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Visual responses from cells in striate cortex of monkeys rendered chronically 'blind' by lesions of nonvisual cortex

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Summary. Chronic 'blindness' can be produced in monkeys by a large cortical removal that spares modality specific visual cortex (striate, prestriate, and inferior temporal cortex). To understand the reasons for the blindness we compared single unit activity recorded from striate cortex of these monkeys with the activity of units recorded from seeing animals. The results indicate that visual processing in the striate cortex of the blind monkeys, with the exception of changes attributable to a partial disruption of the geniculostriate pathway, is similar to that of the normal monkeys. The chronic blindness is therefore probably due not to dysfunction within striate cortex but rather to a disconnection from critical processing stages within the ablated territory. Feedback from this territory is apparently not necessary for information processing to occur in striate cortex.

Key words: Blindness – Cortical blindness – Macaque monkeys – Visual electrophysiology

Introduction

In the companion paper we described chronic 'blindness' in monkeys resulting from a cortical lesion that spared most of the modality specific visual cortex (Nakamura and Mishkin 1985). The effective cortical lesion thus preserved most of striate, prestriate, and inferior temporal cortex, but included all other cortical areas (see Fig. 1a). The lesion was placed in only one hemisphere, while the other hemisphere was left intact but visually deafferented by unilateral optic tract section and forebrain commissurotomy. Despite a preserved retino-geniculo-striate-prestriate-inferior temporal pathway in one hemisphere, animals prepared in this way failed to exhibit any signs of vision for the duration of postoperative survival, which ranged from 300 to nearly 900 days (see for analysis, Nakamura and Mishkin 1986). While it is emphasized that the use of the term 'blind' was not meant to imply that the animals were totally lacking in visual sensation or perception, these results indicated that part or all of nonvisual cortex must play a critical role in visual behavior.

Two explanations might account for the blindness produced by lesions of nonvisual cortex. First, nonvisual cortex could be a necessary link in the pathway through which central visual processes govern behavior, or in other words, visual cortex could have been disconnected from later processing or motor output stages. Second, the visual cortex could have been deprived of a necessary nonretinal input that is normally provided by nonvisual cortex thus preventing the visual cortex from processing the visual input. In order to evaluate these possibilities we recorded single unit activity in primary visual cortex of the blind animals. If the visual cortex was simply disconnected from later processing stages, unit activity within the striate cortex itself should be normal. If the visual cortex had been deprived of an essential nonsensory input, there should be evidence of reduced or altered visual activity.

Material and methods

Subjects

The subjects were four rhesus monkeys (Mx2, Mx3, Mx4, and Mx5) and two cynomolgus monkeys (F4 and F5), all but one of which (Mx5) were described in the preceding report, as were the details of surgery and histology. The rhesus monkeys had received

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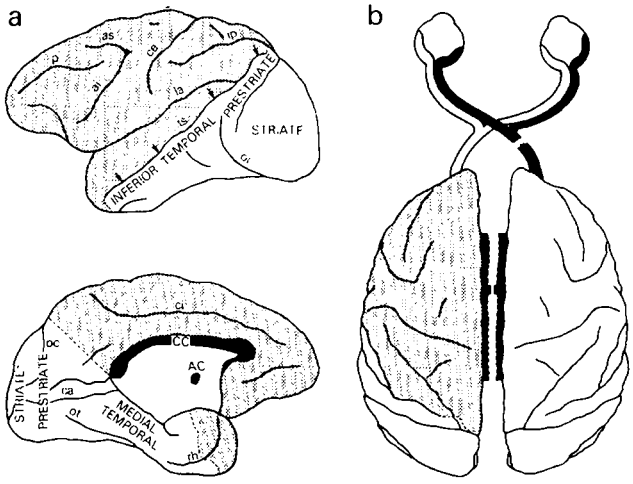

Fig. 1. a Intended nonvisual lesion shown on standard lateral and medial views. The banks of all sulci within the ablated territory were removed, including those at the boundary of the lesion (indicated by arrows). **b** The basic preparation. The nonvisual lesion was placed in the left hemisphere, the forebrain commissures were divided, and the right optic tract was transected

a left hemisphere ablation that spared the modality-specific visual areas (striate, prestriate, and inferior temporal cortex), but included all other cortical areas and the amygdala (Fig. 1a). The cynomolgus monkeys (F4 and F5) received a somewhat smaller lesion that spared the limbic structures removed in Group Mx, including the orbital frontal cortex, cingulate cortex, and the amygdala. The ablation was restricted to one hemisphere in order to prevent the bilateral paralysis that would follow bilateral sensorimotor removal. The right hemisphere was visually deafferented by forebrain commissurotomy and optic tract section (Fig. 1b). Two of the rhesus monkeys (Mx3 and Mx4) did not initially receive the right tract cut. Since these two monkeys could see in the left hemifield, they were used to evaluate normal unit responses of their seeing right hemispheres as well as unit responses of their blind left hemispheres. The right optic tract in these animals was subsequently cut to confirm the effectiveness of the left hemisphere lesion in producing blindness. All animals received their lesions a minimum of six months prior to the beginning of recordings and, with one exception, they all failed the tests for vision for the duration of their survival period which was at least six months after the surgery that produced blindness. The exception was case F4, who showed some signs of movement detection in home-cage testing, although he had failed all tests for vision involving stationary stimuli. The single unit data from this animal did not differ from those of the others. The behavioral data for all monkeys, except animal Mx5, were reported in the earlier study. The exception, Mx5, underwent surgery in a different sequence from the other animals but also showed chronic blindness for the duration of survival (756 days) after surgery.

At least two weeks prior to the first recording session a stainless steel post (to hold the head) and one or more recording wells were attached to the skull with screws and dental cement. As with the neurosurgical procedures, this operation was carried out under barbiturate anesthesia and aseptic conditions.

Unit recording procedure

We recorded units from the animals while they were both paralyzed and lightly anesthetized with procedures modified from those of Desimone and Gross (1979). First, animals were premedicated with atropine and diazepam. They were then lightly anesthetized with ketamine and underwent trachial intubation. The animals were respirated with 70% nitrous oxide and 30% oxygen and then were paralyzed with pancuronium bromide. Temperature of the animals was maintained at approximately 37° C, expired carbon dioxide was maintained around 4.5%, and EKG was monitored. The animals were held in a stereotaxic device by the implanted post. The pupils were dilated and accomodation paralyzed with cyclopontolate hydrochloride, and appropriate contact lenses were inserted to focus the eye on a tangent screen 114 cm away. The recording well was then cleaned with 3% hydrogen peroxide, and a thin slit made in the dura for entry of a varnish coated tungsten microelectrode.

At the end of the recording session the infusion of the paralytic agent was stopped, the electrode was removed, and the dura was again cleaned with 3% hydrogen peroxide. Tetracycline ointment was placed in the well and the well was capped. Once the animal showed some signs of movement, 0.4 ml atropine, 0.2 ml diazepam, and 0.2 ml ketamine was administered. At this time the nitrous oxide was stopped and the monkey was respirated with 100% oxygen. When the animal could breath on its own, it was removed from the respirator and returned to its home cage. Recording sessions were separated by a minimum of five days.

Characterization of cells

Single units in striate cortex were evaluated for their visual responsiveness, orientation selectivity, directionality, ocular dominance, receptive field size, and receptive field location. In addition, cells were classified as unoriented, simple, or complex following the criteria of Hubel and Wiesel (1968) and of Schiller et al. (1976). Cells were classified as unoriented if they responded to flashing lights (spots and bars) and showed no orientation preferences for a moving bar. A cell was classified as oriented if its response to an optimally oriented bar was judged to be at least two times the response to a bar at the orthogonal orientation. All cells that demonstrated orientation specificity were classified as either simple or complex. Cells were classified as simple if they responded to both flashing and moving bars, had spatially separate on- and off-subfields when tested with flashing spots or bars, and had spatially separate light-edge and dark-edge subfields when tested with moving edges. Cells were classified as complex if they responded better to moving than to flashed stimuli and if both light-edge and dark-edge response zones were superimposed. In addition, complex cells were classified as unidirectional or bidirectional. Cells that would have been classified as hypercomplex by the criteria of Hubel and Wiesel (1968) were placed in the complex category.

Ocular dominance was graded using the numerical system of Hubel and Wiesel (1968) (1 = contralateral only, 4 = binocular, 7 = ipsilateral only). In addition, the responsiveness of the cell, or vigor of visual driving, was graded along a 0 (no response) to 4 (strong response) scale. All isolated units were classified. In each penetration, after the first unit was obtained, we systematically sought units at 200 micron intervals.

Results

We initially recorded from 185 single units in four blind hemispheres (Mx3, Mx4, F4, and F5) and 83 units in two seeing hemispheres (Mx3 and Mx4). In the blind hemispheres, 49% of the cells responded

Table 1. Number of cells in which visual responsiveness was evaluated

	Blind hemisphere *left striate*			Seeing hemisphere *right striate*		
	Poor resp.	Good resp.	Total	Poor resp.	Good resp.	Total
Animal						
Mx3	33	37	70	1	42	43
Mx4	9	20	29	3	37	40
F5	4	12	16			
F4	48	22	70			
Total	94	91	185	4	79	83
%	51%	49%		5%	95%	

Table 2. Visual responsiveness of cells in striate cortex[a]

	Responsiveness					
	0	*1*	*2*	*3*	*4*	*Total*
Blind hemisphere						
Cells	36	20	37	53	39	185
%	19%	11%	20%	29%	21%	
Seeing hemisphere						
Cells	2	0	2	5	74	83
%	2%		2%	6%	89%	

[a] '0' represents no detectable response to visual stimulation, while '4' represents a strong reliable response

well to visual stimuli (response classes 4 and 3) while 51% showed little or no response (response classes 2,1, or 0). In the seeing hemisphere, 95% responded well to visual stimuli and only 5% were poorly responsive. Tables 1 and 2 summarize the visual responsivity of the cells.

Much of the difference in visual responsiveness between cells of the normal and blind hemispheres can be attributed to inadvertent damage to the optic radiations arising from infarcts following surgery. These infarcts, which invaded the white matter under the posterior segment of the superior temporal sulcus, damaged the optic radiations representing the lower visual fields and caused degeneration of between 50% and 70% of the lateral geniculate nucleus that represents the lower field (see Table 3 of Nakamura and Mishkin 1985). In accordance with this loss, unresponsive units in the blind hemispheres were concentrated in the lower visual field representation. Table 3 shows the distribution of responsive cells as a function of their location in the visual fields. The proportion of unresponsive units dropped dramatically as the recording site moved from the representation of the upper visual field to the lower

Table 3. Relationship between height in visual field and responsiveness[a]

RF Position	*Cells*	*Responsive %*
Blind hemisphere		
$x \geq 1°$	48	67%
$1° > x > -1°$	46	52%
$-1° \geq x \geq -3°$	53	62%
$x < -3°$	32	6%
Overall	179	49%
Seeing hemisphere		
$x \geq -3°$	58	98%
$x < -3°$	25	88%
Overall	83	95%

[a] Relationship of visual responsiveness of cells to height of the cell's receptive field measured in degrees of visual angle from the horizontal meridian

visual field. At three degrees or more below the horizontal meridian only 6% of the cells were responsive, contrasted with 61% of the cells above. Underrepresentation of unresponsive units was inevitable since we could only classify cells if they were intermingled with responsive cells whose receptive fields could be localized.

Although the small proportion of responsive units in the lower field representation of striate cortex in the blind hemisphere was attributable to damage to the radiations, even in the upper visual field of the blind hemisphere the number of responsive cells (67%) was less than in the seeing hemispheres (95%). This loss in responsivity could be due either to undetected, diffuse damage to the upper visual field radiations, or to some other indirect effect of the lesion.

Since it was likely that optic radiation damage accounted for the poor responsivity of many cells, the analysis of the distribution of cell properties was based only on responsive units (classes 3 and 4). For this analysis an additional 79 responsive cells were included from penetrations in two other blind rhesus monkeys, Mx2 (22 cells) and Mx5 (57 cells), in which no attempt was made to count or study unresponsive units.

The proportions of oriented cells, simple cells, and complex cells in the seeing and blind hemispheres were virtually indistinguishable (Table 4). Of the responsive cells in the blind hemisphere 68% (110 of 161) were orientation selective, compared to 69% (53 of 77) in the seeing hemisphere. Furthermore, of the oriented cells in the blind hemispheres 61% were of the complex type, compared to 63% in the seeing hemisphere.

Table 4. Receptive field characteristics of the cells in our study compared to those found by other investigators

	Seeing hemisphere		*Blind hemisphere*		Hubel and Wiesel (1968)	Schiller et al. (1976)	Dow (1974)	Wurtz and Mohler (1976)
	Cells	%	Cells	%	%	%	%	%
Non-oriented	24	31%	51	32%				
Oriented	53	69%	110	68%	94%	87%	61%	70%
Unidirectional	6	13%	44	59%	10%	42%	37%	46%
Bidirectional	42	87%	31	41%	90%	58%	63%	54%
Simple	11	37%	37	39%		48%		
Complex	19	63%	59	61%		52%		
Monocular	24	30%	98	70%	63%	48%		
Binocular	57	70%	43	30%	37%	52%		

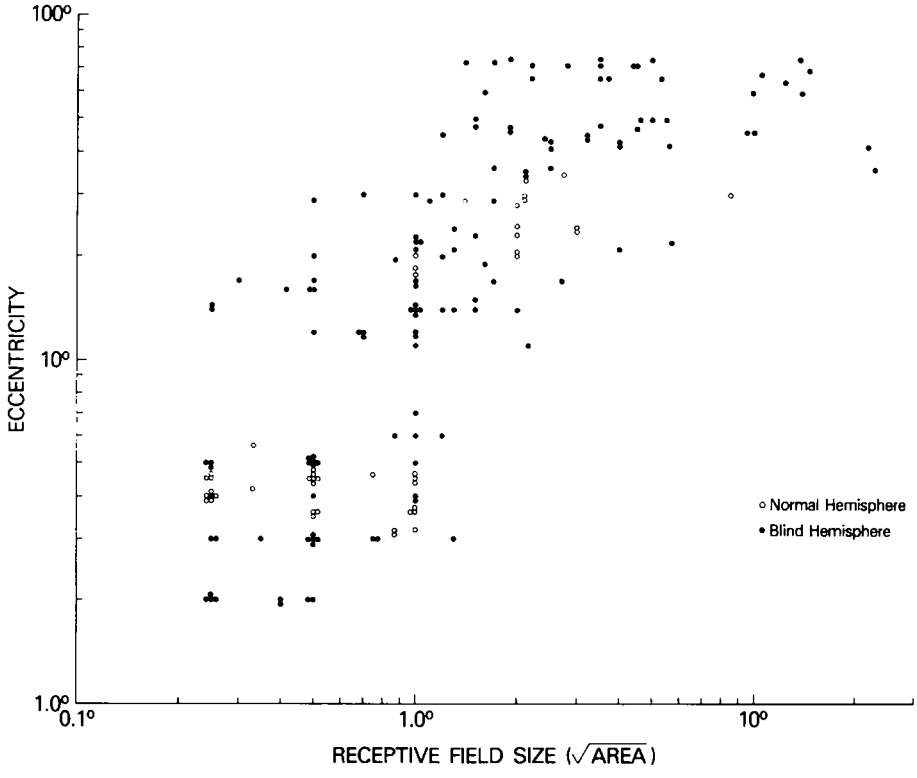

Fig. 2. Receptive field size (square root of area) was plotted against eccentricity from fixation. Filled circles were single cells recorded from the blind hemispheres while open circles represent cells recorded from the seeing hemispheres

The distribution of ocular dominance is shown in Table 4. If we consider ocular dominance categories 1, 2, 6, 7 as predominantly monocular, and categories 3, 4, 5, as binocular, then in the seeing hemisphere 70% (57 of 81) of the cells were binocular, whereas in the blind hemisphere 30% (43 of 141) were binocular. An analysis of the location of the cells recorded in the blind hemispheres showed 50% of cells from the upper visual field were binocular while only 20% of cells from the lower visual field were binocular. The reduced incidence of binocular cells in the lower visual field was expected since the cells would have a lower probability of having input from both eyes spared than would cells from the upper visual field.

The proportion of unidirectional cells, i.e. oriented cells that had one preferred direction of motion, was 59% in the blind hemisphere, which was close to the proportion found by Schiller et al. (1976) in their normal monkeys. We found only 13% of the cells in the seeing hemispheres to be unidirectional for reasons that were not clear.

Receptive field size in striate cortex varies as a function of eccentricity (Hubel and Wiesel, 1974), and we found a similar relationship (Fig. 2) in both

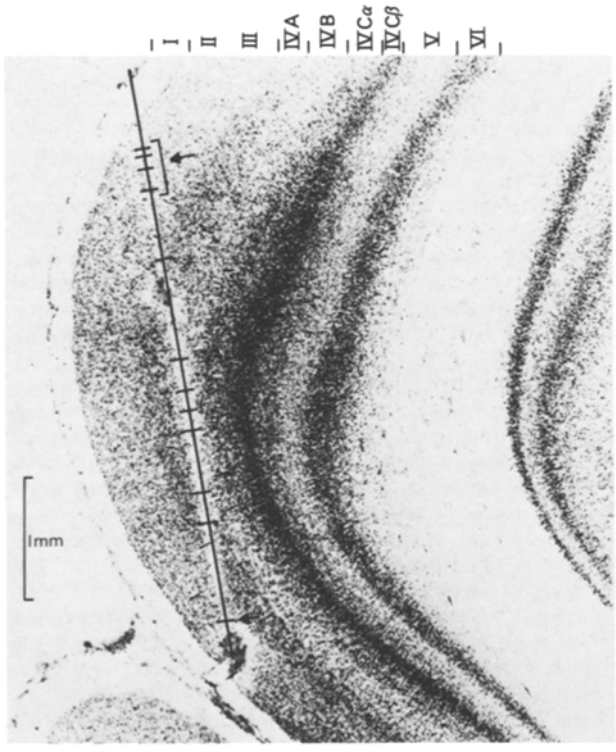

Fig. 3. Histological reconstruction of an electrode track from animal F5 in which responsive units were recorded from cortical layers 2 and 3. Lines indicate locations along the track where responsive units were recorded. Layer boundaries are indicated according to the criteria of Lund et al. (1975)

the blind and seeing hemispheres. There was a highly significant positive correlation ($r = 0.5$, $p < 0.000001$) between receptive field size and eccentricity. As can be seen in Fig. 2, the distribution of receptive field sizes in the blind hemispheres was indistinguishable from that in the seeing hemispheres.

Because each animal was studied over long periods of time, many electrode tracks could not be identified in the histological material, and we therefore were unable to localize many cells within a cortical layer. Therefore, it was conceivable that the unresponsive units in the blind hemispheres were concentrated in the supergranular layers which are the main source of cortico-cortical projections (Lund et al. 1979). However, in one penetration in a blind hemisphere (see Fig. 3) in which small marking lesions were made, we were able to verify the location of several responsive cells in layers 2 and 3. There was therefore no selective loss of responsiveness in the supergranular layers, suggesting that striate cortex was passing on to other cortical visual areas the information that it had processed.

Discussion

We have examined the properties of cells in striate cortex of monkeys made 'blind' by a large cortical ablation that spared striate, prestriate, and inferior temporal cortex. We use the term 'blind' in a restricted sense since the existence of the state in our animals was determined by long-term behavioral testing that cannot be considered exhaustive (see Nakamura and Mishkin 1986). These properties were compared to those of cells recorded from normal hemispheres. The purpose of the study was to determine whether the blindness was due to a disconnection of the visual system from further processing stages in nonvisual cortex or due to lack of processing within the visual system which resulted from the loss of nonvisual input to visual cortex.

First, the results indicate that despite damage to the optic radiations there was a physiologically intact pathway from the retina to the striate cortex in the hemisphere with the nonvisual lesion. This finding eliminated any doubts about the existence of a visual input to striate cortex in these animals. Second, visual information processing appeared to be remarkably normal in striate cortex of the blind hemispheres, as demonstrated by the presence of orientation selectivity, simple and complex receptive fields, binocularity, and directionality. As shown in Table 4, the incidence of cell types in the blind hemispheres of our monkeys was not very different from that found in striate cortex of rhesus monkeys by other investigators. Since all of these properties were thought to arise only as a result of processing within striate cortex (Hubel and Wiesel 1977) it seems clear that our blind animals were continuing to process information in striate cortex.

Although the properties of cells recorded in the blind hemispheres appeared, in general, to be normal, it is possible that our methods were not sensitive enough to detect within the blind hemisphere subtle changes in visual processing resulting from the nonvisual lesion. For example, striate cortex may have lost some modulatory input from nonvisual cortex that could only be detected in recordings from an awake, behaving monkey. Although we cannot reject this possibility, the properties of cells in striate cortex recorded in both the awake (Wurtz and Mohler results in Table 4) and anesthetized paralyzed preparations (all others in Table 4) appear very similar. It is also possible that we have misinterpreted the difference that we did find between the seeing and blind hemispheres. The overall reduction in the responsiveness of striate cortex to visual input in the ablated hemispheres could be related not only to damage to the optic radiations as we have supposed,

but also to loss of cortical feedback. But, since the reduction in responsiveness was so well correlated with degeneration in the lateral geniculate we think the explanation unlikely. Furthermore, the reduction in responsiveness in the upper visual field of our monkeys seems very small in relation to the dramatic behavioral change caused by the lesion.

We conclude, therefore, that the blindness observed in our animals was not due to loss of visual processing within the retino-geniculo-striate pathway. Moreover, preliminary data from recordings in prestriate and inferior temporal cortex indicate that visual processing continues at all levels of modality-specific visual cortex (unpublished observations). The blindness was therefore probably due to the loss of critical processing stages beyond the modality-specific visual system.

The finding of normal unit properties in striate cortex of monkeys that are blind suggests that even this far into the CNS a striking amount of visual processing continues in the absence of behavioral responsivity to visual stimulation. This means that most of the properties of striate units are determined by their input from the retina rather than from feedback generated either by subsequent processing stages or by behavior (see also Sandell and Schiller 1982).

In summary, chronic blindness produced by lesions of nonvisual cortex is accompanied by intact processing in visual cortex and by the ability to make proper behavioral responses to stimulation of non-visual sensory modalities. This strongly suggests that blindness can be produced by disconnection of the visual system from motor output and that visuomotor integration is a corticocortical enterprise.

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