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## Effects of Monocular Deprivation in Kittens\*

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It has long been known to psychologists and clinicians that depriving an animal or man of vision at an early age can lead to profound visual defects. A number of studies have been made in several species by anatomical and behavioral methods, yet very little is known about the physiological effects of sensory deprivation. During the last ten years single-cell responses have been examined and receptive-field arrangements compared at several levels in the cat's visual pathway<sup>1-3,5</sup>. This information provides the necessary background for a study of the immature and the stimulus deprived visual system.

In the present paper we wish to summarize the anatomical and physiological effects of depriving kittens of vision in one eye for various lengths of time and at various ages<sup>7,8</sup>. To begin with it will be necessary to comment briefly on the manner in which lateral geniculate and cortical cells in the adult cat react to visual stimuli.

Since the work of KUFFLER in 1953<sup>5</sup>, it has been known that retinal ganglion cells are of two types, "on-center" and "off-center". Each cell can be influenced by light over a circumscribed region of retina of the order of one millimeter in diameter; this area is called the receptive field of a single cell. Illuminating the center of this region either excites the cell (i.e., increases the rate of impulse firing) or inhibits it, depending on whether the cell is "on-center" in type or "off-center". A similar type of response is evoked if the whole receptive field is illuminated, but the response is always weaker than that which is obtained with a smaller spot just covering the field center. For this reason one can say that retinal ganglion cells are connected to the rods and cones (through the bipolar cells) in such a way that they react not simply to the absolute illumination at a given point, but rather to spatial gradients in illumination.

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\* This paper is dedicated to Professor OTTO KRAYER in appreciation of his friendship and encouragement, and as an expression of our pleasure in being members of his department. The fact that work so far removed from conventional pharmacology originated from his department affords another example of the great breadth of his interests.

At the next stage in the visual pathway, the lateral geniculate body, the cells are organized in a similar manner<sup>2</sup>. They have concentrically arranged receptive fields, and these are again of just two types, "on-center" and "off-center". In these cells, however, there is even greater antagonism of the center response by the receptive-field periphery, so that compared with retinal ganglion cells, cells in the geniculate respond even more feebly to diffuse light.

Cortical cells are vastly more complicated and selective in their responses to retinal stimulation<sup>1,3</sup>. They react only weakly to small spots and hardly at all to diffuse light. They do, however, react strongly and selectively to straight-line stimuli. A given cell may respond best to a dark line, to a bright line, or to a border between light and dark. For a particular cell to be influenced by a line stimulus the orientation of the line on the retina is usually critical. A cell may, for example, respond only if a dark line falls across a particular retinal area in a horizontal direction; an oblique line or a vertical one will generally be incapable of driving the cell, though these stimuli will drive other equally selective cells in the neighborhood.

For the purposes of this study, the binocular properties of cortical cells are important, and will therefore be reviewed in detail<sup>3</sup>. In the lateral geniculate body the two eyes are anatomically and functionally separated: a given cell is generally driven by one eye only, and all of the cells of a given layer respond to just one eye. In the cortex, on the other hand, at least 85% of cells receive some input from the two eyes. For a cortical cell that receives binocular input one can map out and compare the receptive fields in the two eyes. On doing so one always finds that the two receptive fields are located in corresponding parts of the two retinas (so that a given point in the visual field can influence the cell by way of both eyes), and, further, that the fields in the two eyes have similar properties. If two identical stimuli fall on the two retinas in exactly corresponding regions (as happens when one fixes on an object in space), the effects they exert on any cortical cell will be in synergy. The relative dominance of the two eyes over a given cell varies, however. Some cells are driven equally from the two eyes, whereas others consistently give stronger responses to one eye than to the other. Some (the remaining 15%) seem only to be influenced by one eye, which may be ipsilateral or contralateral to the hemisphere from which the cell is recorded. The majority of cells are equally or almost equally driven by the two eyes; of the cells that strongly favor one eye over the other, those responding best to stimulation of the contralateral eye are the more numerous (3, Text-fig. 12). In the experiments to be described we have looked particularly for changes in the normal distribution of cells according to eye preference.

Details of the experimental procedures have already been published elsewhere<sup>3</sup>; here they can be summarized briefly. At the time of an experiment the animal was anesthetized and placed in a head holder with the eyes held open, facing a wide screen on to which various spots and patterns of light could be projected. A microelectrode of the usual metal type for extracellular recording was lowered through the brain until impulse activity was detected. Criteria for recognizing single units were the usual ones of constant amplitude and wave shape from one impulse to the next.

Our original question was whether preventing vision in one eye of a kitten, by sewing the lids of one eye shut for the first three months of life, would produce blindness in that eye and a defect in normal cortical physiology. Lid suture totally abolishes form vision and reduces general retinal illumination by 4 to 5 log units (a factor of 10,000 to 100,000). In acute experiments done after three months of deprivation, single-unit activity was recorded in the striate cortex, and receptive fields of single neurons were examined by patterned light stimulation. The great majority of cortical cells were driven actively from the normal eye; of the total of 84 cells recorded in 4 kittens, only one cell was influenced from the previously closed eye. In these animals a certain number of cells could not be influenced from either eye. Since as far as is known all cells in the striate cortex can normally be influenced by the types of stimuli we used, one wonders if these unresponsive cells were not those that were previously connected exclusively with the sutured eye.

In several kittens we made rough tests of vision in the two eyes. An opaque occluder was placed over each eye in turn, while the other was tested by allowing the animal to walk about examining its surroundings. In each kitten the vision appeared to be completely normal in the eye that had been open, whereas there was no indication of any vision at all in the eye that had been sutured. The pupillary reflex was present, however, indicating that some receptors were functioning. This behavioral result confirms that of several other authors who raised animals in darkness (for review see RIESEN<sup>6</sup>).

At once there arise four questions, which can only be answered by further experiments. First, is the failure to drive cortical cells a manifestation of some cortical abnormality, or might it be due to a defect at earlier levels in the visual pathway? Second, is the abnormality caused by deprivation of light, of form, or both? Third, would similar results have occurred if older cats had been deprived of vision? Finally, is one to assume that the proper connections were not present at birth, and failed to develop in the normal way as a result of disuse, or is it that the connections were there to begin with, at birth, and deteriorated with disuse?

To answer the first of these questions, concerning the site of the abnormality, we studied single cells in the stage just ahead of the primary visual cortex, i.e., the lateral geniculate body. Here the results were quite different; many cells were driven actively from the eye that had been closed, and the receptive fields of these were, with only 2 or 3 exceptions, entirely normal. From this it seems likely that the abnormality is the result of a defect in the cortex itself, perhaps at the synapse between the incoming fibers and the cortical cells. As a by-product one can also draw the interesting conclusion that the retinal and geniculate connections responsible for the specific concentric receptive fields are innate.

In view of this relative normality in geniculate physiology it was surprising to find, on examining the lateral geniculate body histologically, that there were clear and marked morphological abnormalities. The layers receiving input from the eye that had been closed were thinner, partly owing to a loss of interstitial substance, and partly because the cells themselves were shrunken, with a reduction in mean cross sectional area of about 40%. This was unexpected, since in studies on dark reared animals by other workers no such abnormalities were seen. It seems likely that in monocularly deprived kittens the changes are simply much more obvious, since the abnormal layers contrast so strongly with the adjacent normal ones. The presence of morphological abnormalities in the geniculate makes it dangerous to assume that a failure to drive cortical cells was due entirely to a cortical defect; nevertheless the fact that most geniculate cells responded normally suggests that the defect was mainly cortical. No anatomical changes were found in other parts of the visual pathway.

The question as to the relative importance of form and light was approached by raising animals for the first 3 months with one eye covered by a translucent contact occluder. This reduced light by only 1 to 2 log units, but still abolished form vision. Again, the result was a total displacement of the ocular-dominance histogram to the right, indicating a complete failure to drive cortical cells from the abnormal eye. In the lateral geniculate body the layers receiving input from the previously occluded eye were again abnormal even to simple microscopic inspection, but much less abnormal than in kittens deprived of sight by eye suture. Here the mean cross-sectional area was reduced by only 10–15%. Taken with the cortical recordings, this result would tend to suggest that for the cortical abnormality it is form deprivation that is important, whereas for the geniculate the morphological changes are related primarily to light deprivation. This is a satisfying result, since it fits well with the physiology—the fact that most geniculate cells respond to diffuse light, even if feebly in some cases, whereas cortical

cells for all intents and purposes do not. Thus for cortical cells deprivation of form means deprivation of the adequate stimulus.

To assess the importance of visual experience we deprived kittens of vision in one eye at various times after birth, and for various lengths of time. In one kitten the lids of one eye were closed at an age of 9 weeks for a period of 1 month. While a number of cells were driven from both eyes, the balance was nevertheless still grossly abnormal, with an unusually large proportion of cells strongly preferring the normal eye. In this animal the lateral geniculates were almost normal, both to inspection and by measurement of cell cross-sectional area, suggesting again that the abnormality of ocular-dominance distribution is related to a defect in the striate cortex, rather than one in the retina or geniculate. Finally, it was found that a few months of deprivation in an adult cat were not enough to produce any cortical deficit or any morphological changes in the geniculate. These experiments, then, indicate that very young kittens are particularly susceptible to the effects of deprivation, and that the susceptibility decreases with each month of life, possibly even vanishing in the mature animal. It has long been known that in man, too, the effects of deprivation fall off with age, as shown by the profound visual deficit revealed when congenital cataracts are removed from children, as opposed to the good restoration of vision following removal of cataracts acquired late in life.

The problem of whether these cortical abnormalities represent a failure of connections to develop or a disintegration of innate connections was attacked directly by recording from the cortex of very young visually naïve kittens<sup>4</sup>. One of these was studied at the age of 8 days, just as the eyes were beginning to open. Two others were deprived of vision with translucent occluders until they were one or two weeks older. In all three kittens it was possible to drive cortical cells with retinal stimulation, and the receptive fields of these cells had most of the properties of cells in the adult cat. The majority of cells could be driven from both eyes, just as in the mature animal. This makes it very likely that at birth the connections are present, and that they deteriorate with disuse. It is surprising that this possibility seems never to have been considered seriously by those who have raised animals under conditions of sensory deprivation; it has instead been assumed, often explicitly, that the development of vision in the early weeks or months depends on the establishing of new connections, and that this does not occur in the absence of normal input. While it seems very likely that in at least some parts of the central nervous system the formation of neural connections depends intimately on experience, it is perhaps not surprising to find that the main afferent visual pathway is innately determined.

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