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THE PERIOD OF SUSCEPTIBILITY TO THE PHYSIOLOGICAL EFFECTS OF UNILATERAL EYE CLOSURE IN KITTENS

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SUMMARY

1. Kittens were visually deprived by suturing the lids of the right eye for various periods of time at different ages. Recordings were subsequently made from the striate cortex, and responses from the two eyes compared. As previously reported, monocular eye closure during the first few months of life causes a sharp decline in the number of cells that can be influenced by the previously closed eye.

2. Susceptibility to the effects of eye closure begins suddenly near the start of the fourth week, remains high until some time between the sixth and eighth weeks, and then declines, disappearing finally around the end of the third month. Monocular closure for over a year in an adult cat produces no detectable effects.

3. During the period of high susceptibility in the fourth and fifth weeks eye closure for as little as 3–4 days leads to a sharp decline in the number of cells that can be driven from both eyes, as well as an over-all decline in the relative influence of the previously closed eye. A 6-day closure is enough to give a reduction in the number of cells that can be driven by the closed eye to a fraction of the normal. The physiological picture is similar to that following a 3-month monocular deprivation from birth, in which the proportion of cells the eye can influence drops from 85 to about 7 %.

4. Cells of the lateral geniculate receiving input from a deprived eye are noticeably smaller and paler to Nissl stain following 3 or 6 days' deprivation during the fourth week.

5. Following 3 months of monocular deprivation, opening the eye for up to 5 yr produces only a very limited recovery in the cortical physiology, and no obvious recovery of the geniculate atrophy, even though behaviourally there is some return of vision in the deprived eye. Closing the normal eye, though necessary for behavioural recovery, has no detectable effect on the cortical physiology. The amount of possible recovery in the striate

cortex is probably no greater if the period of eye closure is limited to 7 weeks, but after a 5-week closure there is a definite enhancement of the recovery, even though it is far from complete.

INTRODUCTION

Neurophysiological studies of single cells indicate that the highly specialized neurones in the cat visual cortex establish their proper connexions through innate mechanisms (Hubel & Wiesel, 1963). During the first months after birth these connexions are vulnerable, and can be disrupted through various procedures of visual deprivation such as closing the lids of one or both eyes, or surgically producing a strabismus (Wiesel & Hubel, 1963*b*; Hubel & Wiesel, 1965). For example, after an eye has been closed for the first 10–12 weeks of life only a small fraction of recorded cortical cells can be driven from that eye, while nearly all cells can be driven from the normal eye. In the adult cat, in contrast, there is no such sensitivity to deprivation; the cortical cells retain their inborn ability to respond to stimulation of an eye that has been closed for 3 months.

The disruption of cortical connexions following early eye closure is not accompanied by any anatomical changes that can be seen with stains for Nissl substance or myelin. In contrast, cells in the lateral geniculate body are virtually normal in their responses but show marked morphological changes (Wiesel & Hubel, 1963*a*). Again, such abnormalities are not seen following a comparable period of closure in the adult.

These experimental results show that there must be a critical vulnerable period in the first 10–12 weeks, after which the animal is immune to deprivation procedures. In the present paper we set out to examine the timing more precisely. We wished to learn when the susceptibility was greatest, how long it lasted, the duration of deprivation necessary to produce a severe deficit, and the relation between timing of deprivation and ability to recover.

METHODS

Experiments were done on twenty-one monocularly deprived kittens and on two normal 4-week-old kittens. The deprived animals all had their right eyes closed by lid suture at various ages and for varying lengths of time. In some animals the right eyes were subsequently reopened to test recovery, and in some of these the left eye was closed at the time the right eye was opened ('eye reversal').

At the time of recording the kittens were anaesthetized with thiopentone and paralysed with intravenous succinylcholine to prevent eye movements. Recordings were made from single cells with extracellular tungsten micro-electrodes. Receptive fields were mapped by projecting white-light stimuli upon a wide flat white screen which the animal faced from a distance of 1·5 m. A white background light was kept at mesopic levels (-1 to $+1$ $\log_{10}$ cd/m^2) and the intensity of the stimulating light was 1–1·5 log units brighter than the background. As in previous studies (Wiesel &

Hubel, 1963*b*) recordings were usually made in the hemisphere contralateral to the previously closed eye. In the normal cat about twice as many cells are dominated by the contralateral eye as by the ipsilateral, so that a shift in favour of the ipsilateral eye is all the more significant.

At the end of the experiments the animals were perfused with normal saline followed by 10 % formalin, the brains were embedded in celloidin, sectioned at 25 μ and stained with cresyl violet. The histological material was used for reconstruction of electrode tracks and for studies of morphologic changes in the lateral geniculate bodies.

RESULTS

In the normal adult cats about four fifths of the cells in the striate cortex can be influenced from both eyes (Hubel & Wiesel, 1962). The relative influence of the two eyes on cortical cells varies from one cell to

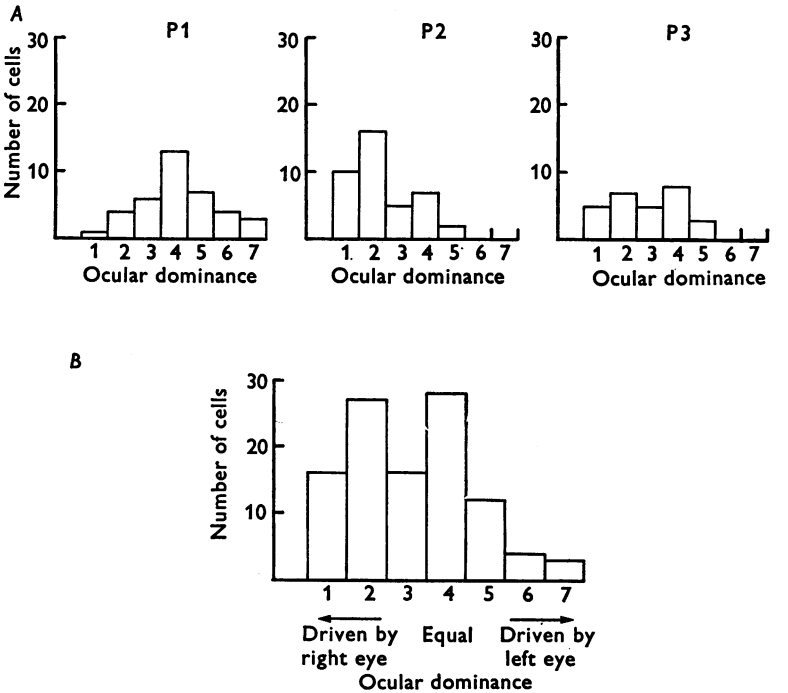

Fig. 1. Upper three histograms: ocular-dominance distributions of cells from three penetrations in striate cortex of two normal kittens, 3–4 weeks old. Lower histogram: sum of above three histograms. (Definition of ocular-dominance groups: cells of group 1 were driven only by the contralateral eye; for cells of group 2 there was marked dominance of the contralateral eye; for group 3, slight dominance. For cells in group 4 there was no obvious difference between the two eyes. In group 5 the ipsilateral eye dominated slightly; in group 6, markedly, and in group 7 the cells were driven only by the ipsilateral eye.)

the next. Some cells receive roughly equal inputs from the two eyes, while in others one eye is strongly dominant or completely so. Cells dominated by one eye show a tendency to be grouped in columns (Hubel & Wiesel, 1965), so that in any micro-electrode penetration perpendicular to the surface of the cortex most or all of the observed cells prefer one eye, though over half show some response to the other.

These findings apply also to kittens with no patterned visual experience, for example animals examined close to the time of birth (Hubel & Wiesel, 1963). We conclude from this that the connexions underlying the observed responses are innate. In the present study many of the deprived kittens

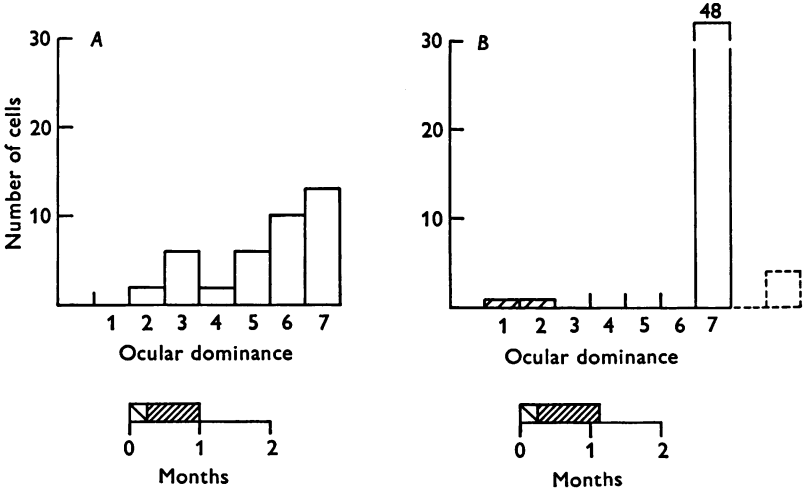

Fig. 2. Ocular-dominance distribution of cells recorded in the left visual cortex of two kittens, litter-mates, in which the right eye was closed (*A*) from the 10th to 31st day; (*B*) from the 10th to 37th day. □ normal response; ▨ no orientation; ⬚ no response. Coiling as in Fig. 1.

were recorded from at an age of 4–6 weeks. We therefore began by recording from normal kittens at this age, to rule out the unlikely possibility that the ocular-dominance distribution might differ from that of either newborn kittens or adult cats. Figure 1*A* shows the ocular-dominance distribution obtained in three micro-electrode penetrations in two normal kittens 3–4 weeks old. The composite histogram for all three penetrations is shown in Fig. 1*B*. As expected, the results are similar to those previously obtained in new-born kittens and in adult cats (Hubel & Wiesel, 1962, 1963).

Monocular closure from birth, for periods of varying length

In ten kittens from five litters the lids of the right eye were sutured together at about 10 days and recordings were made at various times during the next 2–3 months. For any given period of deprivation during the sensitive period there was some variation in results from one kitten to the next, which was minimized by first comparing individuals within the same litter, and then comparing litters. The earliest recordings, made at about one month of age, were already abnormal. Figure 2*A* shows the results obtained from a kitten whose right eye was closed from day 10 to

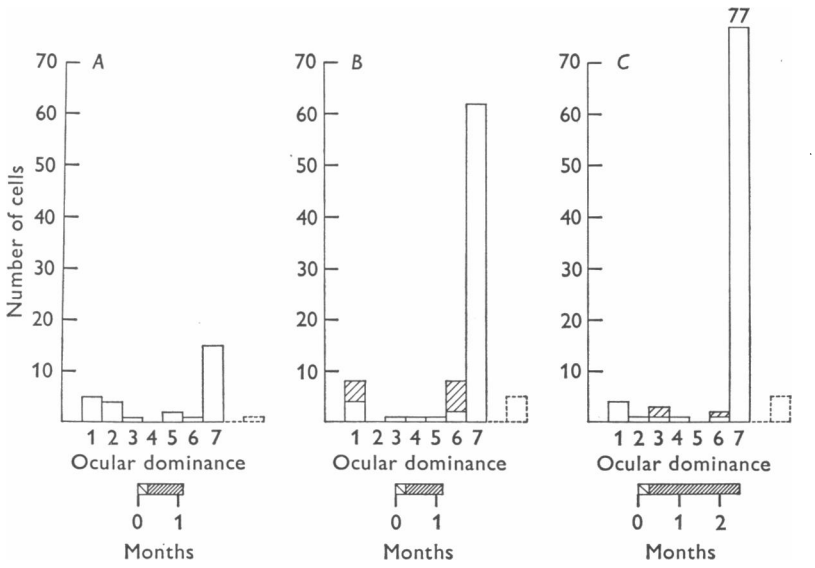

Fig. 3. Ocular-dominance histograms for cells in the left visual cortex in three kittens, litter-mates, deprived by right-eye closure during days (*A*) 10 to 37; (*B*) 10 to 41; (*C*) 10 to 75. Coding of responses as in Fig. 1.

day 31. The thirty-eight cells recorded in two penetrations gave a lopsided histogram showing clear dominance of the normal eye. Moreover, the responses from the right eye were generally more sluggish and fatigued more easily than those from the left, which seemed entirely normal.

Six days later, at 37 days, a litter-mate of this kitten gave the results shown in Fig. 2*B*. Now the shift in favour of the left eye was virtually complete, with only two cells out of fifty-four driven by the closed eye. Four cells were uninfluenced by either eye, an abnormality commonly found in monocularly deprived kittens (Wiesel & Hubel, 1963*b*).

Results from a second litter, also with right eye closure from birth, are

shown in Fig. 3. The first kitten in this litter (Fig. 3*A*) was studied at 37 days of age. Here the shift was not as marked as that of Fig. 2*B*, even though the duration of closure was the same. The histogram was nevertheless abnormal, with a shift in favour of the open eye and a dropping out of most binocularly driven cells. Four days later (41 days) a second member of the litter showed decidedly more advanced changes (Fig. 3*B*), though again some cells were still driven from the right eye. Many of these cells, however, responded sluggishly to the right eye and failed to show the usual selectivity to oriented line stimuli, whereas the responses seen from the left eye were normal. In a third animal, taken from the same litter at 75 days, the changes were still more pronounced (Fig. 3*C*). Now even fewer cells could be driven from the right eye, and with one exception all cells responded weakly from that eye, with none of the usual preference for a specific stimulus orientation. In this litter, then, the most dramatic changes seem to have occurred during the sixth week of life, between the recordings of Fig. 3*A* and *B*.

The results shown in Figs. 2*B*, 3*B* and 3*C* agree with our previous studies in 2–3 month deprived kittens. They are at variance with the findings of Ganz, Fitch & Satterberg (1968), who, using comparable durations of deprivation, found a roughly equal number of cells activated from the deprived and normal eyes. The reason for this difference in results is not clear, but in any case there is agreement that responses from the deprived eye are grossly abnormal.

Figures 2 and 3 illustrate the variations that can occur from one litter to the next. The earliest abnormalities were found in two litter-mates deprived from days 10–30 and 10–32 (not illustrated). In both of these kittens almost all the cells observed were driven by only the eye that had been open, giving a histogram similar to that of Fig. 2*B*.

The results from all five litters suggest that the changes begin by about the fifth week of life, and can become very marked in a matter of a few days.

Monocular closure during the sensitive period

Our next step was to close an eye for only a few days in normal animals 3–5 weeks old, comparing various ages and durations of closure. The histogram of Fig. 4*A* shows the results of a 3-day closure in the 4th week (days 23–26). Even with such a brief period of deprivation the results were abnormal, comparable to those from an animal deprived from birth to 37 days (Fig. 3*A*). In this animal and in several others with eye closure from birth (e.g. the animals of Fig. 3*A* and *B*), there was not only some shift in favour of the normal eye, but also a marked decline in the number of binocularly driven cells, especially those in which the two eyes make

almost equal contributions (groups 3 to 5). At this stage, before the normal eye has taken over completely, the ocular-dominance distribution thus tends to resemble that of animals with strabismus (Hubel & Wiesel, 1965). It is as though connexions from the open eye were in some way competing with connexions from the closed eye, hastening their disruption. By this line of reasoning, one might expect that cells with little or no input from the open eye (groups 1 and 2) would be less vulnerable to the effects of eye closure (Wiesel & Hubel, 1965*a*).

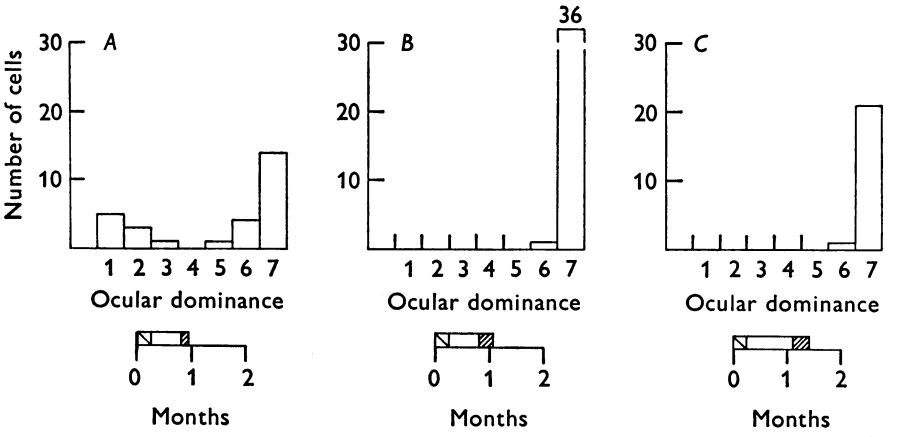

Fig. 4. Ocular-dominance histograms for cells in the left visual cortex in three kittens deprived by right-eye closure during days (*A*) 23 to 26; (*B*) 23 to 29; (*C*) 30 to 39. Kittens *B* and *C* were litter-mates. Coding as in Fig. 1.

In a second animal, from a different litter, monocular deprivation from day 23 to 29 gave the result shown in Fig. 4*B*. Here the shift in ocular dominance was almost complete. A similar result was seen in a litter-mate deprived during days 30–39 (Fig. 4*C*). These experiments show that the sensitive period has a duration of at least several weeks, during which a few days of closure causes marked cortical changes.

Upper limit of sensitive period

Our earlier work indicated that the period of sensitivity to monocular eye closure was limited (Wiesel & Hubel, 1963*b*). In an adult cat a 3-month closure produced no physiological or anatomical abnormalities. At two months of age, closure for 1 month gave the abnormal ocular-dominance distribution shown in Fig. 5*A*, but the changes were far from the extreme ones produced in the present study by much briefer periods of deprivation during the second month. Closure at 2 months for 4 months

produced little additional damage (Fig. 5*B*), suggesting that the sensitive period may decline at about 3 months of age.

In the present series (Fig. 6) we closed an eye of a 4-month-old kitten for a period of 3 months. This was followed by 16 months in which both eyes were open and during which extensive behavioural tests showed normal vision in the two eyes (Dews & Wiesel, 1970). When the animal was

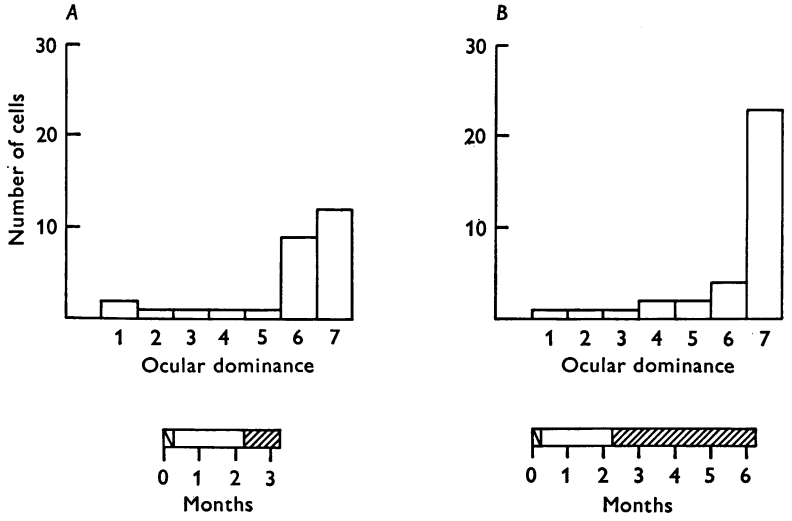

Fig. 5. Ocular-dominance histograms for cells in the left visual cortex of two kittens, not litter-mates, deprived by right-eye closure (*A*) from age 2 months to 3 months; (*B*) from age 2 months to 6 months. Coding as in Fig. 1. (From Wiesel & Hubel, 1963*b*.)

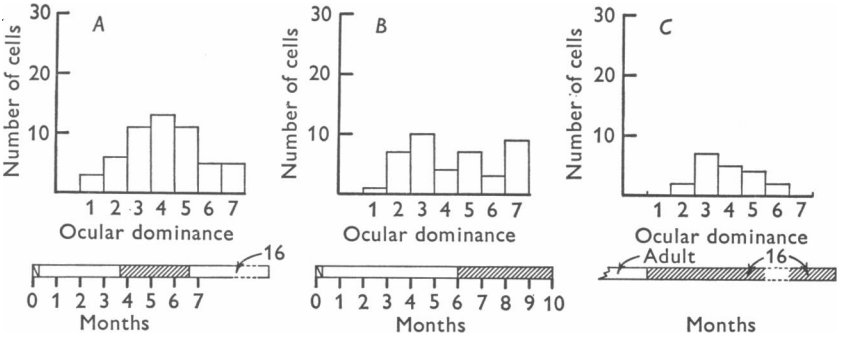

Fig. 6. Ocular-dominance histograms for cells in the left visual cortex of cats deprived by (*A*) right-eye lid suture at 4 months, eye opened at 7 months and recordings made at 2 years of age; (*B*) right-eye lid suture at 6 months, recording at 10 months; (*C*) right-eye lid suture in adult, recording 16 months later. Coding as in Fig. 1.

finally studied physiologically at almost 2 years of age the ocular-dominance histogram, shown in Fig. 6*A*, was also normal. The studies on recovery described previously (Wiesel & Hubel, 1965*b*) and in the next section make it most unlikely that any significant physiological recovery occurred after the deprived eye was opened.

A second kitten had one eye closed at 6 months of age for a period of 4 months. None of the receptive fields in the closed eye were abnormal, and the histogram, shown in Fig. 6*B*, is probably within normal limits. Finally, a 16-month closure in an adult cat likewise produced no abnormalities (Fig. 6*C*). A 6-month-old kitten and an adult cat were deprived for periods comparable to those of Fig. 6*B* and *C*, and then were tested behaviourally immediately after the deprived eye was opened. These animals had normal vision in the deprived eye.

We conclude that the susceptibility to the effects of deprivation, which appears rather suddenly near the beginning of the fourth week and is very great during that week, begins to fall some time between the sixth and eighth week, continues to decline during the third month, and has disappeared by the end of that month. An adult cat seems completely resistant to monocular deprivation.

Recovery from monocular deprivation of various durations

The effects of monocular deprivation for the first 3 months of life tend to be permanent, with very limited morphological, physiological, or behavioural recovery (Wiesel & Hubel, 1965*b*). It seemed important to ask whether the recovery would be greater in animals deprived only for the minimum time necessary to give severe physiological changes. For this purpose we used two litter-mates of the kitten whose 10–37 day deprivation effects are shown in Fig. 2*B*. These kittens had their right eyelids sutured at 10 days and reopened at 37 days; one was studied physiologically after a 12-month recovery period, the other after 14 months. Recordings were almost identical in the two animals (Fig. 7*A* and *B*), and indicate a recovery that was clearly greater than that seen after 3 months deprivation, although it was still very limited. The degree of recovery is perhaps greater than indicated by the histograms alone, since a high proportion of the cells driven by the right eye were normal in their responses and stimulus requirements, and also since the number of cells that could not be driven by either eye was low compared with what is usually seen immediately after monocular deprivation. This decrease in unresponsive cells after a recovery period has been a consistent finding (Wiesel & Hubel, 1965*b*).

In both animals the scarcity of binocular cells is striking; only about one fifth of the cells, instead of the normal four fifths, received inputs from both eyes. Thus it appears that the normal binocular connexions are

not only among the first to go (Figs. 3*A* and 4*A*), but are the least likely to recover. In these penetrations the cells that were driven exclusively by the closed eye tended to occur in groups, as though they were clustered together in the cortex. Normally cells tend to be grouped according to eye dominance (Hubel & Wiesel, 1965), so that presumably the cells that re-establish functional connexions with the deprived eye are those that were strongly dominated by that eye in the first place.

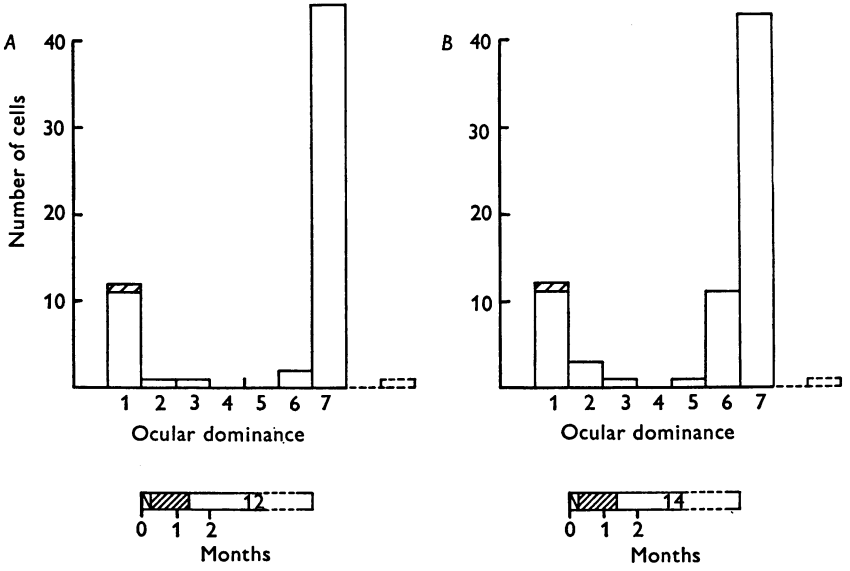

Fig. 7. Ocular-dominance histograms for cells in the left visual cortex of two litter-mates of kitten of Fig. 2*B*. Right-eye suture at 10 days, opened at 37 days. Recordings made at (*A*) 12 months (cat no. 13, Dews & Wiesel, 1970); and (*B*) 14 months after eyes were opened (cat no. 12, Dews & Wiesel, 1970). Coding as in Fig. 1.

The effect of an additional 2 weeks of deprivation upon subsequent recovery is seen in Fig. 8. Here a pair of litter-mates were monocularly deprived between days 10 and 51, and then one was recorded from and the other allowed to recover after opening the lids for 11 months. As expected, the deprivation in the first kitten resulted in virtually complete domination by the left eye (Fig. 8*A*). After 11 months there was some minor recovery in the litter-mate, but considerably less than that seen in the animals of Fig. 7. Many of the cells driven by right eye showed abnormal responses. Thus in the critical period even a slight increase in duration of deprivation, to an age of 7 weeks as opposed to 5, may be important in further limiting the recovery. This is supported by the behavioural studies of some of these same animals (Dews & Wiesel, 1970).

Finally, in two kittens (not litter-mates) the right eyes were closed for the first 3–4 months of life and then opened. In one animal both eyes then remained open for the next 30 months. In the other, the left eye was closed for a year and then opened, and from then on both eyes were open for the next 58 months. When these animals were ultimately studied physiologically neither showed any spectacular recovery (Fig. 9), but just the usual slight increase in cells driven by the originally closed eye and a decline in the number of unresponsive cells. Eye reversal, comparable to

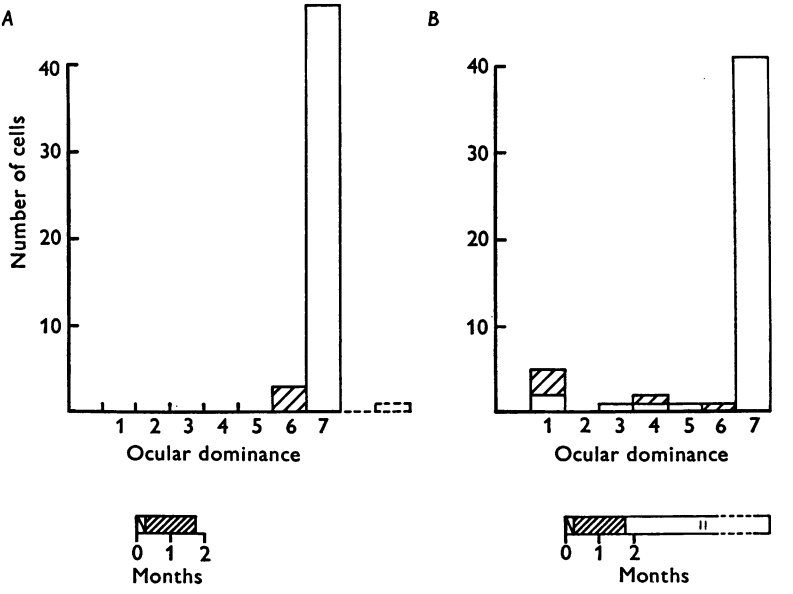

Fig. 8. Ocular-dominance histograms for cells in the left visual cortex of two litter-mates. (*A*) Right eyelids sutured from day 10 to day 51. (*B*) Right eyelids sutured from days 10 to 51, right eye than opened for 11 months. Coding as in Fig. 1.

patching an amblyopic human eye, thus had no detectable effects in the physiological studies. In contrast there was a clear difference in the behavioural recovery of the two animals, for the first (not reversed) cat remained completely and permanently form-blind in the deprived eye whereas the reversal in the second cat led to some return of vision in the originally deprived eye (Dews & Wiesel, 1970). It is worth emphasizing this disparity between the physiological and behavioural recovery in the eye-reversed cat. Such an animal either learns to do very well with the few cortical cells that recover their connexions or else learns to use some other less damaged part of its visual system.

Morphologic changes in lateral geniculate body following monocular deprivation

Our previous studies (Wiesel & Hubel, 1963*a*) showed that after three months of monocular closure from birth the geniculate layers receiving input from the deprived eye are thinner, and the cell bodies within these layers are smaller and stain less deeply with basic dyes. The atrophy was

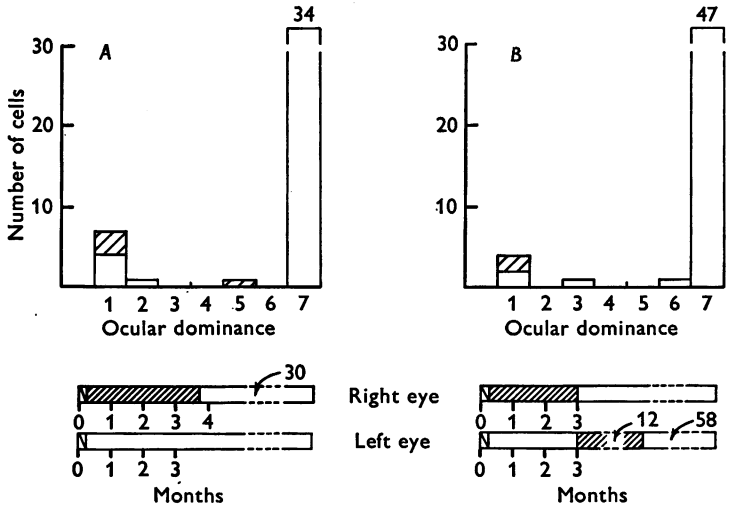

Fig. 9. Ocular-dominance histograms for cells in the left visual cortex of two kittens whose right eyes were closed for the first 3–4 months and then opened. (*A*) Both eyes were then kept open for 30 months (cat no. 10, Dews & Wiesel, 1970). (*B*) Left eye was then closed for 1 year, and then opened. From then on both eyes remained open for the next 4 years and 10 months. The cat was finally recorded from at age 6 years and 1 month (cat no. 1, Dews & Wiesel, 1970). Coding as in Fig. 1.

less marked the later the closure, with no changes in an adult cat deprived for 3 months. Most (though not all) of the cells in the affected layers responded well to visual stimulation and had the usual centre-surround receptive fields. There is considerable additional evidence that the physiological changes seen in cortical cells depend on cortical rather than on geniculate abnormalities; for example, form deprivation with a translucent occluder led to only slight shrinkage in geniculate cells but gave a cortex just as abnormal physiologically as that following eye closure. Again, binocular occlusion gave surprisingly less cortical abnormality than would have been predicted from monocular closures, but resulted in just as severe shrinkage in all geniculate layers (Wiesel & Hubel, 1965*a*). The

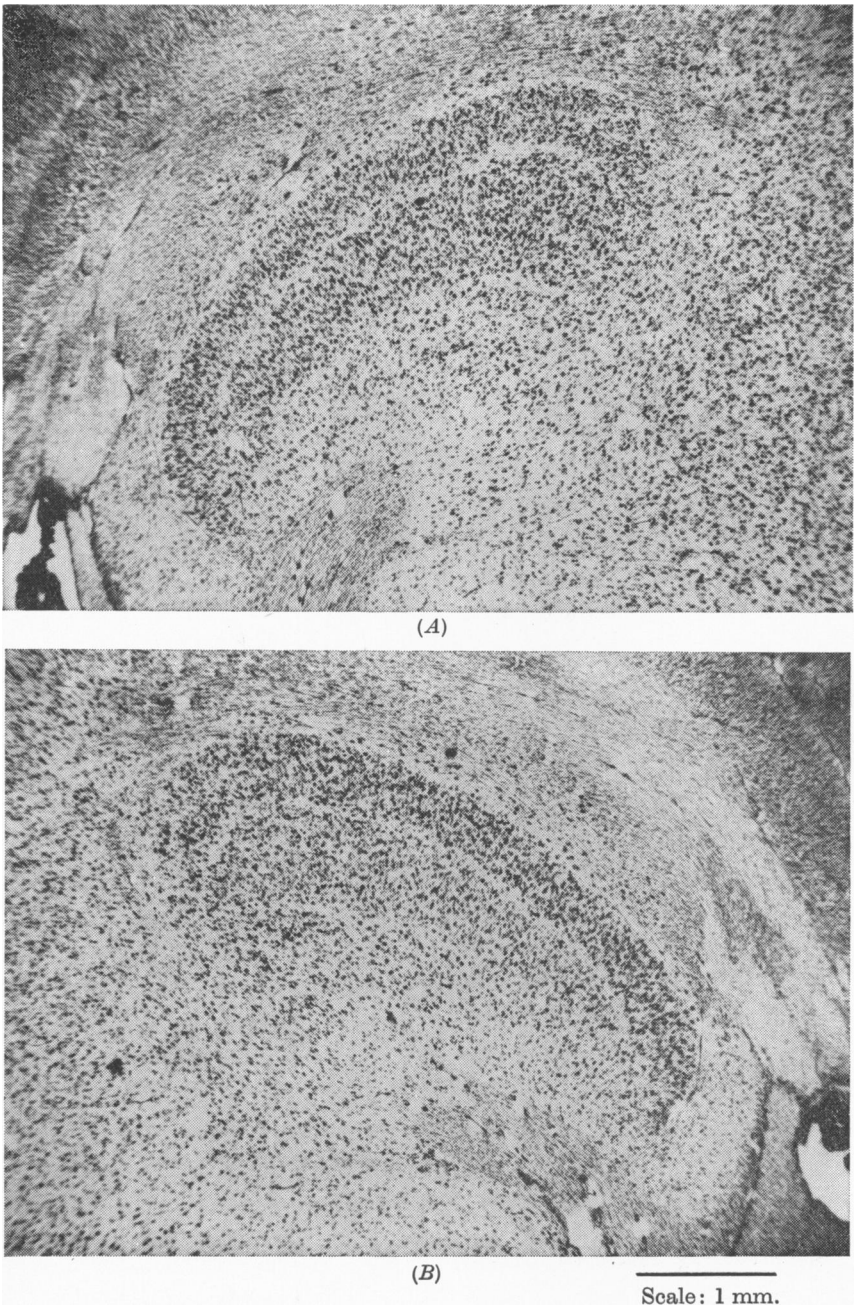

Fig. 10. Coronal section through (*A*) left and (*B*) right lateral geniculate bodies of a kitten whose right eye was closed from days 23–26; same cat as in Fig. 4*A*; cresyl violet.

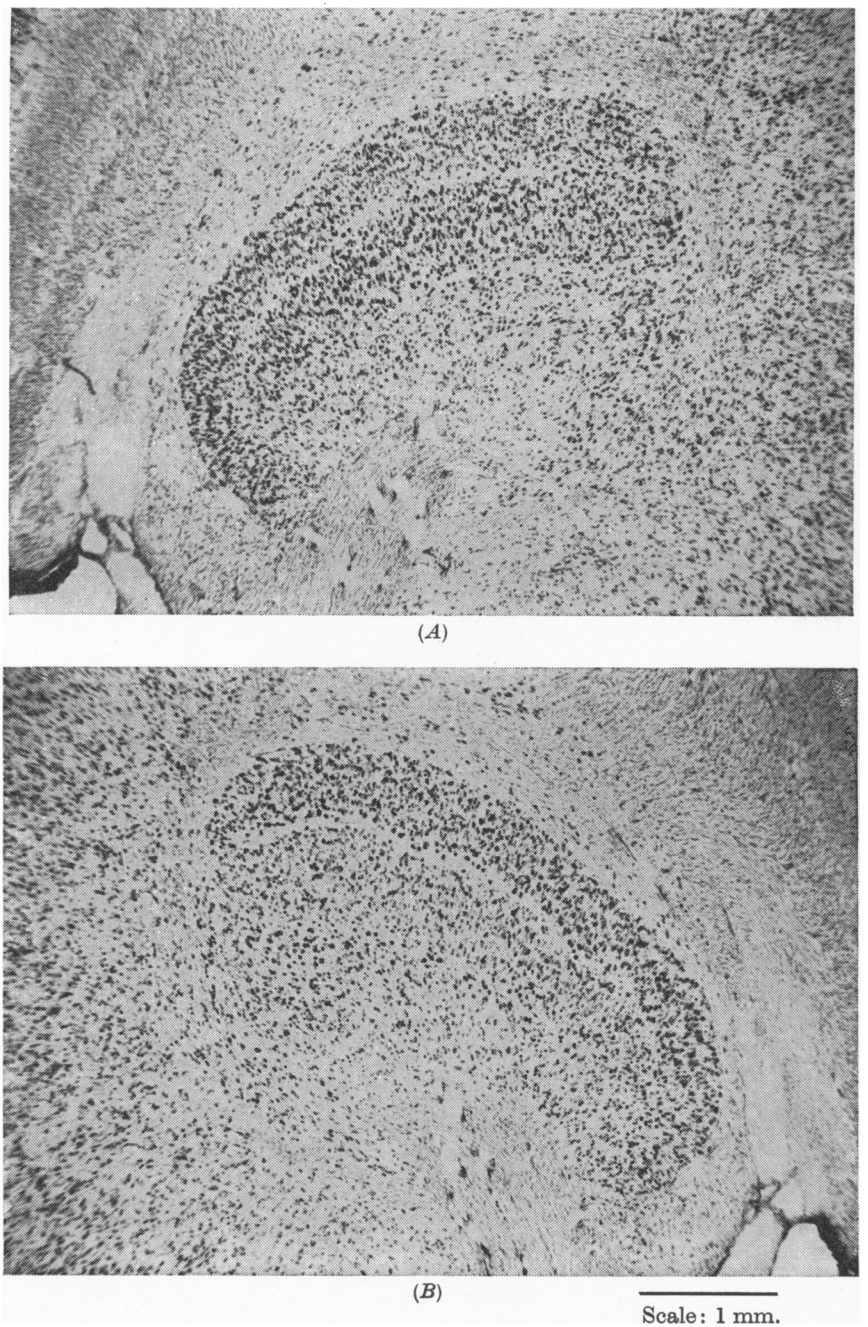

Fig. 11. Coronal section through (*A*) left and (*B*) right lateral geniculate bodies of a kitten whose right eye was closed from days 23–29; same cat as in Fig. 4*C*; cresyl violet.

absence of geniculate abnormalities in animals raised with strabismus affords still another example of the lack of parallel between geniculate morphological and cortical physiological abnormalities.

The effects of deprivation on geniculate cells seem to involve both a retardation in normal growth and also atrophy in the usual sense (Wiesel & Hubel, 1963*a*; Kupfer & Palmer, 1964). At birth the cells are about one fourth adult size, in terms of cross-sectional area; they grow rapidly to about half size in 2–3 weeks and to full size in about 8–10 weeks. During the first 3 weeks eye closure seems to have little effect on this normal growth, not surprisingly perhaps, since even after the tenth day, when the eyes normally open, the animal sleeps or suckles most of the time, often in a dimly lit hiding place. After the third week sensory deprivation gives an irreversible arrest in growth, so that by the second month there is a 30–40 % reduction in size relative to the normal. A kitten deprived at 2 months of age for one month shows a reduction in cell size (Wiesel & Hubel, 1963*a*) and this must be termed atrophy in the strict sense, since normal growth is practically complete at about 2 months.

During the most critical period for physiological changes in the cortex even a few days of deprivation gave a distinct difference between geniculate layers. Figure 10 gives the results of 3 days' deprivation (days 23–26) in the animal of Fig. 4*A*. While not approaching the shrinkage seen following a 3-month deprivation the effects are still obvious at a glance, particularly in the right geniculate, which was for some reason more seriously affected than the left. In Fig. 11 the deprivation lasted 6 days (days 23–29, same cat as in Fig. 4*C*); here the shrinkage was bilateral and more marked, though the change was still not so severe as that seen after a 3-month deprivation. It seems unlikely that differences as large as these could result simply from a cessation of growth during these brief periods, and we assume that there was in addition some atrophy.

Lateral geniculate bodies were examined histologically in both the animals of Fig. 9, in which the recovery period was protracted. Both showed the usual marked reduction in cell size and inability to take up Nissl stain in layers receiving input from the eye that was deprived in the first few months. This agrees with our previous findings (Wiesel & Hubel, 1965*b*). Even in the animal (Fig. 9*B*) whose right eye was closed only for the first 3 months and then the left eye closed for a year, the layers corresponding to the right eye were collapsed and the cells shrunken, compared to the other layers. It seems evident that the abnormalities produced by the original closure are virtually irreversible. Furthermore, the normal appearance of the layers receiving input from the left eye indicate that after 3 months of age, eye closure causes no appreciable changes. This fits well with the absence of any changes in the geniculate of a cat with an eye sutured at

4 months of age for 3 months (Fig. 6*A*), or in an adult cat with one eye shut for 16 months (Fig. 6*C*). Here the evidence is especially compelling since one can compare adjacent deprived and non-deprived layers. Burke & Hayhow (1968) have kept adult cats in darkness for over 2 years without finding any morphological changes in the lateral geniculate.

DISCUSSION

The most surprising result of this paper is the high degree of sensitivity a kitten shows to a few days of monocular deprivation during a very restricted period in life. The susceptibility begins suddenly near the start of the fourth week, at about the time a kitten begins to use its eyes, and persists until some time between the sixth and eighth weeks; it then begins to decline, disappearing ultimately around the end of the third month. After 4 months cats seem to be insensitive even to very long periods of monocular deprivation as tested by behavioural, physiological or morphological criteria.

An ability to recover from the physiologic effects of monocular deprivation seems to be closely related to this vulnerable period. Deprivation for the first 2–3 months produced virtually irreversible defects even when the normal eye was closed during the period of attempted recovery. When the deprivation period was shorter (Fig. 7) the recovery was greater, though it was still relatively slight. Perhaps this difference in ability to recover is simply an expression of a lesser degree of permanent damage from the shorter deprivation period. On the other hand, it may be that between the fourth and eighth weeks an animal's nervous system is better able to recover, just as it is more susceptible to damage. The immunity to deprivation effects after the third month and the failure to recover after that period may both be manifestations of a similar rigidity.

The observation of a critical period of susceptibility to deprivation or abnormal experience is by no means new. Examples have been found in many animals, including birds, dogs, monkeys, and man. The period of susceptibility to deprivation varies from animal to animal and no doubt from system to system within a given species. One extreme is seen in 'following responses' of certain birds, where the critical period peaks sharply within the first day of hatching (Lorenz, 1935). The other extreme is found in man, in whom language capabilities, for example, can be laid down in the non-dominant hemisphere following injury in the dominant one during early childhood, but not after the age of about 8–10. The present studies indicate an age of maximum susceptibility to visual deprivation between the fourth and eighth weeks. It is common experience that kittens handled extensively by humans during this period are subsequently tamer and more tractable than ones isolated from humans, and

behavioural studies such as those of Scott & Fuller (1965) indicate a similar critical period for social development in dogs. It may be that the critical period coincides with the time when a particular system is being formed and developed and that use during this time is essential for its full maturation and sustenance.

One may reasonably ask whether mechanisms in which neural connexions become impaired through abnormal experience can possibly serve any use, or possess any survival value. Here one can only speculate, but it is worth emphasizing that in monocular deprivation the failure of cortical connexions from the closed eye may well be accompanied by an enhancement of connexions from the normal eye. It seems from the results of binocular closure that the failure of connexions from the closed eye is largely dependent on the other eye's being open (Wiesel & Hubel, 1965*a*). The abnormalities we see may thus be part of a larger process of adjustment to the loss or impairment of one eye. Similarly in animals reared with strabismus from birth, the falling out of connexions responsible for mixing of inputs from the two eyes may have the advantageous effect of overcoming double vision. But while it is easy to think of advantages to the animal in possessing some flexibility, it is difficult to understand why the sensitive period should decline so completely after a few months. A second possibility is that the flexibility is important for certain fine adjustments in the neural connexions from the eyes relative to each other. Such adjustments might be important early in life, and once made, might be sufficient to last a lifetime.

As yet we know nothing about the chemical changes and have only begun to learn about the morphologic changes that occur in the cortex as a result of visual deprivation. Light microscopic observations in dark-raised mice indicate that the visual cortex is thinner than in the normal animal (Gyllensten, Malmfors & Norrlin, 1965). It has been reported by Valverde (1967) that in such mice the number of spines on apical dendrites of layer V pyramidal cells are reduced in the parts passing through layer IV. Globus & Scheibel (1967), studying dark-raised rabbits, found that in the portions of the apical dendrite receiving geniculate input the spines were abnormal in size and shape but not reduced in numbers; otherwise cortical cells were normal in size and dendritic branching.

In considering the possible implications of studies like the present one for human development it is important to stress that in the cat, within the critical period between the fourth and eighth weeks, a deprivation as brief as a few days can have marked effects. This implies that for normal development normal environmental conditions must prevail throughout the critical period and not just during some small part of it. What an analogous critical period might be in man is of course not known though

experience with squint would suggest that it is longer, possibly several years. We are now attempting to define this period in the macaque monkey; from the few animals already studied it is clear that 2 weeks of monocular deprivation during the first 5 weeks of life produces at least temporary blindness in the eye that has been closed and an absence of responses of cortical cells to stimulation of that eye. This suggests that the sensitive periods of cats and monkeys may not be too dissimilar.

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