Visual Neuroscience (2002), **19**, 85–96. Printed in the USA.

DOI: 10.1017.S095252380119108X

Topographic map reorganization in cat area 17 after early monocular retinal lesions

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(RECEIVED May 21, 2001; ACCEPTED December 10, 2001)

Abstract

Neither discrete peripheral retinal lesions nor the normal optic disk produces obvious holes in one's percept of the world because the visual brain appears to perceptually "fill in" these blind spots. Where in the visual brain or how this filling in occurs is not well understood. A prevailing hypothesis states that topographic map of visual cortex reorganizes after retinal lesions, which "sews up" the hole in the topographic map representing the deprived area of cortex (cortical scotoma) and may lead to perceptual filling in. Since the map reorganization does not typically occur unless retinotopically matched lesions are made in both eyes, we investigated the conditions in which monocular retinal lesions can induce comparable map reorganization. We found that following monocular retinal lesions, deprived neurons in cat area 17 can acquire new receptive fields if the lesion occurred relatively early in life (8 weeks of age) and the lesioned cats experienced a substantial period of recovery (>3 years). Quantitative determination of the monocular and binocular response properties of reactivated units indicated that responses to the lesioned eye for such neurons were remarkably robust, and that the receptive-field properties for the two eyes were generally similar. Moreover, excitatory or inhibitory binocular interactions were found in the majority of experimental units when the two eyes were activated together. These results are consistent with the hypothesis that map reorganization after monocular retinal lesions require experience-dependent plasticity and may be involved in the perceptual filling in of blind spots due to retinal lesions early in life.

Keywords: Topographic map reorganization, Area 17, Retinal lesions, Cats, Filling-in

Introduction

Although the topographic map in the visual cortex in adult cats and monkeys are known to reorganize after being totally deprived of their normal sources of retinal activation (Kaas et al., 1990; Chino et al., 1992, 1995; Gilbert & Wiesel, 1992; Darian-Smith & Gilbert, 1994, 1995; Chino, 1997), a deprivation of feedforward signals from a small restricted region of the retina (<7 deg) in *one* eye typically leaves deprived neurons in area 17 of adult cats responsive only to the nonlesioned eye when tested monocularly (Chino et al., 1992; Gilbert & Wiesel, 1992; Darian-Smith & Gilbert, 1995; Chino, 1997). Under some conditions, visual responses to the lesioned eye have been reported (Calford et al., 2000), although these responses to the lesioned eye appear to be weaker and more variable than those to the normal eye and depend heavily on the conditions of testing.

In this study, we asked whether we could produce conditions where neurons that had their normal afferent inputs eliminated from one eye would reliably respond to each eye under *monocular* testing conditions, and if so, how would the responses to each eye compare and how would the signals from the two eyes interact when both eyes are stimulated together. We felt that the results of a successful study would relate importantly to efforts to understand the mechanisms and modes of visual cortex plasticity, as well as suggest what happens in the visual cortex of many humans with monocular lesions of the retina that occur at birth or early in life.

Our experiments were designed to maximize the probability that monocularly deafferentated neurons would acquire new receptive fields, and to mimic certain conditions that are common to an early pathological lesion in the retina. Specifically, we monocularly deprived cortical neurons of feedforward activity by placing a restricted lesion in the retina at 8 weeks of age when the visual system is known to be relatively stable but well within the traditionally defined "critical period" for modifying the cortical substrate for binocular vision in cats (Daw, 1995). Because plastic changes in sensory systems may continue to emerge after many months (Kaas et al., 1990; Chino et al., 1992, 1995; Gilbert & Wiesel, 1992; Darian-Smith & Gilbert, 1994, 1995; Chino, 1997,

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1999) or possibly even years of recovery, we waited 3 years to record from cortex. We found that monocularly deprived neurons acquired new receptive fields that were generally similar to those in the nonlesioned eye even when the sources of activation were retinotopically mismatched. The overall responsiveness of the newly acquired receptive fields were surprisingly robust, but their peak firing rate and contrast sensitivity were substantially lower in many of the reorganized units compared to the responsiveness of the normal receptive fields for the nonlesioned eye. Facilitatory or suppressive binocular signal interactions were found between the lesioned and nonlesioned eyes when the new receptive fields and the normal receptive fields were stimulated together.

Methods

Subjects and retinal lesion

Three domestic kittens received a unilateral retinal lesion and two kittens received retinotopically matched bilateral lesions at 8 weeks of age. An Argon blue/green laser (HGM Model PC) was used to make retinal lesions under anesthesia [ketamine hydrochloride (30 mg/kg)/xylazine (4 mg/kg) mixture] (Chino et al., 1995). The lesions (about 1 mm in diameter and subtended about 5 deg in visual angle) were located in the nasal retina centered about 5–7 deg from the center of the area centralis (Fig. 1A). The animals were maintained in normal visual environment for over 3 years prior to the recording experiments. Five normal adult cats that did not receive laser lesions served as controls in the binocular interaction experiments.

Neurophysiology

We employed extracellular single- or multi-unit recording methods to map cortical topography and investigated the receptive-field properties of individual cortical neurons (see Chino et al., 1995). Briefly, the cats were initially anesthetized with an intramuscular injection of ketamine hydrochloride (15–20 mg/kg) and acepromazine maleate (0.15–0.2 mg/kg) and a superficial vein was cannulated. All subsequent surgical procedures including a tracheotomy and a small craniotomy and durotomy were carried out under sodium thiopental (2.5% solution) anesthesia. Following all surgical procedures, the animals were paralyzed by an intravenous infusion (IV) of pancuronium bromide (a loading dose of 0.1–0.2 mg/kg followed by a continuous infusion at the rate of 0.1–0.2 mg/kg/h). The animals were artificially respired with a mixture of 59% N_2O, 39% O_2, and 2% CO_2 to maintain an end-tidal CO_2 between 4.0% and 4.5%. Their core body temperature was kept at 37.6°C. Throughout the recording session, the anesthesia was monitored and maintained by the continuous IV infusion of sodium pentobarbital (2–4 mg/kg/h). Cycloplegia was produced by 1% atropine sulfate and the animal's 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. Tungsten-in-glass microelectrodes were used to record activity from single or multiple cortical neurons. Action potentials were extracellularly recorded and amplified using conventional technology.

Mapping procedures

We optically projected the experimental retinal lesion on the tangent screen, which appeared as a clear dark circle primarily due to damage to the tapetum (Fig. 1A). The visible borders of the projected lesions were distinct and matched well with the extent of retinal damage. Multi-unit activity was recorded at about 200-μm intervals over the 6–7 mm distance of each penetration along the medial bank (Fig. 1C). The receptive fields of units were mapped for both eyes using hand-held stimuli. The penetrations were spaced 500–1000 μm apart on the cortical surface. At each site, the minimum response field was mapped on the tangent screen with hand-held stimuli (Fig. 1B). The A-P and M-L coordinates for penetrations were systematically altered to cover the visual field in the superior to inferior direction around the deactivated zone.

Receptive-field properties

We isolated activity from individual neurons in the reactivated zones. The neuron's responses, converted into standard pulses by a window discriminator, were sampled at a rate of 100 Hz (10-ms bin widths) by a lab-computer and compiled into peristimulus time histograms (PSTHs) that were equal in duration to, and synchronized with, the temporal cycle of the sine-wave grating. The amplitudes and phases of the temporal response components in the PSTHs were determined by Fourier analysis. In all experiments, the stimuli were presented multiple times in a randomly ordered sequence. These procedures were followed by quantitative measurements using drifting sine-wave gratings (temporal frequency = 3.1 Hz; contrast = 0.3–0.5).

Orientation tuning characteristics (i.e. the preferred orientation and tuning bandwidth) were determined by measuring the orientation response functions at 12 different orientations with a near-optimal spatial frequency and fitting each function with the following equation (Swindale, 1998):

$$G(\theta) = m_1 * \sum_{n=-\infty}^{n=+\infty} \exp[-(\theta - m_2 + n * 180)^2/(2 * m_3^2)],$$

where θ is the orientation, m_1 is the amplitude, m_2 is the preferred orientation, and m_3 is the standard deviation of the Gaussian function.

The orientation bandwidth was measured at the response level equal to one-half the maximum response amplitude.

Spatial-frequency response functions were measured using the preferred orientation and the preferred drift direction. The cell's optimal spatial frequency was determined by fitting each spatial-frequency response function with the following equation (DeAngelis et al., 1995):

$$G(m_0) = m_1 * \exp[-(m_0 - m_2)^2/(2 * m_3^2)],$$

where m_0 is the spatial frequency, m_1 is the amplitude, m_2 is the optimal spatial frequency, and m_3 is the standard deviation of the Gaussian function. In seven out of 29 reorganized units that were quantitatively analyzed, the response functions for the lesioned eye could not be adequately fit because of low firing rates and/or irregular tunings, although the new receptive fields for the lesioned eye could be mapped without difficulty using a hand-held stimuli. The data from these units could not be included in Figs. 2, 3, and 6.

Binocular response properties were investigated with a pair of sine-wave gratings. The details of the methods for determining the nature of binocular signal interactions can be found elsewhere (Chino et al., 1994, 1997; Smith et al., 1997). Briefly, responses were collected for dichoptic sine-wave gratings of the optimal spatial frequency and orientation for the nonlesioned eye as a function of the relative interocular spatial phase for the grating

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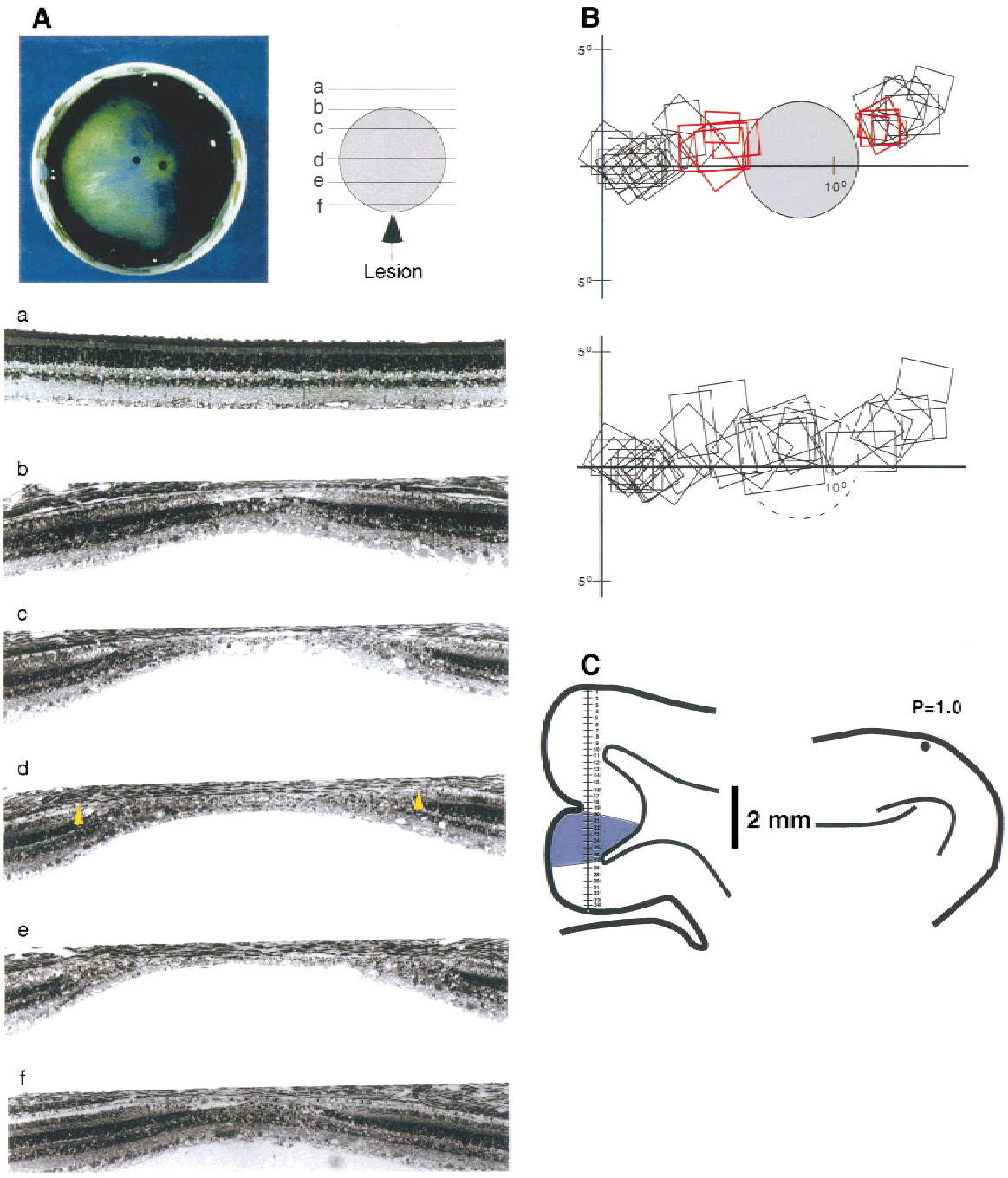

Fig. 1. Topographic map reorganization in area 17 following an early onset unilateral lesion in retina. **A:** The extent of retinal damage. Photograph of an eye with an experimental lesion in one cat (top left). The small retinal lesion (the small "hole" to the left of the optic disk and approximately 5 deg in diameter) was located in the nasal retina. Diagram illustrating the approximate locations of the retinal cross sections shown below (a–f) (top right). The extent of damage caused by the laser burn (bottom). Note that retinal damage occurred in all retinal layers including the ganglion cell layer. Arrows indicate the edges of the burn in the tapetum. **B:** Topographic maps of area 17 following 3 years of recovery. The map on the top was obtained for the lesioned eye (see Fig. 1C for the locations). The shaded circles represent the optically projected laser burn which corresponded well to the area of the visual field that was deprived of feedforward input due to the retinal lesion ("cortical scotoma"). Receptive fields with thick red lines represent the newly activated fields. The map on the bottom shows the receptive fields of the same units mapped for the nonlesioned eye. The circle with the dotted line indicate the area that retinotopically matched the cortical scotoma in the lesioned eye. **C:** Diagram illustrating a typical penetration through the medial bank of the postlateral gyrus (left). The blue shaded area roughly corresponds to the zone of the cortex which was deprived of the feedforward input from the lesioned eye. Top view of the left postlateral gyrus of the cat showing the approximate location of the penetration that resulted in the topographic maps in 1B (right).

pair. In addition, monocular stimuli for each eye and one zero-contrast control were included in each stimulus parameter file. For descriptive and analytical purposes, a single cycle of a sine wave was fit to each neuron's phase tuning function. The amplitude of the fitted sine wave was used to calculate the degree of binocular interaction (*BII*, binocular interaction index = amplitude of the fitted sine wave/the average response amplitude). To determine whether binocular signal interactions were excitatory or inhibitory in nature, the ratios of the mean binocular response amplitudes over the dominant monocular response amplitude (*B/M*) were calculated for each unit.

Histology

At the end of the recording experiments, the animals were given an overdose of sodium pentobarbital (80–100 mg/kg, IV) and perfused through the heart initially with saline and, then, with a mixture of 2% paraformaldehyde and 0.5% glutaraldyde in 0.1 M phosphate buffer (pH = 7.4). The eyes were enucleated, opened by an encircling cut, and the posterior eyecups were immersed in the fixative. After a few days, the eyecups were sectioned into a smaller piece which included the experimental lesion. The tissue was then dehydrated and infiltrated with Spurr's resin and hardened in molds. The embedded tissue was sectioned at 2 μm outside the lesion and at every 1 μm through the lesioned area. Sections were mounted and stained with Toludine blue to determine the extent of retinal cell damage.

To assess the extent of cell damage in the retina, on a series of sections made through the lesioned area, we first measured the largest retinal distance covered by the lesion of the retinal ganglion cell layer. Then, we examined individual retinal ganglion cells around the edge of the lesion for possible signs of neuronal damage (e.g. swelling or shrinkage, reduction of stained Nissl bodies, and/or more obvious structural disintegration).

Results

Retinal lesions and topographic map reorganization in area 17

In all three subjects, new receptive fields were acquired by monocularly deprived neurons. Data for a representative animal are illustrated in Fig. 1. The unilateral retinal lesion was about 1 mm in diameter and extended through all neuronal layers including the ganglion cell layer (Fig. 1A). The nature of the tissue damage due to a laser lesion in 8-week-old kittens was very similar to that in adult cats (see Figs. 1 & 2 in Chino et al., 1995). This retinal lesion created a small circular hole in the cortical topographic representation of visual space (cortical scotoma) in which no receptive fields could be mapped for the lesioned eye (shaded circle in Fig. 1B). However, in all electrode penetrations that entered the cortical scotoma (Fig. 1C), receptive fields could be mapped for the lesioned eye at the great majority of recording sites (i.e. no silent areas were found). Units that would have normally received feedforward signals from the damaged retinal region had acquired new receptive fields at the edge of the cortical scotoma.

Specifically, in each penetration, as our electrode advanced along the medial wall of the postlateral gyrus (Fig. 1C), receptive fields could be mapped through either eye and receptive-field locations progressed systematically toward the periphery until the edge of the projected retinal lesion was encountered (Fig. 1B). With further electrode advancements, the normal shift of receptive fields occurred only for the nonlesioned eye (Fig. 1B, bottom), while no receptive fields were mapped for the lesioned eye inside the projected cortical scotoma area. Instead, because of topographic reorganization, the movement of our electrode into the monocularly deafferentated cortical zone resulted in a pile up of receptive fields at both the central and peripheral edges of the scotoma (Fig. 1B, top). The reorganization involved an area about 2 mm in cortical distance (Fig. 1C). In other penetrations, new receptive fields appeared and progressed along the upper or lower edges of the scotoma as electrodes advanced. In all cases, unlike in normal zone, measurable distances developed (i.e. retinotopic mismatch) between the receptive fields of individual units between the two eyes. Thus, the nature of the map reorganization in these cats with the early unilateral retinal lesions was very similar to that found in area 17 of cats and monkeys with the adult onset *bilateral* retinal lesions (Chino et al., 1992; Gilbert & Wiesel, 1992; Darian-Smith & Gilbert, 1995; Kaas et al., 1990; Chino, 1997).

Monocular response properties

Whether or not these reactivated neurons can influence visual functions depends on how well these neurons can respond to visual stimuli and whether their tuning properties are normal. Because the majority of cortical neurons in normally reared cats can be activated by either eye and the receptive fields for the two eyes show very similar tuning properties and stimulus preferences (Hubel & Wiesel, 1962: Ohzawa & Freeman, 1986; Chino et al., 1994), we asked whether the newly activated receptive fields mapped for the lesioned eye were functionally similar to those mapped for the nonlesioned eye.

Orientation response functions

Fig. 2A shows the orientation response functions of a complex cell located in the reorganized cortical zone. The preferred stimulus orientation and bandwidth for its newly activated receptive field (left) were similar to those found for the nonlesioned eye (right). The plots in Fig. 2B (top left) compare the preferred orientations of the recovered receptive fields in the lesioned eye with those of the normal receptive fields in the nonlesioned eye for all units. The preferred orientations were very similar between the two eyes in the great majority of our sample neurons for both the reorganized ($r = 0.96$, $P < 0.001$) and normal zone of cortex (top right) ($r = 0.96$, $P < 0.001$). However, their orientation bandwidths (Fig. 2B, bottom) were not as well matched between the two eyes ($r = 0.38$ for reorganized units and $r = 0.56$ for units in normal zone, $P < 0.05$). There were no significant differences in the average orientation bandwidths between the two eyes in either the reorganized or normal zone of cortex (One-way ANOVA, $P = 0.1$).

Spatial-frequency response functions

Fig. 3A illustrates the spatial-frequency response functions of a complex cell found in the reorganized zone of cortex. The newly activated receptive field of this unit for the lesioned eye (left) showed very similar tuning properties to that of the normal receptive field for the nonlesioned eye (right). The plots in Fig. 3B (top), which compare the optimal spatial frequencies of sample units between the two eyes, indicate that the new and old receptive fields have similar optimal spatial frequencies in the reorganized cortex (left) ($r = 0.72$, $P < 0.001$). The optimal spatial frequencies of units in the normal zone of cortex showed a comparable match between the right and left eyes (right) ($r = 0.61$, $P < 0.005$).

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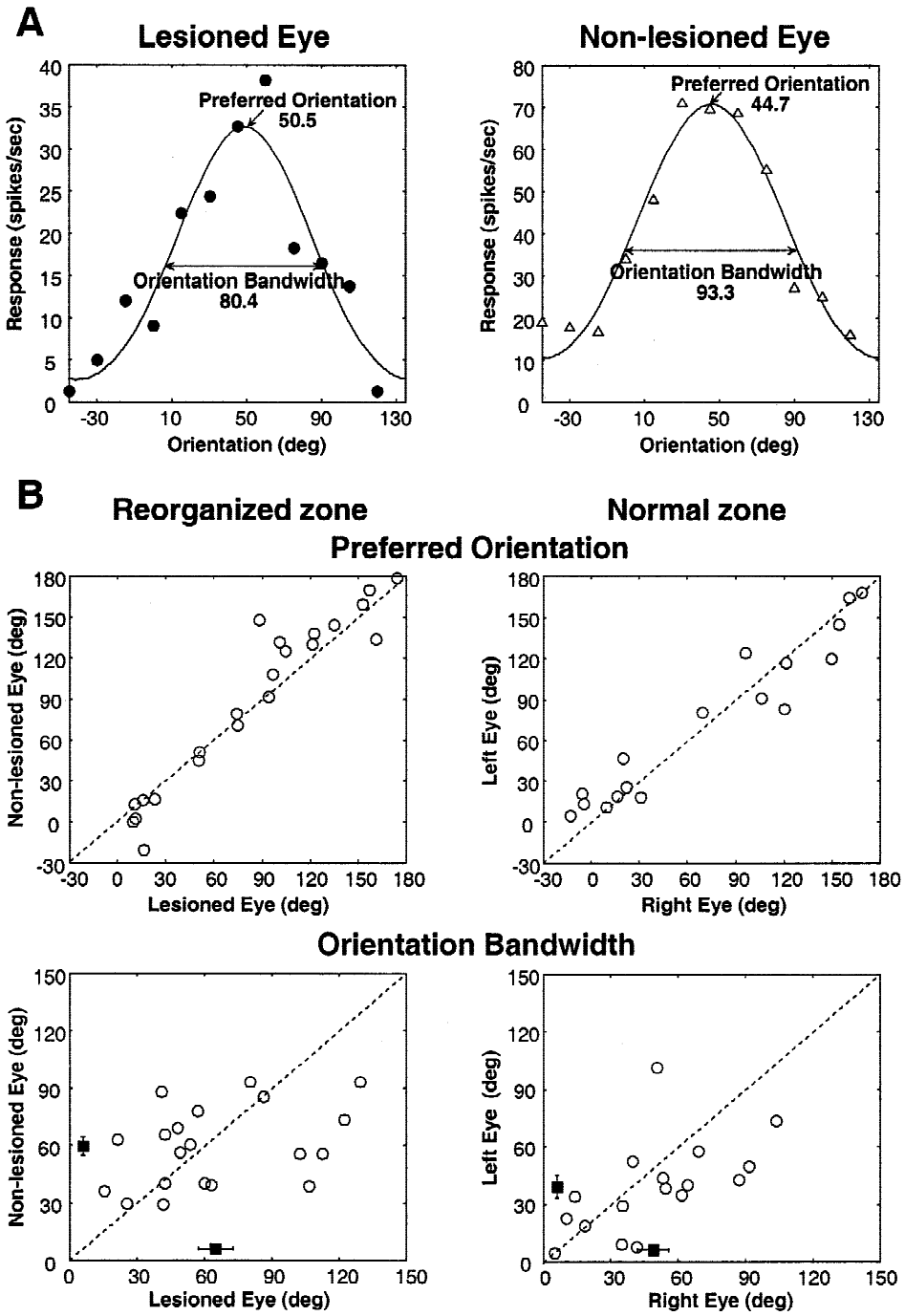

Fig. 2. Orientation tuning of reorganized units. A: Orientation response functions of a complex cell recorded in the reorganized zone are shown for the lesioned (left) and nonlesioned eyes (right). B: Scatter plot comparing the preferred orientations of individual units between the receptive fields mapped for the lesioned and nonlesioned eyes (top left). Similar plot for units in the normal zone (top right). Scatter plot illustrating the relationship between the orientation bandwidths (bandwidth in degrees at the half amplitudes of the orientation tuning functions) for the lesioned and nonlesioned eyes (bottom left). Similar plot for units in the normal zone (bottom right). Mean (±SE) orientation bandwidths are indicated with filled symbols.

The middle panels of Fig. 3B (left) show that the spatial resolutions of the new receptive fields were not substantially different from those of the normal receptive fields of the reorganized units ($r = 0.72$, $P < 0.001$). Not surprisingly, units in the normal zone of cortex (right) showed similar spatial resolutions between the two eyes ($r = 0.61$, $P < 0.005$). The spatial-frequency bandwidths of the new receptive fields (Fig. 3B, bottom) were relatively well matched to those for the nonlesioned eye (left) ($r = 0.62$, $P < 0.005$). A similar match between the two eyes was found for units in the normal cortical zones (right) ($r = 0.65$, $P < 0.005$).

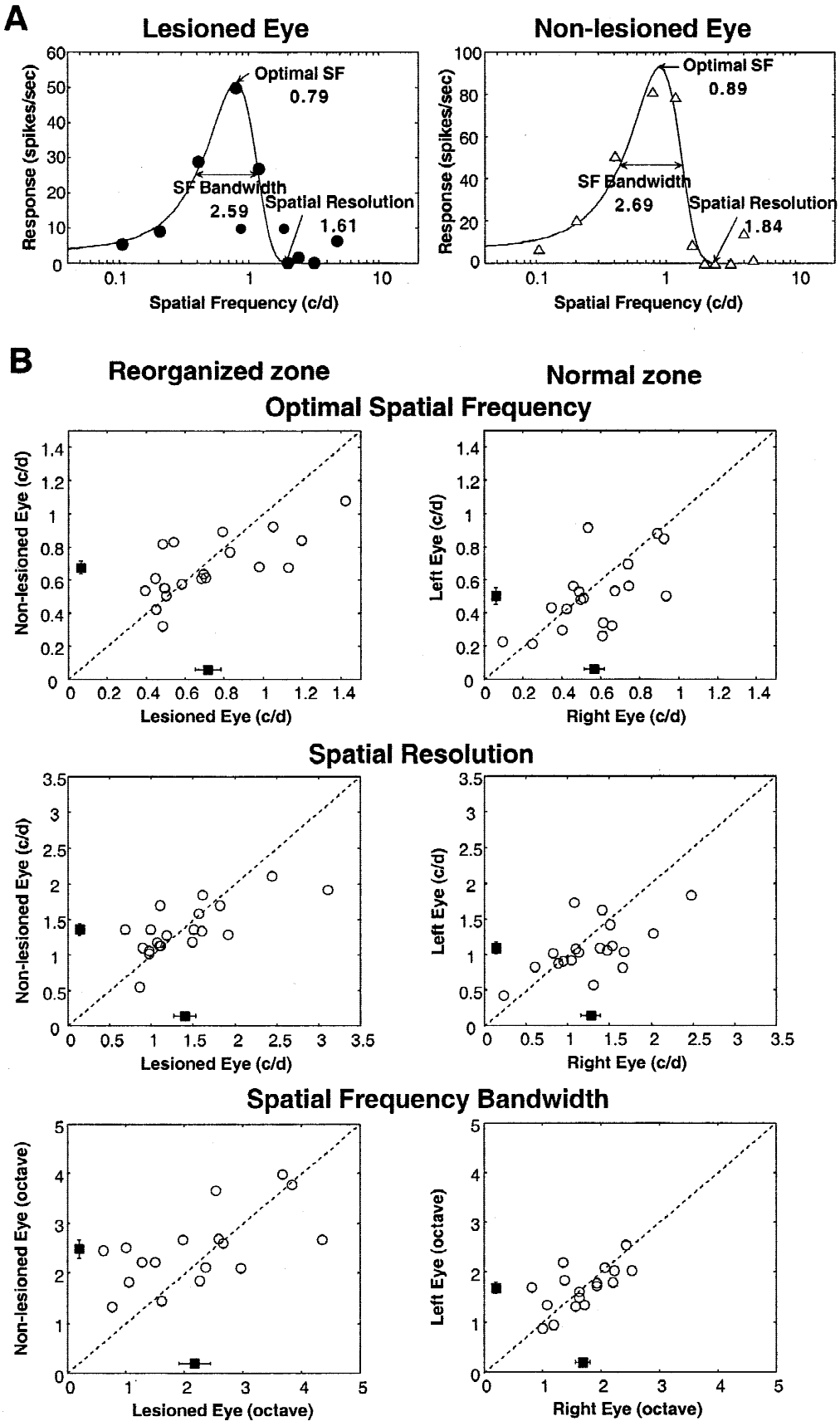

Fig. 3.

No significant interocular differences were found for the mean optimal spatial frequencies, spatial resolutions, or spatial-frequency bandwidths in either reorganized units or units in the normal cortical zone (One-way ANOVA, $P > 0.1$).

These results are consistent with the idea that map reorganization following early retinal lesions results from the activation of normally subthreshold long-range horizontal connections within the visual cortex that are known to functionally interconnect neurons that have similar stimulus preferences (Chino et al., 1995; Darian-Smith & Gilbert, 1994, 1995; Das & Gilbert, 1995; Chino, 1997).

Contrast sensitivity and peak firing rate

The overall responsiveness of neurons to stimuli in the new receptive fields, however, was substantially lower in many of the reorganized units compared to that of the normal receptive fields regardless of whether we measured the minimum stimulus contrast required to initiate neural responses (contrast threshold) or the neuron's peak firing rate. Fig. 4A illustrates the results for a typical complex cell. The contrast threshold for its new receptive field (left) was higher (i.e. its contrast sensitivity was lower) than that for the nonlesioned eye (right) (6.1% *vs.* 1.5%). The cell's peak response for the lesioned eye was strong but was only about one third of that for the nonlesioned eye.

Fig. 4B (top) compares the contrast thresholds between the two eyes for all reorganized units (left). About half of the units showed similar contrast thresholds between the two eyes. However, the remaining units showed clear imbalance between the two eyes favoring the nonlesioned eye. Consequently, the overall correlation between the two eyes was relatively low ($r = 0.22$, $P < 0.02$). In addition, the average contrast threshold for the lesioned eye was significantly higher than that for the nonlesioned eye (One-way ANOVA, $P < 0.005$). Individual units in the normal zone (right) showed similar contrast thresholds between the two eyes ($r = 0.62$, $P < 0.001$) and no significant differences were found for the mean contrast thresholds between the two eyes (One-way ANOVA, $P > 0.1$).

The bottom panels in Fig. 4B compare the peak firing rates between the two eyes for reorganized units (left) and units in the normal cortical zone (right). The newly activated receptive fields in about half of our sample units were far less responsive compared to those in the normal receptive fields for the nonlesioned eye ($r = 0.43$, $P < 0.02$). The average peak firing rate for the lesioned eye was significantly lower than that for the nonlesioned eye (One-way ANOVA, $P < 0.001$). The scatter plots for units in the normal zone did not show a comparable interocular imbalance in responsiveness. However, the overall match in the peak firing rate between the two eyes was very low ($r = 0.12$, $P < 0.05$), a result which can be predicted from the normal distribution of ocular dominance of individual units in area 17.

Effects of bilateral lesions on responsiveness of recovered units

Since competitive binocular interactions play a substantial role in cortical maturation, we tested the hypothesis that neurons that became responsive to new, displaced receptive fields in the eye with the retinal lesion could attain normal levels of responsiveness after long use and recovery if the competitive influence of the other eye was eliminated. To test this idea, we made an identical experimental lesion in one eye of two 8-week-old kittens, and in order to eliminate potential interocular suppressive influences (Chino et al., 1992; Chino, 1997), we removed all the competing neural signals from the other eye by creating a much larger lesion that was centered on the retinotopically matched region in the contralateral eye (Fig. 5). After more than 3 years of recovery, we found that the cortical map for the eye with the small lesion was completely reorganized in both cats (Fig. 5A) and that the tuning properties of the recovered neurons were not different from normal control units (Fig. 5B). However, the average contrast threshold for the reorganized units was still higher than that for the normal controls (Fig. 5C) (One-way ANOVA, $P < 0.01$) and was very similar to that of the animals with early unilateral lesions (Fig. 4B). Thus, the reactivated neurons were not completely normal even under these most favorable conditions of recovery.

Binocular response properties

How do neural signals evoked by stimulation of the newly activated, displaced receptive fields interact with responses from the nonlesioned eye? Since no previous study has addressed this important question, we quantitatively analyzed two primary properties of binocular responses, disparity sensitivity, and the nature of signal interactions (i.e. excitatory or inhibitory). To determine the nature of binocular signal interactions, we measured the response amplitudes of individual units as a function of relative interocular spatial phase disparity for a dichoptic pair of optimized sine-wave gratings (Fig. 6A, top).

Neural signals from the newly activated receptive fields in the lesioned eye of a representative unit clearly interacted with the responses from the nonlesioned eye (Fig. 6A, bottom left). However, in comparison to many control units, reorganized units were not sensitive to interocular disparity (Fig. 6A, bottom right). The majority of the reorganized units did not show a substantial degree of disparity sensitivity (Fig. 6B, left). In area 17 of normal cats, about 70% of all units were sensitive to interocular image disparity (Fig. 6B, right).

As found in normal controls, the binocular response amplitudes of the majority of reorganized units were either higher (binocular excitation) or lower (suppression) than the dominant monocular response amplitudes (Figs. 6A, 6C, & 6D). About 40% of sample

Fig. 3. Spatial-frequency tuning of reorganized units. **A:** Spatial frequency response functions of a complex cell recorded in the reorganized zone are shown for the lesioned (left) and nonlesioned eyes (right). **B:** Scatter plot comparing the optimal spatial frequencies of individual units between the receptive fields mapped for the lesioned and nonlesioned eyes (top left). Similar plot for units in the normal zone (top right). Mean (±SE) optimal spatial frequencies are indicated with filled symbols. Scatter plot comparing the spatial resolutions of individual units between the receptive fields mapped for the lesioned and nonlesioned eyes (middle left). Similar plot for units in the normal zone (middle right). Mean (±SE) spatial resolutions are indicated with filled symbols. Scatter plot comparing the spatial-frequency bandwidths of individual units between the lesioned and nonlesioned eyes (bottom left). Similar plot for units in the normal zone of cortex (bottom right). Mean (±SE) spatial-frequency bandwidths are indicated with filled symbols.

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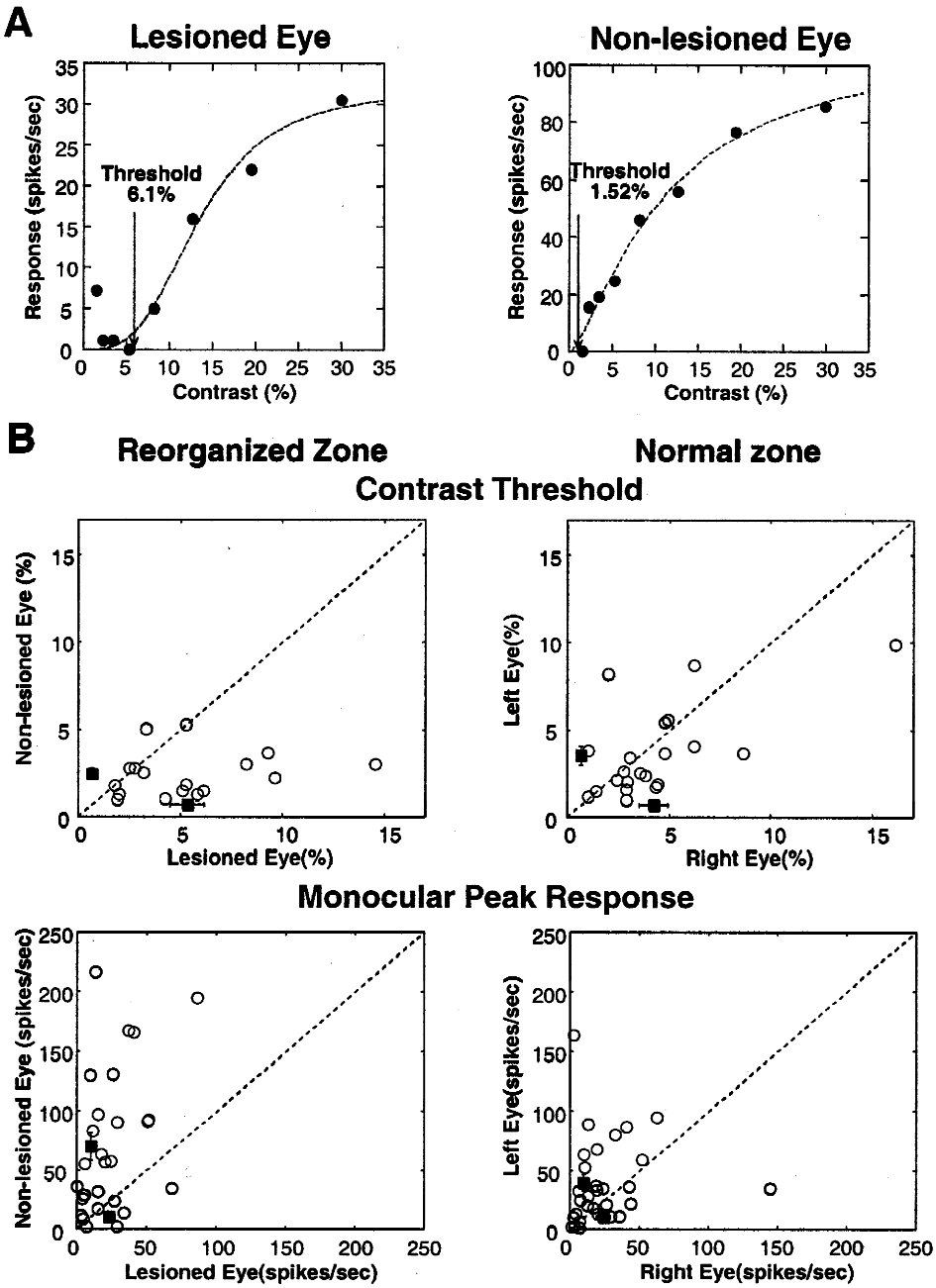

Fig. 4. Responsiveness of new receptive fields in reorganized units. **A:** Contrast response functions for the new receptive field of the lesioend eye (left) and the normal receptive field of the nonlesioned eye for a typical reorganized unit (right). **B:** Relationship between contrast thresholds for individual units determined for the lesioned and nonlesioned eyes in the reorganized zone (top left) and for units in the normal zone (top right). Mean (±SE) thresholds are indicated with filled symbols. Scatter plots comparing the peak response amplitudes of individual units for the lesioned eye with those for the nonlesioned eye of the reorganized zone (bottom left) and for units in the normal zone (bottom right). Mean (±SE) peak firing rates are indicated with filled symbols.

units in both reorganized and normal cortex showed suppressive binocular interactions.

The nature of binocular signal interactions in reorganized units varied as a function of the distance between the new receptive fields for the lesioned eye and the normal receptive fields in the nonlesioned eye of reorganized units. Fig. 6D plots the binocular/monocular ratios (B/M) of individual units as a function of interocular receptive-field separation in degrees. Three units with clear binocular suppression had receptive-field separation greater than 3 deg, while eight out of 11 units showing clear excitatory interactions had the receptive fields separated by equal to or less than 3 deg. This broad relationship between the level of excitatory interactions and interocular receptive-field separation ($r = 0.41$, $P < 0.05$) is consistent with our previous finding in which subthreshold binocular signal interactions were demonstrated in area 17 of monocularly lesioned *adult* cats (Chino, 1997). Finally, for about six units, the B/M values did not substantially deviate from the value of 1.0 (i.e. no binocular interactions).

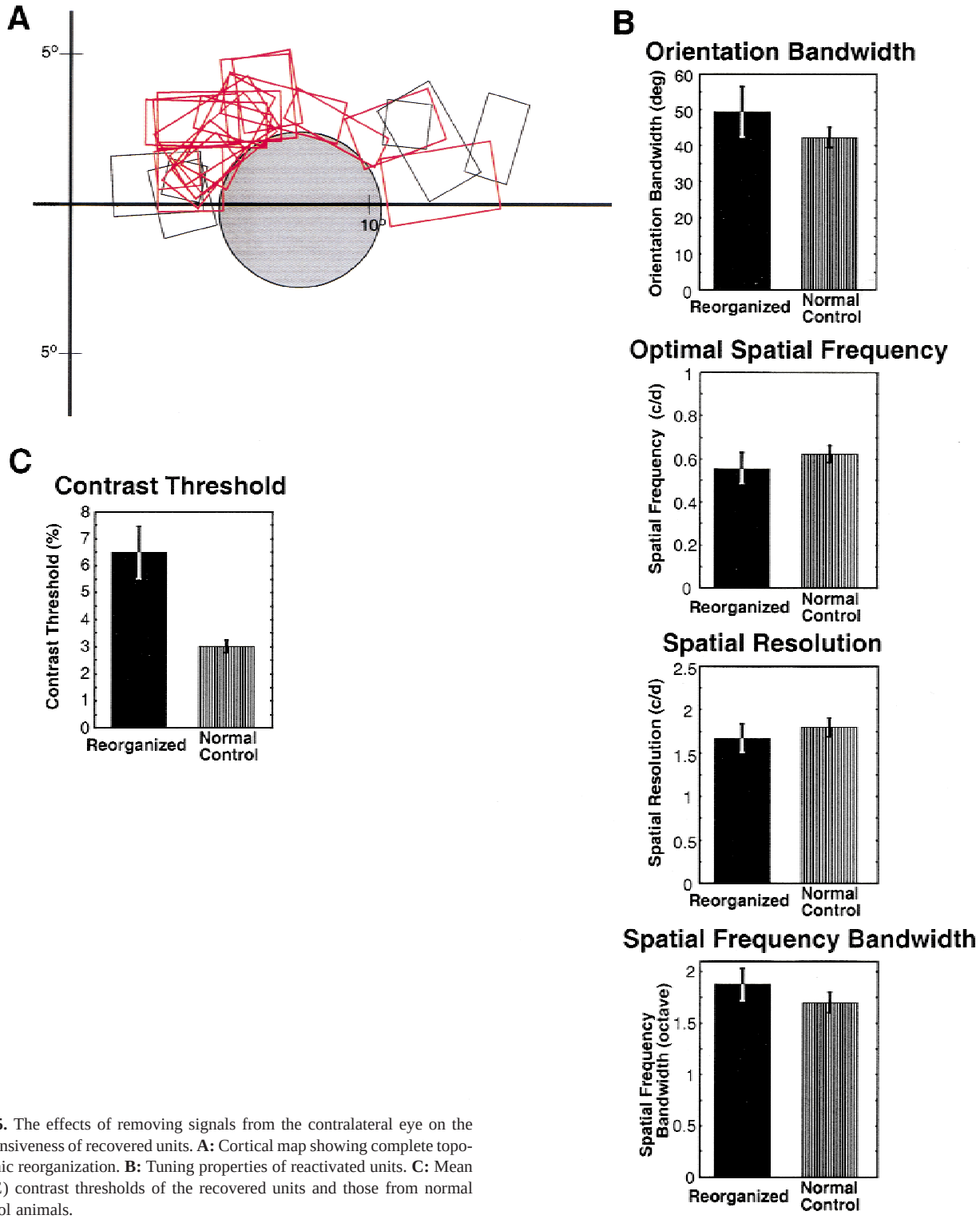

Fig. 5. The effects of removing signals from the contralateral eye on the responsiveness of recovered units. **A:** Cortical map showing complete topographic reorganization. **B:** Tuning properties of reactivated units. **C:** Mean (±SE) contrast thresholds of the recovered units and those from normal control animals.

Discussion

We demonstrated that cortical neurons deprived of part of their feedforward neural activity by a small unilateral lesion of the retina during early development acquired new, displaced receptive fields that are generally similar in tuning characteristics to their original receptive fields in the normal eye. Although the responses of the newly acquired receptive fields were surprisingly robust, their overall responsiveness was substantially reduced compared to that for the receptive fields in the normal eye. However, stimulation of the displaced receptive fields in the lesioned eye and the normal receptive fields in the nonlesioned eye together initiated excitatory or inhibitory binocular signal interactions in the majority of neurons.

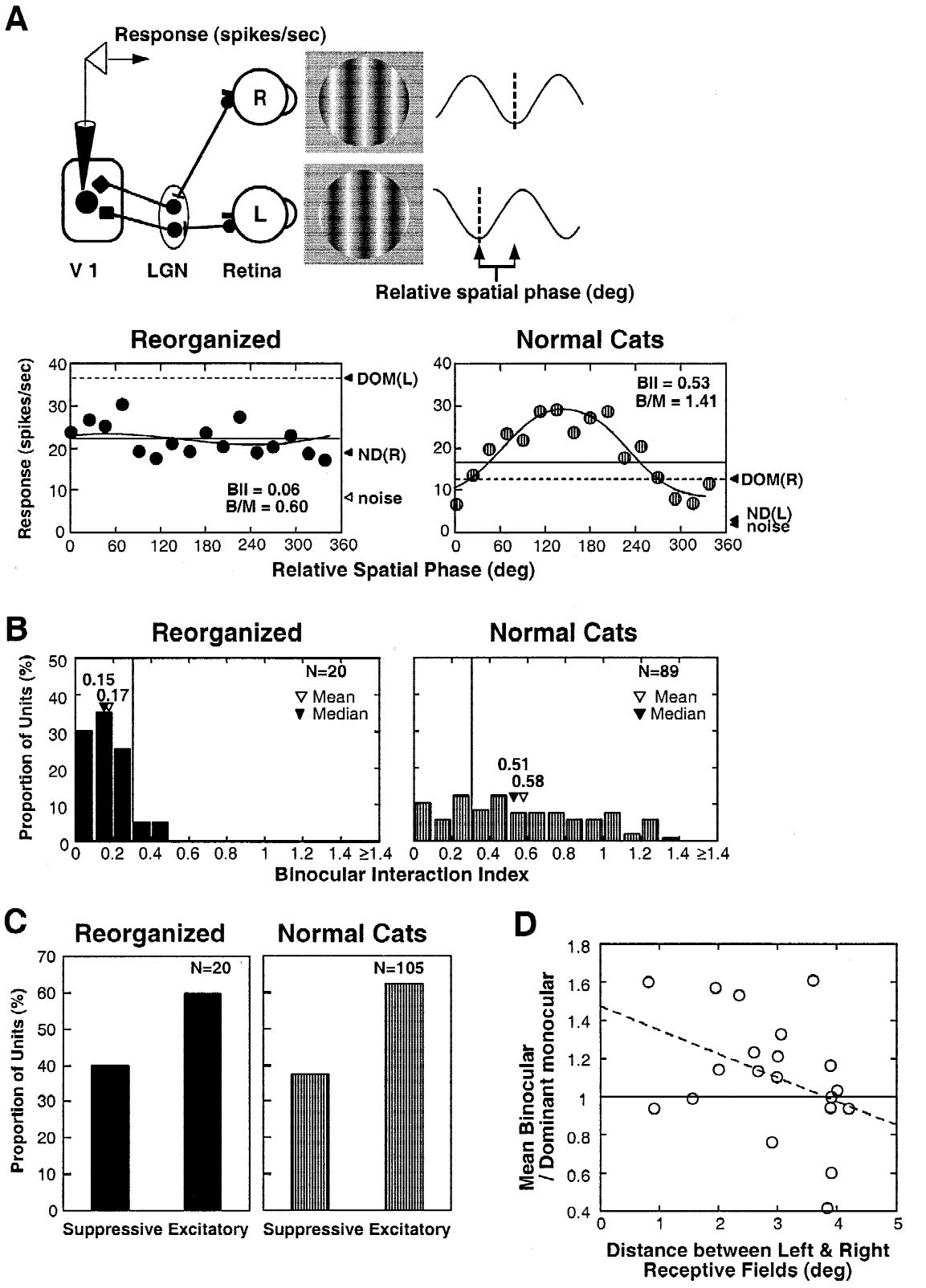

Fig. 6. Binocular signal interactions between the recovered receptive fields of the lesioned eye and the normal receptive fields in the nonlesioned eye. **A:** Methods used to measure the nature of binocular interactions (top) and the binocular responses of representative units from the reorganized cortex of an experimental subject and that of a normal control cat (bottom). **B:** Frequency distributions of BII values for the recovered units in the reorganized cortex (left) and for the normal control cats (right). Units with BII values equal to or greater than 0.3 are traditionally considered to be sensitive to interocular image disparity. **C:** The nature of binocular interactions in units from the reorganized cortex and normal control cats (left). **D:** Binocular/monocular values of individual reorganized units as a function of the distance between the right and left receptive fields. The dotted line represents the best linear fit.

Monocular versus binocular lesions

Previously, responses of monocularly reorganized cortical neurons to the lesioned eye in adult cats and monkeys have been variously described as absent (Chino et al., 1992; Gilbert & Wiesel, 1992; Darian-Smith & Gilbert, 1995; Chino, 1997), fragile or subnormal (Calford et al., 1999, 2000), or suppressed by inputs from the normal eye (Chino, 1997). How did monocularly deprived neurons acquire new relatively robust receptive fields in this study but not in the previous studies? In adult cats and monkeys, new receptive fields emerge following *bilateral* retinal lesions apparently because the normally subthreshold long-range intrinsic horizontal connections are activated by removals of the normal afferent inputs, and functionally strengthened by a use-dependent increase in synaptic efficacy during recovery (Kaas et al., 1990; Chino et al., 1992, 1995; Darian-Smith & Gilbert, 1994, 1995; Das & Gilbert, 1995). Similar alterations in the intrinsic cortical connections are likely to be involved in the case of early monocular lesions (but see Eysel & Mayer, 1981). The apparent differences in the consequences of *monocular* lesions between studies, however, may have resulted from such variables as the size of the lesions, the age at which retinal lesions were made, the duration of postlesion recovery, the stimulus conditions and response criteria employed in the experiments. Thus, conditions for maximizing reactivation, that is, placing lesions in younger animals (8 weeks of age *vs.* $>$ 1 year of age), and allowing much longer recovery time (3 years *vs.* $<$ 6 months) were likely to have contributed to the nearly complete cortical map reorganization observed in this study. The present experiments, however, did not allow us to determine which condition was more important in maximizing reactivation.

Perceptual consequences

The emergence of monocularly deprived neurons with relatively strong responses to either eye is somewhat surprising, given that having two displaced receptive fields is maladaptive. One consequence of the emergence of new, displaced receptive fields would be that fine, discrete retinotopic information may be distorted or blurred. With binocular viewing, there is a local region in which directional cues are imprecise, possibly creating a phenomenon of binocular confusion (i.e. two different objects perceived in the same visual direction). In the developing visual cortex of Siamese cats, cortical neurons with two different retinotopic inputs generally respond only to one eye (Kaas & Guillery, 1973). In contrast, scattered inputs from the skin, due to nerve injury and regeneration may result in somatosensory cortical neurons that have two or more distinct receptive fields in adult monkeys (Florence et al., 1998). These differences in outcome indicate that the rules governing input selection and strengthening certainly require closer attention.

Blind spots which are caused by congenital unilateral lesions in the retina (e.g. coloboma) or associated with the normal optic disk are known to be perceptually filled-in when viewed with the affected eye alone. Moreover dichoptic contour interactions can be demonstrated between the area surrounding a scotoma in one eye and the small region of the other eye that retinotopically corresponds to the center of the blind spot of the affected eye (Tripathy & Levi, 1994, 1999). What may the present findings tell us about where and how these perceptual events are mediated in the brain? With respect to the perceptual filling-in of a scotoma, it has been hypothesized that the blind spot is actively "sewed-up" by low level cortical processes (e.g. reorganization of V1 topographic map). Alternative theory posits that the perceptual filing-in depends on high-level cognitive or "associative" processes while the normal retinotopic spatial values around the blind spot are maintained (i.e. it does not depend on low-level topographic map reorganization) (Dennett, 1991; Ramachandran, 1992; Komatsu & Murakami, 1994; Murakami et al., 1997). Our data are consistent with the first hypothesis, although our findings do not rule out an additional involvement of higher order visual areas. Moreover, a recent study in awake monkeys demonstrated that some V1 neurons representing the optic disk responded to the large uniform stimuli that covered the blind spot and induced perceptual filling-in (Komatsu et al., 2000).

Our new findings on the binocular signal interactions between the new displaced receptive fields in the lesioned eye and the normal receptive fields in the nonlesioned eye parallel the dichoptic contour interactions that occurs across unilateral retinal lesions or the normal optic disk in humans (Tripathy & Levi, 1994, 1999). Our results are consistent with the hypothesis that these dichoptic contour interactions in humans with retinal scotoma may reflect binocular signal interactions in the primary visual cortex that depend on the lateral signal transmission *via* the long-range horizontal connections in and around the cortical representation of a blind spot (Tripathy & Levi, 1994, 1999; Komatsu et al., 2000).

Acknowledgments

This work was supported by NIH grants EY 08128 (Y.C.), EY-03611 (E.L.S.), EY-07551(CORE), and EY-02686 (J.H.K.). We thank Dennis Levi for comments on the earlier version of this manuscript.

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