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REVERSAL OF THE PHYSIOLOGICAL EFFECTS OF MONOCULAR DEPRIVATION IN THE KITTEN'S VISUAL CORTEX

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SUMMARY

1. Twenty-three kittens were monocularly deprived of vision until the age of 4, 5, 6 or 7 weeks. Their deprived eyes were then opened, and their experienced eyes shut for a further 3–63 days. After this time physiological recordings were made in the visual cortex, area 17. Three control kittens, monocularly deprived for various periods, showed that at the time of reverse-suturing, few neurones could be influenced at all from the deprived eye.

2. Following reverse-suturing, the initially deprived eye regained control of cortical neurones. This switch of cortical ocular dominance was most rapid following reverse-suturing at the age of 4 weeks. Delaying the age of reverse-suturing reduced the rate and then the extent of the cortical ocular dominance changes.

3. The cortex of reverse-sutured kittens is divided into regions of cells dominated by one eye or the other. The relative sizes of these ocular dominance columns changed during reversed deprivation. The columns devoted to the initially deprived eye were very small in animals reverse-sutured for brief periods, but in animals that underwent longer periods of reversed deprivation, the columns driven by that eye were larger, while those devoted to the initially open eye were smaller.

4. Clear progressions of orientation columns across the cortex were apparent in many of the kittens, but, in contrast to the situation in normal or strabismic kittens, these sequences were disrupted at the borders of eye dominance columns: the cortical representations of orientation and ocular dominance were not independent.

5. Binocular units in these kittens were rather rare, but those that could be found often had dissimilar receptive field properties in the two eyes.

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Commonly, a cell would have a normal orientation selective receptive field in one eye, and an immature, unselective receptive field in the other. Cells that had orientation selective receptive fields in both eyes often had greatly differing orientation preferences in the two eyes, occasionally by nearly 90°.

6. During the reversal of deprivation effects, the proportion of receptive fields exhibiting mature properties declined in the initially experienced eye, while the proportion increased in the initially deprived eye. Similarly, the average band width of orientation tuning of receptive fields in the initially deprived eye decreased, while that of receptive fields in the initially experienced eye increased.

7. One kitten was reverse-sutured twice, to demonstrate that cortical ocular dominance may be reversed a second time, even after one reversal of ocular dominance.

8. It is suggested that the sensitive period for cortical binocular development consists of two phases. In the first phase, all cortical neurones may be modified by experience, but the rate at which they may be modified decreases with age. In the second phase, an increasing number of cortical neurones becomes fixed in their properties, while those that remain modifiable are as modifiable as they were at the end of the first phase.

9. It is further suggested that, while the innate endowment of cortical neurones is important for the normal course of development, it is overshadowed by environmental factors, since cortical neurones may develop normal mature receptive fields different from the ones that they were initially given, after the innate connexions have been abolished by deprivation.

INTRODUCTION

Most neurones in the primary visual cortex of the cat are functionally connected to both eyes. Many of them are sensitive to binocular disparity, and may thus signal the depth of an object in visual space, and underlie the processes of binocular fusion and stereopsis (Hubel & Wiesel, 1962; Barlow, Blakemore & Pettigrew, 1967; Pettigrew, Nikara & Bishop, 1968). In very young, visually naive kittens, a similarly high proportion of cortical neurones may be binocularly activated, but their properties are immature in that they lack sensitivity to binocular disparity (Hubel & Wiesel, 1963*b*; Pettigrew, 1974; Blakemore & Van Sluyters, 1975). The development of this binocular specificity, and the retention of the innate binocular connexions of cortical neurones depends upon binocular visual experience during a 'sensitive period' early in a kitten's life. Disrupting the normal pattern of experience by causing one eye to deviate, or by alternately occluding one eye and then the other, day by day, leaves the

great majority of cortical neurones functionally connected to one eye or the other, but rarely to both (Hubel & Wiesel, 1965). Furthermore, if one eye is covered, even for a few days at certain times in the sensitive period, few neurones in the cortex may be driven at all by that eye, and none may be strongly driven through it (Wiesel & Hubel, 1963*b*, 1965*a*; Hubel & Wiesel, 1970).

These physiological effects of monocular visual deprivation are not significantly reversible by visual experience obtained after the end of the sensitive period. Wiesel & Hubel (1965*b*) found little or no restoration of the influence of the deprived eye in the cortex following either extended periods of binocular vision, or of forced usage of the deprived eye. Furthermore, Hubel & Wiesel (1970) found that a long period of binocular vision *within* the sensitive period leads to a surprisingly small physiological recovery, even if the initial period of deprivation lasts only 4 weeks.

Blakemore & Van Sluyters (1974) examined the extent to which monocular deprivation effects can be reversed within the sensitive period when kittens are forced to use their deprived eyes. They showed that, so long as the deprived eye is opened before the age of 6 weeks, total or near-total reversal of deprivation effects is possible. Delaying the age at which deprivation is reversed reduces the extent of recovery (see also Wiesel & Hubel, 1965*b*; Chow & Stewart, 1972).

The reversal of deprivation effects is potentially of the greatest importance, since it is one of the few definite examples of the functionally effective restitution of a physiologically disconnected neuronal pathway in the mammalian central nervous system. Reinnervation in the nervous systems of lower vertebrates is possible after surgical disconnexion, but results in the formation of connexions that reproduce, so far as that is possible, the original connectivity pattern (see Jacobson, 1969). But Blakemore & Van Sluyters (1974) observed several unusual features in the reinnervated cortex of their animals that suggest that the new neuronal pattern in this system may not merely restore the old one, but rather represents a functional reorganization of connexions. I have investigated this functional reinnervation in greater detail, with a view to examining the nature of the new connexions, the rate and manner in which they are formed, and their relevance to the processes underlying neuronal development and plasticity in the central nervous system. This paper will examine several aspects of the neuronal organization of the visual cortex in animals undergoing this reinnervation, and the rate at which it proceeds in kittens of different ages. In the following papers some behavioural and morphological correlates will be examined (Movshon, 1976; Dürsteler, Garey & Movshon, 1976).

Some of these results have been briefly reported elsewhere (Movshon & Blakemore, 1974; Blakemore, Van Sluyters & Movshon, 1976).

METHODS

Animals and rearing conditions

The kittens used in these experiments were all caged with their mothers in an open colony room until the age of weaning (usually about 10 weeks); afterwards they freely roamed the colony, which was artificially illuminated on a cycle of 18 hr light and 6 hr dark each day. Their health was checked daily, and they were routinely vaccinated against enteritis at weaning.

Visual deprivation. Eyelid suture was performed by the method of Wiesel & Hubel (1963*a*) as described by Blakemore & Van Sluyters (1975). Animals were anaesthetized with halothane (Fluothane, I.C.I.) and the lid margins were trimmed and opposed with sutures after the eye was infiltrated with an antibiotic suspension (penicillin or aureomycin) and a local ophthalmic anaesthetic (amethocaine). In experiments involving lid-suture of more than 1 week duration, the conjunctiva was dissected from the eyelids and sutured under the closed lids to provide insurance against any extraneous visual experience that might result from a 'window' opening of the lids. In the few cases where windows did appear, they were resutured immediately.

Eyelid suture prevents patterned optical stimulation of the retina, and reduces the mean level of retinal illumination by between 4 and 5 log units (Wiesel & Hubel, 1963*a*).

In experiments involving reversal of lid suture, the lids of the sutured eye were parted under halothane anaesthesia and those of the other eye sutured together. Particular care was taken to prevent the development of infections of the lid margins of the initially deprived eye, which was infiltrated daily with both penicillin and cortisone ointment until the lid margins had healed.

Surgical preparation and maintenance

These procedures were similar to those that have been detailed elsewhere (Blakemore & Van Sluyters, 1975). On the day of recording, the kitten was taken from the colony and its sutured eyelids opened under halothane anaesthesia. When it was fully awake the kitten was photographed and tested behaviourally using methods described in the following paper (Movshon, 1976). During this procedure the kitten received no more than 5 or 10 min of binocular visual experience.

After premedication with atropine (10 $\mu g.kg^{-1}$, I.P.), anaesthesia was induced again with halothane and the radial vein was cannulated; the animal was then transferred to I.V. anaesthetic, either barbiturate (Brietal, Lilly) or steroid (Althesin, Glaxo), infused as needed during surgery. Needles were inserted into one forelimb and one hind limb for e.c.g. recording, the trachea was cannulated and, in most experiments, the cervical sympathetic trunks were divided bilaterally to minimize eye movement. The animal was placed in a conventional stereotaxic headholder using miniature ear bars, and the skull was exposed and reinforced with a cap of dental acrylic. A small craniotomy and durotomy were made over the central projection area of area 17, at Horsley-Clarke co-ordinates P3–5, L1–2, and screws inserted for e.e.g. recording.

For recording, I.V. anaesthesia was discontinued and the animal paralysed with gallamine triethiodide (Flaxedil, May and Baker: 5–10 $mg.kg^{-1}$); the animal was artificially ventilated with a mixture of 75–80% N_2O/19–23% O_2/1–2% CO_2 (Blakemore, Donaghy, Maffei, Movshon, Rose & Van Sluyters, 1974) at a rate and

stroke volume selected from the formula provided by Cleland & Levick (1974). This normally served to maintain the kitten's peak expiratory P_{CO_2}, measured through a narrow-gauge tube placed in the trachea and led to a Beckman LB-1 or LB-2 I.R. gas analyser, at between 5·0 and 5·5%; deviations from this range were compensated by varying stroke volume or the CO_2 concentration in the inspired gas mixture. Paralysis was maintained by continuous infusion of Flaxedil (10 mg.kg^{-1}.hr^{-1}) in 6% glucose in Ringer solution (2 ml.hr^{-1}). E.e.g. and e.c.g. were monitored continuously, and oral temperature was maintained at 37° C with a thermostatically controlled heating blanket.

Recording

Single units and multiple-unit background activity were recorded with tungsten-in-glass micro-electrodes of the type described by Levick (1972), with an exposed tip between 15 and 30 μm in length. They were mounted in a hydraulic microdrive of conventional design, and driven into the cortex through a sealed chamber over the small craniotomy and durotomy. The display and amplification of unit activity were conventional, and no quantitative methods of analysis were normally employed – the responses of the units were simply judged by listening to their activity relayed over an audiomonitor.

In searching for units, the electrode was slowly advanced while a board displaying a number of contours of varying length, width and orientation was moved in front of the animal in a continuously varying pattern of direction and velocity. Using this technique in adult cats it is extremely rare to injure a unit which has not previously been activated by the search stimulus.

Optics

The optical quality of the cat eye is excellent and reaches adult levels between the sixth and twelfth weeks of life, but before then it is less good, largely due to persistent clouding of the lens. Ophthalmoscopic inspection of the fundus is possible after the age of 3 weeks, and it was not difficult to visualize the fundus, locate retinal landmarks and obtain an estimate of the refractive state of the eye even in the youngest kitten in this series, which was 29 days old at the time of recording.

The corneae were protected with clear contact lenses of zero power, pupils dilated with topical homatropine sulphate, and the eyelids and nictitating membranes retracted with phenylephrine hydrochloride. The refractive state of the eyes was assessed by direct ophthalmoscopy, and supplementary spectacle lenses were placed in front of the eyes to focus them on a tangent screen 57 cm away. Artificial pupils of 3 or 5 mm diameter were routinely used to reduce light scatter and increase depth of focus (Enroth-Cugell & Robson, 1974). Young kittens normally appeared hypermetropic during refractive examination, by as much as 6 D; older animals tended to be nearly emmetropic.

The projections of the *areae centrales* and, sometimes, the optic disks were plotted with a reversible ophthalmoscope, and usually rechecked once or twice during the course of an experiment, which lasted between 12 and 30 hr. Most receptive fields were within 10° of the *area centralis*, and all of them were within 19°.

Visual stimulation

Visual stimuli were back-projected on to a tangent screen by manipulation of patterns placed in the object plane of an overhead projector; these commonly consisted of bright or dark bars, edges and spots, and occasionally more complex patterns were devised. Stimuli could be moved over the visual field or flashed on and off

by the experimenter. The luminance of the bright part of a stimulus was commonly between 2 and 20 cd.m^{-2}; the dim part ranged in luminance between 1 and 2 cd.m^{-2}. The luminance difference was normally kept below 0·5 log units, except for particularly refractory or insensitive units.

A clear Perspex sheet in the beam of the overhead projector cast an image of the stimulus down on to a plotting sheet for marking of the receptive fields on metric squared paper for permanent records.

Receptive field plotting

When a unit had been satisfactorily isolated, each eye was occluded in turn and the visual field systematically searched with moving and flashing stimuli. The receptive fields were mapped and classified into one of the following groups.

(1) Orientation selective: simple, complex or hypercomplex.
(2) Direction selective.
(3) Orientation bias.
(4) Non-oriented.
(5) Inhibitory.
(6) Visually unresponsive.

Orientation selective cells were classified by the criteria of Hubel & Wiesel (1962, 1968).

Simple cells have receptive fields which can be subdivided into spatially separated excitatory and inhibitory regions by their response to flashed stimuli. It is not always possible to obtain off-responses from inhibitory regions, but their presence can often be demonstrated by their attenuation of responses obtained from excitatory regions. It is possible to demonstrate spatial summation within and antagonism between these receptive field regions. Three patterns of receptive field organization are common in this group of cells: *on-centre* – a central excitatory region flanked by two inhibitory areas; *off-centre* – the converse of on-centre; and *edge-detector* – an excitatory and an inhibitory region of approximately equal strength side-by-side. This classification is to some extent arbitrary, since there is probably a continuous gradation from on-centre fields, through fields with one strong and one weak flank to edge-detectors, and then again to off-centre fields (J. A. Movshon & D. J. Tolhurst, in preparation).

Complex cells have, on average, rather larger receptive fields than simple cells. Their receptive fields cannot normally be subdivided into separate regions in the same way as simple cells; if they respond to flashed stimuli, they give the same kind of response, normally an on–off discharge, anywhere within the field. Complex cells tend to be selective for stimuli smaller than their receptive fields, and exhibit complicated summation and antagonism between stimuli presented within apparently homogeneous regions (J. A. Movshon & D. J. Tolhurst, 1975 and in preparation).

Hypercomplex cells resemble simple and complex cells except that they appear to have inhibitory regions at one or both ends of their receptive fields which give them selectivity for the length of stimuli. Dreher (1972) suggested that they can be subdivided into two groups according to their resemblance to either simple or complex cells, and this classification was used in this study, although it is not always possible to apply unambiguously.

Direction selective cells resemble the on–off direction selective ganglion cells of the rabbit retina (Barlow, Hill & Levick, 1964), and respond with equal vigour to almost any stimulus moving in the appropriate direction. These cells are most common in the deeper layers, and some of them may be the corticocollicular units described by Palmer & Rosenquist (1974).

Orientation bias cells are a class devised by Blakemore & Van Sluyters (1974) to

describe the rather poor orientation selectivity and responsiveness of some neurones in kitten cortex; they are rare or absent in the adult. These neurones exhibit a definite preference for stimuli of one orientation, but unlike the orientation selective neurones described above, give some response to stimuli oriented orthogonal to the preferred axis. A very few examples of the normal orientation selective types occasionally respond weakly to orthogonally oriented stimuli, and I normally classified these cells as simple or complex, reserving the orientation bias category for those rather unspecific and unresponsive neurones common in the cortex of visually inexperienced kittens.

Non-oriented units which are not afferent geniculate fibres are probably rare in the cortex of adult cats, but are not uncommon in young or visually deprived kittens. Afferent geniculate fibres may be distinguished from these cells by several characteristics: (1) brief monophasic or diphasic action potentials, (2) clear concentric receptive field organization, (3) brisk responsiveness and (4) monocular drive. Cortical non-oriented units are commonly binocularly activated, often have receptive fields without clear concentric organization, and may sometimes give prolonged injury discharges to contact with the electrode. They are usually rather unresponsive, and not easily mistaken for geniculate afferents.

Inhibitory units are very rare, in either adult or kitten cortex. They have rather high resting discharge rates, and their discharge can only be reduced by visual stimulation. They resemble in general character the 'uniformity detectors' of the rabbit retina (Levick, 1967).

Visually unresponsive units may only be unambiguously classified if they signal their presence by spontaneous activity, and if the visual field is systematically and carefully searched with a variety of visual stimuli. In the cortex of deprived kittens it is not, however, uncommon to injure a previously undetected unit when searching slowly and carefully through the cortex. In view of their absence in normal cats and kittens, I have classified such units as visually unresponsive, despite the fact that some of them may merely have been poorly responsive or very stimulus selective.

The following information was normally noted for each visually responsive unit.

(1) Receptive field type in each eye.

(2) Location and size of each minimum response field (Barlow *et al.* 1967).

(3) Ocular dominance, according to the classification scheme of Hubel & Wiesel (1962).

(4) Frequency of maintained activity.

(5) Preferred orientation and/or direction of movement.

(6) Degree of direction preference.

(7) Orientation or direction selectivity. The directions or orientations either side of the best which gave liminal responses were noted. For orientation bias units, the worst orientation was recorded.

Correction for eye rotation

The eyes of a paralysed cat or kitten are often rotated inwards, approximately about the visual axes. As a result, the orientations plotted for the two receptive fields of a binocular unit must be corrected for this torsion before any estimates of the real differences between their preferred orientations can be made. The method of Blakemore, Fiorentini & Maffei (1972) was used to assess this torsion.

After the behavioural testing was completed, a photograph was taken of the kitten's eyes and the orientation of the slit pupils measured. This can be a difficult operation to perform on young kittens, particularly if they have had sutured eyelids,

and topical applications of phenylephrine and pilocarpine were often helpful in opening the eyes wide and constricting the pupils. A second photograph was taken of the kitten after paralysis, but before the application of topical atropine, and the orientations of the pupils on the two photographs compared.

This technique is probably no more accurate than 5°, so measured torsions of less than 5° were neglected; if the torsion was more than 5°, the orientations of the receptive fields were corrected for this during analysis. The average value for this torsion was about 10° *in* (i.e. the animal's eyes rotated so as to bring the superior tips of the pupils medial), and ranged from 7° *out* to 22° *in*. About two fifths of the kittens showed torsions of less than 5°, and therefore did not require correction.

Reconstruction of electrode penetrations

At the end of a micro-electrode penetration, between two and five electrolytic lesions were made at points along the electrode track by passing DC current through the electrode tip (5–10 μA for 5–10 sec, tip negative).

At the end of the experiment, the animal was anaesthetized with Nembutal (50–100 mg.kg^{-1}) and perfused through the heart with 10% formalin in buffered Ringer solution. The skull was removed, the point of entry of the electrode marked with ink and the brain photographed.

A block of brain containing the electrode track was cut with its anterior surface roughly parallel to the plane of penetration, and frozen sections were cut at 40 μm and stained with cresyl violet. The electrolytic lesions were identified by the gliosis they showed, and their positions marked on an outline tracing of a section from the middle of the penetration made using a projection microscope.

Most penetrations were confirmed to lie mostly or wholly within area 17 as outlined by Reinoso-Suarez (1961), and Otsuka & Hassler (1962); in five cases, histological confirmation was not obtained, but the site of entry of the penetration and the steady drift of receptive fields into the contralateral visual field indicated that they, too, lay mostly or completely within area 17.

RESULTS

Experimental design

Physiological recordings were obtained from 858 single units in the visual cortex of twenty-seven kittens reared in the manner described below. A further 242 units from eleven adult cats and older, normal kittens were used as a control sample.

Two kittens had the eyelids of their right eyes sutured shut near the time of natural eye opening, and were recorded as controls at the ages of 28 and 35 days. A third kitten was monocularly deprived for the 2 weeks immediately preceding recording at the age of 6 weeks. The ocular dominance histograms obtained from these three kittens are illustrated in Fig. 1, and show that the initial period of monocular deprivation used in these experiments was sufficient to disconnect physiologically all but a handful of neurones from the geniculate input from the deprived eye.

In twenty-two experimental kittens, the right eye was closed from the time of natural eye-opening to the age of 4, 5, 6 or 7 weeks, at which point it was opened and the left eye closed for a further period of between

3 and 63 days. Recordings were taken from the right hemisphere, ipsilateral to the initially deprived eye. Two kittens reared differently will be discussed in a subsequent section.

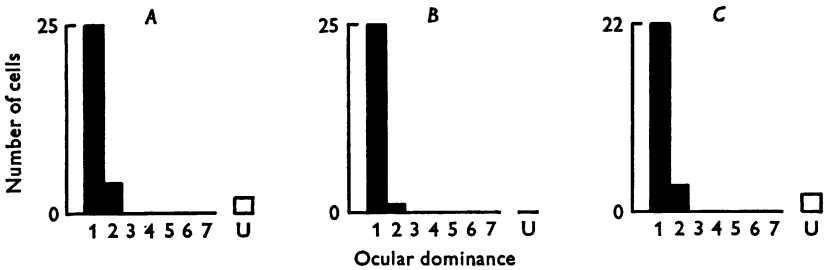

Fig. 1. Ocular dominance histograms obtained from the right hemispheres of three kittens deprived of vision in the right eye. *A*, deprived between the ages of 8 and 28 days. *B*, deprived between the ages of 7 and 35 days. *C*, deprived between the ages of 29 and 42 days. The ocular dominance classification is that of Hubel & Wiesel (1962). Group 1: cells that can only be driven from the contralateral eye. Group 2: cells that can be driven much more effectively from the contralateral eye than from the ipsilateral eye. Group 3: cells that can be driven slightly more effectively from the contralateral eye than from the ipsilateral eye. Group 4: cells that can be driven equally effectively from either eye. Group 5: cells that can be driven slightly more effectively from the ipsilateral eye than from the contralateral eye. Group 6: cells that can be driven much more effectively from the ipsilateral eye than from the contralateral eye. Group 7: cells that can only be driven from the ipsilateral eye. Cells in the column labelled U were unresponsive to visual stimuli.

A number of inferences will be drawn in the following pages about the constitution of neural populations, based on the properties of between 18 and 45 units recorded in single electrode penetrations between 1·8 and 6 mm in length. Since neighbouring cells in the cortex tend to be similar in ocular dominance and orientation preference, the extent to which the recorded sample truly represents the population must be considered (Hubel & Wiesel, 1962, 1963*a*, 1965). Furthermore, since neurones in the cortex of reverse-sutured kittens are often segregated into clear eye dominance columns, the problem may be severe. In the course of these experiments, several steps were taken to minimize the bias of the recorded sample.

(1) All penetrations were angled medially down the medial bank of the post-lateral gyrus, after starting, usually, on its crest; the electrode therefore travelled obliquely across the cortex after the first 0·5–1 mm. Since it is rare to record units closer than 200 μm to the cortical surface, and since I often did not isolate units until the electrode was between 300 and 700 μm below the surface (due either to persistent deep anaesthesia or, occasionally, to cortical trauma during the preparation), most of my recordings were obtained from penetrations that proceeded at an angle of more than 45° to the radial fascicles in the cortex.

(2) In animals with mixed eye dominance, and obvious eye dominance columns, I attempted to sample units equally from a number of these columns by terminating the experiment shortly after entering a cortical column dominated by the eye that dominated the first units encountered in the penetration.

(3) In animals with strongly skewed ocular dominance distributions, I normally attempted to seek out the small regions dominated by the weaker eye by terminating the electrode penetration with a series of deliberate advances of 250 or 500 μm in order to examine a wider area of cortex.

Residual sampling error must remain, and it is possible that some of the ocular dominance distributions presented in the following pages do not satisfactorily represent the underlying distributions. The over-all trends in the data are, however, clear, and major errors are likely to be rare.

The rate of reversal of deprivation effects

The rate at which the initially deprived eye came to dominate the cortex after reverse-suturing was examined in four series of animals, reverse-sutured at the ages of 4, 5, 6 and 7 weeks.

The left-hand column of Fig. 2 shows the ocular dominance distributions obtained from four animals reverse-sutured at the age of 4 weeks, at which time their ocular dominance distributions presumably resembled that of the control animal shown in Fig. 1*A* – virtually all cells could be driven only through the left eye. The animals were forced to use their initially deprived eyes for the periods indicated above each histogram. Within 3 days, the initially deprived eye had come to dominate more than half the cortical neurones sampled, and in the kitten recorded after 6 days of vision through the deprived eye, that eye dominated all but two of the neurones recorded. The ocular dominance distribution of the animal reverse-sutured for 12 days was indistinguishable from that of an animal monocularly deprived in the contralateral eye – only two neurones could be influenced at all from the eye that had been open for the first 4 weeks.

The second column of Fig. 2 shows similar histograms obtained from six kittens monocularly deprived until the age of 5 weeks. The rate at which the cortex was physiologically reinnervated by the initially deprived eye of these kittens was clearly slower than it had been in the kittens reverse-sutured at the age of 4 weeks. Nevertheless, after only 3 days of reversed deprivation, more than half the neurones sampled could be influenced from the initially deprived eye, and between 6 and 9 days after reverse-suturing, a roughly equal proportion of cells was dominated by each eye. The switching of ocular dominance was virtually complete within three weeks of the beginning of the period of forced use of the initially deprived eye, and the ocular dominance distribution of the kitten that used its

Fig. 2. Ocular dominance histograms obtained from the right hemispheres of twenty-two kittens deprived of vision in the right eye for the period indicated in weeks at the top of each column of histograms, and then reverse-sutured and forced to use their initially deprived right eye for the period indicated in days over each histogram. The ocular dominance classification is described in the legend to Fig. 1.

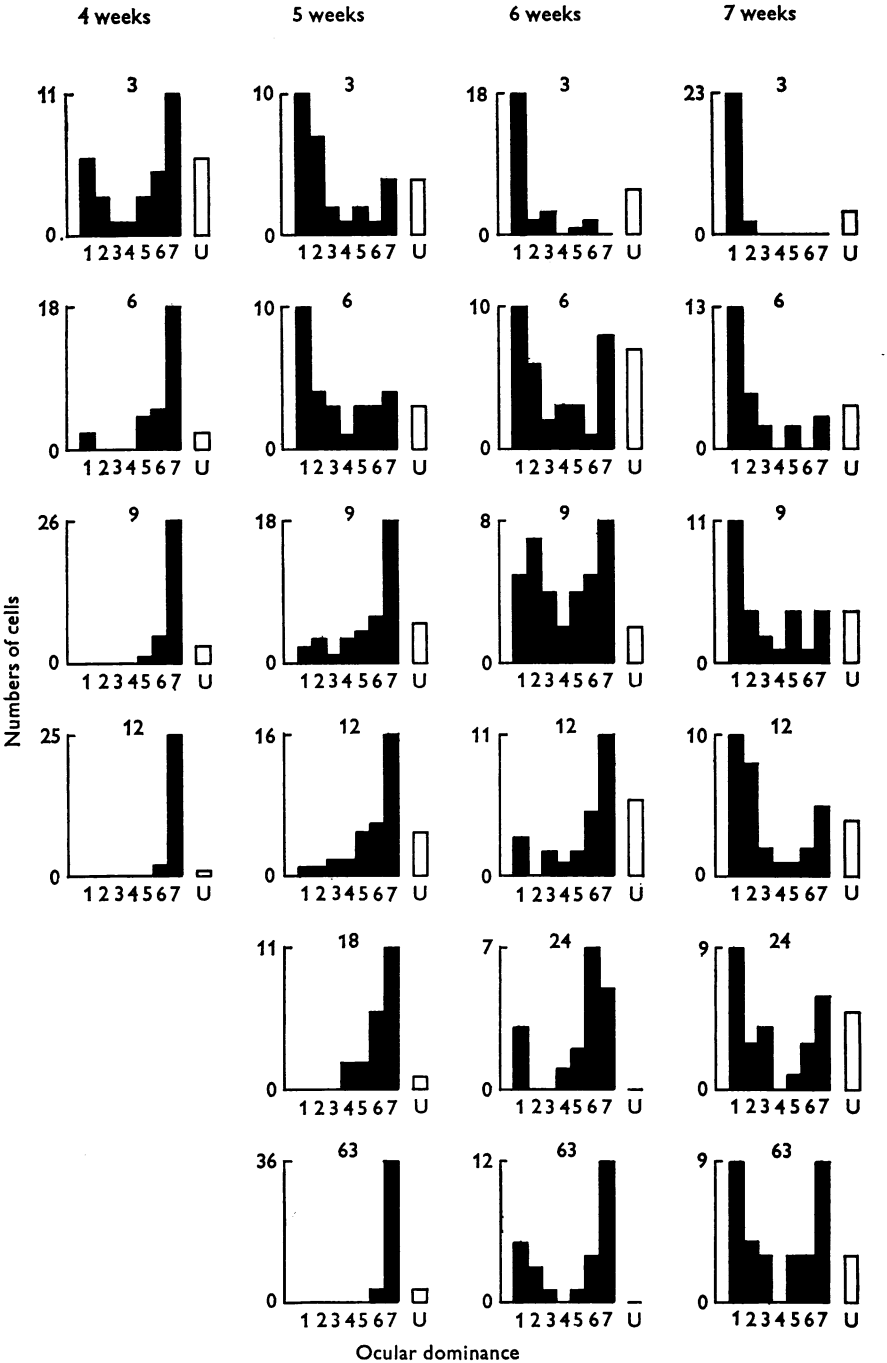

Fig. 2. For legend see facing page.

initially deprived eye for a further 9 weeks, throughout the remainder of the sensitive period, was similar to that obtained from a kitten monocularly deprived in the contralateral eye alone. The initial period of deprivation of the ipsilateral eye had no detectable residual effect on cortical organization.

The third column of histograms in Fig. 2 shows the results obtained from six kittens reverse-sutured at the age of 6 weeks. The rate at which the deprived eye gained influence in the cortex was perceptibly slower than it had been at the age of 4 or 5 weeks. After 3 days, fewer than 25 % of the neurones recorded could be influenced from the initially deprived eye. After 9 days of vision through the initially deprived eye, the process of reversal was about half-complete, but even 9 weeks of vision through that eye did not suffice completely to bias the cortical ocular dominance distribution – more than half the cells sampled could still be influenced from the second eye to be closed.

The fourth column of histograms in Fig. 2 shows similar data from six kittens initially deprived to the age of 7 weeks. The reversal of cortical dominance took place even more slowly in these animals, and reversed deprivation for 3 days had no detectable effect. After 6 days of reversed deprivation, a substantial number of cells could be influenced from the initially deprived eye. But after 9 weeks, only half the cells sampled were dominated by the second eye to be opened.

The pattern that emerges from these results is clear. Near the peak of the sensitive period (Hubel & Wiesel, 1970) it is possible to shift completely the ocular dominance of the recorded population of cortical neurones in less than 2 weeks. As the reversal of suture is delayed, the shift in cortical dominance takes place less rapidly and, then, after further delay in reverse-suturing, is not complete even after 9 weeks of reversed deprivation. At the end of the sensitive period, substantial numbers of cells remain functionally connected to the first eye to be open.

Fig. 3 shows these results graphically for the four series of animals. For each animal the reversal index (the proportion of visually responsive cortical units dominated by the initially deprived eye) is plotted against the period of reversed lid-suture that preceded the recording session.

The graph of the data from the 4-week reversal animals rises rapidly to unity; those describing data from the other series rise progressively less and less rapidly as the initial period of deprivation is lengthened. The graphs of the two last series appear to saturate at some value of reversal index less than 1.

The rate of the reversal process at different ages correlates well with the sensitive period (Hubel & Wiesel, 1970), which is derived from data describing the *extent* of the deprivation effects obtainable at different ages.

There appears to be a relationship between the absolute susceptibility of the visual system to deprivation effects at a given age, and the rate at which those effects take place.

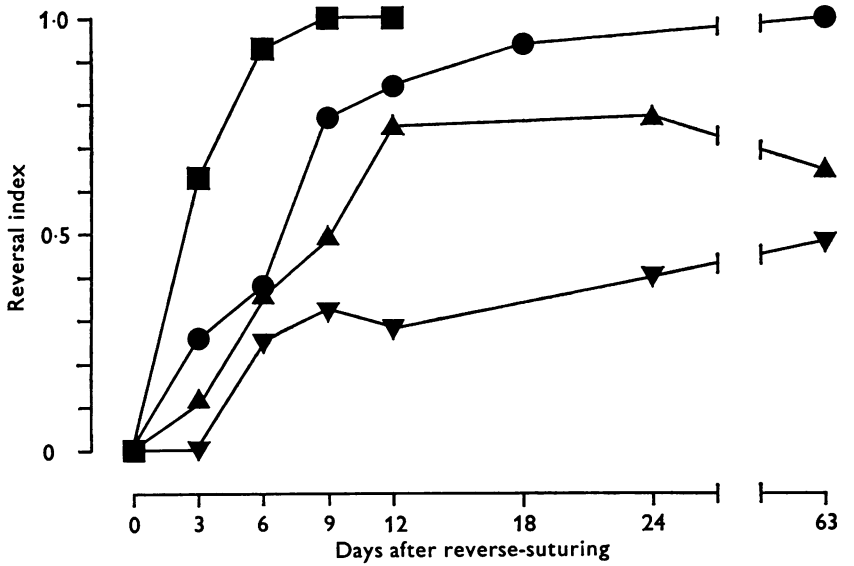

Fig. 3. The rate of reversal of the physiological effects of monocular deprivation. The reversal index (the proportion of visually responsive neurones dominated by the initially deprived, right, ipsilateral eye) is plotted against the period of time subsequent to reverse-suturing that preceded the recording session for each of the twenty-two kittens whose ocular dominance histograms are shown in Fig. 2. Kittens reverse-sutured at the age of 4 weeks: ■; at 5 weeks: ●; at 6 weeks: ▲; at 7 weeks: ▼.

Cortical functional architecture during the reversal of deprivation effects

The grouping of functionally related neurones in the cortex of a reverse-sutured kitten is very striking. Blakemore & Van Sluyters (1974) noted that, when cells dominated by both eyes were encountered in such a kitten, they tended to be grouped together in clusters – the ocular dominance columns first noted by Hubel & Wiesel (1965) in animals with reduced binocularity due to strabismus or alternate monocular occlusion.

Ocular dominance columns were apparent in most of the penetrations in these experiments in which neurones dominated by both eyes were encountered. In animals with strongly skewed ocular dominance distributions, I often encountered long reaches of penetration in which one eye dominated very markedly, interspersed with other, shorter regions where dominance was more mixed.

The cortical ocular dominance organization in three kittens, reverse-sutured at the age of 5 weeks for 3, 6 and 9 days, is illustrated in Fig. 4. All three penetrations showed a clear grouping of cells by ocular dominance, and the brackets on the right-hand side of the ocular dominance diagrams indicate the approximate extent of the columns devoted to the contralateral (C) and ipsilateral (I) eyes. The cortical representations of these

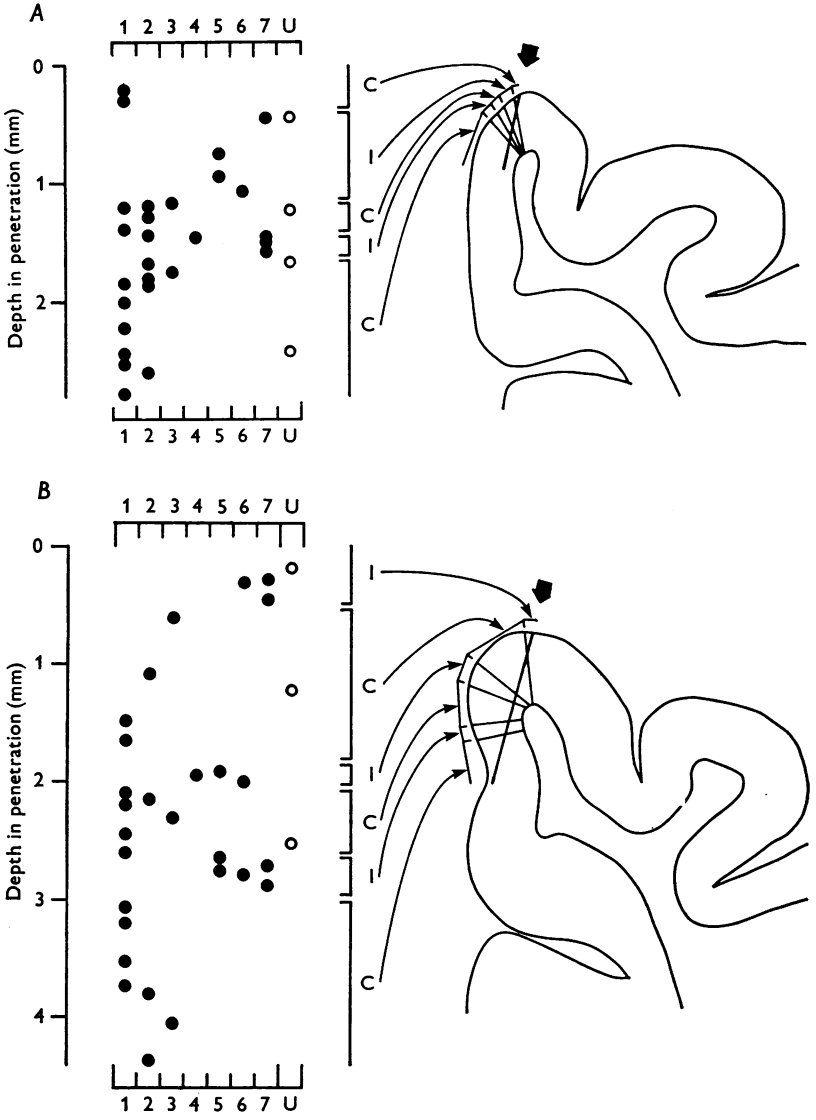

Fig. 4 *A* and *B*. For legend see facing page.

columns have been derived and drawn on to tracings of the histological sections containing the penetrations (arrows leading to the right-hand part of each Figure). The cortical extent of each column was determined by assuming that the borders of columns are parallel to the radial fascicles of the cortex.

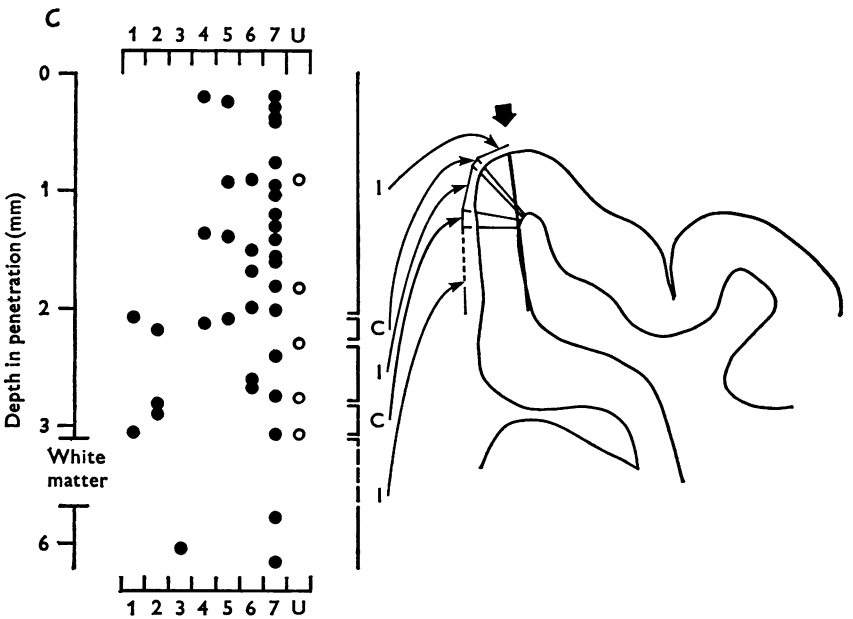

Fig. 4. Reconstructions of three electrode penetrations made in kittens reverse-sutured at the age of 5 weeks for 3, 6 and 9 days (*A*, *B* and *C*, respectively). The ocular dominance of each unit encountered is plotted against electrode depth on the left-hand side of each diagram, as are the positions of visually unresponsive neurones (open symbols, right-hand column). Regions of contralateral (C) and ipsilateral (I) eye dominance are bracketed on the right of the diagrams of ocular dominance sequence. Tracings of the coronal sections of the right hemispheres of the kittens are shown on the extreme right, and the electrode track is indicated by a heavy line and arrow. Ocular dominance columns are reconstructed on these tracings from the regions defined from the unit recordings depicted on the left, and their cortical extent indicated, based on the assumptions that their borders run parallel to the radial fascicles of the cortex from surface to white matter.

Several features are apparent from these reconstructions. Ocular dominance columns devoted to the eye that dominated the majority of cortical neurones were, on average, larger than those devoted to the less-represented eye. In the first two kittens (A and B), the contralateral eye dominated; the ipsilateral eye dominated the third kitten's cortex (C). The

first three columns whose extent was defined in the first kitten were of roughly equal extent, but the electrode then entered a long region devoted to the ipsilateral eye, which persisted to the end of the penetration. Four columns were defined in the second kitten: the two contralaterally driven ones were larger than the two ipsilaterally driven ones. Furthermore, they were flanked by a small region of ipsilateral dominance (at the beginning of the penetration) and an extensive region of contralateral dominance (at the end of the penetration). Three columns were defined in the third kitten: two small regions of contralateral dominance and one extensive region of ipsilateral dominance. This area was flanked on both sides by columns of ipsilateral dominance, interrupted on one side by 2·5 mm of white matter in which the cortical dominance was, of course, not determined.

The penetrations in the second and third kittens contained regions within large eye dominance columns in which the dominance was briefly more mixed, and both single neurones and unresolved background activity could be binocularly driven. These regions are apparent at depths of around 4 mm in the second kitten, and of 0·3, 0·9 and 1·3 mm in the third kitten. They may have been vestiges of eye dominance columns devoted to the initially dominant contralateral eye.

There was a tendency for visually unresponsive neurones (open circles in the columns labelled U) to occur near the borders of eye dominance columns. This was particularly clear in the third penetration, in which the only unresponsive neurone encountered more than 150 μm from a column border was in one of the small regions of mixed dominance. This pattern can be discerned in other penetrations; it was generally the case in these experiments that neurones were rather more difficult to activate near the borders of eye dominance columns than they were in the bodies of columns.

In twelve kittens, it was possible to define the extent of at least one eye dominance column dominated by each eye, and to define the extent of those columns on the cortical surface using the method shown in Fig. 4 to combine and relate histological and physiological data. Several factors prevented an analysis of eye dominance columns in the other kittens, including inadequate histological reconstruction, or poor definition of the border regions of columns devoted to one eye or the other. Furthermore, any column in which the penetration began or ended, or near which the electrode entered or left white matter, could not be delimited in one direction. The sizes of thirty-one satisfactorily determined columns from twelve kittens are listed in Table 1.

The results are clear. The animals with a low reversal index, whose cortices were dominated by the initially open left eye, columns devoted to the left eye were larger; animals with reversal indices near 0·5 had columns of roughly equal size in the two eyes, and animals with higher

reversal indices had larger columns devoted to the right eye than to the left. There was a clear correlation between the ratio of the mean column-sizes of each eye, with the right eye as the numerator, and the reversal index of each kitten ($r = 0{\cdot}84$, $n = 12$, $P < 0{\cdot}001$). There was some variation in the size of one column cycle (the sum of left and right eye columns), which may reflect variation in the angle at which the electrode penetration intersected the columns. The most common column cycle was about 1 mm, which corresponds closely to previous estimates of the extent of one column cycle in monkey striate cortex (Hubel & Wiesel, 1972; LeVay, Hubel & Wiesel, 1975).

TABLE 1. Reconstructed column sizes in reverse-sutured kittens. The extent of each defined ocular dominance column is given in millimetres projected to the cortical surface in twelve kittens. The animals are arranged in order of increasing reversal index, their rearing conditions are indicated in the left-hand column as: age (weeks) at reverse-suturing + days of reversed suture. The left eye was the contralateral, initially experienced eye in all cases

		Column sizes	
Animal	Reversal index	Left eye	Right eye
7+6	0·25	1·6	0·3
5+3	0·26	0·4	0·5, 0·5
7+9	0·32	1·2	0·6
6+6	0·36	0·5	0·5
5+6	0·38	1·4, 0·9	0·5
7+24	0·40	0·9	0·6
7+63	0·48	0·6, 0·4	0·5
6+9	0·49	0·4	0·4
4+3	0·63	0·1, 0·4	0·5
6+63	0·65	0·7, 0·3	0·7
6+12	0·75	0·2, 0·3	0·7
5+9	0·77	0·3, 0·6	1·4

This systematic change in the size of ocular dominance columns during reversal of deprivation seems to reflect complementary shrinkage and expansion of columns devoted to the first and second eye to be opened. After brief periods of reversed lid-suture, small islands of cells dominated by the newly open eye appear and, during the course of the shift in cortical ocular dominance, they gradually expand at the expense of neighbouring columns driven by the initially open eye, until they come to occupy the whole cortex. That this expansion represents a reorganization as well as a reappearance of the residual input from the initially deprived eye is strongly suggested by the pattern of the orientation columns observed in these kittens.

Hubel & Wiesel (1963*a*, 1974) presented evidence that the orientation columns of the cat's striate cortex are systematically organized, although

not so clearly as they are in the monkey (Hubel & Wiesel, 1974). It is not uncommon to encounter regular sequences of preferred orientation in oblique penetrations, and there is a strong tendency for nearby units to have similar orientation preferences. This organization was apparent in the striate cortex of kittens undergoing reversal of deprivation effects.

The overlapping systems of eye dominance and orientation columns in the cortex of normal cats and monkeys appear to be independent of each other (Hubel & Wiesel, 1965, 1974). The upper histograms in Fig. 5 illustrate an analysis of the changes in preferred orientation between successively recorded units in normal cats. Small changes predominate. Furthermore, changes in ocular dominance of four or more groups (which must shift from dominance by one eye to dominance by the other, and will tend to be the borders of eye dominance columns; Fig. 5*B*) are not accompanied by changes in preferred orientation any larger than those accompanying small changes in ocular dominance (Fig. 5*A*). The two distributions do not differ in their variance ($F = 1{\cdot}05$, d.f. = 186, 12, $P > 0{\cdot}05$). The system and sequence in the representation of orientation across the cortex is thus not affected by the borders of eye dominance columns.

In animals with experimentally reduced binocularity due to an artificial strabismus, eye dominance columns are more exaggerated, but remain independent of orientation columns (Hubel & Wiesel, 1965: Figs. 1, 2 and 3). Orientation thus appears to be coded across the cortex without regard to the eye from which the visual information arrives. In reverse-sutured kittens, binocular interaction is much reduced and eye dominance columns are also rather exaggerated. These columns might be expected to show the same indifference to orientation columns that is found in normal and strabismic animals; each eye might take over the appropriate orientation sequence from the other near the borders of eye dominance columns.

This is not the case. The lower histograms in Fig. 5 (*C* and *D*) present an analysis similar to that in Fig. 5*A* and *B* for 580 unit-pairs recorded from reverse-sutured kittens. In these animals, nearby units that were similar in ocular dominance tended, like all unit-pairs in normal cats, to have similar orientation preferences. When nearby units differed substantially in eye dominance, this was less clearly the case; large changes in preferred orientation were much more common. The variance of these two distributions is significantly different ($F = 1{\cdot}84$, d.f. = 42, 536, $P < 0{\cdot}01$). In reverse-sutured kittens, the cortical representation of orientation is disrupted at the borders of eye dominance columns.

The lower histogram in Fig. 5*D* is not flat; there was *some* tendency for neighbouring units to have similar preferences. One half of the changes

in preferred orientation were smaller than 37° when they were accompanied by large dominance changes. But 50 % of the changes *not* accompanied by large shifts in ocular dominance were smaller than 18°.

In the course of these experiments, it was often my impression that, when preferred orientations could be established for both eyes (either from binocularly driven single units, from nearby units of opposite eye preference, or from unresolved background activity), the orientations in the two eyes were often very different. The properties of binocularly activated single units will be discussed below, but evidence for the relative

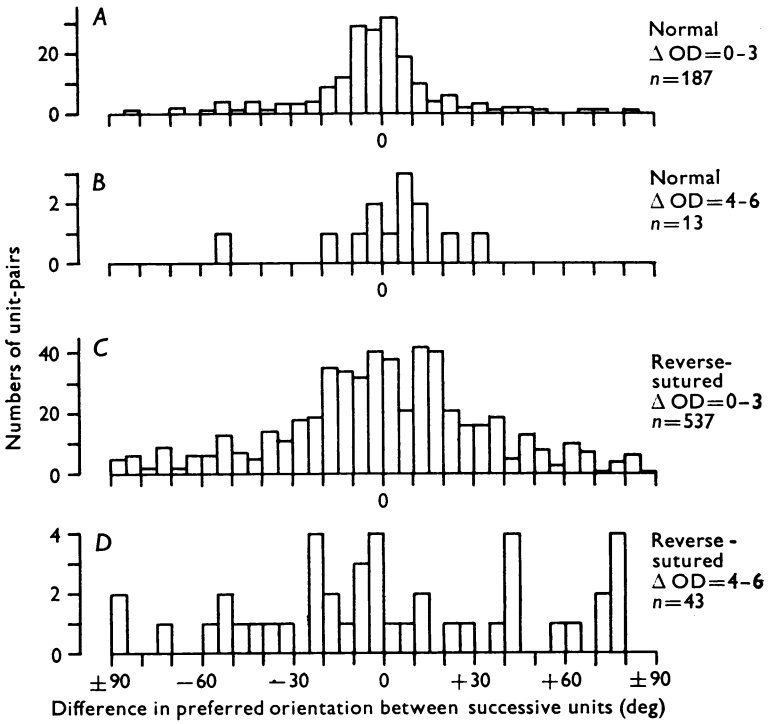

Fig. 5. Histograms showing the distributions of differences in preferred orientation between successively recorded units in normal cats (*A* and *B*) and in reverse-sutured kittens (*C* and *D*). The data were derived from unit pairs recorded less than 200 μm apart in the cortex. Histograms *A* and *C* show the distributions of differences obtained from unit pairs whose ocular dominance (OD) did not differ by more than three groups, and were therefore presumed to be in the same ocular dominance column. Histograms *B* and *D* were obtained from unit pairs whose ocular dominance differed by four groups or more, and were thus presumed in many cases to cross the borders of ocular dominance columns. Differences of positive sign represent clockwise shifts in orientation; differences of negative sign represent anticlockwise shifts.

independence of orientation coding in the two eyes is presented here, using the graphical technique introduced by Hubel & Wiesel (1974).

Fig. 6 plots the preferred orientations of each receptive field encountered

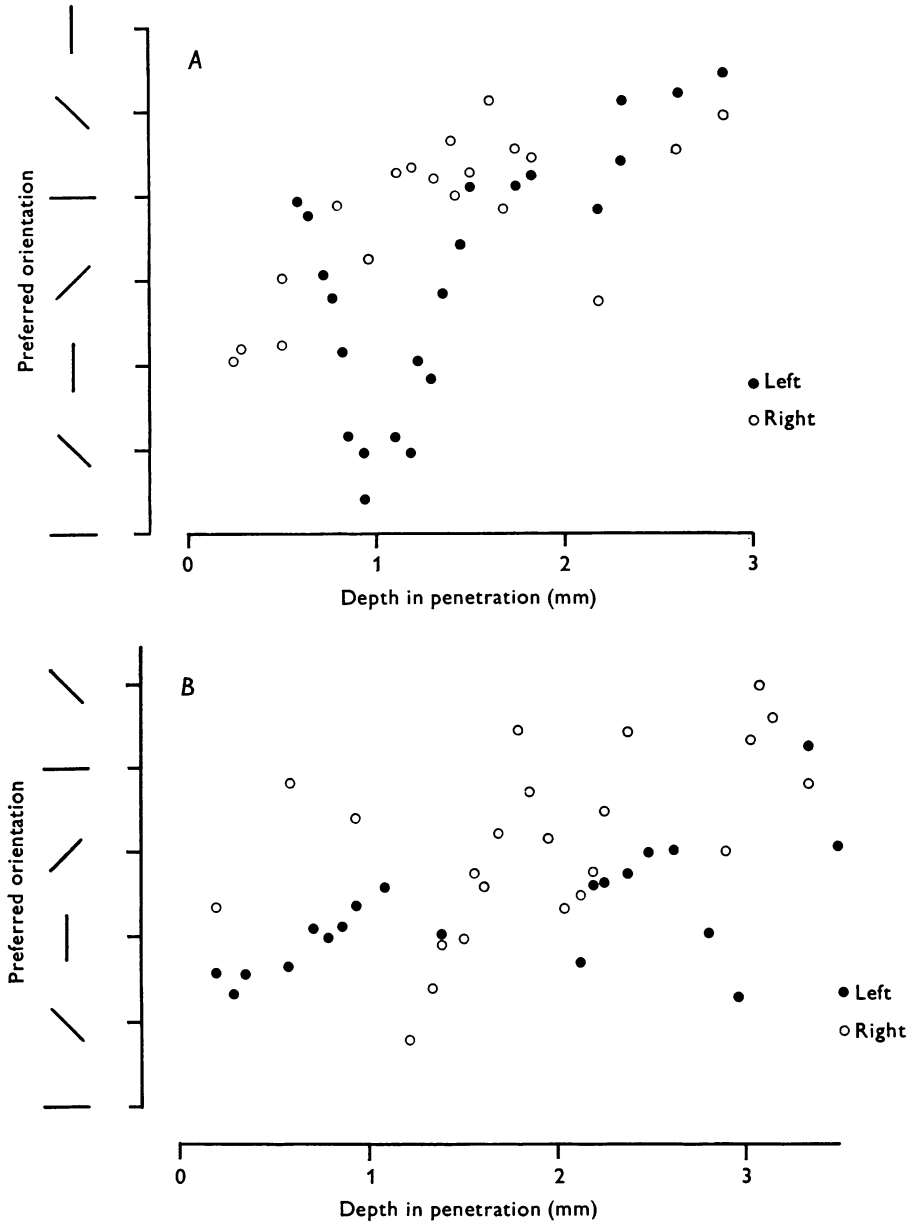

Fig. 6*A* and *B*. For legend see facing page.

in the left and right eyes during three cortical penetrations in reverse-sutured kittens. Fig. 6*A* presents data obtained from a kitten reverse-sutured for 6 days at the age of 6 weeks. Progressions of receptive field orientations in both eyes were apparent. The sequences were clearly different in the two eyes, at least for the first 1·5 mm of the electrode penetration. While the orientation sequence in the left eye exhibited two long progressions, first in an anticlockwise and then in a clockwise direction, that for the right eye showed a gradual continuous clockwise drift with much shallower slope.

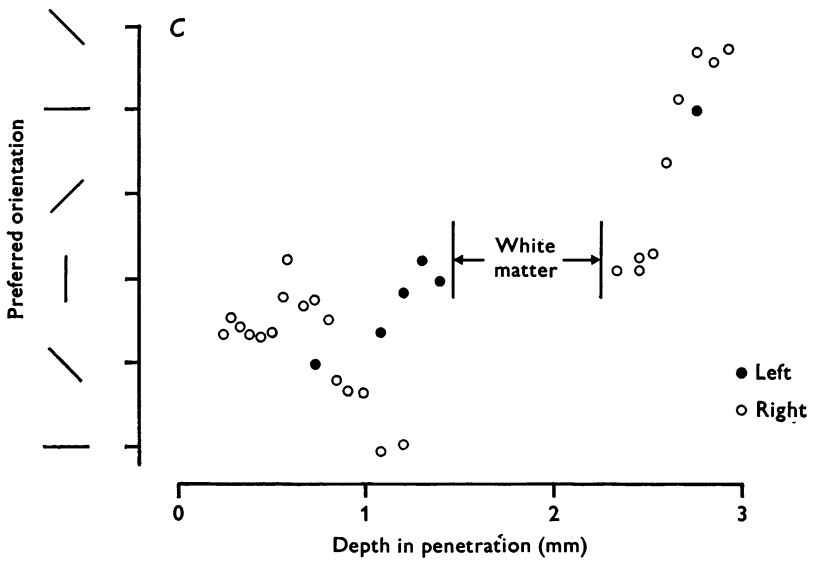

Fig. 6. Diagrams of the sequences of preferred orientation encountered during micro-electrode penetrations through the visual cortex of three reverse-sutured kittens. The preferred orientations for the two eyes are shown separately, filled circles for the initially experienced left eye; open circles for the initially deprived right eye. Kitten A was reverse-sutured for 6 days at the age of 6 weeks. Kitten B was reverse-sutured for 9 days at the age of 6 weeks. Kitten C was reverse-sutured for 6 days at the age of 4 weeks.

Fig. 6*B* illustrates the electrode penetration made in the kitten reverse-sutured for 9 days at the age of 6 weeks. The pattern of ocular dominance columns in this experiment was particularly striking, and there were long stretches of the penetration in which one eye possessed many more orientation selective receptive fields than the other. During the initial and final stages of the penetration, the left eye was dominant, and a gradual clockwise drift of orientation was apparent. The central section of the penetration, dominated by the right eye, exhibited a completely different

pattern of orientation change, with a considerably steeper slope. Furthermore, at depths near 2 mm, where eye dominance was rather mixed, the left and right eye systems were both present, and clearly independent of each other.

Fig. 6*C* illustrates the penetration from the kitten reverse-sutured for 6 days at the age of 4 weeks. The right eye dominated the cortex, and had developed a clear spatial organization in its coding of orientation. The vestigial orientation columns of the left eye showed a different pattern of organization. It should be noted that these three electrode penetrations were among the clearest examples of independent orientation sequences that were encountered. In a number of other kittens, the sequence of orientation columns in one eye or both was more haphazard, and the two eyes did not seem entirely unrelated in the spatial arrangement of their orientation coding. Indeed the fact that, overall, the orientation preferences in the two eyes of the experimental kittens were not entirely uncorrelated (see below and Fig. 5*D*) suggests that there cannot be *complete* independence of the two eyes' orientation columns in reverse-sutured kittens.

Fig. 7 illustrates a similar penetration diagram compiled from data obtained from a kitten reared with a divergent strabismus and recorded at the age of 8 weeks by R. C. Van Sluyters and C. Blakemore, who kindly provided the data. There was a clear sequence of orientation in this penetration and, despite obvious eye dominance columns and greatly reduced binocularity, the orientation columns for the two eyes were identical. Experimental reduction of binocular interaction does not necessarily disrupt the orientation column structure of the cortex. Reinnervation during the process of monocular deprivation clearly does.

Neuronal properties during the reversal of deprivation effects

In view of the unusual cortical functional architecture described above, it is not surprising that a substantial proportion of the neurones encountered in the cortices of these animals had unusual properties. The most striking abnormality was that noted by Blakemore & Van Sluyters (1974): a marked dissimilarity between the two receptive fields of binocularly activated neurones.

An interocular comparison of the receptive field properties of 254 binocular neurones is presented in Table 2. Inspection of the data reveals that 121 of these cells (48 %) had different types of receptive field in the two eyes. Of the 133 cells with similar receptive fields in the two eyes, sixteen (6 % of the total) had non-specific receptive fields (non-oriented or orientation bias). Only 117 neurones (46 %) had orientation or direction selective receptive fields in both eyes.

Fig. 8 illustrates an example of one of the most common of these

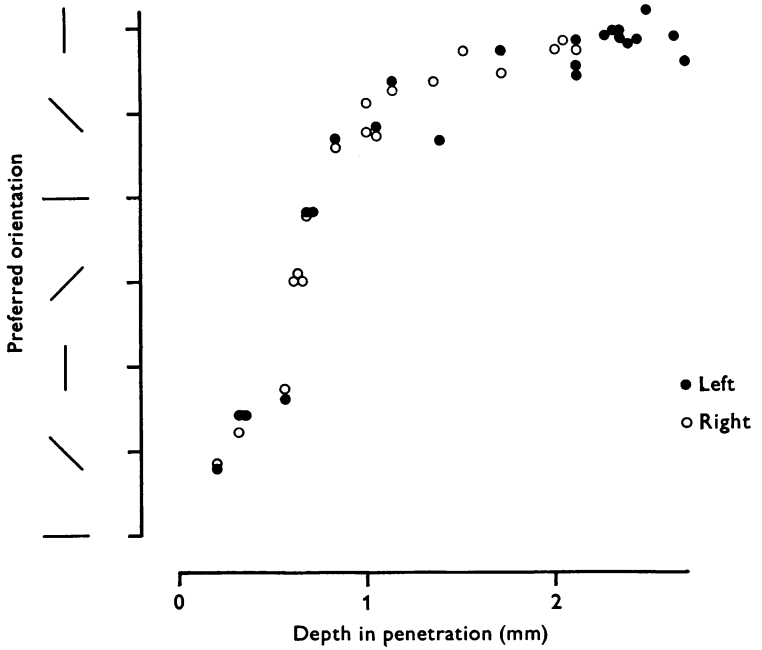

Fig. 7. A diagram similar to those shown in Fig. 6 showing the sequences of preferred orientations in the two eyes of a kitten given a divergent strabismus at the age of 13 days and recorded at the age of 8 weeks (unpublished results of R. C. Van Sluyters and C. Blakemore).

TABLE 2. An interocular comparison of the receptive field properties of 254 binocular neurones recorded from 23 kittens reverse-sutured at various ages for various periods of time. The bottom row of the table gives the percentages of the cells in each column that possessed non-specified (orientation bias or non-oriented) receptive fields in the non-dominant eye

	Receptive field in dominant eye						
	Simple	Complex	Hyper-complex	Direction selective	Orientation bias	Non-oriented	Total
Receptive field in non-dominant eye							
Simple	20	—	—	—	—	—	20 (8%)
Complex	—	81	—	—	—	—	81 (32%)
Hypercomplex	—	—	4	—	—	—	4 (2%)
Direction selective	—	—	—	12	—	—	12 (5%)
Orientation bias	6	16	—	—	1	—	23 (9%)
Non-oriented	32	50	4	1	12	15	114 (45%)
Total	58 (23%)	147 (58%)	8 (3%)	13 (5%)	13 (5%)	15 (6%)	254 (100%)
Unspecified field in non-dominant eye (%)	66	45	50	8	100	100	54

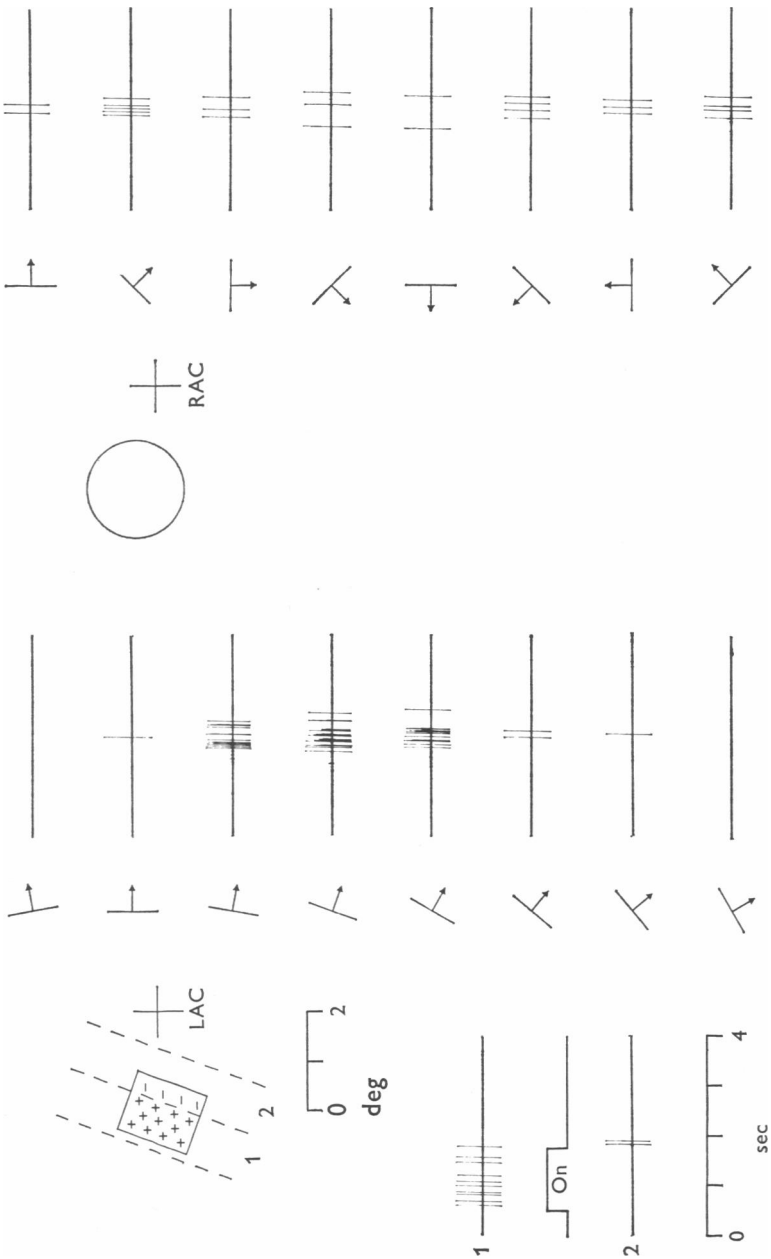

Fig. 8. For legend see facing page.

binocular cell types: a cell with an orientation selective receptive field in the dominant eye and a non-oriented receptive field in the weaker eye. The left-hand part of the Figure shows the responses of this neurone to stimulation of the left eye; note the precise orientation tuning and responses to flashed stimuli typical of a cortical simple cell. The right-hand part of the Figure shows the rather weak and unselective responses given to stimulation of the right eye: similar responses were evoked by stimuli of all orientations, and no responses to flashed stimuli could be obtained.

Even the 117 cells with orientation selective receptive fields in both eyes were often unusual in one important respect, exemplified by the neurone whose responses are illustrated in Fig. 9. This cell, a complex cell recorded from a kitten reverse-sutured for 9 days at the age of 7 weeks, had normal orientation selective receptive fields in both eyes (Fig. 9*A*), and was unusual in that it was in ocular dominance group 4, being equally responsive to stimulation of either eye. The preferred orientations of the two receptive fields, however, differed by over 70°. The receptive field in the left eye (upper panel) had a preference for stimuli tilted approximately 72° clockwise from vertical, while that of the right eye preferred stimuli that were nearly vertical in orientation. This cell also showed a preference for small spots moved along an axis of the receptive field orthogonal to the preferred orientation, although this preference was less precise than that for line orientation. The responses of both receptive fields to moving spots are shown in Fig. 9*B*. The receptive field in the left eye preferred movement in a downward and rightward direction; that of the right eye preferred horizontal movement. The cell therefore had some 'axial

Fig. 8. The responses of a binocularly driven neurone recorded from the cortex of a kitten reverse-sutured at the age of 4 weeks for a period of 3 days.

The left-hand part of the diagram shows responses of the receptive field in the left eye, which was of the simple type and is shown at the upper left. The records at the bottom left show the responses to a bright bar 10° long and 1° wide flashed on and off at the positions indicated on the receptive field diagrams. The stimulus trace between the two records is approximate. The central column of records illustrates the responses of the left eye to a bright slit 10° long and ¼° wide moved across the receptive field at the orientations and directions indicated at a velocity of approximately 1 deg.sec^{-1}. No responses were evoked to stimuli moving upward and to the left (not shown).

The right-hand part of the diagram shows the neurone's responses to stimulation of the receptive field in the right eye, whose location and size are approximately indicated by the circle. The stimulus was the same 10° by ¼° slit, moved at 1 deg.sec^{-1} in the directions indicated; no reliable responses were obtained to stimulation of the right eye with flashed patterns.

Crosses indicate the plotted positions of the left (LAC) and right (RAC) *areae centrales*.

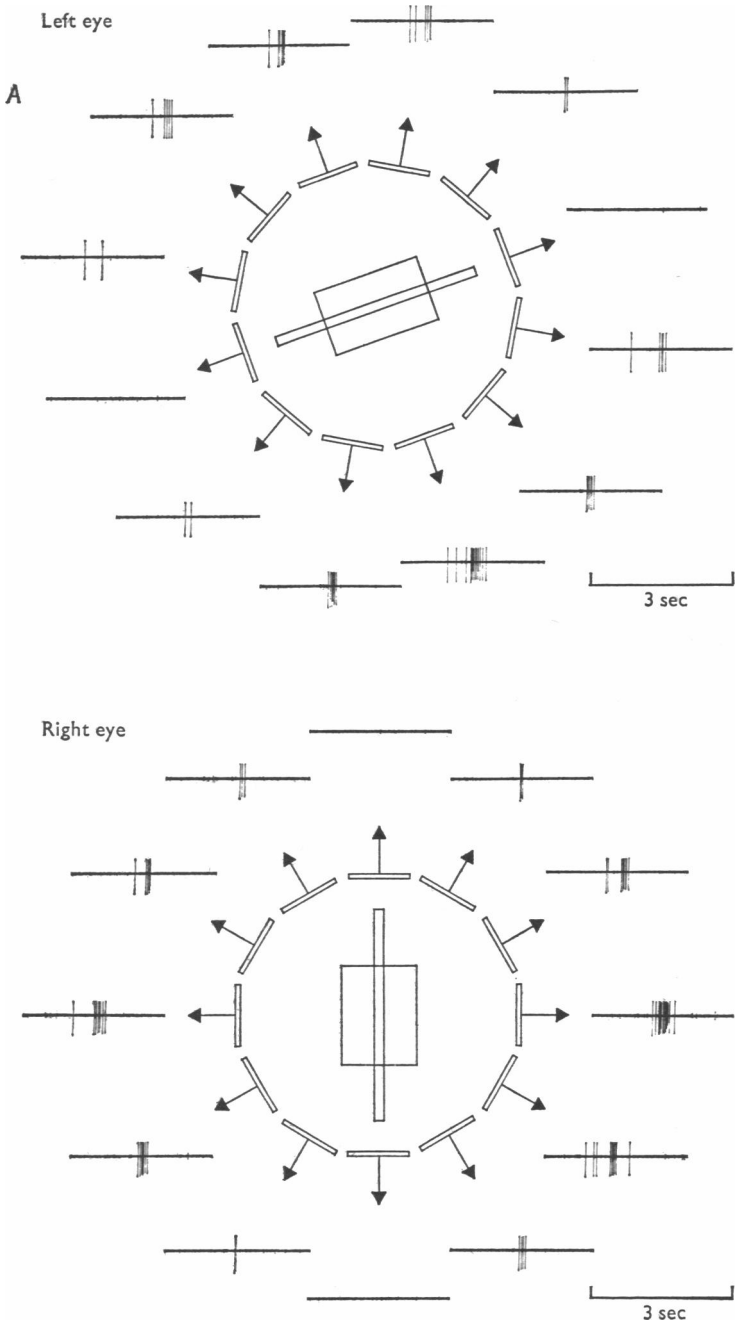

Fig. 9*A*. For legend see page 152.

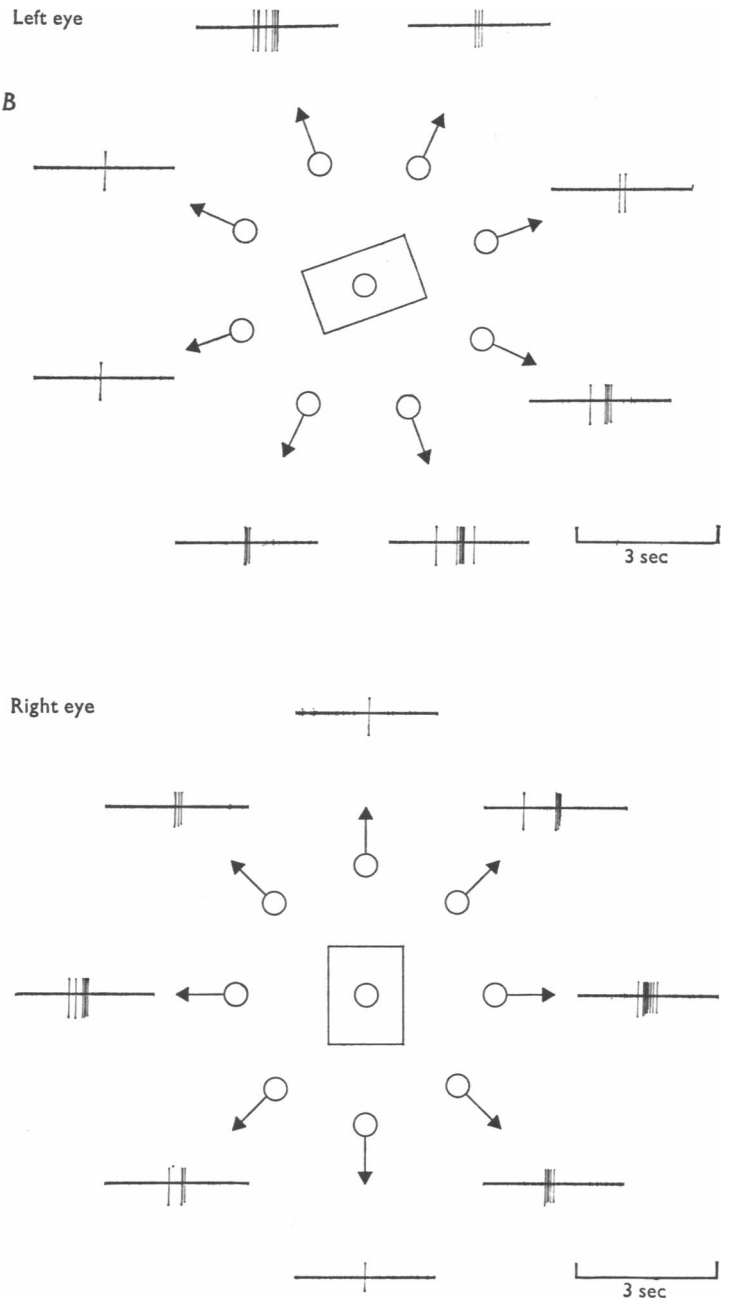

Fig. 9*B*. For legend see page 152.

direction selectivity', and bore some resemblance to the 'double direction selective' neurones described by Van Sluyters & Stewart (1974) in the rabbit's visual cortex. The fact that it was more selective for the direction of line movement than for the direction of spot movement does, however, indicate that it possessed genuine orientation selectivity (cf. Barlow & Pettigrew, 1971; Palmer & Rosenquist, 1974; Henry, Bishop & Dreher, 1974).

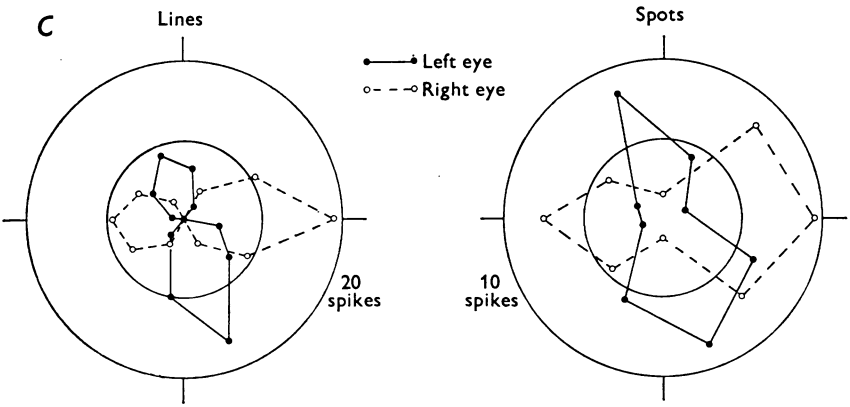

Fig. 9. The responses of a binocularly driven complex cell recorded from the cortex of a kitten reverse-sutured for 9 days at the age of 7 weeks.

A, the responses of the two receptive fields (which are shown diagrammatically in the centre of each group of records) to a bright slit $4\frac{1}{2}°$ long and $\frac{1}{4}°$ wide (which is illustrated to scale superimposed on the receptive fields), moved in the directions indicated at approximately 2 deg.sec^{-1}. Note the marked difference in preferred orientation between the two receptive fields.

B, the responses of the two receptive fields to a bright spot, $\frac{1}{2}°$ in diameter, moved in the directions indicated at approximately 2 deg.sec^{-1}. Note the difference in preferred direction between the two receptive fields.

C, polar diagrams of the responses of the two receptive fields of the neurone to moving lines (*A*) and spots (*B*) described above. The responses plotted are the mean responses to between four and six presentations of each stimulus. Note that the angular co-ordinate in both plots is the direction of stimulus movement. Both receptive fields were more selective for the direction of line movement than for that of spot movement, but showed a definite preferred axis for the direction of movement of a spot.

Fig. 9*C* shows polar diagrams of the responses of the two receptive fields of this cell to moving lines (left) and spots (right). The graphs are based on the average response to between four and six sweeps of a hand-moved stimulus, as described in the legend. The radically different orientation and direction preferences of the two receptive fields of this neurone are obvious.

The preferred orientations of the two receptive fields of binocular cells

in normal adult cats do not generally differ by more than 15°; differences of even this magnitude are rare (Blakemore *et al.* 1972). Fig. 10 compares the interocular differences in preferred orientation for samples of units

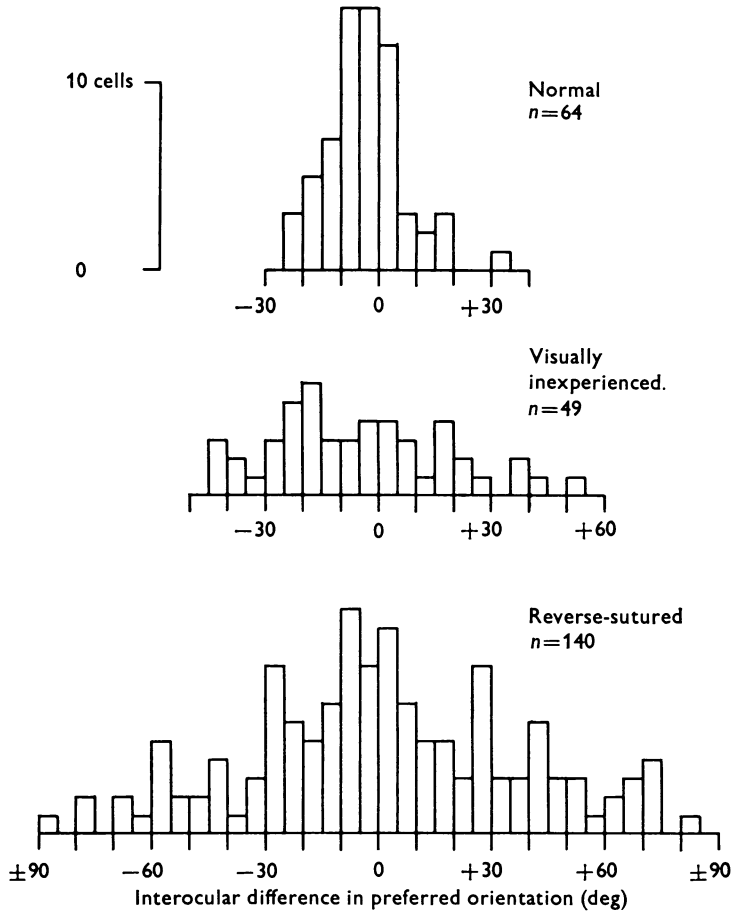

Fig. 10. Histograms of the differences in preferred orientation between the two receptive fields of: (top) 64 units recorded from three normal kittens, aged 19, 26 and 32 days; (middle) 49 units recorded from seven kittens without visual experience before recording at between 9 and 72 days (from Blakemore & Van Sluyters, 1975); (bottom) 140 units from twenty-three kittens reverse-sutured for various periods of time. Differences of positive sign occur when the receptive field in the right eye is tilted clockwise with respect to that in the left eye; negative differences are anticlockwise. The histograms include all orientation selective, orientation bias and direction selective units from these kittens. Direction selective units could have preferred directions differing by as much as 180° in the two eyes (Pettigrew, 1973), and were assigned 'orientations' orthogonal to their preferred directions of movement; no differences of more than 90° were, in fact, observed.

from three kittens, aged 19, 26, and 32 days, reared with normal visual experience (top); from seven kittens binocularly deprived of visual experience from birth to the time of recording at the age of between 9 and 72 days (middle, from Blakemore & Van Sluyters, 1975); and from twenty-two kittens reverse-sutured for various periods (bottom). The differences among these distributions are obvious. The distribution obtained from the rather unselective population of neurones from visually inexperienced kittens is significantly broader than that of the normal population ($F = 4{\cdot}93$, d.f. = 48, 63, $P < 0{\cdot}001$), and the distribution obtained from reverse-sutured kittens is significantly broader than either (*vs.* normals: $F = 11{\cdot}52$, d.f. = 139, 63, $P < 0{\cdot}001$; *vs.* inexperienced: $F = 2{\cdot}34$, d.f. = 139, 48, $P < 0{\cdot}001$). Blakemore & Van Sluyters (1974) noted a similarly broad distribution of differences in their small sample of binocular neurones from reverse-sutured kittens.

It is crucial for some of the inferences that I shall draw to show that this large range of interocular orientation differences is not due to errors. The bottom histogram of Fig. 10 includes all 140 neurones that exhibited some orientation preference in both eyes. Fig. 11 illustrates the distributions for certain subgroups of this population.

The upper histogram shows the distribution of orientation differences for 117 neurones that exhibited orientation or direction selectivity in both eyes. This distribution is not different from that obtained from the twenty-three cells possessing at least one orientation bias receptive field (not illustrated; $F = 1{\cdot}10$, d.f. = 22, 116, $P > 0{\cdot}05$). It seems unlikely that the errors inherent in the determination of the preferred orientations of these cells contributed greatly to the breadth of the distribution.

Of these 117 specified units, thirty-five were in ocular dominance groups 2 or 6, and had rather weak and occasionally ill-defined receptive fields in the non-dominant eye. These cells are compared with the eighty-two cells in the three middle ocular dominance groups in the second and third histograms of Fig. 11; the distributions do not differ significantly in their variance ($F = 1{\cdot}09$, d.f. = 34, 81, $P > 0{\cdot}05$).

The bottom four histograms in Fig. 11 compare the distributions of differences for cells of each of the four 'specified' types. Simple, complex and hypercomplex cells all appear to have similar distributions, but direction selective cells have a somewhat tighter clustering of differences near zero. Their distribution of 'orientation' differences (see legend to Fig. 10) has a significantly smaller variance than that of the other specified cell types ($F = 2{\cdot}53$, d.f. = 104, 11, $P < 0{\cdot}05$). In view of the relative immunity of the superior colliculus to disruption of binocular function (Wickelgren-Gordon, 1972; Gordon & Gummow, 1975), and the probability that many of the neurones classified here as direction selective

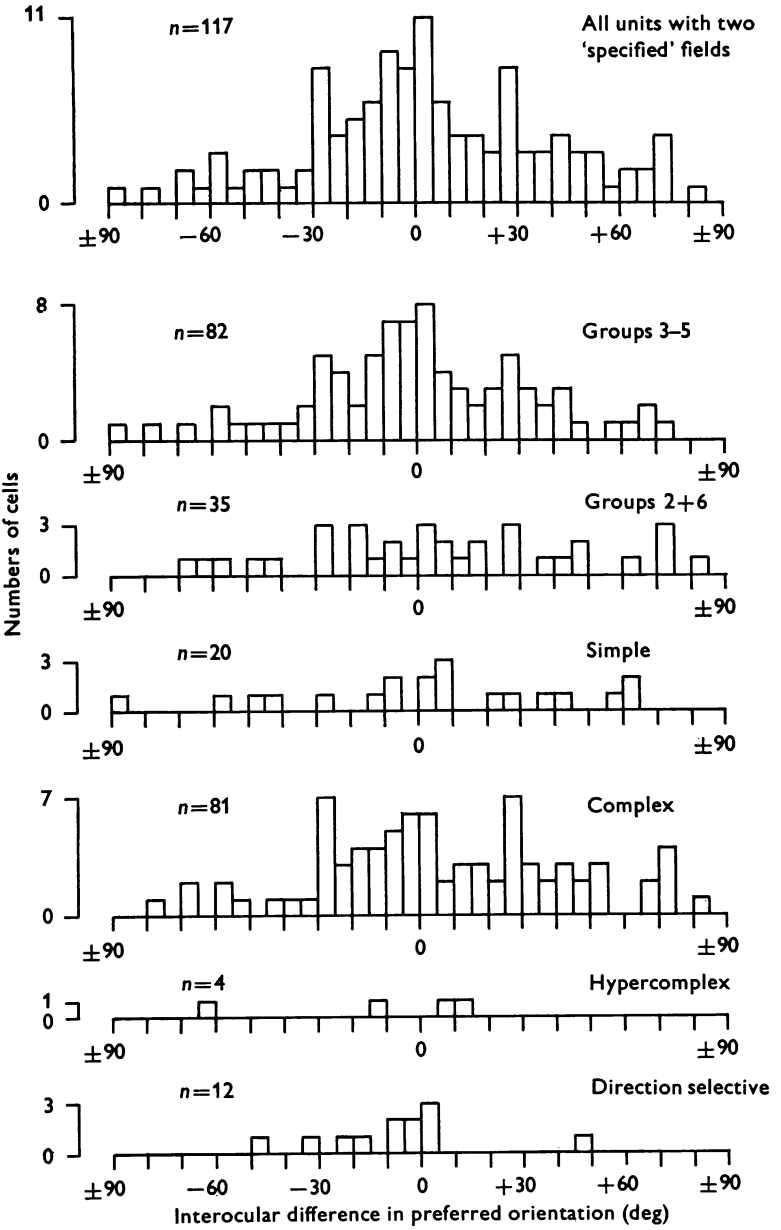

Fig. 11. Histograms of the interocular differences in preferred orientation for the 117 units from reverse-sutured kittens with orientation or direction selective receptive fields in both eyes (top), and for various subgroups of that population, including cells in ocular dominance groups 3, 4 and 5 or 2 and 6, and simple, complex, hypercomplex and direction selective cells. Conventions as in Fig. 10.

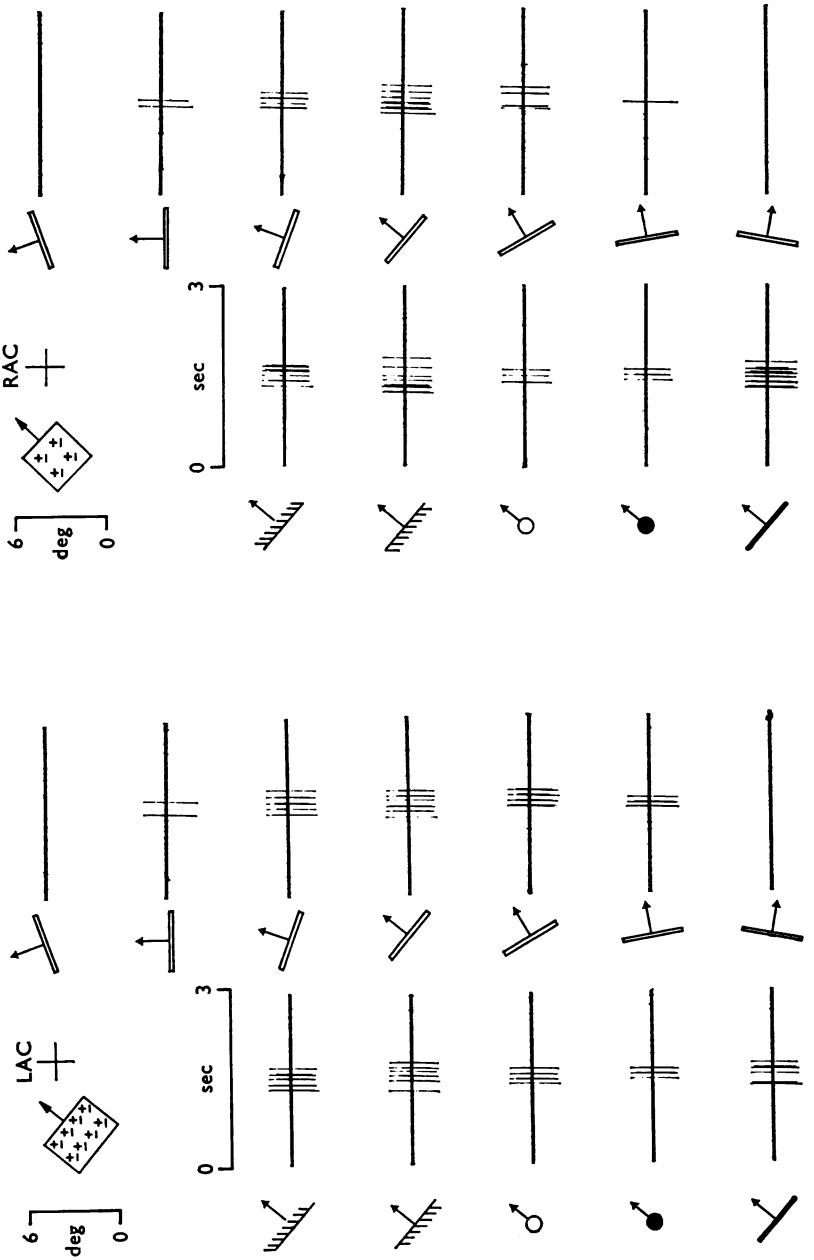

Fig. 12. For legend see facing page.

were corticocollicular projection neurones (Palmer & Rosenquist, 1974), it seems likely that the cortical outflow to the tectum is less susceptible to environmental effects. The responses of a direction selective cell (cf. Palmer & Rosenquist, 1974) recorded from a kitten reverse-sutured for 12 days at the age of 7 weeks are illustrated in Fig. 12. The preferred directions of movement of this neurone's receptive fields in the two eyes differed by only 4°, and it was in ocular dominance group 4. It was one of the very few of the 254 binocular neurones encountered in reverse-sutured kittens that could have been recorded in the cortex of a normal cat.

The pattern of binocular interaction in reverse-sutured kittens is disrupted in a unique manner, and it seems likely that the pattern of disruption is related to the peculiar structure of cortical orientation columns described above (Fig. 6). When different systems of columns from the two eyes overlap, abnormal binocular interaction occurs. The distributions of interocular orientation differences shown in Figs. 10 and 11 are not flat, and there was a clear, if abnormally weak, tendency for the two receptive fields of a binocular neurone to have similar preferred orientations: the preferred orientations in the two eyes were significantly correlated ($r = 0{\cdot}70$, $n = 140$, $P < 0{\cdot}01$). Similarly, the distribution of orientation changes accompanied by large ocular dominance changes shown in Fig. 5*D* is not flat: small changes were slightly more common than large ones.

It is of some interest to assess the degree to which the reinnervated input from the second eye is normal in character and specificity, and to attempt to outline the processes by which new receptive fields are built up and old ones destroyed. We have already seen that the initially deprived eye is capable of organizing an orderly sequence of orientation columns (e.g. Fig. 6*C*), although in some instances that order appears to be less clear than normal (Fig. 6*A*). The data obtained from the twenty-two kittens whose ocular dominance distributions are illustrated in Fig. 2 can be combined and considered by ocular dominance group, since the

Fig. 12. The responses of a direction selective neurone recorded from the cortex of a kitten reverse-sutured for 14 days at the age of 6 weeks. The left- and right-hand parts of the diagram show the cell's responses to stimulation of the receptive fields of the left and right eyes, respectively, which are shown at the top left of each part, along with the positions of the *areae centrales*. The stimuli used in the left-hand columns of each part of the Figure were: leading light and leading dark edges, 20° long; bright and dark spots, 1° in diameter, and dark bars, 10° long and ¼° wide. The right-hand column of each part of the figure depicts the selectivity of each receptive field for the direction of movement of a 10° by ¼° bright slit, moved, as were all other stimuli, at a velocity of approximately 5 deg.sec^{-1}. Note the very similar responses of the two receptive fields to all types of stimulus.

paradigm used in those experiments ensured that the first eye to be open was the contralateral eye. Cells in groups 1, 2 and 3 were therefore dominated by that eye; cells in groups 5, 6 and 7 were dominated by the initially deprived eye. It is possible to compare the different cell types encountered in the cortex with respect to ocular dominance, and such a comparison is presented in Fig. 13.

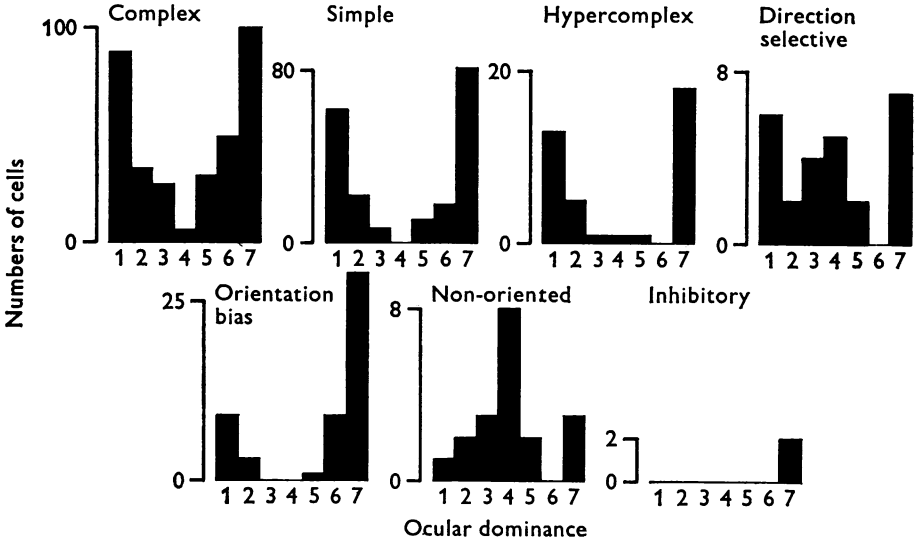

Fig. 13. Ocular dominance histograms for all visually responsive neurones recorded from the right hemispheres of twenty-two kittens deprived of vision in the right eye until the age of 4–7 weeks, and then reverse-sutured for a further variable period. The neurones are classified according to receptive field type; when the two receptive fields differed in type, that of the dominant eye was used for classification purposes. Note that cells in ocular dominance group 1 were driven solely by the first eye to be open; cells in group 7 were driven solely by the initially deprived eye.

It is clear that the four 'specified' receptive field types (top row of histograms) each have similar proportions of cells dominated by the two eyes. There is no evidence that one or the other type of cell failed to develop receptive fields in the second eye to be opened. However, there were marked differences among the cell types in the proportions of each that were strongly binocular. Simple and hypercomplex cells in groups 3, 4 and 5 were very rare, while complex cells were more commonly classed in one of these groups. Direction selective neurones, in keeping with the suggestion made above that they are less susceptible to the effects of disordered binocular input, were often binocularly activated.

The three non-specific receptive field types showed characteristically

different behaviours. Orientation bias cells were much more commonly dominated by the initially deprived eye than the initially experienced eye. This may be related to the overall loss of selectivity exhibited by the initially deprived eye's receptive fields (see below). Non-oriented cells were commonly strongly binocular, but my reluctance to classify monocularly driven units with concentric receptive fields as cortical cells unless they produced an injury discharge in response to the advance of the electrode may have led me to overestimate the binocularity of this type of cell. Both of the inhibitory cells encountered were influenced solely from the initially deprived eye. One of these units was orientation selective in its inhibitory responses, and that orientation was similar to that of the surrounding units and background activity. These cells may have been abnormal cells whose excitatory drive had been disconnected, but whose inhibitory input remained functional (cf. Blakemore & Tobin, 1972; Bishop, Coombs & Henry, 1973; Creutzfeldt, Kuhnt & Benevento, 1974). They were only revealed by their high rate of maintained discharge (between 12·5 and 20 spikes/sec), and the possibility must be noted that many of the neurones I classified as visually unresponsive, but that had low resting discharge rates, may have had functional inhibitory connexions which were impossible to reveal without some artificial elevation of the resting discharge (Bishop, Coombs & Henry, 1971; Hess & Murata, 1974).

In reverse-sutured kittens, the complementary development and degradation of receptive fields affects all receptive fields driven through the eye in question. Figure 14 illustrates this process, showing the proportion of specified receptive fields, of both monocular and binocular neurones, driven by each eye of the reverse-sutured kittens. The data are presented separately for the four series of kittens reverse-sutured at different ages.

Reverse-suturing at the age of 4 weeks caused a rapid loss of specified receptive fields in the left (initially experienced) eye, and a complementary and even more rapid increase in the proportion of these receptive fields in the right eye. A similar process took place more slowly and less completely as the reversal of lid suture was delayed, and the specified receptive fields in the left eye were virtually immune to this loss of specificity by the age of 7 weeks (although the absolute number of receptive fields in that eye, of course, decreased: Fig. 2). Furthermore, the proportion of specified receptive fields in the initially deprived eyes of animals reverse-sutured at the age of 7 weeks never approached 100 %, as it did in younger kittens.

This process may not be confined merely to a complementary loss and development of certain types of receptive fields in reverse-sutured kittens, but may be reflected in the general level of stimulus selectivity, even among receptive fields of the 'specified' types. I did not make quantitative observations of orientation selectivity during these experiments, but I

did note the limits of the orientation tuning curves for the great majority of specified and orientation bias neurones in these animals. Qualitative observations of this kind may, for our purposes, give an adequate representation of the selectivity of neurones.

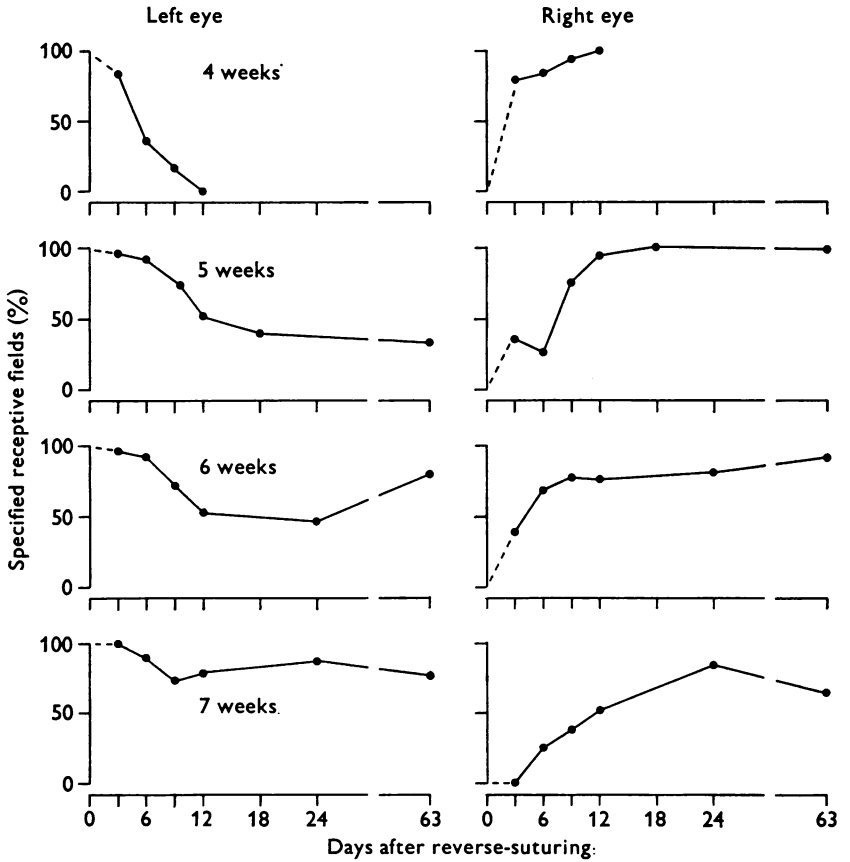

Fig. 14. Graphs showing the proportion of 'specified' receptive fields in the left and right eyes (left and right columns, respectively) of the twenty-two kittens whose ocular dominance histograms are presented in Fig. 2. The proportion of specified (orientation or direction selective) receptive fields in each eye is plotted for each series of kittens as a function of the survival period after reverse-suturing.

D. Rose (personal communication, 1975) has found that there is a high correlation between the quantitatively and qualitatively determined orientation selectivity of cortical neurones. Moreover, the mean orientation band width predicted from the quantitative data on orientation selectivity that has been published (Rose & Blakemore, 1974; Henry, Dreher &

Bishop, 1974; Watkins & Berkley, 1974) is 68° – the mean orientation band width of a population of 109 cortical cells from adult cats determined qualitatively in the present study was 72°.

Orientation band width may therefore give an adequate measure of cortical orientation selectivity, and in Fig. 15 this measure is used to examine the changes in selectivity in the cortical receptive fields of the two eyes of reverse-sutured kittens. The format of this Figure is similar to that of Fig. 14: each point indicates the mean orientation band width of the receptive fields of one eye of one kitten; the vertical bars indicate plus and minus one standard error of the mean, and give some idea of the scatter of selectivities obtained; the number of receptive fields used in the calculations is indicated under each point.

Consider first the left-hand column of curves, which describe orientation selectivity in the initially experienced left eye. In the kittens reverse-sutured for 3 days, the mean band widths were between 67 and 86°, but increasing periods of deprivation caused an increase in this mean, and cells tended to become less selective. This degeneration was particularly rapid in younger animals, and the series of animals reverse-sutured at the age of 7 weeks showed very little over-all decline in orientation selectivity.

The right-hand column shows a complementary process. The first receptive fields to appear in the initially deprived eye tended to be very broadly tuned for orientation, but their numbers and selectivities increased rapidly, although the increase was slower in older animals. It is noteworthy that the smallest mean band widths attained by kittens reverse-sutured at 4 or 5 weeks of age were between 57 and 68°, and thus comparable to normal adult levels of selectivity. The final orientation band width attainable appeared to increase with increasing age at reverse-suturing, to 79° after 6 weeks of deprivation and 98° after 7 weeks. It seems that the cortex is not capable of delaying indefinitely the development of orientation selectivity: the longer it is delayed, the less selectivity is gained.

Double reversal of monocular deprivation effects

The results of Blakemore & Van Sluyters (1974) and those discussed above demonstrate that the sensitive period is not an all-or-none phenomenon, a period in which a cell must determine the nature of its input once and for all. Rather, it is clear that visual experience can disconnect a set of functional inputs, and then restore that or a closely related set of inputs to a state of complete functional normality. I decided to establish whether this process of disconnexion could be pressed one step further, by reversing the cortical pattern of ocular dominance in a kitten in which that pattern had already been reversed.

That this intricate series of biasing, disconnexion and reconnexion of

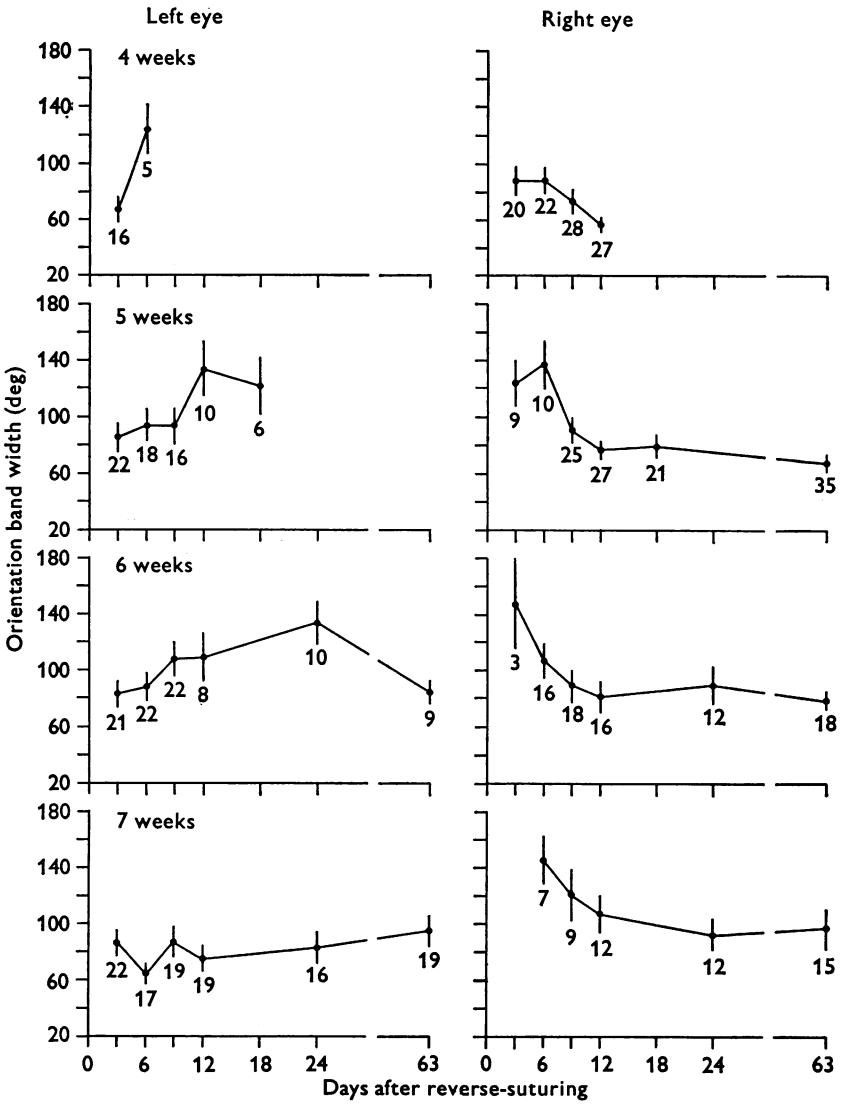

Fig. 15. A plot of the mean orientation band widths determined for the receptive fields of all neurones in the left (left column) and right (right column) eyes of the twenty-two reverse-sutured kittens whose ocular dominance histograms are illustrated in Fig. 2. Most receptive fields with a preference for the orientation of line stimuli are included; orientation bias receptive fields are given a value of orientation band width of 180°. The vertical bars about each point indicate plus and minus one standard error of the mean, and the number of receptive fields for which measurements of band widths were made in each eye of each kitten is indicated under each point.

ocular dominance is possible is shown by the data in Fig. 16, which presents the ocular dominance distributions obtained from four kittens (left) and diagrams their respective periods of visual experience (right).

Kitten A was monocularly deprived in the ipsilateral eye for 28 days, and physiological recordings taken at that time indicate that the effects of that period of deprivation were sufficient completely to shift cortical ocular dominance. Kitten B was deprived in the ipsilateral eye until the

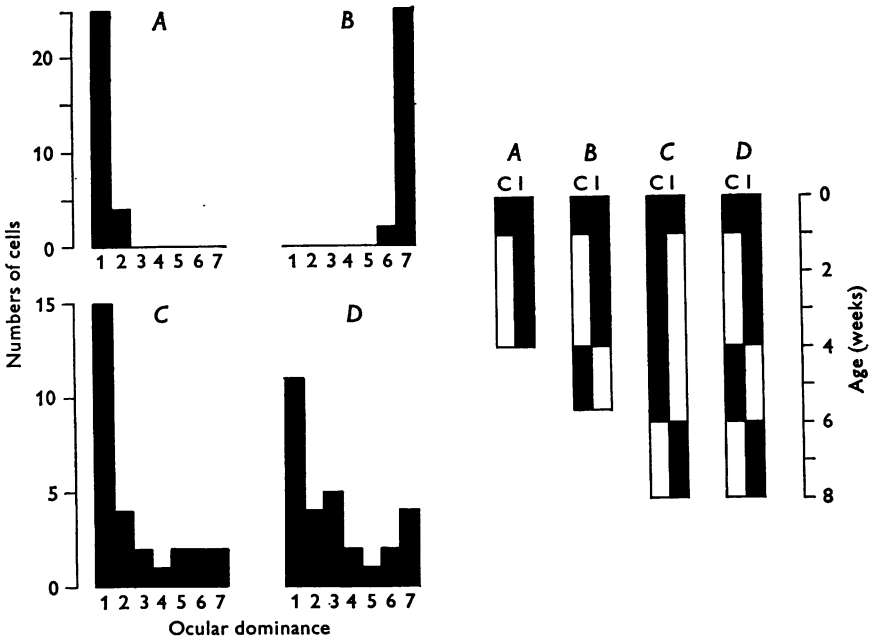

Fig. 16. Ocular dominance histograms obtained from four kittens whose visual experience through the contralateral (C) and ipsilateral (I) eyes is shown on the right. Filled regions indicate periods of eye closure.

age of 28 days (at which point its cortical ocular dominance distribution presumably resembled that of kitten A), and then reverse-sutured for 12 days, which sufficed to shift the ocular dominance of all the cortical neurones to the other, ipsilateral side of the distribution. Kitten C was monocularly deprived in the contralateral eye until the age of 6 weeks, at which point its ocular dominance distribution presumably resembled that of kitten B, and then reverse-sutured for a further 14 days, which caused a large but not total shift in cortical ocular dominance toward the contralateral eye. Kitten D was, like kitten A, monocularly deprived in the ipsilateral eye for the first 28 days of life. Then, like kitten B, it was

reverse-sutured for a period of 14 days. Finally, the initially deprived eye, which had been opened at the age of 4 weeks, was resutured shut and the initially experienced eye was reopened for a further 14 days.

The ocular dominance distributions obtained from kittens C and D were very similar, indicating that the initial period of monocular deprivation made almost no contribution to the cortical ocular dominance of kitten D. This may be taken as further confirmation that the cortex of an animal reverse-sutured at the age of 4 weeks for 2 weeks is virtually identical to that of an animal simply deprived of vision in one eye to the age of 6 weeks (Fig. 2). The 2 weeks of reversed monocular deprivation abolish all traces of connectivity which might be utilized by the eye deprived for that period to accelerate its recapture of the cortex. As suggested by Blakemore & Van Sluyters (1974), 'the sensitive period is, then, a time when the afferent connexions of cortical cells are utterly plastic', at least with respect to ocular dominance.

DISCUSSION

The behaviour of individual neurones during deprivation reversal

In the absence of direct evidence (obtained perhaps from long-term chronic single unit recording) it is impossible to be certain of the stages through which a single neurone passes in the course of the reversal of deprivation effects. It is nevertheless possible to infer the nature of some of these stages from the series of observations described in the preceding pages.

It seems probable, as concluded from studies on the modifiability of neural populations by other authors (e.g. Wiesel & Hubel, 1963*b*; Hubel & Wiesel, 1965; Blakemore & Cooper, 1970; Pettigrew, Olson & Hirsch, 1973) that the properties of individual neurones change during the reversal process. Although micro-electrodes record from a small proportion of the neurones they pass during a penetration, an account of the physiological consequences of monocular deprivation or strabismus based on the loss of inappropriately connected neurones and the retention of others would require that a loss of more than 80% of the normal complement of functional cortical cells should pass unnoticed; some of the results reported above would require that an even higher proportion of cells be lost. Furthermore, the patterns of cortical functional architecture that result from monocular deprivation or strabismus change in a manner that strongly suggests that individual cortical neurones change their properties as a result of visual experience (Hubel & Wiesel, 1965).

Assuming that the phenomena observed during the reversal of monocular deprivation effects reflect changes in the functional connexions of

single neurones, what inferences can be drawn about the rate and manner in which cells shift eye dominance?

The rate and extent of the reversal of cortical ocular dominance depend, as described above, on the age of the animal at reverse-suturing. Fig. 3 shows a graphical representation of the reversal process following reverse-suturing at different ages. Note that the cortical ocular dominance distributions obtained from the series of animals reverse-sutured at 4 or 5 weeks

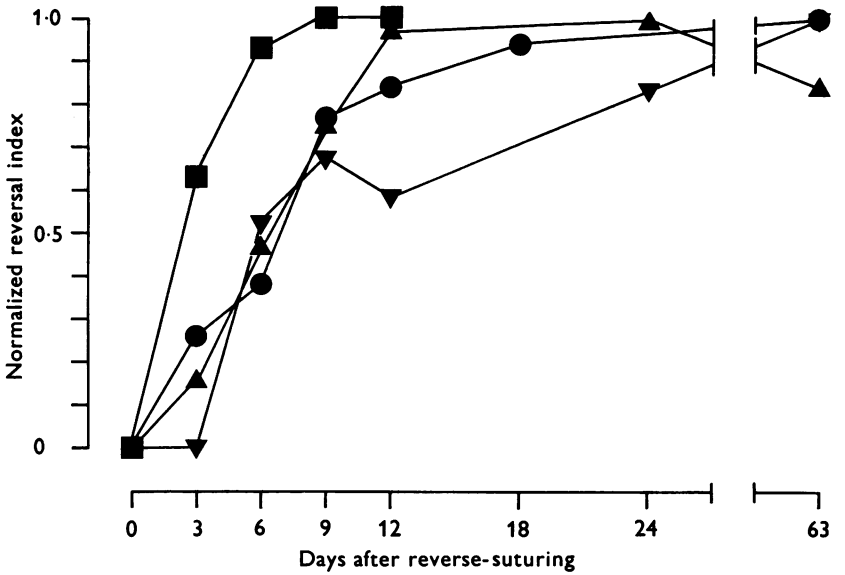

Fig. 17. The normalized rate of reversal of the physiological effects of deprivation. The curves from Fig. 3 have been scaled so that their highest points have a value of normalized reversal index of 1, and the other points adjusted accordingly. Kittens reverse-sutured at the age of 4 weeks: ■; at 5 weeks: ●; at 6 weeks: ▲; at 7 weeks: ▼.

of age (Fig. 2) come to shift completely to the right-hand side of the histograms. In the last few animals of each series, every cell recorded had become dominated by the initially deprived eye. On the other hand, no kitten reverse-sutured at the age of 6 or 7 weeks showed this complete reversal of deprivation effects; a substantial proportion of cortical cells remained dominated by the initially experienced eye, even after 9 weeks of reversed deprivation.

We can neglect these cells that do not shift ocular allegiance, and consider only those cells in 6 and 7 week reversal kittens that ultimately come to be dominated by the initially deprived eye, by normalizing the graphs shown in Fig. 3 to the maximum value of reversal index obtained in each series. Fig. 17 plots the reversal index normalized in this way for the four

series of experimental kittens. The normalization does not affect the graphs for the 4 and 5 week reversal series, since they reach a value of unity in any case. It scales the results of the 6 and 7 week series in such a way as to superimpose the graphs describing their reversal upon that describing reversal at 5 weeks, particularly over the first section of the graphs.

The sensitive period for visual development could be represented at the level of single neurones in two ways. All cells could be modifiable to roughly the same extent at all times, with modifiability declining throughout the neuronal population after the age of 4 or 5 weeks until all cells became more or less fixed in their functional connectivity. Alternatively, all cortical cells could be modifiable early in the sensitive period, but they could lose their ability to alter their functional connexions at different times. The 'sensitivity' of the sensitive period determined from the behaviour of neuronal populations would appear to decline as more and more cells became fixed in their connectivity, despite the fact that others might remain as modifiable as they had been early in the sensitive period.

If all cortical cells are modifiable to roughly the same degree at all times in the sensitive period, then even after a manipulation like normalization that highlights the behaviour of one population of neurones, that population should behave in a different way from a similarly defined population at a different time. Specifically, the rate of reversal of deprivation effects should appear to be slower in older animals, even among those cells that ultimately shift ocular dominance. On the other hand, if some cells become fixed at different times from others, then normalization should reveal the activity of a population of neurones that remain modifiable; the rate of reversal of this population might be much the same at different ages.

The data presented in Fig. 17 suggest that both kinds of process take place, at different times in the sensitive period. After reverse-suturing at 4 weeks, the whole neuronal population appears to shift eye dominance more rapidly than it does after reverse-suturing at 5 weeks. All neurones are therefore more modifiable – they can shift ocular dominance more rapidly – during the fifth week than they are during subsequent weeks. But the population of cells that are capable of shifting eye dominance following reverse-suturing at 5, 6 or 7 weeks all appear to do so at roughly the same rate. Through these weeks an increasing number of neurones becomes committed to dominance by one eye, while other neurones remain as modifiable as they were at the age of 5 weeks. The proportion of cells fixed with respect to ocular dominance is around one third at the age of 6 weeks, and one half at the age of 7 weeks. If the same pattern holds for older animals, then about four fifths of neurones are fixed by the age

of 8 weeks, and few, if any, neurones are modifiable after the age of 10 or 12 weeks (Wiesel & Hubel, 1965*b*; Blakemore & Van Sluyters, 1974).

Note also that the rate at which cells switch ocular dominance appears to be unaffected, within limits, by the length of the period of monocular deprivation they have undergone. Some fraction of the neuronal population is capable of switching eye dominance as rapidly after 7 weeks of deprivation as it is after 5 weeks. These results, and those on double reversal of deprivation, indicate that, beyond a certain stage, further monocular deprivation has no effect on ocular dominance, or on the degree to which ocular dominance is entrenched.

The pattern of cortical ocular dominance columns in reverse-sutured kittens suggests that this gradual specification of the ocular dominance of certain neurones is spatially organized: the cells that remain dominated by the initially experienced eye after an extended period of reversed deprivation are grouped into eye dominance columns. The specification of the final functional state of neurones in normal kittens may proceed similarly; neurones in the centre of regions dominated by one eye or the other might be the first to be specified, and these nuclei of fixed neurones could expand and come to occupy the whole cortex. The fact that the first specified receptive fields encountered in very young kittens tend to be strongly monocular (and perhaps in the centres of eye dominance columns) provides some support for this notion (Blakemore & Van Sluyters, 1975).

The reversal of deprivation effects and neuronal plasticity

The sequences of orientation columns in the cortex of reverse-sutured kittens are, unlike those in normal or strabismic animals, disrupted by changes in cortical ocular dominance. During the reversal process eye dominance columns expand and contract in a complementary fashion; the positions of the borders between them, and therefore the points at which orientation sequences are disrupted, move across the cortex. Thus one point in the cortex, and the neurones there, can represent different orientations at different times during the reversal process.

Innate factors provide most cortical neurones in young, visually inexperienced kittens with at least a rudimentary orientation preference, and something like the adult columnar orientation structure is probably present (Hubel & Wiesel, 1963*b*; Blakemore & Van Sluyters, 1975). Furthermore, the orientation preferences of the two receptive fields of binocular neurones are roughly matched. A period of monocular deprivation commencing at this time will destroy one of these receptive fields, while that in the other eye will become increasingly selective as a result of visual experience; experience will presumably refine a preference for the orientation toward which the receptive field was biased before eye-opening.

Following reversal of lid-suture, the receptive field in the initially experienced eye becomes less selective and degenerates. Concurrently, a receptive field appears and then develops orientation selectivity in the initially deprived eye. If this new receptive field were merely a reactivated version of the rudimentary receptive field that had been present before the period of monocular deprivation, it should show as great a tendency as do receptive fields in visually inexperienced kittens to share the preferred orientation of the receptive field in the other eye.

The distribution of interocular orientation differences in the cortex of visually inexperienced kittens is rather broader than that seen in young normal kittens (Fig. 10). Part of this increased variance is no doubt due to the rather vague orientation selectivity of most neurones in inexperienced kittens, and a reduction in the variance effected by visual experience might in any case be attributed to small changes in the preferred orientation of one receptive field or the other resulting from simultaneous, correlated stimulation by one contour, the necessary stimulant for the retention and refinement of innate binocular connexions. The distribution of orientation differences in reverse-sutured kittens is much broader than that of visually inexperienced kittens (Fig. 10). Monocular deprivation must therefore destroy much of the innate tendency for the receptive field in the deprived eye to share the orientation preference of that in the experienced eye.

It could be argued that the broad distribution of interocular orientation differences shown in Fig. 10 could be due to the inability of the developing input from the initially deprived eye to 'read' the innately specified pattern of connexions with the accuracy possible under normal rearing conditions. The newly developed receptive fields might then be generally but imprecisely related in their orientation preference to those developed earlier by the initially open eye. In that case, however, the sequences of preferred orientation across the cortex should be similar in general character in the two eyes; the sequence developed by the new eye should be a rather sloppy imitation of that possessed by the old one. But deprivation must also destroy the rudimentary columnar organization of orientation in the deprived eye, for the pattern of orientation columns that develops in the initially deprived eye following reverse-suturing can be new and different from that in the initially experienced eye, and not merely a disordered version of it (Fig. 6).

It is not possible to account for the observed patterns of orientation columns and interocular orientation differences by assuming that visual experience following reverse-suturing reactivates synapses made ineffective but not disorganized by the initial period of deprivation, and merely 'tunes up' those connexions to reform orientation columns and orientation

selectivity. The second period of visual experience appears rather to stimulate the development of a new visual cortex, whose functional properties and general characteristics are similar to those of the old one in general, but crucially different in detail.

The effects of strabismus, monocular deprivation and deprivation reversal appear to reflect a binocular competition of the kind proposed by Hubel & Wiesel (1965). Furthermore, this competitive process is spatially organized. It is natural to enquire whether that competition is mediated primarily presynaptically, and consists of a battle between the arborizations of geniculate fibres for terminal space on the post-synaptic membrane of cortical neurones (Hubel & Wiesel, 1965) or whether the competition is largely a post-synaptic phenomenon, and the post-synaptic elements of the cortical neurone adjust their character in order to change the effectiveness of different sets of inputs (Stent, 1973).

The reinnervation of the visual cortex during reversed monocular deprivation may reflect a genuine physical regrowth of axonal connexions from the deprived eye. The initial period of monocular deprivation in these experiments commenced between the sixth and twelfth days of life, when each cortical cell possessed only a tiny fraction of its adult complement of synapses (Cragg, 1975), and it is not implausible to suppose that visual deprivation in some way retards the development of axonal arborizations and terminations of fibres from the deprived layers of the lateral geniculate nucleus. The expansion of physiologically determined eye dominance columns might represent a genuine growth rather than a mere functional unmasking of the terminal arborizations of fibres driven by the deprived eye.

Visually inexperienced monkeys and kittens possess a rudimentary eye-dominance column structure (Wiesel & Hubel, 1974; Blakemore & Van Sluyters, 1975), which appears to undergo a systematic distortion and disappearance when they are deprived of vision in one eye (J. A. Movshon & M. R. Dürsteler, in preparation). In the striate cortex of monocularly deprived monkeys, it is difficult to demonstrate anything but a sparse input from the deprived eye, using the autoradiographic technique of Wiesel, Hubel & Lam (1974) (Hubel, Wiesel & LeVay, 1976). There is no evidence that the periodic structure of axonal terminations in layer IV persists in its normal form, with the terminations from the deprived eye somehow made ineffective while present in normal numbers and positions. This may also be the case in monocularly deprived kittens (Shatz, Lindstrom & Wiesel, 1975), in which case the reversal of deprivation effects would have to be interpreted in terms of axonal growth and sprouting, taking place at a rate of up to 100 μm/day (Table 1). This hypothesis seems in many ways to be the most parsimonious explanation of the results, in view of the close correlation between physiologically

determined eye dominance columns and layer IV arborizations in the cat and monkey visual cortex (Hubel & Wiesel, 1972; Wiesel *et al.* 1974; LeVay *et al.* 1975; Shatz *et al.* 1975; Hubel *et al.* 1976), although it would imply a remarkable rate of axonal growth. Furthermore, the distinctive new pattern of cortical organization could very reasonably be expected to follow such an anatomical reinnervation, since it is difficult to conceive of a neurone-to-axon specification so precise as to guide growing geniculate axons to particular terminal sites on neurones, sites vacated by functionally identical input from the initially experienced eye.

Alternatively, axonal terminations from deprived geniculate layers might always be present across the cortex, perhaps in close approximation to cortical cells, and possessing synaptic structures of some kind, whose post-synaptic effectiveness has been destroyed by deprivation (cf. Marotte & Mark, 1970*a*, *b*; Stent, 1973). It is likely that some afferent fibres driven by the deprived eye are always present in the cortical grey matter of a monocularly deprived kitten, since it is occasionally possible to record the activity of such a fibre. The reappearance of functional input from the deprived eye following reversal of lid-suture could then represent a spatially ordered reactivation of these 'silent synapses', proceeding from the centre of innately organized ocular dominance columns, where the projection from the deprived eye would be most dense, out towards their periphery, where this projection would be more sparse.

The different patterns of organization seen in the two eyes of reverse-sutured kittens could be explained in this scheme, since the passive development of connexions from the deprived eye would proceed (both literally and figuratively) 'blind'. In the absence of the crucially important control that visual experience normally exercises over the elaboration of synaptic contacts, these newly developed inputs might be nearly random in their pattern, swamping the rather weak innate organization present before their arrival.

Recent anatomical evidence (Thorpe & Blakemore, 1975) suggests that both mechanisms may operate at different times in the sensitive period. Following monocular deprivation throughout the sensitive period, commencing near birth, horseradish peroxidase (HRP) injected into the visual cortex is retrogradely transported mainly to the layers of the lateral geniculate nucleus driven by the experienced eye, suggesting that neurones in the other layers of the geniculate no longer possess normal axon terminals in the cortex. But, if the onset of the period of monocular deprivation is delayed until the age of 4 weeks, HRP is retrogradely transported from the cortex to *all* geniculate layers, suggesting that under those conditions (which cause virtually identical physiological changes: Fig. 1*C*) the terminals of axons from deprived layers remain in place in the cortex. It is

of interest then that Van Sluyters (in preparation, see Blakemore *et al.* 1976) has found that reinnervation in the visual cortex after reversal of lid suture following an initial period of monocular deprivation starting during the fifth week of life proceeds in a manner very similar to the original connexion pattern, and that the orientation columns of the two eyes in such animals overlap nearly as precisely as they do in normal kittens.

Either scheme must account for the fact that the initially deprived eye seems to be capable of organizing for itself a new visual cortex following its early functional disconnexion. Although the innate specification of receptive field properties and orientations in the cortex of very young kittens is presumably of some importance in guiding the subsequent course of development, it is quite possible, after those innate contacts have been grossly disrupted, for the neurones of the visual cortex to develop normal response properties and stimulus selectivity, which differ considerably from the ones for which they were destined by prefunctionally determined connexions. The visual cortex, then, possesses a considerable neuronal plasticity during the sensitive period in its development, which seems likely to be related to the kinds of plasticity that are apparent following early injury to other parts of the nervous system. The sensitive period is both sensitive and generous, for it allows the visual cortex to develop at least twice, in more-or-less independent ways.

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