a monkey bilaterally form deprived for 7 weeks (B). Increment-threshold spectral sensitivity functions for the nondeprived eye (O) and deprived eye (●) of a monkey unilaterally form-deprived for 8 weeks (C). Standard errors are shown when they are larger than the symbol size.

Fig. 7. The logarithm of the increment-threshold spectral sensitivity ratios for the mean of the monocular sensitivities of the control subjects to the eye with higher sensitivity for each of the bilaterally (BD)- and unilaterally (MD) form-deprived monkeys. The symbol table indicates the type of treatment and duration (in weeks) for each of the subjects. The dashed lines show the ±95% confidence limits for the mean sensitivity of the control monkeys.
tal animals (except BD-6, not used in these experiments) as a function of stimulus wavelength. The plotted data were relatively flat across the entire visible spectrum and within the 95% confidence limits of the control group. These spectral sensitivity data were in sharp contrast to the effects of early monocular form deprivation on the spectral sensitivity of the deprived eye. The data presented in Figure 6C, and our previous studies, show relatively large sensitivity deficits and alterations in the shape of the increment-threshold function for the deprived eyes of unilaterally form-deprived monkeys. Therefore, the comparison of the effects of the two types of experimental form deprivation demonstrate that the greater alterations of the neural processes involved in these monocular visual functions result more from anomalous binocular competition than from direct deprivation.

**Binocular Vision Functions**

Two measurements, binocular summation and stereodetection, were used to assess the binocular vision capabilities of the experimental animals reared with bilateral form deprivation. Binocular summation, ie, the improvement of visual performance under conditions of binocular vision compared with performance with monocular vision, was determined for both spatial and temporal modulation sensitivities. As a reference for the data from the experimental animals, the average binocular sensitivities for monkeys with normal binocular vision are presented in Figures 1A and 4A. In these figures, the squares represent the mean contrast sensitivities with binocular viewing, and the circles represent the mean sensitivities with monocular viewing. The relative positions of the data points indicate that the contrast sensitivities of the eight control subjects were higher with binocular vision than with monocular vision, an average improvement of 0.19 log units for the spatial contrast sensitivity function (Fig. 1A). Therefore, the binocular summation data for the control monkeys provide a reliable demonstration of binocular vision that may be used as a baseline for measurements of binocularity in the experimental animals.

The spatial modulation sensitivity data with binocular viewing, for each of the bilaterally form-deprived monkeys, are presented in Figure 2 (squares) along with the sensitivity data for each of the monocular viewing conditions (open and filled circles). It is apparent that the contrast sensitivities with binocular viewing were intermingled with the data for the eye with higher sensitivity for each of the monkeys. For most of the subjects, the lack of binocular summation for the spatial contrast sensitivity measurements was not surprising; the magnitudes of their interocular contrast sensitivity differences were not compatible with binocular summation for monkeys with normal binocular vision. In this respect, it is important to note that the monkey (BD-6), that had equal spatial contrast sensitivities for each eye, did not have higher sensitivities with binocular viewing compared with monocular viewing. However, for these animals, the investigation of binocular summation with temporal contrast sensitivity measurements provided a clearer indication of the presence or absence of binocularity because the monocular contrast sensitivities of all of the binocularly deprived monkeys, except BD-2, were within the range of normal variability for this measurement. The relationship between binocular and monocular viewing was quantified by the binocular summation ratios presented in Figure 8 for both the spatial and temporal modulation sensitivity functions. The summation ratios, defined as the logarithm of the ratio of the sensitivity with binocular viewing to the sensitivity of the less-affected eye at each spatial frequency, were calculated from sensitivity values derived from the fitted functions. Based on the data from the control subjects, the range of binocular summation ratios expected for animals with normal binocular vision were delineated by the 95% confidence limits, and these are marked off by the horizontal dashed lines in the two panels of Figure 8. The data for the experimental animals, for both spatial and temporal modulation sensitivity functions, clustered below the normal binocular summation confidence limits, indicating that binocular viewing did not improve visual performance above monocular vision levels for either of the measures of vision function.

The absence of functional binocular vision, suggested by the failure to find binocular summation on the contrast sensitivity task, was confirmed by investigations of stereodetection using dynamic random-dot stereograms. Stereodetection data were collected on four of the five experimental animals and one control animal. For an unknown reason, although she did well on the other parts of the experiment and was given extensive practice, the fifth experimental animal (BD-13) was unable to learn the basic detection task on the paradigm which included a paired luminance cue. Consequently, BD-13 could not be included in this part of the study of binocular vision.

Figure 9 illustrates the typical stereodetection performance, with 6 min of retinal disparity, for control and bilaterally deprived monkeys. The final detection rates for each of the animals are presented in Table 2. The control monkey (Fig. 9A) exceeded 90% detection rate with either a LED luminance cue or a grating test pattern when viewing the display without the colored filters, ie, detection based on monocular form or luminance cues. Subsequently, insertion of the ana-
glyphic filters resulted in only a minor reduction in the detection rate regardless of whether the grating was presented with crossed (ODR) or uncrossed (ODG) disparities. Additional evidence that the detection performance was based on binocular disparity cues was provided by monocular viewing trials or sessions in which the animal viewed the random-dot display with red or green filters before both eyes. For either of the control conditions, the monkey's detection rate fell to chance levels.

Figure 9B shows comparable data for one of the experimental animals (BD-16) on the stereodetection task. The initial data indicated that this monkey was able to achieve detection rates similar to those of the control monkey when the monocular cues were available. These data showed that the animal learned the behavioral task, and his responses were under stimulus control. However, in contrast with the results from the monkey with normal binocular vision, when the detection task depended on stereoscopic vision (filled symbols in ODR and ODG columns), the detection rates dropped to chance levels and remained there even with extensive practice with crossed and uncrossed disparity gratings. The results for the other three bilaterally deprived animals were similar to those of BD-16 and the final detection rates with and without associated monocular luminance cues are presented in Table 2.
A

GRATING

ODR

ODG

RED BILAT

% CORRECT

B

GRATING

ODR

ODG

BLOCK OF TRIALS
Table 2. Stereo-detection rates and standard deviations for a control monkey (NC-1) and bilaterally form-deprived monkeys (BD-2, BD-6, BD-13, BD-16)

<table>
<thead>
<tr>
<th>Subject</th>
<th>Luminance cued</th>
<th>Binocular disparity cued</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC-1</td>
<td>94.5% ± 3.5%</td>
<td>87.5% ± 7%</td>
</tr>
<tr>
<td>BD-2</td>
<td>71.0% ± 14%</td>
<td>9.5% ± 6.5%</td>
</tr>
<tr>
<td>BD-6</td>
<td>84.0% ± 8%</td>
<td>6.0% ± 5%</td>
</tr>
<tr>
<td>BD-7</td>
<td>86.0% ± 7%</td>
<td>2.0% ± 3%</td>
</tr>
<tr>
<td>BD-16</td>
<td>80.0% ± 11%</td>
<td>3.5% ± 3.5%</td>
</tr>
</tbody>
</table>

Although the interocular spatial vision asymmetries could have been a factor in reducing the stereocuities of these animals, the large matrix elements of the stereograms (3 min of arc) make it unlikely that the interocular asymmetries would have precluded stereodetection for an animal with normal binocular vision. In addition, BD-6, with normal monocular spatial contrast sensitivities for each eye, also performed the stereo task at a chance level. Based on these results, the stereodetection experiments were interpreted as showing that the period of bilateral form deprivation disrupted the normal development of stereopsis mechanisms in all of the experimental animals.

Taken together, the absence of binocular summation and the inability to detect stereotargets are strong evidence for the lack of functional binocular vision in these bilaterally form-deprived monkeys. The absence of binocular vision was not the result of an observable strabismus, and the behavioral data agreed with the results of subsequent electrophysiologic investigations of the ocular dominance of neurons in the striate cortex that showed very small numbers of binocularly driven cells.13

**Discussion**

These psychophysical investigations showed several alterations of visual function as a consequence of early, bilateral form deprivation in the primate. The most significant of these alterations occurred in the animals' spatial vision functions and binocular vision; their temporal vision and spectral sensitivity functions appeared to be relatively normal. Because deficits in spatial vision were present for both eyes of some animals, particularly the ones deprived for longer periods of time, the results demonstrate that form deprivation per se can cause functional abnormalities. However, the effects of bilateral form deprivation on spatial vision were less severe than those caused by unilateral form deprivation of similar duration. In addition, unilateral form deprivation produced deficits in temporal vision and photopic spectral sensitivity that were not present for the bilaterally form-deprived monkeys. The differences in the severity of visual deficits resulting from unilateral and bilateral form deprivation indicate that binocular competition is a more powerful force than direct deprivation in modifying visual-processing mechanisms during the sensitive period of development, i.e., when neural plasticity is present. This basic principle of development was illustrated clearly by data from MD-2 and BD-2. The former had only 2 weeks of unilateral form deprivation, from 4-6 weeks of age, and developed severe amblyopia of the deprived eye. Similarly, BD-2, who had a short period of incomplete monocular deprivation as a result of an eyelid irritation at 6 weeks of age, also developed a moderate amblyopia of the affected eye.

The rationale for using bilateral eyelid suture as the method of establishing binocular form deprivation was to produce a balanced and equal deprivation for each of the two eyes. It was, therefore, surprising to find that four of the five experimental monkeys had interocular asymmetries in their spatial contrast sensitivity functions that were outside the range of interocular differences found for normally reared, control animals. An obvious, potential explanation for the monocular deficits would be that some posttreatment factor, e.g., anisometropia or strabismus, allowed binocular competition mechanisms to influence the subsequent development of visual processes after the lids were parted. Neither of these specific conditions were observable, however, at the time of the psychophysical experiments. The subjects' refractive errors were small and approximately equal for the two eyes, and they all appeared to have normal binocular fixation with unrestricted eye movements. However, the possibility of a microstrabismus could not be excluded. It also was not possible to exclude completely the presence of some type of binocular competition during, or after, the form deprivation phase of the experiment. In this respect, a natural or surgically induced difference in the optical densities of the eyelids or an eye preference may have been factors contributing to the interocular asymmetries of the spatial modulation sensitivity functions. The possibility of residual binocular competition effects during bilateral lid suture in kittens was suggested previously. However, it is also important to note that asymmetric binocular competition influences were apparently absent for one animal, BD-6. The spatial contrast sensitivity functions were equal between this animal's two eyes and minimized for the other animals. The interocular asymmetries were much less severe than would have occurred with equal durations of unilateral form deprivation.
In addition to bilateral lid suture, rearing animals in total darkness also has been used to produce binocular visual deprivation. In the study most comparable to ours, monkeys dark reared from 2 weeks of age to 3 or 6 months of age were tested. Shortly after the end of the rearing period, the monkeys' visual acuities, measured under binocular viewing conditions with a preferential looking procedure, were about 1–2 octaves lower than those for age-matched control subjects. The visual acuities of our monkeys bilaterally deprived for 7 weeks or longer were about 1–2 octaves below the acuities of the control animals (Fig. 2). Although, under the specific conditions used in the two experiments, both dark-rearing and bilateral lid suture produced comparable sensory deficits, most of the dark-reared monkeys also developed oculomotor abnormalities (either strabismus or intermittent nystagmus) that probably contributed to the magnitudes of the sensory deficits. The occurrence of strabismus may have been related to differences in the ages at onset of deprivation (2 weeks for dark rearing versus 1 month for bilateral lid suture); deprivation-induced oculomotor anomalies are also common in monkeys form deprived within the first week of life, but not at later ages.

The patterns of visual deficits produced by bilateral form deprivation generally are similar in monkeys and cats. As in monkeys, bilaterally lid-sutured cats have deficits in spatial and temporal resolution. In both species, the reductions in photopic temporal resolution (critical fusion frequency) usually are smaller than those observed in spatial resolution, and in general, the temporal and spatial deficits associated with bilateral deprivation are milder than those produced by equivalent periods of unilateral deprivation, although there are exceptions. In both cats and monkeys, bilateral lid suture results in abnormal binocular vision even when the animals have essentially equal and normal visual acuities in each eye. There is perhaps one difference between bilateral form deprivation effects in cats and monkeys. In cats the effects of binocular form deprivation on visual acuity are greater with lid suture than dark rearing. In monkeys the two types of form deprivation appear to produce essentially equal effects. However, there is insufficient evidence to conclude that this is a true interspecies difference because the data from cats comes from comparisons using identical rearing histories and behavioral procedures. The comparative data for lid suture and dark rearing in monkeys involved somewhat different deprivation histories and behavioral techniques.

The results of our behavioral experiments agree with the results of previous physiologic investigations of bilateral form deprivation in monkeys and with the subsequent electrophysiologic data from the monkeys used in the present experiments. In essence, these electrophysiologic measures of ocular dominance showed that approximately equal numbers of cortical neurons were influenced by each of the two eyes, but few of them retained binocular inputs. The monocular sensitivity data from the behavioral experiments were compatible with such ocular dominance distributions of cortical neurons because the two eyes of the bilaterally form-deprived monkeys were equally sensitive for temporally modulated or spectral stimuli, although some interocular differences were found for spatially modulated stimuli. With respect to sensory, binocular vision processes, the absence of binocular vision may be explained readily as a result of the absence of binocularly driven neurons in the visual cortex. The correlation of the electrophysiologic and psychophysical data suggest that the development and/or maintenance of binocular vision processes require normal fusion stimulation during the sensitive period, just as the development of normal spatial vision requires adequate stimulation. Sensory, binocular vision processes of the primate appear to be extremely vulnerable to the effects of early abnormal visual experience. Our current investigation, and our previous behavioral studies on the effects of abnormal visual experience, showed that binocular vision functions, such as stereopsis and binocular summation, are affected adversely even when all of the monocular functions appear to be completely normal.

From a practical point of view, the data show that in the development of functional amblyopia, anomalous binocular competition produces more severe alterations than direct deprivation. Although direct deprivation mechanisms may produce spatial vision deficits, the deficits are milder than those produced in conjunction with anomalous binocular competition. In addition, the data suggest that if the deprivation could be balanced, the developing visual system may tolerate brief periods of bilateral occlusion without permanent monocular spatial vision defects (Fig. 2, BD-6). This situation is different from the effects of monocular occlusion where, as demonstrated by the results in BD-2, a brief period of incomplete monocular deprivation caused a substantial degree of amblyopia. Therefore, the practical application of the results of these experiments suggests that when ocular conditions in young children require occlusion as part of the treatment (except for patching treatment for amblyopia), both eyes should be occluded, even if the specific conditions affected only one eye.

These results on the effects of bilateral form deprivation in infant monkeys support several clinical observations in humans. For instance, bilateral uncorrected high hyperopia or bilateral congenital...
cataracts in humans cause bilateral amblyopia. However, brief periods of bilateral patching during infancy are without consequences for visual acuity in humans but usually have an adverse effect on stereopsis. Whether there are differences between the effects of bilateral total occlusion and the bilateral diffusion of light through closed lids must await experimental confirmation. However, it is interesting that a newborn infant treated with complete occlusion for 17 days, although developing normal visual acuity, had no stereopsis.

The relatively greater sensitivity of the immature visual system to abnormal binocular competition from unbalanced visual inputs versus bilateral form deprivation has some therapeutic implications. For example, we would predict from clinical observations and our experimental findings that brief periods of bilateral patching may prevent amblyopia from asymmetric visual inputs in infants with unilateral hyphema or vitreous hemorrhage or in those who have had one congenital cataract removed and are awaiting surgery on the other eye. Although the susceptibility of the human visual system to the effects of unbalanced visual input has been fairly well delineated by retrospective clinical studies, similar information regarding the effects of bilateral form deprivation is not available. Therefore, at this time, we do not know the duration of bilateral patching that may be tolerated before bilateral amblyopia and/or the loss of stereopsis occurs in human infants, nor at what age the visual system remains sensitive to such manipulations.

Key words: amblyopia, monkeys, animal psychophysics, contrast sensitivity, binocular vision

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References