

EXTENT OF RECOVERY FROM THE EFFECTS OF VISUAL DEPRIVATION IN KITTENS¹

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INTRODUCTION

IN KITTENS, deprivation of form and light over several months can lead to marked abnormalities in the visual pathway. These include behavioral blindness, morphological changes in the lateral geniculate body, and disruption of innately determined cortical connections (2, 6-8). This type of plasticity seems to be greatest in the early months of life and to decline rapidly with age; an adult cat deprived for similar periods showed no changes at all. We were naturally interested in whether the deprivation effects were permanent or whether they could be reversed by allowing normal stimuli to reach the retina again. Several kittens were therefore raised with the lids of one or both eyes sutured together for 3 months, as in previous experiments (6), and then the closed eye was reopened and the animals were allowed to live for another 3-14 months before making observations.

METHODS

Seven kittens were used, and the various procedures of deprivation and subsequent studies are summarized in Table 1. In six animals the lids of one eye were closed for the first 3 months of life. In the recovery period two of these kittens had the deprived eye opened. The other four had the deprived eye opened and the other (previously open) eye was closed. The seventh animal had both eyes closed for 3 months; the right eye was then opened. Recovery periods varied from 3 to 18 months. The animals were all kept together in a large, bright room, and were frequently played with by attendants and passersby.

Anatomical and physiological methods are described in other papers (1, 6, 8). Behavioral studies consisted mainly of observing the animal's use of vision to guide his activities. Tests of visual discrimination using operant-conditioning techniques are still being made on several animals; these will be reported elsewhere.

RESULTS

Behavior

The first kitten of this series had the right eye sutured shut from the tenth day up to 3 months of age. The lids were then separated under anesthesia. As with all the animals in this study the cornea was moist and clear; the fundus appeared normal, as were the direct and consensual pupillary

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light reflexes. At the outset the animal appeared to be blind in the deprived eye (7). The first signs of any recovery were noticed only after 2-3 weeks. With the good eye covered, the animal then seemed to be alerted by large objects moved in front of it, and at times would appear to follow them. These following movements showed some slight improvement with time, until after 3 months a large object was occasionally followed for several seconds. Even then, the animal did not always lock in on the object, but tended to lose it and go looking about wildly. Visual placing never returned. When put on the floor to roam freely, the animal would at times avoid large obstacles, but at other times would collide with them. It seldom avoided small objects such as chair legs. Placed on a chair, it would slide down, feeling its way with its forepaws. If the good eye was uncovered, the kitten would promptly jump to the floor.

Table 1. Summary of procedures performed on the seven experimental animals

Animal No.	Deprivation			Recovery			Procedure		
	Right eye	Left eye	Time, months	Right eye	Left eye	Time, months	Anatomy	Physiology	Behavior
1	Closed	Open	3	Open	Open	3	x		x
2	Closed	Open	3	Open	Open	18			x
3	Closed	Open	3	Open	Closed	3	x	x	x
4	Closed	Open	3	Open	Closed	8	x		x
5	Closed	Open	3	Open	Closed	14	x	x	x
6	Closed	Open	3	Open	Closed	18			x
7	Closed	Closed	3	Open	Closed	14	x	x	x

This behavior was typical of all animals tested. Animal 2 (Table 1) was allowed to go for 18 months after the deprived eye was opened, but it showed little if any recovery after the first 3 or 4 months.

To test the possibility that, with both eyes open, the animals might in some way be "neglecting" the previously deprived eye, we sutured closed the normal eye at the time of opening the deprived one. This was done in four kittens (no. 3-6, Table 1). Following the eye reversal these animals did just as badly as the others, indicating that they could not be forced to use the deprived eye. The change in behavior was dramatic, especially for cat 6, which during the first 3 months had been the leader of about a dozen animals. This large, husky animal lost his prominent position in the group, became meek and cowardly, and even after 18 months is still subdued and anxious. Finally, the same kind of slow and inadequate recovery was seen in one animal (no. 7) that was initially deprived by bilateral suture, following which one eye was opened for over a year.

Single-unit recordings

Recovery after monocular deprivation. Cortical recordings were made from 3 of the 7 animals. In kitten 3 (Table 1) the right eye had been closed for the

first 3 months, after which that eye was opened and the left eye closed for another 3 months. Two penetrations were made in striate cortex, one in each hemisphere, and 54 cells were recorded. The great majority of cells (45 of 54) were still driven exclusively from the left eye. Only 9 cells could be driven

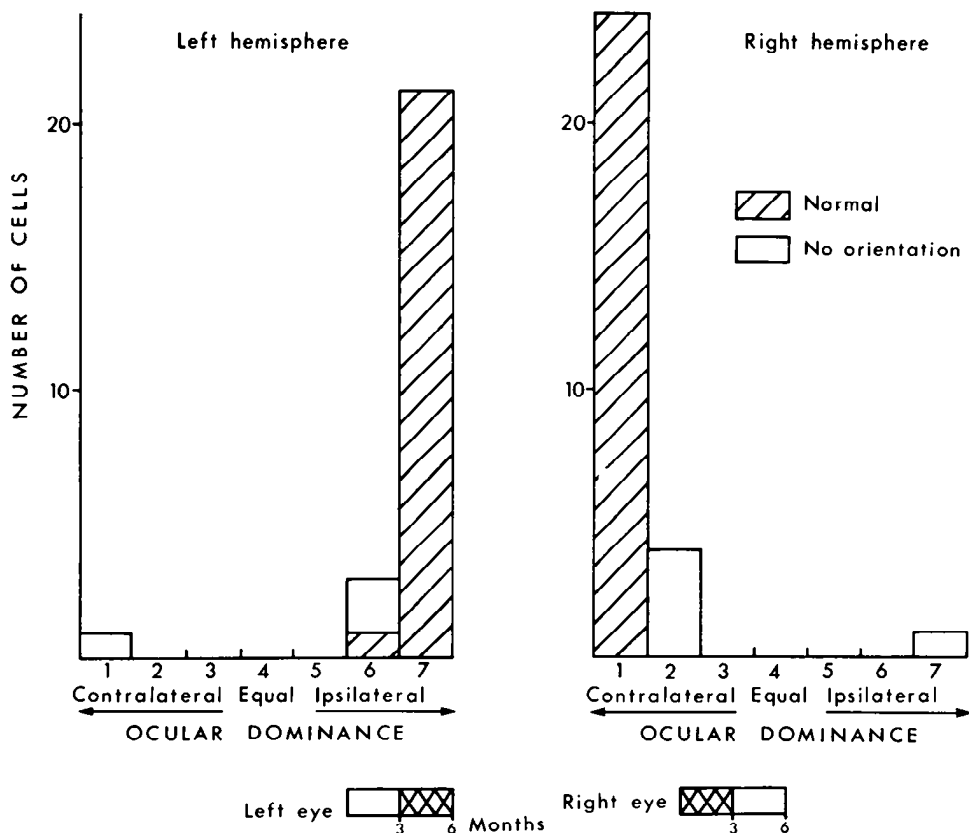


FIG. 1. Ocular-dominance distribution of 54 cells recorded from a 6-month-old cat (no. 3) in which the right eye was closed for the first 3 months of life, following which the right eye was opened and the left eye closed for the next 3 months. (Definitions of the ocular-dominance groups are as follows: cells of group 1 are driven only by the contralateral eye; for cells of group 2 there is marked dominance of the contralateral eye; for group 3, slight dominance. For cells in group 4 there is no obvious difference between the two eyes. In group 5 the ipsilateral eye dominates slightly; in group 6, markedly, and in group 7 the cells are driven only by the ipsilateral eye.)

from the right eye; of these 8 were abnormal, and 7 were still strongly dominated by the left eye. Two cells were exclusively driven by the right eye. The ocular-dominance distribution, given in Fig. 1, was thus still highly abnormal; indeed it was probably not significantly different from that of animals monocularly deprived for 3 months, as can be seen by comparing this

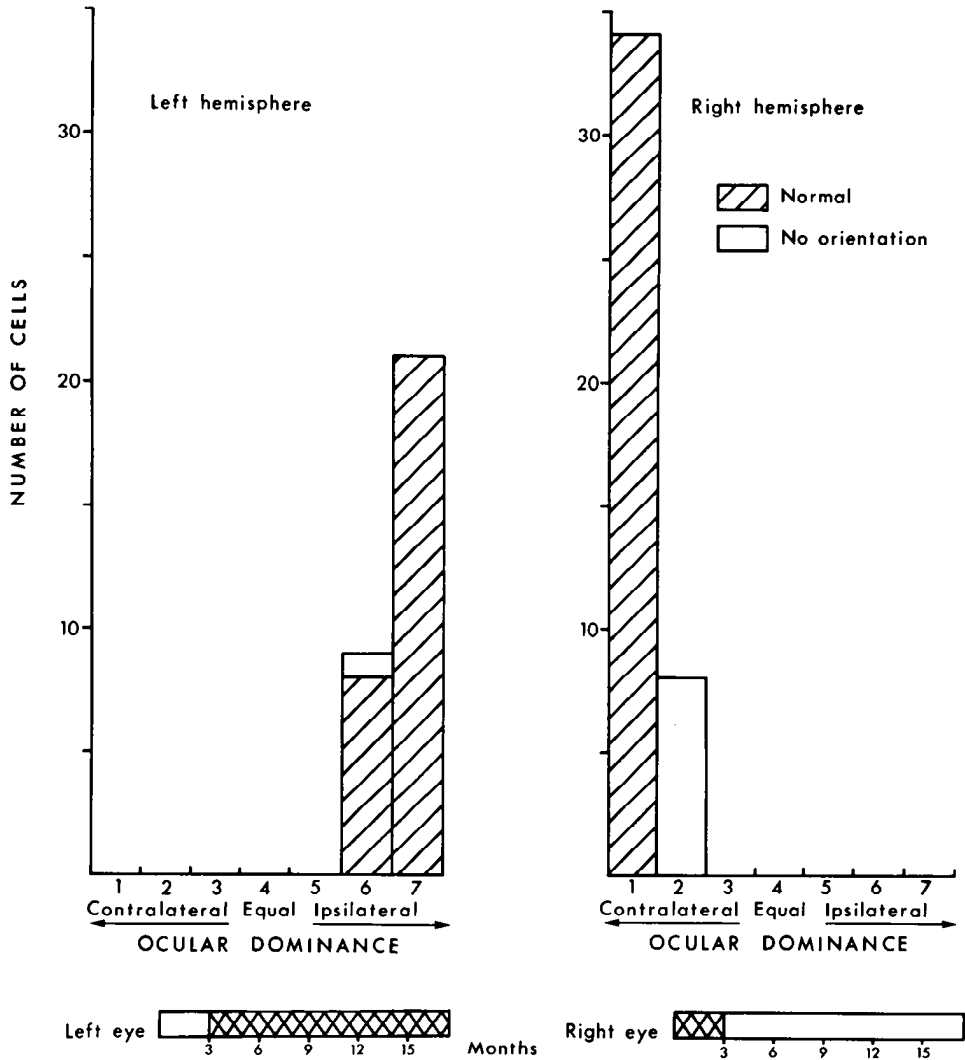


FIG. 2. Ocular dominance of 72 cells recorded from a cat (no. 5) in which the right eye was closed for the first 3 months of life, following which the right eye was opened and the left eye closed for the next 14 months.

figure with Fig. 2 in the paper on binocular deprivation (8). The 8 abnormal cells responded to a line stimulus regardless of its orientation; and showed a strong tendency to fatigue. That it was the connections between these cells and the right eye that were abnormal, rather than the cells themselves, is shown by the fact that the cells were driven in a perfectly normal manner by the left eye, having a precise receptive-field orientation and showing little tendency to fatigue. The 3 months' deprivation of the left eye immediately

preceding the recording apparently had little or no effect on that eye's ability to drive cortical cells, despite the marked atrophy of the geniculate layers connected to the left eye (see below). In contrast to this, a simple closure of one eye following several months of normal vision produces a marked cortical defect (7). Taken together, these two results reinforce our conclusions from the binocular closures and strabismus experiments (8, 3) in suggesting a strong interdependence in the pathways originating from the two eyes.

Kitten 5 likewise had the right eye closed for the first 3 months, after which the right eye was opened and the left closed. It was then kept for over a year before recordings were made. The results of observing 72 cells in 2 penetrations are shown in Fig. 2. Again, the effects of the original deprivation to the right eye appear to have been irreversible or nearly so.

One result common to these two experiments is the absence of unresponsive cells. This contrasts with the usual monocular closure, in which some 10% of cells were not driven by either eye.

Recovery after binocular deprivation. It will be recalled that the cortical effects of depriving both eyes for the first 3 months of life are not at all what one would have predicted from the monocular deprivations (8): instead of only a very few responsive cells, 73% of the cells could be driven, and 41% responded normally. These results are summarized in the left-hand part of Table 2. In studying the cortical effects of reopening an eye one therefore begins with a totally different situation from that following monocular closure.

Cat 7 was brought up with both eyes closed for the first 3 months, at which time the right eye was opened. The animal then went for over a year with the left eye closed. Ninety-nine cells were studied in the two hemispheres, with the results shown in Fig. 3 and Table 2. The histograms show no striking predominance of the opened eye, indicating that, just as in the monocular closures, there was little tendency for recovery. On the other hand, an examination of Table 2 suggests that opening the eye did produce some changes. As in the other recovery studies, unresponsive cells were diminished, amounting to 10% of the cells instead of 27%. At the same time, cells with abnormal responses (lack of receptive-field orientation) went from 32% to 60%. The abnormal responses came mainly from the right or opened eye, which accounted for twice as many abnormal fields as the left (52 as opposed to 25). Normal cells were, if anything, slightly reduced, and fewer of these were driven by the right eye (15%) than by the left (30%).

The asymmetry in the two eyes is further illustrated by the 31 cells that were driven from both eyes. Eight of these were driven normally from the left eye and abnormally from the right, having in that eye fields that lacked any clear orientation. The reverse was not true for any of the cells. Moreover, in our study of binocularly deprived animals without recovery there were none of these asymmetric cells, normal for one eye, but abnormal for the other. Here again it is as though the number of abnormal connections from the opened eye had greatly increased.

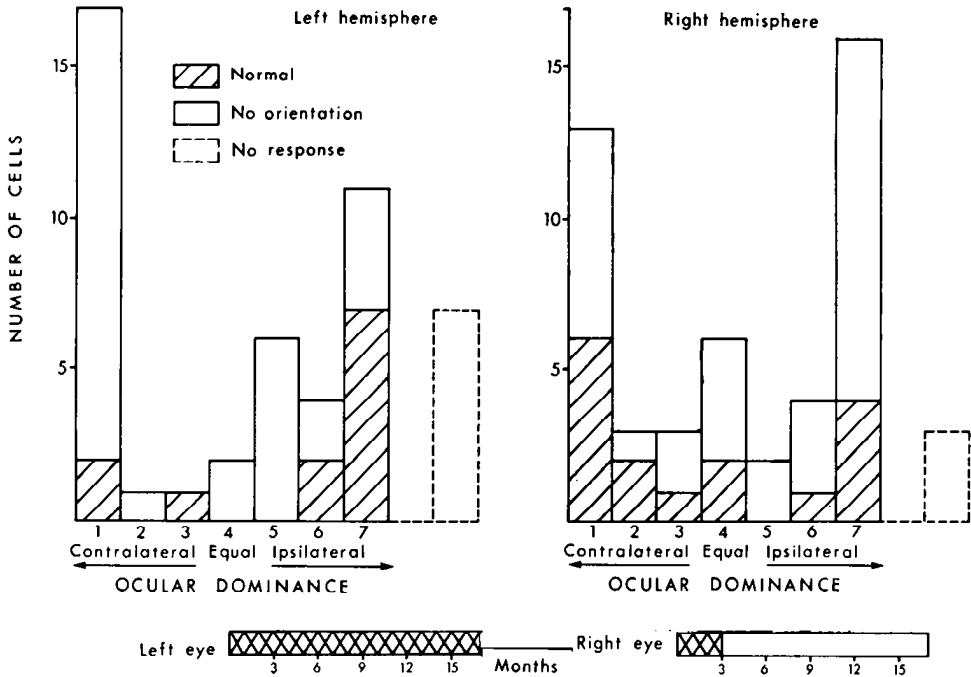


FIG. 3. Ocular-dominance distribution of 99 cells in a cat (no. 7) in which both eyes were closed for the first 3 months of life, following which the right eye was opened for the next 14 months.

In summary, it would seem that the recovery process had re-established connections between cortical cells and the opened eye, but that these connections were distorted ones. The fact that following recovery fewer cells were driven normally from the opened (right) eye than from the closed one is at first glance surprising. The "normal" category is, however, somewhat arbitrary and, in animals before the recovery period, it might include cells

Table 2. Comparison of single-cell responses following 3-month binocular deprivation, with and without periods of recovery

	3-Month Binocular Deprivation (8)		3-Month Binocular Deprivation Followed by 14 Months Recovery of Right Eye (cat 7)	
	Cells	Percent	Cells	Percent
Normal cells	57	41	28	30
Abnormally driven	45	32	61*	60
Unresponsive	37	27	10	10
Total cells	139	100	99	100

* Includes cells that were driven abnormally by one eye and normally by the other, as well as cells driven abnormally by both eyes.

that had lost some connections and therefore responded less briskly than normal but with full specificity. If during the recovery process the lost connections were re-established, but in distorted form, one would have an increase of abnormal cells at the expense of the normal category. It does seem unlikely that opening an eye would cause abnormal connections to be established between that eye and otherwise normal cells.

Table 3. Effects of the various experimental procedures on size of cells in the two dorsal layers of the lateral geniculate body

Description of Cat	Layer	L. Side, μ^2	R. Side μ^2	Diff. Between Sides, %	Dev. From Assumed Normal of $300\mu^2$, %	
					Left	Right
Control: simple suture R. eye closed 3 months L. eye open 3 months	A	184 \pm 8	279 \pm 12	37 (t = 4.8)	39	
	A ₁	316 \pm 14	198 \pm 9	38 (t = 5.6)		34
Cat 1: simple eye opening R. eye closed 3 months, open 3 months L. eye open throughout	A	183 \pm 7	254 \pm 9	28 (t = 6.3)	39	
	A ₁	284 \pm 12	198 \pm 8	30 (t = 5.7)		34
Cat 3: eye reversal R. eye closed 3 months, open 3 months L. eye open 3 months, closed 3 months	A	171 \pm 8	192 \pm 7	11 (t = 0.6)	43	36
	A ₁	210 \pm 11	158 \pm 8	25 (t = 1.2)	30	47
Cat 5: eye reversal R. eye closed 3 months, open 14 months L. eye open 3 months, closed 14 months	A	160 \pm 5	191 \pm 10	16 (t = 2.8)	47	36
	A ₁	203 \pm 11	172 \pm 10	15 (t = 2.1)	33	43
Cat 7: binocular R. eye closed 3 months, open 14 months L. eye closed throughout	A	172 \pm 7	185 \pm 8		43	38
	A ₁	201 \pm 7	202 \pm 9		33	33

* Assumed normal based on average of 10 cats ranging in age from 3 months to 1½ years. According to our measurements any growth in cells after 3 months is negligible.

Finally, this animal showed a marked increase in the proportion of cells driven only by one eye, cells of groups 1 and 7. The change resembles that seen in animals raised with squint or with alternating contact occluders (3), both conditions in which the synergic action of the two eyes is eliminated without the complication of complete disuse. Three months of binocular occlusion gave no comparable defect (8), suggesting that in the present experiment the relative increase in groups 1 and 7 must have taken place during the recovery period. Perhaps the process simply requires more time when the lack of synergy is produced by disuse, a point that could easily be settled by binocular deprivation for longer periods.

Morphology of the lateral geniculate body

Of the 5 animals whose brains have been sectioned so far, 4 were studied by examining the Nissl-stained sections and by measuring cross-sectional areas of 50 cells in each geniculate layer. The results were unanimous in failing to show the least evidence for any recovery. They are summarized in Table 3. For comparison, figures are included from an animal whose right eye was closed for the first 3 months. The average cell size of the dorsal pair of layers (A and A₁) in the normal cat at 3 months or older is about 300 μ^2 . (As discussed previously (6), cell sizes vary to some extent from one animal to the next, partly, no doubt, because of differences in fixation. We have found no evidence that cells increase significantly in size beyond 3 months of age. This seems to be confirmed by comparing in Table 3 the size of normal cells in the 3-month-old control cat with the normal cell size in the 6-month-old cat 1.)

The simplest assessment of recovery can be made for cat 1, in which the right eye was closed for the first 3 months and was open for the next 3, the left having been open at all times. Coronal sections of the two geniculata are shown in Fig. 4. The degeneration of layers A on the left and A₁ on the right is roughly the same as in animals with one eye closed for 3 months, and no recovery period (see ref. 6, Fig. 1). Cell sizes in corresponding layers on the two sides still differ by some 30%.

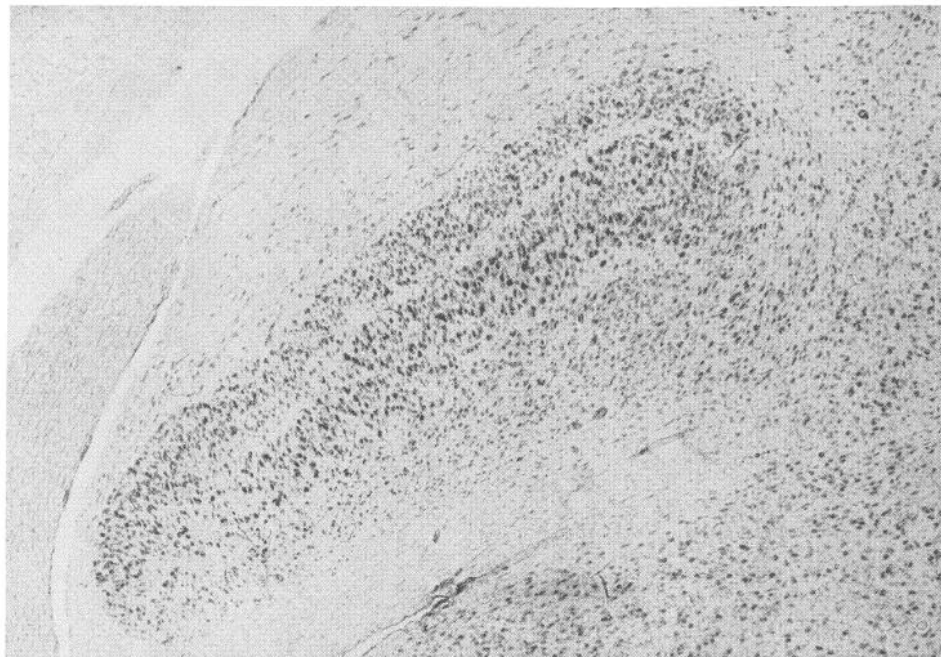
The other three animals confirm this finding, and show that if growth of cells is retarded by eye suture for the first 3 months, there is little or no subsequent recovery even if the eye is reopened for over 1 year. This is particularly impressive in cat 7 in which both eyes were closed for 3 months and the right eye was then opened for 14 months. Here there was no significant difference in corresponding geniculate layers on the two sides. A coronal section through the right lateral geniculate is shown in Fig. 5, and actual cell sizes are given in Table 3.

Finally, the eye-reversal results (cats 3 and 5) confirm our previous impression that late eye closure can produce an actual atrophy of cells (as opposed to the failure to grow produced by closure). The shrinkage is not as pronounced as that produced by initial closure, as can be seen directly in coronal sections of the geniculata of cat 5 (Fig. 6), and also from the actual measurements of cell size given in Table 3. A comparison of the atrophy in cats 3 and 5 indicates that the main atrophic changes occur within the first 3 months of the late closure. Comparing cats 5 and 7 suggests that it makes little difference to the abnormality produced, whether an eye is closed for the first 3 months or the first 17.

DISCUSSION

The absence of any great degree of recovery in this study was surprising, since previous reports on behavioral recovery following deprivation in man (5) and in animals (4) had led us to expect some return of function, slow and

A



B



1 mm

FIG. 4. Coronal sections of left (*A*) and right (*B*) lateral geniculate bodies of a 6-month-old kitten (no. 1) in which the right eye was closed for the first 3 months of life and open for the next 3, the left being open at all times. Celloidin, cresyl violet.

perhaps incomplete, to judge from human experience, and prompt and virtually complete, to judge from the animal experiments. It is difficult to reconcile these results. The human material is particularly hard to assess, since one frequently does not know certain crucial facts such as the age of onset of cataracts, the degree of reduction of retinal illumination, and the final extent of return of vision after cataract removal. In behavioral studies in ani-

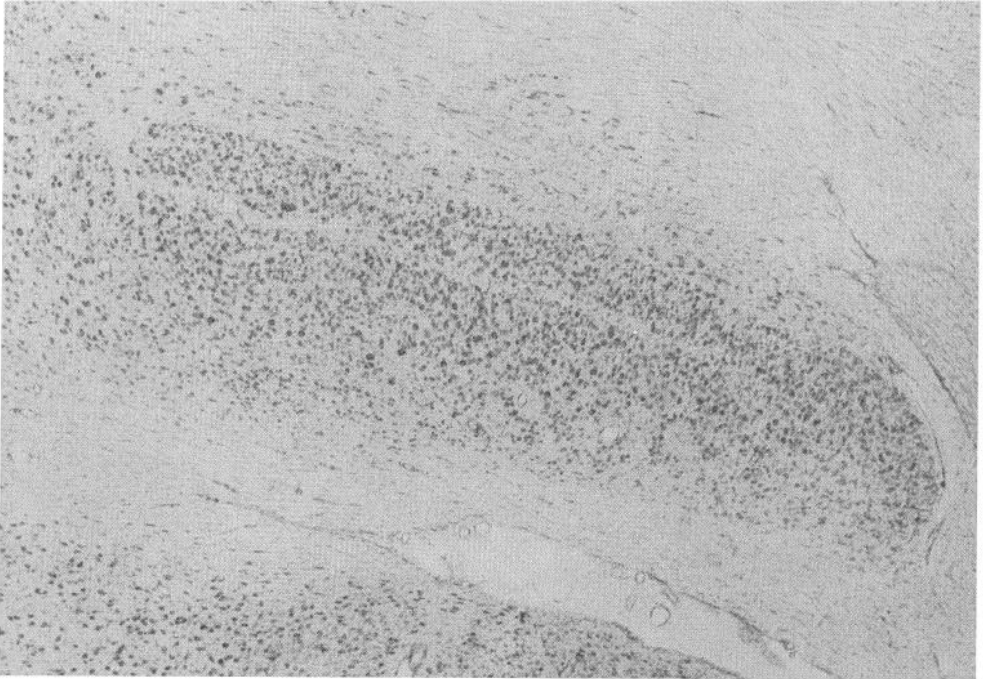
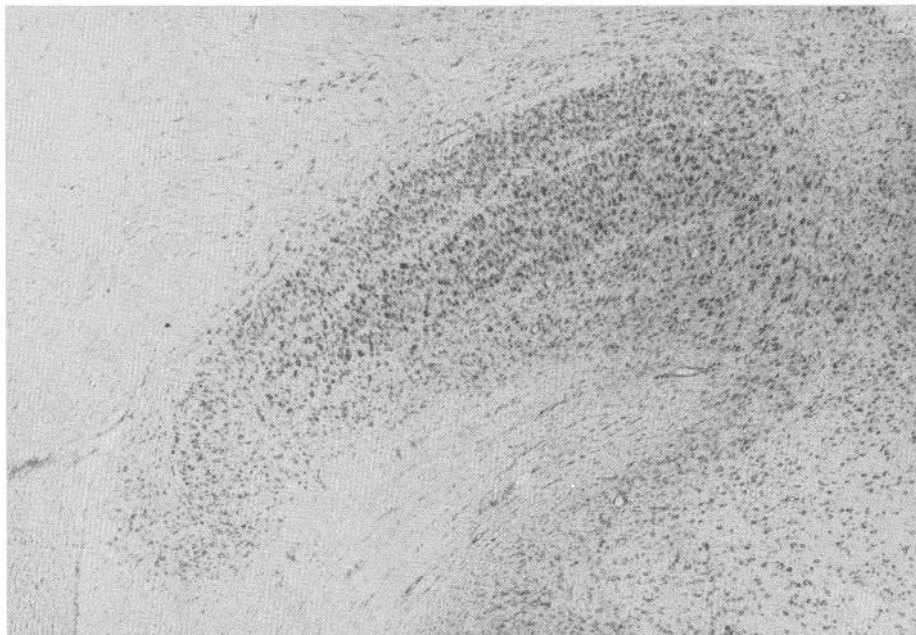


FIG. 5. Coronal sections through right lateral geniculate body of a cat (no. 7) in which both eyes were closed for the first 3 months of life, and then the right eye was opened for the next 14 months. Note that cells in the middle layer (A_1), corresponding to the right eye, appear no different from those of the dorsal layer (A). Celloidin, cresyl violet.

mals a direct comparison of results is not possible, since schedules of visual deprivation and testing procedures have differed from those used in the present experiments. The evaluation of visual abnormalities in animals is in any case difficult, there being no generally accepted or well-evaluated procedures for testing vision in normal animals.

All three phases of the present study—the behavioral, the physiological, and the morphological—agree in indicating only very minimal recovery from the effects of eye closure during the first 3 months of life. In the cortex such connections as did reform apparently did so in a distorted manner.

A**B**

1 mm

FIG. 6. Coronal sections through left (A) and right (B) lateral geniculate bodies of a cat (no. 5) in which the right eye was closed for the first 3 months of life, following which the right eye was opened and the left eye closed for the next 14 months. Note the small size of cells in the dorsal layer of the left geniculate and the middle layer of the right, corresponding to the originally closed right eye. Celloidin, cresyl violet.

There would seem to be two possible interpretations. Either connections, once lost, are incapable of properly re-establishing themselves, or the failure of recovery may simply be a matter of age—another manifestation of the decline in flexibility that occurs in the system some time between the third month and the first year. Experimentally it is difficult to know how to decide between these interpretations, since it probably requires a month or two to produce the abnormalities, by which time the period of flexibility may well be almost over.

SUMMARY

In kittens, monocular or binocular deprivation by lid suture for the first 3 months of life leads to virtual blindness, marked morphological changes in the lateral geniculate body, and a severe deterioration of innate cortical connections. In seven kittens whose eyes had been sutured at birth for 3 months, six unilaterally and one bilaterally, an attempt was made to assess the extent of recovery by reopening an eye and allowing the animals to live for another 3–15 months. In two of the monocular closures the deprived eye was opened and the normal eye closed.

In all kittens there was some slight behavioral recovery during the first 3 months, but the animals remained severely handicapped and never learned to move freely using visual cues. There was no morphological improvement in the lateral geniculate body. Our previous impression that atrophy can develop with deprivation beginning at 3 months was confirmed. In monocularly deprived animals a few cells in the striate cortex may have recovered responses to stimulation to the originally deprived eye, but in many of these cells the responses were abnormal. In the binocularly deprived kitten there was a marked increase in the proportion of cells responding abnormally to the eye that was reopened, without any obvious increase in the total number of cells responding to that eye.

We conclude that the animals' capacity to recover from the effects of early monocular or binocular visual deprivation, whether measured behaviorally, morphologically, or in terms of single-cell cortical physiology, is severely limited, even for recovery periods of over a year.

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