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Effects of monocular deprivation on the lateral geniculate nucleus in a primate

(visual development/amblyopia/monocular eyelid closure/galago/bush baby)

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ABSTRACT **In many mammalian species, rearing with one eyelid closed produces a loss of vision in the deprived eye and a change in cell size in the lateral geniculate nucleus (LGN). In cats, the reduction in the size of deprived LGN cells has been correlated with a loss of one functional class of cells, Y cells. In primates, such as galago, LGN cells also exhibit marked changes in size with deprivation. In the present study we recorded from single cells in the LGN of monocularly deprived galagos to determine if such changes in cell size would be accompanied by changes in physiological properties. The results revealed no alterations in the distribution or functional properties of any cell class. The differences in the effect of monocular deprivation on the function of LGN cells in cats and primates are most easily explained by a fundamental difference in visual system anatomy. In cats, different classes of retinal afferents (X vs. Y) are in a position to compete for postsynaptic LGN neurons: in primates, segregation of cell classes into different layers may preclude such developmental interactions.**

Rearing infant mammals with one eyelid closed has proved a useful paradigm for studying the interaction of experience and genetically determined organization on the morphology and function of the developing visual system. Such an abnormal visual environment produces a number of anatomical, physiological, and behavioral changes that appear to result, in part, from an imbalance in the competition between afferents from the two eyes during development (for reviews, see refs. 1–3).

Behaviorally, monocular lid closure during early postnatal development produces a permanent loss of vision (amblyopia) in the deprived eye if the lid closure extends past a critical period in early development (4–11). It has been argued that binocular competitive interactions produce changes in the lateral geniculate nucleus (LGN) where cells innervated by the deprived eye are smaller than their nondeprived counterparts in the binocular segment—i.e., that part of the nucleus innervated by both eyes (6, 12–24). At the cortical level, the terminal arbors of these deprived LGN cells occupy less space in cortex (20, 21, 25–30).

At present, it is unclear how LGN cell size changes produced by monocular deprivation relate to the functional changes found in LGN cells. For example, in cats, changes in LGN cell size have been correlated with the loss of one functional class of LGN cells, Y cells. Normally, two physiological classes of cells, X cells and Y cells, are intermixed in the main laminae of the LGN in cat. Evidence has been published showing that the largest cells in the cat LGN are Y cells (3, 31). After monocular deprivation, Y cells show the greatest change in cell size (32, 33) and are the most affected physiologically by monocular deprivation (22, 32, 34–36). On the other hand, other forms of deprivation in cats, such as binocular lid closure or dark-rearing, also produce a functional loss of Y cells without producing dramatic changes in LGN cell size (33, 37–40).

In the present study, we were interested in determining in a primate whether the LGN cell size changes produced by monocular deprivation are correlated in any logical way with changes in the physiological properties of cells. In the primate LGN, cells are segregated into different laminae according to size [e.g., the magnocellular and parvocellular laminae (41)]. After monocular deprivation, the mean cell size in the deprived magno- and parvocellular laminae is always significantly smaller than that in corresponding nondeprived laminae (17, 23, 24). If cell size changes are directly related to physiological abnormality, one would expect cells in both the deprived magno- and parvocellular laminae to exhibit functional abnormalities after monocular deprivation.

To examine the functional changes produced by monocular deprivation in primate LGN cells, we studied the receptive-field properties of LGN cells in monocularly lid-sutured greater galagos. In normal galagos, we previously found that Y-like and X-like functional classes are segregated in the magnocellular laminae (nos. 1 and 2) and parvocellular laminae (nos. 3 and 6) (42). In this species, there is an additional set of koniocellular or smallest-size cell laminae (nos. 4 and 5) that contain W-like cells. The basis for our nomenclature has been discussed elsewhere (42–45). For the purposes of this paper we will focus primarily on the effects of deprivation on the X- and Y-like cell classes because our data are too limited at present to assess the effects of monocular deprivation on the wide variety of W-like cells in the koniocellular laminae.

MATERIALS AND METHODS

We used extracellular recording techniques to examine the receptive-field properties of neurons in the binocular segment of the LGN of four greater galagos (*Galago crassicaudatus*) that received monocular eyelid closure within the first 2 postnatal days and were monocularly deprived for 1–4 years. During the recording session, the galagos were anesthetized, paralyzed, artificially respired, and held securely in stereotaxic coordinates. The battery of tests used to identify cells in our monocularly deprived animals and the histological

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Abbreviations: D, deprived (cells); LGN, lateral geniculate nucleus; ND, nondeprived (cells); PTI, phasic-tonic index; MIN, medial interlaminar nucleus.

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procedures used to localize the site of recorded neurons were identical to those employed in our study of normal animals (42) and are described there in detail.

Briefly, we used a battery of measures to identify cells as W-, X-, or Y-like. These measures include: orthodromic latency to optic chiasm shock, antidromic latency to striate cortex shock, the response to rapidly moving (>150°/sec) visual targets of appropriate sign, responses to standing con-

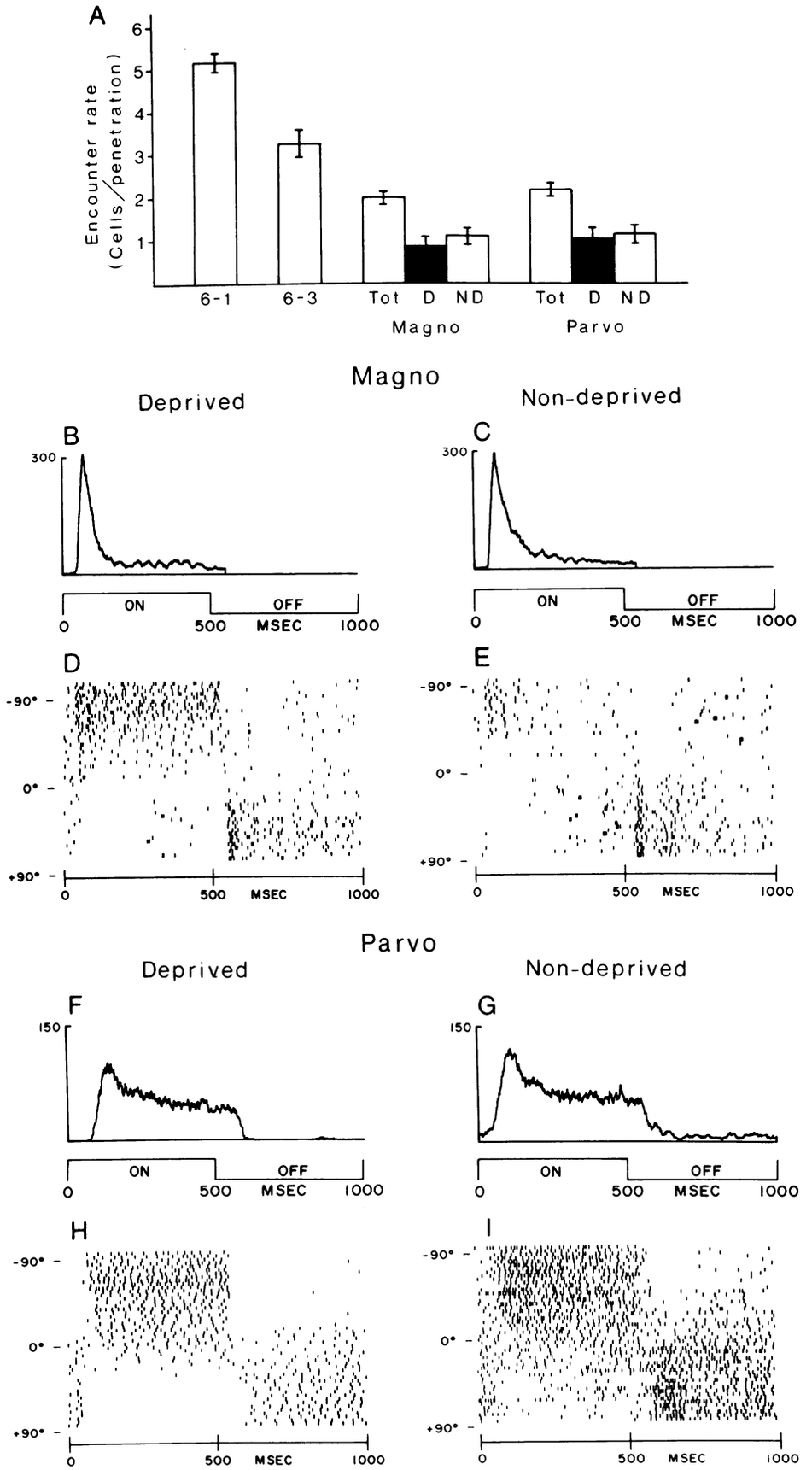

FIG. 1. (*A*) The encounter rate (all cells per penetration) of D and ND cells for penetrations through all six laminae (19 penetrations, 96 cells) and through laminae 6–3 (excluding the magnocellular laminae) (23 penetrations, 78 cells). Encounter rates within D and ND magno- and parvocellular laminae are shown separately. Standard error bars are indicated. (*B*, *C*, *F*, and *G*) Response histograms to a flashing spot (500-msec duration) for both D and ND Y-like and X-like cells. PTI values were determined by using such histograms. To calculate the PTI from poststimulus response histograms we used the formula: PTI = 100 − (tonic component − maintained activity/phasic component − maintained activity) × 100. A large initial phasic burst resulted in a large PTI, whereas a small phasic burst produced a small PTI. The ordinate indicates firing rate in spikes per sec. (*D*, *E*, *H*, and *I*) Responses of D and ND Y-like and X-like cells to a test for linearity of spatial summation. To test this, a high-contrast (60–80%) sine-wave grating was produced on a Tektronix 608 monitor and square-wave counterphased every 500 msec. The grating was stepped across the receptive field through 180° of phase angle to determine whether there was a null position where the cell linearly summed the balanced increments and decrements in luminance within the receptive field. For each cell the spatial frequency of the grating was selected so that it was near (usually within 0.5 cycles/degree) the maximal spatial frequency to which the cell would respond. All examples had a null or showed inhibitory doubling.

trast (>15-sec duration), phasic-tonic index (PTI), and linearity of spatial summation.

RESULTS

An initial question was whether, despite being shrunken, cells in the deprived LGN laminae were responsive to visual stimuli and could be sampled normally with extracellular microelectrodes. We found that visually evoked activity appeared normal in all laminae. Encounter rates for deprived (D) and nondeprived (ND) cells in the magno- and parvocellular laminae are illustrated in Fig. 1*A*. We did not find statistically significant differences in encounter rate between cells

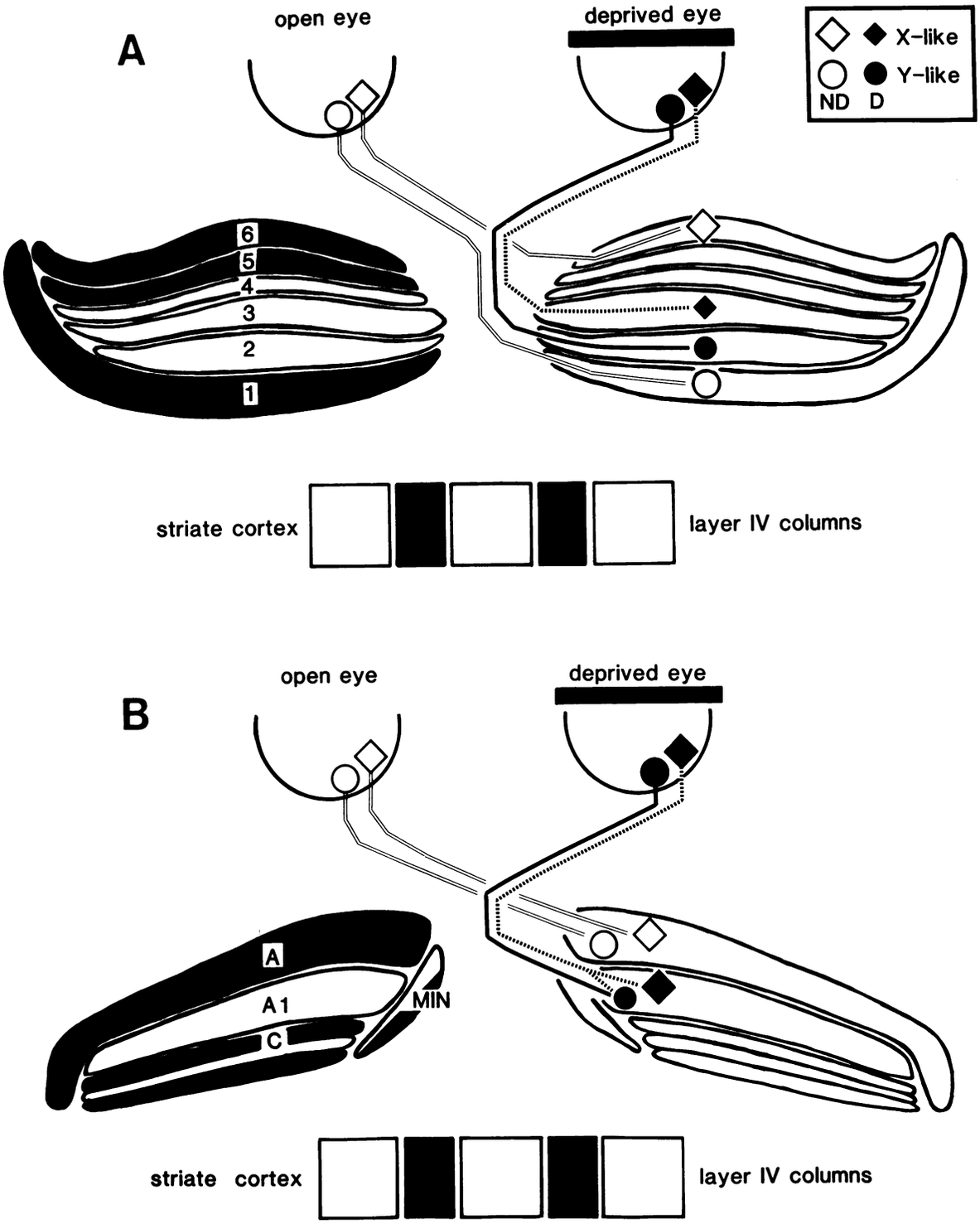

FIG. 2. A schematic diagram comparing the visual system anatomy of monocularly deprived galagos (*A*) and cats (*B*). D cells and structures are indicated by filled symbols; ND cells and structures are indicated by open symbols. The projection of retinal ganglion cells to the LGN is shown by a solid line (D Y-like), a dashed line (D X-like), and a double line (ND Y- and X-like). The connections of each visual system have been simplified and some connections omitted to avoid confusion. Not shown are connections of ganglion cells to cat C laminae or the medial interlaminar nucleus (MIN). Projections from W or W-like retinal ganglion cells have also been omitted from diagrams of both cat and galago. The extent of the terminal arbors of LGN relay cells in columns in striate cortex layer IV is represented by the solid (D) and the open (ND) blocks. A fundamental difference between galago and cat is that X- and Y-like cells and their inputs are segregated into separate laminae in galago LGN but are intermixed in cat LGN.

driven from the deprived eye and cells driven from the nondeprived eye in these laminae.

Examination of the receptive-field properties also revealed no differences between D and ND cells: both appeared identical to cells in normal animals. Several examples of our data are provided in Fig. 1.

As in normal galagos, D and ND Y-like cells had short optic chiasm latencies (mean D = 1.66 msec; ND = 1.67 msec) and short visual cortex latencies (mean D = 1.40 msec; ND = 1.42 msec). Most responded to rapidly moving stimuli, responded transiently to stationary stimuli, and showed a large initial phasic burst to a flashing spot (mean PTI: D = 83.0; ND = 83.4) (Fig. 1 *B* and *C*). Fig. 1 *D* and *E* show the responses of D and ND Y-like cells examined for linearity of spatial summation by using a counterphased, high-contrast sine-wave grating (46). In normal galagos, nonlinear cells are rare (≈11%) and are restricted to the Y-like and W-like cells (42). Of the 13 Y-like cells tested (8 D and 5 ND), none exhibited the excitatory doubling characteristic of nonlinear spatial summation. Because nonlinear cells are rare in normal galago LGN, we cannot be certain if their absence in *both* deprived and nondeprived laminae is a result of deprivation or a small sample size. However, it is noteworthy that both nonlinear and linear W-like cells were encountered.

Also, as in normal galagos, D and ND X-like cells had moderate optic chiasm latencies (mean D = 2.96 msec; ND = 3.10 msec) and visual cortex latencies (mean D = 2.36 msec; ND = 2.47 msec). These cells typically did not respond to rapidly moving stimuli, gave a sustained response to standing contrast, and showed little or no initial phasic burst in response to a flashing spot (mean PTI: D = 49.5; ND = 50.7) (Fig. 1 *F* and *G*). Fig. 1 *H* and *I* show the responses of D and ND X-like cells that were examined for linearity of spatial summation. Again, as in normal galagos, all of these cells either had a null region or gave inhibitory doubling in response to counterphased, sine-wave gratings.

Finally, comparisons of D and ND cells on all the other parameters that we examined failed to reveal any differences that could be related to monocular deprivation. We are impressed with the overall normality of the cells in the deprived laminae. Blakemore and Vital-Durand (47) also found little effect on the receptive-field properties of X cells in the LGN of young patas monkeys after varying periods of monocular deprivation. However, their sample of Y cells was insufficient for meaningful comparison. In contrast, it has been reported that the acuity and contrast sensitivity functions of LGN X and Y cells are altered in the deprived laminae in monocularly deprived cat (35, 36, 48, 49). Our preliminary study in galago of the contrast sensitivity function and the response latency of flashed light spots failed to reveal any difference between D and ND LGN cells (50).

DISCUSSION

Our data provide no compelling evidence of a loss of any functional class of LGN cells or of changes in LGN receptive field properties after monocular deprivation in a primate. Thus, the marked cell size changes [30% or more (17)] found in the magnocellular and parvocellular LGN laminae after deprivation do not appear to produce any functional changes in these cells. Because both galagos and cats show changes in LGN cell size with deprivation, whereas only cats exhibit a loss of one functional class of LGN cells (Y cells), it is likely that Y-cell loss in cats is not due solely to changes in cell size. Evidence has recently been provided suggesting that in cat, deprived retinal X and Y axons compete for functional synaptic sites on D LGN Y cells (32, 51, 52). This is modeled in Fig. 2, which illustrates the similarities and differences in geniculo-striate organization of a monocularly deprived galago and cat. Interactions between X-like and Y-like retinal afferents are presumably precluded in galago because X-like and Y-like cells and their retinal afferents are segregated within different laminae (42). This laminar segregation is a fundamental difference in LGN organization of galago and cat. Consistent with this model is the finding that Y-cell loss also occurs in the tree shrew after monocular deprivation, a species in which X and Y cells appear to be mixed in specific LGN laminae (18). The model may also account for the loss of Y cells seen in cats after other forms of deprivation, such as binocular suture or dark-rearing (33, 34, 37–40). However, the model does not account for Y cell loss that occurs in the MIN of the cat LGN after monocular deprivation because X cells do not appear to project to MIN (53). Whether this means that Y cells in cat are actually more sensitive as a group to the effects of monocular deprivation (54) or that Y cells in MIN are different from Y cells in the main laminae of the cat LGN remains to be determined.

Although species differences are apparent in the physiological effects of monocular deprivation on LGN relay cells, galagos, cats, and other species studied using the same paradigm all exhibit profound loss of vision after monocular lid closure. Because this amblyopia does not always appear to correlate with loss or changes in the functional properties of deprived LGN neurons, it seems likely that deprivation-related changes in LGN physiology, such as Y cell loss, are specific to species such as cats and tree shrews, in which retinal afferents of different functional classes can compete for domination of a postsynaptic target. The amblyopia that results from early monocular eyelid closure presumably is due to changes at the cortical level. These changes could be at the geniculocortical synapse, where D LGN cells might be less successful in activating striate cortex neurons, or due to other changes in cortex resulting from reduced input from the deprived LGN laminae.

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