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Cortical Representation of a Myopic Peripapillary Crescent

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Purpose: To determine how formation of an acquired myopic crescent adjacent to the optic disc affects metabolic activity in the primary visual cortex.

Design: Laboratory animal study.

Participants: Three macaque monkeys.

Methods: The blind spot region in the primary visual cortex was labeled by cytochrome oxidase (CO) histochemistry analysis or [^{3}H]proline autoradiography.

Main Outcome Measures: Visualization of the representation of the blind spot and myopic peripapillary crescent in the visual cortex.

Results: In high myopia, a region resembling the myopic peripapillary crescent was visible in cortical sections processed for CO. In this region, metabolic activity was reduced in ocular dominance columns that normally would be driven by input from retina corresponding to the myopic peripapillary crescent.

Conclusions: The formation of a myopic crescent is accompanied by loss of metabolic activity in the cortex supplied by the affected retina. This observation confirms that retinal tissue is damaged by the development of a myopic crescent, rather than simply translocated in a temporal direction. The cortical defect matches the myopic peripapillary crescent in size and shape, indicating that fill-in of the retinotopic map by healthy, surrounding retina does not occur. *Ophthalmology 2016;■:1–6 © 2016 by the American Academy of Ophthalmology.*

The optic disc in each eye gives rise to a natural scotoma, the blind spot. In the primary striate visual cortex, the contralateral eye's blind spot appears as an oval region, centered at 15° along the representation of the horizontal meridian.[1] The alternating pattern formed by the ocular dominance columns is interrupted in this zone, because 1 eye contributes no input. In humans with a history of vision loss in 1 eye, the blind spot can be labeled at autopsy by processing the cortex for cytochrome oxidase (CO), a metabolic enzyme.[2,3] In animals, it also can be labeled by transneuronal autoradiography after [^{3}H]proline injection into 1 eye.[4] At birth, the blind spot representation is present already, indicating that it is hard wired into the cortex.[5]

Subjects with high myopia resulting from axial elongation usually demonstrate a crescent-shaped region of peripapillary temporal atrophy, sometimes with tilting of the optic disc.[6–8] There are no photoreceptors in this atrophic zone, and there is partial or complete absence of other retinal layers.[9–12] Consequently, the blind spot becomes enlarged.[13,14] This phenomenon has been described in monkeys as well as in humans.[15] However, it is unknown whether enlargement of the blind spot, a process that occurs after the critical period for plasticity of ocular dominance columns, can be detected in the primary visual cortex.[16] Herein, we describe the cortical representation of the blind spot in 3 macaque monkeys. Two animals were

normal, but the third had acquired peripapillary atrophy resulting from high myopia.

Methods

Experiments were conducted in 3 adult male macaques who were engaged in unrelated neurophysiologic studies in our laboratory. All procedures followed protocols approved by the University of California, San Francisco, Institutional Animal Care and Use Committee. To ensure correct refraction for neurophysiologic testing, the animals underwent periodic streak retinoscopy after dilation of the pupils with 1% cyclopentolate and 2.5% phenylephrine.

The neurophysiologic studies were followed by histologic examination of striate cortex. In 2 animals, 2 mCi [^{3}H]proline in 30 μl sterile saline were injected intravitreally to label the cortical ocular dominance columns. In 1 animal, the columns were double-labeled by reacting the cortex for CO activity after enucleation of 1 eye. All procedures were performed under local and general anesthesia, and the animals were treated afterward with an analgesic, buprenorphine (0.02 mg/kg).

For processing of brain tissue, the animals received a lethal dose of pentobarbital intraperitoneally and then were perfused transcardially with 1 liter saline followed by 1 liter 0.5% paraformaldehyde in 0.1 M phosphate buffer (pH, 7.4). Striate cortex was removed, unfolded, flattened, and cut tangentially to the pial surface with a freezing microtome. Individual 30-μm sections were mounted on slides for autoradiography or CO histochemistry analysis.[16] Digital photographs were obtained of each section. The
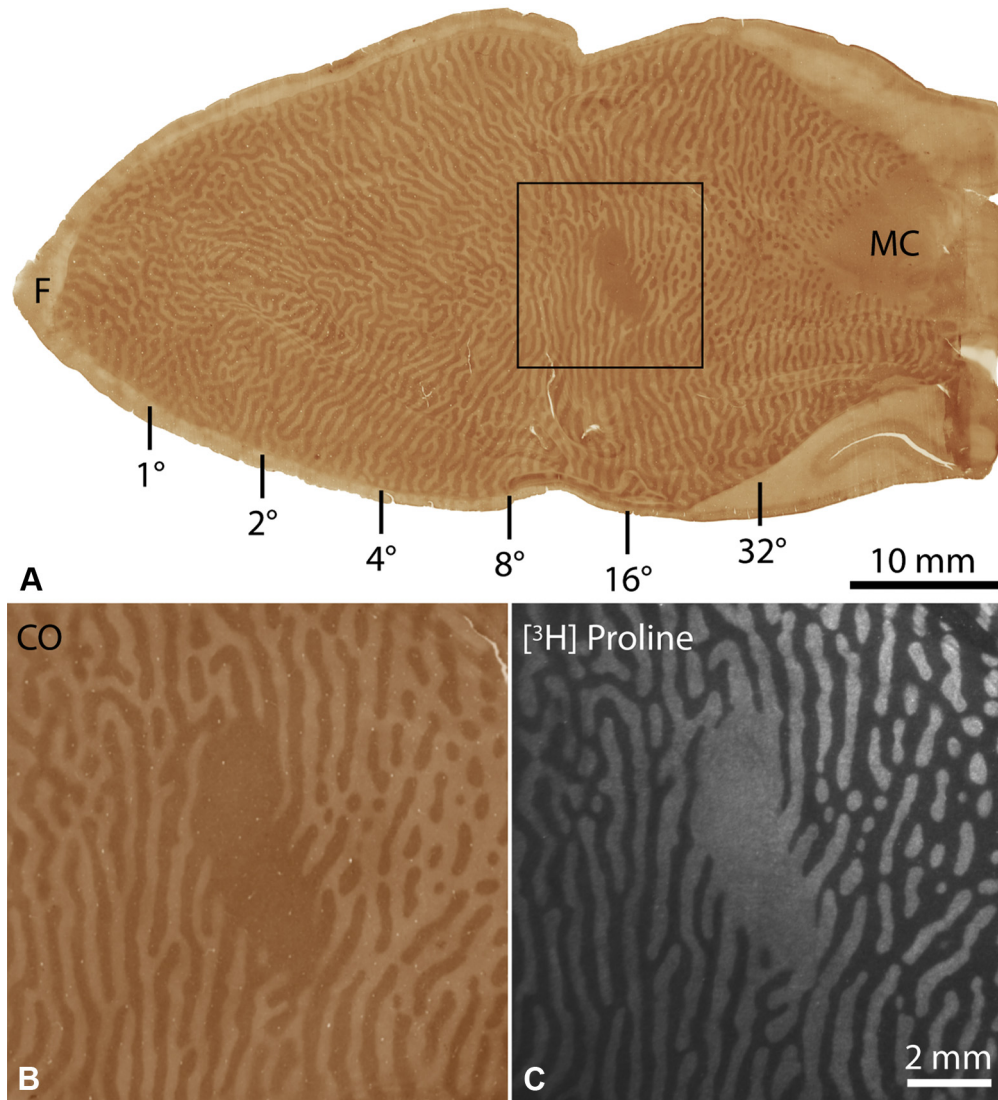
Figure 1. Double-labeling of the cortical optic disc representation in monkey 1. **A**, Montage of flattened layer 4C of left striate cortex showing ocular dominance columns labeled by cytochrome oxidase (CO) after enucleation of the right eye. F = fovea, MC = monocular crescent. **B**, Boxed region above, centered on the optic disc representation of the right eye. **C**, Montage of alternate sections, showing bright label after transneuronal transport of [³H]proline from the left eye, which coincides with dark CO in (**B**). The right eye's blind spot representation is supplied only by the left eye.

cortical layer 4C, containing the ocular dominance columns, was reconstructed by montaging serial images using Photoshop CS (Adobe Systems, San Jose, CA).

Results

The pattern of metabolic activity revealed by levels of the mitochondrial enzyme, CO, was examined in the vicinity of the blind spot representation in striate cortex of 3 monkeys.

Monkey 1

This animal had a stable refraction of +0.50 sphere in each eye measured repeatedly by streak retinoscopy. The optic discs were normal, with no evidence of a peripapillary crescent. The ocular dominance columns were labeled by injection of [³H]proline into the left eye and by enucleation of the right eye. The animal survived for 10 days after these procedures. This was necessary for transport of [³H]proline to the primary visual cortex, via synapses in the lateral geniculate nucleus. It also allowed sufficient time for cortical levels of CO to change after enucleation of the right eye.

Ocular dominance columns were present in CO montages of layer 4C as a result of reduction of metabolic activity after loss of the right eye. In the left striate cortex, columns were present everywhere, except in the regions corresponding to the monocular crescent and the blind spot of the right eye (Fig 1A). The latter appeared as a solid dark oval, where columns were absent (Fig 1B). The intensity of CO activity within the blind spot representation was equal to the level present in the surrounding ocular dominance columns of the left eye. The blind spot representation was approximately 3 to 4 pairs of columns wide.