Receptive Field Development and Individual Experience

Visual experience begins before development is over and may participate in assuring adaptive outcomes.

Paul Grobstein and Kao Liang Chow

For more than 10 years, investigators of nervous system development have known that samples of neurons in the striate cortex of cats which have had abnormal early visual experience may display a quite different spectrum of receptive field properties from those with normal visual experience. The original observation was that the proportion of binocular neurons was dramatically reduced when kittens received incongruous experience through their two eyes (*1*). Later it was reported that, when kittens received visual experience restricted to lines of a single orientation, it was not possible to detect neurons specific for orientations very different from those experienced (*2, 3*). In the past few years, it has been claimed that a number of other aspects of receptive field organization may also be affected by abnormal early visual experience (*4*). These observations have reawakened interest in a classical hypothesis of developmental neurobiology: that individual experience participates to some extent in patterning the intricate interconnections of the nervous system. The observations have not, however, established the proposition as an accepted principle of nervous system development.

Basically, there are three reasons for reservations. One is that the observations have to do with the responses of cortical neurons to visual stimulation; the extension to neuronal interconnections is inferential. We will not, in this article, treat the legitimacy of this inference, but simply note that it is not entirely unsupported by anatomical studies (*4*). The second reason for reservation, particularly in the case of restricted orientation experience, is that there has been some doubt whether the observed changes in distribution of receptive field properties actually indicates that individual neurons have been modified in the relevant properties. Finally, and most generally, there is considerable uncertainty as to whether the processes responsible for abnormal distributions of receptive field properties in abnormally experienced animals actually operate during normal development. This uncertainty, in turn, is largely due to two conclusions drawn from the original investigation of sensitivity to abnormal visual experience in the cat: that the visual pathways are essentially fully developed before visual experience begins and that the effect of abnormal visual experience is to produce a deterioration of the fully developed state (*5*). From this perspective, during normal development, visual experience may be necessary to maintain the developed state but it certainly is not responsible for producing it.

For the past several years, we have been studying the development of receptive field organization in the rabbit visual cortex (*6*) and the role of sensory experience in the process (*7, 8*). This work has produced quite different conclusions about the degree of receptive field development present before first visual experience occurs and about the effects of subsequent abnormal visual experience. The similarity between our results in the rabbit and recent results in the cat (*9*) suggest that a new perspective may be warranted, one which recognizes receptive field development as continuing well into the time of, and being significantly influenced by, initial visual experience. In this article, we attempt to justify this alternative point of view, sketch its broad outlines, and indicate where uncertainties still remain.

Rabbit Receptive Field Development

The rabbit differs from the cat in having laterally placed rather than frontally placed eyes, so that very little visual field is seen by both eyes. As might be expected from this, the retinal projections are almost fully crossed and the great bulk of the visual cortex contains neurons that are exclusively activated by the contralateral eye (*10*), unlike in the cat where most neurons are binocularly activated (*11*). Our studies have been restricted to areas of rabbit visual cortex which represent visual field seen only by the contralateral eye (*12*). This has allowed us to focus attention on the role of visual experience through one eye, without the complication, present in the cat, of interactive effects between two eyes. A second difference between the cat and the rabbit is that in cats most neurons require a properly oriented stimulus bar or edge for maximal activation (*11*), whereas this is true for only about one-third of the neurons in rabbits (*10*). Most of the remainder of the neurons in the rabbit are maximally responsive to stationary spots of light, to moving spots of light, or to spots moving in a particular direction (*13*). Several things follow from this. One is that we have routinely distinguished between directional and orientation specificity, which has only recently been done in cat (*9*). A second consequence of the diversity of receptive field types is that the original investigators of adult cortex were motivated to describe the relative frequencies with which neurons falling into them were encountered (*10*). This allowed us to pose our questions in terms of the developmental time courses over which these frequencies were attained. Finally, the presence of both orientation-specific and nonorientation-specific neurons in the rabbit cortex made it possible to recognize an involvement of visual experience restricted to the development of orientation specificity.

In our initial developmental studies (*6*), we concentrated on the relative numbers of orientation-specific, direction-specific, and nonorientation-specific receptive fields present at various ages. In particular, we were concerned with ages in the vicinity of about 10 days, when rabbit pups normally open their eyes and patterned visual experience first becomes available. Figure 1 shows the time course of receptive field development in rabbit visual cortex. It illustrates the general conclusion that the process is not complete when the animals open their eyes. Specifically, neurons displaying orientation specificity were not detectable until after eye-opening, and they increased in relative numbers over the subsequent several weeks. The same was true of directional cells. Nonoriented cells, on the other hand, are present before eye-opening in frequencies near levels characteristic of

---

Dr. Grobstein is an assistant professor in the Department of Pharmacological and Physiological Sciences, University of Chicago, Chicago, Illinois 60637. Dr. Chow is a professor in the Department of Neurology, Stanford University Medical School, Stanford, California 94305.

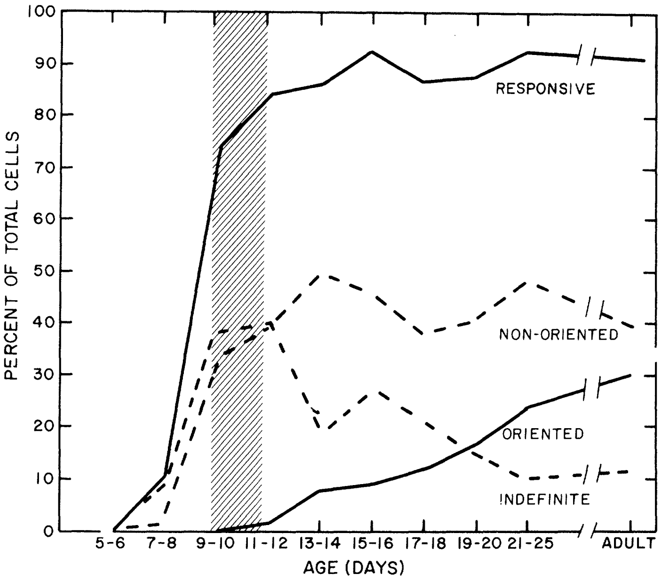

Fig. 1. Normal development of receptive field organization in rabbit visual cortex. The four curves illustrate changes as a function of age in the properties of samples of cortical neurons recorded in rabbits undergoing normal development. The abscissa represents age in days after birth. The ordinate represents the percentage of the total number of neurons recorded at any given age. Shading indicates the age at which rabbits open their eyes. The upper curve shows the percentage of the neurons encountered which were responsive to visual stimulation of any kind. The lower three curves indicate the percentage of neurons encountered which were categorized as nonoriented, oriented, or indefinite as described in the text and in (*13*). Direction-selective neurons are not shown [modified slightly from (*6*)].

adult animals. A second difference between young animals and normal adults was the high percentage of neurons (indefinite cells) which, while visually responsive, were too unreliable in their response properties to place in any of the standard receptive field categories. These declined in frequency over a period quite similar to that for the appearance of orientation-specific neurons. Finally, in the young animals, of all the neurons encountered, a slightly lower proportion than in adults were responsive to any form of visual stimulation.

These findings prompted us to reexplore the effects of visual deprivation on receptive field organization in rabbit striate cortex (*7*). It was already known that animals deprived by lid suture of patterned visual experience from birth for 3 months or more were indistinguishable from normal adult animals in terms of frequencies of various receptive field types (*8*). We were interested, however, in whether the developmental time courses we had observed in normal development would be affected by delaying eye-opening, in particular whether the events that normally occur during the 2 weeks subsequent to eye-opening would occur during that time if eye-opening was prevented. The nearly complete crossing of the visual pathways in the rabbit already alluded to provided us with the opportunity for an internal control against systemic effects of visual deprivation. We closed one eye by suturing before eye-opening but allowed the other eye to open normally. Both the control cortex, contralateral to the open eye, and the experimental cortex, contralateral to the sutured eye, were sampled in animals 20 to 25 days of age, a time when most of the changes after eye-opening in normal animals have occurred.

The histograms in Fig. 2 show that the visually deprived and visually experienced cortices differ in percentages of responsive neurons, of neurons with oriented and nonoriented receptive fields, and of indefinite neurons. The lines extending to the left show the chronological ages at which these percentages would be found in normally developing animals. These cluster around 20 days for the experienced cortices and around 10 days for the deprived cortices. This we take as strong evidence that the effect of delayed eye-opening (early visual deprivation) is not to produce deterioration of a fully developed cortex, but instead to delay an ongoing developmental process. For the sake of the comparison below with the cat, it is worth mentioning one exception to this rule. Directional cells are present, in normal percentages, in the deprived cortices (*7*).

In the rabbit, then, receptive field development spans the time when visual experience first becomes available. Before that time a significant number of neurons lack normal receptive field organization; these are either indefinite or nonresponsive. Subsequent to eye-opening, cells with oriented fields appear, coincident with a decline in indefinite and nonresponsive neurons. These two correlated events can be delayed, but not prevented, by delaying eye-opening.

Methodological Considerations

Before we consider the generality and significance of these findings, we call attention to an important methodological aspect of these studies. We have attempted to focus on the cortex as a complete neuronal population by emphasizing quantitative changes in the percentages of neurons in various receptive field categories. The reason for this is that the number of neurons in the visual cortex of a mammal is enormously large compared to the number actually observed by microelectrode sampling. To draw meaningful conclusions by comparing microelectrode samples from animals of different ages or subjected to different experience regimes, it is necessary to assume that the samples adequately represent the same population of neurons in the different animals. In the present instance, we are inclined to the conclusion that many indefinite and nonresponsive neurons in the animal before eye-opening subsequently develop into neurons with oriented receptive fields. An alternate possibility is that we are sampling different populations of neurons in, for example, 10-day-old and 25-day-old animals.

A sampling bias may come about in several ways. One is a subtle form of experimenter bias. Unless an investigator is alert to the likelihood of neurons with atypical response characteristics, he may discard them. Moreover, neurons in young animals generally have low levels of spontaneous activity. Because neurons must fire to be detectable with a microelectrode, nonresponsive neurons (particularly those with low spontaneous activity) may be missed altogether. In our studies, we are careful to take note of every neuron encountered, no matter how atypical its response. It was this that made us recognize indefinite neurons as a significant component of the cortical population prior to eye-opening in the rabbit and to detect the correlation between the decline of indefinite neurons and the appearance of orientation-specific neurons. We also make it a practice, particularly in quite young animals, to advance the electrode slowly, with long waits; even so, we may have underestimated the frequencies of nonresponsive neurons.

A second source of sampling bias is electrode bias. An increase in size of neurons of a particular class, for example of orientation neurons, might bring them above the level of detectability with an electrode. One might erroneously conclude that the class has newly developed, when in fact, it was present all along but simply not detected. This can never be absolutely excluded as a possibility; a careful population analysis may, however, indicate that such an explanation is unlikely. To account for our rabbit data on this basis would, for example, require an involved and ad hoc scheme of correlated adjustments in the detectability of other classes. In particular, there is only a small increase in the percentage of visually responsive units during the time that oriented units appear, so there would have to be a decrease in detectability of some other class. Neurons in the indefinite class are candidates, but then there should be an increase in percentage of nonoriented units, which does not in fact occur.

In short, there do indeed seem to be changes in the response characteristics of individual cortical neurons in the rabbit, the time course of which, in the case of oriented neurons, can be affected by abnormal visual experience. The question of sampling bias in connection with the effects of more sophisticated paradigms of abnormal visual experience used in cats, as well as with regard to the degree of development in the cat visual cortex before eye-opening, is discussed below.

Development in Cat and Monkey

The degree of receptive field development at the age when visual experience first becomes available, and the effects of delaying the onset of visual experience, have recently been investigated in the monkey (*14*) and reinvestigated in the cat (*9*). The recent results in the cat are strikingly similar in several ways to those we have obtained in the rabbit. Those from the monkey differ somewhat. We will consider the cat first and then go on to discuss the monkey. Like the cat, the monkey is largely a binocular organism. For the moment, we ignore results bearing specifically on binocularity and treat only aspects of receptive field organization which have parallels in the rabbit.

Cats, like rabbits, open their eyes during the second week after birth. The original investigation of receptive field organization at this age involved recordings from a single animal (*5*). Many fewer neurons were isolated in a penetration than in adults and some isolated neurons displayed less selectivity to line orientation. The investigators chose, however, to emphasize the existence of neurons as specific in their orientation selectivity as adult units. The legitimacy of this characterization has been called into question by Barlow and Pettigrew and by Pettigrew (*9*), who pointed out that directional selectivity is confounded with orientation selectivity when moving bars are used as stimuli. With data from more animals, they report that directional neurons first appear about the time of eye-opening in the kitten. Orientation specificity, in the strict sense, is not observed until 2 weeks after eye-opening. Directional specificity is present in 2- to 6-week-old animals despite prevention of eye-opening by lid suture. Occasional orientation-specific neurons are found, but their frequency is much lower than in normally reared animals of the same age. There is still some uncertainty as to whether any neurons in the cat are orientation-specific before eye-opening (*14*). What does seem clear, if all units encountered by an electrode are included, is that many neurons develop orientation specificity after eye-opening and that this development can be prevented from occurring at the normal time by delaying eye-opening.

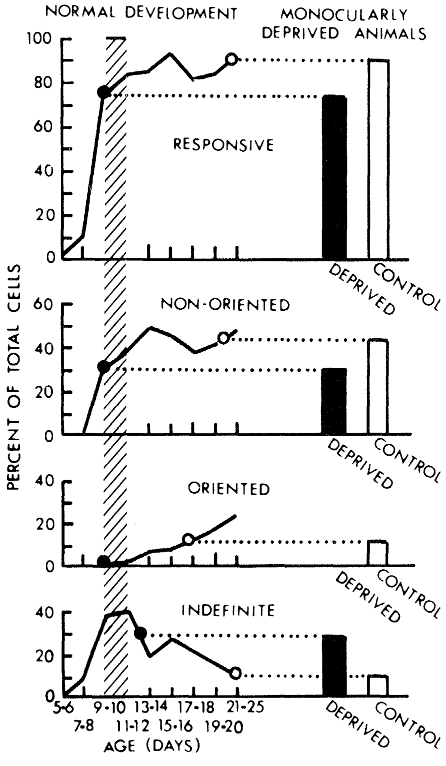

Fig. 2. Effects of short-term delayed eye-opening on receptive field development in the rabbit visual cortex. The histograms on the right show the percentages of responsive neurons and of neurons falling into nonoriented, oriented, and indefinite categories in the deprived (closed bars) and control (open bars) cortices of 20- to 25-day-old rabbits in which one eye was prevented from opening by lid suture. Horizontal lines extending to the left intersect the curves redrawn from Fig. 1, indicating the ages during normal development when the values indicated by the histograms would be expected. The clustering of these intersections above 17 days (open circles) for the control cortices and below 12 days for the deprived cortices (closed circles) indicates retardation of development [modified slightly from (7)].

It is worth entertaining the possibility that the parallels between cat and rabbit development encompass more than the late development of orientation selectivity and its sensitivity to delayed eye-opening. In binocularly deprived cats of 2¼ to 4½ months of age, 27 percent of the neurons are nonresponsive, 32 percent are "abnormal" but responsive, and 41 percent are "normal" (*15*). The high percentages of nonresponsive and poorly responsive neurons have been interpreted as being indicative of deterioration due to deprivation. In the deprived rabbit, however, high percentages in these categories are indicative of retarded development; they are highest at the age when eye-opening would normally occur and decline with time under delayed eye-opening, although more slowly than with normal visual experience. Conversely, orientation-specific neurons increase as a percentage of the population.

The percentage of nonresponsive neurons in kittens before eye-opening is not known. However, a penetration through the cortex of a young kitten encounters 10 percent or less of the number of neurons in an adult cortex (*5*). One possible explanation is that there is a quite high percentage of nonresponsive neurons having very low spontaneous activity. A small sample of neurons in 12- to 18-month-old binocularly deprived cats yielded 12 percent nonresponsive (*16*), so that the value for binocularly deprived 2¼- to 4½-month animals (27 percent) may well be on a declining curve. It is more difficult to ascertain whether percentages of orientation-specific and atypical neurons are increasing or decreasing under continued deprivation, since available information about long-term deprivation comes from experiments that predate the attempt to distinguish between directional and orientation specificity. However, some neurons exhibit orientation specificity in the strict sense in a 6-week-old deprived cat (*9*). In 12- to 18-month deprived cats, 88 percent of the neurons respond to only one or two of four tested directions of movement (*17*), a value higher than the 41 percent "normal" in the intermediate age animals.

These data are very suggestive that in the cat, as in the rabbit, some orientation-selective neurons will develop, albeit later than normal, despite delayed eye-opening. It is within the realm of possibility that all of the results in 2¼- to 4½-month binocularly deprived cats represent an intermediate point in a lengthened developmental sequence, rather than a deterioration. If this should turn out to be the case, two things would follow. One is that 27 percent is an absolute lower limit for the number of nonresponsive neurons present at the age when eye-opening normally occurs. The other is that the delay in development caused by deprivation is much longer in the cat than in the rabbit (*16*).

The monkey differs from the cat and rabbit in that it is born with its eyes open. Recordings have been made from a single 2-day-old animal as well as from 3- to 4-week-old animals binocularly deprived essentially from birth (*14*). In the latter, 10 to 15 percent of the neurons were poorly responsive or had less than normal orientation selectivity. In the former, of 23 neurons, none were unresponsive, sluggish, or nonoriented. In this case, there is no strong evidence that visual experience affects the development of orientation selectivity. Indeed, the presence of atypical neurons in the binocularly deprived animals and their absence, together with the presence of neurons displaying normal selectivity in the 2-day-old animal, might lead one to the conclusion stated generally earlier that orientation selectivity develops in advance of visual experience and is subject only to subsequent degradation by abnormal visual experience.

We believe, however, that it is premature to conclude that the monkey is qualitatively different from the cat and rabbit in these ways. It certainly appears to be the case that some orientation-specific neurons are present at an earlier age in the monkey than they are in the cat or rabbit. What is not clear is whether there is an additional population of neurons that develops orientation selectivity subsequently, over a time course which can be prolonged by visual deprivation. This question can be settled only by experiments like those in the cat and rabbit which determine the percentage of cortical neurons displaying orientation specificity as a function of age during normal development and then looking for deprivation effects against this baseline. The possible existence of a reservoir of nonresponsive neurons of low spontaneous activity in the young monkey makes it unclear whether atypical neurons in the older deprived animals have lost previously typical receptive field characteristics or instead have failed to develop them.

To summarize the available developmental studies, the development of orientation-selective cells in the rabbit and of at least some in the cat follows the onset of visual experience. For both the cat and the rabbit, the development does not occur at the normal time if eye-opening is delayed. These results imply, at a bare minimum, that visual experience participates in the normal development of functional connectivity related to orientation specificity; it is not accurate to say that it functions only to maintain previously established functional circuitry. On the other hand, the evidence on normal development and the effects of delayed eye-opening do not permit the conclusion that visual experience influences the pattern of functional connections which represents some end state of development, since orientation selectivity may develop, albeit later than normal, despite continued deprivation.

Development of Binocularity

In addition to orientation specificity, there is a second aspect of receptive field organization, binocular specificity, which has been shown to develop over a time course that can be modified by delayed eye-opening. For most striate cortical neurons in the adult cat, a visual stimulus must be precisely placed on both retinas to elicit the maximal response. One measure of this is the size of the region on one retina which gives a maximal response when stimulated simultaneously with a fixed position on the other. Pettigrew has shown that this area is quite large for neurons in cats before eye-opening and narrows to adult levels over succeeding weeks. The narrowing fails to occur in animals binocularly deprived to 6 weeks (*9*).

The recognition of binocular specificity is relatively recent. However, recognition of binocularity—the fact that cortical neurons are activated through either eye from roughly the same region of visual space—is older, and the phenomenon has played an important part in studies of the role of experience in visual system development. Indeed, it was the phenomenon of binocularity, rather than that of orientation specificity, that most clearly exemplified the perspective of a nervous system fully developed before the onset of visual experience. At present, these original studies, coupled with the newer studies on the development of binocular specificity, provide the strongest evidence that the final pattern of functional circuitry in the visual system is normally influenced by visual experience.

The original observation by Hubel and Wiesel was that kittens before the onset of visual experience display approximately the same pattern of binocular neurons as do normal adults (*5*), whereas kittens subjected to early monocular deprivation have an enormous, and nearly irreversible, reduction in the percentage of neurons that can be activated by the deprived eye (*1*). Monocular deprivation, of course, may lead to a developmental retardation of the kind described above in the rabbit. In the cat, the fact that both eyes project ultimately to the same cortex adds the complication that there may be a retardation of development of functional circuitry of one eye relative to the other. If the majority of cortical neurons will accept functional connections related to either eye, this alone may account for the effects of monocular deprivation (*18*).

Two additional abnormal experience regimes, however, indicate that relative retardation of development is not the sole factor influencing binocularity. Animals reared with day-by-day alternation of the deprived eye exhibited a severe reduction of binocularly activated neurons, without any relative loss of either eye's ability to activate neurons and without the presence of nonresponsive or indefinite neurons (*19*). More strikingly, the same effect was seen in animals with a surgically induced strabismus, so that both eyes were simultaneously activated but were looking at quite different parts of visual space (*19*).

An important link between these early experiments and the more recent developmental studies was provided by Shlaer, who inferred from the earlier work that stable binocular connections onto single neurons were established when the afferents representing the two eyes were simultaneously activated by the same stimulus in visual space (*20*). He tested this inference by raising kittens with prisms over their eyes which displaced the visual world a small amount on one retina with respect to the other. He then determined the position on the retinas of the receptive fields of cortical neurons through each eye with respect to a retinal landmark (the nerve head). In normal animals, he found the receptive fields to be located roughly the same distance from the nerve head on both retinas. In the prism-reared animals the fields were shifted in such a way as to tend to compensate for the displacement produced by the prisms (*20*). These experiments, unfortunately, have never been fully reported and need to be confirmed with the use of the same measure of binocular specificity as in the more recent developmental studies. They are, however, concordant with the more recent studies which show a gradual increase in the precision of binocular fusion with age and visual experience. Together, it seems to us, they establish a fairly strong case that, during normal development, it is left to individual experience to establish exactly which pairs of retinal regions activate single cortical neurons.

If we assume that this tentative conclusion about the development of binocularity withstands further experimental test, there are two implications about the role of individual experience in nervous system development which we propose may have general applicability. One of these we might call the principle of restricted potential. By this we mean to emphasize that the developing nervous system is not a tabula rasa, free to reflect whatever individual experience dictates. Rather, the development of the nervous system is a process sharply constrained by a genetic program. At certain points, the genetic program permits a range of possible realizations, and individual experience acts only to specify the outcome within this range.

We deduce this principle from the observations of Shlaer and Pettigrew on the one hand and those of Hubel and Wiesel on the other, particularly those with strabismic animals. The difference between prism-reared animals and those with a surgically induced strabismus is largely one of degree. Both have a relative displacement of the visual world on the two retinas. In prism-reared animals, the relative displacement is rather small (4° to 6°) and a compensating adjustment of inputs to cortical neurons appears. In strabismic animals, the relative displacement is much larger and binocular connections largely break down. Thus there appears to be a small range within which individual experience operates to assure proper binocular fusion. The displacements induced by Shlaer were of the order of the size of binocular facilitation fields found by Pettigrew in naive animals; it would be interesting to know if these fields define the permissible range. For displacements greater than the permissible range, the system breaks down (*21*).

The second principle we propose attempts to define the circumstances in which such windows to individual experience are likely to be present in the genetic program for nervous system development. Many experiments in developmental neurobiology have led to the conclusion that individual experience does not affect nervous system development. What is special about binocular specificity, it seems to us, is that individual experience is probably indispensable in its development. The two eyes have independent developmental histories; their relative positions, optics, and retinal structures are presumably all subject to minor variations. Under these circumstances, to determine which pairs of retinal regions are actually stimulated by a single region in visual space seems not possible, except by trying out the system. In short, genetic information is probably intrinsically inadequate to assure functionally appropriate connections. It is in such cases, we propose, that developmental programs contain a mechanism for incorporating "ontogenetic information" into the developing nervous system.

Development of Orientation Specificity

We now return to the question of the role of visual experience in the development of orientation specificity. As we indicated previously, the developmental studies indicate that, in the cat and the rabbit, orientation specificity does not develop at the normal time if eye-opening is delayed. This indicates that visual experience is normally involved in the development of this aspect of receptive field organization. We can add now that this implies that there are two processes sensitive to visual experience. One is concerned with matching inputs through the two eyes. The other, since it is present in the nonbinocular portions of rabbit cortex, must not be. In fact, the conclusion we arrive at is that it is not clear what the adaptive value of the latter process is.

There have been two independent reports of dramatic effects of rearing kittens in ways that restricted their experience to either horizontal or vertical bars. Hirsch and Spinelli (*3*) reared kittens whose only visual experience was through goggles which presented vertical stripes to one eye and horizontal stripes to the other. Many cortical neurons in these animals were activated monocularly and had receptive fields oriented in accord with the orientation of the bars the eye had experienced. In addition, Hirsch and Spinelli found some neurons lacking oriented fields and noted silent regions of cortex in which neurons were not encountered. Blakemore and Cooper (*2*) reared kittens with visual experience restricted to periods inside tubes with either horizontal or vertical stripes on the walls. In these animals, neurons were normally binocular, but no neurons had orientation specificity for the nonexperienced orientation. Silent regions were reported not to be present.

There are several possible interpretations of these experiments. One is that orientation specificity itself is a product of visual experience, that neurons tend to be responsive to linear contours because linear contours are common in the environment. This seems highly unlikely, in view of the fact that orientation selectivity develops in the deprived rabbit, is already present in the neonatal monkey, and probably is present in the visually naive cat. A much more likely interpretation, in analogy with the development of binocular specificity, is that there is some genetically determined range of possible orientation specificities for an individual neuron within which the actual orientation specificity is realized by experience. The experimental evidence, however, is less compelling than in the case of binocular specificity.

In the case of goggle-reared animals, there is considerable question whether the failure to find neurons selective for nonexperienced orientations indicates that all neurons have become selective for the experienced orientation. The finding of neurons with no orientation selectivity as well as of silent cortical regions, which may contain nonresponsive neurons, makes it possible that a sampling bias accounts for the lack of neurons selective for nonexperienced orientations. By this we mean that there may be a relative retardation of the developmental time course of neurons which would normally be specific for nonexperienced orientations. There is some support for this in the finding that goggle-reared animals, after a subsequent period of normal binocular experience, do not have silent regions, possess more binocular units, and seem to have a wider scatter of orientation selectivities (*22*).

Goggle-reared animals, however, undoubtedly are displaying several effects, including some related to asymmetry of inputs to the two eyes. In tube-reared cats, which have the opportunity for synchronous binocular input, silent areas have not been found nor have significant numbers of indefinite neurons. In these animals, the evidence strongly suggests that the orientation selectivity of individual cortical neurons can be influenced at least within a small range (roughly 45° of orientation selectivities, centered around the nonexperienced orientation, is missing) by visual experience (*23*).

The question then is the significance of this observation for normal development. It has been suggested that the process may operate to increase the proportion of neurons selective to orientations which are prevalent in the environment in order to increase visual acuity for such orientations (*2*). This seems unlikely on both experimental and theoretical grounds. Rabbits do not show the dramatic effects of tube-rearing obtained in cats (*24*). Very young monkeys show the ordered progression of orientation selectivities across cortical columns characteristic of adults (*14*). In the former there is no evidence that proportions of neurons selective for particular orientations is influenced by visual experience and, in the latter, it seems unlikely. Even in cats, there is evidence for establishment of a range of orientation specificities not matched to visual experience. Leaving aside the previously considered questions of the existence of orientation specificity prior to visual experience and of its development despite delayed eye-opening, it has been reported that exposure to restricted orientations, if done at a time later than in the experiments previously described, results in development of a full range of orientation specificities (*25*).

On theoretical grounds, it seems unlikely that a process making use of individual visual experience to match the visual system to the environment in this way would be particularly useful (and hence unlikely that it would have evolved). The environment, after all, has not been notably variable in the prevalence of particular orientations. If a match of neuronal orientation selectivities to environmental prevalence is useful, one would expect such a match to be produced by genetic information. In short, the interpretation does not satisfy our proposed principle that individual experience participates in nervous system development only when genetic information is inadequate to assure functionally appropriate connection patterns.

An alternate interpretation which does satisfy the genetic inadequacy principle is that there is a certain potential range of orientation selectivities left by genetic mechanisms in order to assure that inputs from the two eyes have matched orientation specificities (*26*). This may be true for the cat, although it is experimentally unsupported. The interpretation does not, however, account for the situation in the predominantly monocular rabbit cortex where, as in the cat, development of orientation specificity is delayed by delayed eye-opening. It is possible that the similarities between cat and rabbit in this regard are coincidental; indeed, we have already noted that it is apparently less possible to influence orientation selectivity by selective orientation rearing in the rabbit. The similarities are striking, however, and there is mounting evidence of other kinds for effects of abnormal sensory experience in circumstances where binocular interactions are not present (*27*).

We are left therefore with the uncomfortable feeling that there is a role played by visual experience in the normal development of orientation selectivity, but that we have no good notion of what it is. It is probably not the creation of line detectors and probably not the matching of acuity to common orientations. Perhaps it is some more subtle role, such as aligning some fundamental retinal axes, against which orientation selectivities are defined, with body axes or some other axes relevant to motor control. If this is the case, then the apparent identity of the developmental end state reached by normally experienced and longer term deprived rabbits reflects our failure to use assay techniques appropriate to reveal their differences (*28*).

Summary and Conclusions

We believe that the trend of experimental evidence, as exemplified by studies reviewed in this article, as well as others (*4*), is toward establishing that individual sensory experience is a creative factor in establishing the functional organization of the mammalian visual pathways. At the present time, however, as we have attempted to make clear, there are varying degrees of uncertainty associated with the supporting arguments.

Our strongest conclusion is that the normal adult functional organization is not present in cat or rabbit cortex before the age at which eye-opening normally occurs. We emphasize the presence of high percentages of atypically responsive and of nonresponsive neurons as evidence for this, but note as well that two particular aspects of receptive field organization, binocular and orientation specificity, are either not present or are present in a much smaller fraction of neurons than in normal adults. We conclude with equal assurance that, in both the cat and the rabbit, the time course of the appearance of normal percentages of orientation-specific units is markedly delayed by delaying eye-opening. The same is true for binocular specificity in cats, which may be prevented altogether from developing. Accompanying the delayed development of orientation specificity in rabbits are elevated percentages of atypical and nonresponsive neurons. These represent a retention of the neonatal state, not a deterioration. The same may be true in the cat.

The effect of these findings on normal development and delayed eye-opening is to remove one barrier to acceptance of the proposition that individual experience participates in visual system development. So long as it seemed that the visual system was fully developed in advance of visual experience, the effects of subsequent abnormal visual experience could only be interpreted as destructive. It now appears certain that development normally continues well into the time when visual experience becomes available and that at least some of the effects of abnormal visual experience, in particular delayed eye-opening, should be interpreted as a retention of the developmental state present before the initiation of visual experience.

While this allows the strong conclusion that visual experience normally participates in development, we explicitly note that it does not allow the conclusion that the end state of the developmental process is normally influenced by individual experience. The development of orientation selectivity in the rabbit, and perhaps in the cat despite continued deprivation, is a case in point. It is necessary to show that the end state reached differs when individual experience differs. In particular, it is necessary to show that the behavior of individual neurons has been influenced by visual experience; possible sampling bias must have been excluded.

There are two aspects of receptive field organization for which we believe this has been accomplished, both in the cat. Strabismic animals reach an end state characterized by a vast reduction in binocularity, and tube-reared animals reach an end state with an absence of neurons selective for nonexperienced orientation. Even this, however, is not sufficient to establish that visual experience influences the end point in normal development. This final step in the argument requires the demonstration that there is some element provided by experience, what we have termed ontogenetic information, which is essential to the correct functioning of the system.

At this point, the conclusions are, unfortunately, more tentative. In the case of binocularity, we believe the critical piece of ontogenetic information has probably been identified: which pairs of retinal regions are in fact stimulated by single regions in visual space. While further experimental verification is needed, it seems likely that this is indeed a critical piece of ontogenetic information, that genetic information alone cannot assure appropriate function. On the other hand, if our interpretation of this body of evidence is correct, the incorporation of ontogenetic information is not unbounded; it occurs by selection of one realization within a genetically determined range.

In the case of orientation specificity, the critical piece of ontogenetic information is simply not clear and we regard this as the principal challenge at the present time. We have suggested that there is probably a common phenomenon in the cat and the rabbit, despite the lack of a dramatic response to selective orientation rearing in the latter. The lack may reflect a smaller potential range of variations in the rabbit, or a difference in its manner of interacting with the selective environment. Perhaps one of the key problems, if the hypothesis of a common phenomenon is correct, is to establish the differences between a normally reared and a visually deprived rabbit.

References and Notes

1. T. N. Wiesel and D. H. Hubel, *J. Neurophysiol.* **26**, 1003 (1963).
2. C. Blakemore and G. F. Cooper, *Nature (Lond.)* **228**, 447 (1970).
3. H. V. B. Hirsch and D. N. Spinelli, *Science* **168**, 869 (1970); *Exp. Brain Res.* **13**, 509 (1971).
4. In this article, we will not attempt to provide a comprehensive literature review, but rather will focus on what we think are the important examples illustrative of the points we are trying to emphasize. In so doing, we concentrate on physiological studies of the development of cortical neuronal receptive field organization and of the effects of abnormal visual experience on binocularity and orientation specificity. For more comprehensive reviews of the effects of abnormal visual experience on neuronal physiology, see J. D. Pettigrew, *Ann. N.Y. Acad. Sci.* **228**, 393 (1974); C. Blakemore, *Br. Med. Bull.* **30**, 152 (1974); P. Grobstein and K. L. Chow, in *Development of Neural and Behavioral Specificities*, G. Gottlieb, Ed. (Academic Press, New York, in press). For a review of the effects of abnormal visual experience on anatomy, see R. W. Guillery, in *Essays on the Nervous System*, R. Bellairs and E. G. Gray, Eds. (Clarendon, Oxford, 1974).
5. D. H. Hubel and T. N. Wiesel, *J. Neurophysiol.* **26**, 994 (1963).
6. P. Grobstein, K. L. Chow, P. D. Spear, L. H. Mathers, *Science* **180**, 1185 (1973); L. H. Mathers *et al., Exp. Brain Res.* **19**, 20 (1974).
7. P. Grobstein, K. L. Chow, P. C. Fox, *Proc. Natl. Acad. Sci. U.S.A.* **72**, 1543 (1975).
8. K. L. Chow and P. D. Spear, *Exp. Neurol.* **42**, 429 (1974).
9. H. B. Barlow and J. D. Pettigrew, *J. Physiol. (Lond.)* **218**, 98P (1971); J. D. Pettigrew, *ibid.* **237**, 49 (1974).
10. K. L. Chow, R. H. Masland, D. L. Stewart, *Brain Res.* **33**, 337 (1971); A. Hughes, *Doc. Ophthalmol.* **30**, 33 (1971).
11. D. H. Hubel and T. N. Wiesel, *J. Physiol. (Lond.)* **160**, 106 (1962).
12. For studies on the small region of rabbit cortex containing binocular neurons, see R. Van Sluyters and D. L. Stewart, *Exp. Brain Res.* **19**, 196 (1974).
13. In practice, we place neurons in one of nine categories depending on their responses to visual stimulation. Of these categories, seven are well-defined receptive field types: uniform, concentric, motion, directional, simple, complex, and oriented-directional. For detailed descriptions, see (*10*). "Oriented-directional" has replaced the earlier name "hypercomplex" [see (*6*)]. Of the seven receptive field types, the last three require properly oriented linear contours for maximal response; they are here collectively termed "oriented." The first three do not require oriented stimuli and are here collectively termed "nonoriented." These collective terms have been adopted as a result of our recent deprivation studies (*7*) and differ respectively from the "asymmetric" and "symmetric" supercategories used earlier (*6*) only in that the directional receptive field type has been excluded from the former and is treated independently. The two remaining categories are "nonresponsive," meaning unaffected by visual stimulation, and "indefinite," meaning responsive to visual stimulation but too unpredictable to identify as one of the seven receptive field types.
14. T. N. Wiesel and D. H. Hubel, *J. Comp. Neurol.* **158**, 307 (1974).
15. ——, *J. Neurophysiol.* **28**, 1029 (1965).
16. Our intention in this analysis of the effects of long-term deprivation is to call attention to the possibility that they may represent in part delayed development rather than degradation of previously developed behavior. We wish to explicitly note, however, that in addition to delaying development, continued deprivation may subsequently cause degradation. Separation of these two effects may require a well-resolved temporal analysis of the percentages of the cortical neuronal population exhibiting various behaviors in binocularly deprived animals.
17. L. Ganz, M. Fitch, J. A. Satterberg, *Exp. Neurol.* **22**, 614 (1968).
18. There are two somewhat distinct ways that retardation of development could yield the observed results of monocular deprivation, that is, the virtual domination of neurons by one eye. They differ with respect to the fate of the binocularly activated neurons present before eye-opening. One possible interpretation is that these neurons are unaffected by the deprivation but that the hypothesized large population of nonresponsive neurons all develop inputs only from the open eye. The observed result would then be largely a sampling effect and should not be interpreted as deterioration. The other is that the developmental retardation puts the deprived eye at a disadvantage even in maintaining functional inputs to neurons it was once capable of activating. Because of the sampling problem, these are not distinguishable interpretations at present.
19. D. H. Hubel and T. N. Wiesel, *J. Neurophysiol.* **28**, 1041 (1965).
20. R. Shlaer, *Science* **173**, 638 (1971).
21. There is a second difference between prism-reared animals and those with strabismus produced surgically by cutting one extraocular muscle. In the latter the animal's ability to produce coordinate movement of the two eyes has been reduced. Experiments over a range of prism displacements are needed to verify that it is the magnitude of the displacement which accounts for the difference between prism-reared and strabismatic animals.
22. J. D. Pettigrew, C. Olson, H. V. B. Hirsch, *Brain Res.* **51**, 345 (1973); D. N. Spinelli, H. V. B. Hirsch, R. W. Phelps, J. Metzler, *Exp. Brain Res.* **15**, 289 (1972).
23. At the April 1975 meeting of the Association for Research in Vision and Ophthalmology, M. P. Stryker and H. Sherk reported that, using somewhat different techniques for sampling neurons, they were unable to detect the effect reported by Blakemore and Cooper (*2*). Other laboratories have, however, observed the effect [see (*24*)]. A resolution for these contradictory results may be forthcoming in the near future.
24. R. R. Mize and E. H. Murphy, *Science* **180**, 320 (1973). Whether this reflects a qualitative difference between cats and rabbits has been thrown into some question by the report of failure to obtain effects of tube rearing in cats (*23*).
25. C. Blakemore, in *The Neurosciences: Third Study Program*, F. O. Schmidt and F. G. Worden, Eds. (MIT Press, Cambridge, Mass., 1974), pp. 105–113.
26. —— and R. C. Van Sluyters, *J. Physiol. (Lond.)* **237**, 195 (1974).
27. R. W. Guillery and J. H. Kaas, *J. Comp. Neurol.* **154**, 443 (1974); S. M. Sherman, K.-P. Hoffmann, J. Stone, *J. Neurophysiol.* **35**, 532 (1972).
28. Van Sluyters and Stewart (*12*) have reported that, in binocular areas of monocularly deprived rabbits, the distribution of direction selectivities of neurons driven by the deprived eye is different from the distribution of neurons driven by the experienced eye or that obtained in a normally experienced animal. Because of slightly differing terminologies, many of the neurons included in their samples probably would qualify as orientation-specific in our classification scheme. We are reevaluating whether, in monocular cortical areas, there is an abnormal distribution of directional or orientation specificities.

29. We thank E. H. Murphy, P. C. Fox, and W. B. Kristan, Jr., for helpful discussion. We thank C. Bailey for secretarial assistance. This article grew out of research done while P. G. was an NIH postdoctoral fellow at Stanford University. Supported by PHS grants NS 18512 and EY 00691 and NASA grant NGR-05-020-435 to K.L.C.

NEWS AND COMMENT

Sakharov: Scientists Welcome Award of Nobel Peace Prize

Soviet physicist Andrei D. Sakharov achieved a form of secular sainthood on 9 October when the Norwegian parliament announced that he had won this year's Nobel peace prize. Reportedly, the Norwegians passed over an Indian nun, the International Boy Scouts, and a number of prime ministers in favor of Sakharov. After helping to develop the Soviet hydrogen bomb in the 1950's, Sakharov began a one-man campaign against nuclear testing, against the Cold War arms race, and in favor of individual liberties, activities which have incurred him the hostility of the Soviet authorities.

American scientists, many of whom when in Moscow pilgrimage to see him as a way of maintaining contact, reacted jubilantly to the news. They said it would strengthen Sakharov's international stature and protect him from further indignities.

"This is a great man," said Philip Handler, the president of the National Academy of Sciences, "His voice has spoken for all people." At the height of détente, in late 1973, Handler led the NAS in protesting an official Soviet anti-Sakharov campaign, despite the fact that official U.S. policy was to downplay what had been happening (*Science*, 28 September 1973).

Victor F. Weisskopf, former chairman of the physics department at the Massachusetts Institute of Technology, reacted with enthusiasm to word of the award. "I think it's wonderful that he got it. He does something for peace, you know. His constant preaching of openness, that only openness in every respect will bring peace, is wonderful. Openness is the credo of the scientific world as well."

Also delighted was Marvin Goldberger, chairman of the physics department at Princeton, which has invited Sakharov for a sabbatical but received no reply. Goldberger, a former high-level government defense consultant, says, "Sakharov has been a forthright and fearless opponent of the Soviet military industrial complex. He has fought for arms control and international cooperation . . . in the face of extreme pressures from his government. One can only hope that, in similar circumstances, one would be as brave."

The presentation of the award will prove a test of Soviet sincerity about the Helsinki accords, signed last summer, which are widely interpreted as pledging the Soviets to show greater respect for human rights, including the right of travel. The Soviet government may allow Sakharov to go to