Visual acuity and behavior of monocularly deprived monkeys after retinal lesions

Anita Hendrickson, John Boles, and E. B. McLean

One eyelid of each of three Macaca nemestrina monkeys was sutured shut at 3 weeks of age. One animal had the central 10° of the open eye retina lesioned at 3 weeks of age (EL1), a second at 9 months of age (LL1), and the third had no lesion (MD1). After a reverse suture at 9 months of age, the deprived eye was tested for grating acuity, visual behavior, and visual field. EL1 tested positively on all behavioral tasks by 1 month and showed good visual ability to negotiate a playroom but never performed better than 20/1,250 on grating acuity. MD1 showed little visual behavior in the playroom but tested at 20/400 acuity. LL1 rapidly recovered all aspects of visual behavior and tested at 20/80 visual acuity. Perimetry shows that LL1 and EL1 respond mainly in the central portion of the deprived eye visual field but not to the periphery or the monocular segment. We conclude that removal of the open eye retina after the critical period allows much visual recovery by the deprived eye but that removal of the open eye retina within the critical period does not prevent many of the effects of monocular deprivation.

Key words: visual acuity, amblyopia, visual deprivation, monkey visual system.

There is now a large body of evidence showing that when one eyelid of a cat or monkey is sutured within the first 6 weeks after birth, the functional capacity of the closed eye is sharply reduced when the lid is reopened. Moreover, this functional loss is permanent even after forced use of the deprived eye. Recently three experimental procedures have demonstrated ways of preventing or reversing the effects of lid closure in cats. In the first, Sherman and associates, using 1-week-old kittens, lesioned part of the retina of the open eye and sutured the other eye. When the closed eye was opened in the adult cat, the portion of the visual system driven by the deprived retina which is homologous to the lesion in the open eye retina (critical segment) had anatomical, electrophysiological, and behavioral characteristics similar to those of the open eye or to the monocular segment of the closed eye which earlier had been shown to be unchanged after deprivation. Since the possibility of competition between open
and closed eye retinal afferents was removed in the critical segment by the lesion and never existed in the monocular segment, it follows that removing binocular competition prevents the effects of monocular deprivation in cats.

At least partial reversal of deprivation in the adult cat has been shown neurophysiologically by two other methods. When the open eye is enucleated, the number of cortical units responsive to the deprived eye increases within hours from 10 percent before enucleation to 20 to 45 percent the day after, but no further increase in responsive units was found even a year later. After the intravenous infusion of the γ-aminobutyric acid–receptor blocking agent bicuculline, the deprived eye began to drive cortical units within a minute; this effect lasted for up to 30 minutes, after which the open eye resumed the usual neurophysiological domination of the unit. The receptive field characteristics of most of the cortical units driven by the deprived eye were clearly abnormal in the enucleation experiments but were less so in the bicuculline study. Behavioral effects of these reversal experiments have not been reported, but anatomically, the deprived dorsal lateral geniculate nucleus (dLGN) neurons showed very little increase in cell size 14 months after the open eye optic nerve was crushed.

There is much less information on prevention or reversal of deprivation in the monkey. The only experiments reported thus far are dLGN cell size measurements following the production of a critical segment in the deprived eye. Von Noorden and associates have shown that the deprived parvocellular neurons within the dLGN critical segment are the same size as open eye neurons whereas deprived neurons outside of the critical segment are 35 percent smaller than the open eye neurons. Hendrickson and associates found that in both parvocellular and magnocellular layers, the deprived critical segment neurons were close to, but did not equal, the size of the open eye neurons.

Our laboratory has begun a series of experiments to study the effect of retinal lesions during and after the critical period for monocular deprivation in monkeys and to analyze these effects with behavioral, electrophysiological, and anatomical methods. This is a preliminary report on the first set of animals to complete behavioral testing.

Methods

The left eyelid of three Macaca nemestrina monkeys was surgically closed in the third week after birth, with standard techniques. At the same time, in one animal (EL1) the central 10° of the open right eye retina received a full-thickness lesion by an argon laser. At 9 months of age all animals had the lids of the deprived eyes surgically opened and the previously open lid sutured (reverse suture). A second animal (LL1) received a similar lesion in the open eye at the time of reverse suture, and the third (MD1) served as a monocular deprived control. MD1 became terminally ill 5 months after reverse suture and was sacrificed for anatomical studies.

All acuity testing used a two-alternative, forced-choice paradigm with either apple juice or raisins as reinforcement. Just before reversal, the right eye of MD1 was tested in a lever-pull operant box, and LL1 was tested binocularly at 2 weeks of age by preferential looking. EL1 at all times and MD1 and LL1 after reversal were tested in a modified Wisconsin General Test Apparatus (WGTA). The positive stimuli were 5 by 6 inch test cards consisting of photographically reproduced black and white stripes of various widths, which at the 7 inch working distance of the WGTA yield a Snellen acuity of 20/40 to 20/5000. The positive stimulus was paired with a 20/20 card for presentation in a semirandom series. Twelve trials of each of four stripe widths were run daily; criterion was set at 90 percent correct 3 days in a row for a given stripe width. The end point of testing in a given time period was reached when for 10 days in a row an animal achieved criterion on larger stripe widths and chance (corrected for guessing to 67 percent) on a smaller stripe width in a given series.

In addition, a second series of tests was used to assess more complex visual behavior, including visuomotor behavior. These were identical to tests previously described, with the addition of "raisin retrieval" which consisted of holding the monkey within reaching distance of a yellow tabletop on which lay several raisins in a random pattern. A positive score consisted of an accurate reach and pickup of an individual raisin at a distance at
Follow light Follow object Visual placing Avoidance of object Retrieve raisins

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Days after reverse suture: 8 16 24 32 32 46

Fig. 1. Recovery of performance of the deprived eye on visual tasks in the first 46 days after reverse suture.

which olfactory cues were not operative. Each test was run every day until the animal was positive for 7 days in a row. The monkeys were also observed while playing as a group in a 6 x 6 foot room containing four platforms of different heights, a swinging chain, and an assortment of other objects like balls, boxes, and toys. Finally, gross perimetry was done by attracting the monkey's attention to one person so that it looked straight ahead with the deprived eye and then bringing (by a second person) a raisin into the field of view of the eye from the periphery toward the central retina. This test was done after the animals reached and performed successfully on raisin retrieval; a positive point in the field was taken as the most peripheral point at which the monkey reached for the raisin or moved his head to fixate on it before reaching for it.

Results

Behavior in playroom. All three monkeys had been placed in this room twice a week from 1 month of age and were very familiar with it. They all exhibited excellent coordination before reversal. After reversal MD1 exhibited severe depression when placed in this room; he usually refused to move about and often lay immobile on the floor. When he did move, he paced in a straight line back and forth along one wall. If a novel object was placed along this path, he bumped into it. ELI at first was fearful and cautiously exploratory, but by 2 months after reversal he was moving about the room and platforms with no difficulty but not with the frequency and confidence of his prereversal activity. LLI regained her prereversal level of activity and exploration within a month.

Behavior on complex tasks. The striking differences between LLI and the other two animals can be seen in Fig. 1. MD1 was the slowest to recover positive responses on all tests, with most not positive until 1 month after reverse suture. Visual placing was still not clearly positive when he was sacrificed. ELI had a variable pattern of test scores; visual placing returned early, but recovery for other tasks was delayed. In contrast LLI was positive on all but visual placing by 1 week.

Grating acuity. These results are presented in Table I. The interpretation of the time course of acuity recovery for LLI and MD1 was limited by a delay in testing caused by a quarantine of the entire infant colony due to a viral epidemic shortly after reverse suture and the unexpected refusal of the animals to work at the operant lever-pulling task which necessitated a shift to the WGTA apparatus. Several months were lost in shaping the animals to their new task. The first point at 4 months after reversal for LLI and MD1 reflects these delays. MD1 performed well in the WGTA, reaching a final acuity of 20/400 just before sacrifice. LLI learned the WGTA task rapidly and performed at 90 percent correct on all stripes as fast as they were introduced into the paradigm until she reached 20/80, at which acuity...
Table I. Best acuity achieved by infant monkeys before and after reverse suture

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<th>Animal</th>
<th>Open eye before reverse suture</th>
<th>Deprived eye after reverse suture</th>
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<tr>
<td></td>
<td>1 week</td>
<td>1 month</td>
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<tr>
<td>LLl</td>
<td>20/80↑</td>
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<td>MD1</td>
<td>20/25§</td>
<td>20/500</td>
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<tr>
<td>ELI</td>
<td>20/200</td>
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*The open and closed eyes were tested monocularly except for the prereverse testing of LLl.
†Tested by preferential looking at 2 weeks of age.
‡First presentation for learning WGTA task.
§Tested with operant conditioning test apparatus at 7-8 months of age.

she has remained. ELI, who had been trained in the WGTA previous to reversal, performed at chance on the largest stripes 1 day after reversal and by 2 months had reached no better than 20/1250. ELI had difficulty in fixating objects after reverse suture, but this has improved with time. It does not seem to be the reason for his poor grating acuity, since that has remained unchanged at 20/1250 over the same period.

Perimetry. The results were very clear in LLl; she seemed to respond to stimuli only in a central cone of the visual field ranging from 20° nasal to 40° temporal, and she ignored stimuli outside of this central area, including the far temporal periphery which is the monocular crescent. ELI did not respond to raisins coming into the nasal field until they were straight ahead of this gaze. Raisins moved into the peripheral temporal field did not cause a response until about 45° off central gaze. MD1 responded, but never sharply, to any raisins moved within normal visual field boundaries.

Discussion

These preliminary results must be accepted with great caution until they are repeated in a number of animals and the eyes and brains of all of the animals are anatomically studied to verify the presence and location of the retinal lesion. However, they do suggest two conclusions. First, in monkeys as in cats, recovery from monocular deprivation is possible in older animals if the open retina is physically removed. This recovery is accompanied by improvement in grating acuity and is meaningful for the behavior of the monkey.

From her general behavior we believe that LLl was indistinguishable from a normal monkey within 2 weeks after reverse suture. Since she performed at 90 percent for every stripe width down to 20/80 on the first day that it was presented, we infer that at the time of acuity testing she already had achieved 20/80 acuity. It is known that at the time of reversal the deprived eye would input onto shrunken dLGN neurons and that these in turn would synapse on a much smaller volume of striate cortex than the open eye neurons. Even though these deprived-eye dominance columns are small, it is significant that receptive field characteristics within them appear to be normal. The question of whether the size of the deprived dLGN neurons or the striate columns change after a late lesion will have to await anatomical studies, but from the rapid course of visual recovery it appears unlikely that anatomical reorganization is the primary cause.

Second, removing binocular competition at the time of eyelid suture by a retinal lesion in the open eye does not give a monkey an advantage either in general visual behavior or in visual acuity when compared to a monocularly deprived monkey. The deprived monocular segment likewise appears nonfunctional. However, in light-deprived monkeys which show poor general visual behavior, nearly normal visual acuity can be demonstrated if the testing methods do not demand much visuomotor coordination. It may be that the WGTA
task requires more coordination than ELI possesses and that his acuity is really much better than he can demonstrate. Although his behavior in the playroom and his responses on the visuomotor tasks argue against it, we are planning to examine this possibility by using acuity testing methods that require no motor response at all. One explanation for this finding may be the observations that in monkeys\textsuperscript{4, 5} the dLGN neurons of the monocular segment receiving input from the closed eye shrink 12 to 20 percent, whereas in cats they change very little in size.\textsuperscript{2} We suggest that in monkeys there is a substantial direct monocular retinal component of deprivation as well as an effect from binocular competition. Although the deprived dLGN neurons of the critical segment are more normal in size\textsuperscript{6, 7} and presumably occupy a normal or even supernormal amount of striate cortical space,\textsuperscript{10} either these changes are not significant for improved visual behavior or our testing procedures were insufficient to detect such improvement.

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REFERENCES

(End of Symposium Part II)