13. Respective HLA types of these two subjects were (subject a) HLA A1,29; B13,35; Cw1,w4; DR1,5; DRw52; DQw1,3 and (subject b) HLA A1,29; B14,44; Cw5,−; DR1,7; DQw1,2; DRw53. Allogeneic target cells representing matches at all the respective HLA class I and class II loci were tested except: (subject a) Cw1; (subject b) HLA B14.
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The Nasotemporal Division in Primate Retina: The Neural Bases of Macular Sparing and Splitting

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In primates, each hemisphere contains a representation of the contralateral visual hemifield; unilateral damage to the visual pathways results in loss of vision in half of the visual field. Apparently similar severe, unilateral lesions to the central visual pathways can result in two qualitatively different central visual field defects termed macular sparing and macular splitting. In macular sparing a 2° to 3° region around the fovea is spared from the effects of unilateral damage to the visual pathways. In macular splitting there is no such spared region and the scotoma produced by unilateral brain damage bisects the fovea. The patterns of decussation of the different classes of retinal ganglion cells in both New World (*Saimiri sciureus*) and Old World (*Macaca fascicularis*) monkeys have been determined by horseradish peroxidase injection. In both species the distributions of ipsilaterally and contralaterally projecting ganglion cells in the central retina are different from those in other mammals and suggest neural bases for macular sparing and splitting, respectively.

IN PRIMATES, THE CELLS IN THE NASAL retina project contralaterally, and those in the temporal retina project ipsilaterally. As a result, the postchiasmal visual pathways in each hemisphere represent the contralateral visual hemifield. There is very little bilateral representation, and thus unilateral damage to the visual pathways in man results in a profound loss of vision in the contralateral visual hemifield. In their paper describing the visual field defects produced by penetrating wounds of the brain, Koerner and Teuber (*1*) note "the age-old problem of macular sparing and splitting" or, more correctly, as they point out "foveal sparing" and "foveal splitting." In macular (foveal) sparing a 2° to 3° region around the fovea is spared from the effects of unilateral damage to the visual pathways. In less commonly observed macular (foveal) splitting there is no such spared region, and the scotoma produced by unilateral brain damage bisects the fovea. In advanced primates, the fovea comprises the central 3° of retina and is a roughly circular region devoid of ganglion cells (the foveal pit) surrounded by a multilayered, annular region of densely packed ganglion cells (the foveal slope).

We have studied the central projections of retinal ganglion cells in both New World (*Saimiri sciureus*) and Old World (*Macaca fascicularis*) monkeys after electrophoretic injection of horseradish peroxidase (HRP) into the lateral geniculate nucleus and superior colliculus. A total of eight animals were studied; the results for all animals were similar.

The procedures used for the surgery, extracellular single unit recordings, electrophoretic injection of HRP, histology, histochemistry, and computer-aided morphometric analysis are standard and have been described (*2–4*). All animals were deeply anesthetized.

The retinas of New World and Old World monkeys contain classes of ganglion cells with similar morphologies and patterns of central projection (*5*). Retinal ganglion cells in *S. sciureus* and *M. fascicularis* can be classified as A cells (p α), B cells (p β), C cells (p γ), or E cells (p ϵ) (*2, 6*). In both species, A cells project heavily to the magnocellular laminae of the lateral geniculate nucleus (LGNd) and have large cell bodies, large dendritic trees, and coarse axons. B cells project to the parvocellular laminae of the LGNd and have small cell bodies, very small dendritic fields, and medium-gauge axons. Within central retina, B cells are "midget" ganglion cells (*5–7*). C cells project to the superior colliculus and pretectum and constitute a heterogenous group of cells with small- to medium-sized cell bodies, large dendritic fields, and fine axons. E cells also project to the superior colliculus and pretectum. They have medium-sized cell bodies, large dendritic fields, and rather fine axons.

We determined the patterns of decussation of the different classes of primate retinal ganglion cells that were labeled as a result of large, unilateral injections of HRP into the LGNd of adult monkeys (Fig. 1). In the adult, the nasotemporal overlap is smallest (about 1° wide) adjacent to (but not within) the fovea (*8, 9*). As in the cat (*4, 10*), the region of overlap was wider in peripheral than in paracentral regions of retina. For example, 6 mm from the fovea, the region of overlap increased in width to about 2° because contralaterally projecting A and C cells extended farther into the temporal retina than they did more centrally. Occasionally, isolated, contralaterally projecting cells were observed up to 8° into temporal retina at far peripheral elevations (*11*).

Injections of HRP into the LGNd of both *S. sciureus* and *M. fascicularis* revealed that most of the foveal pit was located in temporal retina and that a 0.5° (125 μm) wide "ring" of densely packed, ipsilaterally projecting cells circled the nasal side of the foveal pit (Fig. 1, A and C). Some ipsilaterally projecting midget cells were always found throughout the foveal pit. Such a ring of cells was not observed after injections into the superior colliculus, and there was no ring of contralaterally projecting cells around the foveal pit in temporal retina after LGNd injections (Fig. 1, B and D). Only 40% of the foveal pit was surrounded by contralaterally projecting cells and they were in the nasal retina. In addition, the foveal pit ipsilateral to LGNd injections contained

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more labeled ganglion cells than did the foveal pit contralateral to LGNd injections (Fig. 1). The ipsilaterally projecting cells within and around the foveal pit were virtually all B (midget) ganglion cells. Their dendrites ramified in the inner plexiform layer (IPL) in the same region of retina in which their cell bodies were located. Similarly, the dendrites of the contralaterally projecting cells on the nasal side of the foveal pit arborized in the same regions as their cell bodies.

Previous studies of the distributions of ipsilaterally and contralaterally projecting cells in primate retina have not accounted for the clinical phenomena of foveal sparing and splitting (*8*), although a bilateral representation of central retina in the monkey central visual pathways has been reported (*9*). In this study, in *M. fascicularis* a small number of retinal ganglion cells on the temporal and nasal sides of the fovea were found to project contralaterally and ipsilaterally, respectively (*12*). Although these results help to explain foveal sparing (*9, 13*), they are inconsistent with foveal splitting (*9*). Also, because the HRP technique was new at the time, the quality of HRP staining did not allow visualization of the dendrites of the labeled cells. This is important because we have observed midget ganglion (B) cells within the fovea with principal dendrites that extend hundreds of micrometers from their cell bodies before arborizing in the IPL; one must know where in the IPL the dendrites of labeled cells arborize in order to determine the regions of retina that they subserve.

Thus, our results indicate that ipsilaterally projecting cells in and around the fovea can generate 2° to 3° of bilateral representation in the geniculocortical pathways, because they are intermingled with contralaterally projecting cells on the nasal side of the foveal pit. In our material the dendrites of these are well filled; they arborize in regions of the IPL that suggests that they subserve the regions of retina in which they are located (*14, 15*). In addition, contralaterally projecting retinal ganglion cells in temporal retina cannot generate bilateral representation in the central visual pathways because there is no intermingling of ipsilaterally and contralaterally projecting cells on the temporal side of the foveal pit.

The results of our studies of primate central retina differ from those in the cat. For example, within the area centralis region in the cat, there are contralaterally projecting cells in the temporal retina but virtually no ipsilaterally projecting cells in the nasal retina. Also, most of the area centralis projects contralaterally, not ipsilaterally, in the cat. Finally, the width of the region of nasotemporal overlap is smallest, not largest, in the center of the cat area centralis (*4, 10*). There are, thus, marked differences in the patterns of central projection of retinal ganglion cells in primate and nonprimate species.

Our findings provide possible neural bases for both foveal sparing and foveal splitting; damage to the visual pathways in one hemisphere of primates should result in foveal splitting in the eye ipsilateral to the lesion and foveal sparing in the eye contralateral to the lesion. In fact, a number of studies exist in which the two eyes of patients suffering unilateral optic tract or cortical lesions were tested separately. In some of these cases evidence for ipsilateral foveal splitting and contralateral foveal sparing has been presented (*16*). Additional studies of the visual field defects produced in the two eyes by unilateral destruction of the visual pathways in monkeys and man are required to confirm our hypothesis and solve the "age-old problem of macular sparing and splitting."

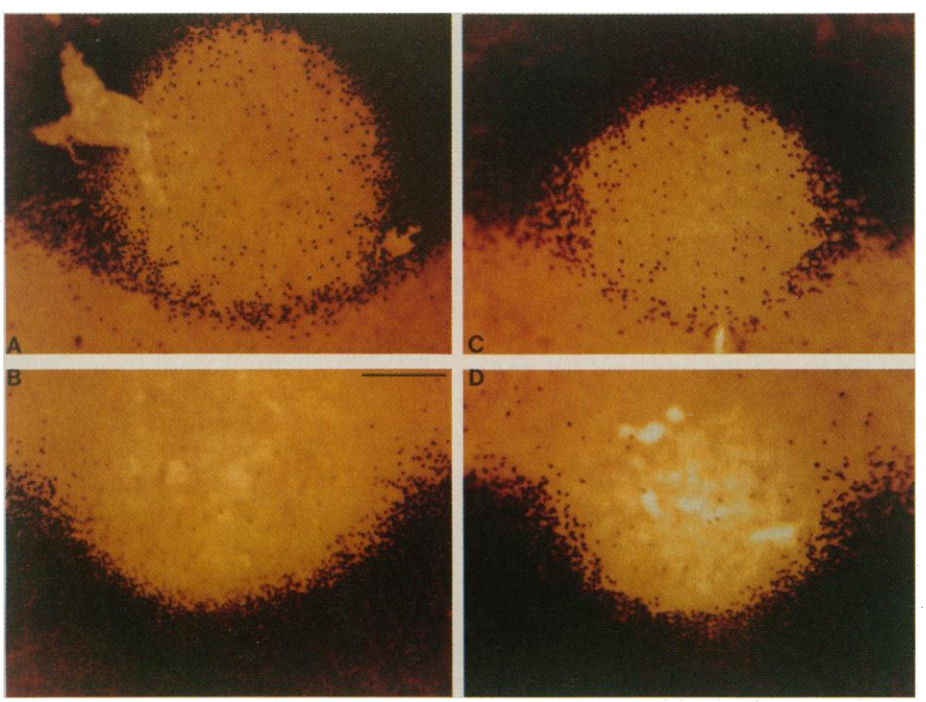

Fig. 1. Ipsilaterally (**A**) and contralaterally (**B**) projecting retinal ganglion cells labeled by injections of HRP into one LGNd of a normal adult New World monkey (*S. sciureus*). Ipsilaterally (**C**) and contralaterally (**D**) projecting retinal ganglion cells labeled by injections of HRP into one LGNd of a normal adult Old World monkey (*M. fascicularis*). In both species (A and C), the foveal pit is mostly in the temporal retina and contains ipsilaterally projecting cells, and a ring of ipsilaterally projecting cells surrounds the nasal side of the foveal pit. The dendrites of these cells arborize in regions of the IPL close to their cell bodies. In both species (B and D), virtually no contralaterally projecting cells are found within or on the temporal side of the foveal pit. (A) to (D) are at the same magnification; scale bar, 200 μm.

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14. Neurophysiological evidence supporting this point has been reported by A. Cowey [*J. Neurophysiol.* **27**, 366 (1964)] in his study of *S. sciureus*.
15. To determine the exact position of retina subserved by retinal ganglion cells in the macular region it is also necessary to know the trajectories of the bipolar cell axons and Henle fibers (cone axons) that ultimately provide their inputs.
16. See, for example, figures 15-10 and 15-23 in D. O. Harrington [*The Visual Fields* (Mosby, St. Louis, ed. 5, 1981), pp. 337 and 347] and case 3 in W. Penfield *et al.* [*Arch. Neurol. Psychiatry* **33**, 816 (1935), pp. 822–824].

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