chemotherapeutic drug selected have a mode of action compatible with IF induction of its various intracellular mediators (*12*). Also, IF may prove of particular value in controlling neoplasms involving stem cells such as leukemias of myeloid origin.

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Cortical Plasticity in Monocularly Deprived Immobilized Kittens Depends on Eye Movement

Abstract. *A marked reduction of binocular cells in striate cortex is found if 4-week-old kittens are visually stimulated monocularly while anesthetized and held in a stereotaxic apparatus. If the kittens are paralyzed and artificially respirated, changes are not found unless an eye is moved mechanically. It appears that eye movement and visual stimulation are necessary conditions for deactivation of binocular connections, but neither is sufficient to induce such changes alone.*

A relatively brief period of monocular deprivation can cause marked changes in the visual cortex of a 4-week-old kitten (*1*). Study of this phenomenon, which could reflect cellular mechanisms similar to those involved in learning and memory, would be greatly facilitated if the consequences of the visual deprivation were measured as they developed. However, attempts to produce alterations in the visual cortex while recording from single neurons have been largely unsuccessful (*2*). Since monocular occlusion for 8 hours causes physiological changes if an animal is alert (*3*), but not if it is paralyzed and anesthetized, one or both of the latter conditions must interfere with the process that deactivates some afferent pathways.

We tested the hypothesis that the cortical effects of brief periods of monocular occlusion are prevented by paralysis or anesthesia or both. Two groups of normally reared 4-week-old kittens were held stereotaxically while they viewed a visual stimulus monocularly for 12 hours. Then, using standard procedures, we studied a sample of cells in their visual cortex. One group of kittens breathed a mixture of nitrous oxide and oxygen during the stimulation but remained unparalyzed. Results from this group showed a significant numerical reduction of binocularly activated cells but not of neurons responsive through the occluded eye. The second group was prepared in the same way as the first group, but the kittens were paralyzed during the exposure to visual stimuli. In this case, no breakdown of binocularity was found. We conclude that some aspect of the paralysis somehow interferes with the effects caused by monocular deprivation.

In the first experiment, ten kittens were anesthetized with halothane; anesthesia was maintained by intravenous infusion of methohexital sodium while a tracheal tube was inserted and EEG electrodes were attached to the skull. The kittens were then positioned loosely in a stereotaxic apparatus. All wound areas were infiltrated with a local anesthetic (zyljectin). Five of the kittens were paralyzed with gallamine triethiodide (10 mg/kg per hour) and were given a mixture of N_2O (75 percent) and O_2 (25 percent) through a respirator. The other five kittens were not paralyzed and were given the gas mixture through a reservoir and a one-way valve arranged so that room air could not enter. (Cursory observation indicated that under the latter condition, irregular eye movements of moderate scope and slow velocity occurred.) All ten kittens were given a very small amount of methohexital sodium (0.75 mg/kg per hour, intravenously) in a mixture of lactated Ringer's solution. Contact lenses were placed on both eyes but the left lens was opaque, occluding the entire palpebral aperture.

Visual stimuli were presented in one of two forms (Fig. 1). The first was a cathode-ray tube (CRT) display of a bright (75 cd/m^2) horizontal grating high in contrast and low in spatial frequency (0.5 cycle per degree), whose bars drifted continuously downward at 1 Hz. The second display was a projected high-contrast pattern of random elements that rotated and moved up and down at about 5° per second. The temperature, expired CO_2, EKG, and EEG of all the kittens were monitored. Visual stimulation was begun when there were no signs of barbiturate anesthesia (spindles) in the EEG.

After presentation of the visual stimuli, we prepared the animals according to standard procedures (*1*) for the study of single neurons. A small section of skull over the hemisphere contralateral to the occluded eye was removed and the dura mater excised. The kittens that had breathed through the reservoir-and-valve apparatus were paralyzed and artificially ventilated. A tungsten-in-glass microelectrode was inserted into the brain to measure action potentials from individual cells. These potentials were amplified, displayed, and fed into audio monitors. The receptive fields of sampled cells were located within an estimated 10° of the area centralis. Subjective estimates were made of absolute and relative response strengths for each eye. Using the estimate for the latter, we assigned ocular dominance ratings (Fig. 1) to indicate whether a cell was monocularly or binocularly activated. It is important to note that for all kittens studied, we decided jointly the ocular dominance category of each cell.

In normal 4-week-old kittens, as in adults, most cells are binocularly activated (*1*) (Fig. 1b). However, with only 8 hours of monocular occlusion while kittens are kept alert (*3*), there is a substantial reduction in the number of binocularly activated cells and a shift to the unblocked eye (see Fig. 1a). In this case, only 36 percent of the cortical cells tested were binocularly activated; 70 percent were activated by the nonoccluded eye. Results for the experiment in which anesthetized kittens viewed a grating monocularly for 12 hours indicate that

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the occlusion caused a significant reduction (38 percent of the total) in the number of binocularly activated cells (Fig. 1c). But in the paralyzed kittens, 76 percent were binocularly activated—comparable to the value of 77 percent determined for the normal control (Fig. 1b). In contrast to the results for kittens that were monocularly occluded while kept alert, the findings for anesthetized kittens showed no tendency for the unblocked eye to predominate. The first consequence of deprivation of vision in one eye is probably a breakdown of binocularity before the unblocked eye gains control of most of the cells (*4*). Therefore, it appears that the effect of monocular occlusion of the anesthetized kittens was relatively weak. A grating was used to see if alteration of binocular connectivity was linked to spatial properties of the stimulus. However, analysis of orientation and direction selectivity of the cells showed no bias. It appears, then, that a functional breakdown of binocular connections is the only marked effect.

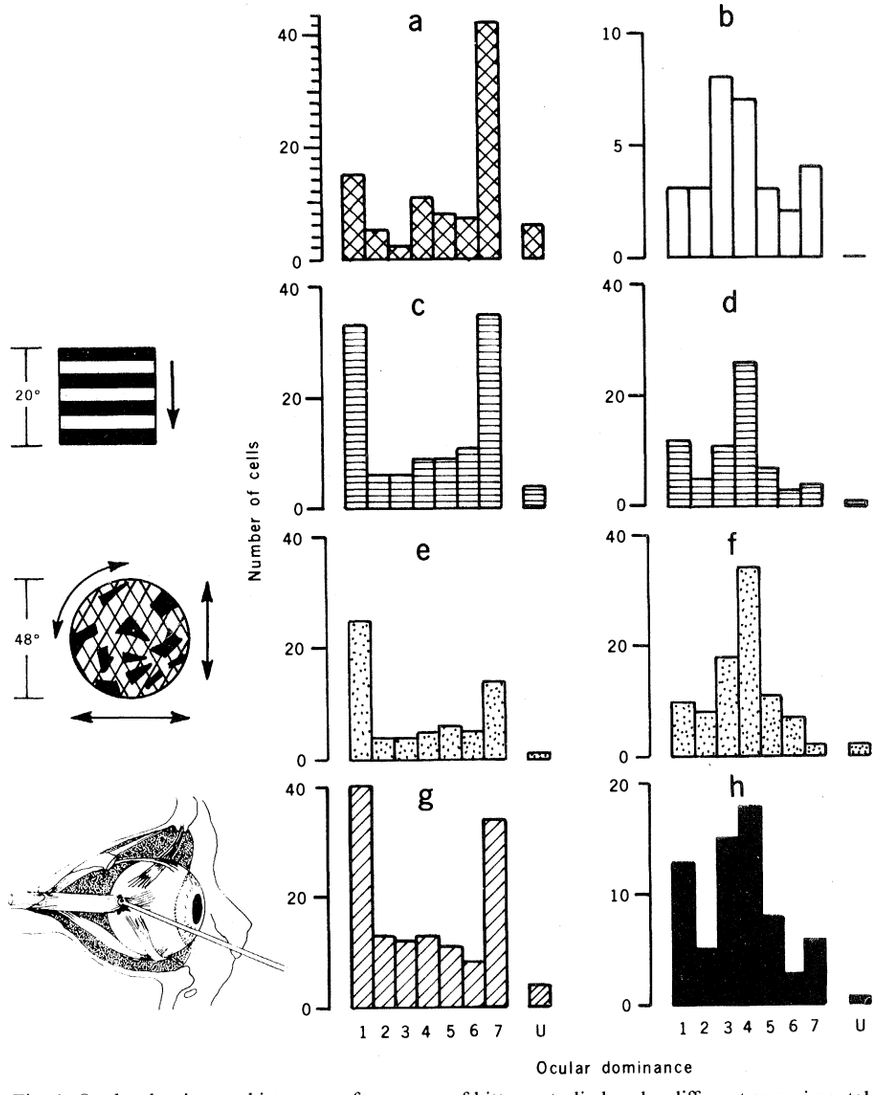

Fig. 1. Ocular dominance histograms for groups of kittens studied under different experimental or control conditions. In all cases, results within each group are very similar. Subjective ratings were made of the degree to which each cell responded to the optimal stimulus presented to each eye. Monocular cells activated through the eye contralateral or ipsilateral to the hemisphere in which the electrode was placed are designated group 1 or 7, respectively. Group 4 indicates equal control by both eyes. Binocularly activated cells that were dominated by the contralateral or ipsilateral eye are in groups 2 and 3 or groups 5 and 6, respectively. Visually unresponsive cells are group *U*. For all monocularly occluded kittens, recordings were made in the hemisphere contralateral to the blocked eye. (a) Histogram for three kittens studied after 8 hours of monocular occlusion while kept alert. The dominance percentages for binocularly activated cells were 30, 33, and 45. (b) Histogram for a 4-week-old, normally reared control animal. (c) Histogram for three kittens monocularly occluded and presented with the grating stimulus (shown to left) while they were held in a stereotaxic apparatus and given N_2O (75 percent) and O_2 (25 percent) to breathe. Binocularly activated cells comprised 29, 41, and 43 percent of the total. (d) Histogram for two kittens studied as in (c), but paralyzed and artificially respirated during the occlusion period. Binocularly activated cells constituted about 76 percent of the total in each kitten. (e and f) Results for two and three kittens, respectively, studied as in (c) and (d), respectively, except that the visual stimulus was a moving random element pattern (shown to left). Binocularly activated cells comprised 27 and 48 percent of the total in (e) and 80, 87, and 93 percent of the total in (f). (g) Results for four kittens that were monocularly occluded while paralyzed, but whose unblocked eye was mechanically moved during the exposure session by a rod attached to the lateral rectus muscle (preparation shown to left). Three of the kittens were shown the grating and the fourth the random element pattern. Binocularly activated cells comprised 50, 44, 41, and 39 percent of the total. (h) Results for two kittens tested as in (g), except that both eyes were occluded. Binocularly activated cells comprised 63 and 82 percent of the total.

It could be argued that a visual display richer than a grating might cause a shift in dominance toward the unblocked eye or a breakdown of binocular connections in a paralyzed animal. We therefore tested a second series of kittens, using as the stimulus a high-contrast random element pattern with many contours of various orientations. The pattern was placed in the object plane of a rear projector and rotated and moved asynchronously along x and y axes by driving a system of pen motors attached to mirrors with three waveform generators, each running at a different frequency. Results for this series of kittens (Fig. 1, e and f) closely resemble the results obtained when the grating stimulus was used. Once again, when the kittens are not paralyzed the main effect is a loss of binocularly activated cells without dominance by the unblocked eye. In fact, the number of cells activated by the contralateral (deprived) eye is slightly higher (Fig. 1e). When the kittens are paralyzed, even fairly vigorous visual stimulation still seems insufficient to cause a loss of binocular connections (Fig. 1f).

Why is there no reduction of binocularity in the paralyzed kittens? It could be the result of a central effect of the drug used to maintain paralysis, since gallamine triethiodide has been reported to influence the cerebral cortex (*5*). Another possibility is prevention of normal eye movement per se. To distinguish between these possibilities, we devised an experiment in which the unblocked eye in four paralyzed kittens was mechanically moved during the entire 12-hour exposure period. After exposing the lateral rectus muscle of the right eye, a suture was passed under the belly of the muscle near the area of its insertion and tied to the end of a rod that was attached to the voice coil of a loudspeaker. A triangle wave drove the coil and caused slow (0.1 Hz) horizontal motion (2 mm) of the rod,

which in turn oscillated the eyeball at about 4° per second over a range of 16° (Fig. 1). All other procedures were identical to those used on the other paralyzed kittens.

Figure 1g shows the results of this experiment. As in the kittens that were not paralyzed, binocular connections are clearly reduced: binocularly activated cells comprise 44 percent of the total. Therefore a central influence of gallamine triethiodide cannot be of primary importance in preventing the deprivation effect. Rather, the effect seems to depend upon activation of pathways associated with movement of the eye. It is possible that this activation by itself could cause a breakdown of binocular connections. To determine the role of eye movement alone, we paralyzed two kittens and oscillated their right eyes for 12 hours with both eyes occluded. Subsequent study of cortical cells showed that a large proportion (72 percent) were binocularly activated (Fig. 1h). Eye movement alone is therefore not sufficient to cause cortical changes during short-term monocular occlusion.

In conclusion, we have shown that a brief period of monocular deprivation can produce substantial alterations of binocular connections in the visual cortex of anesthetized kittens. It should be possible to monitor these changes in individual neurons. The effect does not occur in a paralyzed kitten unless an eye is mechanically moved while the stimulus is presented. Eye movement and visual stimulation are necessary conditions for cortical changes, but neither is sufficient to induce such changes alone. It is intuitively obvious that visual stimulation should be required, but the additional requirement of eye movement suggests that indirect pathways are also involved. A relationship between extraocular muscle function and changes in ocular dominance has been proposed (*6*). The extraocular muscles of the cat have spiral endings responding to stretch (*7*), and afferent responses from these muscles have been reported from recordings in the cerebellum (*8*). In addition, it has been shown that lateral geniculate activity is modulated by oculomotor centers (*9*) and that electrical stimulation of motor branches of extraocular muscles evokes some response in visual cortex (*10*). Some of the pathways suggested by these studies could be involved in a gating system that controls the degree to which striate cortex is receptive to visual input.

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Genetic Component of Bee Odor in Kin Recognition

Abstract. *The primitively social sweat bee,* Lasioglossum zephyrum, *blocks the entry into its nest of most conspecifics from other colonies. Laboratory inbreeding of these bees produced lines which showed a positive linear relationship between the coefficient of relationship of bees tested and how often they permitted non-nestmates to pass them. The most probable mechanism is a genetically determined odor coupled with a learned component by which guard bees discriminate between odors of close kin and other bees.*

The concept of altruism in sociobiological theory is usually based on the relatedness of individuals; for example, the "inclusive fitness" of a sterile individual can be enhanced if a close relative is prolific (*1*). Given the many examples of altruism in animal behavior, the question arises whether there are specific mechanisms to ensure that related individuals cooperate with one another. In a recent review Sherman states that, although there are many examples of recognition of nestmates or siblings in animals, "recognition of more versus less similar siblings has not been demonstrated in any creature" (*2*). I infer such discrimination, however, because of evidence (presented below) of a genetic component for chemical recognition of relatives in a primitively social sweat bee, *Lasioglossum zephyrum*, which permits bees to recognize degree of relatedness even though they have not previously met. This species lives in burrows in soil guarded by one or more individuals that commonly exclude natural enemies as well as conspecifics from other nests (*3*).

Earlier work with this bee demonstrated the probable existence of individual or group odors involved in mating, nest defense, and nest recognition (*4–6*). Particularly relevant are Bell's findings that, among bees killed by freezing, nonresidents elicited aggressive responses by guards more often than residents did (*7*). Nonresident bees were also rejected when only far-red light was used, presumably simulating darkness to the bees. Bell concluded that contact chemoreception or olfaction were the modalities of recognition.

Bees were raised in the laboratory year-round in artificial nests consisting of burrows in a layer of soil between two sheets of glass; the nest entrances consisted of plastic tubes 4 mm in diameter (*8*). The two family lines used for inbreeding were originally collected from field sites about one-half mile apart (1 mile = 1.6 km). Additional colonies were started with pupae collected at widely separated locations. The latter were used to measure recognition between distantly related bees. All bees lived in mixed soil from a single site, and were fed from a single stock of *Typha* pollen and honey water.

New laboratory colonies were started with callow (young) bees which generally do not meet adults before digging out of their cells in their second day; for this experiment they were removed from their cells within 24 hours of eclosion. They were put into new nests one at a time until a colony of six sister bees was established. Each bee was marked on its thorax with a drop of enamel, a different color for each.

Inbred lines were developed by first observing these new colonies until queen determination was made (*9*). These young queens readily mated in small cages (16 by 12 by 13 cm) containing males from the same parental colony (presumably brothers). After a single mating, the females were returned to their original nests. At least 5 days were allowed for a new colony to establish itself before any tests were made. These inbred lines did not seem more difficult to raise than others, nor did any obvious deleterious traits develop.