

REVERSAL OF THE PHYSIOLOGICAL  
EFFECTS OF MONOCULAR DEPRIVATION IN KITTENS:  
FURTHER EVIDENCE FOR A SENSITIVE PERIOD

BY COLIN BLAKEMORE AND RICHARD C. VAN SLUYTERS\*

*From the Physiological Laboratory, University  
of Cambridge, Cambridge CB2 3EG*

*(Received 20 August 1973)*

SUMMARY

1. It was confirmed that suturing the lids of one eye (monocular deprivation), until only 5 weeks of age, leaves virtually every neurone in the kitten's visual cortex entirely dominated by the other eye. On the other hand, deprivation of both eyes causes no change in the normal ocular dominance of cortical neurones, most cells being clearly binocularly driven.

2. Kittens were monocularly deprived until various ages, from 5 to 14 weeks, at which time *reverse suturing* was performed: the initially deprived right eye was opened and the left eye closed for a further 9 weeks before recording from the visual cortex.

3. Reverse suturing at 5 weeks caused a complete switch in ocular dominance: every cell was dominated by the initially deprived right eye. Reverse suturing at 14 weeks, however, had almost no further effect on ocular dominance: most cells were still driven solely by the left eye. Animals reverse sutured at intermediate ages had cortical neurones strongly dominated by one eye or the other, and they were organized into clear columnar groups according to ocular dominance.

4. Thus, between 5 weeks and 4 months of age, there is a period of declining sensitivity to both the effects of an initial period of monocular deprivation and the reversal of those effects by reverse suturing.

5. The small proportion of binocular cells in reverse sutured kittens (which have never had simultaneous binocular vision) often differed considerably in their receptive field properties in the two eyes. In particular, if the cells were orientation selective in both eyes the two preferred orientations could differ by up to 70°.

6. The relative importance of innate and environmental contributions to the properties of cortical cells is discussed.

\* National Institutes of Health Special Research Fellow, 1972–1974.

## INTRODUCTION

If a young kitten is deprived of visual experience in one eye the physiological organization of its visual cortex is dramatically altered. In a very young, visually inexperienced kitten the majority of cortical neurones can clearly be influenced by either eye (Hubel & Wiesel, 1963; Barlow & Pettigrew, 1971) and this degree of binocularity even persists if both eyes are deprived of vision by suturing together the eyelids (Wiesel & Hubel, 1965*a*). However, monocular deprivation leads to almost a total loss of binocular neurones (Wiesel & Hubel, 1963*a*, 1965*a*; Ganz, Fitch & Satterberg, 1968). In the visual cortex of such kittens most cells can only be influenced through the experienced eye, although they are apparently normal in every other way. Moreover, such an animal appears behaviourally blind when forced to use its deprived eye (Wiesel & Hubel, 1963*a*, 1965*a*; Dews & Wiesel, 1970).

In a careful series of experiments Hubel & Wiesel (1970) discovered a distinct period of susceptibility to these effects of monocular deprivation. Their technique was to close one eye for a time, reopen it and record from the cortex some time later. They found that there were changes in cortical ocular dominance only if the deprivation occurred during a 'sensitive period', extending from about 3 weeks to about 4 months of age. In fact as little as 3 days of closure during the fourth week was enough to induce these remarkable changes.

These same experiments showed that the reorganization of the cortex persisted despite a period of binocular vision after the initial deprivation. Even if the deprived eye was reopened for a year there was only a small increase in the number of cortical neurones that it could influence. This procedure also caused only a small improvement in the behavioural capacity of the cat through the originally deprived eye (Wiesel & Hubel, 1965*b*; Dews & Wiesel, 1970; Ganz & Fitch, 1968). On the other hand Ganz *et al.* (1968) reported a considerable percentage of cortical cells driven by the initially deprived eye in cats subjected to intensive behavioural testing through both eyes, after a period of monocular deprivation.

A potentially more powerful method of cancelling the effects of monocular closure might be to follow the deprivation by a period of 'reverse suturing' in which the deprived eye is re-opened and the other eye is closed. Certainly this procedure produces some behavioural improvement even if it is applied after the end of the sensitive period (Dews & Wiesel, 1970; Ganz & Fitch, 1968; Chow & Stewart, 1972).

Despite this behavioural recovery cells in the cortex remain almost uninfluenced by the originally deprived eye (Hubel & Wiesel, 1970),

although Chow & Stewart (1972) reported some increase in the representation of the deprived eye after extremely prolonged periods of reverse suturing.

In the present experiments we have applied the technique of reverse suturing within the sensitive period itself in order to optimize the chances for recovery of cortical function.

## METHODS

### *The kittens*

All the animals in this study were domestic tabby kittens, bred in an isolated laboratory colony. They were housed in large cages, with their mother and litter-mates, until the age of about 10 weeks, when they were released into the open colony. The room was illuminated by artificial light for 18 hr each day.

*Monocular lid suture and reverse suturing.* For the five experimental animals, at the time of natural eye opening (usually about 8–10 days) the lids of the right eye were sutured together, using the technique of Wiesel & Hubel (1963*b*). Reverse suturing was performed at a different age for each kitten (5, 6, 8, 10 and 14 weeks of age): the lids of the right eye were reopened and those of the left eye sutured shut. Every animal was then allowed 9 weeks of vision with its newly opened right eye before the neurophysiological experiment took place. At all stages the sutured eyelids were checked very carefully for 'window' openings, and in the very few cases where a window developed it was repaired immediately. Every precaution was taken to ensure that the kittens had virtually no simultaneous binocular vision.

*Control animals.* To act as controls, and to confirm previous observations, we studied three other rearing conditions:

- (1) *Normal rearing.* Three kittens were reared in the colony with neither eye deprived of vision. They were recorded from at 3 to 5 months of age.
- (2) *Binocular deprivation.* The lids of both eyes were sutured at 1 week of age in one kitten and they were not re-opened until recording, at 8 weeks.
- (3) *Monocular deprivation.* One kitten had the right eyelids alone sutured and the recording was carried out at 5 weeks of age, without reverse suturing.

### *Simple behavioural tests*

The kittens' visual abilities were checked by a number of simple behavioural tests. These were performed both before and after reverse suturing, thus testing the initially non-deprived and deprived eyes separately. They were performed again on the two eyes separately and with both eyes open after the eyelids were re-opened following the 9-week period of reverse suturing.

The tests used were as follows.

- (1) *Visual following:* movement of the head to follow a large object, usually a shaking hand, moving back and forth in front of the kitten.
- (2) *Visual startle:* reflex withdrawal of the head and eye blink, in response to the sudden approach of an object.
- (3) *Depth perception:* avoidance of stepping on to a transparent surface covering a drop, in a simplified version of the 'visual cliff' (Gibson & Walk, 1960).
- (4) *Triggered visual placing:* extension of the forelimbs to reach a surface towards which the kitten was lowered (Hein & Held, 1967).
- (5) *Optokinetic nystagmus:* smooth following eye movements (with fast phases

in the opposite direction) in response to a large pattern of black and white stripes (square-wave, approximately 0.2 cycles/degree) moving slowly in front of the eyes.

#### *Recording techniques*

The animals were anaesthetized with Fluothane and then i.v. Brietal (methohexitone sodium) during the preparation, and with nitrous oxide during recording (Blakemore, Donaghy, Maffei, Movshon, Rose & Van Sluyters, 1974). Animals older than 3 months were artificially ventilated with a mixture of 80% N<sub>2</sub>O/19% O<sub>2</sub>/1% CO<sub>2</sub>, but with younger kittens slightly lower proportions of nitrous oxide (70–75%) were adequate to maintain a slow-wave electroencephalogram. E.c.g., as well as e.e.g. was monitored continuously and body temperature was maintained at 37° C.

The animal was paralysed by a continuous i.v. infusion of Flaxedil (7.5 mg/kg.hr made up in 6% glucose-Ringer solution). Eye drift was further minimized by bilateral cervical sympathectomy. The corneae were protected by contact lenses and the eyes corrected for a distance of 57 cm by means of additional spectacle lenses. Mydriasis and cycloplegia were induced by means of homatropine and phenylephrine (Neosynephrine) and 3 mm artificial pupils placed before the eyes. The approximate projection of the area centralis in each eye was plotted on a screen at a distance of 57 cm with a reversible ophthalmoscope.

Cut-out patterns were moved by hand across the stage of an overhead projector in order to back-project moving spots, bars, edges, etc., on to the translucent screen in front of the cat. The dark parts of the patterns had a luminance of about 6 cd.m<sup>-2</sup>, the bright parts about 20 cd.m<sup>-2</sup>. A beam-splitter in the projector beam at an angle of 45° cast an identical image of the stimulus down on to a large pad of graph paper where the receptive fields were plotted for permanent records.

Single units were recorded with tungsten-in-glass micro-electrodes (Levick, 1972) advanced hydraulically through a sealed chamber positioned over a small craniotomy and durotomy, about 2 mm in diameter. In very young animals the thin skull was reinforced with a covering of dental acrylic cement before the craniotomy was drilled. We used conventional methods of amplification and display of action potentials and simply judged responses by listening to the bursts of spikes.

#### *Histology*

At the end of the experiment the animal was sacrificed by an i.v. injection of Nembutal and perfused through the heart with Ringer solution followed by buffered 10% formalin. The brain was frozen, sectioned at 40 μm, stained with fast luxol blue and counter-stained with cresyl violet. The micro-electrode penetrations were reconstructed by searching for several small electrolytic lesions made by passing current through the micro-electrode (d.c., electrode negative, usually 5 μA for 5 sec) at several points along the track.

## RESULTS

### *The consequences of binocular and monocular deprivation*

Simply to confirm previous observations and to provide controls, we studied:

- (a) three kittens reared normally until 3–5 months of age,
- (b) one animal binocularly deprived from birth until recording at 8 weeks and

(c) one kitten monocularly deprived in the right eye until recording at 5 weeks.

### *Ocular dominance*

The results of the experiments are summarized in Fig. 1, using Hubel & Wiesel's (1962) method of classifying the neurones' ocular dominance. Cells of Group 1 can only be driven directly through the contralateral eye, those of Group 7 only through the ipsilateral eye. Neurones in Group 4 are equally influenced by both eyes. So, proceeding from Group 1 to 7, there is a spectrum of relative influence from the contralateral and ipsilateral eyes.

Clearly, just as has previously been described (Hubel & Wiesel, 1962; Blakemore & Pettigrew, 1970), the normal animals (Fig. 1*A*) had a large majority of binocular neurones (Groups 2–6), with a slight bias in favour of the contralateral eye (Groups 2 and 3). The binocularly deprived kitten (Fig. 1*B*) also had a quite normal ocular dominance distribution, confirming that visual experience is not necessary for the maintenance of binocular input (Wiesel & Hubel, 1965*a*; Barlow & Pettigrew, 1971). On the other hand, monocular deprivation (Fig. 1*C*) led to virtually a total loss of direct influence from the deprived eye. For this kitten the recording electrode was in the right hemisphere (as in all experiments described below), so the deprived right eye was ipsilateral. The dominance histogram shows that virtually every cell could be driven only through the contralateral, non-deprived, left eye.

### *Receptive field properties*

We studied the responses of all neurones very carefully, through both eyes, using flashing and moving spots, slits, bars and edges. The receptive fields were then classified into one of the following categories.

(1) *Orientation selective*. (a) Simple; (b) complex and (c) hypercomplex.

We used Hubel & Wiesel's (1962, 1965*a*) criteria as summarized by Blakemore, Fiorentini & Maffei (1972), for classifying these cells. They all responded better for a moving oriented target than for a moving spot and had no discernible discharge to an edge orthogonal to the best orientation. Many of these cells also preferred one direction of movement to the other. In the ocular dominance histograms, orientation selective cells are shown as unfilled blocks.

(2) *Orientation bias*. In the binocularly deprived animal we found, in agreement with Hubel & Wiesel (1963), Wiesel & Hubel (1965*a*) and Barlow & Pettigrew (1971), that a large number of cells responded almost equally to edges of all orientations, but some had just a slight preference for one angle. These neurones usually responded almost as well to moving

spots as to oriented stimuli and on these grounds could not reasonably be classified as orientation selective. In general their responses were weak, they suffered rapid habituation and they rarely responded at all to flashed stimuli. In the histograms these cells are plotted as cross-hatched blocks.

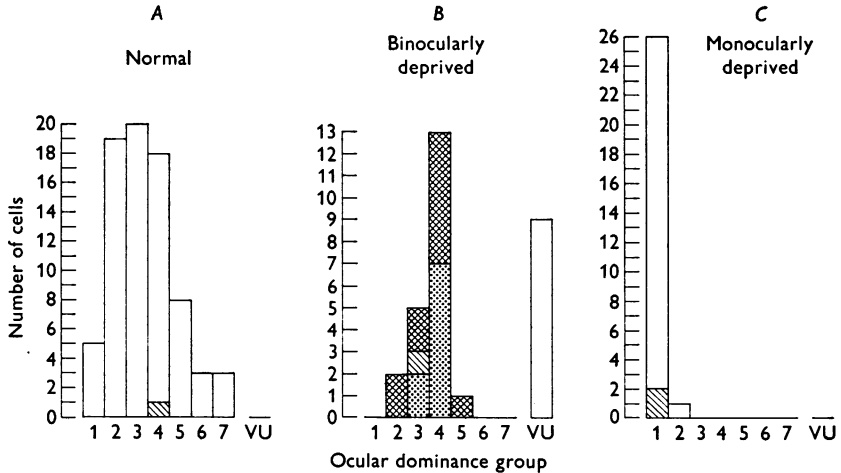


Fig. 1. Histograms, showing the number of neurones, their ocular dominance groups and the types of receptive fields classified on the basis of responses in the eye dominating the cell. Cells in groups 1 and 7 are monocularly driven, being excitable only through the contralateral (left) eye or ipsilateral (right) eye respectively. Cells of group 4 are equally driven by the two eyes. Group 3 and 5 cells are slightly more strongly driven by the contralateral and ipsilateral eyes respectively; group 2 and 6 neurones are very strongly dominated by the contralateral and ipsilateral eyes respectively. Receptive field types: *orientation selective* = open blocks; *orientational bias* = cross-hatched blocks; *pure direction selective* = diagonally striped blocks; *non-oriented* = stippled blocks; *visually unresponsive* = open blocks under a separate column labelled V.U. *A*, seventy-six neurones from three normal kittens aged 3–5 months. *B*, thirty neurones from a kitten binocularly deprived until recording at 8 weeks. *C*, twenty-seven neurones from a kitten monocularly deprived by suturing the right (ipsilateral) eyelids until recording at 5 weeks.

(3) *Pure direction selective*. These were cells that responded almost equally to spots, bars and edges of either contrast but they had an obvious, though often broadly tuned, preferred direction of movement, giving virtually no discharge in the reverse, null direction. If they responded at all to flashing stimuli they usually gave ON-OFF responses over the whole receptive field. There is a small percentage of these neurones even in the normal adult cat cortex. They are shown in the histograms as diagonally striped blocks.

(4) *Non-oriented*. These cells, shown as stippled blocks in the histograms, responded to all moving stimuli, usually better to edges than to spots, but had no preference whatever for any particular orientation of contour or direction of movement. They rarely gave any response to flashing stimuli.

(5) *Visually unresponsive*. With very careful searching and slow penetration it is extremely rare in area 17 of the normal adult to find any spontaneously active cell that cannot be driven by visual stimuli, or to injure a neurone that had no spontaneous firing and whose presence was unknown until it produced an injury discharge. However, such cells are occasionally found in animals that have endured deprivation in either one or both eyes. They are shown as empty blocks in the histograms, under a separate column, labelled V.U.

In all of these experiments we have excluded from the analysis of ocular dominance a small number of units, almost all recorded in the white matter, which had fibre wave forms, were monocularly driven and had the briskly responding centre-surround receptive fields of afferent geniculate fibres.

To summarize the results of these control experiments, we found that the normal kittens (Fig. 1*A*) had almost entirely orientation selective cells with a tiny proportion of pure direction selective units.

The binocularly deprived animal had no cell that could reasonably be classified as orientation selective, though it did possess a number (11 units: 37%) of orientation bias cells, which exhibited a rudimentary kind of orientational preference. Many of the cells (9 units: 30%) were non-oriented, and the remainder were pure direction selective (1 unit: 3%) or visually unresponsive (9 units: 30%).

In terms of receptive field properties, the monocularly deprived kitten's neurones were quite normal (Fig. 1*C*): almost all of them displayed precise orientation selectivity. Indeed virtually the only unusual feature of this animal's visual cortex was its total domination by the non-deprived eye.

### *The effects of reverse suturing*

#### *Ocular dominance*

The results of our main experiment are shown in Fig. 2 as a series of ocular dominance histograms. The first animal (Fig. 2*A*) is the control kitten, monocularly deprived in the right eye until 5 weeks of age. All the other animals were initially deprived in the right eye and then reverse sutured at different ages: 5, 6, 8, 10, 12 and 14 weeks as shown in Fig. 2*B-F*. All these animals were permitted 9 weeks following reverse suturing in which to use their initially deprived right eye before the

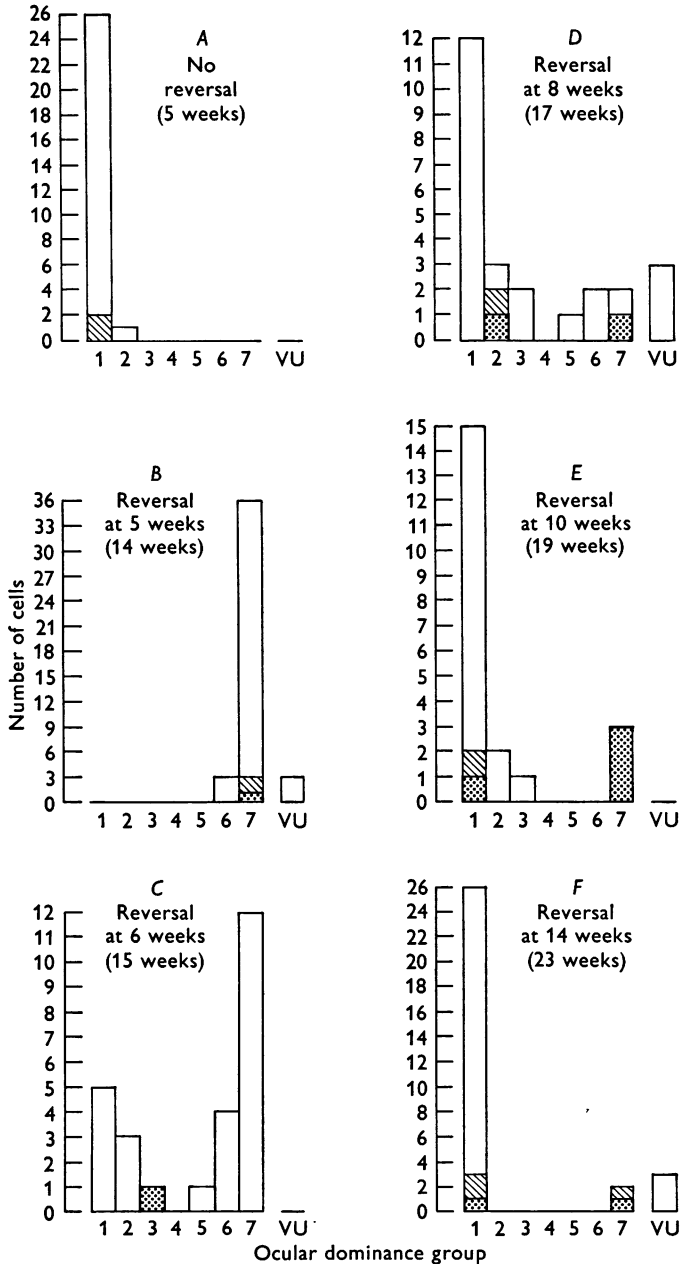


Fig. 2. Ocular dominance histograms with the same conventions as in Fig. 1. *A*, the dominance distribution for the control animal, monocularly deprived in the right eye until 5 weeks, reproduced here for comparison (see Fig. 1*C*). *B-F*, results for five kittens monocularly deprived in the right (ipsilateral) eye until 5, 6, 8, 10 and 14 weeks, respectively, and then reverse sutured. In each case the kitten was then allowed 9 weeks of vision using its right (ipsilateral) eye following reverse suturing (left eyelids closed), before recording at the age indicated in parentheses above the histogram.



recordings were taken. The electrode penetration was always in the right hemisphere, so the right eye was ipsilateral, the left eye contralateral.

It is evident that reverse suturing at 5 weeks caused total reversal of the form of the dominance distribution (compare Fig. 2*A* and 2*B*). With reverse suturing at progressively later ages, however, the switch from contralateral (left) eye to ipsilateral (right) eye was less and less complete. Indeed, reversal at 14 weeks left the dominance distribution virtually unaltered (compare Fig. 2*A* and *F*). For no animal was there a large proportion of binocular neurones.

The reversal index is defined as the ratio of the number of units falling in groups 7, 6 and 5 (dominated by the more recently experienced right eye) to the total number of visually responsive units. It is therefore an indication of the degree of takeover by the originally deprived eye. We calculated the reversal index for each kitten and the results are displayed graphically in Fig. 3. The interrupted line shows the index (0.0) for the control animal, deprived in the right eye until 5 weeks (see Fig. 2*A*). The kitten that was reverse sutured at 5 weeks had a reversal index of 1.0, as if the original period of deprivation in the right eye had never occurred. The curve traced out by reverse suturing at progressively later ages presumably describes the degree of residual plasticity of binocular properties in the cortex and thus provides a description of the form of the latter part of the sensitive period.

#### *Receptive field properties*

The histograms of Fig. 2 also describe the types of receptive field properties. In general the units driven only by the eye that over-all was more dominant (the ipsilateral for Fig. 2*B* and *C*, the contralateral for Fig. 2*D–F*) had quite normal orientation selective receptive fields. But cells that were driven monocularly by the eye that in general was less influential, tended to have non-oriented fields.

It is fascinating to consider the degree of similarity of the receptive fields in the two eyes for the small proportion of binocular cells in these reverse sutured animals, for such neurones have never enjoyed simultaneous binocular stimulation. In the histograms of Fig. 2 the classification of receptive field types is based entirely on the responses through the eye that dominated the cell. However, a number of the binocular units certainly did not have identical receptive field characteristics through both eyes. Table 1 analyses the degree of similarity in the two eyes for all the binocular units. It is in the form of a contingency table, showing for each cell, the field type in the eye that dominated the neurone and the type in the non-dominant eye. In normal animals all neurones have almost identical characteristics in the two eyes, but in these kittens there

were many cells that did not have the same properties in both eyes. The commonest category of such dissimilar cells was, in fact, neurones that were orientation selective in the dominant eye and non-oriented in the non-dominant eye ( $N = 8$ : 36% of all binocular cells). However, it is particularly impressive that the cells that were orientation selective in both eyes ( $N = 11$ : 50%) were always of the same type (simple, complex or hypercomplex) in the two eyes.

TABLE 1. Interocular comparison of receptive field properties.  
N = Reverse sutured animals. (N) = Binocularly deprived animal

Non-dominant eye	Dominant eye					
	Orientation selective			Pure direction selective	Orientalional bias	Non-oriented
	Simple	Complex	Hyper-complex			
Orientation selective						
Simple	1	—	—	—	—	—
Complex	—	7	—	—	—	—
Hypercomplex	—	—	3	—	—	—
Pure direction selective	—	—	—	(1)	—	—
Orientalional bias	1	—	—	—	(11)	—
Non-oriented	1	4	3	1	—	1 (9)

Table 1 also shows (in italics) the comparison of receptive field properties for the 21 binocular units from the binocularly deprived control animal (compare Fig. 1*B*). These data reveal that *all* binocular neurones had very similar fundamental properties in the two eyes. Here then is a basic difference between binocular neurones in animals that have had no visual experience and those that have had vision through both eyes, but never simultaneously.

For each binocular cell that was orientation selective or had an orientational bias in both eyes we analysed carefully the preferred orientations of the two receptive fields. In order to correct for any possible rotation of the eyes after paralysis we routinely photographed the kitten before anaesthesia and after the preparation, and assessed the degree of rotation from the angles of the fissurated entrance pupils. All the measurements of preferred orientation have been corrected for the small amounts of rotation introduced by paralysis. Fig. 4 shows the analysis of the similarity of receptive field orientation in the two eyes for the three normally reared control animals (Fig. 4*A*), for the binocular units in the kittens that had undergone reverse suturing (Fig. 4*B*), and for

the orientational bias cells in the binocularly deprived control animal (Fig. 4C). The sign convention of Blakemore *et al.* (1972) is used to measure the differences in preferred orientation, as described in the Figure legend. In a much more rigorous analysis of interocular differences

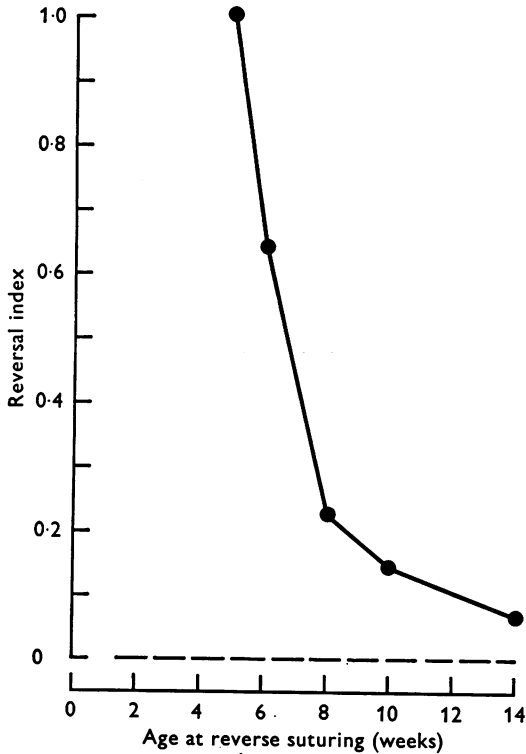


Fig. 3. The time course of the latter part of the sensitive period. The reversal index is the ratio of the number of neurones dominated by the more recently experienced right eye (groups 7, 6 and 5) to the total number of visually responsive cells, and thus provides an indication of the degree to which the initially deprived eye recaptured the cortex. The interrupted horizontal line shows the same ratio calculated for the control animal, monocularly deprived until 5 weeks, which had no neurones in groups 7, 6 or 5 (index = 0.0).

in the normal adult cat, Blakemore *et al.* (1972) found a range of about  $\pm 15^\circ$ . Clearly the three normal kittens produced rather similar results although the range was slightly broader (approximately  $\pm 20^\circ$ ), probably due to less exact techniques of measurement and the inclusion of several quite broadly tuned units in which the preferred orientation was hard to determine. On the other hand, the reverse-sutured animals had a very much wider range of differences in orientation, with some cells having

virtually orthogonally oriented fields in the two eyes. The two distributions (Fig. 4*A* and *B*) are, in fact, significantly different in their variances ( $P < 0.001$ :  $F$  test; d.f. 11, 65). It is important to note that in Fig. 4*B* the neurones found to have the most extreme interocular differences in preferred orientation were nevertheless very orientation selective in both eyes. Thus, these large orientational differences cannot be solely accounted for by cells which had only a crude, and therefore possibly imprecisely determined, orientation preference.

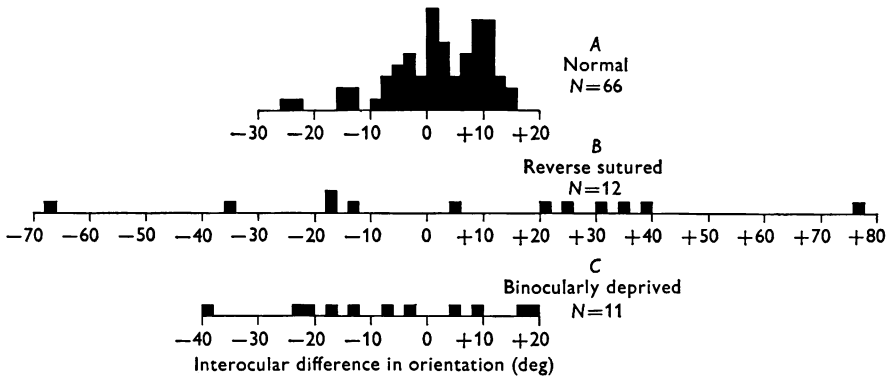


Fig. 4. Histograms showing differences in preferred orientation in the two eyes for: *A*, sixty-six binocular neurones from three normal kittens; *B*, twelve binocular cells from five reverse sutured kittens; *C*, eleven binocular cells from a binocularly deprived kitten. In each case the receptive field orientations were corrected for any rotation of the eyes. Orientations clockwise from horizontal are negative, those anticlockwise are positive. The preferred orientation in the left eye was subtracted from that in the right to obtain the interocular difference plotted on the abscissa.

Fig. 4*C* shows the analysis of binocular cells with an orientation preference in both eyes for the binocularly deprived animal. The distribution, though somewhat less broad than Fig. 4*B*, is still significantly different from the distribution for normal animals ( $P < 0.05$ .  $F$  test, d.f. 10, 65). Less weight can, however, be attached to these results because all these neurones had only a weak orientational bias in each eye.

#### *Cortical architecture*

It is interesting to consider the organization of orientation columns (Hubel & Wiesel, 1962) and ocular dominance columns (Hubel & Wiesel, 1965*b*) in reverse-sutured animals, whose neuronal connectivity has been so totally modified. We reconstructed the micro-electrode penetrations

by searching for the electrolytic lesions placed at a number of points along each track. Figs. 5, 6 and 7 show some typical examples, each one having a sketch of the brain with the position of the penetration indicated, a coronal section with the lesions and the track marked, and, on the right, a schematic reconstruction of the penetration, showing the position and properties of each unit recorded. In these reconstructions the short continuous lines show the preferred orientations of orientation selective

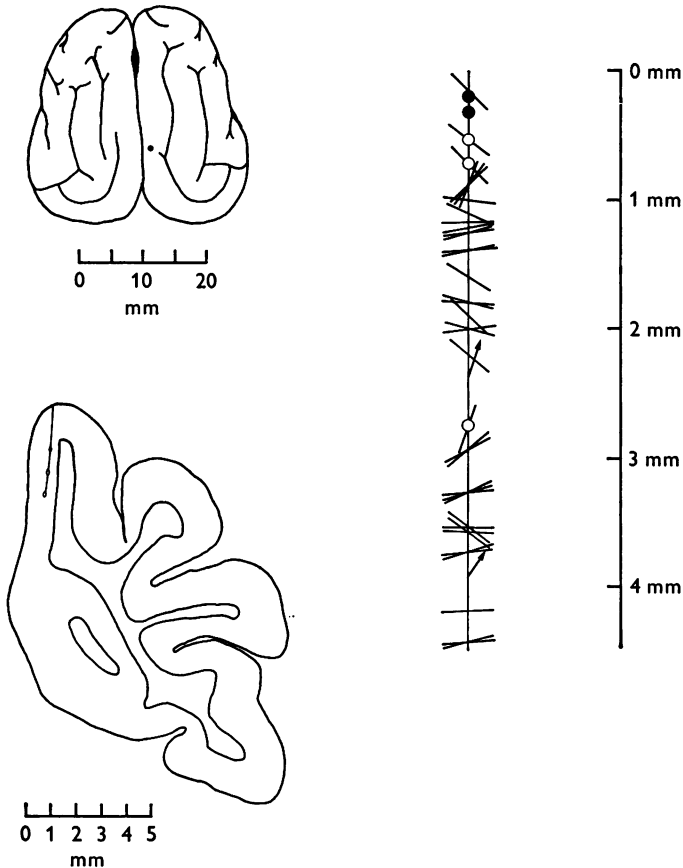


Fig. 5. Penetration reconstruction for the kitten reverse sutured at 5 weeks (see Fig. 2B). The sketch of the cerebral hemispheres shows the position of the penetration (upper left) and the coronal transection through the right hemisphere shows the whole penetration, with three electrolytic lesions marked on it (lower left). The penetration is schematically reconstructed on the right where each symbol indicates the position at which a unit was recorded and its receptive field type in the dominant eye. *Orientation selective* = continuous line at the preferred orientation; *pure direction selective* = arrow in the preferred direction; *non-oriented* = filled circle; *visually unresponsive* = open circle.

cells, the arrows show the preferred directions for pure direction selective units, the empty and filled circles represent visually unresponsive and non-oriented cells respectively and the concentric rings indicate the positions of recordings from afferent geniculate fibres. Cells that had different receptive field types in the two eyes are described on the basis of the properties in the dominant eye.

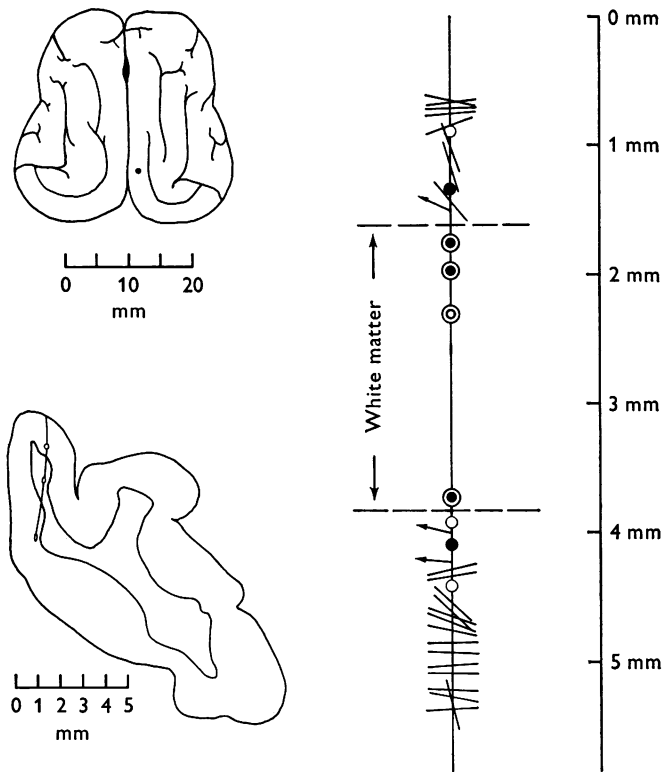


Fig. 6. Penetration reconstruction for the kitten reverse sutured at 14 weeks (see Fig. 2*F*). All the symbols are as in Fig. 5 with the addition of: *afferent geniculate fibre, ON-centre* = concentric circle with open centre; *afferent geniculate fibre, OFF-centre* = concentric circle with filled centre. This penetration, as shown in the coronal section, passed through white matter. The points at which the electrode entered and left the white matter are indicated by interrupted lines on the schematic reconstruction.

The first example (Fig. 5) is from the kitten that was reverse-sutured at 5 weeks (see Fig. 2*B*). Just as in the monocularly deprived animal with no reverse suturing, this animal had no obvious regions of silent cortex. In other words, there was no indication of any subdivision into ocular dominance columns. Certainly, then, the changes occurring during

monocular deprivation and its reversal cannot simply be explained by the silencing of neurones originally dominated by the deprived eye. One eye can take over total control of virtually every neurone and this process can be utterly reversed. On the other hand, the reconstruction shows that, just as in the normal animal, sequentially recorded neurones tended to have very similar preferred orientations. Thus, the organization of the cortex into orientation columns persisted despite wholesale reversals of ocular dominance.

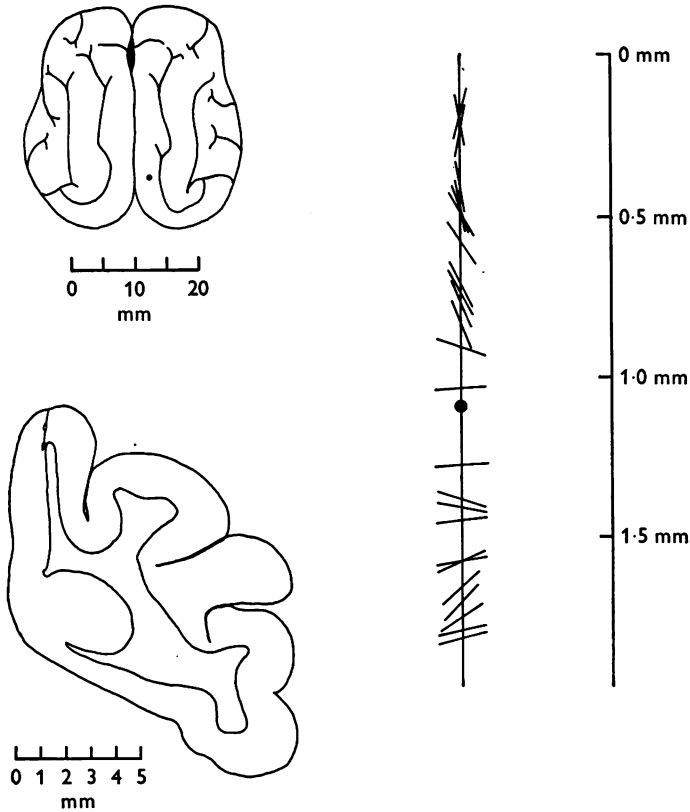


Fig. 7. Penetration reconstruction for the kitten reverse sutured at 6 weeks (see Fig. 2C). The symbols are as in Fig. 5.

Fig. 6 illustrates the results for the animal that was reverse sutured at 14 weeks (see Fig. 2F). This penetration clearly passed through a large region of white matter (indicated by dashed lines on the reconstruction) within which the only units recorded were afferent geniculate fibres. However, in the grey matter itself there was again clear evidence of columnar organization according to orientational preference, but there





the cortex but again orientation columns were very evident. In this case there was also a very distinct grouping of cells according to their ocular dominance. Fig. 8 shows the same penetration reconstructed to illustrate the ocular dominance of the cells. Each filled circle represents the position of a unit along the penetration and the abscissa shows its ocular dominance group. There are occasional sudden transitions from a cluster of cells dominated by one eye to a group dominated by the other eye. These ocular dominance columns are shown as bracketed regions in Fig. 8.

*Simple behavioural observations*

We tested the visual behavioural repertoire of every experimental animal in the originally open, left eye immediately before reverse suturing. Every kitten, including the one reverse sutured at 5 weeks had excellent visually guided behaviour at this stage and they all passed each of the tests described in the Methods. Their visual ability through the initially

TABLE 2. Visual behaviour immediately before recording

Age of the kitten at reverse suturing	Behavioural tests				
	Visual following	Visual startle	Depth perception	Visual placing	Optokinetic nystagmus
5 weeks { Right eye	x	x	x	x	x
{ Left eye	—	—	—	—	x
6 weeks { Right eye	x	x	x	x	x
{ Left eye	—	—	—	—	x
8 weeks { Right eye	x	x	x	x	x
{ Left eye	x	x	x	x	x
10 weeks { Right eye	x	x	x	x	x
{ Left eye	—	—	x	x	x
14 weeks { Right eye	—	—	—	x	x
{ Left eye	—	x	x	x	x

deprived, right eye was tested immediately after reverse suturing and occasionally at intervals during the following 14 week period. In general all the kittens were behaviourally blind in the right eye when it was first opened, but the animals reverse sutured very early (at 5–8 weeks) showed fast progressive recovery of visual function. All the kittens were tested thoroughly using each eye separately, and then with both eyes open, when the left eye had been reopened just before recording. Table 2 summarizes the visual performance of all the kittens, at that stage. In this Table a cross indicates that the particular visual behaviour was present, while no entry indicates that it was absent.

There is fairly good correspondence between the relative visual

capabilities through the two eyes and the cortical physiology. The animals that were reverse sutured at 5 and 6 weeks had no visual capacity (except for clear optokinetic nystagmus) using the left eye, which had been robbed of its representation in the cortex, but had excellent visuomotor coordination using the right eye. The cats reverse sutured at 8, 10 and 14 weeks had at least some vision through both eyes but with progressively less visual ability in the newly experienced right eye. In every case visual behaviour with both eyes open was as good as with the better eye alone.

#### DISCUSSION

Our experiments have confirmed Wiesel & Hubel's (1965*a*) observations that binocular connexions are established and maintained in the cortex without any patterned visual experience, but that quite a brief period of monocular deprivation early in life can lead to total domination of the cortex by the experienced eye. Hubel & Wiesel (1970) have also demonstrated very convincingly that the consequences of monocular deprivation are severe only if the period of deprivation occurs sometime between about 3 weeks and 4 months of age (Hubel & Wiesel, 1970), and that the susceptibility decreases considerably in the latter half of this sensitive period.

We wondered whether the sensitive period might be a time during which binocular cells have the capacity to abandon, once and for all, their connexions from one of the eyes, or whether it is a period of true neuronal plasticity, during which connexions can be broken and re-made any number of times. In fact we have found that reverse suturing early in the sensitive period causes total re-establishment of the effectiveness of the deprived eye (Fig. 2). The degree to which the initially deprived eye recaptures cortical neurones dramatically declines as the act of reverse suturing is delayed (Fig. 3) thus tracing out a sensitive period apparently very similar to that for the actual first induction of the effects of monocular deprivation. The sensitive period is, then, a time when the afferent connexions of cortical cells are utterly plastic. The pattern of connectivity gradually gels, and finally sets sometime after 14 weeks of age.

To what extent any modifiability remains in the adult cat's cortex is a question of debate; but, given the roughly exponential decline early in life, it is not wholly surprising to find that extremely prolonged periods of reverse suturing can lead to some recapture of the cortex by a deprived eye, even in the adult (Chow & Stewart, 1972).

The present experiments provide no information about the rate at which a deprived eye can recapture cortical neurones after early reverse

suturing. However Pettigrew, Olson & Barlow (1973) have demonstrated changes in ocular dominance for some cortical neurones, following very brief periods of monocular stimulation in anaesthetized kittens. Current experiments here in Cambridge (J. A. Movshon, in preparation) have shown that recapture is virtually complete only a week or so after reverse suturing at 5 weeks.

Binocularity is certainly an innate characteristic of the cortex, but the exact receptive field properties seem to be only partially specified on the basis of genetic information alone. We found only a crude form of orientational preference in the visually inexperienced kitten's cortex and many of the neurones in such an animal have totally non-oriented receptive fields. It is interesting to find that in our reverse sutured animals, whichever eye was in general less dominant tended to have these same infantile receptive field properties. So it seems that as an eye loses its control over cortical cells the receptive fields in that eye revert from an adult to a more primitive form: likewise, as the input from the second eye begins to recapture the cortex its receptive fields pass through an infantile stage before developing normal adult properties. So it is unlikely that the effects of monocular deprivation and its reversal are due simply to the silencing of a set of well specified connexions from the initially deprived eye and their perfect re-establishment after reverse suturing. Rather it seems that certain receptive field properties are independently determined by each eye's experience.

In that case, are there any innate limitations on the receptive field properties that a neurone can adopt? The fact that orientation selectivity can be modified, after selective visual experience of edges at one angle, suggests that receptive field characteristics are indeed extremely plastic (Hirsch & Spinelli, 1971; Blakemore & Cooper, 1970; Blakemore & Mitchell, 1973). However our present data do point out certain genetic constraints on the properties of cortical cells. For instance, for the few binocular cells in our animals (which had never experienced simultaneous vision through both eyes), if both receptive fields were orientation selective, then the basic receptive field type (simple, complex or hypercomplex) was *always* the same in the two eyes (Table 1). Therefore this basic quality of a cortical neurone does seem to be innately determined – hardly a surprising conclusion if these different classes of cortical unit represent anatomically distinguishable neuronal types in the adult (Van Essen & Kelly, 1973).

On the other hand, our experiments provide further evidence for the immense plasticity of orientation selectivity. When neurones in our animals were clearly orientation selective in both eyes the preferred orientations could differ by more than  $70^\circ$  in the two eyes (Fig. 4B).

There appears then, to be an extremely loose genetic hold on the orientation selectivity of a cell and, within very broad limits this preference can be altered, even independently in the two eyes, and even after it has been specified completely in one of the eyes. This finding incidentally argues against the notion that the preferred orientation of a cell is determined solely by the shape of its dendritic tree (Colonnier, 1964), even though this may be the case in the squid (Young, 1973). It appears, rather, that this property is dependent mainly on the particular set of effective incoming fibres, and that it can differ markedly for the inputs from the two eyes.

Why then does the normal cat have such a small range of differences in preferred orientation (Fig. 1A and Blakemore *et al.* 1972)? Presumably this characteristic is a function of normal simultaneous binocular vision, with correct ocular alignment, in which both of the receptive fields would be likely to experience retinal images of similar orientation – the images of single objects in space. In that case, the real biological function of the modifiability of preferred orientation might be to ensure that the two receptive fields of a binocular cell do indeed adopt very similar preferred orientations in the two eyes – a necessary property for their role in binocular fusion and stereopsis (Barlow, Blakemore & Pettigrew, 1967).

One intriguing finding was that aggregations of neurones according to ocular dominance reappeared as the cortex was partially recaptured by the second eye (Fig. 8), even though the cortex had certainly gone through a stage at which every neurone was entirely dominated by the other eye. Of course one cannot conclude that these newly formed ocular dominance columns are identical in arrangement to those originally present: but some process must ensure that neighbouring neurones tend to be reoccupied to about the same extent. Thus, as one eye gains more and more influence over the visual cortex, the size of its ocular dominance columns increases at the expense of those of the other eye.

It was gratifying to see some correspondence between the physiology of the visual cortex and the behavioural capacities of our animals (Table 2). The only really surprising result was that animals reverse sutured rather late in the sensitive period made roughly equal use of both eyes, despite the fact that the right eye had regained almost no influence in the cortex and its receptive fields were in general very poorly specified.

The sensitive period is clearly established as a time of extraordinary neuronal plasticity in the kitten's cortex. It seems that the period during which environmental modification of preferred orientation can be induced (Blakemore, 1973, and in preparation) coincides remarkably with the 3 week to 4 month sensitive period for the induction or reversal of the

consequences of monocular deprivation. It is within this same period that the media of the eyes are clearing completely and the visual axes becoming properly aligned (Sherman, 1972). Why then does the sensitive period start and end when it does? In teleological terms it would be disastrous for it to begin much earlier because normal lid opening, at about 10 days, does not necessarily occur simultaneously in both eyes. If the critical period had already begun, such natural asynchrony in lid opening could cause changes in cortical binocularity. Also the extreme divergence of the visual axes present before 3 weeks would act as a condition of strabismus, which also causes a loss of binocularity if it occurs during the sensitive period (Hubel & Wiesel, 1965*b*). The termination of the sensitive period, very gradual though it is, is more difficult to explain, even in such teleological terms. However, the normal animal, by the age of 2 months or so, has clear ocular media and properly aligned visual axes: it has had sufficient visual experience to stamp in the binocularity of its cortical neurones, to specify their receptive field properties and to ensure that binocular neurones have adopted very similar properties in the two eyes. It is ready to deal with the visual world.

This work was supported by a Programme Grant (No. G972/463/B) to C.B. from the Medical Research Council, London. We are grateful to R. D. Loewenbein, J. S. Dormer and R. M. Cummings for their expert technical assistance.

## REFERENCES

- BARLOW, H. B., BLAKEMORE, C. & PETTIGREW, J. D. (1967). The neural mechanism of binocular depth discrimination. *J. Physiol.* **193**, 327-342.
- BARLOW, H. B. & PETTIGREW, J. D. (1971). Lack of specificity of neurones in the visual cortex of young kittens. *J. Physiol.* **218**, 98-100*P*.
- BLAKEMORE, C. (1973). Developmental factors in the formation of feature extracting neurons. In *The Neurosciences: Third Study Program*, ed. SCHMITT, F. O. & WORDEN, F. G. Cambridge, Mass., M.I.T. Press (in the Press).
- BLAKEMORE, C. & COOPER, G. (1970). Development of the brain depends on the visual environment. *Nature, Lond.* **228**, 477-478.
- BLAKEMORE, C., DONAGHY, M. J., MAFFEI, L., MOVSHON, J. A., ROSE, D. R. & VAN SLUYTERS, R. C. (1974). Evidence that nitrous oxide can be an adequate anaesthetic after induction with barbiturates. *J. Physiol.*, **237** (in the Press).
- BLAKEMORE, C., FIORENTINI, A. & MAFFEI, L. (1972). A second neural mechanism of binocular depth discrimination. *J. Physiol.* **226**, 725-749.
- BLAKEMORE, C. & MITCHELL, D. E. (1973). Environmental modification of the visual cortex and the neural basis of learning and memory. *Nature, Lond.* **241**, 467-468.
- BLAKEMORE, C. & PETTIGREW, J. D. (1970). Eye dominance in the visual cortex. *Nature, Lond.* **225**, 426-429.
- CHOW, K. L. & STEWART, D. L. (1972). Reversal of structural and functional effects of long-term visual deprivation in cats. *Expl Neurol.* **34**, 409-433.

- COLONNIER, M. (1964). The tangential organisation of the visual cortex. *J. Anat.* **98**, 327-344.
- DEWS, P. B. & WIESEL, T. W. (1970). Consequences of monocular deprivation on visual behaviour in kittens. *J. Physiol.* **206**, 437-455.
- GANZ, L., FITCH, M. & SATTERBERG, J. A. (1968). The selective effect of visual deprivation on receptive field shape determined neurophysiologically. *Expl Neurol.* **22**, 614-637.
- GANZ, L. & FITCH, M. (1968). The effect of visual deprivation on perceptual behaviour. *Expl Neurol.* **22**, 638-660.
- GIBSON, E. J. & WALK, R. D. (1960). The 'visual cliff'. *Sci. Amer.* **202**, 64-71.
- HEIN, A. & HELD, R. (1967). Dissociation of the visual placing response into elicited and guided components. *Science, N.Y.* **158**, 390-392.
- HIRSCH, H. V. B. & SPINELLI, D. N. (1971). Modification of the distribution of receptive field orientation in cats by selective visual exposure during development. *Expl Brain Res.* **13**, 509-527.
- HUBEL, D. H. & WIESEL, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J. Physiol.* **160**, 106-154.
- HUBEL, D. H. & WIESEL, T. N. (1963). Receptive fields of cells in striate cortex of very young, visually inexperienced kittens. *J. Neurophysiol.* **26**, 994-1002.
- HUBEL, D. H. & WIESEL, T. N. (1965*a*). Receptive fields and functional architecture in two non-striate visual areas (18 and 19) of the cat. *J. Neurophysiol.* **28**, 229-289.
- HUBEL, D. H. & WIESEL, T. N. (1965*b*). Binocular interaction in striate cortex of kittens with artificial squint. *J. Neurophysiol.* **28**, 1041-1059.
- HUBEL, D. H. & WIESEL, T. N. (1970). The period of susceptibility to the physiological effects of unilateral eye closure in kittens. *J. Physiol.* **206**, 419-436.
- LEVICK, W. R. (1972). Another tungsten microelectrode. *Med. & Biol. Engng* **10**, 510-515.
- PETTIGREW, J., OLSON, C. & BARLOW, H. B. (1973). Kitten visual cortex: short-term, stimulus-induced changes in connectivity. *Science, N.Y.* **180**, 1202-1203.
- SHERMAN, S. M. (1972). Development of interocular alignment in cats. *Brain Res.* **37**, 187-203.
- VAN ESSEN, D. & KELLY, J. (1973). Correlation of cell shape and function in the visual cortex of the cat. *Nature, Lond.* **241**, 403-405.
- WIESEL, T. N. & HUBEL, D. H. (1963*a*). Single-cell responses in striate cortex of kittens deprived of vision in one eye. *J. Neurophysiol.* **26**, 1003-1017.
- WIESEL, T. N. & HUBEL, D. H. (1963*b*). Effects of visual deprivation on morphology and physiology of cells in the cat's lateral geniculate body. *J. Neurophysiol.* **26**, 978-993.
- WIESEL, T. N. & HUBEL, D. H. (1965*a*). Comparison of the effects of unilateral and bilateral eye closure on cortical unit responses in kittens. *J. Neurophysiol.* **28**, 1029-1040.
- WIESEL, T. N. & HUBEL, D. H. (1965*b*). Extent of recovery from the effects of visual deprivation in kittens. *J. Neurophysiol.* **28**, 1060-1072.
- YOUNG, J. Z. (1973). Receptive fields of the visual system of the squid. *Nature, Lond.* **241**, 469-471.