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# Effects of Brief Periods of Unilateral Eye Closure on the Kitten's Visual System

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## SUMMARY AND CONCLUSIONS

*1.* The effects of brief periods of eye closure on the visual system of kittens were examined in animals monocularly deprived by eyelid suture for between 6 h and 8 days, starting on the 29th day of life. Before that time, the kittens had normal visual experience. At the end of the deprivation period, the kittens were permitted 2 days consolidation with both eyes closed before physiological recordings were undertaken in the visual cortex, area 17. After the brief recording sessions, the kittens were sacrificed and prepared for histology. Measurements were made of the distributions of cell areas in the layers of the lateral geniculate nuclei (LGNs) innervated by the two eyes.

*2.* Perceptible shifts in cortical binocularity were seen following as little as 1 day of eye closure, and these effects were increasingly marked in kittens deprived for longer periods. A period of 4 or 8 days of deprivation was sufficient to cause cortical changes comparable to those seen following much longer periods of deprivation.

*3.* Neuronal receptive fields activated through the deprived eye appeared to lose much or all of their stimulus selectivity before disappearing altogether. Many neurons in the kittens deprived for 1, 2, or 4 days possessed normal orientation-selective receptive fields in the eye that had been open and nonoriented or poorly selective receptive fields in the eye that had been closed.

*4.* The changes in cortical binocularity were accompanied by changes in the distribution of physiologically revealed ocular-dominance columns. In kittens that showed marked deprivation effects, the neurons that were dominated by the deprived eye tended to be clustered together in small groups and flanked by larger areas strongly dominated by the experienced eye.

*5.* Significant differences in cell size between layers of the lateral geniculate nuclei driven by the two eyes were apparent in all kittens deprived for longer than 12 h. These effects were larger in kittens deprived for longer periods: the areas of cells in layers driven from the deprived eye were smaller, on average, than those in layers driven from the experienced eye by about 10% after 1 or 2 days of deprivation, by about 20% after 4 days of deprivation, and by nearly 30% after 8 days of deprivation.

*6.* The close correlation between the changes in cortical binocularity and the changes in geniculate cell size observed in these animals lends support to the hypothesis that these effects share a common origin, perhaps related to the competition for terminal space in the cortex reflected in physiological and morphological changes in the relative extent of the cortical regions dominated by the two eyes in deprived animals.

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## INTRODUCTION

Depriving a kitten of vision in one eye causes profound physiological changes in its visual cortex: most neurons, which may normally be influenced by visual stimuli delivered to either eye, can only be driven through the eye that was open (31, 32). It appears that this effect is not due merely to the disappearance of the cells that were originally driven from the deprived eye. Rather, there seems to be a shift in the extent to which each cortical neuron may be driven from the two eyes, such that most neurons lose their contacts from the deprived eye and perhaps strengthen their contacts from the open eye. Thus, the great majority of cortical neurons can still be influenced by visual stimulation after a period of deprivation.

In addition to the effects of monocular deprivation on the binocularity of cortical neurons, there are striking morphological changes in the lateral geniculate nucleus, the thalamic nucleus that relays information from the retina to the visual cortex. In the LGN of a deprived kitten, cells in the layers of the nucleus driven from the deprived eye are 25–40% smaller in cross-

sectional area than cells in layers driven from the open eye (17, 30). The physiological changes in the LGN are subtle compared to those in the visual cortex. Most neurons, irrespective of the eye that drives them, have normal receptive-field properties. The recorded distribution of two functional types of LGN cells, X- and Y-cells, is altered by deprivation: Y-cells become much more difficult to record from in the deprived layers (27). This effect is probably due to the fact that Y-cells, which are normally the largest cells in the LGN and are thus most frequently recorded, appear to shrink (or fail to grow) much more markedly during deprivation than do X-cells (5).

Both the physiological and morphological effects of deprivation may be produced by surprisingly brief periods of eye closure. During the fifth week of life, when the kitten's visual system appears most susceptible to environmental influence, a few days of deprivation are sufficient to cause effects that are very similar to those produced by much longer periods of deprivation (15, 21). We were interested in determining the rate at which these two kinds of changes take place during brief periods of monocular deprivation, with a view toward examining the hypothesis that the two effects of deprivation are causally related (3, 9, 26). We also wished to examine the nature of the changes in the receptive-field properties of individual neurons that accompany their change in binocularity and the progressive alteration in cortical functional architecture that occurs during deprivation.

## METHODS

Ten kittens were used in this study. Of these, seven were deprived for various periods of time and were studied both physiologically and morphologically. Three normal kittens were also used. Physiological recordings were obtained from two of them (ages, 26 and 32 days), while the third (age, 28 days) was perfused without prior recording and used only for morphological analysis. All deprived kittens had normal vision until the age of 29 days. At this point, the right eye was closed for a period of 6 h to 8 days. The left eye was then closed, and the kittens were left with both eyes closed for 2 days to permit "consolidation" of the effects of the deprivation period (23, 24) before physiological recordings were taken. Following the recording experiment, which varied in duration between 10 and 14 h, the animal was perfused and the brain prepared for histological measurements. In all cases save one, recordings were taken from the right hemisphere, ipsilateral to the deprived eye. The periods of deprivation in the series were (in hours): 6, 12, 24, 48, 96 (2 kittens), 192. It should be noted that the kittens were asleep for about half the period of deprivation; the deprivation periods for the kittens deprived for 6 and 12 h began in the early morning, and these kittens were checked periodically during the deprivation period and awakened when necessary to ensure that they received at least 4 and 8 h of deprivation, respectively.

Our procedures for depriving kittens of vision, obtaining physiological recordings from single units in the striate cortex, and analyzing cell-size changes in the LGN were identical to those that we have detailed elsewhere (3, 20).

Visual deprivation was produced by suturing together the eyelids under halothane anesthesia, using the method of Wiesel and Hubel (30). In addition, when the deprivation was to be of more than a few days duration, the conjunctiva was dissected away from both lids and sutured over the cornea to provide a second layer of protection against extraneous visual experience. Each kitten was carefully checked each day for openings in the lids: none of the animals in this series had any such openings.

On the day of recording, the kitten was anesthetized with halothane and then, after venous cannulation, with a short-acting barbiturate (brietal) or steroid (Althesin) anesthetic. A cannula was placed in the trachea, the skull was reinforced with a cap of dental acrylic, and a small craniotomy and durotomy opened over the central projection area of the striate cortex. Screws were inserted over the cortex lateral to area 17 for EEG recording.

During recording, the kittens were placed in a conventional stereotaxic head holder using miniature ear bars, and intravenous anesthetic was discontinued. The animals were paralyzed with an intravenous infusion of gallamine triethiodide (Flaxedil, 10 mg/kg·h) in 6% glucose-Ringer solution (2 ml/h). Light anesthesia was maintained by artificially ventilating the animals with a mixture of $N_2O$, $O_2$, and $CO_2$ (approximately 75:23:2). Peak expired $P_{CO_2}$ was measured with a Beckman infrared gas analyzer and maintained between 4.5 and 5.5% by varying the stroke volume of the respiration pump or the $CO_2$ concentration in the gas mixture. ECG and EEG were monitored continuously throughout the experiment. When necessary, cardiac arrhythmia (which sometimes accompanied the initial paralysis) was abolished with a single iv dose of isoprenaline HCl (3–10 $\mu$g/kg).

Single-unit activity was recorded in area 17 with tungsten-in-glass microelectrodes (19) having an exposed tip approximately 25 $\mu$m long. The recording was amplified and displayed on an oscilloscope and relayed to an audiomonitor. The electrodes were driven hydraulically into the cortex through a sealed chamber over the craniotomy and durotomy.

The optical quality of the eyes of the kittens in this study, which were between 26 and 38 days old at the time of recording, was not as good as that of adult cats. Nevertheless, it was not difficult to visualize the fundus, locate retinal landmarks, and obtain an estimate of the refractive state of the eyes in any of the kittens. During recording, the pupils were dilated, accomodation paralyzed, and the nictitating membranes and eyelids retracted with topically applied homatropine sulfate and phenylephrine HCl. The corneas were protected with clear contact lenses behind artificial pupils (diameter, 3–5 mm), and the retinas made conjugate with a tangent screen 57 cm distant through the use of appropriate supplementary lenses.

Visual stimuli were back projected onto the tangent screen by manipulating cut-out patterns in the object plane of an overhead projector. An image of the stimuli was cast down onto plotting paper for permanent records of receptive-field properties. The luminance of the dimmest and brightest parts of the stimuli was normally approximately 1–2 and 5–10 cd/m$^2$, respectively. Brighter stimuli were occasionally used to stimulate particularly insensitive units.

Receptive fields were analyzed using flashed and moving bars, edges, and spots and classified into three groups: orientation selective (simple, complex, or hypercomplex), orientation bias, or nonoriented. Orientation-selective cells were classified according to the criteria of Hubel and Wiesel (13). Orientation-bias receptive fields are a class devised by Blakemore and Van Sluyters (1) to discriminate the erratic responsiveness and poor orientation selectivity of many receptive fields in visually deprived kittens: these cells, like the normal orientation-selective receptive-field types, have a preference for stimuli of one orientation. They differ from normal cells, however, in that they respond to stimuli of all orientations, including that orthogonal to their preferred orientation, and often respond with equal vigor and selectivity to a moving spot. Nonoriented cortical cells are rarely encountered in the cortex of normal adult cats, but they are not uncommon in deprived kittens. They may be discriminated from afferent fibers from the LGN by the fact that they are commonly binocularly driven, often lack clear concentric receptive-field organization, and have action-potential waveforms characteristic of cell-body recordings. Activity was occasionally recorded from units identified as geniculate afferents; these units were excluded from the analysis. Due to their virtual absence in adult cats, we refer to orientation bias and nonoriented receptive fields as "unspecified"; normal orientation-selective receptive fields are "specified." The effectiveness of each of the two eyes in driving cells was assessed, and each cell was classified by eye dominance into the seven-category scale of Hubel and Wiesel (13).

One microelectrode penetration was made in each kitten. The penetrations were all angled medially down the bank of the postlateral gyrus, crossing the radial fasciculi of the cortex at an angle of 30–90°. The penetrations varied in length between 1.9 and 3 mm, during which approximately 30 single units were isolated. At the end of the recording session, the electrode tracks were marked with electrolytic lesions made by passing current through the electrode tip (5 $\mu$A for 5 s, tip negative), and the animals were then sacrificed with Nembutal (pentobarbital sodium) and perfused through the heart with Ringer solution followed by 10% buffered formalin. The recording sessions were limited to less than 14 h duration in order not to prejudice measurements of LGN cell sizes. Blocks of visual cortex containing the electrode tracks were cut out, frozen, sectioned at 40 $\mu$m, and stained with cresyl violet. All electrode penetrations were verified to lie entirely within area 17, as defined by standard cytoarchitectonic criteria (22).

A second block containing the thalamus was cut from each of the brains of the deprived kittens, embedded in paraffin, and sectioned coronally at 20 $\mu$m. Every fifth section over the LGN was mounted and stained with cresyl violet. The identity of each LGN block was concealed from the experimenter who was to analyze it.

We sampled cells from the LGN using a technique modified from that of Guillery and Stelzner (10). Two levels were chosen for measurement, one rostral and one caudal to the middle of the nucleus, approximately 1 mm apart. The whole nucleus was traced through a drawing tube at a magnification of 60, and the outlines of layers A and A1 defined. Layer A was further subdivided into a medial, binocular segment opposed to layer A1 and a lateral monocular segment extending beyond the lateral border of layer A1. All the measurements reported below refer only to the binocular segment of layer A; the monocular segment does not show major changes in cell size after monocular deprivation (10). Layer A1 was treated as a whole.

Each of the two segments was divided by a line midway between its dorsal and ventral borders. The lines were then divided into four equal lengths, and cells sampled from a single high-power field at the center of each. The sample thus excluded cells from the medial interlaminar nucleus and large cells from within the LGN layers that lie near laminar borders and that may be binocularly activated (7, 8, 11). The central 12 or 13 somata in each high-power field were drawn at a magnification of 1,000; cells were only drawn if the nucleus and nucleolus were clearly visible. In this way, 50 cells were sam-

pled from each of the four chosen sections (both nuclei in rostral and caudal sections); 400 cells were sampled from each brain. The cross-sectional area of each outline was determined with a Quantimet 720 particle size-measuring computer.

## RESULTS

### *Rate of induction of deprivation effects in visual cortex*

Recordings of 270 units from nine kittens were taken. Figure 1*A* shows the ocular-dominance distribution obtained from the two normal kittens and confirms previous observations that young normally reared kittens have normal cortical binocularity, apparently identical to that seen in the adult cortex. Figure 1*B–G* shows the ocular-dominance distributions obtained from the six kittens deprived of vision in the eye ipsilateral to the cortical recording site for periods of time between 6 h (kitten *B*) and 8 days (kitten *G*). It is difficult to detect any significant shift in the ocular-dominance distributions of the kittens deprived for 6 or 12 h (*B* and *C*): these distributions resemble that of the normal kittens shown in *A* and are well within the range of variability of ocular-dominance distributions obtained from similar-sized samples of units from normally reared cats and kittens. The ocular-dominance distributions shown in Fig. 1*D* and *E*, obtained from kittens deprived for 24 and 48 h, are rather more skewed toward the contralateral eye than is normal. In kitten *C*, 69% of the units and in kitten *D*, 83% of the units were dominated by the open, contralateral eye; only 44% of units in the two normal kittens were so dominated. The ocular-dominance distributions obtained from kittens *F* and *G* (deprived for 96 and 192 h, respectively) were both strongly skewed toward the open, contralateral eye: that eye dominated virtually all neurons recorded in both these kittens. This is in agreement with the results of Hubel and Wiesel (15), who reported a similarly dramatic effect following 6 or 8 days of deprivation.

Hubel and Wiesel (15) and Olson and Freeman (21) both noted a tendency for a few residual units to remain monocularly driven by the deprived eye when the period of deprivation did not result in a complete shift in cortical eye dominance. Thus, the effects of monocular deprivation on binocularity may be more rapid than those on relative eye dominance. There is no real suggestion of this behavior in our data: the ocular-dominance distributions merely became more and more skewed after longer periods of deprivation and exhibited no particular tendency to become U shaped (15, 21). This difference between results may reflect a difference in the responses of the contralateral and ipsilateral projections to the visual cortex during monocular deprivation, since the reports cited were based largely on recordings made in the cortex contralateral to the deprived eye.

### *Hemispheric differences*

Figure 2 compares the ocular-dominance distributions for two kittens briefly deprived in the right eye for 4 days. Recordings were taken from

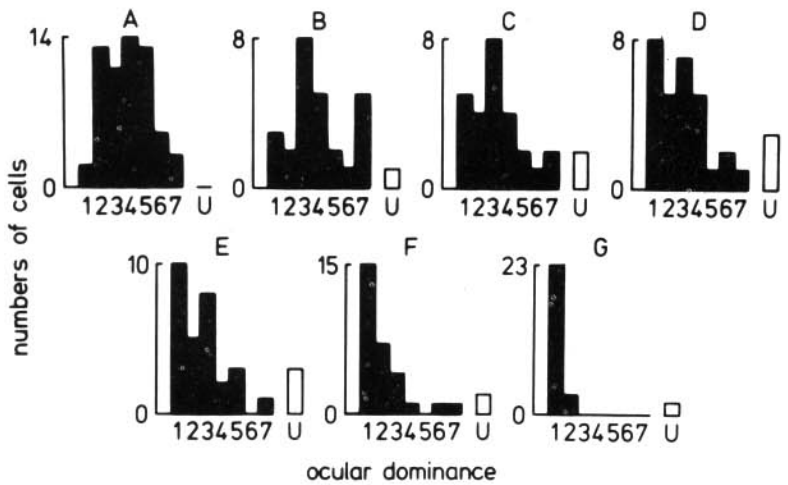


FIG. 1. Ocular-dominance histograms showing the distribution of cortical binocularity in two normal kittens, *A*, ages 26 and 32 days, and in six kittens deprived of vision in the ipsilateral eye for various periods of time; *B:* 6 h; *C:* 12 h; *D:* 24 h; *E:* 48 h; *F:* 96 h; *G:* 192 h. The ocular-dominance classification is that of Hubel and Wiesel (13), in which group 1 represents total dominance by the contralateral eye, group 7 total dominance by the ipsilateral eye, and intermediate groups intermediate levels of dominance by one eye or the other. Cells in the unshaded columns labeled U were unresponsive to any visual stimuli we could devise.

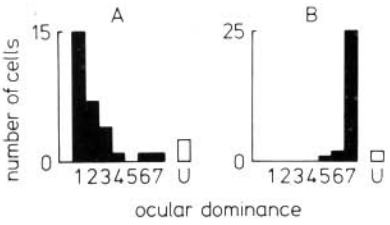


FIG. 2. Ocular-dominance histograms from two kittens deprived in the right eye for 96 h. In kitten *A*, recordings were taken from the right hemisphere, ipsilateral to the deprived eye; in kitten *B*, recordings were taken from the left hemisphere, contralateral to the deprived eye. Conventions as in Fig. 1.

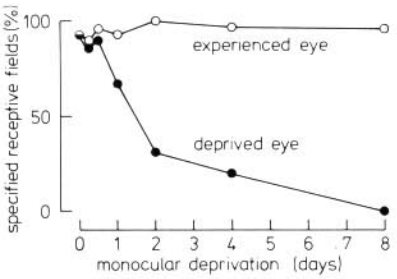


FIG. 3. Degradation of receptive fields driven through the deprived eye is shown for the eight kittens whose ocular-dominance distributions are illustrated in Fig. 1. The proportion of specified receptive fields—those showing normal orientation-selective properties—in the deprived eye is shown as a function of the duration of the period of monocular eye closure.

the right hemisphere of animal *A* and the left hemisphere of animal *B*. Contrary to expectation, the effect of deprivation on the phylogenetically older and stronger contralateral projection appeared to be more rapid than it was on the ipsilateral projection. In animal *B*, only three cells could be influenced at all from the deprived contralateral eye, whereas more than half of the visually responsive cells in animal *A* had receptive fields in the deprived ipsilateral eye.

It is probably unwise to place too much reliance on a finding based on small samples of cells from only two animals, but it may be noteworthy that Olson and Freeman (21) observed a far more marked effect of 1 day of deprivation on the contralateral projection than is shown in Fig. 1*D* for the ipsilateral projection. It is possible that the ipsilateral projection is, oddly, less susceptible to the early effects of monocular deprivation than the contralateral projection; certain of our morphological observations also suggest that this might be the case, at least for brief deprivation periods.

### *Receptive-field properties*

Wiesel and Hubel (31, 32) noted that cells driven by the deprived eye in monocularly deprived animals tend to have rather unusual receptive-field properties. In animals deprived from birth this is not surprising, since the receptive fields in the deprived eye have never received any visual experience. It is interesting to note that a similar pattern was observed in these experiments. While cells dominated by the experienced eye tended to have apparently normal orientation-selective receptive fields, the receptive fields in the deprived eye of cells dominated by the experienced eye showed an increasing tendency to have immature or nonspecific receptive-field properties, possessing nonoriented or orientation-bias receptive fields in that eye and normal orientation-selective receptive fields in the other.

Figure 3 graphically demonstrates this point by plotting the proportion of the receptive fields in the two eyes which exhibited specified properties (orientation-selective receptive fields) as a function of the period of deprivation; the nonspecific receptive fields were either orientation bias or nonoriented. After brief periods of deprivation, most receptive fields in the deprived eye had normal orientation-selective properties, but after more than 2 days of deprivation, the majority of receptive fields in this eye was nonspecific. Although many of these receptive fields were nondominant for the neurons they drove, it is worth stressing that all of the cells recorded in the animals deprived for 6 or 12 h had similar receptive-field properties in the two eyes; the cortex of these animals was not obviously different from the cortex of a normal animal of the same age (2). It was only after more extended periods of deprivation that deprived receptive fields lost their selectivity.

### *Functional architecture*

The few cells dominated by the deprived eye in the cortex of monocularly deprived kittens tend to be aggregated together in small groups, which may correspond to the cores of the ocular-dominance columns initially controlled by that eye (14, 32). The progressive change in cortical ocular-dominance organization seen in these experiments lends weight to this hypothesis.

Figure 4 illustrates the sequences of ocular dominance seen in the penetrations made in the six animals recorded in the right hemisphere. All the microelectrode penetrations were similar in position, angle, and extent, proceeding obliquely across the medial side of the crest of the postlateral gyrus. The two left-hand penetrations, from the animals deprived for 6 and 12 h, exhibited no marked clustering of cells with respect to ocular dominance. There was some tendency for cells of similar ocular dominance to occur together, and in the penetration diagram for the 12-h ani-

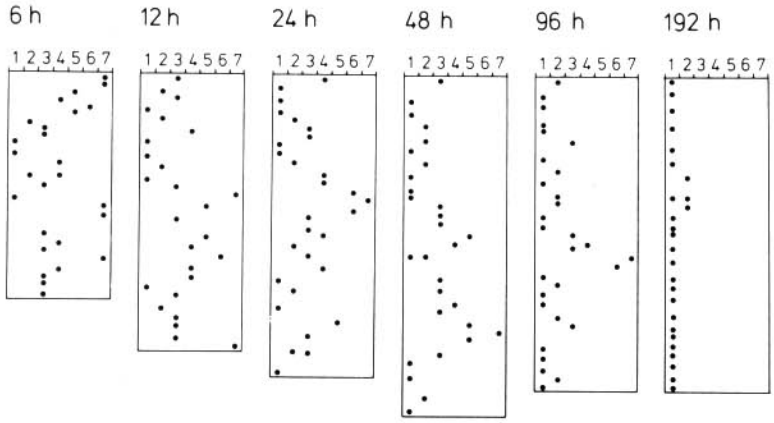


FIG. 4. Diagrams illustrating sequences of ocular dominance seen in cortical penetrations through the right hemispheres of the six kittens deprived in the ipsilateral eye. All penetrations proceeded medially down the bank of the postlateral gyrus, crossing the radial fasciculi of the cortex at an angle of approximately 30° near the cortical surface and an angle of roughly 90° near the end of the penetration. Lengths of penetrations illustrated vary between 1.8 mm (for the 6-h-deprived kitten) and 2.7 mm (for the 48-h-deprived kitten). The ocular-dominance classification is that used in Figs. 1 and 2.

mal, about one cycle of a gradual oscillating pattern can be discerned. These penetrations bear a close resemblance to those typically seen in normal kittens and adult cats. The third penetration diagram, from the animal deprived for 24 h, shows a slightly clearer pattern of ocular-dominance columns; almost all the cells dominated by the deprived eye were encountered in a short section near the middle of the penetration. A similar organization was present in the penetration made in the 48-h-deprived animal. The ocular-dominance pattern in the cortex of the 96-h-deprived animal was very clear: almost all the cells that could be substantially influenced from the deprived eye were grouped together in one short stretch of the penetration and surrounded by much longer reaches of cells heavily dominated by the experienced eye. And it may be noteworthy that the only three cells recorded in the cortex of the 192-h-deprived animal which had visual receptive fields in the deprived eye were encountered within 300 $\mu$m of each other.

This evidence suggests that regions dominated by the deprived eye may undergo a shrinkage, whereas regions devoted to the experienced eye expand and, ultimately, occupy the whole cortex. Cells with extreme ocular dominance are clustered together, and those with intermediate dominance occupy intervening regions.

### *Morphological observations*

Table 1 summarizes the results of measurements made of the cross-sectional area of 3,200 cells from seven deprived kittens and one normal kitten 28 days old at the time of perfusion.

TABLE 1. *Measurements of cross-sectional area in LGN layers*

| | Right LGN | | Left LGN | | % Difference | |
|---|---|---|---|---|---|---|
| Expt, h | A, experienced | A1, deprived | A, deprived | A1, experienced | A | A1 |
| Normal | 128 ± 4.4 | 145 ± 4.6 | 134 ± 4.4 | 142 ± 4.9 | 4* | 2* |
| 6 | 146 ± 4.8 | 151 ± 4.1 | 140 ± 3.7 | 163 ± 6.1 | 4* | 7* |
| 12 | 136 ± 5.0 | 124 ± 3.9 | 119 ± 3.5 | 143 ± 4.7 | 12‡ | 13‡ |
| 24 | 149 ± 5.3 | 149 ± 4.5 | 138 ± 3.9 | 167 ± 5.3 | 7† | 11‡ |
| 48 | 142 ± 4.1 | 129 ± 3.9 | 124 ± 3.3 | 143 ± 5.0 | 13§ | 10† |
| 96 | 153 ± 4.6 | 137 ± 4.2 | 119 ± 4.5 | 156 ± 6.2 | 22§ | 12‡ |
| 96 | 108 ± 3.2 | 91 ± 3.2 | 76 ± 2.4 | 103 ± 3.6 | 29§ | 12‡ |
| 192 | 137 ± 4.6 | 118 ± 3.9 | 116 ± 3.3 | 199 ± 10.9 | 15§ | 41§ |

Values (in square micrometers) are means ± SE ($n$ = 100 in each case) in the different layers of the LGN of the eight experimental kittens. Measurements from layer A were taken only from the portion of that layer representing the binocular visual field. The period of monocular deprivation undergone by each kitten is shown in the first column, and the differences between the LGN layers on the two sides (expressed as a percentage of the greater mean) and the significance of the differences on Student's $t$ test are shown in the last two columns. * $P > 0.05$. † $P < 0.05$. ‡ $P < 0.01$. § $P < 0.001$.

The mean and standard error of cell size in the four binocular layers of each nucleus of each animal is given (for 100 cells in each case), along with differences between segments on the left and right hand sides and the significance of the differences on the Student $t$ test.

In the 28-day-old control kitten, our results are similar to those of previous authors. There are no perceptible differences between the layers on the two sides of the brain, and cells in the A1 laminae appear slightly larger than those in the A laminae. Histograms showing the distributions of cell section areas from the four layers (left and right A and $A_1$) of this kitten are shown in Fig. 5*A*. In this and the other cell-size histograms in Fig. 5, the order of segments from top to bottom is arranged so that layers driven from the left eye are displayed above data from the comparable layer driven by the right eye. The second and fourth histograms in each part of Fig. 5 represent cells driven by the deprived right eye; the first and third histograms represent cells driven by the experienced left eye.

Inspection of the LGNs of the kitten deprived for 6 h reveals nothing of significance—these nuclei are indistinguishable from those of the normal control kitten in cell size and staining density. A few large cells, as in the normal kitten, are visible scattered throughout all layers of the nuclei, although these cells are less clearly distinguishable here, as in the other experimental kittens, than they are in adult LGNs. In the left LGN, as in those in the normal kitten, cells in layer $A_1$ are slightly larger than those in layer A; this difference is less clear in the right LGN. Measurement of cell sizes reveals a very small difference between cells driven by the two eyes. Those driven by the deprived eye tend to be slightly smaller, but this difference, although appropriate in direction, does not attain significance on a $t$ test.

The LGNs of the kittens deprived for 12, 24, and 48 h all appear similar on qualitative examination. In each case, a perceptible difference between the layers innervated by the deprived and experienced eyes is apparent, with cells in deprived layers appearing slightly smaller than those in experienced layers. In the right LGNs of these kittens, differences in the density of Nissl substance are apparent between layers A and A1; no such difference is visible in the left LGNs, despite the presence of cell-size differences. There are also fewer large neurons visible in the deprived layers than in the experienced layers. Measurement reveals that cells in the deprived layers of these kittens are, on average, approximately 10% smaller than their counterparts in experienced layers. The cell-size histograms shown in Fig. 5*B* for the kitten deprived for 12 h confirm the qualitative impression and reveal a clear monocular deprivation effect, albeit one much smaller than is seen after longer periods of deprivation.

Two kittens deprived for 96 h were examined, and both animals' LGNs appear very similar. The cells in deprived layers appear considerably smaller than those in experienced layers and are much less densely stained. Measurement reveals differences averaging approximately 20% between the sizes of cells in deprived and experienced layers, and the cell-size histograms for one of these kittens shown in Fig. 5*C* show the clear cell-size differences observed.

The LGNs of the kitten deprived for 192 h appear very similar to those of a kitten deprived for much longer periods (3, 6, 10, 30), although the difference between the A1 layers appears more marked than that between the A layers. Large cells, common in the experienced left layer, A1, are virtually absent from the deprived layers. The cell-size histograms for this kitten shown in Fig. 5*D* reveal a clear (15%) difference between the A layers and a very large (41%) disparity between cell areas in the A1 layers, although this value may be an overestimate due to the unusually large number of large neurons measured.

The data shown in Table 1 indicate that the effects of deprivation were more marked in the A layers of the LGN than in the A1 layers of the LGN when the duration of eye closure was 4 days or less; deprivation for 8 days appeared to have a more marked effect on the A1 layers. Furthermore, there is a marked reduction in staining density in the deprived A layers of the kittens deprived for 2 days or less that is not accompanied by any similar change in the deprived A1 layers. We would be inclined to regard these phenomena as a problem in our measurements rather than a real difference were it not for the observations of Wan and Cragg (29) who recently showed a very similar pattern of cell-size changes in the A and A1 layers of the LGN following brief periods of eye closure at the age of 23 days. It may be that the different behavior of the two LGN A layers in response to deprivation is related to recent reports that area 18 of the visual cortex receives much more of its input from layer A1 than layer A, whereas area 17 receives similar projections from both layers (4, 12). We might, thus, expect the effects of monocular deprivation on binocularity in area 18 to be slower in onset than in area 17. Moreover, the fact that the effects of periods of deprivation shorter than 8 days are more severe in the contralaterally driven A laminae than they are in the ipsilaterally driven A1 laminae correlates with the observation that the effects of these periods of deprivation on cortical binocularity may be less severe in the ipsilateral striate cortex than they are in the contralateral cortex (Fig. 2; cf. ref 21), although further recordings from

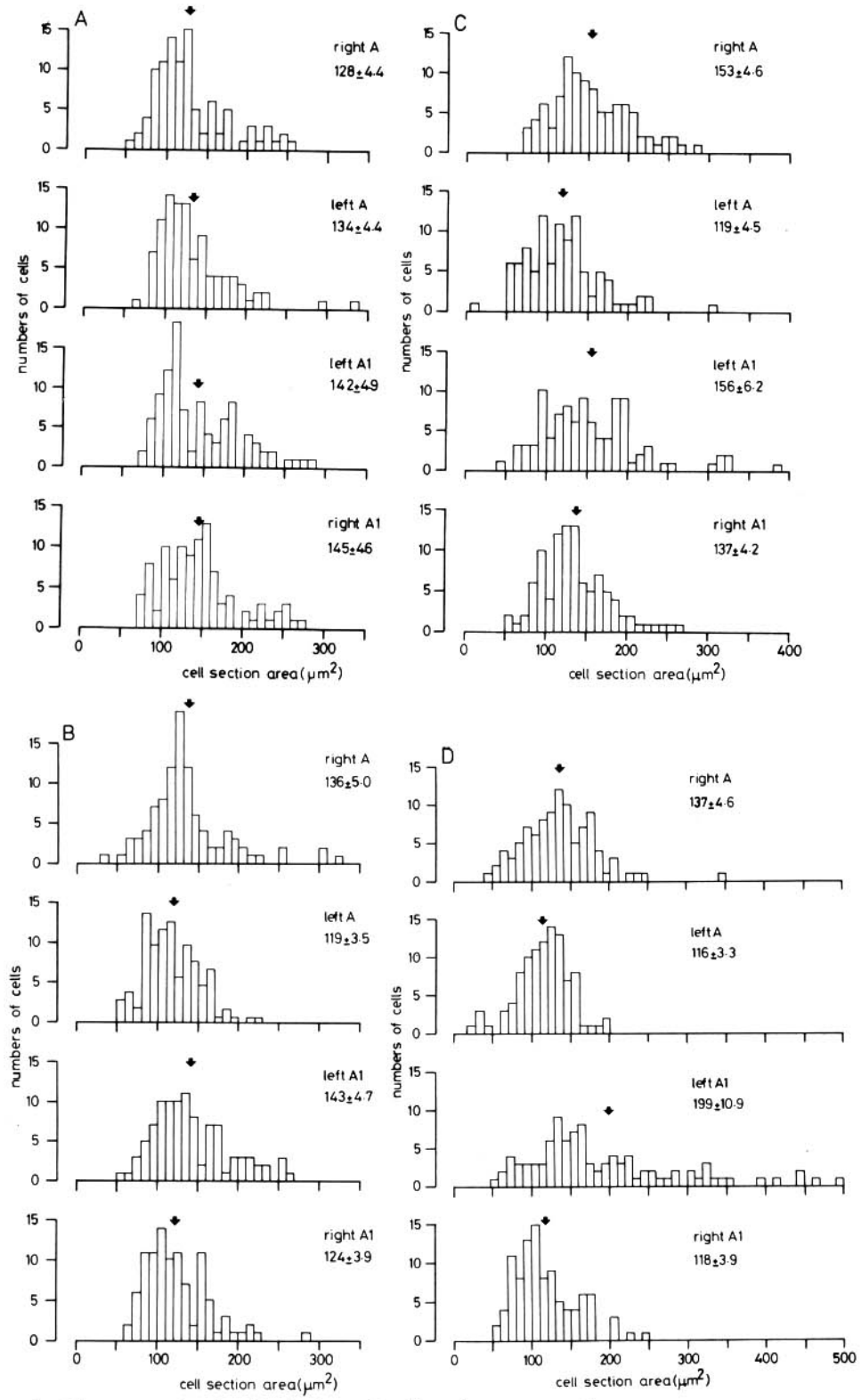


FIG. 5. Histograms showing distributions of cell section areas ($\mu m^2$) for neurons in the four binocular laminae of the LGNs of four kittens. In each case, the order of histograms from top to bottom is right layer A

both hemispheres of deprived kittens would be needed to establish this point with certainty.

In summary, then, our quantitative measurements of the LGNs of these animals reveal that significant morphological effects may be seen following periods of deprivation as brief as 12 h and that effects may be seen in kittens deprived for 4 or 8 days that are nearly identical to those observed following much longer periods of deprivation (3, 6, 10, 30). The quantitative results for the animals deprived for 4 or 8 days also confirm Hubel and Wiesel's (15) qualitative observations on kittens deprived for similarly brief periods.

## DISCUSSION

### *Relationships between physiology and morphology*

The extent of the physiological and morphological effects of monocular deprivation observed following brief periods of monocular deprivation seems to be very similar. No perceptible morphological or physiological effects may be observed following 6 h of monocular deprivation, but periods between 12 and 48 h produce relatively subtle effects on both cortical dominance and geniculate cell size. Near-total effects of deprivation on both cortex and LGN may be seen following deprivation lasting 4 days or more.

To facilitate comparison between these two effects, we have calculated an "induction index" for each. The physiological induction index (23) is simply the proportion of visually responsive cells in each sample that is dominated by the experienced left eye. In the experiments involving recordings from the right hemisphere, the index is the number of cells in groups 1, 2, and 3 divided by the total number of responsive neurons. The morphological induction index is the mean of the ratios of all possible pairs of experienced- and deprived-layer cell sizes, with the experienced layer set as the numerator (3). For these kittens, deprived in the right eye, the formula is

$$\frac{\frac{\text{right A}}{\text{left A}} + \frac{\text{left A1}}{\text{right A1}} + \frac{\text{right A}}{\text{right A1}} + \frac{\text{left A1}}{\text{left A}}}{4}$$

This measure compensates for any differences in effect between different sides of the brain or different LGN layers that may be present. Figure 6 plots these two induction indexes as a function of the duration of the deprivation period, and it readily may be seen that the morphological and physiological changes take place over the same time period. It appears at first sight that the changes in cortical dominance take place slightly more rapidly than the changes in geniculate cell size, but in view of the unknown metric that might relate the two measures of the effect of deprivation, this conclusion must be extremely tentative. It should also be borne in mind that the 2-day period of consolidation in these experiments might have allowed time for the effects in one structure to "catch up" with the effects in the other, although the similarly close relationship between physiological and morphological effects seen in experiments on reversed monocular deprivation without a period of consolidation (3) tends to cast doubt on this possibility.

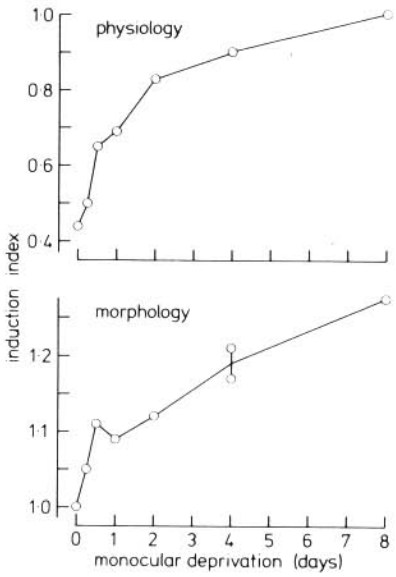


FIG. 6. Graphic representations of the rate of induction of the cortical physiological and geniculate morphological effects of monocular deprivation. The induction indices reflect the extent of cortical dominance by the experienced eye (physiological) and the extent of cell-size differences between deprived and experienced geniculate layers (morphological) and are defined in the text.

In any case, the close correlation between physiological and morphological effects lends further weight to the notion that the two effects are produced by a common causal factor, which may be the competition by the axons of LGN cells for terminal space in the visual cortex (3, 9, 14, 26). The mechanism by which cortical connectivity changes might affect the distributions of cell size in the LGN is unknown, but in view of the absence of a clear time lag between the

(experienced), right layer A1 (deprived), left layer A1 (experienced), and left layer A (deprived). Histograms in *A* represent a normal 28-day-old kitten, those in *B* represent the 12-h-deprived kitten, those in *C* represent one of the 96-h-deprived kittens and those in *D* represent the 192-h-deprived kitten. Measurements of cells in layer A were restricted to those portions of the layer that receive input from the binocular region of the visual field (10).

two effects, it must be the case that this mechanism acts rapidly, within a period of hours or days. It is also possible, of course, that the changes in LGN cell size produced by deprivation are unrelated to those in the cortex and are produced by some interaction between the layers of the geniculate. The failure of this study or of any other to demonstrate a clear dissociation between cortical and geniculate effects must, however, leave the status of this theory in some doubt (3, 26, 30–32).

### *Progressive cortical changes during deprivation*

The rate at which the experienced eye takes over control of the cortex during monocular deprivation is rather rapid: after 4 days, nearly all cells are dominated by the experienced eye. The progressive changes that accompany this shift in dominance are remarkable in several respects.

The receptive-field properties of cells in the deprived eye seem to undergo a progressive degradation which is similar in character to the progressive specification of receptive fields by visual experience in young kittens (2) but seen in reverse. In kittens allowed very brief periods of vision through one eye only, and otherwise completely deprived of vision, some receptive fields develop specified properties in that eye, producing binocularly activated neurons with orientation-selective receptive fields in one eye and nonspecific receptive fields in the other (23). The degradation of the deprived eye's receptive fields that accompanies monocular deprivation after a period of normal visual experience seems to produce a very similar kind of binocular interaction in some cells, which might indicate that they pass back through a similar stage during the loss of connections from the deprived eye, even though those connections had developed to a normal degree during the first 28 days of life.

The ocular dominance organization of the cortex of kittens undergoing monocular deprivation is distorted in a systematic fashion. Columns of cells driven by the open eye swamp those columns devoted to the deprived eye and ultimately leave only small regions of mixed ocular dominance between reaches of cortex in which the open eye is totally dominant. In cat, as in monkey, ocular-dominance columns are reflected morphologically in a periodic variation in the relative density of the geniculate arborizations in layer IV of the cortex from the layers of the geniculate driven by the two eyes (25). In both these species, the relative sizes of ocular-dominance columns devoted to the two eyes, revealed anatomically, appear to be affected by deprivation in just the way that would be expected on the basis of our results: the columns devoted to the deprived eye shrink, while those devoted to the experienced eye expand and come to occupy most of layer IV of the cortex (16, 25). It may be that this expansion and contraction of the terminal arborizations of geniculate cells is the stimulus that triggers the changes in cell size in the LGN during deprivation: as the cortical extent of an axon's terminal arborization shrinks or expands, the size of the soma necessary to maintain that terminal could reasonably be expected to shrink and expand in a similar fashion. The signal for the change in soma size (and also the change in the density of Nissl substance, the rough endoplasmic reticulum, which is the site of protein synthesis in the cell) might be carried by the retrograde transport of some factor from the terminals in the cortex to the soma (18). It is intriguing to imagine that this factor might be the central nervous system's analogue of nerve growth factor, which appears to govern a very similar process in the sympathetic nervous system (28), and that the monocularly deprived visual system might be the structure in which the identity and mode of action of this factor could be revealed.

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