

Synaptic Competition in the Kitten's Visual Cortex

Colin Blakemore, Richard C. Van Sluyters and J. Anthony Movshon

Cold Spring Harb Symp Quant Biol 1976 40: 601-609 Access the most recent version at doi:10.1101/SQB.1976.040.01.056

References	This article cites 28 articles, 16 of which can be accessed free at: http://symposium.cshlp.org/content/40/601.refs.html
Email alerting service	Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article or click here

To subscribe to Cold Spring Harbor Symposia on Quantitative Biology go to: http://symposium.cshlp.org/subscriptions

Synaptic Competition in the Kitten's Visual Cortex

COLIN BLAKEMORE, RICHARD C. VAN SLUYTERS* AND J. ANTHONY MOVSHON[†] Physiological Laboratory, University of Cambridge, Cambridge CB2 3EG, England

Plasticity of Synaptic Input to Cells in the Kitten's Visual Cortex

A large fraction of the cat's visual field is shared between the two eyes; correspondingly, the majority of neurons in the part of the visual cortex representing the binocular field have input from both eyes (Hubel and Wiesel 1962). Most of these cortical neurons have receptive fields that are highly selective for the orientation of a moving edge and they often have preferences for many other aspects of the visual stimulus, such as its direction, length and velocity of movement (Hubel and Wiesel 1962, 1965a; Pettigrew et al. 1968a; Rose 1974; Movshon 1975). Remarkably, in most cases the stimulus requirements of these binocular neurons are exactly matched in the two eyes. The preferred orientation, the optimal width and contrast of the stimulus and the best velocity of movement are usually similar for the two receptive fields of a single cell (Hubel and Wiesel 1962; Noda et al. 1971; Blakemore et al. 1972). In addition, the receptive fields are on roughly corresponding regions of the two retinae, so each cell is likely to be stimulated simultaneously by the two retinal images of a single object in space. Indeed, there can be strong interaction between the two synaptic inputs, so that some binocular cells exhibit facilitation when stimulated with a correctly positioned image shown simultaneously to the two eyes, whereas inappropriate relative positioning can produce powerful occlusion of the response (Barlow et al. 1967; Pettigrew et al. 1968b). This creates a preference for the retinal disparity of the stimulus, which, together with the fact that the optimal disparity varies somewhat from cell to cell, has led to the suggestion that binocular neurons are involved in the analysis of stereoscopic cues to the distances of objects in space (Barlow et al. 1967; Nikara et al. 1968; Joshua and Bishop 1970).

There is no doubt that most cat cortical neurons, even those in very young kittens, are innately supplied with input from both eyes, though there is much debate about the degree of stimulus specificity that these synapses bestow upon the cells (Hubel and Wiesel 1963; Barlow and Pettigrew 1971; Pettigrew 1974; Blakemore and Van Sluyters 1975). Indeed, in kittens and monkeys without visual experience, the visual cortex is already organized into the pattern of "ocular dominance columns" found in the adult cat and, even more obviously, in the monkey (Hubel and Wiesel 1965b; Wiesel et al. 1974; LeVay et al. 1975). Neurons tend to be grouped together according to the eye that provides the stronger input. Thus, during a long penetration through the cortex, there are shifts in ocular dominance from neurons more strongly influenced by one eye to those dominated by the other. Figure 1 shows reconstructions of microelectrode penetrations in two very young kittens (9 and 19 days old) that had not had prior visual experience. Each visually responsive neuron was classified into one of the seven ocular dominance groups of Hubel and Wiesel (1962) (see figure legend). The two penetrations are schematically reconstructed in a form showing the position of each cell recorded and its ocular dominance group. In these inexperienced kittens, it is clear that there were progressive shifts in ocular dominance as pronounced as those seen in the adult cat. In monkeys, the actual pattern of termination of axons from the laminae of the lateral geniculate nucleus seems to correlate exactly with the arrangement of ocular dominance columns (Hubel and Wiesel 1972; Wiesel et al. 1974; LeVay et al. 1975). Perhaps the arrangement of binocular neurons observed in neonatal kittens reflects the genetically guided distribution of afferent terminals in the visual cortex.

Binocularity is, then, well established in the cortex by the time a kitten opens its eyes. Moreover, binocular connections usually survive over long periods of deprivation of binocular visual experience (Wiesel and Hubel 1965; Pettigrew 1974) or normal visual experience. However, there is immense plasticity of synaptic input to the visual cortex in the first few months of a kitten's life-plasticity that can rob the cortex almost entirely of its binocularity. A variety of procedures will rapidly reduce the proportion of binocular cells: the induction of an artificial strabismus or alternating occlusion of the two eyes produces a very exaggerated pattern of ocular dominance columns, so that most neurons are purely monocularly driven (Hubel and Wiesel 1965b); presentation of dissimilar images to each of the two eyes or rotation of one eye has much the same effect (Hirsch and Spinelli 1970; C. Blakemore, R. C. Van Sluyters, C. K. Peck and A. Hein, in prep.). Perhaps the most dramatic rearrangement is produced simply by covering one eye (Wiesel and Hubel 1963, 1965). Even very brief monocular deprivation sometime during the second or third month of life can utterly transform the arrangement of ocular dominance columns in a kitten's visual

Present addresses: *School of Optometry, University of California, Berkeley, California 94720; †Department of Psychology, New York University, New York, New York 10003.

602

BLAKEMORE ET AL.



Figure 1. Ocular dominance columns in the visual cortex of very young kittens with no previous visual experience. (A) Nineday-old kitten at the time of natural lid opening. (B) Nineteen-day-old animal reared in total darkness.

On the right in both A and B is a coronal cross section of the right hemisphere, which shows the course of the microelectrode penetration as reconstructed from the electrolytic lesions indicated by filled circles on the track. On the left, the sequence of neurons recorded in the penetration is shown by dots that plot the depth of each cell and its ocular dominance group, using the seven-point scale introduced by Hubel and Wiesel (1962): 1 and 7-monocularly driven solely by either the contralateral (left) or ipsilateral (right) eye, respectively; 2 and 6-binocularly driven, but are much more strongly influenced by either the contralateral or ipsilateral eye, respectively; 3 and 5-slightly dominated by either the contralateral or ipsilateral eye. The columns are added to produce the ocular dominance histograms below.

In A, the electrode passed briefly through the fiber layer under the cortex, marked "white matter" on the reconstruction. In B, the microelectrode was deliberately advanced three times without stopping, marked by downward arrows, to increase the region of cortex sampled.

cortex. Almost all neurons become completely dominated by the input from the experienced eye (Hubel and Wiesel 1970; Olson and Freeman 1975).

Figure 2 shows ocular dominance histograms from four animals deprived of patterned visual experience in one eye. The first two animals had the lids of the right eye sutured closed (A) from before natural eye opening until 4 weeks and (B) for just 48 hours on the 28th and 29th days of life. The other two animals were deprived in the left eye: the first (C) had both eyes closed until 29 days, when the right eye was opened for only 6 hours (Peck and Blakemore 1975), and the final animal (D) received visual experience only when wearing goggles containing a translucent diffuser over the left eye and a matched, transparent, neutral density filter over the other eye (ensuring that both retinas received the same mean level of illumination, but that the left eye and a matched, transparent, neutral density images). In each case, the results were the same: the eye that had been deprived of patterned visual experience lost control over cortical cells. Hubel and Wiesel (1965b) have suggested that there is some kind of competition between the synaptic input to the cortex from each

eye. The necessary condition for binocularity to be maintained is that the two convergent pathways onto each cortical cell should reliably receive simultaneous, correlated signals. This can only be achieved if both eyes are correctly aligned and if the condition of the two retinal images is very similar. These requirements must normally be adequately met for it is very unusual to find an ordinary adult cat with obviously reduced binocularity in the visual cortex.

The experiments to be described in this paper are concerned with the nature of the rearrangement of synaptic input that might underlie changes in cortical ocular dominance.

METHODS

Our general procedures have been detailed elsewhere (Blakemore and Van Sluyters 1975). Kittens were reared in an isolated breeding colony of domestic tabby cats, maintained on an artificial day/night cycle of 18 hours light and 6 hours dark.

Monocular deprivation was achieved by the conventional technique of suturing together the lids of one



Figure 2. Ocular dominance histograms for neurons (all recorded in the right hemisphere) from four monocularly deprived kittens. (A) The right (ipsilateral) eyelids were sutured closed from before natural lid opening until recording at 4 weeks. (B) The right eyelids were sutured for 48 hr on days 28 and 29, after previous normal binocular vision. (C) Both eyes were closed until day 29, when only the right eye was opened for 6 hr. (D) This kitten was reared in total darkness and received its only visual experience wearing goggles with a translucent diffuser over the left eye and a transparent neutral density filter, producing the same overall attenuation of flux as the diffuser, over the right eye. In each example, the ocular dominance histogram is shifted in favor of the eye that received patterned retinal images.

eye. In addition, we usually took the precaution of suturing together, over the cornea, the dissected flaps of conjunctiva underneath the lids. This ensured that if a "window" developed in the sutured eyelids, the cornea would still be covered with a diffusing sheet of conjunctiva, so the kitten would not obtain any extraneous visual experience before the window could be repaired (Blakemore and Van Sluyters 1975).

The animals were prepared for electrophysiology under Fluothane and then barbiturate (Brietal sodium) or steroid (Althesin) anesthesia. During the actual recording, they were artificially respirated with approximately 75% N₂O/23% O₂/2% CO₂. Eye stability was achieved by continuous infusion of Flaxedil, 10 mg/kg · hr, in 6% glucose solution, together with bilateral cervical sympathectomy. Contact lenses, artificial pupils and additional correcting lenses were used to preserve good retinal image quality. Simple cutout stimuli, such as spots, edges and slits, were back-projected from an overhead projector onto a tangent screen 57 cm in front of the cat.

The responses of cortical neurons were analyzed qualitatively. Each eye was covered in turn, and the

receptive field was mapped out with moving and flashing stimuli. Cells were classified as simple, complex, hypercomplex (Hubel and Wiesel 1962, 1965a), pure direction selective, orientational bias or non-oriented (Blakemore and Van Sluyters 1975), and qualitative records were kept of the preferred orientation, the angular selectivity and the preference of the cell for stimulus size, velocity and direction of movement.

RESULTS

The effects of prolonged reverse suturing. It has been demonstrated (Blakemore and Van Sluyters 1974) that the reorganization imposed on the cortex by a period of monocular deprivation can be partially or completely reversed by opening the deprived eye and closing the experienced eye, as long as this reverse suturing is performed within the "sensitive period" originally described by Hubel and Wiesel (1970). All the animals in this series were monocularly deprived by suturing the lids of the right eye until a certain age, when that eye was reopened and the left eye closed. The age at reverse suturing varied between 5 and 14 weeks (that is, from approximately the most sensitive age for the actual effects of initial monocular deprivation to the age at which monocular deprivation no longer has severe consequences for an animal that has previously had normal binocular vision).

Figure 3 shows ocular dominance histograms for six kittens in this series. In every case, recordings were taken from the right hemisphere, contralateral to the originally experienced left eye. As shown in Figure 3A, the effect of the initial period of deprivation in the right (ipsilateral) eye was to make virtually all cortical neurons totally dominated by the contralateral (left) eye, shifting nearly all of them into Group 1 of the ocular dominance histogram. On the other hand, the animal reverse sutured at 5 weeks and allowed a further 9 weeks to use its initially deprived right eye showed a complete reversal of ocular dominance: almost every cell belonged to Group 7, being dominated by the newly experienced, ipsilateral right eye (Fig. 3B). At the other end of the scale, the animal reverse sutured at 14 weeks and again allowed a further 9 weeks to use its newly experienced ipsilateral eye still had a cortex dominated by the contralateral (left) eye, which first had visual experience and was open throughout most of the sensitive period (Fig. 3F). The other animals illustrated in Figure 3, all of which had their right eye reopened for a period of 9 weeks, show that the value of this procedure in restoring the input to cortical cells from the deprived eye decreases progressively between 5 and 14 weeks of age.

In Figure 4, the results of this experiment are summarized and compared with those of Hubel and Wiesel. In the upper graph are plotted the data of Hubel and Wiesel (1963, 1970) and Wiesel and Hubel (1965). The animals in their experiments were simply monocularly deprived, after an original period of binocular vision, by closing the eye contralateral to the

604

BLAKEMORE ET AL.



Figure 3. Ocular dominance histograms after long-term reverse suturing at different ages. In each case, recordings were taken from the right hemisphere. (A) Right eyelid closed from the time of natural eye opening until 5 weeks, then immediate recording without reverse suturing; (B) right eye closed until 5 weeks, left eye closed from weeks 5-14; (C) right eye closed until 6 weeks, left from weeks 6-15; (D) right eye closed until 8 weeks, left from weeks 8-17; (E) right eye closed until 10 weeks, left from weeks 10-19; (F) right eye closed until 14 weeks, left from weeks 14-23. The small number of visually unresponsive cells found in these kittens is not included in these diagrams.

hemisphere to be recorded from in the future. Each bar on this graph shows, on the abscissa, the period for which the animal was monocularly deprived. The ordinate is the induction index, defined as the ratio of the number of cells dominated by the experienced eye to the total number of visually responsive neurons. The curve fitted to these results defines the sensitive period, which rises to maximum sensitivity around the fourth and fifth weeks of life and then declines slowly until about 4 months of age. The lower graph shows the data from Figure 3 presented in a form similar to the upper graph. The abscissa is now the period for which the animal was reverse sutured; the ordinate plots the reversal index, defined as the proportion of visually responsive neurons dominated by the second eye to be opened. These two graphs agree quite well in their general form, defining the time course of the change in sensitivity to the effects of monocular deprivation, or its reversal, during the latter half of the sensitive period. Apparently this time in a kitten's life represents a period when the synaptic input to cortical cells is extremely plastic.

The speed of recapture after reverse suturing. Experiments have shown that ocular dominance can be changed by long periods of enforced use of the deprived eye alone (Blakemore and Van Sluyters 1974). But a single episode of monocular deprivation, even if very brief (Fig. 2B,C), can have dramatic effects. It is natural to ask whether the time course of the reversal of these effects is similar to the time course of their onset. This question has been examined in some detail (Movshon and Blakemore 1974; J. A. Movshon, in prep.) by reverse suturing animals at different ages for different periods of time. The basic plan of the experiments was the same as that already described: the right eye was sutured first and then it was opened and the left eye closed. Recordings were always taken from the right hemisphere. Figure 5 illustrates the results for a series of animals reverse

sutured at the age of only 4 weeks. Results for a control animal, which was not reverse sutured but from which recordings were taken at the age of 4 weeks (immediately after the first period of monocular deprivation), are shown in Figure 2A.

It can be seen from this series of four reversesutured animals that the newly experienced ipsilateral eye rapidly recaptures cortical neurons. Within 3 days, more than half the cells are dominated by the newly experienced eye; only 9 days after reverse suturing, the process of takeover is virtually complete. The results are shown graphically below the ocular dominance histograms, using the same ordinate (the reversal index) as in the lower graph in Figure 4. The abscissa shows the amount of time that the animal used its initially deprived eye after reverse suturing.

Thus early in the sensitive period, at 4 or 5 weeks of age, reestablishment of synaptic input from a deprived eye can be rapid and total. The process is somewhat slower when reverse suturing is done at 5 weeks rather than at 4 weeks (Movshon and Blakemore 1974), but in either case, it is virtually complete within 3 weeks after reverse suturing. Later in the sensitive period not all cells are recaptured, even within 9 weeks (Fig. 3C-F), but in that fraction of the population that does switch ocular dominance, the rate of changeover is not markedly different from that after reversal at 5 weeks. Thus from 5 weeks on, there may be a decreasing fraction of labile cells still capable of switching ocular allegiance, whereas the speed with which they are able to make the change may not be radically altered throughout the rest of the sensitive period.

The strategy of reinnervation. After reverse suturing, the initially deprived eye does not reestablish its connections randomly, but in an ordered morphological pattern. The probability of a neuron being recaptured depends on its position in the visual cortex. Immediately after reverse suturing, there is, of course, no evidence of ocular dominance columns in the visual



Figure 4. The sensitive period for the effects of initial monocular deprivation and reverse suturing. The upper graph plots the results of Hubel and Wiesel (1963, 1970) and Wiesel and Hubel (1965). Kittens were monocularly deprived by suturing the lids of the eye contralateral to the future recording site. The period of monocular deprivation (sometimes very brief) is plotted as a bar on the abscissa. The induction index is the proportion of all visually responsive cells that belonged to Groups 5, 6 and 7. The interrupted line shows the same index calculated for 224 cells from normal cats. The lower graph shows, on the same abscissa, the results of Blakemore and Van Sluyters (1974). Each kitten had only the contralateral eye open until the age indicated by the beginning of the solid bar. It then was reverse sutured and allowed a further 9 weeks of vision, as indicated by the length of the bar. The reversal index is the proportion of cells dominated by the ipsilateral eye, the second one to be open. The interrupted line is the same index calculated for a control animal monocularly deprived in the ipsilateral eye until 5 weeks with no reverse suturing.

cortex: all neurons are heavily dominated by the experienced eye. However, if reverse suturing has occurred early enough, this situation is completely reversed within a short time: all neurons become controlled by the new eye, and again there is no evidence of ocular dominance clustering. But while this reversal is occurring, a remarkably systematic process takes place. When cells dominated by the newly experienced eye first make their appearance, they do so in small clusters situated among the many unchanged neurons. Thus during a long penetration through the cortex, ocular dominance does not switch randomly from one cell to the next. The clusters of neurons dominated by



Figure 5. Results of J. A. Movshon (in prep.) showing the consequences of short periods of vision following reverse suturing. The four ocular dominance histograms apply to kittens that had the ipsilateral eye closed until 4 weeks and then were reverse sutured and allowed normal vision for the number of days shown above each histogram and plotted on the abscissa of the graph below. The reversal index is defined in Figure 4.

the new eye appear to grow in size in a regular fashion, expanding until they finally occupy virtually the whole surface of the visual cortex. Figure 6 shows reconstructions of two penetrations from animals reverse sutured at the age of 5 weeks. These kittens were allowed 6 days (Fig. 6A) and 9 days (Fig. 6B) to use their ipsilateral eyes. If the sequential alternation between cells strongly dominated by one eye and those dominated by the other can be taken as evidence of ocular dominance columns, then such columns have clearly been reestablished during the period of reinnervation.

Thus an ocular dominance column cannot be looked upon as an immutable element of cortical organization. Columns can appear, expand, and swamp the cortex in just a few days.

In the normal adult monkey, there seems to be a very close correspondence between these physiologically determined ocular dominance columns and the anatomical layout of axonal arborizations from the ipsilaterally and contralaterally driven laminae of the lateral geniculate nucleus (Hubel and Wiesel 1972; Wiesel et al. 1974; LeVay et al. 1975). Does this mean, then, that the appearance and growth of physiological ocular dominance columns in the reverse-sutured kitten represent the appearance or growth of afferent axons from the deprived laminae of the geniculate nucleus? This would seem to be the most parsimonious explanation of our results. However, it demands a quite unprecedented speed of axonal growth. The small islands of newly dominated 606

BLAKEMORE ET AL.



Figure 6. Penetration reconstructions, of the type shown in Figure 1, for two reversesutured animals. (A) Contralateral eye alone open until 5 weeks, then the ipsilateral eye alone was open for 6 days; (B) contralateral eye alone open until 5 weeks, then the ipsilateral eye alone open for 9 days.

On the schematic reconstructions in both A and B, visually unresponsive cells are shown as open circles under the column labeled "U." The regions heavily dominated by either the contralateral (C) or ipsilateral (I) eye are bracketed, and arrows indicate their positions in the coronal section of the cortex and the presumed radial divisions into ocular dominance columns. The heavy line on the coronal section, marked by a large filled arrow, is the penetration track.

cells are usually encountered at roughly 0.5- to 1-mm intervals (see Fig. 6). If this represents the approximate center-to-center distance between neighboring ocular dominance columns (or, more correctly, slabs, if they have the same shape in the cat as in the monkey), then the borders of each expanding column would have to approach those of its neighbors at up to $50-100 \ \mu m$ per day. If this pattern does represent invasion by a new set of afferent axons, it implies a remarkable speed of axonal growth.

There is an alternative hypothesis to explain the form of the recapture of cortical cells by a previously deprived eye. Axonal terminals from the deprived geniculate laminae may always be present all across the visual cortex, but their degree of postsynaptic efficiency and specialization might be modified by the relative input to each of the two eyes. Thus after some period of monocular deprivation, terminals from the deprived eye, although still present in close proximity to cortical cells and perhaps even morphologically indistinguishable from normal, might be silenced and therefore ineffective in exciting the membranes of cortical neurons. Indeed, it is likely that some afferent fibers from the deprived eye are always present in the cortex of a monocularly deprived kitten; on rare occasions it is even possible to record the activity of such a fiber. The reappearance of input from the deprived eye could then be regarded merely as a spatially sequential reactivation of these "silent synapses," proceeding from the center of the genetically determined ocular dominance columns, where terminals might be expected to be the most dense, out towards its periphery, where innately directed fibers would be more sparse.

The initial period of monocular deprivation in the reverse-sutured kittens described above began at or

before the time of natural eye opening, when each cortical cell has only a tiny fraction of its adult complement of synapses (Cragg 1972), and, physiologically, the visual cortex is rather primitive (Hubel and Wiesel 1963; Barlow and Pettigrew 1971; Blakemore and Van Sluyters 1975). Passive maturation of connections to cortical cells, in the absence of patterned visual stimulation (Cragg 1975), is ineffective in donating to them the highly selective receptive field properties found in normal cats (Wiesel and Hubel 1965; Pettigrew 1974; Imbert and Buisseret 1975; Blakemore and Van Sluyters 1975). Thus after reverse suturing, the newly opened eye is receiving its first patterned visual experience. The kind of silent synaptic input from this initially deprived eye that one might expect to be revealed by reverse suturing should therefore be hardly different from the input present at birth.

In the animals considered thus far, the recapture of the cortex by the initially deprived eye more closely resembles the normal deployment of specificity in the cortex of a young kitten than the reestablishment of a previously specified input. It would therefore be of interest to consider the reinnervation of the visual cortex by an input that had formerly been highly specific. Fortunately, it is possible to produce a complete shift in cortical ocular dominance (qualitatively similar to that resulting from prolonged monocular deprivation from the time of natural eye opening) by briefly suturing one eye near the peak of the "sensitive period" after previous normal binocular vision (see Fig. 4). The cortex of a kitten more than 3 to 4 weeks old is physiologically very similar to that of a normal adult (Blakemore and Van Sluyters 1975). Therefore monocular deprivation after this time should "silence" a relatively specified complement of synapses, and reversal of eyelid suture should reactivate them, permitting a comparison of the properties of reinnervation following disconnection of a specified input with those following gross retardation in the development of any organized input from the deprived eye.

R. C. Van Sluyters (in prep.) has performed this experiment as follows: Kittens were allowed normal vision until the age of 32 days, at which time the cortex was shown to be essentially mature in all respects. They were then monocularly deprived for 10 days, causing a total shift in ocular dominance similar to that shown in Figure 2A. Then at the age of 6 weeks, the animals were reverse sutured and forced to use the deprived eye alone for 6 to 14 days. It is important to note that after the start of the first period of monocular deprivation, these animals never had natural binocular vision. The rate of reversal of ocular dominance in these animals was similar to that seen in kittens monocularly deprived for 6 weeks and then reverse sutured, and the form of the reinnervation seemed rather similar. The expansion of eye dominance columns was perhaps less regular, though they were clearly in evidence at all stages. Despite the superficial similarity in the recapture of cortical cells

after brief monocular deprivation and prolonged monocular deprivation, the receptive field properties donated to the cells from the initially deprived eye are organized very differently in the two conditions.

The reestablishment of receptive field properties after prolonged deprivation. When reverse suturing follows monocular deprivation from the time of natural eye opening, the receptive fields of each cortical neuron seem to undergo a systematic change. In these reverse-sutured kittens, binocularly driven neurons often have different receptive field properties in each eye. The eye that dominates the cell almost invariably has a normal orientation-selective receptive field, whereas the nondominant eye has a receptive field with much less mature properties, often lacking orientation or direction preference. This seems to imply that when synaptic input first arrives from the initially deprived eye, it provides a weak and poorly specified receptive field, but that this field soon develops more normal properties. Concomitantly, the receptive field of the other eye undergoes a progressive degradation until it is nonselective and finally disappears. The chance of finding a cell with normal orientation selectivity in both eyes is relatively low; in any one animal, such cells rarely constitute more than 25-30% of the population. Nevertheless, these cells are of the greatest interest, for they provide information about the innate restrictions on the receptive field properties of cortical cells. Here are binocularly driven neurons, with stimulus selectivity in both eyes, that have never experienced simultaneous, correlated binocular input.

The range of interocular differences in preferred orientation in the normal cat has been examined quantitatively (Blakemore et al. 1972) and found to be on the order of $\pm 15^{\circ}$. Using qualitative techniques (Blakemore and Van Sluyters 1974), a range of about $\pm 20^{\circ}$ was found. The uppermost histogram in Figure 7 shows the distribution of orientation differences for three kittens, aged 19, 26 and 32 days, with normal visual experience. In seven visually inexperienced kittens, aged 9 to 72 days (Fig. 7, second histogram), the distribution is somewhat broader, covering a range of $\pm 45^{\circ}$, although a part of this extra scatter is probably accounted for by the relatively imprecise orientation tuning of cortical cells in binocularly deprived animals. The distribution shown in the third histogram of Figure 7 for 151 cells recorded from 26 reverse-sutured kittens deprived from the time of natural eye opening is obviously much broader than either of the other two, covering virtually the entire range of $\pm 90^{\circ}$; however, the mode of the distribution is clearly close to zero-the same orientation preference on the two retinae.

It does not seem likely that the receptive fields that these cells gain in the initially deprived eye are the same ones they possessed prior to the first suture simply reactivated by visual experience. If that were so, they would be expected to show the

BLAKEMORE ET AL.



same distribution of interocular orientation differences as cells in visually inexperienced kittens, and this is not the case. If these receptive fields do represent the activation of silent synapses, those synapses must undergo extensive reorganization, perhaps akin to that seen in the development of stimulus specificity in the normal, very young kitten (Blakemore and Van Sluyters 1975). If they represent the growth of new connections, as previously proposed (Movshon and Blakemore 1974), then the extent to which these cells have different orientation preferences in each of the two eyes may represent the absolute range of orientational modifiability permitted each cortical cell.

The reestablishment of receptive field properties after brief monocular deprivation. In kittens monocularly deprived and reverse sutured following a period of normal binocular vision, the properties of binocular neurons closely resemble those in a normal cat (R. C. Van Sluyters, in prep.). Most binocular cells have well-specified receptive fields in each eye; neurons with nonspecific receptive fields in one eye, like those in kittens initially deprived from the time of natural eye opening, are relatively rare.

Furthermore, as is shown in the bottom histogram of Figure 7, the distribution of interocular orientation differences of 54 cells in three such kittens is clearly different from that in kittens deprived from the time of natural eye opening; it closely resembles that seen in normal kittens (uppermost histogram) and adult cats. It might have been expected that binocular neurons in these animals would be as likely to have widely discrepant orientation preferences in each of the two eyes as those in animals that had never had binocular visual experience. This is clearly not the case; the restored synaptic input seems to provide each cell with Figure 7. Histograms of differences in preferred orientation in the two eyes for binocularly driven cortical neurons. In each case, zero on the abscissa indicates that the receptive field has the same orientation on both retinae.

The first histogram is for 64 binocular cells from three normal kittens aged 19, 26 and 32 days. The second is for 49 cells from seven visually inexperienced kittens aged 9 to 72 days. The third is for 151 neurons from 26 kittens that never had simultaneous binocular vision: they were monocularly deprived from the time of lid opening and then reverse sutured. The final histogram is for 54 cells from three animals that had normal binocular vision until 32 days of age, were monocularly deprived until 42 days, and then reverse sutured.

properties nearly identical to those it lost during the initial period of monocular deprivation. It is possible that axons growing back to a group of cortical neurons might somehow be guided in their pattern of reinnervation, just as retinotectal axons in some lower vertebrates seem to be guided to their target neurons (see, e.g., Gaze 1970). However, far more parsimonious is the proposal that synapses from the initially deprived eye were never removed from their cortical terminals nor significantly disrupted, but that the initial period of deprivation merely decreased their efficiency in driving cortical cells.

DISCUSSION

While these experiments have provided further evidence for the great plasticity of input to cortical neurons in the kitten, they have not unambiguously answered two basic questions: What functional role does modifiability play? And what are the structural rearrangements underlying it? A workable hypothesis is that the synaptic input from one eye is capable, if predominantly active, of silencing terminals from the other eye relatively rapidly, but without displacing them from their terminal sites or disrupting their organization. Over longer periods of deprivation, the synapses may or may not become physically detached from their sites on the cell but they certainly become grossly disorganized and disrupted.

If silent synapses are merely reactivated during reinnervation, the ordered morphological pattern of their reactivation may reflect the spatially periodic pattern of terminal arborizations of fibers from the ipsilaterally and contralaterally driven geniculate laminae. The terminals formed by the lower order branches of any axon, closer to its point of entry to the cortex, may be

somehow more resistant to deprivation effects. Under conditions that disrupt the binocular input to cortical cells, the more distal terminals (far from the axon's point of entry) might be more vulnerable and therefore the first to be inactivated. The orderly shift in the borders of eye dominance columns seen during the period of reverse suturing would then reflect the switching off of the terminal ramifications of axons from the initially experienced eye in an orderly fashion from the periphery of their arborizations toward their origin; the arborizations of axons from the initially deprived eye would undergo a complementary change.

In any case, it is clear that two periods of monocular deprivation that produce identical physiological effects on the binocularity of cortical neurons can represent very different phenomena at the synaptic level. In the case of brief deprivation following a period of normal development, little seems to change apart from synaptic effectiveness; deprivation from birth causes a more profound disruption of the synaptic organization of the cortex.

Acknowledgments

We are grateful to P. A. Taylor, R. M. Cummings and J. S. Dormer for technical help and to the Medical Research Council, London, for providing a grant (No. G972/463/B) which supported this work. R. C. V. S. held a National Institutes of Health Special Research Fellowship, and J. A. M., a Research Studentship from the Wellcome Trust.

REFERENCES

- BARLOW, H. B. and J. D. PETTIGREW. 1971. Lack of specificity of neurones in the visual cortex of young kittens. J. Physiol. 218:98P.
- BARLOW, H. B., C. B. BLAKEMORE and J. D. PETTIGREW. 1967. The neural mechanism of binocular depth discrimination. J. Physiol. 193:327.
- BLAKEMORE, C. and R. C. VAN SLUYTERS. 1974. Reversal of the physiological effects of monocular deprivation in kittens: Further evidence for a sensitive period. J. Physiol. 237:195.
- . 1975. Innate and environmental factors in the development of the kitten's visual cortex. J. Physiol. 248:663.
- BLAKEMORE, C., A. FIORENTINI and L. MAFFEI. 1972. A second neural mechanism of binocular depth discrimination. J. Physiol. 226:725.
- CRAGG, B. G. 1972. The development of synapses in cat visual cortex. Invest. Ophthalmol. 11:377.
- ——. 1975. The development of synapses in kitten visual cortex during visual deprivation. Exp. Neurol. 46:445.
- GAZE, R. M. 1970. The formation of nerve connexions. Academic Press, New York.
- HIRSCH, H. V. B. and D. N. SPINELLI. 1970. Visual experience modifies distribution of horizontally and vertically oriented receptive fields in cats. *Science* **168**:869.
- HUBEL, D. H. and T. N. WIESEL. 1962. Receptive fields,

binocular interaction and functional architecture in the cat's visual cortex. J. Physiol. 160:106.

- . 1965a. Receptive fields and functional architecture in two non-striate visual areas (18 and 19) of the cat. J. Neurophysiol. 28:229.

- ------. 1972. Laminar and columnar distribution of geniculo-cortical fibers in the Macaque monkey. J. Comp. Neurol. 146:421.
- IMBERT, M. and P. BUISSERET. 1975. Receptive field characteristics and plastic properties of visual cortical cells in kittens reared with or without visual experience. Exp. Brain Res. 22:25.
- JOSHUA, D. E. and P. O. BISHOP. 1970. Binocular single vision and depth discrimination. Receptive field disparities for central and peripheral vision and binocular interaction on peripheral single units in cat striate cortex. *Exp. Brain Res.* 10:389.
- LEVAY, S., D. H. HUBEL and T. N. WIESEL. 1975. The pattern of ocular dominance columns in Macaque visual cortex revealed by a reduced silver stain. J. Comp. Neurol. 159:559.
- MOVSHON, J. A. 1975. The velocity tuning of single units in cat striate cortex. J. Physiol. 249:445.
- MOVSHON, J. A. and C. BLAKEMORE. 1974. Functional reinnervation in kitten visual cortex. Nature 251:504.
- NIKARA, T., P. O. BISHOP and J. D. PETTIGREW. 1968. Analysis of retinal correspondence by studying receptive fields of binocular single units in cat striate cortex. *Exp. Brain Res.* 6:353.
- NODA, H., O. D. CREUTZFELDT and R. B. FREEMAN, JR. 1971. Binocular interaction in the visual cortex of awake cats. *Exp. Brain Res.* **12**:406.
- OLSON, C. R. and R. D. FREEMAN. 1975. Progressive changes in kitten striate cortex during monocular vision. J. Neurophysiol. 38:26.
- PECK, C. K. and C. BLAKEMORE. 1975. Modification of single neurons in the kitten's visual cortex after brief periods of monocular visual experience. Exp. Brain Res. 22:57.
- PETTIGREW, J. D. 1974. The effect of visual experience on the development of stimulus specificity by kitten cortical neurones. J. Physiol. 237:49.
- PETTIGREW, J. D., T. NIKARA and P. O. BISHOP. 1968a. Responses to moving slits by single units in cat striate cortex. Exp. Brain Res. 6:373.
- . 1968b. Binocular interaction on single units in cat striate cortex: Simultaneous stimulation by single moving slit with receptive fields in correspondence. *Exp. Brain Res.* 6:391.
- ROSE, D. 1974. The hypercomplex cell classification in the cat's striate cortex. J. Physiol. 242:123P.
- WIESEL, T. N. and D. H. HUBEL. 1963. Single-cell responses in striate cortex of kittens deprived of vision in one eye. J. Neurophysiol. 26:1003.
- . 1965. Comparison of the effects of unilateral and bilateral eye closure on cortical unit responses in kittens.
 J. Neurophysiol. 28:1029.
- WIESEL, T. N., D. H. HUBEL and D. LAM. 1974. Autoradiographic demonstration of ocular dominance columns in the monkey striate cortex by means of transsynaptic transport. Brain Res. 79:273.