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SHORT COMMUNICATION

An albino-like decussation error in the optic chiasm revealed by anomalous ocular dominance columns

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Abstract

We report a unique anomaly in the ocular dominance column pattern of a single, normally pigmented macaque monkey. The column pattern contained large monocular areas inserted between the normal columns and the dorsal V1 border. These monocular regions received transneuronal input from the contralateral eye, indicating that a small population of temporal ganglion cells erroneously decussated at the optic chiasm. Projection of the column pattern back onto the visual field showed that the monocular wedges represented a ~5-deg sector of ipsilateral field. This corresponded to the extent of naso-temporal overlap of ganglion cells in the normal retina, suggesting an error in axon guidance affecting cells close to the vertical midline of the retina. The consequences of the crossing error in this animal were threefold: it produced an anomalous monocular zone near the V1 border, the vertical meridian was not represented at the V1 border, and points near the vertical meridian were represented twice in the brain, once in each hemisphere.

Keywords: Primary visual cortex, Cytochrome oxidase, Stereopsis, Axon guidance, Albino

Introduction

Ocular dominance columns in primary visual cortex (V1, striate cortex) have been particularly instructive for probing neural development and plasticity. Changes in transneuronal retinal input to V1 can be investigated by labeling ocular dominance columns. Reconstruction of column patterns has become the standard means for assessing the effects of visual deprivation, and for defining the critical period in mammals (Hubel et al., 1977). In many primate species, the columns form a stereotypical pattern with respect to retinotopic landmarks, making it relatively easy to detect abnormalities. For instance, in macaques the columns terminate abruptly at right angles to the V1 border (Fig. 1A) (LeVay et al., 1985), where the vertical meridian is represented precisely (Talbot & Marshall, 1941; Daniel & Whitteridge, 1961; Dow et al., 1985). When extreme abnormalities occur, it always indicates that some form of miswiring has occurred in the visual pathways. For example, in albinos the ocular dominance columns are absent in portions of V1, because of a decussation error at the chiasm (Guillery et al., 1984).

The columns can be revealed by enucleating one eye and processing V1 for the metabolic enzyme, cytochrome oxidase (CO) (Fig. 1B) (Horton, 1984). The enucleated eye's columns appear pale, because their physiological activity is reduced. The pattern of columns labeled by this approach corresponds precisely to the retinal input supplying the cortex. This can be shown by injecting [^{3}H]proline into the vitreous of the remaining eye (Wiesel et al., 1974). Proline imbibed by retinal ganglion cells is transported transneuronally to the cortex where it labels a pattern of columns identical to that revealed with CO (Fig. 1C). Thus, aberrations in the retinal input to V1 can be discovered simply by examining CO-labeled columns.

In the central visual field representation, the area occupied by the columns serving the two eyes is nearly equal (Horton & Hocking, 1996). Here we report a unique anomaly in the pattern of ocular dominance columns in a macaque monkey. In both hemispheres of this animal, a wedge of monocular tissue supplied by the contralateral eye was juxtaposed between the normal columns and the V1 border, leading to a misrepresentation of the visual field in V1. This error shows that accurate mapping of sensory fields along the midline is not a trivial feat.

Methods

The anomalous monkey came to light in connection with an unrelated study, examining projections from V1 to V2 (Sincich & Horton, 2002). It was a normally pigmented, adult male *Macaca fascicularis*, obtained from a feral colony on the island of Mauritius. Enucleation of the right eye was performed under isoflurane

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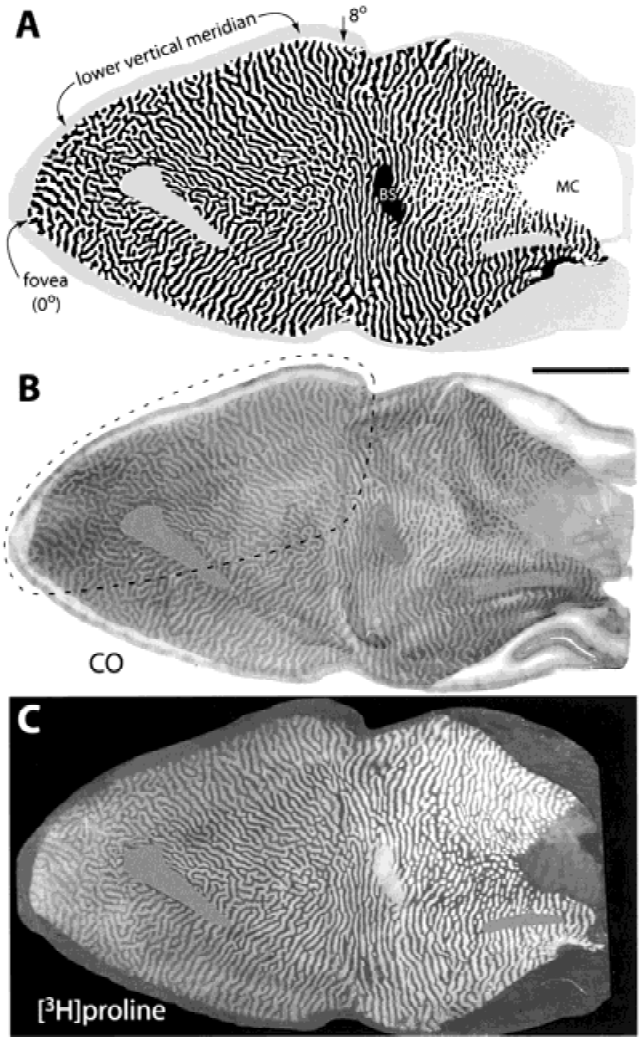

Fig. 1. The left cortex of a normal macaque monkey showing ocular dominance columns supplied by the left (black) and right eye (white). (A) Columns are present everywhere except in the representation of the monocular crescent (MC) and the blind spot (BS). The left half of the cortex represents from the fovea (0 deg) to the central 8 deg of the contralateral visual hemifield. (B) CO montage of a V1 flatmount after right eye enucleation showing the column pattern used to produce A. Dashed line indicates the area of V1 shown in Fig. 2 for the anomalous monkey. (C) Autoradiograph prepared from alternate sections after injection of [^{3}H]proline into the remaining left eye. The perfect match between B and C shows that CO can be used to map retinal input. Scale: A–C, 1 cm.

anesthesia, as previously described (Horton & Hocking, 1996), followed by a 3-day survival time.

The normal monkey (Fig. 1), described for comparison, also had its right eye removed under general anesthesia. Weeks later an intravitreal injection of 2 miCu [^{3}H]proline was made in the remaining left eye, followed by a 10-day survival for transneuronal transport. All surgical procedures in both monkeys followed protocols approved by the University of California, San Francisco Committee on Animal Research.

The animals were given a lethal dose of pentobarbital intraperitoneally, then transcardially perfused with 1 l saline followed by l l 1% paraformaldehyde in 0.1 M phosphate buffer (pH 7.4). Visual cortex was removed, unfolded, and flattened prior to histological processing for cytochrome oxidase (Horton & Hocking, 1996) or autoradiography (normal monkey only) (Wiesel et al., 1974).

Montages of the ocular dominance columns were made from images of individual sections cut through layer 4Cβ, using Adobe Photoshop 6.0. Rendering the column patterns onto the visual field was done with Elastic Reality 3.0 (www.avid.com). This procedure required assignment of points on the cortical surface to corresponding retinotopic points in the visual hemifield. The fovea (0 deg) was set at the lateral-most apogee of V1 (Tootell et al., 1988). The horizontal meridian was placed in a location where it bisected V1 into dorsal and ventral halves. Although ventral V1 was only partially retained, we estimated its perimeter by examining other V1 column montages prepared in our laboratory (Horton & Hocking, 1996). Normally, the vertical meridian corresponds to the V1 border. However, we elected to place the vertical meridian along the transition in cortex between normal ocular dominance columns and the anomalous zone of contralateral ocular input. In the Discussion, we explain why the vertical meridian was placed in this location. Its exact location was admittedly a matter of judgement, because the transition was not abrupt.

After locating the fovea, horizontal meridian, and vertical meridian, we used published cortical magnification data (Hubel & Freeman, 1977) to determine the eccentricity of points situated every 5 mm along five principal polar meridia (upper vertical, lower vertical, horizontal, and two obliques). Cortical magnification factor was adjusted to account for the 1.5:1.0 anisotropy along the vertical meridian versus the horizontal meridian in striate cortex (Van Essen et al., 1984; Tootell et al., 1988; Blasdel & Campbell, 2001). A total of 31 correspondence points, forming a ring-and-ray pattern, provided the data set for the computer transformation of the cortical surface onto visual space.

Results

In a mirror-symmetric fashion, both hemispheres contained a wedge of V1 cortex which was largely monocular, containing only a few column islands serving the other eye (Figs. 2A–2D). The peculiarity was present along the dorsal V1 border, in a region representing the central 8 deg of the lower vertical meridian. It began 8 mm from the foveal representation and widened gradually with increasing eccentricity. It could not be followed beyond 8 deg, because the peripheral cortex was not retained. The columns were narrow in this animal (mean = 390 μm), at the low end of the range for normal macaques (Horton & Hocking, 1996). The monocular wedge was supplied by the contralateral eye in each hemisphere. This was determined by observing that it was pale in the left hemisphere (pale = enucleated right eye) and dark in the right hemisphere.

To estimate the visuotopic extent of the monocular wedge, the V1 column pattern was projected back into the visual fields (Fig. 2E). The wedge translated into a roughly 5-deg sector along the lower vertical meridian in each visual hemifield. Thus the ocular dominance pattern, and the cortical retinotopic map, were altered over a region of visual space corresponding to 5 deg. The backprojected width of the monocular wedge is a direct product of the cortical magnification factor for macaque V1.

The nature of the mapping error responsible for the anomalous column pattern in this animal is explained in the Discussion. It resulted in a shift in location of the vertical meridian representation, and inclusion of 5 deg of ipsilateral visual field in each cortex. Consequently, a 5-deg sector of visual space along the

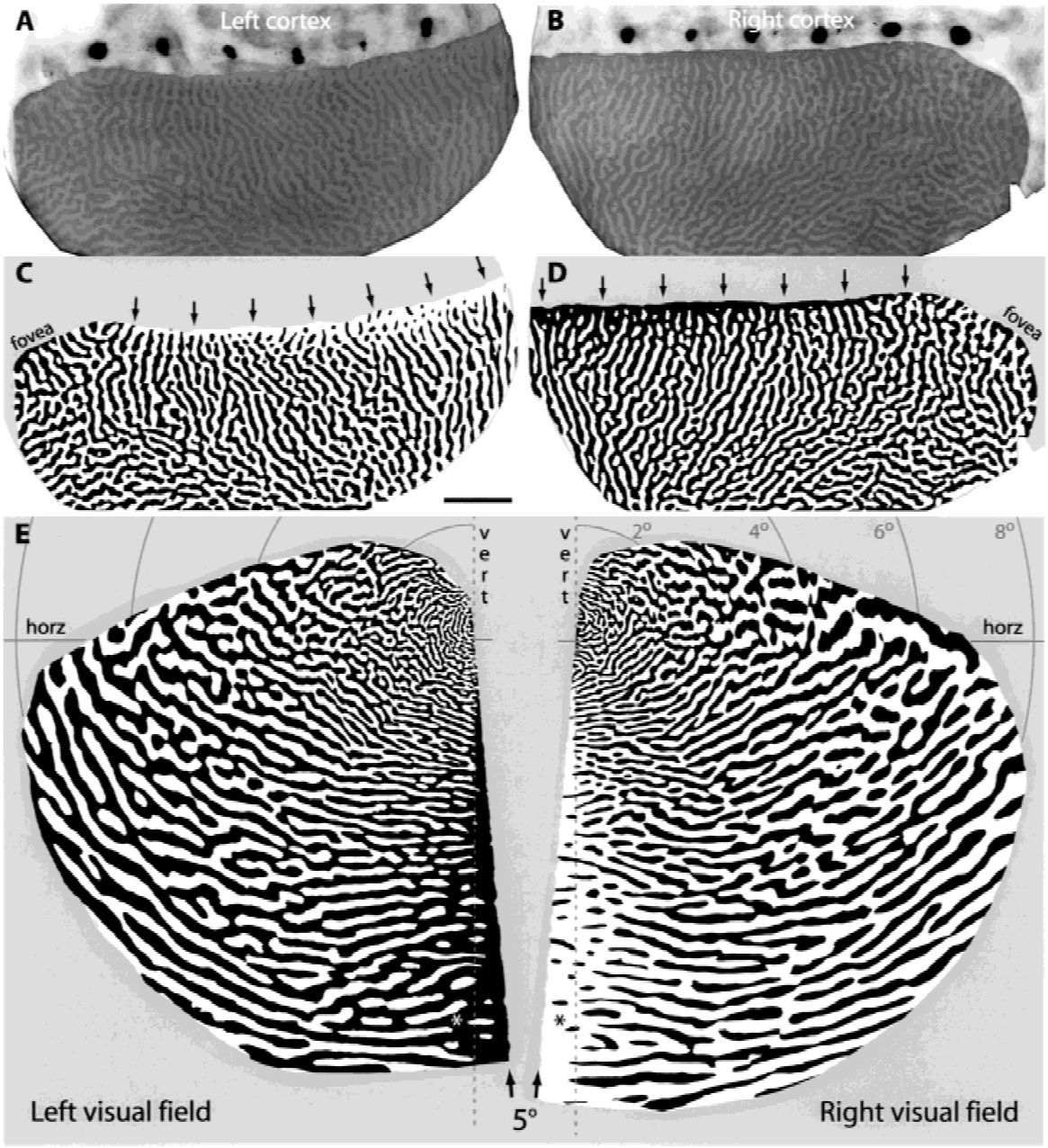

Fig. 2. An anomalous wedge of monocular input to V1 is present along the dorsal V1 border in a normal macaque. (A,B) CO montages from the left and right hemispheres after right eye enucleation. Black spots in V2 are tracer deposits from an unrelated study. (C,D) Thresholded images of the ocular dominance columns labeled by CO. Arrows point to the abnormal monocular strip situated between the V1 border and the normal column pattern. (E) Projection of the V1 columns back into the visual fields. Each monocular zone corresponds to a 5-deg sector along the lower vertical meridian, extending into the ipsilateral visual field. Eccentricity from the fovea is marked out to 8 deg. Points near the vertical meridian (e.g. asterisks) are represented twice, once in each hemisphere. Scale: A–D, 5 mm.

lower vertical meridian was dually represented in this animal, once in each hemisphere. An example of a dually represented point is denoted by the pair of asterisks in Fig. 2E.

Discussion

How did this anomaly arise? The possibilities are constrained by the fact that the anomaly in the cortex is bilateral and symmetric. No abnormality, confined to just one eye, could be responsible. The zone of monocular input to each cortex could have arisen by excessive input from the contralateral eye, or by loss of input from the ipsilateral eye. The choice of mechanism determines the placement of the vertical meridian with respect to the V1 border in the cortex.

Consider first the possibility that input was lost from the ipsilateral eye, leaving a zone of pure contralateral eye input in the

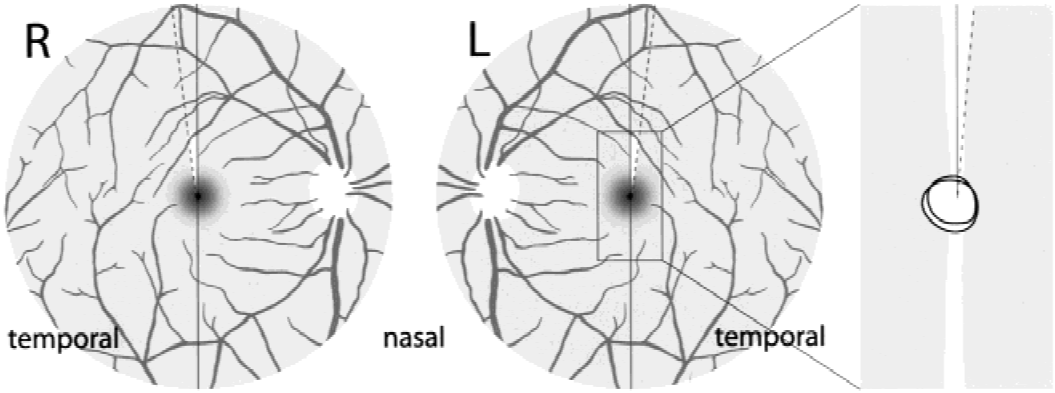

Fig. 3. Projection of the 5-deg monocular visual field sectors onto the retinae showing the zones between the vertical meridia and the dashed lines that contain ganglion cells in temporal retina presumed to decussate incorrectly. (Detail) For comparison, the normal zone of overlap between ipsi- and contra-projecting ganglion cells is shown in white (Fukuda et al., 1989).

cortex. In this case, the representation of the vertical meridian would remain at its normal location along the V1 border. One might postulate focal loss of ganglion cells in a narrow sliver of retina, just temporal to the vertical meridian in each retina (Fig. 3). This would reduce ipsilateral eye input along the dorsal V1 border in each hemisphere. However, we found no evidence of focal ganglion cell depopulation along a sector near the vertical meridian in temporal retina. It is also conceivable that selective loss of geniculate cells might account for our findings. However, this mechanism would require cell loss restricted to the three ipsilateral laminae, along a narrow retinotopic sector in the lateral geniculate body. It is hard to imagine a lesion likely to produce this pattern of cell loss.

Another possibility is that visual deprivation induced shrinkage of columns serving the ipsilateral eye. Hubel and Wiesel (1977) have shown that monocular lid suture, a model for childhood amblyopia, results in shrinkage of the deprived eye's columns. However, the columns shrink *everywhere*, not just in a local portion of the cortex. It is impossible to explain how a narrow sliver of temporal retina in each eye, abutting the vertical meridian, could have been selectively deprived. With near convergence, the top of the vertical horoptor tilts away from the median plane, but this should not induce selective deprivation of temporal retina. Thus, we can reasonably exclude postnatal visual deprivation as a cause of the column anomaly.

Having argued against loss of input from the ipsilateral eye, the most likely explanation for the column anomaly is excessive input from the contralateral eye. We suggest that a population of ganglion cells in each eye, located in a sliver of retina just temporal to the normal vertical meridian, decussated incorrectly at the optic chiasm. Shifting the decussation line about 5 deg into the temporal retina of each eye would produce a pattern of ocular dominance columns exactly like that shown in Figs. 2A–2D. Such a decussation abnormality would result in a small wedge of ipsilateral visual field representation in each cortex, served by the contralateral eye. Under these circumstances, the representation of the vertical meridian would no longer coincide with the V1 border, but would be displaced to the border of the normal, binocular column pattern.

In normal monkeys, the vertical raphe between ganglion cells projecting ipsilaterally and contralaterally is not precise (Stone et al., 1973; Bunt et al., 1977). There is an overlap zone in the retina where ipsi- and contra-projecting ganglion cells are intermingled (Fukuda et al., 1989). In Fig. 3, we have superimposed the overlap zone onto the retina corresponding to the monocular cortical wedge in the anomalous monkey. There is a striking coincidence between the extent of the normal overlap and the magnitude of the postulated decussation error in our animal.

The existence of an overlap zone in normal animals implies that the molecular cues guiding decussation do not operate with perfect accuracy. Some cells in temporal retina are induced to cross at the chiasm, although their numbers fall sharply with increasing distance from the vertical meridian (Fukuda et al., 1989). We do not know why the midpoint of the decussation was shifted temporally in this anomalous monkey. Either the guidance cues in the chiasm itself lost some specificity (Wizenmann et al., 1993; Marcus et al., 1999), or some temporal ganglion cells expressed "crossing receptors" erroneously. The only clue is that the shift was equal to the maximum temporal limit of decussating cells in normal monkeys, suggesting that too many fibers responded to a signal present in a normal location.

Newton pointed out that placement of the decussation raphe along the vertical midline, with crossing of nasal ganglion cells only, leads to a single, binocular representation of each point in visual space within the opposite hemisphere of the brain (Newton, 1704, p. 136). In normal monkeys, less than 0.5 deg of ipsilateral visual field is represented in the striate cortex (Dow et al., 1985). In the monkey which we describe, errant decussation of a small population of temporal ganglion cells near the midline should produce an anomaly in the representation of the visual fields: a 5-deg monocular wedge of ipsilateral field inserted between the normal contralateral visual field representation and the V1 border. A similar contralateral eye zone of ipsilateral visual field representation exists in cats (Whitteridge & Clarke, 1982; Anderson et al., 1988; Payne, 1990), ferrets (White et al., 1999), ungulates (Pettigrew et al., 1984), and tree shrews (Bosking et al., 2000). In all these species, a population of cells in temporal retina decussates. These decussating cells are located from 4–15 deg temporal to the midline, depending on the species, and account for the ipsilateral field representation in the visual cortex. The pattern of retino-geniculo-cortical projections in these nonprimate species is the best explanation for the wiring anomaly in our monkey. This conclusion could be proven by injection of a retrograde tracer, such as WGA-HRP, into the anomalous monocular cortical zones in striate cortex (LeVay & Voigt, 1990). Transneuronal retrograde transport would be expected to reveal labeled cells in the temporal retina of the contralateral eye.

As a result of the decussation anomaly, points near the vertical meridian are represented twice in V1, once in each hemisphere (Fig. 2E). The two eyes do not contribute equally to this dual representation, but rather, the contralateral eye dominates. The lack of ipsilateral eye input to this interpolated wedge of ipsilateral field may lead to impaired stereopsis along the lower vertical meridian (Blakemore, 1969). However, normal function could be preserved, by transcallosal projections conveying input from the other eye. If one could screen normal animals using *in vivo* imaging techniques, it would be worthwhile to identify animals with this rare column anomaly, so that stereopsis could be tested along the vertical meridian.

The miswired animal in this study was obtained from a feral colony in Mauritius, established in the 17th century (Houghton, 1988). The anomaly is a *forme fruste* of the crossing error present in albinos (Guillery et al., 1984), where a large segment of the ipsilateral visual field is inserted along the V1/V2 border (Hubel & Wiesel, 1971; Ault et al., 1995). However, this monkey was fully pigmented, had well-developed foveae, and appeared entirely normal. Over the past decade, we have reconstructed the ocular dominance columns in ~ 40 macaques in the context of various experiments. No other animal has shown the abnormality described here, although occasionally a few ipsilateral eye columns fall short of the dorsal V1 border (Horton & Hocking, 1996). We suspect that small decussation anomalies occur on a sporadic basis in otherwise normal primates. This case provides a glimpse of nature's error rate in the wiring of the retinogeniculate projection. It is worth pointing out that it was discovered only because the geniculate input to V1 is arranged into orderly columns, making it easy to spot an aberration. It would have been far more difficult to detect this subtle decussation error in a subprimate species, or by screening with tracer injections in the lateral geniculate bodies.

Acknowledgments

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