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Very Brief Visual Experience Eliminates Plasticity in the Cat Visual Cortex

Abstract. *Rearing cats in the dark extends the critical period for development of visual cortical neurons, which indicates that the experience of visual input is necessary to begin the developmental process. A single brief pulse of visual input (6 hours) during a period of dark-rearing eliminates delayed development in the visual cortex. Light therefore seems to rapidly trigger the developmental process, and once triggered, that process runs to completion in the absence of further input.*

Postnatal development of the central visual pathways depends on the quality of the visual environment. In cats reared with the lids of one eye sutured closed, the physiology of visual cortical cells is dramatically altered. In normal cats, most cells respond to stimulation of either eye; in monocularly deprived (MD) cats, virtually every cortical cell responds only to stimulation of the initally open eye (*1*). This effect reflects a permanent developmental abnormality and cannot be reversed even by forcing use of the initially closed eye in later life (*1*).

The time period when neural development is susceptible to environmental manipulation is termed the plastic or critical period. It is restricted to very early life. In cats, plasticity appears to be maximal at around 1 month of age and then declines over the next 3 months, after which time the visual pathways are virtually immutable (*2*). During this plastic period, every major response property of cortical cells (ocular dominance, orientation selectivity, direction selectivity, disparity sensitivity) can be modified by manipulation of the visual environment (*3*).

These observations define one of the roles of visual input in cortical plasticity: to determine the final response properties of the developing neurons. In addition to this role, several recent studies have indicated that visual input also plays an essential role in the underlying process of plasticity itself. Animals reared in complete darkness beyond the critical period (until 4 to 10 months of age) and then allowed monocular visual experience show delayed susceptibility to the effects of MD in the visual cortex (*4, 5*). It is as if the critical period has been delayed or slowed in the absence of visual input. These results indicate that the plastic period is not a simple age-dependent maturational process; rather, visual input in some way controls the underlying events that allow for or eliminate neuronal plasticity. The environmental trigger seems to be simply the experience of light. If cats are reared with binocular eyelid suture throughout early life (which allows them to experience only diffuse light), the visual cortex shows dramatic degradation and there is no delayed susceptibility to MD (*5*).

This study was designed to further explore the role of visual input in triggering neural plasticity in visual cortex. We compared visual cortical physiology in cats who experienced prolonged dark rearing with that in cats who experienced very brief visual exposure during prolonged dark-rearing. These two types of cats were compared in electrophysiological studies at the end of the rearing period (to assess development during the restricted visual experience) and after a prolonged period of MD in a normal light-dark cycle following the initial rearing period (to assess the capacity for delayed development and plasticity). We found that very brief periods of visual experience triggered neural development and that once triggered, the plastic period ran its full course in the absence of further visual input.

Nineteen cats were studied. Six received no visual experience throughout the first 4 to 5 months of life [dark-reared (DR)]. Of these, three were used in physiological studies at the completion of the rearing period (DR cats). The other three had the lids of one eye sutured at the end of the rearing period (under ketamine anesthesia, 25 mg/kg) and were allowed prolonged monocular vision prior to physiological study (DR → MD cats). Three cats were reared in darkness for 4 to 5 months, but at the age of 6 weeks they received one day (6 hours) of binocular visual experience in a normally lighted laboratory room. After this rearing, two of them were used in electrophysiological studies [DR(6) cats], then recovered from anesthesia and paralysis and allowed prolonged monocular vision [DR(6) → MD cats]. The third cat simply had one eye sutured after the rearing period [DR(6) → MD]. Four cats were reared in darkness for 4 to 5 months, but at the age of 6 weeks they received two consecutive days (12 hours) of visual experience. Three of these were studied at the end of the rearing period [DR(12) cats], and the other experienced prolonged monocular vision prior to recording [DR(12) → MD cat]. Six other cats were used as comparison animals. In all cats who experienced MD, the period of monocular vision lasted a minimum of 3 months.

Studies of the visual cortex were done with the animals anesthetized (sodium pentobarbital, 25 mg/kg initially, supplemented by 3 mg/kg-hour) and paralyzed (gallamine triethiodide, 10 mg/hour). Recordings were restricted to one hemisphere; in all cats who experienced MD, the hemisphere contralateral to the deprived eye was studied. A minimum of two oblique penetrations (2 mm in extent) were made. Within penetrations, single units were sampled at 100-μm intervals, and all cells studied had receptive fields located 4° to 8° from the area centralis. The same search stimulus (0.5° by 20° white slit) and matched microelectrodes (3 to 5 megohm at 1000 Hz, tungsten) were used in all cats. This procedure ensured representative sampling of ocular dominance clusters within animals and provided objective comparative data among animals. We determined two major receptive field characteristics for each visual cortical cell: ocular dominance (the degree to which the cell responded to visual stimulation of one or

the other eye) and receptive field specificity (the degree to which the response of the cell depended on stimulus shape, orientation, and direction of movement).

In DR cats (Fig. 1A), most cells were visually responsive and binocularly activated. Cells in these animals were typically nonselective for the direction or orientation of the visual stimulus, and their responses frequently fatigued. In DR → MD cats (Fig. 1B), there were two strong indications of delayed development after the dark-rearing period. (i) The majority of cells were responsive only to the eye that had been opened during the period of MD. (ii) Most of these cells had orientation-selective receptive fields. Thus, at an age at which neural plasticity is eliminated in normal cats, dark-reared cats showed clear developmental changes as a result of MD.

After the initial rearing period, the physiology of DR(6) cats was not very different from that of DR cats (Fig. 1C). Most cells were binocularly activated and nonselective for stimulus shape, orientation, or direction. Differences between these two rearing conditions were evident in the cats who experienced subsequent MD. Unlike DR → MD cats, there was no selective development of connections from the open eye in DR(6) → MD cats (Fig. 1D). In these cats, most cells were binocularly activated and lacked orientation selectivity, being similar to those seen after the initial rearing period in DR(6) cats. Thus, there was no evidence for an effect of MD in cats who experienced 6 hours of vision during dark rearing.

In the DR(12) cats, there was a loss of binocular cells and a high incidence of visually unresponsive cells (Fig. 1E). After prolonged MD, there was no physiological recovery in visual cortex [DR(12) → MD] (Fig. 1F). The loss of binocular cells in these cats could reflect several factors (*6*). In the present context, the important points are the irreversible degradation of receptive field properties and the loss of susceptibility to the effects of MD.

In normal cats at 4 to 5 months of age, most cells were binocularly driven and orientation selective cells strongly predominated (Fig. 1G). MD imposed after 4 to 5 months of normal vision had relatively little effect (Fig. 1H). This result indicates that the effect of monocular vision in DR → MD cats cannot be attributed to residual normal plasticity after 4 to 5 months of age. As a result of MD throughout the first 4 to 5 months of life the open eye took over completely (Fig. 1I).

The major point of this study is the dramatic difference [χ^2 (10) = 120.1, $P < .001$] in the effect of MD between cats who experienced more than 4 months of dark rearing and those who experienced 6 or 12 hours of visual input during that time (*7*). The former showed obvious developmental changes as a result of subsequent MD—effects similar to those found in cats who experienced monocular vision throughout early life. The latter showed no clear sign of any development as a result of subsequent MD. The elimination of susceptibility to MD in the cats who experienced 6 or 12 hours of vision was as complete as that in cats who experienced 4 to 5 months of binocular vision followed by MD. Thus, plasticity was prolonged in the dark-reared group and eliminated in the group who experienced 6 or 12 hours of vision during dark rearing.

The results suggest a simple interpretation of the way in which visual input interacts with the timing of the critical period. Light seems to be the adequate stimulus for triggering the period. When darkness is experienced from birth, neural plasticity persists. A brief pulse of light is sufficient to activate the critical period, which then runs to completion with or without further input. In darkness, the end product of this developmental process is abnormal and immutable receptive fields. Thus, it appears that visual input is necessary for the initiation of the critical period and for the development of normal receptive field properties. However, visual input is not necessary for the progression of the critical period once it has been initiated.

This interpretation is supported by studies of orientation tuning in dark-reared cats (*8*). When a cat is reared in darkness until 6 weeks of age, orientation-selective cells are few. A 6-hour period of vision leads to a rapid (1 day) increase in orientation selectivity approaching normal levels. If the cats are returned to the dark, receptive field

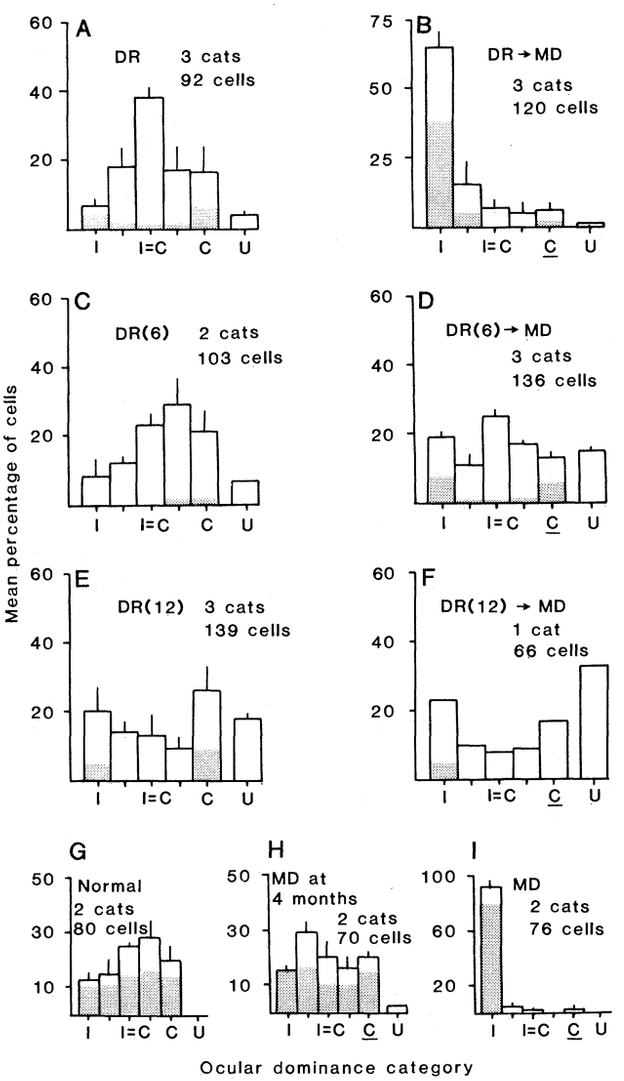

Fig. 1. Summary of physiological results in visual cortical cells. For ocular dominance, six categories were used: *U*, visually unresponsive cells; *I*, cells driven only by the ipsilateral eye; *C*, cells driven only by the contralateral eye. Intermediate categories indicate various degrees of binocular responsiveness, with category $I = C$ indicating cells equally responsive to both eyes. For each cat, we determined the percentage of cells in each category. These values were then averaged by category, among animals in each group. Each bar in the figure represents that mean and its standard error. Underlining indicates the deprived eye. Shaded areas are the proportion of cells in each ocular dominance category that were orientation selective. To be considered so, a cell had to fail to respond to visual stimuli (slits of light) oriented perpendicular to the optimal orientation and had to show sharper tuning to slit than to spot stimuli.

properties degenerate over the next 6 weeks. This result indicates that the pulse of light rapidly triggers development and that continued visual input is necessary to maintain normal receptive fields. Once the cells have degenerated in darkness, they are no longer capable of developing normal response properties (*8, 9*).

Visual input seems to act as a switch that rapidly activates the underlying biochemical events that control neural plasticity in the visual system.

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6. It is not clear why there was a loss of binocular cells and a high incidence of unresponsive cells in cats who received 12 hours of visual experience during dark rearing. The 12-hour condition resulted in more severe abnormalities than the 6-hour condition [χ^2 (5) = 28.4, $P < .001$]. The difference between these conditions could therefore be related to the longer visual exposure or to a consolidation effect because vision was experienced on two successive days in the 12-hour condition. Additionally, since the eyes of dark-reared cats are frequently misaligned, effects of strabismus may be more manifest in the 12-hour condition.
7. Observations of visuo-motor behavior indicated differences between the DR and DR(6, 12) rearing conditions that were consistent with the physiological data. After several weeks of monocular vision, DR → MD cats showed clear signs of visuo-motor behavior [J. Van Hof-Van Duin, *Brain Res.* **104**, 233 (1976); G. D. Mower, C. J. Caplan, G. Letsou, *Behav. Brain Res.* **4**, 209 (1982)] and became indistinguishable from cats who experienced MD from birth on a variety of simple tasks (placing, jumping, tracking, obstacle avoidance). DR(6, 12) → MD cats, on the other hand did not show such behavioral recovery and still failed these tasks at the end of the period of MD.
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Inhibitory Influence of Unstimulated Rods in the Human Retina: Evidence Provided by Examining Cone Flicker

Abstract. *In the parafoveal retina of human observers, cone-mediated sensitivity to flicker decreases as rods become progressively more dark-adapted. This effect is greatest when a rod response to flicker is precluded. These results indicate that rods tonically inhibit cone pathways in the dark.*

Several different mechanisms permit rod- and cone-related signals to interact within the visual system (*1, 2*). Rods as well as cones contribute to color vision (*3, 4*), and separate rod and cone responses interact in determining threshold (*5*) and the sensation of flicker (*6*). In the most thoroughly studied psychophysical examples (*3, 5, 6*), the underlying process always has two features. (i) Rod- and cone-related signals interact most strongly when both types of photoreceptors are photically stimulated. This is surprising since both rods and cones release a neurotransmitter most rapidly in the dark (*7*), and dark-release of both an excitatory and an inhibitory neurotransmitter is documented in the vertebrate retina (*8*). (ii) Photic stimulation of both rods and cones leads to a response of similar effect (whether inhibitory or excitatory) at some common neural locus. In fact, with only one well-documented exception (*9*), intracellular neurophysiological studies have shown rod-cone interaction to involve summation.

We now demonstrate a type of rod-cone interaction in the human visual system with a different mechanism. We have found that unstimulated, dark-adapted rods maximally inhibit cone-mediated sensations of flicker.

A sinusoidally flickering light 2°20′ in diameter was presented 7° from fixation in the temporal field (*10*). Modulation depth was fixed at 87 percent, and the observer adjusted illuminance so that the light appeared to barely flicker (*11*). Although we have obtained similar data from 20 observers, including 15 with no psychophysical training, Figs. 1 and 2 represent data from S.H.G., an experienced psychophysical observer with normal vision.

We found that flicker sensitivity was determined by three variables: the extent of dark adaptation, the spectral distribution (*10*) of the stimulus, and flicker frequency. For example, after being exposed to a bleaching field of 46,000 trolands, the observer tracked sensitivity to flicker throughout the time course of dark adaptation. Data obtained with a 5-Hz flickering green stimulus (Fig. 1) resembles usual dark-adaptation curves (*12*). The upper limb (less than 6 minutes in the dark) can be attributed to the adaptational properties of cones, and the lower limb to those of rods. Such an increase in sensitivity throughout the entire time course of dark adaptation was obtained only with green or yellow stimuli flickering at frequencies below 7 Hz. The sensitivity to red flicker also increased during the cone recovery stage of dark adaptation but, during the rod recovery period of dark adaptation, sensitivity decreased (Fig. 1). This phenomenon was most pronounced with higher flicker frequencies: using other response measures, we have obtained a similar suppression in sensitivity to flicker with frequencies up to 40 Hz (*11*).

To ascertain the mechanism underlying these data, we first determined the types of photoreceptors involved. The experiment with 20-Hz red flicker was repeated with green or yellow flickering stimuli (*10*). When data were plotted in photopic units (reflecting the sensitivity of human cones), results were uninfluenced by stimulus wavelength, indicating that cones were detecting flicker. Additionally, the bleaching field used prior to dark adaptation was varied in wavelength; scotopic trolands illuminance (influence on human rods) was fixed, but photopic illuminance was varied. Regardless of the bleaching wavelength, data corresponding to the rod recovery stage of dark adaptation remained unaltered (*13*).

The controls described above show that the data reflect rod-cone interaction but do not specify mechanism. Rod- and cone-related flicker signals can sum in the retina (*6, 14*). Since the latency of rods is longer than that of cones, rod and cone responses can either enhance or cancel each other depending on flicker frequency. We rule out this explanation for our data for two reasons. (i) We have collected similar data with red stimuli of many different frequencies and have always observed flicker sensitivity to decrease monotonically during rod adaptation (*15*). (ii) We used a control procedure throughout the entire study, but data are shown only for 20-Hz flicker in Fig. 1. Red and green flickering stimuli were presented 180° out of phase: the time-averaged scotopic illuminance of