EXPERIMENTAL NEUROLOGY 72, 308–317 (1981)

Relationship of Aberrant Retinotectal Projections to Visual Orienting after Neonatal Tectal Damage in Hamster

B. L. FINLAY AND S. J. CAIRNS[1]

Department of Psychology, Cornell University, Ithaca, New York 14850

Received May 6, 1980; revision received October 6, 1980

The relationship of visual orienting to the extent of physiologically functional aberrant retinotectal connectivity was determined in hamsters subjected to large lesions of their superior colliculi on the day of birth. No relationship was found. The extent of visual field over which visual orienting could be evoked was always markedly smaller than the extent of visual field over which a physiologic evoked response could be found in the neonatally damaged superior colliculus. No evidence was found that aberrant retinal projections to the deep layers of the superior colliculus produced by neonatal damage contribute substantially to visual-orienting behavior.

INTRODUCTION

If abnormal neuroanatomic projections resulting from early brain damage could be shown to produce normal behavior, the implications for the significance of neuronal plasticity and for therapeutic approaches to early brain damage would be immense. One of the few possible cases of this phenomenon was reported by Schneider (10–12). After neonatal lesions of the superficial layer of the superior colliculus, aberrant retinal projections to the residual deep layers of the remaining superior colliculus were found, a type of connectivity never found in a normal hamster. Animals with this neonatal lesion and the resulting aberrant retinal projections were capable of orienting to stimuli presented in the central and lower visual fields, and Schneider hypothesized and presented some evidence that these aberrant retinal projections were the substrate of the preserved orienting capacity (11, 12).

[1] This work was supported by National Science Foundation grant BNS 77 07066. We thank Anne T. Berg for her assistance with the electrophysiology and Pat Moran for her secretarial help.

0014-4886/81/050308-10$02.00/0

This hypothesis has been clouded by the observation that adult animals with lesions of similar extent lacking abnormal retinal projections also show orienting in the central visual field (2, 5, 7, 8). Nevertheless, the abnormal retinal projection appears to be physiologically functional in that postsynaptic visual responses can be elicited in the residual tectum, with a spatial distribution similar to the distribution of the aberrant retinal projection (1, 6). The projection is physiologically and topographically abnormal and represents a variable amount of the central and nasal visual fields (1). Because the superior colliculus normally contributes substantially to visual orienting, it is reasonable to investigate the effect of this aberrant projection on the residual orienting of animals with neonatal lesions.

If the aberrant retinal projection and the residual tectal fragment contribute to visual orienting, the extent, amount, or quality of behavioral orienting should covary with some feature of the representation or organization of the visual field in the residual tectum. We investigated the relationship of the extent of visual field represented in the residual tectum, assessed electrophysiologically, with the extent of visual field over which orienting can be elicited. The volume of the remaining tectum and the size and topographic organization of the residual visual fields were also compared with behavioral orienting.

METHODS

Subjects. In seven hamsters residual tectal volume and visual-orienting behavior were assessed. In four, electrophysiologic assessment of visual field was added. Each tectum and its contralateral visual field was treated as an independent observation because the responsive visual field for each eye at no time overlapped, and the areas of behaviorally responsive visual field for each eye in each hamster were uncorrelated (Spearman's rank-order correlation, $R_s = 0.30$, not significantly different from 0, $P > 0.05$).

Neonatal Surgery. Within 24 h of birth, hamster pups were removed from their mother and given bilateral heat lesions of the superficial layers of the superior colliculus, in the manner described by Schneider (10). The pup was cooled to provide anesthesia, limit mobility, and reduce blood flow, and a small incision was made in the scalp and the skin retracted so as to reveal the confluence of the transverse and sagittal sinuses and the occipitointerparietal suture. These landmarks define the boundaries of the superior colliculus in the neonatal hamster, which is not covered dorsally by cortex as it is in the adult. The superficial gray layer and variable amounts of intermediate and deep layers of the superior colliculus were

then destroyed bilaterally by application of heat through the paper-thin cranium. The skin wound was then closed with sutures and the animal warmed and returned to the mother. At maturity and after testing, the extent of each lesion was determined.

Assessment of Visual Orienting. Beginning at 3 months of age, the hamsters were trained to stand on a small elevated platform and hold their noses relatively motionless in a hole in a small upright panel. The visual stimulus was a small gray plasticine sphere, about 1 cm in diameter, in which a sunflower seed was inserted. The stimulus was suddenly introduced into the hamster's visual field and jiggled slightly. An overhead camera and a frontal camera videotaped the seed position as well as the evoked orienting movement. Only orienting movements initiated within 2 s of stimulus presentation were scored. The hamster was rewarded with the sunflower seed as rapidly as possible when he ceased his head movement, regardless of the accuracy of the turn. Stimulus position and verification of head movement was determined by slow and stop-motion playback of the videotape. Because the hamster's eye movements are not monitored in this procedure, this perimetry procedure yields maps based only on head coordinates of positions yielding reliable turns. Measurements of amplitudes of spontaneous saccades in hamsters give a normal range of 1 to 7° (13). An average of 83 stimulus presentations per hemifield was accumulated for each hamster. The total area of responsive visual field was determined on a unit sphere, expressed as a percentage of total area where one hemisphere = 100%.

Electrophysiology. The hamsters were anesthetized [for electrophysiology] with urethane (0.7 g/ml, 0.3 ml/100 g body weight) mixed with prednisolone (Depo-Medrol, 4 mg/ml, 0.2 ml/100 g body weight) which reduced inflammation and cerebral edema. Tectal unit responses are influenced only minimally by urethane, and unit responses remain vigorous and constant for extended periods (to 8 h) with one anesthetic dose. The cranium overlying the residual superior colliculi was removed, and the sagittal sinus was ligated, cut, and retracted.

Overlying visual cortex was then aspirated for the following reasons: (i) The midbrain undergoes considerable plastic deformation as a result of the neonatal lesion. Removal of overlying cortex gives a clear view of the tectal area. (ii) The projection of interest is the aberrant retinotectal projection and its relation to orienting behavior. There is a normal visual corticotectal projection to the dorsal segment of intermediate gray not of interest in this experiment. (iii) A question might be raised concerning the physiologic normality of the residual tectum consequent to acute visual cortex removal. Although this experiment has not been done in the animals with early lesions, in the normal hamster the consequences of such a re-

moval are subtle, and gross responsivity, such as that tested here, is not affected (9).

Axes of the visual field were defined by the following techniques. Two small marks were made on the corneal margins at the midpoints of the attachments of the lateral and medial rectus muscles, which define a nasotemporal meridian, not the same as "true" horizontal as defined with respect to gravity in an alert animal. The eye was sutured in place, the pupil was dilated with a dilute solution of atropine, and the cornea protected with a contact lens of zero refractive power. The optic disc was then located with a reversible ophthalmoscope, and it and the rectus marks were plotted on a translucent hemisphere centered about the hamster's eye; thus both eye position and rotation could be kept constant.

Visual stimulation was done in a darkened room, and the principal visual stimulus used was a hand-held 3 to 8° white spot, back-projected on the translucent hemisphere.

Electrode penetrations were made approximately perpendicular to the surface of the residual midbrain with the skull inclined 30°, nose up, from the normal stereotaxic horizontal (10). The electrodes were tungsten-in-glass, 1 to 2 μm at the tip. Multiunit evoked potentials were used to define receptive field boundaries. Fields were plotted by moving the light spot into the receptive field from the periphery at low velocity (4 to 10°/s); the first point where a reliable evoked response (three responses per four presentations with a 5- to 10-s interpresentation interval) could be evoked, however small, was counted as the field boundary. The surface of the residual tectum was plotted in 0.2-mm steps, until all surrounding boundaries were contacted (inferior colliculus, brachium of the inferior colliculus, and the pretectal and lateralis posterior nuclei). The depth of the responsive residual colliculus at each recording site was measured and any changes in receptive field location or extent with depth were plotted. The total area of responsive visual field was determined on a unit sphere, expressed as a percent of total area where one hemisphere = 100%. The average receptive field diameter was calculated.

Microlesions for subsequent reconstruction of the electrode placements were made at the end of each recording session.

Histology. The hamsters were killed immediately after electrophysiologic recording and perfused with saline followed by 10% formol–saline. Coronal sections in the plane parallel to the angle of electrode penetration were cut frozen at 30 μm. Every fifth section was stained with cresylecht violet and used for reconstruction. All electrode placements were verified, and the extent of the neonatal damage reconstructed. Volume of the residual superior colliculus was estimated by taking the smallest rectangle that would enclose the residual tectal tissue in

TABLE 1

Animal	Physiologic visual field (%)	Tectal volume	Behavioral visual field (%)
35.11 L	15.3	0.68	5.1
R		0.89	
34.1 L	13.3	2.33	7.3
R	12.6	0.66	13.1
35.6 L	49.1	0.53	12.7
R		0.53	
35.5 L	26.9	0.70	7.9
R	25.9	1.02	4.0
32.3 L		0.94	12.7
R		2.99	5.5
58.3 L		1.24	8.3
R		1.09	40.2
58.5 L		1.06	17.3
R		1.21	18.8

each section, including, but not exceeding, the stratum griseum profundum, multiplying this area by the intersection distance, and summing the resultant volume for all sections containing superior colliculus. This method was chosen because the shape of the residual tectum in these animals approximated a rectangle. A normal superior colliculus has an estimated volume by this method of 4.6 mm^3.

RESULTS

Reconstruction of the Early Lesion. From a number of animals with early bilateral tectal damage, those with complete removal of the superficial gray layer and sparing of some intermediate and deep gray were chosen for correlation, because this is the type of preparation which is likely to show the aberrant retinotectal connectivity described by Schneider (11). The resultant volumes of the remaining superior colliculi in all but two of the eight animals included in this study clustered between 0.5 and 1.5 mm^3, which was 10 to 33% of normal volume (Table 1). An example of such a lesion for animal 35.5L is shown in Fig. 1. No evidence of the normal organization or cell types of the superficial gray was evident. Most dorsally, a fiber layer was present in which the optic tract axons coursed (11). Large cells characteristically found in the deep gray layer were

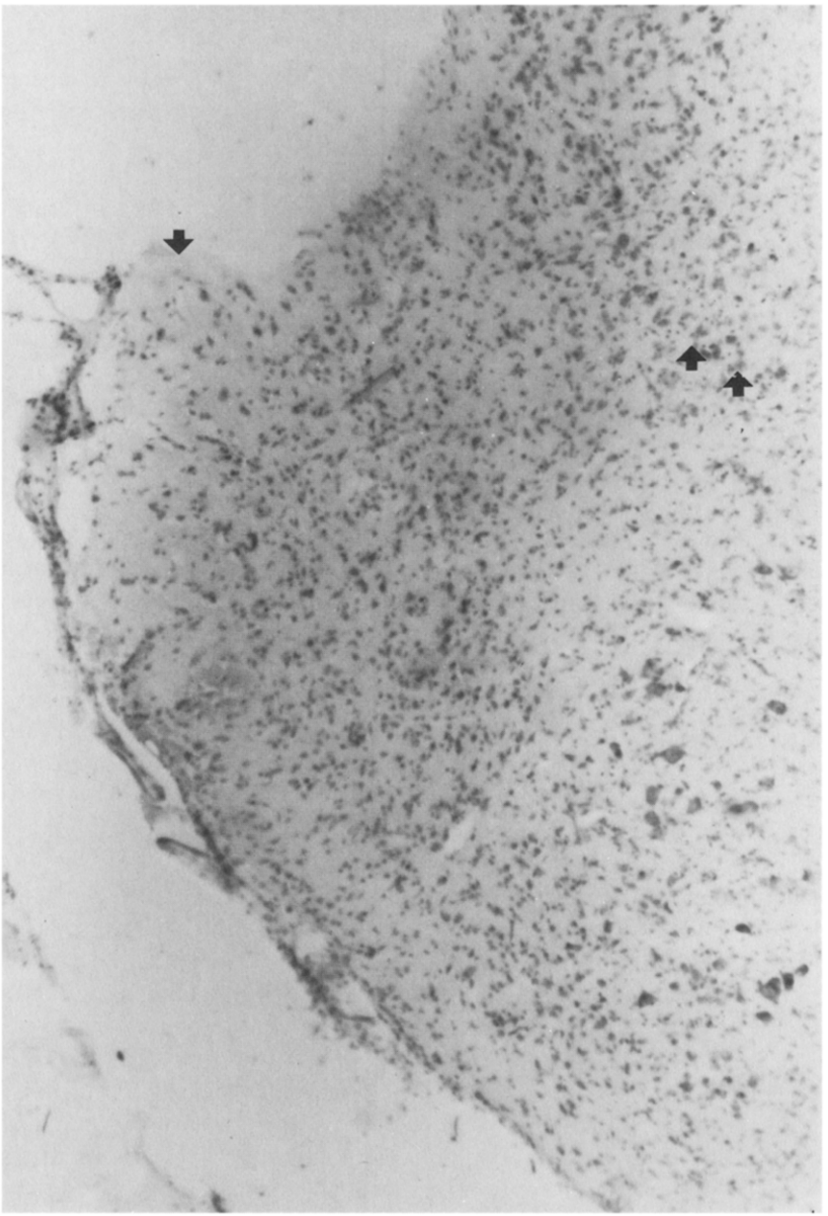

FIG. 1. Representative section of residual superior colliculus in a hamster with a neonatal lesion. The right edge of the photomicrograph is the animal's midline. This section is taken from the midpoint of the rostrocaudal extent of the residual colliculus. The double arrows mark the edge of the central gray, the single arrow the anomalous dorsal fiber layer. Centrally, there is a small electrolytic lesion marking an electrode penetration. A normal superior colliculus would present approximately twice the dorsal surface to the central gray extent seen here.

evident laterally; medially the lesion extended to the dorsal aspect of the central gray. Two animals proved to have one superior colliculus with greater residual volume, 2.3 and 2.9 mm^3. Because both these cases showed complete destruction of the superficial gray layer, they were included in this analysis.

In all damaged superior colliculi but two, visual responses could be elicited and receptive fields plotted. On reconstruction the two animals with no recordable visual responses in one colliculus proved to have several electrode penetrations in the residual colliculus yielding no response. However, because neither colliculus proved to have been completely explored, they were not included in the following data analysis.

Visual Representation in the Superior Colliculus and Visual Orienting. In a normal hamster visual evoked responses in the tectum from a single eye can be found over an area approximately 70% of a hemisphere (4). The normal hamster will orient regularly to sunflower seeds over a somewhat smaller area of visual field, 48% of a hemisphere for each eye separately. For the behavioral measurement an overlap of the field of view of the two eyes of 40° about the vertical midline is estimated (15). In the normal hamster, thus, the hamster orients over a somewhat smaller area than it shows a visual evoked response in the tectum; the ratio of these two areas is 0.68.

In the animals with neonatal lesions, the ratio of behavioral to physiologically responsive areas averaged 0.3, with only one observation close to normal (0.71); the others ranged from 0.11 to 0.38. The hypothesis that this group comes from a population with an overall mean of 0.68 can be rejected ($t = -4.23$; $P < .0043$). Thus, a substantially larger than normal visually responsive area in tectum is not expressed in behavioral orienting.

In animals with early lesions, the correlation of physiologic visual field to behavioral visual field was $r_s = -0.08$ (Spearman's rank order correlation) indicating no relationship between these two variables ($P > 0.05$). Similarly, residual tectal volume within the limited range examined in this study proved to be unrelated to orienting behavior ($r_s = -0.05$, not significantly different from 0, $P > 0.05$).

Receptive Field Size. In prior studies of animals with smaller lesions, a relationship of tectal volume to receptive field size was observed. In the normal animal, average receptive field diameter was 8.6° (4). Animals with 30% reductions in tectal volume showed an increase in receptive field diameter to 9.9° (3). Volume reductions of 40 to 50% yielded receptive field diameters of 12.4° (2). The present group, with volume reductions of 67 to 90%, yielded an average receptive field diameter of 27°. Within this group, receptive field diameter as an index of "normality" did not predict amount of orienting (Pearson's $r = 0.31$); a negative value of r would be expected if small receptive fields were associated with normal orienting.

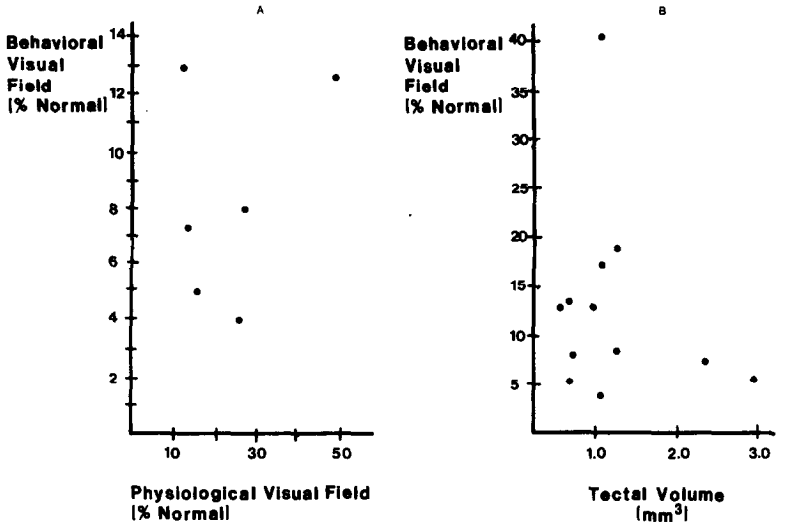

FIG. 2. A—relationship between electrophysiologic visual field recorded in the neonatal-lesion superior colliculus, and the extent of visual field over which the animal would visually orient, expressed as percentage of the normal area for both capacities. B—relationship between residual tectal volume and area of the visual field over which the animal would orient.

DISCUSSION

We can find no evidence for a simple relationship between visual orienting and visual representation in the remaining tectum in animals with neonatal tectal lesions. Because this is a negative result, unusual care should be taken to verify assumptions and justify data collection procedures. For the following reasons, we believe these data accurately reflect a lack of relationship.

(i) The measurement techniques were appropriate and adequate. Physiological representation of an area of visual field in the tectum is presumably a sine qua non for its behavioral expression in orienting. If the data presented here gave any hint of relationship between physiology and behavior, it might be profitable to further investigate some feature of "normality" of receptive field organization and relate it to behavior. No such hint exists. The mapping and receptive field plotting procedures used in this study, although not mechanized, were systematized. Since regularities were observed in the relationship of individual receptive field sizes to tectal volumes, it is likely the physiologic assessment procedures were sensitive enough to accurately reflect differences in amount of visual field representation in the remaining tectum.

(ii) A larger portion than normal of the physiologic visual field recorded

in these damaged colliculi does not appear to have a behavioral expression in orienting. This observation is all the more compelling in that the physiologic visual field is likely to be systematically underestimated due to the punctate nature of sampling of the residual tectum, whereas the behavioral visual field is probably systematically overestimated due to the possibilities of small eye movements.

(iii) Adult animals given lesions of similar extent to these neonatal lesions show preserved orienting (3). It is interesting that the abnormal connectivity in the residual tectum at least does not appear to be deleterious to the preserved visual orienting of the neonatal lesion group; the amount of responsive visual field in tectum and behavioral visual field is not negatively correlated.

Schneider described two types of visual orienting in hamsters subjected to neonatal tectum lesions (11). In the first type, "wrong way" turning occurs when retinal fibers are induced to recross the tectal midline to innervate the superficial layer of the ipsilateral superior colliculus. These projections, although topographically abnormal, are not typologically abnormal, as the superficial gray layer of the superior colliculus is a normal target area for optic tract axons. Schneider convincingly demonstrated that these recrossing axons underly "wrong way" turning behavior (12), and we have not investigated this type of projection.

We investigated a second type of projection from retina to deep tectum, hypothesized to contribute to slow, but correct direction turning, in the central nasal visual field. Because the deep tectum is not a normal retinal target, this projection is both topographically and typologically aberrant. If this entirely abnormal projection did contribute to adaptive behavior, it would be extremely interesting. With the exception of one animal, given a partial undercut of the deep tectum, that lost some correct-direction orienting, Schneider's evidence for adaptive function of this projection is indirect (12). We found no evidence in support of a role for this projection in visual orienting.

These results must be evaluated in the larger context of work in neuroplasticity and the functional consequences of early brain damage. Though there are numerous cases of apparently spared behavioral capacities after early brain damage that would be lost after adult damage (12, 14), there are as yet no reported cases of demonstrably normal behavior dependent solely on demonstrably abnormal neuronal connectivity. It may be that coping with early trauma by gross anatomic reorganization is not a likely property of the nervous system. Further study of those cases of behavioral sparing potentially associable with central nervous system reorganization is essential to demonstrate the extent of contraints on plasticity of brain function.

REFERENCES

1. FINLAY, B. L. 1979. Experimental manipulation of the development of ordered projections in the mammalian brain. Pages 391–402 in R. D. FREEMAN, Ed., *Developmental Neurobiology of Vision*. Plenum, New York.
2. FINLAY, B. L., K. MARDER, AND D. CORDON. 1980. Acquisition of visuomotor behavior after neonatal tectum lesions in hamster: the role of visual experience. *J. Comp. Physiol. Psychol.* **94:** 506–518.
3. FINLAY, B. L., S. SCHNEPS, AND G. SCHNEIDER. 1979. Orderly compression of the retinotectal projection following partial tectal ablation in the newborn hamster. *Nature (London)* **280:** 153–154.
4. FINLAY, B. L., S. SCHNEPS, K. WILSON, AND G. SCHNEIDER. 1978. Topography of visual and somatosensory projections to the superior colliculus of the golden hamster. *Brain Res.* **142:** 223–235.
5. FINLAY, B. L., D. SENGELAUB, A. BERG, AND S. CAIRNS. 1980. A neuroethological approach to hamster vision. *Behav. Brain Res.* **1:** 479–496.
6. FINLAY, B. L., K. WILSON, AND G. SCHNEIDER. 1979. Anomalous ipsilateral retinal projections in Syrian hamsters with neonatal lesions: topography and functional capacity. *J. Comp. Neurol.* **183:** 721–740.
7. GOODALE, M., AND R. MURISON. 1975. The effects of lesions of the superior colliculus on locomotor orientation and the orienting reflex in the rat. *Brain Res.* **88:** 243–261.
8. MORT, E., S. CAIRNS, H. HERSCH, AND B. FINLAY. 1980. The role of the superior colliculus in visually guided locomotion and visual orienting in the hamster. *Physiol. Psychol.* **8:** 20–28.
9. RHOADES, R., AND L. CHALUPA. 1978. Functional and anatomical consequences of neonatal visual cortical damage in superior colliculus of the golden hamster. *J. Neurophysiol.* **41:** 1466–1494.
10. SCHNEIDER, G. 1970. Mechanisms of functional recovery following lesions of visual cortex or superior colliculus in neonate and adult hamsters. *Brain Behav. Evol.* **3:** 295–323.
11. SCHNEIDER, G. 1973. Early lesions of the superior colliculus: factors affecting the formation of abnormal retinal projections. *Brain Behav. Evol.* **8:** 73–109.
12. SCHNEIDER, G. 1979 Is it really better to have your brain lesion early? A revision of the "Kennard Principle." *Neuropsychologia* **17:** 557–583.
13. STEIN, B., AND J. MCHAFFIE. 1981. The control of eye movements by the superior colliculus in hamster and rat. *Behav. Brain Res.*, in press.
14. STEIN, D., J. ROSEN, AND N. BUTTERS, Eds. 1974. *Plasticity and Recovery of Function of the Central Nervous System*. Academic Press, New York.
15. TIAO, Y.-C., AND C. BLAKEMORE. 1976. Functional organization in the superior colliculus of the golden hamster. *J. Comp. Neurol.* **168:** 459–482.