
The efficacy of brief periods of reverse occlusion in promoting recovery from the physiological effects of monocular deprivation in kittens. DAVID P. CREWTHER, SHEILA G. CREWTHER, AND DONALD E. MITCHELL.*

For over two centuries the accepted treatment for amblyopia has included occlusion of the better eye for a time in order to force the child to use the ambylopic eye. Although it is generally agreed that greater improvement in the vision of the ambylopic eye is achieved with full-time occlusion, a growing body of evidence indicates that even brief daily periods of patching can be quite effective. Since brief periods of patching are far more acceptable to a child than full-time occlusion, it is important to explore this approach in greater detail including identification of its neuropathological basis through animal models.

Kittens monocularly deprived by eyelid suture from near birth to 5 weeks of age or more appear behaviorally blind when first forced to employ their deprived eye. This functional blindness is accompanied by striking physiological changes in the visual cortex, where the vast majority of cells can be excited only by visual stimuli presented to the formerly open eye. However, substantial recovery can be observed both behaviorally and physiologically after termination of the period of monocular occlusion, particularly if the animal is forced to employ its formerly deprived eye by occlusion of the other eye, a procedure generally referred to as reverse occlusion. In this situation the distribution of ocular dominance of cortical cells can be completely reversed, so that all cells are now excited only by visual stimuli delivered to the formerly deprived eye. (Ocular dominance refers to the relative excitatory influence of each eye on a cortical cell.) The dramatic shift in the ocular dominance of cortical cells is also accompanied by equally rapid improvements in visual behavior and acuity. Most studies of the physio-
logical recovery from monocular deprivation have
owned full-time reverse occlusion. In order to
explore the possible neurophysiological basis for
the visual improvements achieved with minimal
occlusion therapy in amblyopia, we investigated
the relative effects of short daily periods of reverse
occlusion in promoting recovery from the effects of
monocular deprivation.

Methods. A total of 22 kittens of nonspecific
breed, born and raised in a closed laboratory col-
ony, were monocularly lid-sutured at about the
time of natural eye opening (7 to 10 days of age).
The operations were performed under halothane
anesthesia after sedation with 2% xylazine. On
awakening, the kittens were returned immediately
to the mother in cages in a room that was illumi-
nated for 12 hr/day. When 21 of the kittens were 5
weeks old, the eyelids of the deprived eye were
parted and those of the formerly open eye were
sutured closed under anesthesia (a reverse eyelid
suture). The kittens were immediately placed with
their mothers in cages in a completely dark room.
Each kitten was taken from the darkroom and
placed in an illuminated environment for a fixed
period of time each day, after which they were
returned to the darkroom. During the period of
visual exposure the animals were under constant
observation and were stimulated by noises or tac-
tile contact when necessary in order to keep them
awake.

The kittens were prepared for physiological re-
cording within 24 hr of the final period of daily
visual exposure, by using procedures that have
been described extensively elsewhere. Briefly,
the kittens were prepared for recording under 2%
halothane anesthesia in a 2:1 nitrous oxide to oxy-
ogen mixture and were then hyperventilated during the recording session with a 3:1 N2O to 5% CO2 in O2 gaseous mixture after paralysis with a continuously infused isotonic solution of 10 mg/kg · hr gallamine triethiodide (Flaxedil) in glucose and saline. Tungsten in glass microelectrodes were used to record extracellular potentials. Typically, penetrations of at least 3 mm were angled down the medial bank of the postlateral gyrus at 5° to 10° medial and 10° to 15° anterior to ensure sampling of as many ocular dominance columns as possible and also to prevent excessive sampling of any single cortical layer. Recordings were usually made from both hemispheres, although in a few cases only the hemisphere contralateral to the initially deprived eye was sampled. The variation in results obtained from the two hemispheres was not greater than the individual variation between cats, and so the data from both were combined and displayed as if the recordings were made from the hemisphere contralateral to the initially deprived eye.

The first experiment, performed on 11 kittens, examined the relative effect on cortical ocular dominance of daily periods of reverse occlusion of different durations. Each kitten was exposed to light each day for 20 days for a period of either 0.5, 0.75, 1.0, 2.0, or 4 hr. Thus, although the formerly deprived eye of each animal received visual experience daily for 20 days, the total visual experience it received during this time was not the same for each group of animals, ranging from 10 to 80 hr.

The second series of experiments included data from 12 kittens, two of which participated in the first experiment. The total duration of visual exposure of the formerly deprived eye was the same for each animal (20 hr) but was distributed over a different number of daily sessions. The total period of exposure of 20 hr was divided into either 2, 3, 4, 5, 7, 10, 20, or 40 sessions, which with the exception of the last category, the animal received 40 sessions each of 30 min duration, distributed over a period of 10 days.

Results. Periods of reverse occlusion as brief as 30 min per day for 20 days were found to produce substantial physiological recovery. Cortical ocular dominance histograms from each group of kittens in the first experiment are shown in Fig. 1, together with the ocular dominance distribution sampled from a control kitten. This animal was recorded immediately on termination of the initial period of monocular deprivation at 5 weeks of age. As expected, virtually all cells encountered in this animal could be excited only by stimuli presented to the nondeprived eye. However a significant shift in cortical ocular dominance away from the initially open eye was observed even in the three animals that received only 30 min daily forced visual experience through the formerly deprived eye. With increasing durations of daily visual exposure of the formerly deprived eye, a progressively greater shift in cortical ocular dominance was observed toward the formerly deprived eye, with almost complete dominance established with about 4 hr daily exposure. The degree of ocular dominance shift can be specified in terms of a reversal index, which is defined as the percentage of visually responsive cells dominated by the initially deprived eye. In terms of the histograms displayed in Fig. 1, this index (R) is defined as follows:

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R = \frac{\text{Number of cells in OD groups 1 to 3}}{\text{Total number of visually responsive cells}} \times 100
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A reversal index was calculated for each of the conditions displayed in Fig. 1 and has been plotted in Fig. 2 as a function of the number of hours of daily forced visual exposure of the initially deprived eye.

The striking effects of short daily periods of reverse occlusion in promoting physiological recovery in the visual cortex were even more apparent in the results from the second series of experiments in which the total duration of visual expo-
Fig. 3. Cortical ocular dominance distributions obtained from two groups of two kittens that were reverse-sutured at 5 weeks of age and which subsequently received a total of 20 hr visual experience through the initially deprived eye but distributed differently in time. The physiological recordings were made on the day after the last exposure, at either 38 or 56 days of age. Ocular dominance groups are as described in Fig. 1. The results are displayed as if the recordings were all made from the hemisphere contralateral to the initially deprived eye. n, Number of cells sampled.

Discussion. The first experiment indicated that a substantial degree of physiological recovery was achieved with daily periods of reverse occlusion as short as 30 min. With further increase in the amount of daily exposure, the extent of reversal of ocular dominance increased in an approximately logarithmic fashion (Fig. 2); almost total dominance by the initially deprived eye was achieved with 4 hr of daily visual exposure. An interesting feature of the ocular dominance distributions obtained from all the animals except those that received 4 hr daily experience was the relatively high proportion (about 40%) of cells that were binocular. A similar observation was also made by Movshon on animals that were reverse-sutured for brief periods of time. This high proportion of binocular cells is quite remarkable in view of the fact that the animals never received simultaneous binocular vision.

The relative efficacy of short daily periods of reverse occlusion is made even more prominent when the results of Figs. 1 and 2 are compared to results obtained by Movshon from animals reverse-sutured at the same age and thereafter allowed virtually continuous exposure (18 hr/day) to light. For example, the degree of reversal of cortical ocular dominance shown by the animals that received 30 min of daily exposure for 20 days (a total exposure of 10 hr) was comparable to that

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shown by animals that were reverse sutured for 6 days during which time they were exposed to light for 108 hr. This similarity seems even more remarkable in light of the fact that in the latter condition the reverse occlusion was imposed for 6 days at a time when binocular cortical connections are close to being at their peak vulnerability to disruption by monocular eye closure. 

The considerable recovery observed in kittens that received only brief periods of reverse occlusion indicates that the extent of physiological recovery depends not only on the total duration of reverse occlusion but also on the way in which it is distributed in time. This point was emphasized by the results of the second set of experiments in which the total duration of reverse occlusion was constant but distributed over a different number of sessions. Each animal was recorded the day after the last exposure session rather than at the same age because of the claim that the effects of monocular deprivation may decay if the animal is placed in darkness afterward for a prolonged period. Virtually no shift in ocular dominance was observed at all in the animals in which the reverse visual exposure was received over two sessions each lasting 10 hr (Fig. 3). However, substantial reversal (40%) was observed in the animal in which the reverse visual exposure was distributed over three sessions. Thereafter, with further increase in the number of daily exposure sessions, there was a gradual increase in the reversal index (Fig. 4). The greatest shift in ocular dominance was observed in animals in which the visual exposure was distributed over 20 hourly sessions. The darkroom environment in which the kittens lived between exposure sessions must not be overlooked as a factor contributing to the extent and speed of recovery from deprivation effects.

The results of these experiments, particularly the second, indicate that distributed periods of reverse occlusion produce a greater degree of physiological recovery than an equivalent total period of occlusion that is massed in only two sessions. As such, this finding is relevant to the recent resurgence of interest in minimal occlusion therapy for amblyopia. In addition, our findings bear a formal resemblance to a ubiquitous property of learning that has long been recognized to occur faster with distributed than with massed trials.

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REFERENCES

Previous work showed that despite good visual acuity, many healthy older people require more contrast to see gratings of low and intermediate spatial frequencies than do younger observers. Here we report that a daily perceptual activity, which relies on lower spatial frequency information, is also adversely affected: as compared to young individuals, many older individuals require more contrast to see sinusoidal gratings of low and intermediate frequencies than do younger individuals.

Therefore low-contrast conditions could pose a special problem for the elderly, forcing them to rely on visual mechanisms specialized for processing lower spatial frequencies, precisely those mechanisms of diminished sensitivity. Here we explore this possibility by examining the effects of contrast reduction on face perception for young and old observers.

Materials and methods. We tested two groups of observers: 14 young observers (mean age = 20.5; S.D. = 1.9) and 13 older observers (mean age = 74.2; S.D. = 4.1). Young observers were student volunteers whose most recent eye exams (on average, 10 months before our tests) revealed no ocular pathological conditions. Older observers were healthy active individuals recruited from a senior citizen meeting center. Detailed ophthalmological exams of the older observers of our experiment within 3 months were generally unremarkable. Most older subjects had traces of cataract; three had early senile macular degeneration (SMD); all had intraocular pressures within the normal range (mean = 16.3 mm Hg; S.D. = 3.2). All older observers had normal visual fields when tested with a 1 mm diameter white target on a tangent screen.

Observers' acuities were measured at a distance of 3 m with a Sloan letter chart (120 cd/m²). Since all subsequent testing was done with binocular viewing, we report only binocular acuities here. Observers wore appropriate corrections during the experiment, their own spectacles or contact lenses or lenses in trial frames. Expressed as minimum angle resolvable, acuities were 0.84 min arc for young observers (S.D. = 0.10) and 0.94 min arc for older observers (S.D. = 0.17). Included in the mean for the older group are the acuities for the three observers with early SMD: 1.09, 1.04, and 1.02 min arc.

The face perception task was divided into two parts, detection and discrimination. To measure detection, eight slides of single faces were rear-projected one at a time onto a translucent screen 115 cm from the subject. Faces were relatively large targets, subtending a visual angle of approximately 5 x 7.4 degrees. The faces were of middle-aged, Caucasian males having no beards, moustaches, eyeglasses, or unusual hairstyles. All males who were photographed wore a gray cloth around their shoulders to prevent the observer from making discriminations based on apparel. Our apparatus consisted of two matched slide projectors positioned so that their beams coincided on the rear-projection screen. Fixed linear polarizers positioned in front of each projector.