Cortical Effects of Brief Daily Periods of Unrestricted Vision During Early Monocular Form Deprivation

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Sakai, E., H. Bi, I. Maruko, B. Zhang, J. Zheng, J. Wensveen, R. S. Harwerth, E. L. Smith III, and Y. M. Chino. Cortical effects of brief daily periods of unrestricted vision during early monocular form deprivation. J Neurophysiol 95: 2856–2865, 2006. First published February 1, 2006; doi:10.1152/jn.01265.2005. Experiencing daily brief periods of unrestricted vision during early monocular form deprivation prevents or reduces the degree of resulting amblyopia. To gain insight into the neural basis for these “protective” effects, we analyzed the monocular and binocular response properties of individual neurons in the primary visual cortex (V1) of macaque monkeys that received intermittent unrestricted vision. Microelectrode-recording experiments revealed significant decreases in the proportion of units that were dominated by the treated eye, and the magnitude of this ocular dominance imbalance was correlated with the degree of amblyopia. The sensitivity of V1 neurons to interocular spatial phase disparity was significantly reduced in all treated monkeys compared with normal adults. With unrestricted vision, however, there was a small but significant increase in overall disparity sensitivity. Binocular suppression was prevalent in monkeys with constant form deprivation. Microelectrode-recorded frequency and orientation tuning functions to determine whether specific we quantitatively examined the ocular dominance distribution of V1 units in favor of the nondeprived eye (form-deprivation amblyopia) and a dramatic shift in the ocular dominance distribution of V1 units in favor of the nondeprived eye (for reviews see Kiorpes and McKee 1999; Kiorpes and Movshon 2003; Movshon et al. 1987; Smith et al. 1997b). No clear consensus has been reached as to the extent of spatial filter deficits in animal studies. However, the nature of abnormal visual experience during early development (such as monocular form deprivation, anisometropia, or strabismus) has a large impact on how the functional circuits of the visual brain are reorganized and what is the nature of perceptual deficits that manifest (Kiorpes and McKee 1999; Kiorpes and Movshon 2003; Levi and Klein 2003). Experiencing early monocular form deprivation leads to a severe reduction of visual sensitivity in the deprived eye (form-deprivation amblyopia) and a dramatic shift in the ocular dominance distribution of V1 units in favor of the nondeprived eye (for reviews see Kiorpes and McKee 1999; Kiorpes and Movshon 2003). However, recent studies have demonstrated that daily brief periods of unrestricted vision during monocular form deprivation can prevent or greatly reduce the degree of resulting amblyopia in monkeys (Smith et al. 2002; Wensveen et al. 2005) and in cats (Mitchell et al. 2003). To understand the cortical mechanisms that are responsible for the observed “protective effects” of daily brief periods of unrestricted vision during form deprivation, we conducted microelectrode-recording experiments in V1 of monkeys that demonstrated behaviorally confirmed protective effects of unrestricted vision. Specifically we quantitatively examined the ocular dominance index and the characteristics of binocular signal interactions to define the binocular response alterations, and the spatial frequency and orientation tuning functions to determine whether spatial filter properties of individual neurons were altered. We asked which of these cortical response properties could best...
explain both the observed behavioral loss of visual sensitivity and the protective effects of unrestricted vision.

Another important question we asked was whether there was any functional or cortical recovery for the deprived eye in monkeys that experienced constant form deprivation if deprivation began a few weeks after birth (but not at birth) and normal binocular unrestricted vision was restored during the critical period of vision development in monkeys. Previous studies in ferrets and cats reported a robust recovery of cortical binocularity under similar conditions (Kind et al. 2002; Liao et al. 2004; Mitchell and Gingras 1998; Mitchell et al. 2001). In monkey V1, recovery of the functional connections from the deprived eye after monocular deprivation was possible only if reverse deprivation was imposed during the early segments of the critical period in monkeys (Blakemore et al. 1981). Resolving these apparently conflicting observations are important in our understanding of the cortical mechanisms underlying amblyopia in primates and also the protective effects of brief periods of unrestricted vision. We found that constant monocular form deprivation results in a large shift in ocular dominance distribution in favor of the nondeprived eye and also a severe amblyopia of the deprived eye (i.e., little or no recovery), but that only 1 h of unrestricted vision every day during the deprivation period dramatically improved contrast sensitivity of the deprived eye and reduced the ocular dominance imbalance in V1. Preliminary data were previously reported in abstract form (Watanabe et al. 2004).

METH O DS

All experimental and animal care procedures were in compliance with the Guiding Principles for Research Involving Animals and Human Beings and were approved by the Institutional Animal Care and Use Committee of the University of Houston.

Subjects

The details of the rearing procedures were previously described (Smith et al. 2002; Wensveen et al. 2005). Briefly, infant monkeys between 3 and 18 wk of age wore a helmet that secured a diffuser spectacle lens in front of one eye and a plano lens in front of the other eye. The diffuser lens consisted of a plano carrier lens that was covered with a commercially available occlusion foil. Measurements of spatial contrast sensitivity revealed that these diffuser lenses reduced the contrast sensitivity of normal adult humans by more than 1 log unit for gratings of spatial frequencies of 0.125 c/deg, with a cutoff spatial frequency near 1.0 c/deg. The rearing regimen included a daily period of unrestricted vision for 0 (n = 2), 1 (n = 3), 2 (n = 2), or 4 (n = 2) h. The lens removal occurred near the midpoint of the normal 12-h lighting cycle. The experimental monkeys experienced unrestricted vision between birth and 3 wk of age, and between the end of the rearing period (18 wk of age) and the microelectrode recording experiments (around 4 yr of age). Assessment of the eye alignment indicated that all of the experimental monkeys were orthotropic.

Behavioral testing

When the monkeys were ≥18 mo of age, spatial contrast sensitivity functions were determined for each eye using operant procedures (Harwerth et al. 1980; Smith et al. 1985; Wensveen et al. 2005). Substantial portions of the behavioral data were published elsewhere (Wensveen et al. 2005).

Neurophysiology

PREPARATION. The surgical preparation and recording procedures were described in detail elsewhere (Chino et al. 1997; Smith et al. 1997a). Briefly, the monkeys were anesthetized initially with an intramuscular injection of ketamine hydrochloride (15–20 mg/kg) and acepromazine maleate (0.15–0.2 mg/kg). A superficial vein was cannulated and all subsequent surgical procedures were carried out under sodium thiopental anesthesia. A tracheotomy was performed to facilitate artificial respiration and, after securing the subjects in a stereotaxic instrument, a small craniotomy and durotomy were made over the operculum of V1. After all surgical procedures were completed, the animals were paralyzed by an intravenous injection of pancuronium bromide (a loading dose of 0.1–0.2 mg/kg followed by a continuous infusion of 0.1–0.2 mg·kg⁻¹·h⁻¹) and artificially ventilated with a mixture of 59% N₂O, 39% O₂, and 2% CO₂. Anesthesia was maintained by the continuous infusion of sodium pentobarbital (2–4 mg·kg⁻¹·h⁻¹). Core body temperature was kept at 37.6°C. Cycloplegia was produced by the topical instillation of 1% atropine and the animals’ corneas were protected with rigid gas-permeable, extended-wear contact lenses. Retinoscopy was used to determine the contact lens parameters required to focus the eyes on the stimulus screens.

RECORDING AND VISUAL STIMULATION. A typical penetration (angled) was made in each hemisphere within the region representing the central 5–6°. Each penetration in V1 began at the surface and ended when the electrode entered the white matter. Thus we typically sampled through V1 at steps of about 100 μm for a distance of 2.0–2.5 mm. This sampling method was similar for all monkey groups (see Fig. 2). Tungsten-in-glass microelectrodes were used to isolate the activity from individual cortical neurons. Action potentials were extracellularly recorded and amplified using conventional technology. For each isolated neuron, the receptive fields for both eyes were mapped and its ocular dominance was initially determined using handheld stimuli (Hubel and Wiesel 1962). All receptive fields were located within 60° of the center of the fovea.

The visual stimuli were generated using Vision Research Graphics (VRG) software on a monochrome monitor (frame rate = 140 Hz; 800 × 600 pixels, mean luminance 50 cd/m²). Responses to drifting sine-wave gratings (3.1 Hz, 30–40% contrast) were measured to determine the orientation and spatial frequency tuning functions for each unit (Fig. 1, A and B). Cells were classified as simple or complex on the basis of the temporal characteristics of their responses to a drifting sine-wave gratings of the optimal spatial frequency and orientation (Skottun et al. 1991).

Data analysis

ORIENTATION TUNING. The optimal orientation and orientation bandwidth for each receptive field were determined by fitting the orientation tuning functions with wrapped Gaussian functions (Swindale 1998)

\[ G(\theta) = m_1 \sum_{\theta} \exp\left[-(\theta - m_2 + 180\theta \\Omega)^2/(2\sigma^2)\right] \]

where \( \theta \) is orientation, \( m_1 \) is amplitude, \( m_2 \) is preferred orientation, and \( \sigma \) is SD of the Gaussian function.

SPATIAL FREQUENCY TUNING. To determine each cell’s optimal spatial frequency and spatial resolution, the spatial frequency–response data were fitted with Gaussian functions (DeAnglis et al. 1993)

\[ G(m_0) = m_1 \exp\left[-(m_0 - m_3)^2/(2\sigma^2)\right] \]

where \( m_0 \) is spatial frequency, \( m_1 \) is amplitude, \( m_3 \) is optimal spatial frequency, and \( \sigma \) is SD of the Gaussian function. Spatial resolution...
of each unit was determined by locating the highest spatial frequency that evoked responses significantly higher than the average spontaneous firing of the unit (i.e., > ±2 SD).

OCULAR DOMINANCE. The ocular dominance index (ODI) of a neuron was determined with the following formula (Chino et al. 1997; Smith et al. 1997a):

$$\text{ODI} = \left( \frac{R_i - \text{noise}}{R_c - \text{noise}} \right) / \left( \frac{R_i - \text{noise}}{R_c - \text{noise}} \right)$$

where $R_i$ is the peak response amplitude for ipsilateral eye stimulation, $R_c$ is the peak response amplitude for contralateral eye stimulation, and noise is the spontaneous activity. ODI values range from 0.0 (contralateral response alone) to 1.0 (ipsilateral response alone), with 0.5 indicating perfect binocular balance.

BINOCULAR INTERACTIONS. To determine the strength and the nature of binocular interactions, responses were collected for dichoptic sine-wave gratings of the optimal spatial frequency and orientation as a function of the relative interocular spatial phase disparity of the grating pair (Fig. 1C). The sensitivity to relative interocular spatial phase disparities was quantified using a binocular interaction index that was calculated from the sine function fit to the binocular phase tuning data (BII = amplitude of the fitted sine wave/the average binocular response amplitude) (Ohzawa and Freeman 1986; Smith et al. 1997a). To characterize whether binocular signal interactions were facilitatory or suppressive in nature, the peak binocular response amplitude/dominant monocular response amplitude ratios (Peak B/M ratios) were calculated for each unit and expressed in terms of relative strength (db), i.e., 10 log Peak B/M. Negative Peak B/M values signify binocular suppression and positive values indicate binocular facilitation.

Histology

At the end of each penetration, small electrolytic lesions (5 μA, 5 s, electrode negative) were made at three points along the track in V1 for later reconstruction. Experiments were terminated by administering an overdose of sodium pentobarbital (100 mg/kg) and the animals were killed by perfusion through the heart with an aldehyde fixative. Frozen sections were stained for Nissl substance and cytochrome oxidase. The laminar distribution of individual units, obtained by a method similar to that in our previous study (Endo et al. 2000), indicated that our sampling was uniform and similar in all subject groups with respect to cortical layers (Fig. 2).

RESULTS

Unrestricted vision and contrast sensitivity functions

The representative spatial contrast sensitivity functions in Fig. 3 demonstrate the clear-cut behavioral benefits of unrestricted vision during the period of monocular form deprivation. As previously reported (e.g., Harwerth et al. 1981), the deprived eyes of a monkey reared with continuous monocular form deprivation (Fig. 3B) exhibited severe losses of contrast sensitivity and, as a result, only low spatial frequency gratings of high contrasts (<1.0 c/deg) were detected by the treated eyes of these monkeys. However, with only 1 h of unrestricted vision during the deprivation period, there was a dramatic increase in the contrast sensitivity of the deprived eye (Fig. 3C). Two hours of unrestricted vision further improved the
contrast sensitivity of the deprived eye (Fig. 3D) and 4 h of unrestricted vision eliminated interocular differences in contrast sensitivity (Fig. 3E).

Ocular dominance imbalance

Varying the duration of the period of unrestricted vision during monocular form deprivation resulted in graded increases of the proportion of V1 units dominated by the treated eye (Fig. 4). The severely amblyopic monkeys that were reared with continuous monocular form deprivation (Fig. 4B) showed obvious shifts of ocular dominance in favor of the nondeprived eyes (chi-square $\chi^2$ test, $P < 0.001$, against all groups). However, with 1 h of unrestricted vision, this imbalance in ocular dominance between the treated and nontreated eyes became significantly smaller than that for constantly deprived monkeys (Fig. 4C) ($\chi^2$ test, $P < 0.001$). The ocular dominance distribution with 2 or 4 h of unrestricted vision was relatively balanced between the two eyes and was not significantly different from that in normal adults (Fig. 4, D and E) ($\chi^2$ test, $P > 0.1$ for both treatment groups).

The observed ocular dominance imbalance was quantified for each treatment group by calculating the interocular ratios of the summed ocular imbalance indices (OII) for all units (OII = $2|ODI − 0.5|$; DeAngelis and Newsome 1999). The OII values range from 0.0 (no imbalance) to 1.0 (complete imbalance). Because the OII value does not indicate which eye is dominant but it shows only the difference in relative strength of the two eyes in driving the unit, each cell was assigned according to ODI value to either the deprived eye (ODI <0.5) or the nondeprived eye group (ODI ≥0.5). Then all OII values for each group were summed and the interocular ratio (ROI) was calculated for each subject group. The interocular ratios of the summed OII values (ROIs) for the nondeprived eye over the deprived eye indicate the relative strength of the nontreated and treated eyes in driving V1 neurons. The ROI value for the monkeys reared with continuous monocular form deprivation was 8.46 (Fig. 4B), indicating a strong dominance shift toward the nontreated eye. With 1 h of unrestricted vision during the period of form deprivation, the ROI value declined to 1.97 (Fig. 4C). Two hours of unrestricted vision had no additional effect (ROI = 2.08) (Fig. 4D). With 4 h of unrestricted vision, the ocular dominance distribution and the ROI values were similar to those from normal monkeys (1.46 vs. 1.45) (Fig. 4E).

The degree of amblyopia for each treatment group, expressed as a reduction in the contrast sensitivity of the deprived eye (Fig. 3D) and 4 h of unrestricted vision eliminated interocular differences in contrast sensitivity (Fig. 3E).
binocular interaction index (BII), was drastically reduced both in simple and complex cells compared with those in normal monkeys (one-way ANOVA, \( P < 0.001 \)) (Fig. 6). With 1 h of unrestricted vision, there were small but significant increases in the phase sensitivity of both simple and complex neurons compared with monkeys with continuous deprivation (one-way ANOVA, \( P < 0.01 \) for simple and \( P < 0.001 \) for complex). However, longer periods of unrestricted vision had no or little additional effects on the phase sensitivity of simple or complex cells and, consequently, V1 neurons in all of the form-deprived monkeys, regardless of the duration of unrestricted vision, showed significant reductions in disparity sensitivity compared with normal monkeys (one-way ANOVA, \( P < 0.01 \) for simple cells, \( P < 0.05 \) for complex cells).

Reductions in facilitatory binocular interactions and/or aberrant increases in suppressive binocular interactions are commonly observed in the visual cortices of monkeys that experience strabismus early in life (e.g., Kumagami et al. 2000; Mori et al. 2002; Smith et al. 1997b; Zhang et al. 2005b). We compared the amplitudes of binocular and monocular responses of individual units to determine the peak binocular over monocular response ratios and also the percentage of units exhibiting interocular suppression (i.e., binocular response amplitude < monocular amplitude) (Fig. 7).

For simple cells, the mean (±SE) peak binocular/monocular response ratios (Fig. 7A, left) and the percentage of suppressive units (Fig. 7B, left) for all of the treated monkey groups were similar to those in normal monkeys (one-way ANOVA, \( P > 0.05 \); \( \chi^2 \) test, \( P > 0.10 \)). For complex cells, however, the peak binocular/monocular response ratios were significantly reduced in monkeys reared with continuous form deprivation compared with those in normal monkeys (one-way ANOVA, \( P < 0.01 \)) (Fig. 7A, right). Unrestricted vision had significant protective effects, i.e., the mean binocular/monocular response
Monocular response properties of V1 units

Degradation of the spatial response properties of V1 neurons has often been speculated to be one of the major underlying causes of amblyopia (Kiorpes and McKee 1999; Kiorpes et al. 1998; Movshon et al. 1987). Therefore we asked whether the monocular spatial response properties of V1 neurons were abnormal in our treated monkeys when the treated eye was stimulated. To ensure complete interocular comparisons of these response properties, we divided cells into three categories according to their ocular dominance index values and the orderliness of tuning functions (Fig. 8, A–C).

“Monocular units” (ODI = 0.0–0.2 or 0.8–1.0) had no quantifiable responses in one eye (Fig. 8A). Open squares in the scatterplot of Fig. 9 show the optimal spatial frequency (Fig. 9A), spatial resolution (Fig. 9B), and orientation selectivity (Fig. 9C) of these individual monocular units. For those units we determined whether there were interocular differences in the group means for the dominant-eye responses (filled symbols along the axes in Fig. 9). There were no significant interocular differences in the spatial or orientation tuning of these units in any of our treated monkeys (one-way ANOVA, \( P > 0.1 \)).

A substantial percentage of units, including those in monkeys reared with constant monocular form deprivation, responded to stimulation of either eye (ODI = 0.3–0.7). The majority of these units exhibited orderly tuning functions by both eyes that could be fit with Gaussian functions (Fig. 8B). This made possible the direct interocular comparisons of the tuning characteristics for each unit. The open circles in the scatterplots in Fig. 9 show the interocular comparisons of the optimal spatial frequency (Fig. 9A), spatial resolution (Fig. 9B), and orientation selectivity (Fig. 9C) of individual binocular units (ODI = 0.3–0.7). The mean (±SE) values for the treated and untreated eyes for binocular units are indicated by the filled symbols.

In the monkeys reared with constant monocular form deprivation, there was not an overabundance of binocular units exhibiting higher optimal spatial frequencies (Fig. 9A) or imbalance in the mean optimal spatial frequency in favor of the nondeprived eye (paired \( t \)-test, \( P > 0.05 \)). Also the mean optimal spatial frequencies for monocular units were nearly the same in both eyes for all treated monkeys. Similar results were found for spatial resolution (paired \( t \)-test, \( P > 0.05 \)) (Fig. 9B). However, note that the mean spatial resolutions for units in monkeys with constant form deprivation were significantly lower in both eyes than in normal monkeys (one-way ANOVA, \( P < 0.01 \)). The interocular comparisons of orientation bandwidth in each unit (Fig. 9C) yielded very similar results, i.e., there were no significant interocular differences in the orientation tuning characteristics of neurons between any monkey group (paired \( t \)-test, \( P > 0.1 \)).

FIG. 7. Effects of the duration of unrestricted vision during early monocular form deprivation on (A) the mean ± SE (open circles) and median (open triangles) peak binocular/monocular response ratios, and (B) the proportion of interocularly suppressive units (Peak B/M < 0.0 db). Left column: simple cells. Right column: complex cells.
A small percentage of binocular units in the treated monkeys (10–20%) had inconsistent tuning in one eye that could not be fit with any function and therefore interocular comparisons were not possible in these units (Fig. 8C). In monkeys reared with constant form deprivation (0 h), these inconsistent tuning functions were more frequently encountered when the deprived eye was stimulated (Fig. 8D).

**DISCUSSION**

The main findings of this study were that the severity of amblyopia and the “protective” effects of unrestricted vision during monocular form deprivation were correlated with the magnitude of the ocular dominance imbalance of V1 neurons, and that the monocular responses to stimulation of the treated eye were largely normal when the firing rates of a neurons were significantly above the noise levels.

The latter finding is somewhat surprising in light of the previous reports that the spatial filter properties of V1 neurons were degraded in the treated eyes of monkeys reared with chronic monocular atropinization (Movshon et al. 1987) and in the treated eyes of monkeys that experienced surgically imposed strabismus and/or optically induced anisometropia early in life (Kiorpes et al. 1998). Although we found a relatively small number of cells that had degraded spatial filter properties in monkeys reared with constant form deprivation (Fig. 8C and D), these units were the exceptions (8/47 in constantly deprived monkeys) and were not likely to have been a primary cause of amblyopia in these monkeys. As previously pointed out, differences in the nature of abnormal visual experience during early development have a large impact on how the functional circuits of the visual brain are reorganized and the nature of manifest perceptual deficits. It is important to recognize that in monocularly form deprived monkeys the deprived eye is put at a competitive disadvantage at the onset of deprivation and the resulting loss of the functional connections from the deprived eyes are rapid and overwhelming (e.g., in monkeys: Blakemore and Vital-Durand 1981; in cats: Trachtenberg et al. 2000). In contrast, the functional connections in V1 for the treated eyes of either anisometropic or strabismic monkeys are rarely lost, although the percentage of binocularly driven V1 units are drastically reduced in those monkeys (Kiorpes et al. 1998; Kumagami et al. 2000; Mori et al. 2002; Smith et al. 1997b; Zhang et al. 2003). Thus the long-term blur in the treated eyes of anisometropic and strabismic monkeys may degrade the spatial properties of V1 units rather than rapidly disconnecting the input from the disadvantaged eye. Interestingly, a consensus is emerging that the monocular spatial filter deficits in V1 neurons are relatively small even for anisometropic or strabismic amblyopia, and that there are far more severe alterations in neurons beyond V1 that may correlate better with the perceptual abnormalities associated with amblyopia (Kiorpes and McKee 1999; Kiorpes et al. 1998).

**Significance of normal vision before deprivation**

In monocularly form deprived ferrets, the binocularity and orientation selectivity of V1 neurons were restored by experiencing normal binocular vision during or even after the critical period of cortical binocularity (i.e., without reverse depriva-
the early monocular form deprivation (Liao et al. 2002, 2004). However, the same investigators found little or no recovery if monocular deprivation began at eye opening, although “normal” binocular visual experience was allowed during the critical period of binocular vision for ferrets. Thus brief periods of normal visual experience before the onset of abnormal visual experience appear to be a fundamental requirement for the potential recovery from monocular deprivation.

Apparently normal binocular visual experience before form deprivation firmly establishes “some sort of marker” of the functional connections in V1 that are present before or at birth and such markers, which were presumably “suppressed” by monocular form deprivation, are reactivated by subsequent “normal visual experience” (Chalupa 2004). Also these observations in ferrets were interpreted as evidence for the existence of “different mechanisms for the loss and recovery of binocularity in visual cortex” (in cats: Kind et al. 2002; in ferrets: Liao et al. 2002) and challenged the classic theory of competitive synaptic mechanisms for ocular dominance plasticity (Blakemore et al. 1981; Wiesel and Hubel 1965). However, in our monkeys that were reared with constant monocular form deprivation from 3 wk of age, cortical binocularity did not recover, although normal unrestricted vision was restored during the height of the critical period of binocular vision in monkeys (Harwerth et al. 1983). These contrasting results between ferrets and monkeys highlight the potential importance of species differences in the maturational status of visual cortex at birth (Chino et al. 1997; Horton and Hocking 1996; Issa et al. 1999) and of cortical plasticity near birth.

There is another reason for the significance of normal vision before the deprivation for our monkeys. Specifically form deprivation from birth (e.g., alternating monocular form deprivation or binocular deprivation) is known to produce strabismus in monkeys (Mustari et al. 2001). Persistent ocular mis-

**FIG. 9.** Effects of the duration of unrestricted vision during early monocular form deprivation on the monocular response properties of V1 neurons. Interocular comparisons of the tuning functions of “binocular units” (open circles) (ODI = 0.3–0.7) for optimal spatial frequency (A), spatial resolution (B), and orientation bandwidth (C). Filled symbols show mean values (±SE). Open squares on x- and y-axes indicate comparable data for “monocular units” (ODI = 0.0–0.2 or 0.8–1.0). Filled symbols along x- and y-axes show mean values (±SE) for monocular units. Durations of unrestricted vision are indicated at the top.
alignment would drastically reduce or eliminate the possibility of functional recovery (e.g., Kind et al. 2002). In this study, monocular form deprivation was activated at around 3 wk of age. This rearing strategy prevented our infant monkeys from developing ocular misalignments and allowed binocularly correlated input signals to V1 during the brief daily periods of unrestricted vision.

Mechanisms underlying protective effects

The simplest explanation for the observed protective effects on behavior and V1 neurophysiology is that brief periods of daily unrestricted vision reinforced the integrity of the functional connections from the deprived eye by providing binocularly correlated inputs to individual V1 neurons. In this respect, our results on binocular suppression provide an important insight into the observed protective effects. We found that, although constant form deprivation resulted in a high prevalence of binocular suppression in V1, 1 h of daily unrestricted vision dramatically reduced this suppression (Fig. 7). Thus this reduction of binocular suppression brought about by brief periods of unrestricted vision was apparently a key neural factor in “reactivating” the functional connections from the deprived eye. When the strength of suppression is reduced to a certain level (a “threshold” level), normal visual input by the deprived eye is permitted to exert protective effects, i.e., strengthening the functional connections for periods of time each day.

Because the treated monkeys experienced over 3 yr of “normal” vision following the diffuser lens-rearing regimen (during which behavioral testing was given for 2 yr), spontaneous “recovery” after the lens rearing may have caused an overestimation of the protective effects of brief daily unrestricted vision. However, the effects of posttreatment normal vision, if any, are likely to have been negligible. The periods of unrestricted visual experience after the lens treatment were the same for all treatment groups, including monkeys that experienced continuous monocular form deprivation. Moreover, we previously found in monkeys reared with early optical strabismus that over 3 yr of normal visual experience after the removal of prisms resulted in little or no significant recovery in the binocular response properties of V1 neurons (see Kumagami et al. 2000; Mori et al. 2002; Smith et al. 1997b; Zhang et al. 2005b). Although the nature of early binocular imbalance is different between the present and previous studies, our earlier results support the conclusion that the “protective effects” of brief normal vision in this study were largely unaffected by potential spontaneous recovery.

Functional implications

The results of this study have important implications for infant vision development. Our results suggest that, although continuous monocular form deprivation during the critical period, even for short periods, can cause a severe amblyopia (Harwerth et al. 1981, 1986), only a few hours of daily unrestricted vision during form deprivation can prevent or substantially reduce the degree of amblyopia. Our results imply that lifting a drooping eyelid or having infants with a severe case of anisometropes wear corrective lenses for even brief periods every day may have substantial beneficial effects (Wensveen et al. 2005).

Although intermittent, brief periods of normal binocular vision are very beneficial in preventing amblyopia, the results from our binocular interaction experiments (Figs. 6 and 7) suggest that fine binocular vision (e.g., stereopsis) was not likely to have been spared even with 4 h of unrestricted vision. Our experimental monkeys were not behaviorally tested for stereocuity or for the binocular summation of contrast sensitivity. It is important to note that even 4 h of daily unrestricted vision, although sufficient to maintain a near normal ocular dominance distribution, did not prevent the breakdown of the cortical circuits that are necessary for disparity sensitivity or normal binocular facilitation. These results highlight the extremely fragile nature of developing binocular cortical circuits soon after birth (Kumagami et al. 2000; Mori et al. 2002; Smith et al. 1997b; Zhang et al. 2005b).

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References


