Ocular dominance columns in strabismus

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Abstract

During development, the projection from the lateral geniculate nucleus to striate cortex becomes segregated into monocular regions called ocular dominance columns. Prior studies in cats have suggested that experimental strabismus or alternating monocular occlusion increases the width and segregation of columns. In the squirrel monkey, strabismus has been reported to induce the formation of ocular dominance columns. However, these studies are difficult to interpret because no animal can serve as its own control and the degree of inter-individual variability among normal subjects is unclear. We have re-examined the effect of strabismus on ocular dominance columns in a large group of strabismic and normal squirrel monkeys. Five animals rendered strabismic at age one week had well-developed, widely spaced columns. Among 16 control animals, a wide spectrum of column morphology was encountered. Some control animals lacked ocular dominance columns, whereas others had columns similar to those observed in strabismic animals. Natural variation in column expression in normal squirrel monkeys, and potential uncontrolled genetic influences, made it impossible to determine if strabismus affects ocular dominance columns. It was evident however, that strabismus does not affect the binocular projection from the lateral geniculate nucleus to each CO patch in the upper layers. In strabismic monkeys, just as in normal animals, each patch received input from geniculate afferents serving either the left eye or the right eye. In addition, in strabismic monkeys, as in normal animals, patches were not aligned with ocular dominance columns.

Keywords: Squirrel monkey, Striate cortex, V1, Cytochrome oxidase, Patch

Introduction

Ocular dominance columns have been useful for probing the mechanisms that govern the development of the cerebral cortex. Retinal blockade with tetrodotoxin prevents column segregation (Stryker & Harris, 1986). Without visually driven geniculocortical input, it is believed that Hebbian mechanisms that drive column formation via asynchronous activity cannot operate (Miller et al., 1989). An increase in retinal asynchrony, by the same token, may enhance the degree of column segregation. Shatz et al. (1977) noted the unusual clarity of the [3H]proline-labeled ocular dominance columns in a single cat raised after tenotomy of the lateral rectus muscle in one eye. Similar observations were recorded by Löwel (1994) in strabismic kittens. Physiological studies have also shown a greater proportion of monocular cells in animals raised with strabismus or alternating monocular occlusion, consistent with increased column segregation (Hubel & Wiesel, 1965; Van Sluyter & Levitt, 1980; Chino et al., 1994; Sengpiel et al., 1994; Smith et al., 1997).

In the cat, it is difficult to assess the impact of strabismus on the segregation of geniculocortical afferents because the clarity of ocular dominance columns labeled by [3H]proline autoradiography shows marked variation in normal animals. Potentially, the squirrel monkey offers a better opportunity to demonstrate the effects of strabismus. This species has been reported to lack ocular dominance columns entirely (Hubel et al., 1976; Tigges et al., 1977; Hendrickson et al., 1978; Rowe et al., 1978; Hendrickson & Tigges, 1985; Livingstone et al., 1995). To induce their formation, Livingstone (1996) raised four squirrel monkeys with divergent strabismus. One animal developed columns throughout V1, another had columns in part of V1, and two had no columns at all. It was unclear why strabismus produced different effects among this sample of four animals. However, the study provided some evidence that strabismus can induce columns to form in a species where normally they are wholly absent.

In her study of strabismic squirrel monkeys, Livingstone (1996) examined a single control animal for ocular dominance columns. None were found. A contemporaneous report, however, showed that ocular dominance columns can occur in normal squirrel monkeys (Horton & Hocking, 1996c). This finding raises a dilemma: were the columns observed by Livingstone in half her animals a product of strabismus, or did they occur as a phenotypic variant in normal squirrel monkeys? We have examined a larger cohort of normal and strabismic animals to address this issue.

In normal squirrel monkeys, there is no relationship between ocular dominance columns and CO patches, and every CO patch receives geniculate input driven by the left eye and the right eye (Horton & Hocking, 1996c). In the present experiments, we have...
also tested whether strabismus acts to align patches and columns, and whether the geniculate input to the CO patches becomes more monocular.

Materials and methods

Five squirrel monkeys (Saimiri sciureus) from the California National Primate Center, Davis (CNPRC) were rendered strabismic by bilateral medial rectus tenotomy under anesthesia with ketamine HCl (15 mg/kg, i.m.) at age one week. A week after surgery, flash photographs were taken of awake, hand-held monkeys with a ring flash and a 100-mm macro lens to record the angle of exotropia. The magnitude of strabismus was determined by measuring the decentration of the corneal light reflex from the center of the pupil. For adult macaque monkey eyes, it is equal to 14\(^{\circ}/\text{mm}\) (Hirschberg ratio) (Quick & Boothe, 1989). The Hirschberg ratio depends on the distance from the center of the pupil to the center of the corneal curvature. Using fixed eyes, we calculated the Hirschberg ratio to be approximately 20\(^{\circ}/\text{mm}\) in the squirrel monkey. Fig. 1 shows a photograph of Monkey B at age two weeks, demonstrating about 50 deg of divergent strabismus.

After strabismus surgery, infant monkeys were reared with their mothers in a free-ranging indoor colony. They were transferred to UCSF at age ~2 years. Six control monkeys with normal eye alignment were obtained from the same colony. In addition, 10 more control animals were obtained later from two other sources. Upon arrival at UCSF, each monkey was examined while handheld for assessment of pupils and eye movements. Photographs were taken to document eye alignment. Then, cycloplegic retinoscopy, fundus examination, and fundus photography were performed.

To label the ocular dominance columns with cytochrome oxidase (CO), one eye was enucleated under general anesthesia with 1.5% isoflurane and retrobulbar anesthesia with 2% lidocaine with epinephrine 1:100,000. Loss of CO activity induced by eye removal makes the ocular dominance columns visible. In some animals the ocular dominance columns were also labeled transneuronally by injecting the remaining eye with 2 mCi of \(^{3}H\)proline. In a single case, Monkey B, \(^{3}H\)proline was injected without monocular enucleation. Animals were revived to allow time for \(^{3}H\)proline transport and/or a change in cortical CO activity. After regaining consciousness, all animals received an opiate analgesic (buprenorphine HCl, 0.03 mg/kg, i.m.) at least three times per day until fully recovered. After a minimum survival of one week, animals received a lethal dose of sodium pentobarbital (150 mg/kg, i.v.) followed by transcardial perfusion with 1 L of normal saline and 1 L of 1% paraformaldehyde.

In four of five strabismic animals and four of sixteen normal animals the ocular dominance columns were double-labeled with CO and \(^{3}H\)proline. The column patterns yielded by these two anatomical methods were essentially identical in every case. Once this fact became evident, we stopped performing \(^{3}H\)proline eye

![Fig. 1. Monkey B: Photographic assessment of strabismus angle. Photograph taken a week after bimedial rectus tenotomy, demonstrating a large exodeviation. Because the black pupil is poorly visible against the brown iris, contrast and brightness have been increased in the square regions. The ring-flash reflection from the corneal light reflex is deviated nasally 0.85 mm in the right eye and 1.55 mm nasally in the left eye, for a total exotropia of 50 deg (2.4 mm × 20\(^{\circ}/\text{mm}\)). Note that the 4th Purkinje image is visible near the center of each pupil, as well as the reflection of the person holding the monkey in the temporal cornea of the right eye.](image)
injections because the columns could be labeled more easily and inexpensively with CO alone. All monkeys were over age two at the time of eye enucleation. This is well after the critical period for plasticity of ocular dominance columns.

Brains were removed and a region of cortex including V1 and V2 was dissected and flattened onto a glass slide. After further fixation and cryoprotection, the flatmounted tissue was cut at 30–40 μm on a freezing microtome parallel to the pial surface. In animals receiving a [3H]proline eye injection, alternate 20-μm sections were dipped in photographic emulsion (Kodak NTB2) and exposed in a dark room for six weeks for autoradiography. Otherwise, all sections were processed for CO in preparation for montages of layer 4C (Adams & Horton, 2003b). The lateral geniculate nuclei were cut coronally at 40 μm. Alternate sections were processed for CO, Nissl, or autoradiography.

Cortical CO flatmounts were imaged at 600 dots per inch on an Agfa Arcus II flatbed scanner fitted with a transparency adapter to prepare montages of layer 4Cβ. Autoradiographs were photographed with a Diagnostic Instruments Spot RT Slider camera mounted on an Olympus SZH10 microscope. Images were imported into Photoshop 7.0 to compile the montages. In the final images, a dust and scratches filter was used to eliminate blood vessels.

To measure the periodicity of the columns the V1 montage was first excised from the surrounding image. The distribution of pixel values was then adjusted to span the full range of 0–255. To reduce edge effects, each montage was placed on a background adjusted to the mean gray level. The images were blurred using a Gaussian filter of diameter 35 μm to eliminate blood vessels and other high frequency components. Next, the radially-summed Fourier spectrum was plotted for each montage using Matlab. The mean column width was defined as the location of the peak in the Fourier power spectrum (see Fig. 5 later).

**Results**

*Ocular dominance columns in strabismic squirrel monkeys*

It was critical for the success of these experiments to create a large deviation of the eyes, so that doubts would not arise later regarding whether or not an animal was truly strabismic. Amazingly, infant rhesus monkeys can realign their eyes spontaneously after a free tenotomy of the medial rectus muscles (Von Noorden & Dowling, 1970). We confirmed photographically the angle of strabismus in each monkey, a week after surgery and at age 2 years (Fig. 1). In all five monkeys, a large exotropia was present one week after

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**Fig. 2.** [3H]proline autoradiograph of layer 4Cβ from the left striate cortex of a strabismic animal, Monkey G. The right eye was injected with the radioactive tracer, yielding ocular dominance columns, which appear bright in darkfield. Note that columns are present everywhere except in the representation of the blind spot (dark oval) and the monocular crescent (solid, bright label). The boxed region is shown in Fig. 3. The same cortex, with the columns labeled by CO, is shown in Fig. 4A, Monkey G, left cortex.

**Fig. 3.** Autoradiography and CO reveal the same ocular dominance column pattern. A, Boxed region from Fig. 2, showing columns labeled by [3H]proline. B, Same region from Monkey G, delineated by the box in Fig. 4B, with pale columns in the CO montage corresponding to the enucleated left eye. C, Dark shading denotes the unlabeled areas in A, corresponding to the ocular dominance columns of the left eye. Outline marks the borders of the columns in B. The patterns in A and B are similar, indicating that autoradiography and CO yield the same result.
surgery, ranging between 23 deg to 62 deg. All five animals retained a large angle of exotropia into adulthood.

Fig. 2 shows well-formed ocular dominance columns in the left hemisphere of a strabismic animal, labeled by \[^{3} \text{H}\]proline injection into the right eye. In this animal, the columns were double-labeled by enucleating the left eye a week before death. Alternate tissue sections were processed for CO and autoradiography. Comparison of the column patterns labeled by CO and \[^{3} \text{H}\]proline shows that they appear extremely similar (Fig. 3). The same was true in normal squirrel monkeys (compare Figs. 1 and 3 in Adams.

**Fig. 4.** Ocular dominance column patterns in 5 strabismic animals. A, Flatmount montages of layer 4C/b from the left and right striate cortex of each strabismic squirrel monkey, showing well-segregated ocular dominance columns in every animal. In Monkeys A, F, G, & H the cortex was stained for CO after enucleation of the left eye; in Monkey B the right eye was injected with \[^{3} \text{H}\]proline. Monkey F was discovered to have suffered a depressed occipital skull fracture at some time during infancy, damaging striate cortex and partly obliterating the column pattern in the right hemisphere. Except for this case, the column patterns in opposite hemispheres are highly symmetric. Insert for Monkey G shows an autoradiograph of the LGN after \[^{3} \text{H}\]proline injection into the right eye. B, Column mosaics created by Fourier filtering of the images in A. Mean column width is indicated for each animal. BS, blind spot and MC, monocular crescent. All panels to scale.
Strabismus in squirrel monkeys

Fig. 5. Radially summed Fourier spectra of normal and strabismic squirrel monkey column patterns. Strabismic animals have more widely spaced columns than normal animals from the same colony. However, some normal animals (Monkeys N and O), have columns of periodicity similar to those in the strabismic group. Means and standard deviations are shown for each group.

Persistence of binocular input to patches in strabismic animals

In the macaque, CO patches are aligned into rows that fit in register with the ocular dominance columns (Horton & Hubel, 1981; Horton, 1984). After [3H]proline injection into one eye, every other row of patches is labeled, coinciding with the labeled ocular dominance columns in 4C (Horton & Hocking, 1996b). Therefore, the direct konio input to CO patches in layer 2/3 is monocular. In the squirrel monkey, the situation is entirely different. The input to CO patches is binocular, and every CO patch is labeled following tracer injection into either eye (Livingstone & Hubel, 1982; Fitzpatrick et al., 1983; Weber et al., 1983; Horton, 1984; Itaya et al., 1984; Horton & Hocking, 1996c). We tested whether strabismus disrupts the binocular input to patches in the squirrel monkey.

Fig. 6A shows the ocular dominance columns from the right striate cortex of a strabismic squirrel monkey after [3H]proline eye injection. No enucleation was performed in this animal. The columns are crisply segregated. The CO patches in the upper layers appear indistinguishable from those found in normal animals. They form a regular array (Fig. 6B), with mean spacing of 480 µm determined from the peak in the Fourier power spectrum. Comparison with an adjacent autoradiograph shows that every single CO patch is labeled. This means that early disruption of ocular alignment does not cause gross segregation of intermingled left eye and right eye geniculate afferents in the CO patches within layer 2/3. This result was confirmed in one other strabismic monkey. In addition, the patches did not form single rows aligned with the ocular dominance columns (Fig. 6F).

Immense natural variation of columns in normal monkeys

At first glance, the development of striking column patterns in all five strabismic animals seemed to confirm that misalignment of the eyes during infancy increases the segregation and periodicity of ocular dominance columns in the squirrel monkey. However, a remarkable degree of variation in column patterns was encountered among the 12 control animals (see Fig. 1 in Adams & Horton, 2003a). This spectrum of column morphology in normal monkeys was arbitrarily divided into four classes, based on the mean single column width. There were two animals with coarse columns (~600 µm), two animals with medium columns (~450 µm), four animals with fine columns (~250 µm), and four animals with columns so indistinct that no width could be determined. Since publication of this brief communication (Adams & Horton, 2003a), we have examined four more normal squirrel monkeys. All four happened to have indistinct, rudimentary columns.

This heterogeneity of column morphology among normal squirrel monkeys was wholly unexpected. In macaques, column periodicity can vary by twofold, but columns are always present (Horton & Hocking, 1996a). In contrast, half (8/16) the control squirrel monkeys in this study showed virtually no evidence of columns.

In cats, variation in the size of orientation columns among different individuals has been reported. Interestingly, cats from the same litter tend to share the same column spacing, suggesting an influence of heredity (Kaschube et al., 2003). If column spacing is subject to genetic influence, the most informative control animals would be those from the same colony as the strabismic animals. The colony providing our strabismic animals, numbering 60–80 monkeys, was derived from a Peruvian source about a decade ago (Mason & Mendoza, 1998). Six control animals also came from this colony (Fig. 5). The control animals had a mean single column width of 367 µm (range 301–495µm). This value was less than the mean column width of 560 µm in the five strabismic monkeys implying an effect of strabismus on column width.

However, even among the animals in this colony, it is possible that genetic heritage may have played a confounding role. In two cases, controls and strabismics shared mothers (and perhaps fathers). Control Monkey O (mean column width 495 µm) was a half sister of strabismic Monkey A (mean column width 679 µm) (Fig. 7A). It had well-segregated columns in the calcarine cortex,
resembling those found in Monkey A. However, the columns in Monkey O were narrower, and nearly disappeared in the opercular cortex. Control Monkey P (mean column width 344 μm) was a half sister of strabismic Monkey G (mean column width 517 μm). It had clear columns in opercular cortex, which appeared finer than those in Monkey G (Fig. 7B). The columns in the calcarine sulcus were less distinct than those on the operculum (just the opposite of the situation in Monkey O). Two half-sibling control animals, Monkey C (mean column width 312 μm) and Monkey Q (mean column width 258 μm), had very similar columns (Fig. 7C). These examples of column patterns among closely related monkeys indicate that parentage could be a factor. The difference in mean column width between control monkeys and strabismic monkeys might be due in part to inheritance, rather than to strabismus.

Fig. 7 shows four of the control animals from the Peruvian colony. The other two control animals from this colony, shown in Fig. 8, had medium columns: Monkey D (409 μm) and Monkey E (452 μm). All 11 monkeys (five strabismic, six normal) from this colony had ocular dominance columns. To determine if this property might vary by colony, we examined six normal monkeys imported together from Bolivia. Four had essentially no columns (Fig. 9), a fifth had fine columns, and the last (Monkey N) had well-formed, coarse columns of width 528 μm (see Fig. 1A in Adams & Horton, 2003a). Finally, four monkeys were obtained from Guyana. None showed any hint of columns. This sample of control monkeys derived from three different sources provided anecdotal evidence, with the glaring exception of Monkey N, that colony origin might be an important factor.
Ocular dominance columns influence the upper layers

In the macaque, the ocular dominance columns in layer 4C exert a strong influence on the ocular bias of the upper layers. Consequently, after monocular enucleation, pale rows of patches emerge in register with pale ocular dominance columns in 4C (see Fig. 4 in Adams & Horton, 2003b). In squirrel monkeys with fine or absent columns this effect does not occur (see Fig. 3 in Adams & Horton, 2003b), presumably because ocular segregation in 4C is poor and the konio input to the patches is binocular. In such animals, all the patches appear evenly stained after monocular enucleation.

We inquired whether the well-developed ocular dominance columns in our strabismic squirrel monkeys might affect CO activity in the upper layers after monocular enucleation. Fig. 10 shows the ocular dominance columns in layer 4C from an animal with strabismus. In the upper layers, the “ghost” of the ocular dominance column pattern is visible, independent of the patch mosaic. This shows that the ocular dominance columns in 4C can influence metabolic activity in the upper layers. In such animals, optical imaging would be capable of revealing ocular dominance columns in vivo.

This effect also occurs in those normal squirrel monkeys that have well-segregated ocular dominance columns. Fig. 11 shows the ocular dominance columns in layer 4C from a control Monkey N with coarse columns. In layer 2/3, there is a faint fluctuation in CO density that corresponds to the ocular dominance columns. The contrast is not as pronounced as seen in normal macaques after monocular enucleation, and there is no one-to-one spatial relationship between patches and columns. Nonetheless, it is remarkable

Fig. 7. Comparison of ocular dominance columns in half-siblings. CO montages comparing the left hemispheres from 3 pairs of animals that shared the same mothers. Column periodicity was extremely similar in the two control animals, C and Q, suggesting that parentage may influence column width. Even in the normal/strabismic pairs, the columns are similar in some regions of the cortex.
that any influence of the ocular dominance columns is present in layer 2/3, when one considers that each CO patch in the squirrel monkey receives rich binocular input.

**Segregation of geniculate laminae and ocular dominance columns**

In squirrel monkeys, laminae within the lateral geniculate nucleus are less well segregated than in the macaque (Doty et al., 1966; Campos-Ortega & Glees, 1967; Jacobs, 1969). It would be of interest to know if animals with poor ocular segregation of the lateral geniculate nucleus exhibit poor segregation of their ocular dominance columns. In normal animals, we did not observe any striking difference between the geniculate nuclei of animals with columns and without columns. In animals with well-segregated columns, considerable intermingling of ocular inputs was still present in the lateral geniculate nucleus (Fig. 8). However, all the strabismic monkeys showed unusually sharp delineation of ocular laminae in the lateral geniculate nucleus (Fig. 4A, Monkey G).

**Discussion**

To simulate the development of ocular dominance column patterns has posed an irresistible challenge to the field of computational modeling. The utility of this approach is to synthesize the processes involved in column formation and make predictions about how changing variables will affect the resulting pattern. These predictions can then be tested experimentally. A number of models have been proposed, each able to produce a realistic pattern given a few variables (von der Malsburg & Willshaw, 1976; Swindale, 1980; Miller et al., 1989; Goodhill & Willshaw, 1990; Jones et al., 1991; Harris et al., 1997). Most models of ocular dominance column formation operate using an algorithm that allots cortical territory to one eye or the other based on competitive rules. The “Elastic Net” model (Goodhill, 1993) predicts that a decrease in correlated activity between the eyes would serve to increase column periodicity. Initial experimental results appeared to confirm this prediction (Goodhill & Löwel, 1995). Löwel (1994) found that a group of strabismic cats had increased column width compared

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**Fig. 8.** Control monkeys with medium columns. A, Monkey D, left hemisphere, showing CO-labeled columns with a mean width of 409 μm. Insert shows the left lateral geniculate body from this animal, labeled by [3H]proline injection into the right eye. Laminae 3, 4, and 5 were poorly segregated, despite well-formed columns in the cortex. The image of the LGN covers a flaw in the CO mosaic. B, Monkey E, left hemisphere, showing medium columns with a mean width of 452 μm.

**Fig. 9.** Monkey I. A control monkey with essentially no columns. The optic disc representation in the left hemisphere and the monocular crescent representation in the right hemisphere (arrow) are visible because the left eye was enucleated. Note that the stripes in V2 are well demarcated despite the absence of columns in V1.
to a control group. Tieman & Tumosa (1997) later showed a similar, but smaller, effect from alternate monocular occlusion. However, when the natural variation in periodicity of ocular dominance columns among normal cats was fully appreciated, the effect of strabismus became less certain (Rathjen et al., 2002).

The width of ocular dominance columns in normal macaques varies over a two-fold range (Horton & Hocking, 1996a). Studies of macaque monkeys raised with strabismus have not found any evidence of increased column spacing (Tychsen & Burkhalter, 1995; Crawford, 1998; Murphy et al., 1998; Fenstermaker et al., 2001; Crawford & Harwerth, 2004). However, given the natural variation among control animals, a modest effect of strabismus would be difficult to detect. The strongest argument against any effect of strabismus in the macaque is that the ocular dominance columns are present at birth (Horton & Hocking, 1996b). Thus, the layout of the columns is determined prior to visual experience. For strabismus to have any influence, they would have to melt down and reform with a coarser periodicity. This is an unlikely proposition.

In the squirrel monkey, nothing is known about the timing of the formation of ocular dominance columns. In many individuals, geniculocortical afferents remain intermingled throughout life. In such animals, it is conceivable that strabismus could exert a strong effect on the degree of column formation, by promoting the segregation of geniculocortical afferents during an early critical
period of cortical plasticity. Previously, it has been shown that reciprocal exchange of cortical territory occurs between the eyes in response to the local influence exerted by the shadows of retinal blood vessels (Adams & Horton, 2002). Similarly, strabismus might also affect the segregation of columns.

It has been proposed that strabismus induces the development of ocular dominance columns in the squirrel monkey (Livingstone, 1996). Divergent strabismus was produced in three animals by cutting the medial rectus muscles. One animal had clear ocular dominance columns throughout striate cortex. A second animal had ocular dominance columns only in calcarine, but not opercular cortex. The absence of columns in opercular cortex was attributed to the animal’s mild degree of strabismus. However, one should expect, in anything, the opposite result. The macula is represented in the operculum, where receptive fields are small. Here, a small misalignment of the eyes should have a much greater impact, compared with calcarine cortex, where peripheral retina is represented and receptive fields are large. The third monkey showed no ocular dominance columns. The author suggested that this animal might have recovered normal eye alignment. Finally, a fourth monkey was raised with daily alternating monocular occlusion to create strabismus. This animal had no ocular dominance columns either. It was concluded that this monkey probably had some normal visual experience because it removed its contact lens occasionally.

In light of our findings, it is possible that the occurrence of columns in two out of four strabismic monkeys in the earlier-referenced study represents natural variation in the expression of ocular dominance columns, rather than an effect of strabismus. This would explain why two strabismic animals failed to show columns, (about 50% of normal animals lack columns). It would also explain why one animal showed columns in only part of striate cortex. This is a phenotype observed in some normal animals (see Monkey O, Fig. 7).

All five strabismic animals in our study had coarse, well-segregated columns. These data could be construed as evidence for a strong effect of strabismus on the formation of ocular dominance columns. We have resisted this interpretation, because it is not definitive. The effect of monocular lid suture is obvious in individual animals, because deprivation shrinks one eye’s columns and expands the other’s. However, to detect an increase in the width of both eye’s columns is not as straightforward. There is no way to judge the effect of an experimental manipulation in a given animal without knowing first how wide the columns would have been otherwise. We attempted to overcome this problem by studying a relatively large number of normal and strabismic animals. When the degree of natural variation turned out to be much greater than expected, we were foiled.

It is quite likely that column periodicity is subject to genetic influences (Kaschube, 2002, 2003; Rathjen et al., 2002). This means that one must genetically match control and strabismic animals to isolate the effect of strabismus. Although six control animals were from the same colony as the strabismic animals, most had different parents. We should have compared columns in full siblings, raising one animal with strabismus while using the other as a normal control animal. Genetic methods are easily available now to determine the parentage of a given animal in a free ranging colony. However, when we began these experiments we had no inkling of the wide variation that exists in normal animals, so we did not adopt this approach.

We found columns in zero out of 4 normal animals from Guyana, and in two out of six animals from Bolivia. It is possible that there exist subspecies of squirrel monkeys in different regions of South America (Hershkovitz, 1984). However, one of the Bolivian animals (Monkey N) had exceptionally well formed columns so it is unlikely to be a simple question of some subspecies having columns, and others lacking them. Multiple factors may control column width, including (but not restricted to) genetic make-up, post-natal eye alignment, and the degree of cortical development at birth, each of which may vary in individual animals. Caution is warranted when drawing conclusions based on small numbers of animals from different subgroups. After studying five strabismic animals and 16 control animals we are still unsure if strabismus affects the periodicity or segregation of ocular dominance columns.

The effect of strabismus on the geniculate input to CO patches in layer 2/3 was clearer. In strabismic animals, every CO patch was labeled after monocular [3H]proline injection, just as in normal animals. One might have expected each eye to abandon half the patches, based on models of activity-driven segregation. It is possible that, on a microscopic scale, geniculate afferents serving each eye become segregated within patches, to synapse on different cells. This explains the high proportion of monocular cells we have recorded in squirrel monkeys raised with strabismus (Adams & Horton, 2006).

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