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Ocular Dominance Columns in New World Monkeys

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Squirrel monkeys normally lack ocular dominance columns in V1. This study shows that squirrel monkeys can exhibit clear ocular dominance columns if they are made strabismic within a few weeks of birth. Columns were seen only in layer 4Cβ and were coarser than the overlying blob pattern in the same animal. In physiological recordings from layer 4C of a normal squirrel monkey, single units were mostly monocular, but units driven by the two eyes were intermixed. These results suggest that in squirrel monkeys activity-dependent mechanisms do normally segregate geniculate inputs from the two eyes, but on a much finer scale than in Old World primates. Strabismic owl monkeys also showed ocular dominance columns; normal owl monkeys showed variable expression. Because ocular dominance columns, when present in New World monkeys, tend to occur in later-maturing parts of layer 4C, I hypothesize that a difference in the relative timing of the maturation of geniculocortical inputs and intracortical lateral connectivity explains the variability of ocular dominance column expression in New World monkeys.

Key words: ocular dominance columns; New World monkeys; strabismus; owl monkeys; squirrel monkeys; Hebbian models

All Old World primates, including humans, show sharp ocular dominance segregation in layer 4C of the primary visual cortex, but anatomical studies in various New World monkeys show robust, weak, or no ocular dominance columns (for review, see Florence et al., 1986). Squirrel monkeys fall into the last category, in that all anatomical studies to date have failed to find ocular dominance columns in normally reared *Saimiri* (see Discussion for references). It seems strange that such a striking organizational aspect of the primary visual cortex should be so variously expressed in otherwise quite similar creatures. Therefore, one question addressed in this study was whether ocular dominance columns can be induced to form in squirrel monkeys by altering their early visual experience. I used manipulations that increase differences in activity in the two eyes because such procedures increase monocularity in cats (Hubel and Wiesel, 1965; Van Sluyters and Levitt, 1980).

The variable expression of ocular dominance columns in New World primates emphasizes the mystery of their functional significance—no visual differences are known that distinguish species that have ocular dominance columns from those that do not (Allman and McGuinness, 1988). Two prevalent theories on their function are as follows. (1) They are important for stereopsis because they provide a systematic interdigitation of the inputs from the two eyes (Ferster, 1981; LeVay and Voigt, 1988; Poggio et al., 1988). (2) Ocular dominance columns have no functional significance themselves but arise as an epiphenomenon of a developmental program (Swindale; 1980; Miller et al., 1989; Purves et al., 1992).

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The first hypothesis was addressed in a previous study from this laboratory (Livingstone et al., 1995). We measured evoked potentials in a squirrel monkey in response to depth-reversing random-dot stereograms and found that the squirrel monkey showed responses that were consistent with its having stereoscopic depth perception. This result seems contrary to the idea that ocular dominance columns are important for stereopsis.

The second hypothesis, that ocular dominance columns arise as an epiphenomenon of a developmental program, was first strongly suggested by the result of Law and Constantine-Paton (1981) that ocular dominance columns formed when two eyes of a frog were forced to share territory normally innervated by only one eye. Models using activity-dependent sorting of synaptic inputs, as initially proposed by Hebb (1949), economically explain how inputs from neighboring parts of the retina can come to innervate nearby parts of the target zone, and have been shown to result in connectional patterns that are optimal for information extraction (Linsker, 1987; Miller et al., 1989). Moreover, such activity-dependent synaptic modification rules, in the presence of spontaneous activity in the retina, would also inevitably result in the segregation of synapses from the two eyes onto different sets of cells. So the question I have attempted to answer here is as follows: If a Hebbian developmental program is important during development in most species, does the cortex in primates without ocular dominance columns develop in some fundamentally different way, or are particular parameters of the Hebbian mechanism different in these species?

MATERIALS AND METHODS

The experiments were carried out on five squirrel monkeys (*Saimiri sciureus*) and seven owl monkeys (*Aotus trivirgatus*). Abnormal postnatal visual experience was produced for the first 10 weeks to 1 year of life. The resultant ocular dominance distribution was then revealed either by eye injection followed by autoradiography or by monocular enucleation followed by cytochrome-oxidase staining.

Altered visual experience. Four squirrel monkeys and three owl monkeys were given altered postnatal visual experience. These seven monkeys were born in the laboratory and were reared by their mothers. Six were made strabismic by cutting both medial rectus muscles between 6 and 10 d after birth. The surgery was done under halothane anesthesia using

aseptic techniques. After the surgery, the monkey was returned to its mother. Each infant monkey was given antibiotics (2.5 mg/kg Baytril, i.m., daily) for 10 d postoperatively. To evaluate the degree and duration of strabismus after the eye muscle cuts, close-up flash photographs of each monkey were taken once per month after surgery. Misalignment of the two eyes could be seen as a noncorrespondence of the flash reflections relative to the pupils, whereas if the flash reflections were in the same positions on the two eyes I concluded that the eyes were properly aligned.

One newborn squirrel monkey was subjected to alternating monocular occlusion for 6 d/week for the first 10 weeks after birth, by keeping the monkey, and its mother, in complete darkness except for 4–6 hr/d. During those times, an opaque contact lens was put in one of the infant monkey's eyes, with alternate eyes occluded each day. Ophthalmic anesthetic (Ophthaine, 0.5%) was put in the eye before the lens was inserted. The lens was checked hourly, and replaced if the monkey had removed it, which happened about once per day. At the end of each day's light period, the lens was removed and the lights were turned off.

Methods for visualizing ocular dominance patterns. For the alternately occluded squirrel monkey and one of the strabismic owl monkeys, the pattern of retinogeniculocortical inputs was studied by eye injection with radioactive tracer. For these monkeys, 5 mCi of [^{3}H]proline in 20 μl of sterile water was injected into one eye. After a survival period of 2 weeks, each monkey was given an overdose of pentothal and perfused through the heart with saline, followed by 4% paraformaldehyde in 0.1 M sodium phosphate, pH 7.4, and then with 15% sucrose in 0.1 M sodium phosphate, pH 7.4. Frozen sections were cut and mounted on slides, which were dipped in Kodak NTB-2 emulsion and exposed in the dark for 80 d.

In the rest of the monkeys, ocular dominance patterns were visualized by eye removal followed by cytochrome-oxidase staining of sections of the visual cortex. For the eye removal, the monkey was initially anesthetized with Ketamine (0.1 mg/kg), and the surgery was done under halothane anesthesia using aseptic techniques. The eye that was removed was always the left eye. One month after the eye removal, the animal was given an overdose of pentothal (50 mg/kg) and perfused transcardially with (1) warm saline, followed by (2) 0.75% freshly depolymerized paraformaldehyde, 2.25% glutaraldehyde in 0.1 M sodium phosphate, pH 7.4, and then (3) postperfused with 15% sucrose in 0.1 M phosphate buffer, pH 7.4. The occipital lobe of the brain was then removed, gently flattened against a microscope slide, and frozen in dry ice/ethanol-cooled isopentane. Sections were cut parallel to the surface at 75 μm thickness on a freezing microtome. All sections were stained for cytochrome oxidase (Wong-Riley, 1979).

The microscope slides of sections were scanned with a high-resolution digital camera (Leaf Lumina, Southborough, MA). The images of the cross-sectioned material were printed without alteration, and the images of tangential sections were minimally processed using Adobe Photoshop (high-pass-filtered) to eliminate gradual changes in staining density (the amount of alteration can be seen by comparing the cross- and tangential sections). To make the montages of layer 4 shown in Figures 2, 5 and 6, parts of up to three sections showing different areas of layer 4C were aligned using the radial blood vessels. Adobe Photoshop was used to map the blob and ocular dominance patterns: a threshold operation was performed on the high-pass-filtered image, using a threshold level set by eye to correspond best to the raw image. The threshold map was blurred, and then the threshold operation was repeated. The radial blood vessels were also mapped on the same image using another threshold operation, and then the combined maps were warped using Morph software, so that the radial blood vessels in each section were precisely aligned. Then the same sections as were used to make the preceding raw image were combined to show the blob pattern overlaid on the ocular dominance columns. In each image shown, the sections through layer 4C are mapped in black and white, so that white areas indicate lighter staining regions, and should thus correspond to territories innervated by the enucleated (left) eye, and the black regions indicate regions dominated by the right eye. The sections through layer 3 were mapped in an identical way, except that the dark regions, corresponding to the blobs, are mapped in gray, and lighter-staining regions of the sections are left blank.

Measurements of ocular dominance column and blob periodicity were calculated, by Klaus Obermayer and Christian Piepenbrock, from their Fourier spectra. Spectra were obtained by applying a two-dimensional fast Fourier transform (Press et al., 1988) to each cytochrome-oxidase pattern, after the removal of artifacts, such as section edges and the holes left by blood vessels, by blurring and filling in, respectively. After transformation, power spectra and typical wavelengths were then obtained from Fourier spectra and typical wavelengths by procedures described previously in Obermayer and Blasdel (1993). These allowed direct determinations of blob and ocular dominance frequencies and intervals along all axes.

Adult physiology. One normal young adult squirrel monkey was studied electrophysiologically. To record from single units in layer 4C, we made tangential penetrations using fine tungsten electrodes (<10 μm tip diameter, 2–5 MΩ resistance at 1 kHz). The animal was initially anesthetized with Ketamine (0.1 mg/kg) and then maintained under surgical levels of anesthesia, using 1.5–2% isofluorane, for the duration of the recording. Under isofluorane anesthesia, but before paralysis, the remaining surgical procedures were performed: placement of the head in a stereotaxic holder, scalp incision, drilling of a small hole in the skull, and attachment of the microdrive using dental impression compound. Before making incisions, sites were infiltrated with long-lasting local anesthetic (2% lidocaine).

Just before recording began, administration of the paralyzing agent was begun (gallamine, 10 mg/kg, i.v., then 10 mg/kg/hr). For the rest of the experiment, the EEG and ECG were monitored to ensure adequate anesthesia; when the EEG showed signs of impending arousal or the ECG showed tachycardia, the anesthetic was increased. We have monitored the EEG in similarly anesthetized, but unparalyzed, monkeys and found that as long as the EEG does not show prolonged desynchronization, the animal shows no signs of withdrawal to painful stimuli or spontaneous movement or vocalization. We are certain, therefore, that as long as we increase the anesthetic as soon as the animal shows even brief periods of EEG desynchronization, it remains unconscious.

To identify the layers corresponding to different recording sites, lesions were made at various points along the electrode track. At the end of the experiment, the animal was given an overdose of pentothal (50 mg/kg) and perfused as described above, except the tissue was cut parasagittally. The lesions could easily be identified in the cytochrome oxidase-stained sections.

All experiments were carried out according to National Institutes of Health standards for humane treatment of animals as set forth in Guide for the Care and Use of Laboratory Animals and were approved by the Harvard Medical School Standing Committee on the Use of Animals in Research.

RESULTS

The procedures on each monkey and the ages at which they were done are listed in Table 1.

Squirrel monkey anatomy

Clear ocular dominance columns were found in two of the strabismic squirrel monkeys. One showed ocular dominance columns only in the calcarine sulcus; the other had columns throughout V1. Both of these monkeys were still strabismic at 6 months of age, and the one with columns throughout V1 had the more severe strabismus. In this monkey, the left eye deviated >45° laterally for the entire 7 months after the eye muscle surgery. The squirrel monkey that developed columns only in the calcarine sulcus was also strabismic at 6 months of age, but both eyes faced forward, and were only slightly exotropic. The third squirrel monkey that had been made strabismic did not develop ocular dominance columns, but this animal's eye misalignment was mild right after the surgery, and by 4 months of age the eye alignment appeared normal, suggesting that the eye muscles had reinserted. In the animal given alternating ocular occlusion, I also saw no ocular dominance columns. This animal probably had some normal visual experience because it did remove its contact lens occasionally.

Histology sections from the strongly strabismic monkey are shown in Figures 1 and 2. In this monkey, the occipital lobe was flattened against a slide, so the cortex of the opercular surface and the roof of the calcarine sulcus would be cut parallel to the cortical layers, but the medial bank and other parts of the calcarine sulcus were cut in cross-section. In the sections in which the cortex was cut perpendicular, there are clearly alter-

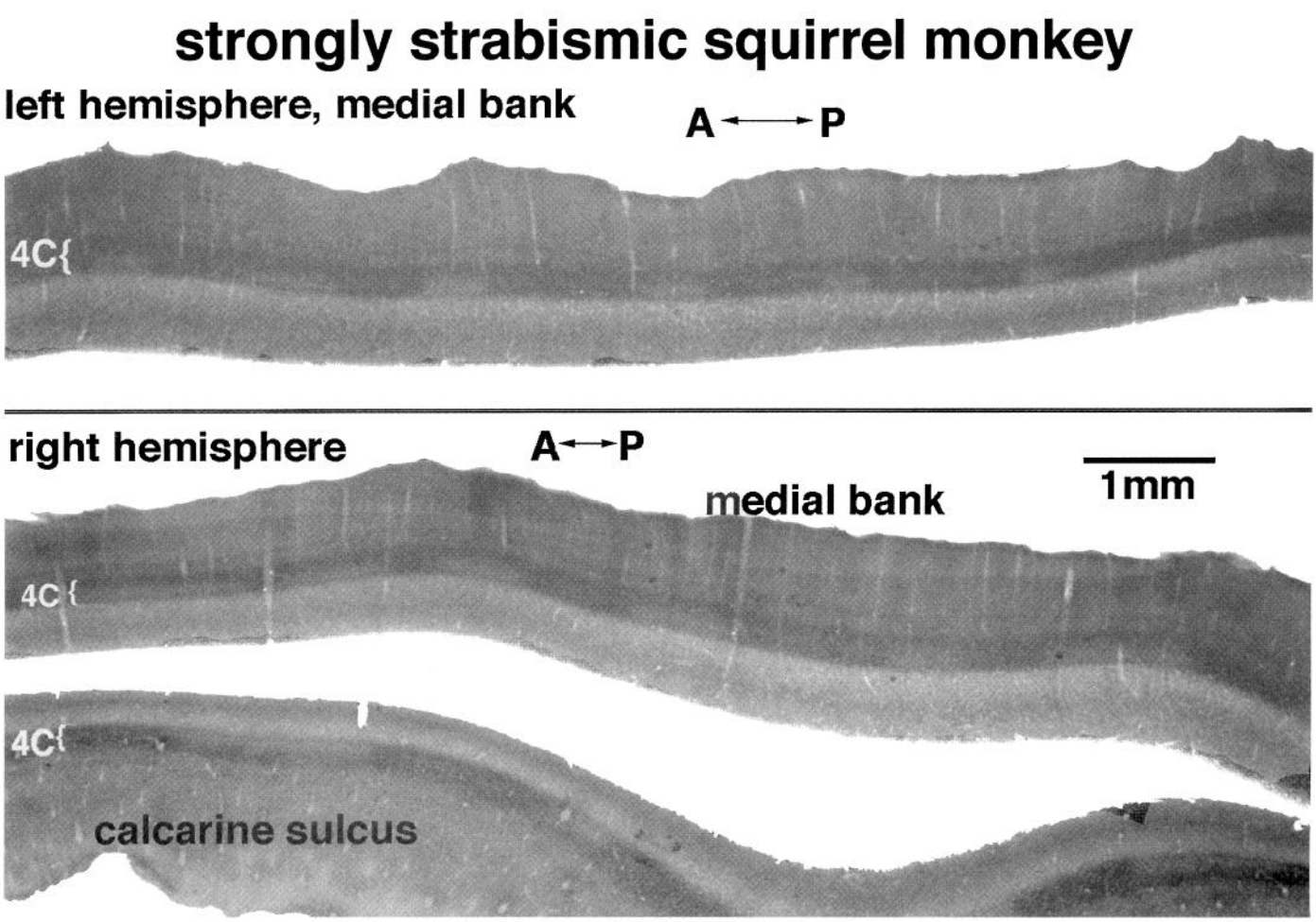

Figure 1. Cross-sections of striate cortex, stained for cytochrome oxidase, from the strongly strabismic squirrel monkey, perfused 1 month after left eye enucleation. The *top section* is from the left hemisphere, and the *bottom section* from the right. Both sections show the medial edge of the opercular surface, just at the point where it first curves sharply, and the section from the left hemisphere also shows part of the underlying calcarine sulcus. Layer *4C* is indicated on each cortical area. These sections are representative of all of V1 of both hemispheres in this monkey in showing periodic changes in density only in the deeper half of layer 4C, layer 4Cβ. (Note: the cortex of the roof of the calcarine sulcus is upside-down, so here 4Cβ is above 4Cα.)

nating regions of light and dark staining in layer 4C, but these periodicities appear only in the lower half of layer 4C, in sublamina β, and not in layer 4Cα (Fig. 1). In normally reared macaques, ocular dominance columns are less well demarcated in layer 4Cα than in 4Cβ, but are nevertheless clearly present in both sublaminae (Hubel et al., 1976). The top half of Figure 2 shows layer 4Cβ of the opercular surface of both hemispheres from this same monkey viewed en face. There is a clear pattern of light- and dark-staining regions in both hemispheres. The eye that was removed (to reveal the columns) was the left eye, so the cytochrome-light regions would correspond to territory driven by the left eye.

The overall pattern of ocular dominance columns is much less regular than in macaques, although in the left hemisphere there is a tendency for the columns to intersect the V1/V2 border at a right angle. The lower half of Figure 2 shows the overlying blob pattern for the same regions of cortex. By inspection, the periodicity of the ocular dominance columns seems coarser than the blob pattern. The average width of the ocular dominance columns in the left hemisphere was 650 μm, and the average width in the right hemisphere was 800 μm. The average interblob spacing was 450 μm in the both hemispheres. For comparison, in the macaque the average ocular dominance width is 550 μm (Hubel and Wiesel, 1972), and the average interblob spacing is also 550 μm (Horton, 1984). Figure 3 shows a computer-generated map of the blob pattern overlaid on the ocular dominance column pattern for both hemispheres. In the sections through layer 3 shown in Figure 2 (*bottom*), there seem not to be two distinct sets of blobs, light and dark, overlying the light and dark regions in layer 4, as there are in monocularly enucleated macaques (Hendrickson et al., 1981; Horton and Hubel, 1981), yet in Figure 3 there is nevertheless a hint that the blobs are sparser overlying the left eye regions. Because cytochrome-oxidase staining density falls off from the center of blobs (Trusk et al., 1990; Edwards et al., 1995), lighter-staining blobs would simply map as smaller blobs.

The squirrel monkey that remained mildly strabismic for 6 months also showed ocular dominance columns, although less distinct than the strongly strabismic squirrel monkey. This

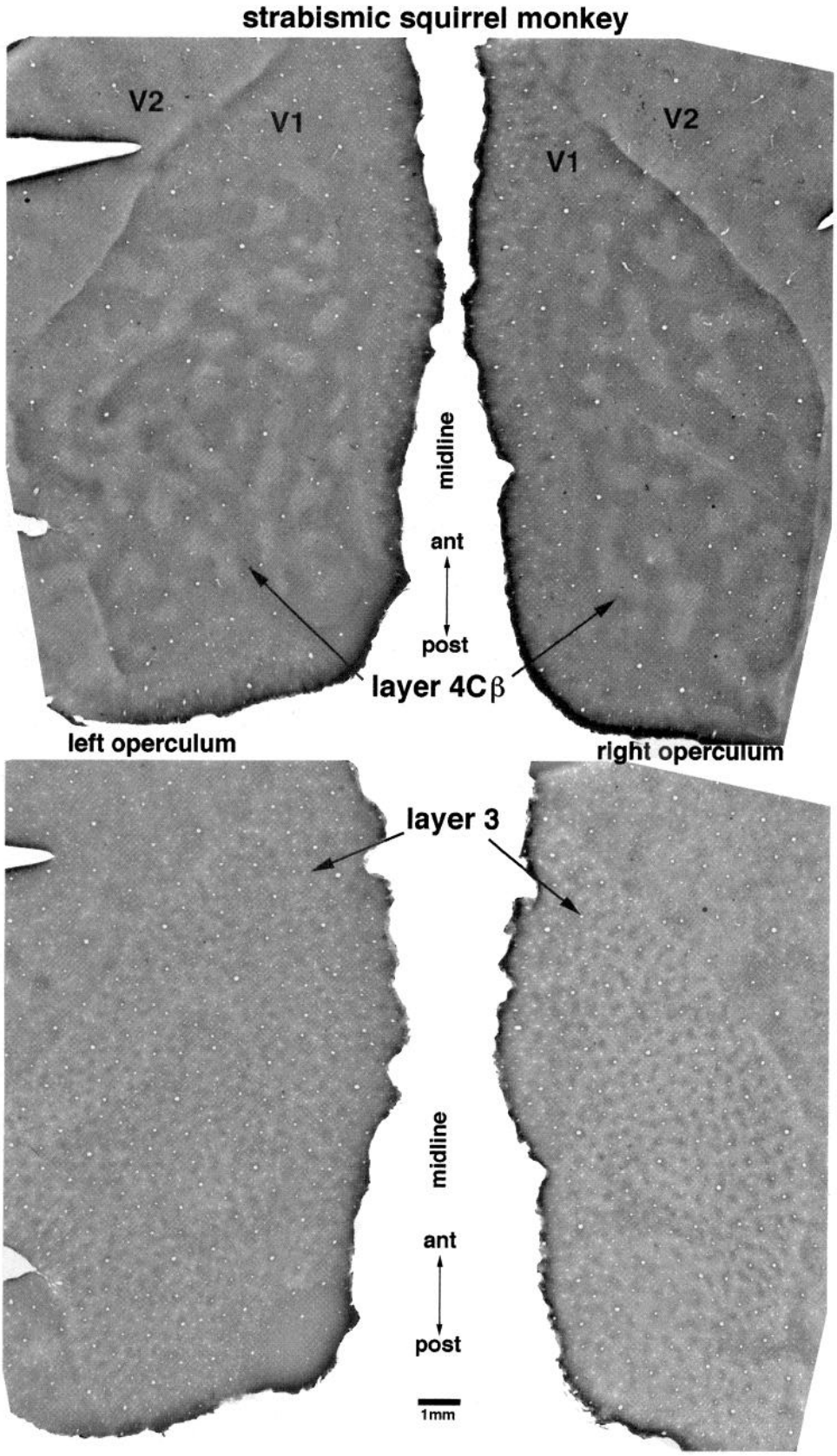

Figure 2. Four sections through the flattened opercular cortex from the strongly strabismic squirrel monkey (same monkey as in Fig. 1). For both pairs of images, the one on the *left* is from the left hemisphere and the one on the *right* is from the right hemisphere. The *top images* are montages of two sections each, and the *bottom images* are each single sections. Each image was high-pass-filtered. Each pair of sections is oriented as the cortex would be in the animal, as viewed from the back. The *top sections* are mostly through layer 4Cβ in V1, and show the pattern of ocular dominance columns en face. The *bottom sections* are more superficial than the top two sections, passing mostly through layer 3, and show the pattern of blobs. The V1/V2 border is the *bowed line* in each section curving outward and downward from the upper midline. The *white triangles* are cuts that were made in the tissue to relieve tension. *ant*, Anterior; *post*, posterior.

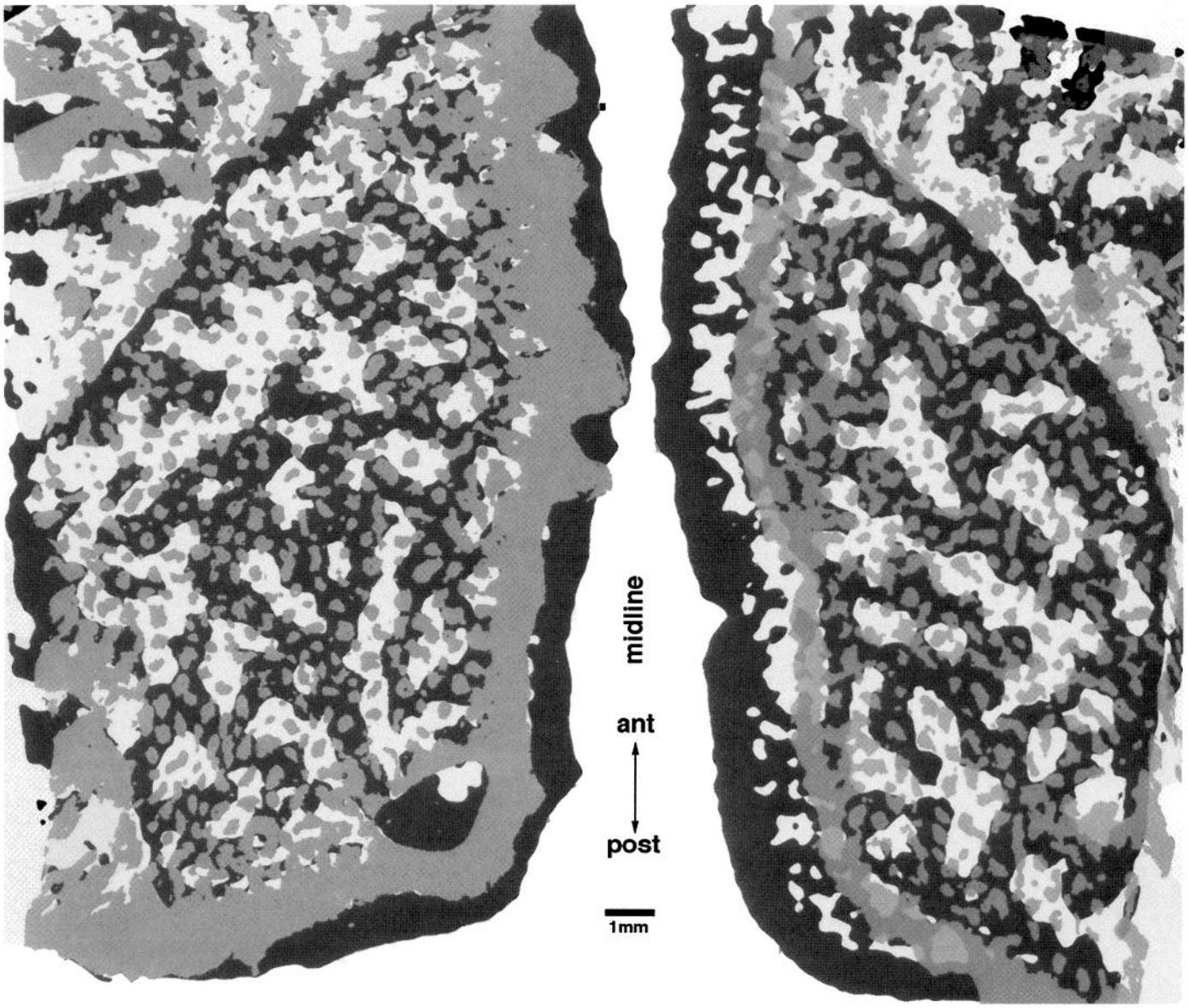

Figure 3. Overlaid maps of computer-generated blob and ocular dominance patterns from the same tissue as shown in Figure 2. A threshold operation was used to map the light- and dark-staining regions of the images shown in Figure 2. The ocular dominance columns are shown in *black* and *white*, and the overlying blobs are shown in *gray*. Note that the ocular dominance columns are coarser than the overlying blob pattern and that the blobs are scarcer over the regions corresponding to the enucleated eye (*white regions*).

monkey showed ocular dominance columns only in the buried cortex of the calcarine sulcus, again only in layer 4Cβ (Fig. 4).

Owl monkey anatomy

I performed similar experiments in owl monkeys. Owl monkeys have been reported in the literature to exhibit either no (Kaas et al., 1976) or faint (Rowe et al., 1978) ocular dominance columns. I made three owl monkeys strabismic postnatally, and visualized the ocular dominance pattern by eye injection at 6 months or by eye removal at >1 year, followed by cytochrome-oxidase staining (Table 1). All three of these strabismic owl monkeys showed clear ocular dominance columns. In two of these animals, the columns were visible in both 4Cα and 4Cβ, throughout V1. Sections from one of these animals are shown in Figure 5. In the section through layer 3 (*top right panel*), the blobs do not seem at first glance to comprise a light- and a dark-staining population, but when the blob pattern is mapped onto the ocular dominance column pattern (*bottom right panel*), it can be seen that the mapped blobs are much sparser over the regions corresponding to the enucleated eye, indicating that the blobs over the enucleated eye regions are probably lighter staining than the blobs over the right eye regions. In the third strabismic animal, the columns were visible only in layer 4Cβ, and primarily in the calcarine sulcus.

I looked at four normally reared owl monkeys, as controls, by removing one eye at 1 year or later, and then staining for cytochrome oxidase. Two control monkeys showed no periodicities in layer 4C anywhere in V1; one of the controls showed very faint columns throughout V1, only in layer 4Cβ, and the fourth control showed clear columns, predominantly in layer 4Cβ. The periodicity of the blob and ocular dominance columns in the strabismic

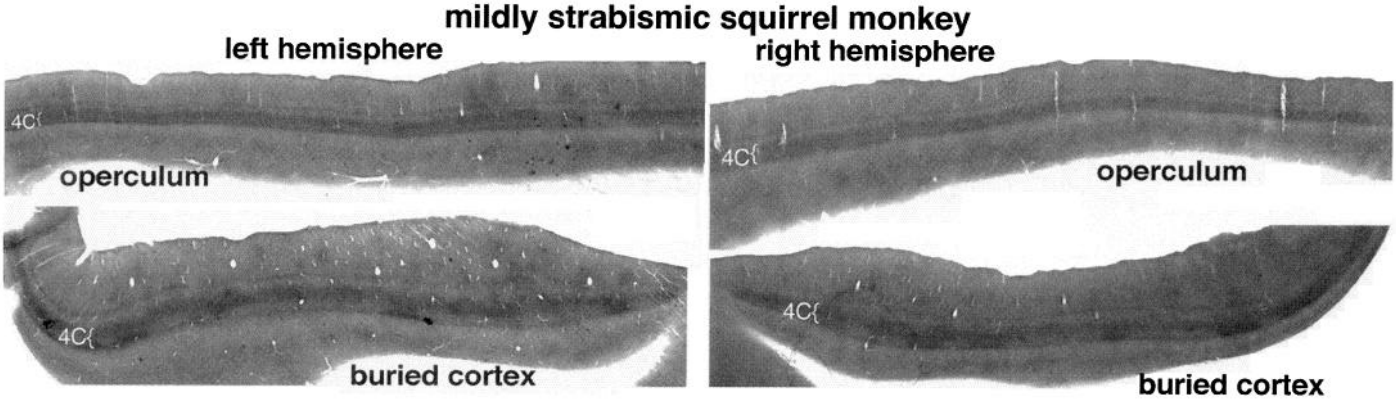

Figure 4. Four cross-sections stained for cytochrome oxidase from the squirrel monkey that had been mildly strabismic for 6 months and then was monocularly enucleated 1 month before perfusion. The sections on the *left* were from the left hemisphere, and the sections on the *right* were from the right hemisphere. The *top sections* were both from the opercular surface, just at the medial edge where it first curves away from the surface. Neither of the sections from the opercular surface shows ocular dominance columns, nor did any tissue examined from the opercular surface. The *bottom sections* were from the buried cortex in the medial bank of the calcarine sulcus. All sections examined from within the calcarine sulcus similarly showed fluctuations in staining density only in layer 4Cβ.

owl monkeys was about equal, as in the sections shown in Figure 5. In the fourth control owl monkey, as in the more strabismic squirrel monkey, the ocular dominance columns were coarser than the overlying blob pattern from the same region of cortex (Fig. 6). Figure 6 (*right*) shows the blob pattern mapped onto the ocular dominance columns. The blobs are sparser over the regions corresponding to the enucleated eye, and the width of most of the ocular dominance stripes is considerably coarser than the spacing of the overlying blobs.

Physiology of layer 4C in a normal squirrel monkey

Because the anatomical experiments in squirrel monkeys showed that squirrel monkeys apparently can express, under some circumstances, ocular dominance columns, I concluded that the mechanisms necessary for activity-dependent geniculocortical segregation are normally present. I therefore asked what degree of ocular segregation is normally present in squirrel monkey layer 4C. Hubel and Wiesel (1978) had previously reported that in normal squirrel monkeys physiological recordings in layer 4 show mild fluctuations in ocular preference, with a periodicity of 500 μm, although all recording sites were to some degree binocular. Hubel and Wiesel (1978) did not, however, use fine enough electrodes to record single units in layer 4C.

In collaboration with David Hubel, I recorded physiologically from layer 4C of a normal squirrel monkey. To record single units from layer 4C, we used very fine tungsten electrodes and positioned the electrodes at an angle of ~45° to the surface. We made two penetrations, each through two thicknesses of V1 (through the operculum and then through the first cortical layer of the roof of the calcarine sulcus). We identified layer 4C by the increase in background activity and the lack of orientation selectivity in the background activity. Small electrolytic lesions were made where we thought the borders of 4C were, and the laminar location of recording sites was subsequently confirmed histologically. In these four passes through layer 4C, we recorded from 41 sites, at intervals of 0.03–0.05 mm. We considered a spike to be a single unit only if it was at least twice as large as the background activity and if the spike showed a consistent size and shape. Above and below layer 4C, we recorded orientation-selective units that were usually driven by both eyes. At the depth at which we began recording an increase in unoriented background activity, the single units we were able to isolate became monocular, even though the background activity was binocular. At 9 of the 41 recording sites, we isolated single units, and all 9 of of these were strictly monocular. The background activity at two of these single-unit sites was also monocular (driven by the same eye as the single unit), and at the other sites the background activity was binocular. At seven recording sites, two single units could be distinguished, by distinctive differences in spike size. At one of these sites, both single units were driven by the same eye (and both were on-center units). In the other six of these two-unit recordings, one unit was driven by one eye and the other unit by the other eye. At three recording sites, the spike activity was on-center in one eye and off-center in the other. For the first two of these on-in-one-eye-off-in-the-other recording sites, we assumed that there were two different units of similar size, one on-center in one eye and the other off-center in the other, but the third unit was quite large, and when the electrode was advanced gradually over almost 100 μm, the spike became even larger, and the spike profile for the on responses to one eye remained identical to the off responses to the other eye; then both responses disappeared simultaneously. So we were forced to conclude that this unit, at least, was on-center for one eye and off-center for the other. At the remaining sites, no single units could be resolved, although at most of these sites the multiunit activity was strongly biased toward one eye or the other, with little input from the other eye. We saw no single units in layer 4C that were binocular and of the same sign in the two eyes.

One potential problem with this physiological study, raised by Michael Stryker, is that it is possible that we recorded from geniculate afferent fibers rather than from layer 4C cells, and geniculate fibers would of course be expected to be monocular. We do, however, have some reasons for believing that most, if not all, of the single units we recorded represented cortical cells rather than geniculate fibers. First, we recorded rich, single-unit activity in the upper and lower layers that was orientation-selective and, therefore, undoubtedly from cortical cells. Second, the electrode did not record fibers in the white matter between the two cortical layers. Third, geniculate fibers have a characteristic firing pattern and spike form, and these units appeared to us to be characteristic of cortical cells. Nevertheless, with the techniques we used, we cannot completely rule out this possibility.

Table 1. Experimental history and observations on animals in anatomical study

Squirrel monkeys

Cut medial recti	Remove 1 eye	Perfusion	Comments	Results
3 weeks	8 months	9 months	eye muscles may have reinserted	no o.d. columns
1 week	6 months	7 months	remained mildly strabismic for all 6 months	o.d. columns in calcarine, not operculum; only in 4Cβ. Figure 4
1 week	7 months	8 months	strongly strabismic for 7 months	clear o.d. columns throughout V1, only in 4Cβ. Figures 1–3
Control	>1 year	1 month later		no o.d. columns

Alternating eye occlusion	[^{3}H]proline eye injection	Perfusion	Comments	Results
Birth to 10 weeks	10 weeks	12 weeks	may have had some normal visual experience	no o.d. columns

Owl monkeys

Cut medial recti	Remove 1 eye	^{3}H eye injection	Perfusion	Results
1 week	15 months		16 months	clear o.d. columns throughout V1; clearer in 4Cβ than in 4Cα. Figure 5
12 d	12 months		13 months	faint o.d. columns throughout V1, in both α and β of 4C
control	>1 year		1 month later	no o.d. columns
control	1 year		13 months	no o.d. columns
control	>1 year		1 month later	very faint o.d. columns, β only, mostly in calcarine
control	>1 year		1 month later	o.d. columns throughout V1, only in 4Cβ. Figure 6
1 week		6 months	12 d later	o.d. columns mostly in calcarine, mostly in 4Cβ

o.d., Ocular dominance.

DISCUSSION

I conclude from the anatomical studies that it is possible, although difficult, to induce ocular dominance columns in squirrel monkeys. Only the one animal with the most disparate input from the two eyes postnatally developed columns throughout V1, and those columns were restricted to layer 4Cβ. Recordings from a normal adult squirrel monkey indicated that there is segregation of the inputs from the two eyes in the cortex but that this segregation is on a much finer scale than in other species, such as Old World monkeys. Such a salt-and-pepper segregation would not, of course, be apparent in the kinds of anatomical experiments previously used to reveal ocular dominance columns.

Owl monkeys, on the other hand, apparently normally show variability in the degree of segregation of the inputs from the two eyes: of four control monkeys, two showed no ocular dominance columns and two showed some columns. The three owl monkeys made strabismic postnatally showed much clearer ocular dominance columns throughout V1.

Previous anatomical studies of the geniculocortical inputs to V1 in New World monkeys, when looked at all together, show an interesting pattern. The following sections summarize the anatomical studies on ocular dominance columns in New World monkeys.

Normal squirrel monkey

No ocular dominance columns have been seen in normal squirrel monkey using a variety of anatomical techniques: monocular tracer injection (Hubel et al., 1976; Tigges et al., 1977; Hendrickson et al., 1978; Rowe et al., 1978); monocular visual stimulation with 2-deoxyglucose (Hendrickson and Wilson, 1979; Humphrey and Hendrickson, 1983); and monocular enucleation followed by cytochrome-oxidase staining (Hendrickson and Tigges, 1985).

Deprived squirrel monkey

In squirrel monkeys that had been monocularly deprived postnatally, there were no ocular dominance columns in V1 except for a few patches of high silver grain density in layer 4Cβ in the calcarine sulcus (Tigges et al., 1984).

Marmosets

Normal marmosets show no evidence for ocular dominance columns in V1, whereas monocularly deprived marmosets show ocular dominance columns, restricted to layer 4Cβ and, by inspection of *their* Figure 2, primarily in the calcarine sulcus and not in opercular cortex (DeBruyn and Casagrande, 1981). Young marmosets can show ocular dominance columns, preferentially in the calcarine sulcus (Spatz, 1989).

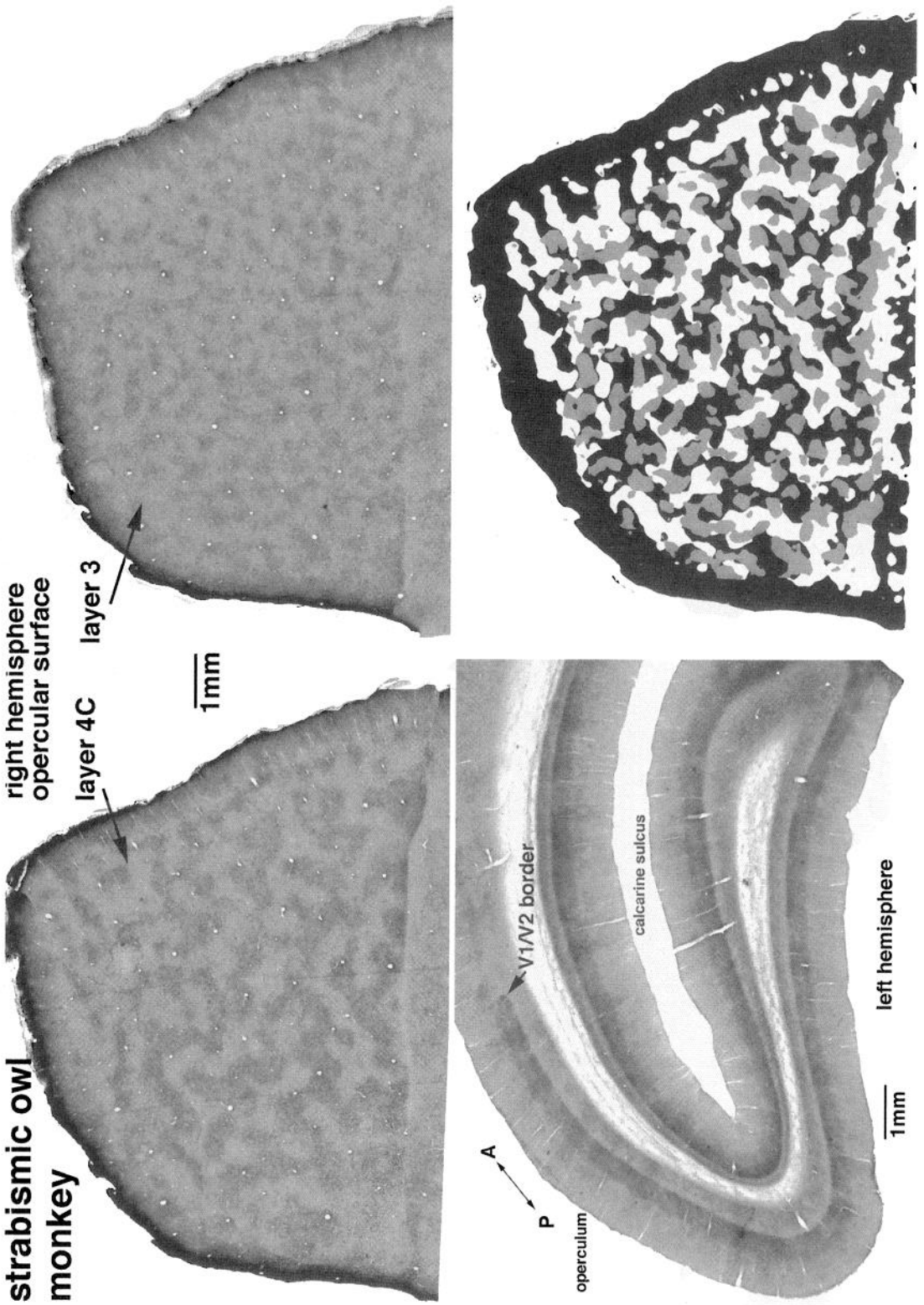

Figure 5. Ocular dominance columns from an owl monkey that had been strabismic from birth until 15 months of age. At 15 months of age, it was monocularly enucleated and perfused 1 month later. The right hemisphere of this monkey was cut tangentially, and the left hemisphere was cut parasagittally. The *top panels* show images from the right hemisphere, and the *bottom left panel* shows one section from the left hemisphere. The left hemisphere section shows the layers in cross-section; columns are present both on the opercular surface and in the buried cortex of the calcarine sulcus, and they span all of layer 4C. The image in the *top left panel* is a montage of three tangential sections through layer 4C, showing the pattern of ocular dominance columns en face. The *top right panel* shows a single section, passing mostly through layer 3, showing the overlying blobs from the same region of cortex. The *bottom right panel* shows computer-mapped images of the blobs (*gray*) and ocular dominance columns (*black* and *white*) from the same right hemisphere sections. The blob pattern and the ocular dominance columns have about the same periodicity, and the mapped blobs are generally smaller over the regions corresponding to the enucleated eye, indicating that they were either lighter or smaller than the blobs over the right eye columns.

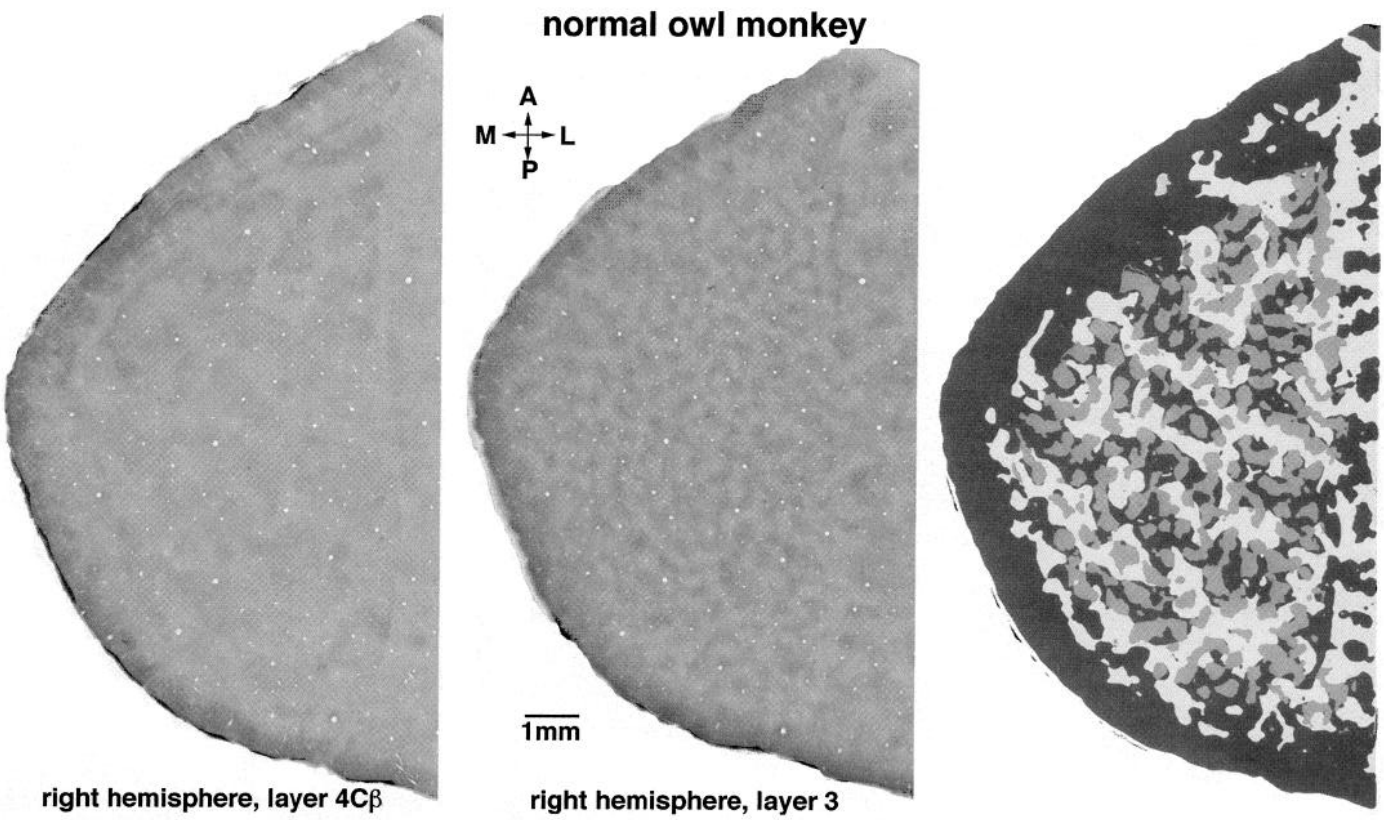

Figure 6. Cytochrome oxidase-stained sections from a normal owl monkey monocularly enucleated at >1 year of age and perfused 1 month later. The *left image* is a montage of three sections through layer 4C and shows clear ocular dominance columns. The *middle image* shows a single section through layer 3 of the overlying blob pattern. The *right image* is a computer-generated map of the ocular dominance columns (in *black* and *white*) and the blobs (in *gray*) from the same sections. The ocular dominance columns are coarser than the blob pattern, and the mapped blobs are generally sparser over the regions corresponding to the enucleated eye.

Owl monkey

Kaas et al. (1976) found no evidence for ocular dominance columns, but Rowe et al. (1978) found ocular dominance columns, only in layer 4Cα of the upper bank of the calcarine sulcus.

Spider monkey

In spider monkeys (*Ateles ater*), Florence et al. (1986) found ocular dominance columns in V1; the columns were faint on the opercular cortex and more striking in the calcarine sulcus, and throughout V1 they were much clearer in layer 4Cβ than in layer 4Cα.

Cebus

Hendrickson et al. (1978) saw no ocular dominance columns in *Cebus albifrons*, but other studies have found ocular dominance columns in *Cebus apella* (Hess and Edwards, 1987; Rosa et al., 1988).

The following is a summary of all of these results. When ocular dominance columns are present in New World monkeys, either normally or after monocular deprivation, they exhibit two gradients. (1) If they are detectable at all, they will be in the calcarine sulcus (which represents the peripheral visual field) in preference to the opercular surface (which represents central vision). (2) If ocular dominance columns are present at all, they are often seen only in layer 4Cβ and not in 4Cα; if they are present in layer 4Cα, they are much clearer in layer 4Cβ (except for the results of Rowe et al., 1978). This pattern is interesting because several lines of evidence indicate that the geniculate inputs to layer 4Cβ mature later than the inputs to layer 4Cα (Rakic, 1977; LeVay et al., 1980; Garey and Saini, 1981). Also, other evidence suggests that the retinal inputs to the representation of the central visual field in the geniculate mature before the inputs representing the periphery (Lachica and Casagrande, 1988). It is not known, however, whether the geniculocortical pathway shows a similar central/peripheral gradient; Rakic (1976, 1977) did not describe any. Nevertheless, it is worth examining the possibility that in New World monkeys, ocular dominance columns tend to develop preferentially in the slowest maturing parts of layer 4C, because that would suggest that a simple timing difference might underlie the differences in ocular dominance column expression.

One possibility is that the relative timing of the geniculocortical projections and the lateral intracortical projections may be critical for the expression of ocular dominance columns. I suggest this because in Hebbian models of ocular dominance column formation (von der Malsburg and Willshaw, 1976; Swindale, 1980; Miller et al., 1989; Obermayer et al., 1995), differences in activity between the two eyes drive the segregation of cortical afferents to a state in which single cells tend to be driven by inputs exclusively from one eye or the other, but it is the lateral connectivity in the cortex itself that drives the tendency for the inputs to cluster into millimeter-wide same-eye regions. That is, in the absence of a factor representing lateral connectivity (or cooperativity) in the cortex, these models produce a salt-and-pepper intermixing of monocular cells rather than ocular dominance columns. Therefore, if in squirrel monkeys, compared to Old World monkeys, the

plastic period for the geniculocortical inputs is earlier relative to the development of the lateral intracortical connections, then one might expect the kind of salt-and-pepper segregation of eye inputs that we saw physiologically in the normal squirrel monkey.

The following scenario of maturational sequences could explain the existing results for squirrel monkey ocular dominance columns: Imagine that in normal squirrel monkeys most of the plastic period for the segregation of the geniculocortical afferents occurs prenatally, but that the lateral intracortical connections mature later, perhaps mostly postnatally. Because eye segregation begins before the lateral intracortical connections are well developed, this timing would result in a salt-and-pepper segregation in layer 4C. The plastic period for the geniculocortical inputs might not be over by birth, but normally the activities of the two eyes become much more correlated after birth because of visual input, so that little further segregation of inputs would happen postnatally. In this model, manipulations that produce significant differences in activity postnatally between the eyes would be expected push the system to develop a coarser (ocular dominance column) eye segregation pattern, because the eyes would have very different patterns of activity at a time when the lateral intracortical connections were also active. According to this scheme, the only difference between animals that express ocular dominance columns and those that do not would be that, in animals that do express ocular dominance columns, the lateral intracortical connections would mature slightly sooner relative to the maturation of the geniculocortical inputs. Moreover, small changes in the relative timing of the maturation of the geniculocortical pathway and lateral intracortical connections might result in a spectrum of ocular dominance expression, even within the same animal, with the later-maturing parts of the geniculocortical projection more likely to develop the coarse pattern and the earlier-maturing parts more likely to develop a salt-and-pepper segregation (which shows up anatomically as no ocular dominance columns). This would explain the tendency for ocular dominance columns to appear preferentially in layer 4Cβ and in the calcarine sulcus.

In previous studies in which ocular dominance columns or patchy labeling was seen in squirrel monkeys or marmosets after monocular deprivation (DeBruyn and Casagrande, 1981; Tigges et al., 1984), it was suggested that the deprivation uncovered a normally weak underlying ocular dominance fluctuation by diminishing the degree of overlap between the two eyes. But I would suggest that in these species, the normal segregation is not "weak" in the sense that most layer 4C cells are binocular with periodic shifts toward domination by one or the other eye but, rather, that the eyes are segregated on a cell-by-cell basis, and that deprivation, instead, coarsens the segregation by prolonging the period when the eyes have disparate activity. I predict, by analogy to the squirrel monkey result, that when layer 4C in an owl monkey or marmoset does not show ocular dominance columns, it would nevertheless show intermixed monocular cells in layer 4C.

In one of the strabismic squirrel monkeys and in one of the normal owl monkeys, the ocular dominance stripes and the blob patterns were clearly of different periodicities, whereas in other owl monkeys, and in all other species examined (Hendrickson et al., 1981; Horton and Hubel, 1981; Horton, 1984), the blob and ocular dominance patterns have the same periodicity. That the blob and ocular dominance column patterns can show variable relative sizes, even within a single species, is consistent with the idea that cortical columns arise from developmental programs rather than represent functional modules or hypercolumns (Purves et al., 1992).

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