J. Physiol. (1981), **310**, *pp.* 215–239
With 2 plates and 8 text-figures
Printed in Great Britain

THE EFFECTS OF EARLY VISUAL EXPERIENCE ON THE CAT'S VISUAL CORTEX AND THEIR POSSIBLE EXPLANATION BY HEBB SYNAPSES

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(*Received 2 June 1980*)

SUMMARY

1. Kittens were dark-reared until 4–6 weeks old, and then for another 4–7 weeks with various combinations of cylindrical lenses, monocular occlusion, and normal vision.

2. Single unit recordings from 816 neurones of the visual cortex (area 17) were obtained after the end of exposure. Clear-cut effects on the distributions of the neurones' ocular dominance and orientation preference were found yielding close correlations with the rearing conditions.

3. It was confirmed that most cortical neurones prefer vertical stimulus orientations when experience is restricted to vertical contours in both eyes. It was further confirmed that, if the experienced orientations are different in the two eyes, each eye dominates over those neurones whose orientation preference corresponds to the orientation this eye has experienced.

4. When one eye is covered while the other sees only contours of one orientation, the ocular dominance distribution of cortical neurones shows a bias towards the open eye. Neurones dominated by this eye prefer orientations corresponding to the experienced range. Neurones preferring other orientations are shared between both eyes.

5. When vision is unimpaired in one eye and restricted to vertical contours in the other, binocularity is common among neurones preferring vertical orientations. Neurones with orientation preferences off the vertical are mainly monocular and dominated by the eye with unrestricted vision.

6. When normal monocular vision of one eye precedes restricted monocular vision of the other eye, only a few binocular units are encountered. Reversal of the initial effects of monocular experience is found only in neurones preferring the orientation that has been experienced by the newly opened eye. The other neurones remain dominated by the originally open eye. Thus, complementary distributions of orientation preferences are found for the two eyes.

7. A good correlation was found between the amount of orientational experience as determined by the number of orientations exposed and the number of normally tuned neurones. Conversely, the number of neurones responding to all orientations decreases with increasing amount of experience.

8. Between 24 and 32 % of all units analysed were unresponsive to light stimulation or did not show any preference for a particular stimulus orientation. In all but one paradigm the number of non-oriented or unresponsive neurones was smaller than the number that is to be expected if the bias in the orientation-distribution after selective experience solely resulted from selective deprivation of those neurones committed to non-experienced orientations. From these quantitative considerations it is concluded that the role of visual experience is not only to maintain innate properties of cortical neurones, but also to specify innately unspecific neurones.

9. A mechanism that could account for *both* roles of visual experience is the matching of patterns of afferent activity with post-synaptic response properties. This is similar to that postulated by Hebb for adaptive synaptic connexions.

INTRODUCTION

After the initial controversial reports of Hubel & Wiesel (1963) and Barlow & Pettigrew (1971) it is now generally accepted that the visual cortex of very young, visually inexperienced kittens contains a certain proportion of neurones with oriented receptive fields (Barlow, 1975; Blakemore & Van Sluyters, 1975; Imbert & Buisseret, 1975; Sherk & Stryker, 1976; Fregnac & Imbert, 1978; Pettigrew, 1978). With the exception of one study (Sherk & Stryker, 1976) most authors agree that the frequency of occurrence of these mature receptive fields is lower than in fully experienced adult animals (Hubel & Wiesel, 1963; Pettigrew, 1974; Blakemore & Van Sluyters, 1975; Buisseret & Imbert, 1976).

During this early phase of post-natal development, the visual system is extremely susceptible to restrictions or alterations in experience. Monocular occlusion causes a nearly complete inactivation of the afferents from the deprived eye (Wiesel & Hubel, 1963, 1965). Strabismus leads to a disruption of cortical binocularity (Hubel & Wiesel, 1965) and, on occasions, to functional amblyopia of the squinting eye (Ikeda & Wright, 1976; Singer, von Grüenau & Rauschecker, 1980). Likewise, selective restriction of visual experience to contours of a single orientation (Hirsch & Spinelli, 1970; Blakemore & Cooper, 1970; Freeman & Pettigrew, 1973; Blasdel, Mitchell, Muir & Pettigrew, 1977) or direction of movement (Tretter, Cynader & Singer, 1975; Cynader, Berman & Hein, 1975; Daw & Wyatt, 1976) has been shown to result in a characteristic distortion of orientation and direction preferences of cortical neurones.

The changes in ocular dominance resulting from monocular deprivation and squint are commonly explained by competitive interactions between the afferents from the two eyes (Guillery, 1972; Sherman, Guillery, Kass & Sanderson, 1974; Cynader & Mitchell, 1977). This conclusion can be drawn since it is well established that binocularity is a preexisting property of most striate cortex neurones and is independent of visual experience (Hubel & Wiesel, 1963; Blakemore & Van Sluyters, 1975; Imbert & Buisseret, 1975).

With respect to experience-dependent changes in the orientation domain no definite agreement has been reached so far. In a recent study, Stryker, Sherk, Leventhal & Hirsch (1978) compared the effects of orientational restriction that was either concordant or discordant in the two eyes. Their results were consistent with a hypothesis of selective deprivation, but they could not rule out additional instructive processes that tune cells to the experienced orientations. In the present experiments an approach was adopted which makes it easier to distinguish between selective and instructive processes because it provides an internal control for the effect of restricted experience in the same animal: our three main paradigms have in common the fact that only one eye receives restricted orientational experience while the other eye experiences normal vision, or is totally deprived of vision. Combining in this way selective experience with asymmetric activation of the two eyes allows us to assess quantitatively the effect of exposure on different subsets of neurones that share either the same ocular dominance or the same orientation preference. The results provide evidence for both selective and instructive processes and could be explained by synapses with the adaptive properties postulated by Hebb (1949).

Part of the present results have previously been reported in brief form (Rauschecker & Singer, 1978, 1979; Rauschecker, 1979).

METHODS

Visual exposure

Eleven kittens were studied. The kittens were housed from birth until the day of eye opening (around 5–10 days of age) together with their mother and their litter-mates in a separate compartment in the normal colony room. Afterwards the families were taken into separate compartments of a dark-room. Special care was taken to assure that the room was absolutely light-proof. During cleaning and food replacement the kittens were kept in light-proof boxes within the room.

Visual exposure was started around the peak of the sensitive period, which lies at about 5 weeks of age (Hubel & Wiesel, 1970). This is also the age at which kittens start to reduce the time spent asleep and become more interested in their environment. During exposure, the kittens wore helmets made of polyurethane foam (Terocor (R), Terosone). For manufacture of the helmets the fluid plastic material was sprayed on a model of a kitten's head; after hardening the masks could be worked thermally and mechanically to ensure that they fitted each individual animal perfectly. At the position of one or both eyes, depending on the experimental scheme, a hole (20 mm diameter) was melted in the mask, in which a cylinder lens was glued with silicone sealer (Dow Corning Aquarium Sealer). Pl. 1*A* shows one of the experimental animals during exposure.

The plano-concave lenses used were 0 and −25 D in the respective orthogonal meridians. This difference goes far beyond the amplitude of accommodation of the cat, even if one takes into account the different optical properties of the kitten eye. Use of negative cylinders avoids the problem at close distances that would be encountered with positive lenses.

The artificial environment, in which the kittens stayed during exposure (shown on Pl. 1*B*), was situated in a brightly lit room. It consisted of a large Plexiglass box (1·5 × 1·5 × 1·0 m) with double walls. Between these walls thin cardboard plates or photographic prints were inserted. On the plates high-contrast patterns were drawn which contained long black and white bars of all orientations grouped together to form 'stars' of 80 cm diameter. The width of the bars increased with distance from the centre of the star, ensuring a continuous range of spatial frequencies. The optical transfer properties of the cylindrical lenses are demonstrated most clearly if such a pattern is viewed directly through one of the lenses. In Pl. 2 this situation is simulated by photographing the exposure pattern through the cylinder (focal length of objective lens: 50 mm; stop: 1/16). The photograph gives an impression of the effect of the cylindrical lens on an optical system with an aperture of 3·1 mm diameter. The kitten's pupil may differ from this, and there are other factors that may influence how important the defocus is.

When the head is tilted the lens rotates with it. There is some reflex counter-rotation of the eye, but this amounts only to 10% of the tilt angle (O.-J. Grüsser, personal communication). Thus the orientation of the stimulus relative to retinal co-ordinates remains virtually constant, independent of head movements.

Three kittens were exposed wearing masks with lenses in front of both eyes: in one case the lenses were oriented at the same angle, in two cases at right angles to each other. In five kittens a lens was applied only to one eye, the other remaining covered by the mask. Three kittens were allowed to see normally with one eye while the other eye viewed the visual environment through a lens. Table 1 gives a summary of the ages and treatments of all the kittens used in this study.

Exposure of at least 100 hr (in two kittens 200 hr) was given in daily sessions of about 8 hr average duration. The masks were securely fixed on the kittens' heads with adhesive tape, such that the animals could not pull them down or even slightly shift them. After the first day of exposure, the kittens were usually fully accustomed to the masks and pursued their normal activities without any sign of disturbance.

Preparation and recording techniques

For surgery, the cats were anaesthetized with a mixture of 10 mg ketamine-base (Ketanest (R)) and 0·15 ml. xylazine (2 %) (Rompun (R)) per kg body weight I.M., after premedication with 0·01 mg atropine S.C. A venous cannule was then placed into one of the forearm veins, and anaesthesia was continued with sodium thiopentone (Pentothal) I.V. After tracheotomy the animal was mounted in a stereotaxic headholder. An initial dose of 20 mg Flaxedil was given and artificial respiration was started with 70 % N_2O and 30 % O_2. Flaxedil infusion of 20 mg/kg . hr was continued throughout the experiment. For nutrition a 4:1-mixture of glucose and Ringer solution was given through an orally inserted gastric catheter. The physical state of the animal was constantly monitored. Body temperature was kept automatically at 38 °C. Special care was given to e.c.g., e.e.g., intrapulmonal pressure and the expiratory CO_2 content, as measured at the tracheal cannula. Cardiac accelerations to minor noxious stimuli were not observed during the experiments. Additional anaesthetic was available, however, if required.

For light stimulation, the nictitating membranes were retracted with neosynephrine and the pupils dilated with atropine. The corneae were protected with black contact lenses, which contained artificial pupils of 2 mm diameter to create standard viewing conditions. The refractive state of the optics of both eyes including spherical and astigmatic aberrations was checked with a Rodenstock refractometer and corrected if necessary to focus the eyes on a tangent screen at 1 m distance. Landmarks of both retinae (blind spot and area centralis) were projected onto the screen by means of a Zeiss fundus camera. Extracellular recordings from single units in area 17 were obtained with 1·5 M-potassium citrate filled micropipettes (impedance 5–15 MΩ), usually in both cerebral hemispheres (see Table 1). A bridge circuit made it possible to inject current (in the range of 1–5 nA) through the electrode to activate cells and thereby to reduce the chance of missing cells that lack spontaneous activity while advancing the electrode.

In order to avoid a sampling bias imposed by the columnar organization of striate cortex (Hubel & Wiesel, 1962), long tracks angled obliquely to the surface of the cortex were made. If, for simplicity, highly regular columnar systems of orientation preference and ocular dominance are assumed (with widths of 50 μm/10° and 500 μm/eye respectively, Hubel & Wiesel, 1974; Hubel, Wiesel & Stryker, 1977), geometrical considerations dictate that a penetration has to have an inclination of at least 27° and thereby a length of at least 2 mm in order to be representative of all orientation preferences and both ocular dominances. These conditions were fulfilled in all of our tracks; many of them were even longer than the minimum, because they were extended down into the medial bank of the lateral gyrus thereby increasing the likelihood of crossing several ocular dominance columns.

Under these circumstances it did not seem necessary to exempt any single neurones from analysis by sampling only in discrete steps of 100 μm (Stryker & Sherk, 1975). Furthermore, with micropipettes (unlike low-impedance tungsten electrodes) it is always possible to identify successively recorded responses as coming from the same or from different neurones. Only single unit recordings were used for analysis, group responses were not taken into account. The mean distance between consecutively recorded cells in the various penetrations was 85 μm ($\pm$ 18·5 μm). To avoid experimenter bias the majority of the experimental paradigms were performed in a blind procedure. During rearing animals and masks were identified only by numbers. During the experiment the experimenter did not know the orientation and, or, ocularity of the exposure stimuli.

Responses were checked first with both eyes open. Then each eye was tested individually to determine the relative degrees of excitability ('ocular dominance') and the orientation selectivity ('preferred orientation' and 'orientation tuning') in the two eyes. Ocular dominance was rated in

TABLE 1. History of experimental animals. The identification number of each kitten contains the number of its litter (first three digits) and a number within the litter (last digit). It can be seen that litter mates were used for most of the exposure paradigms. In the two-stage case (litter 142), start and duration of exposure for the two stages are separated by a slash

Exposure paradigm	|||| |||| R L	|||| ≡ R L	≡ |||| R L	≡ ● R L	|||| ● R L		○ |||| R L		○ ● ● ≡ R L		○ ● ● |||| R L
Kitten	0551	0535	1211	1024	1025	1521	1522	1523	1421	1424	1423
Age at start of exposure (weeks)	6	6	6	4	4	5	5	5	5/6	5/6	5/6
Exposure duration (hr)	102	121	128	223	223	109	109	108	100/100	100/100	100/100
Age at end of exposure (weeks)	10	12	12	11	11	11	11	11	10	10	10
Age at recording (weeks)	12	12	14	11	12	15	15	13	12	14	10
Recorded hemispheres	Both	Both	Both	Both	Both	Left	Right	Both	Both	Left	Both

five classes. 'Preferred orientation' was designated as the orientation of the bar stimulus which gave the maximal number of spikes per sweep. To differentiate between orientation and direction preference it was routinely established whether a moving spot of light gave the same response amplitude as a light slit. The width of 'orientation-tuning' was determined from those two stimulus orientations (if there were any) that just failed to elicit an increase in discharge rate. In evaluation of orientation selectivity, preferred orientations and orientation-tuning were grouped into bins of 22·5°, which equals a sixteenth of the full circle or eight different categories within 180°. Applying the optimal stimulus through the better eye the vigour of each neuronal response was rated on a subjective scale ('response quality'), the best responses being rated as '5', barely detectable ones as '1'.

In most of the cells the receptive field properties were determined initially by hand. If any one of the parameters remained unclear, computer-aided analysis was started by means of peri-stimulus time histograms. This procedure seems to us a fair compromise between the option of purely quantitative data collection and the need to obtain representative samples of neurones for statistical analysis. This is supported by two recent studies (Blasdel *et al.* 1977; Stryker *et al.* 1978) in which no significant difference was found between cell samples obtained with hand plotting and computerized analysis.

Recording from a particular penetration was terminated when the track was at least 3 mm long and no single unit could be isolated for over 500 μm and, or, when activities typical for lateral geniculate nucleus (l.g.n.) fibres (Hubel & Wiesel, 1962) appeared repeatedly. Electrodes were changed when their impedance dropped below 5 MΩ. The experiment was terminated when e.e.g. or e.c.g. showed pathological changes or the optic media became cloudy.

At the end of the experiment, the animal was given 5 ml. Nembutal I.V. and was perfused transcardially with 4 % formaldehyde for later morphological investigation of the lateral geniculate nuclei on either side. Occasionally, Nissl stained sections of the recording site were also made in order to confirm the position of the electrode.

RESULTS

1. *Conflicting and non-conflicting experience in the two eyes*

To make our results as comparable as possible with previous work, three kittens were reared according to the paradigms chosen by Hirsch & Spinelli (1970) and Blakemore & Cooper (1970), but achieving the restriction of visible orientations by cylindrical lenses (see Methods).

Blakemore & Cooper's paradigm

In one kitten, vision was restricted in both eyes to the same orientation. The cylindrical lenses were oriented such that the clearly visible meridian was vertical. Great care was taken to align exactly the axes of both lenses to avoid orientational disparity. The results from this kitten are shown in Fig. 1. The ocular dominance distribution of the neurones encountered in area 17 of both hemispheres looks quite normal; 67 % of the cortical cells could be driven from both eyes. Thus, binocularity is reduced by only 13 % when compared with a normal proportion of about 80 % binocular neurones (Hubel & Wiesel, 1962). If ocular dominance is plotted as a function of contra- and ipsilateral activation (instead of right/left), the normal dominance of the contralateral eye (Hubel & Wiesel, 1962) becomes apparent.

The polar distribution of the neurones' preferred orientations shows a clear bias towards the experienced orientation. Among the oriented cells, independent of ocular dominance, 61 % show a preference for vertical orientations (90 ± 22·5°), whereas only 20 % show a preference for horizontal yielding a ratio between vertical and horizontal neurones of 3·0. If only neurones with good responses (response quality > 1) are considered, precisely the same ratio of 3·0 is found. The bias for vertical orientations is bigger among binocular neurones than among monocular ones, the respective ratios between vertical and horizontal being 3·25 and 1·8.

In order to simulate a situation where neurones are sampled only in discrete steps of 100 μm (Stryker & Sherk, 1975), data analysis was subsequently performed by leaving out all neurones that were found to lie closer than 100 μm to another one. In this case the bias for vertical became even bigger, the vertical/horizontal ratio being 4·3.

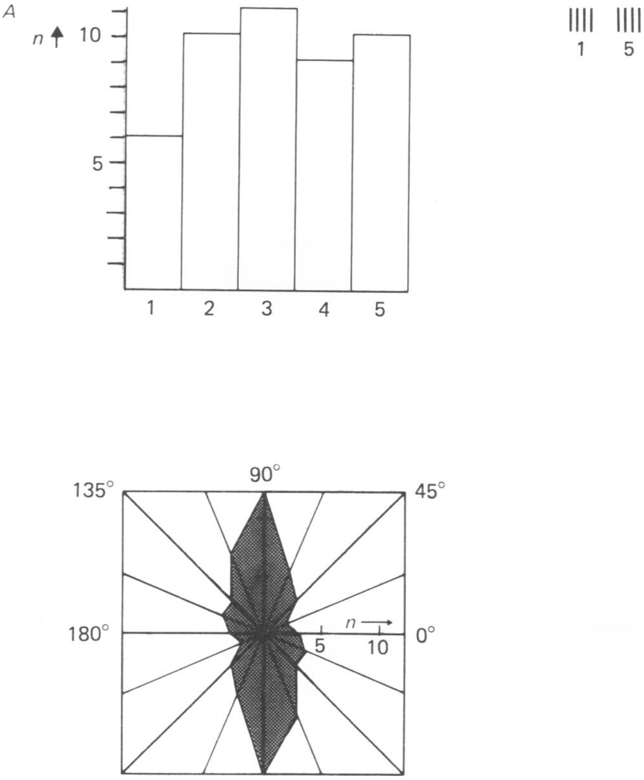


Fig. 1. Results of single unit recording from the striate cortex of a kitten whose visual experience was restricted to vertical contours in both eyes by means of cylindrical lenses. *A*: ocular dominance histograms of all neurones that responded to light stimulation. Ocular dominance is rated in five classes: 1 and 5 refer to monocular neurones driven by the right and left eye, respectively; 2–4 are binocular neurones, whereby 2 and 4 are clearly dominated by the right and left eye, respectively, while class 3 neurones are about equally driven by both eyes. The number of neurones in each of these classes is indicated on the ordinate. *B*: polar histogram of preferred orientations for all neurones with a preference for stimulus orientation. Orientation preference is given in segments of $360°/16 = 22{\cdot}5°$, 0° (180°) corresponding to horizontal, 90° to vertical. The radius at every discrete angle gives the number of neurones with that particular orientation preference; the endpoints are interconnected by straight lines enclosing the dark area. Since direction preference was not taken into account, the polar plot is radially symmetrical around its centre.

Hirsch and Spinelli's paradigm

Two kittens were studied whose vision was restricted to vertical contours in one eye and at the same time to horizontal contours in the other eye. One kitten was raised with the right eye seeing horizontal and the left eye vertical, while in the other kitten the conditions were reversed, and to reduce possible bias the experimenter was unaware of the raising condition during the recording session. Two recent studies by Stryker *et al.* (1978) and Gordon, Presson, Packwood & Scheer (1979) have also been aimed at comparing the effects of concordant and discordant visual stimuli.

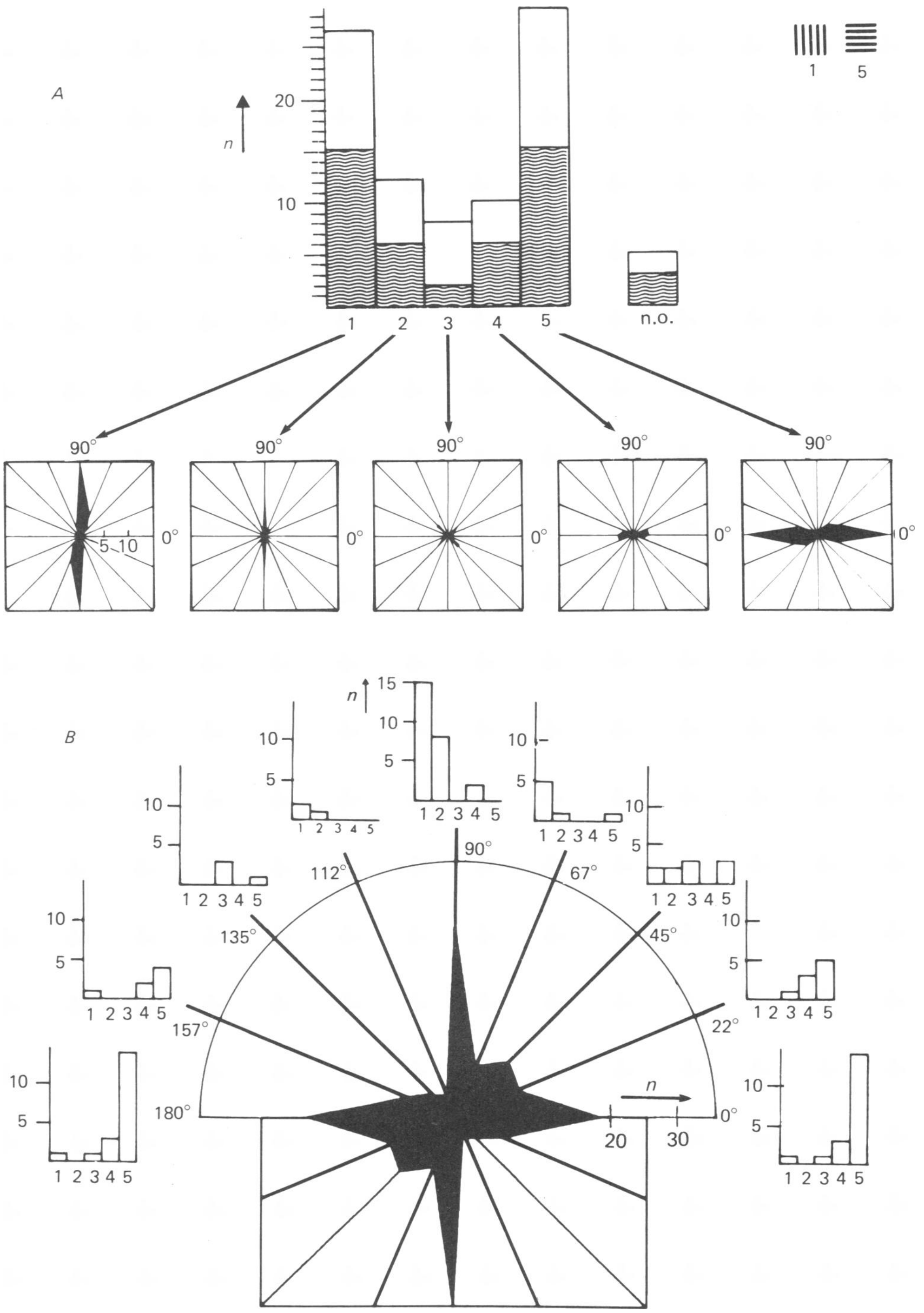
All the major findings of Hirsch & Spinelli (1970) were confirmed in our results. Binocularity was lost in most cortical units (binocular: thirty-four neurones = 35 % of responsive units). The large majority (85 %) of the orientation selective monocular neurones preferred the orientations experienced by the eye to which they had remained connected. Cells that were strongly dominated by one or the other eye followed the same scheme: the orientation that had been experienced by the dominant eye prevailed in 82 % of the oriented units in these two ocular dominance classes ($n = 22$). Of the ten cells that were symmetrically driven from both eyes (which constitute only 8 % of the whole sample of fully analysed neurones), six responded best to oblique orientations (45° or 135°) and two were non-oriented (cf. Fig. 2*A*).

This dependence between orientation preference and ocular dominance is also reflected when ocular dominance distributions are plotted as a function of the neurones' orientation preference. Neurones preferring vertical or horizontal orientations were usually dominated by the eye with corresponding experience; the very few cells with oblique orientation preferences were equally shared between the two eyes (cf. Fig. 2*B*).

2. *Asymmetric non-conflicting experience*

The second group of experiments comprised five kittens that had their visual experience restricted to one orientation in one eye only. Simultaneously, the other eye was either completely deprived of vision (two kittens) or was allowed to view normally (three kittens).

Fig. 2. Results of single unit recording from the striate cortex of two kittens whose visual experience was restricted simultaneously to vertical contours in one eye and to horizontal contours in the other eye by means of cylindrical lenses. The raising condition is displayed symbolically at the upper right corner. Since the eyes which experienced vertical and horizontal contours were different in the two kittens, ocular dominance classes 1 and 5 in this case correspond to the eye with vertical and horizontal experience respectively, and classes 2–4 accordingly. *A*: polar histograms of preferred orientation as a function of the ocular dominance of the particular neurones. Polar plots are constructed in the same way as in Fig. 1*B*. The ocular dominance diagram on top comprises all orientation selective neurones; the number of non-oriented neurones is shown in a separate column to the right. The distributions of the individual kittens are indicated by different shading. *B*: ocular dominance distributions as a function of the orientation preference of the particular neurones. Number of neurones is shown on the ordinates. The polar plot of all orientation selective neurones is given in the centre.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Selective monocular vision

The results of the two kittens with the left eye closed and selective experience in the right eye are shown in Fig. 3. In one kitten the cylindrical lens was oriented vertically, in the other horizontally (see Table 1).

The effect of exposure can be assessed most clearly if, as in the previous case, the neurones' orientation preferences are plotted as a function of their ocular dominance (Fig. 3*A*). Of the neurones dominated by the experienced eye 71 % (59 units) preferred the orientation (±22·5°) visible during exposure was compared to only 43 % (18 units) of the neurones dominated by the inexperienced eye. This complementary relationship becomes most obvious when the ratios between the numbers of neurones preferring the experienced and inexperienced orientations are calculated. This ratio is 4·25 (34/8) for the experienced eye and 0·82 (9/11) for the completely deprived eye. Correspondingly, the large majority of the cells that preferred the experienced orientations (34 units = 71 %) were found to be dominated or driven exclusively by the experienced eye (Fig. 3*B*). The same relation holds if neurones in the two neighbouring categories (±22·5°) of orientation preference are included. For neurones preferring stimulus orientations orthogonal to those experienced the situation is rather different: the large majority of these cells are symmetrically driven from both eyes. This results in an over-all dominance of the experienced eye which is, however, slightly less pronounced than in monocularly deprived cats without further restriction. The same was apparent from morphological inspection of the two l.g.n.s.

Simultaneous selective and normal vision

Three kittens were reared with the right eye open and a cylindrical lens in front of their left eye with vertical as the visible orientation. Fig. 4 shows ocular dominance histograms and orientation preference plots as functions of each other for all cortical neurones found in these three kittens. In one kitten recording was done in both hemispheres, in the other two kittens only in the left or right hemisphere respectively (see Table 1).

Neurones that still possess an input from the eye with restricted vision, in particular those that are dominated by this eye, exhibit a clear bias for the vertical orientation in their polar histograms. On the other hand, neurones that are exclusively driven from the normal eye represent all other orientation preferences (Fig. 4*A*). Correspondingly, neurones with preferences for vertical orientations (90±22·5°) show a normal ocular dominance distribution, the majority (73 %) of neurones being driven by both eyes (Fig. 4*B*). Among all other neurones with oriented receptive fields 78 % (n = 38) were dominated or driven exclusively by the normally seeing eye (n = 38).

After these experiments were completed, a brief report appeared by Cynader & Mitchell (1977). They reared kittens with one eye viewing through a 12 D cylindrical lens (axis vertical), the other eye seeing normally. In spite of the weaker lens their results agree well with ours. In their study, however, neurones with orientation preferences for horizontal (the meridian viewed simultaneously by both eyes), though displaying a symmetrical ocular dominance distribution, were largely monocularly activated. It seems unlikely that this break-down of binocularity could have been

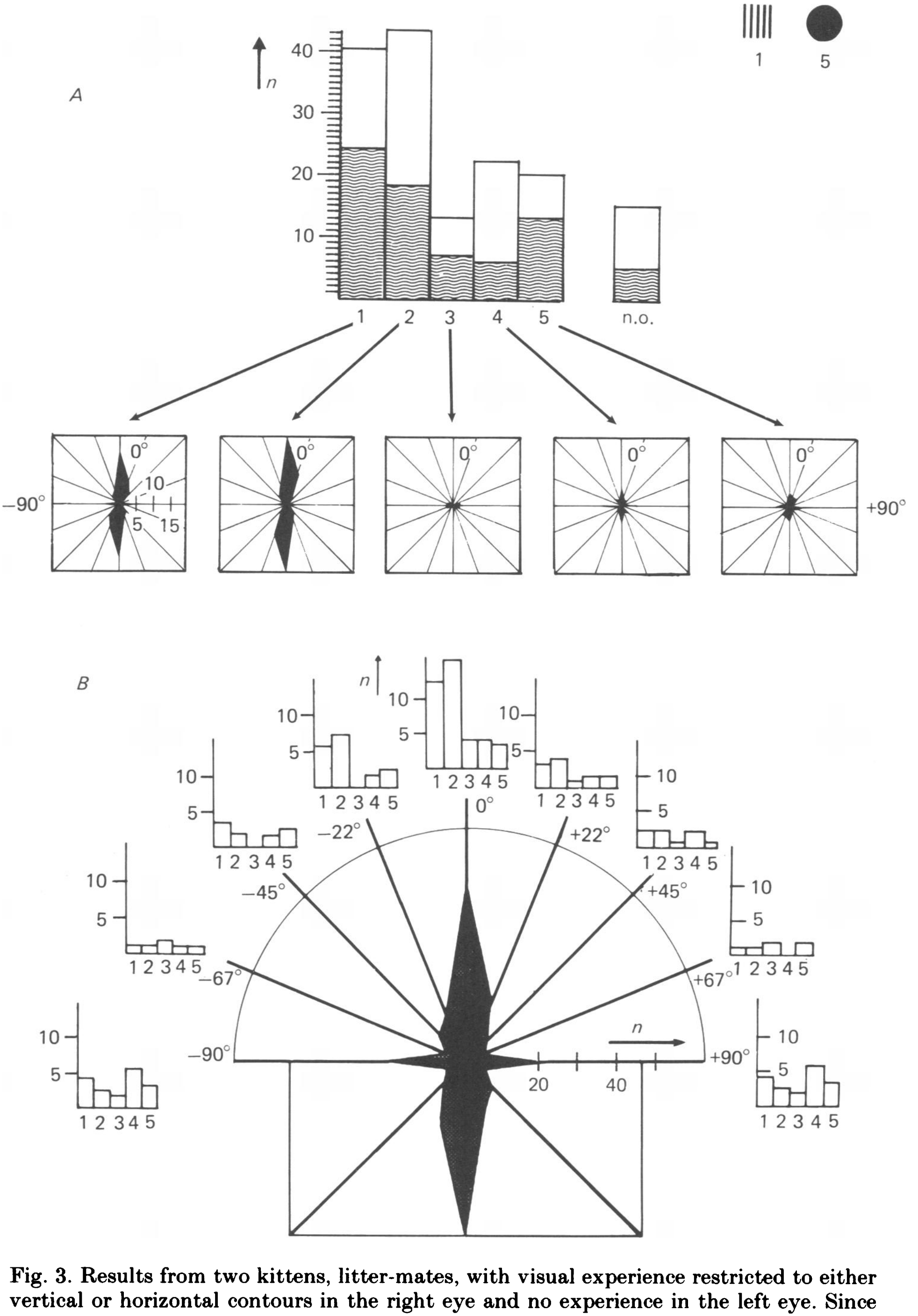


Fig. 3. Results from two kittens, litter-mates, with visual experience restricted to either vertical or horizontal contours in the right eye and no experience in the left eye. Since the experienced orientation was different in the two kittens, orientation preference is given as the difference between experienced orientation and preferred orientation, 0° corresponding to no difference. Only the vertical case is displayed symbolically at upper right corner. Coding of ocular dominance classes as in Fig. 1. Other conventions as in Fig. 2. *A*: polar histograms of preferred orientation as a function of ocular dominance. *B*: ocular dominance distributions as a function of orientation preference.

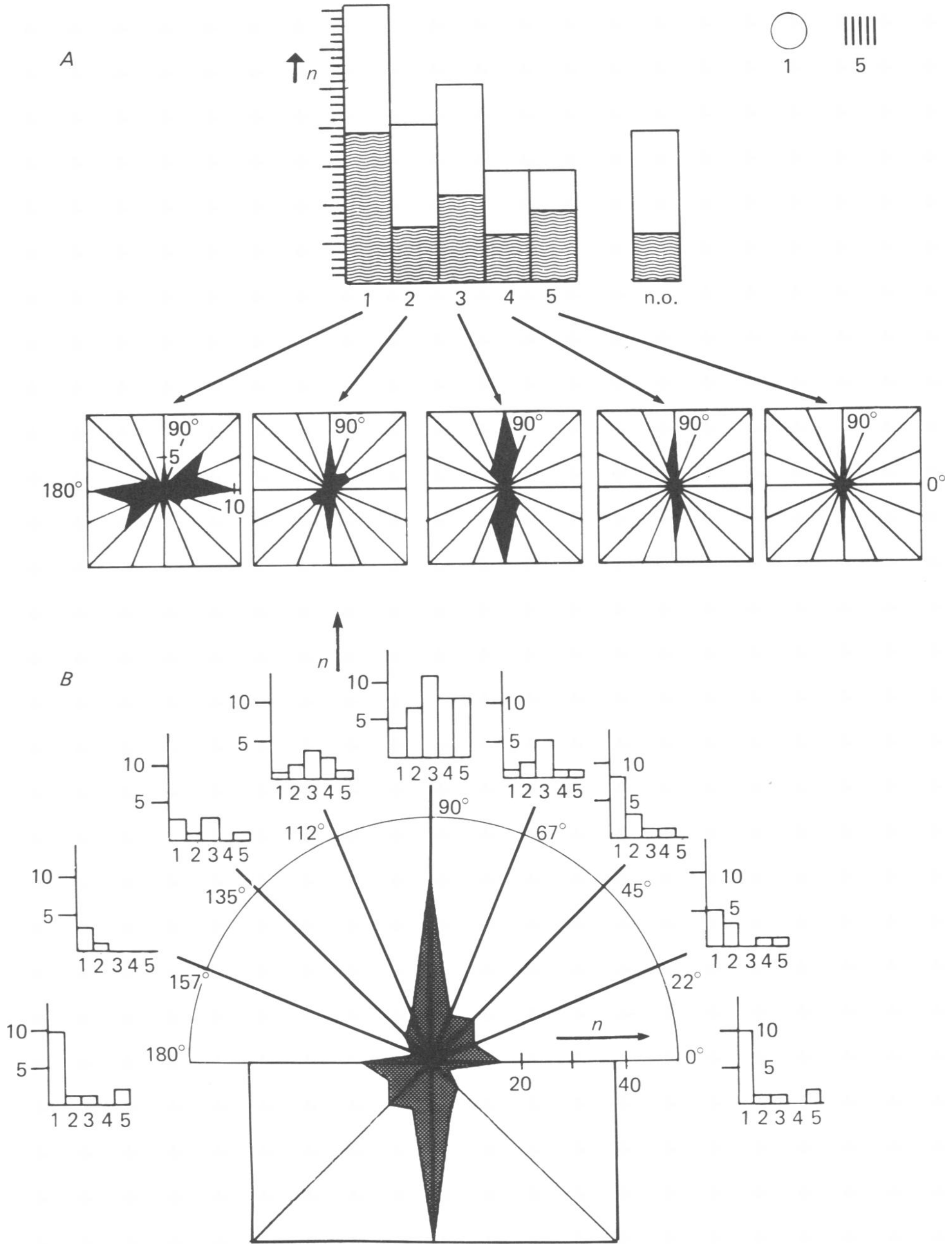


Fig. 4. Results from three kittens, litter-mates, with visual experience restricted to vertical contours in the left eye and normal experience in the right eye. Coding of ocular dominance classes as in Fig. 1. Other conventions as in Fig. 2. *A*: polar histograms of preferred orientation as a function of ocular dominance. In the ocular dominance diagram (on top) of all orientation selective neurones the shaded part comprises the units from the two kittens in which only one hemisphere was recorded from (cf. Table 1). *B*: ocular dominance distributions as a function of orientation preference.

caused by prismatic displacements: the clearly seen meridian is orthogonal to the axis of the cylinder and is therefore unaffected by such displacements. Rotational variations, however, could account for the loss of binocularity.

3. *Selective monocular vision following normal monocular exposure*

The following results are from three kittens whose exposure scheme contains common features from both groups of the previous section 2, but is different in one important aspect. The kittens had normal visual experience with one eye for 100 hr between 5 and 6 weeks of age while the other eye was closed. The originally open eye was then closed and the deprived eye was allowed to view through the cylindrical lens. The visible orientation was horizontal in two kittens and vertical in one kitten.

Alternating occlusion of the two eyes is known to disrupt cortical binocularity (Hubel & Wiesel, 1965; Blakemore & VanSluyters, 1974). Indeed, as shown in Fig. 5*A*, 71 % of the neurones (84 of 118) had become monocular, whereas only six neurones (5 %) could be activated equally from both eyes. Fig. 5*A* shows that the majority (70 %) of neurones dominated by the newly opened eye prefers horizontal orientations ($0 \pm 22{\cdot}5°$) in the two kittens that had viewed horizontal contours; similarly vertical orientation preference (85 %) prevails in the kitten with vertical experience. Neurones still dominated by the other, previously normal, eye show a complementary distribution, with 81 % orientation preferences for the respective orthogonal meridian ($\pm 45°$).

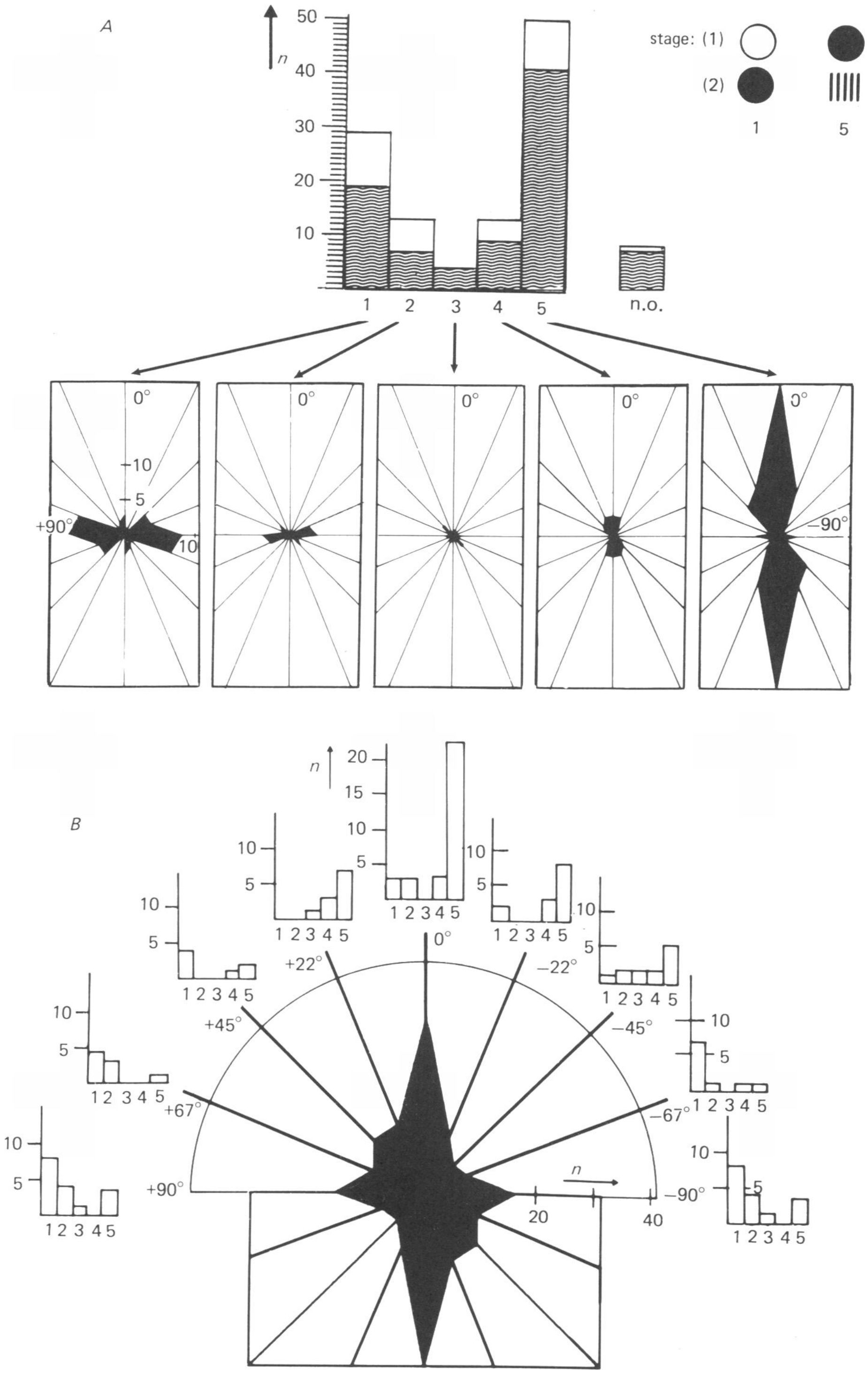
From these complementary distributions it has to be concluded that only neurones preferring orientations within the restricted visible range had selectively recovered from the initial effects of monocular deprivation. Cells with different orientation preferences had remained dominated by the originally open eye (Fig. 5*B*).

4. *Assessment of orientation tuning: proportions of non-oriented and unresponsive cells*

Apart from the neurones' preferred stimulus orientations we were also interested in the range of orientations to which each neurone could respond. The distribution of non-oriented and unresponsive neurones is important since their existence and proportion bears directly on the question of whether visual experience is only necessary to maintain prespecified response properties or whether it can in addition instruct uncommitted neurones.

For every kitten we determined, first, the percentage of neurones whose tuning for orientation was within the normal range (responding only within $\pm 45°$ of the optimal orientation) and, secondly, the proportion of units that responded to all orientations (including those that did show some bias for one orientation). The results for each paradigm were pooled since the numbers within each paradigm did not differ at the 5 % level, applying Fisher's exact test to all pairs of kittens.

As a working hypothesis for the following evaluation it was assumed that the percentage of normally tuned cells should increase with the amount of experience available while the fraction of unselective cells should decrease. The 'amount of experience' was defined as the number of orientations ($n \times 22{\cdot}5°$) that were visible to the kitten in early life yielding an ordinal scale of different amounts of experience for the various exposure paradigms. From the plots in Fig. 6 it is evident that indeed more neurones with normal orientation tuning were found in the kittens that could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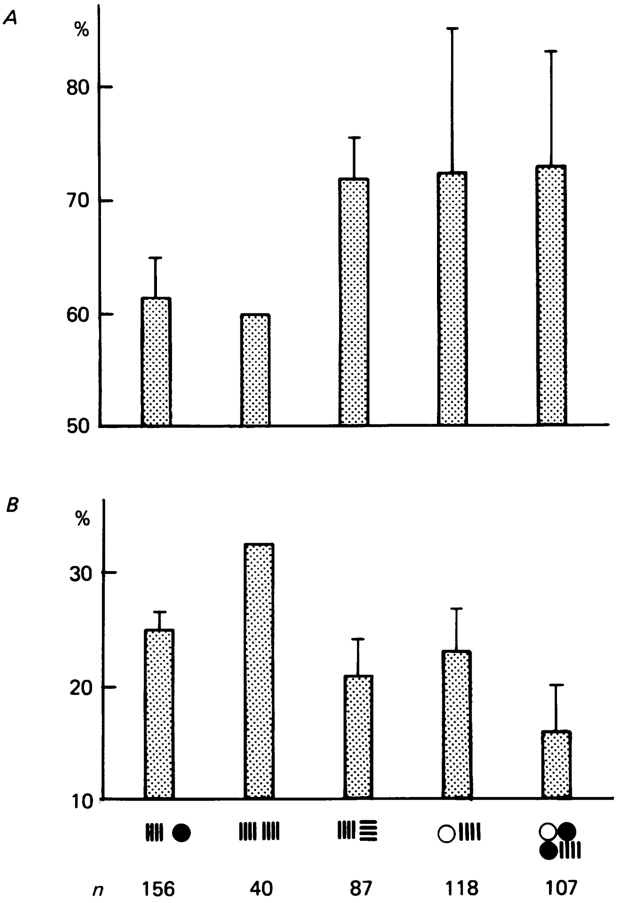


Fig. 6. Orientation selectivity of cortical neurones as a function of the amount of orientational experience. The five experimental paradigms are put in order of increasing number of orientations exposed as shown schematically at the bottom. The total number of units in each paradigm for which orientation tuning was determined is shown under each symbol. *A*: mean percentages of neurones with normal orientation selectivity (responding within ±45° or less around the preferred orientation). *B*: mean percentages of neurones that responded to all orientations, including those with an orientation bias. The scatter between the individual animals is indicated by small bars on top of the columns, giving the maximum percentage found in each paradigm. For the vertical/vertical case error bars cannot be given since only one animal was examined.

Fig. 5. Results from three kittens, litter-mates, which had normal monocular experience in one eye prior to monocular experience with contours of a single orientation in the other eye (two kittens horizontal, one kitten vertical; only vertical case is displayed symbolically at upper right corner). *A*: polar histograms of preferred orientation as a function of ocular dominance. In the ocular dominance diagram on top the shaded part comprises the units from the two kittens with horizontal experience in the second stage of exposure. *B*: ocular dominance distributions as a function of orientation preference. As in Fig. 3 (see legend) 0° corresponds to zero difference between the experienced orientation and that of the unit, not to horizontal as elsewhere.

see all orientations, or at least horizontal and vertical, than in the kittens that had experienced only one orientation. For neurones with a broadly tuned or entirely unselective response the contrary is true. Table 2 compares contingencies between different paradigms. It can be seen that the greatest similarities (least significant differences) exist between the first two and the last two paradigms, the horizontal/vertical case being in between.

TABLE 2. Similarities between the different paradigms in their proportions of orientation selective cells. The matrix shows the results of pairwise comparisons of the results for different paradigms shown in Fig. 6*A* using Fisher's exact test. The hypothesis tested was whether the proportions of cells with normal orientation tuning (within ±45°) were the same or different. Combinations differing on the 0·1-level are marked with one asterisk, differences on the 0·05-level are indicated by two asterisks. It can be seen that there is a clear gradient of significant difference from left to right and bottom to top; no significant differences are found to the right of the oblique dotted line

		IIII ● P_1	IIII IIII P_2	IIII ≡ P_3	○ IIII P_4	○ ● ● IIII P_5
IIII ●	P_1	—	—	—	—	—
IIII IIII	P_2	0·5945	—	—	—	—
IIII ≡	P_3	0·0593*	0·1212	—	—	—
○ IIII	P_4	0·0333**	0·0960*	0·6544	—	—
○ ● ● IIII	P_5	0·0379**	0·0998*	0·6506	0·6868	—

In the two paradigms with experience restricted to one orientation it is possible to compare the orientation tuning in neurones preferring the experienced and non-experienced orientations respectively. As expected, the number of sharply tuned cells (responding with ±30°) was higher in the experienced orientation than in the non-experienced ones (53 % as compared to 37 % for the case with experience in both eyes; 29 and 17 % for the case with experience only in one eye).

These results give some information with respect to selective versus instructive processes. On a purely selective theory it would be expected that the percentages of sharply tuned cells would be multiples of each other. For instance the proportion of sharply tuned cells in the horizontal-vertical case would have to be twice as high as in the vertical-vertical case, but this is clearly not the case.

In the histograms of Figs. 1–5, where ocular dominance and preferred orientation of cortical neurones were presented as functions of each other, naturally none of the non-oriented and unresponsive neurones were included although their proportions were given in each Figure. The percentage of such units was consistently higher than in animals raised under normal conditions. This cannot be due mainly to the periods spent in dark before and after exposure, since animals whose exposure had been started at 6 weeks of age did not show higher numbers of unspecific neurones than those in which exposure had been started earlier. It might be argued, therefore, that the bias in the orientation distributions results from the exclusion of cells which

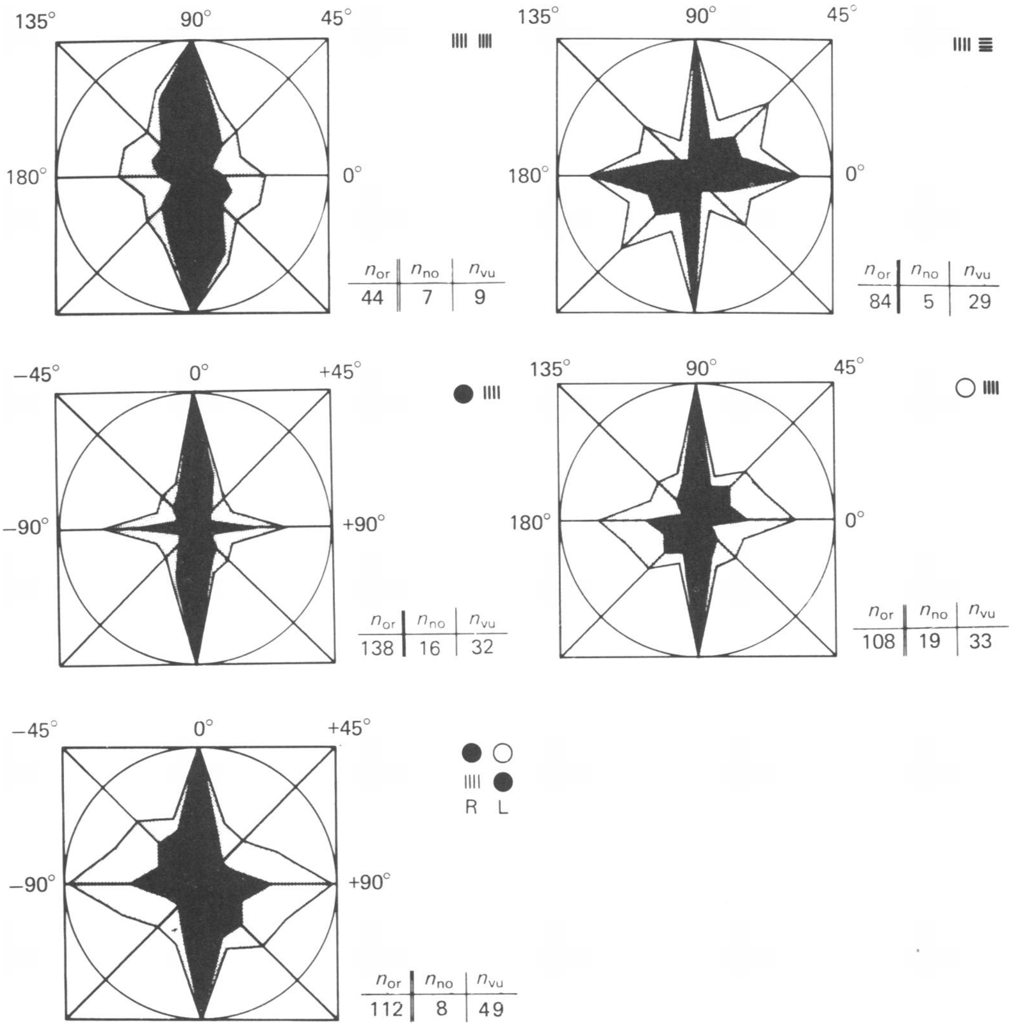


Fig. 7. Quantitative considerations regarding the relative contributions of selective and instructive processes to the origin of the orientation bias in the different raising conditions. The centre diagrams (dark shading) show the distribution of orientation preferences in polar histograms as in Figs. 1–5. Circles with the maximum radius are drawn around the centre to aid visualization of the magnitude of the bias in every case. Assuming a hypothesis of selective deprivation all non-oriented (n_{no}) and unresponsive (n_{vu}) units were spread among the deprived orientations according to the following linear algorithm:

$$n_i = n_{or_i} + (n_{no} + n_{vu}) \times i/K,$$

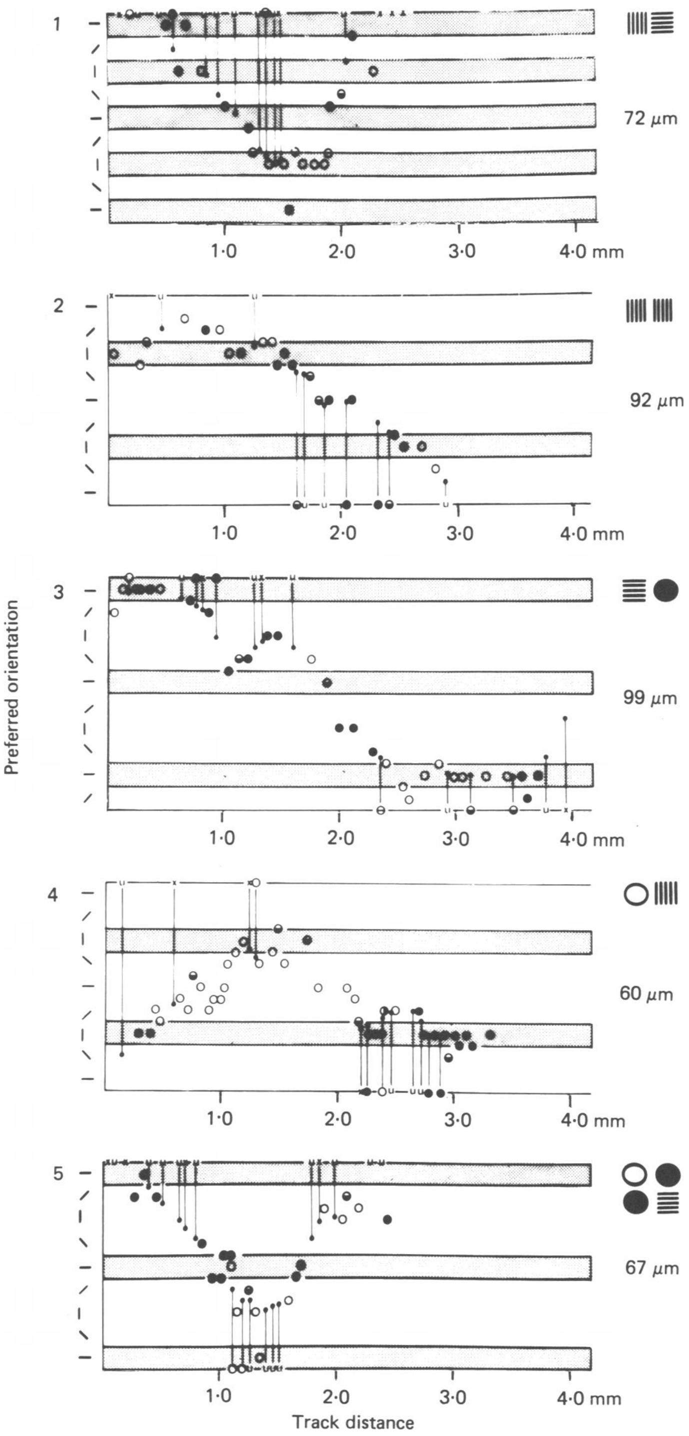
with i being the angle difference between the experienced orientation and a particular orientation in multiples of 22·5°. The numbers of neurones in that particular orientation before and after the addition are n_{or_i} and n_i respectively. For the vertical/horizontal case $K = 8$ is valid, for all other cases $K = 16$. In these latter cases the formula means that a quarter (4/16) of the non-oriented and unresponsive neurones is added to the neurones in the orientation orthogonal to the experienced one; none of them is added to the neurones in the experienced orientations. From the resulting outer graphs (light shading) it can be seen that except in the two-stage paradigm the effects of selective deprivation are too small to explain fully the orientation bias.

'selective deprivation' had rendered non-oriented or unresponsive, since they did not receive affirmative experience. Any apparent bias in the distributions of preferred orientations could only be satisfactorily explained by such a mechanism, if it were possible to quantitatively match the numbers of unselective and unresponsive neurones with the gaps in the skewed distributions. This presupposes of course that all neurones along the path of the electrode were actually detected, which was assured as far as possible by the methods used. In Fig. 7 the polar plots from the previous figures were redrawn and all non-oriented and unresponsive neurones found in the respective kittens were added to the few neurones preferring non-experienced orientations, i.e. assuming that all these cells originated from the pool of neurones that did not receive adequate experience. This evaluation considers the strongest possible case in favour of a selectional hypothesis, since 100 hr of exposure with intermittent periods in total darkness are not comparable to normal experience; even in normal animals there is a certain proportion (5–10 %) of neurones that are visually unresponsive or unselective for orientation. Indeed, for the three kittens that had normal monocular experience before their vision was restricted, the bias can be practically equalized by this procedure except for a slight lack of neurones tuned to oblique orientations. In all other kittens, however, a clear bias for the selectively experienced orientation remains. This is mainly due to the fact that in the two-stage paradigm the proportion of unresponsive units was significantly higher than in all other paradigms (28 % as compared to an average of 18 %).

5. *Track analysis*

Not only to illustrate the data reported above, but also to decide between possible explanations for the changes found in neuronal distributions it is of great interest to analyse the sequence of neuronal response properties (ocular dominance and preferred orientation) along the electrode penetrations. Fig. 8 shows typical examples of track reconstructions from each of the different experimental series. Most tracks show portions of coherent sequences of progressively changing orientation preferences as in normal animals (Hubel & Wiesel, 1974). These sequences are, however, interrupted by clusters of unselective or unresponsive units, especially in the cats that had normal experience before selective exposure. A distinct system of ocular dominance columns was found in practically every kitten. This confirms previous studies which have shown that, at least rudimentarily, orientation and ocular dominance columns are innate facets of cortical organization (Wiesel & Hubel, 1974; Sherk & Stryker, 1976; Shatz, Lindstroem & Wiesel, 1977).

Fig. 8. Examples of penetration reconstructions from each of the five paradigms. Preferred orientation of every neuron is displayed against distance along the electrode track. The exposure paradigm and the mean distance between successively recorded neurones are indicated at the right margin of each graph. The experienced orientations are emphasized by light shading. Ocular dominance is given as follows: ○, right eye; ●, left eye; ◑, symmetrical activation by both eyes (ocular dominance class 3). Crosses represent neurones that were lost before analysis was completed. 'u' refers to unresponsive neurones, and cells lacking an orientation preference are indicated with the respective ocular dominance symbols at the upper and lower margin of the graphs. In all of these cases thin vertical lines are drawn from the margins to linearly interpolated sites between neighbouring orientation-selective cells in order to test the plausibility of a selective deprivation hypothesis (see text).


1
72 µm
1·0
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92 µm
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4·0 mm
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99 µm
1·0
2·0
3·0
4·0 mm
Preferred orientation
4
60 µm
1·0
2·0
3·0
4·0 mm
5
67 µm
1·0
2·0
3·0
4·0 mm
Track distance

From most track reconstructions it appears, however, that this innate system can be filled in and moulded to some extent by visual experience without, however, causing disturbances in the natural periodicity. Depending on individual exposure the columns of the overall dominating eye appeared to be expanded. Moreover, it was quite often observed that portions dominated by an eye with restricted experience contained long sequences of neurones preferring exactly the experienced orientation (± 11·25°). In such cases the change in eye dominance often coincided with an abrupt change in preferred orientation (Fig. 8).

If the extent of cortical tissue devoted to a particular orientation is estimated along one dimension, it is obvious that in all but the two-stage paradigms the 'columns' or slabs corresponding to the selectively experienced orientations occupied more space than those committed to other orientations. Most importantly, they appeared to be expanded not only in *relative*, but also in *absolute* terms when compared to the even distribution which is found in normal animals. The absolute increase in the number of cells responsive to the experienced orientations thus corresponds to an absolute expansion of the respective orientation slabs, partly, it seems, at the cost of cells with broad tuning for oblique orientations. This view is strengthened by current investigations with the [^{14}C]deoxyglucose technique on kittens reared under the same conditions, which visualize this absolute expansion of orientation slabs directly (W. Singer, R. D. Freeman & J. P. Rauschecker, in preparation).

6. *Orientation disparity*

In 90% of all binocular neurones recorded the preferred orientation was the same when tested through either eye. In some cases the tuning borders were different for the two eyes, the tuning usually being broader for the eye with the less appropriate experience. Among all units recorded only two neurones were found in which the optimal orientations differed by more than 22·5°, both being found in kittens which had viewed different orientations simultaneously with the two eyes. This constitutes only 2% of the responsive units in these kittens. But even in these neurones the ranges of orientation where a response could be evoked from one or the other eye were overlapping.

DISCUSSION

Methodological considerations

Because of controversial reports concerning the effect of selective visual experience much emphasis has been put recently on methodology, in particular on the rearing procedure of the kittens and on the sampling of striate cortex cells (Stryker & Sherk, 1975; Sherk & Stryker, 1976; Stryker, Sherk, Leventhal & Hirsch, 1978). In the present experiments the range of visible orientations was restricted with goggles containing strong cylindrical lenses. While assuring a constant and effective control of exposure this method keeps the viewing conditions for the kittens as close to normal as possible. The cylindrical lenses only filter away 'unwanted' aspects of natural objects and do not interfere with visuo-motor integration leaving visual reafference unaffected in the visible spectrum. Normal interaction with the visual world and, thus, also the behavioural relevance of visual experience are unaffected. Finally, the use of cylindrical lenses offers attractive parallels to natural deprivation in humans with congenital astigmatism, who develop meridional amblyopia (Freeman & Pettigrew, 1973; Mitchell, Freeman, Millodot & Haegerstrom, 1973).

To avoid an unrepresentative sample being caused by the columnar organisation of striate cortex we used long, oblique, penetrations (see Methods). Therefore, we do not think it is necessary to exclude any cells from analysis, even if the distance from the previously encountered cell was less than 100 μm. To justify the quantitative approach described above special efforts had to be made to reduce the chance of missing cells along the recording track. Cells lacking spontaneous activity could be activated by currents applied to the electrode. In addition, the use of high-impedance micropipettes increased the selectivity between consecutively recorded cells and reduced the risk of missing small cells (Stone, 1973). This yielded an average distance between successively recorded cells of 60–100 μm with a mean of 85 μm. These values are in the same range as those obtained with identical techniques in normal animals, and we are therefore quite confident that the same proportion of neurones lying on the course of the electrode track was detected in our kittens as in normal cats.

To minimize the experimenter bias different exposure orientations were used within one paradigm and the exact exposure conditions were unknown during receptive field mapping.

Finally, the internal controls resulting from the design of our paradigms indicate that our exposure conditions and the precautions taken during recording have been efficient: (1) In all paradigms with asymmetric exposure of the two eyes there was a strict correlation between ocular dominance, orientation preference and experienced orientations. (2) The high degree of constancy in the exposure conditions is demonstrated by the maintenance of binocularity in the kittens that had binocular vision but with either one or both eyes looking through a cylindrical lens. This internal consistency together with the precautions taken during exposure and recording make us confident that the abnormalities in orientation and ocular dominance distributions are specific results of the restricted viewing conditions.

Selective versus instructive processes

It has become common practice to explain the effects of early restricted visual experience on cortical neurones in terms of either of two theories: (1) *selective* consolidation and, or, deterioration of neuronal response properties already present at birth, (2) *instructive* acquisition of new response properties as a function of visual experience. While a lot of evidence has accumulated in favour of selective processes (Wiesel & Hubel, 1963; Hubel & Wiesel, 1965; Cynader & Mitchell, 1977; Stryker *et al.* 1978), instructive effects are not so widely accepted.

Our results clearly add to the evidence for 'selective' changes, quantitative considerations and careful analysis of the electrode tracks, however, provide evidence for additional 'instructive' effects. In none of the one-stage paradigms, in which dark-rearing preceded restricted experience, was the number of unresponsive and non-oriented neurones high enough to fully account for the orientation bias. Furthermore, there was no proportional relationship between the amount of orientational experience and the number of neurones with mature orientation selectivity or the number of unresponsive and non-oriented neurones respectively. Finally, in segments that were dominated by an eye with restricted experience, long and uninterrupted sequences of neurones were frequently encountered that preferred exactly the experienced orientation. Thus the 'columns' or slabs corresponding to the selectively experienced orientations appeared to be expanded in absolute terms when compared to the even distribution found in normal animals.

The present data therefore suggest that selective and instructive effects may be coexisting rather than mutually exclusive. The relative contribution of the two processes seems to depend mainly on the functional state of the cortex before selective exposure: the possibility of instructive changes decreases as the fraction of neurones already highly specific for a particular orientation increases. Therefore cortical malleability declines during the normal course of the 'critical period' and may be prolonged after prior deprivation (Cynader, Berman & Hein, 1976). Neurones in different layers of visual cortex should show differential plasticity to orientation-selective exposure according to their different degrees of orientation selectivity prior to experience (Blakemore & Van Sluyters, 1975).

The neural mechanism of developmental plasticity

The following arguments suggest that selective and instructive effects are not necessarily different but depend upon the same neuronal mechanism. A set of three simple rules appears to be sufficient to describe this mechanism; their common and crucial assumption is that changes in synaptic efficiency are determined neither by pre- nor by post-synaptic activity alone but depend on the contingency between the two. It is assumed that (1) excitatory synaptic connexions increase their safety factor each time presynaptic afferents and post-synaptic target cell are concomitantly active, (2) synaptic efficiency decreases when the post-synaptic element is active while the pre-synaptic fibre is silent, and (3) synaptic efficiency decreases slowly in time irrespective of pre-synaptic activity when post-synaptic activity is absent.

These rules lead to competitive interactions between convergent afferents whereby those pathways become consolidated, at the expense of others, which possess the highest probability of being active in contingency with the post-synaptic target cell. As discussed previously (Rauschecker & Singer, 1979), the results of the two-stage experiment provide direct evidence for the assumption that circuit changes depend critically on the occurrence of post-synaptic responses. In this case a selective reversal of ocular dominance occurs in those neurones whose orientation preference enables them to respond to the visible range of orientations.

Applying the same three rules to the orientation domain it becomes apparent that they predict correctly and in great detail all results of the present study. It can easily be seen that activity-dependent competition can not only lead to a shift in ocular dominance (Singer, 1976; Singer, Rauschecker & Werth, 1977; Cynader & Mitchell, 1977) but also to a shift in the orientation-preference of broadly tuned cells by asymmetric sharpening of tuning. Furthermore the priming of a particular preference in uncommitted cells can be considered to be the result of such activity-dependent interorientational competition. In both cases pathways conveying the specific activity pattern elicited by the experienced orientation drive the post-synaptic target cell and, according to rule one, these pathways increase their efficiency and finally consolidate. At the same time, because of selective exposure, those connexions remain unstimulated that would be characteristic for other orientations. According to rule two this leads to a gradual decrease of their efficiency. The result is that the cells will become optimally responsive to those input patterns that have been available during selective exposure.

Since, however, all changes in afferent connectivity are gated by post-synaptic activity, the malleability of a neurone's orientation preference by restricted experience depends to a critical extent upon its initial tuning properties. Changes of preference are expected to occur only within the range of a neurone's initial responsiveness. When a cell is not capable of responding to the experienced orientations because of initially high selectivity for another orientation it will either maintain this initial preference or, according to rule three, become unresponsive altogether. Thus, according to the three rules, only two distinct effects of experience are to be expected: (1) adaptation of response properties to available stimulus configurations if the latter are contained in the repertoire of the former and (2) persistence of original response properties and degradation of responsiveness over time when available stimulus configurations fall outside the pre-specified repertoire. We would like to emphasize that the three rules assumed for activity dependent changes in synaptic efficiency are on a formal level identical to Hebb's classical postulates (Hebb, 1949). These postulates were developed in search of a neurophysiological explanation for behavioural changes during operant conditioning. It is tempting to speculate, therefore, that neuronal plasticity during early development is just a special case of the plasticity required for learning and adaptive behaviour: the neuronal mechanisms are governed by the same rules and are therefore likely to be identical. Developmental plasticity would then differ from adult learning and forgetting only because it can already be demonstrated at a rather peripheral level of sensory processing and because it is usually confined to a critical period. This critical period would then serve a twofold purpose in biological terms. The final tuning of the cortical response properties is governed to a certain extent by the external environment in order to adapt the organism to its environment as well as possible. If these requirements exceed the limits set by genetic rules, the respective functional characteristics are eliminated. The seemingly devastating effects of deprivation and the 'paradox of the critical period' (Pettigrew, 1978) would thus appear a little easier to understand.

In conclusion, the results of all exposure paradigms investigated in this study can be accounted for by the above rules defining changes in excitatory transmission as a function of neuronal activity. Processes appearing formerly different at the descriptive level, namely instructive and selective processes, can thus be explained by the same neuronal mechanisms. Therefore, it appears to us that this conceptual dichotomy should no longer be maintained.

We wish to thank Mariele Kremling for editing the manuscript, Linda Walsh for help in rearing the cats, and Susanne Zieglgäensberger for preparing the Figures. We greatly appreciate the valuable suggestions made by G. Dirlich of the Department of Biostatistics concerning statistical analysis and the fruitful discussions on the manuscript with L. Wilson.

This work was partially supported by a research training scholarship from the Max Planck Society to J.P.R. and by a grant from the Deutsche Forschungsgemeinschaft SFB 50, A14 to W.S.

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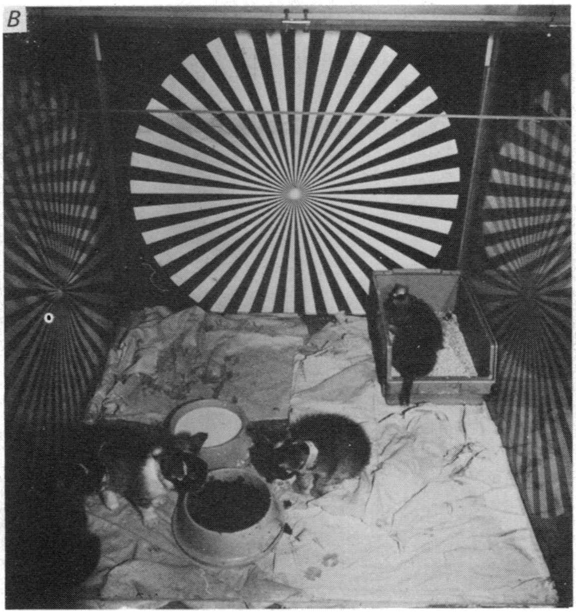
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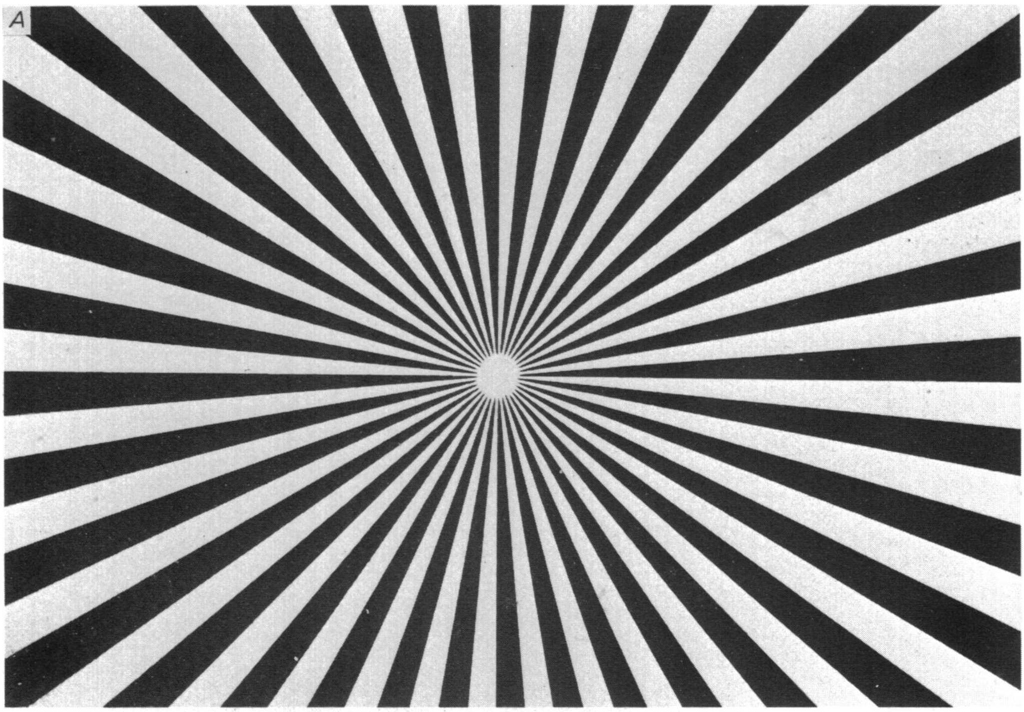

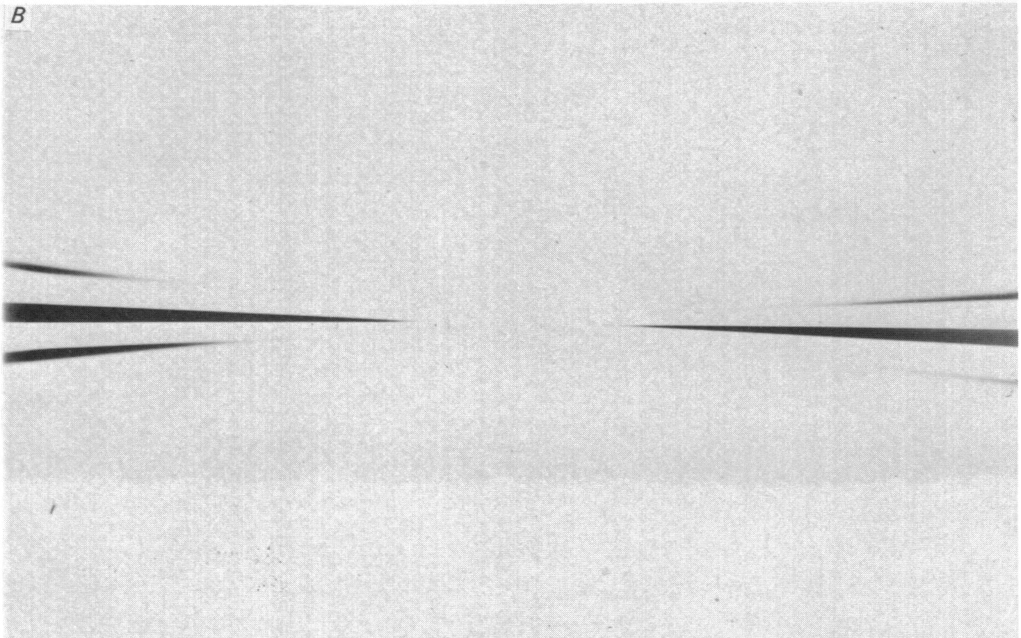

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EXPLANATION OF PLATES

PLATE 1

Illustration of how the experimental animals received their restricted experience. *A*, exposure mask with a cylindrical lens in front of the right eye. *B*, the artificial environment consisting mainly of high-contrast bars of all orientations and of continuously varying spatial frequency.

PLATE 2

Demonstration of the optical filter properties of the cylindrical lenses used for restriction in the orientation domain. *A*, exposure pattern as contained in the visual environment of the kittens under normal viewing conditions. *B*, same pattern photographed with 3·1 mm aperture through a cylindrical lens (−25 D) as worn by the kittens, illustrating the effect of astigmatic blurring (see text).