ALTERED RETINAL CONNECTIONS FOLLOWING PARTIAL TECTUM

LESIONS IN NEONATE HAMSTERS

by

Sonal Ramniklal Jhaveri

B.S., M.I.T., Cambridge, Massachusetts

(1970)

SUBMITTED IN PARTIAL FULFILLMENT

OF THE REQUIREMENTS FOR THE

DEGREE OF MASTER OF SCIENCE

at the

Massachusetts Institute of Technology

September, 1973

Signature of Author ___ Signature redacted
Department of Psychology, September, 1973

Certified by ___ Signature redacted
Thesis Supervisor

Accepted by ___ Signature redacted
Chairman, Departmental Committee
on Graduate Students

CONTENTS

ABSTRACT

Discrete lesions of the retina were produced in 33 normal

adult hamsters (Mesocricetus auratus) by current through an electrode

which penetrated the sclera at positions measured with respect to

muscle attachments. 5 days after surgery, each animal was perfused

and the brain prepared for silver staining of degenerating axons and

terminals in a closely spaced series of sections. Degeneration in

each section was displayed, for 16 lesions, on lateral and dorsal view

reconstructions of the brainstem surface.

Before the axons of the main optic tract have reached their

principal terminal areas, they have become organized such that axons

from dorsal retina are located posteriorly and those from ventral

retina anteriorly. This order is maintained by the sheet of fibers as

it proceeds over both nuclei of the lateral geniculate body (LGB),

bends caudally and extends across the pretectal area and through the

 superior colliculus (SC). Close to the tract in each terminal area, all

or nearly all of the contralateral retina is represented by terminating

fibers, which extend away from the tract along lines of projection.

Axons from nasal retina enter each nucleus of LGB ventrally, those from

temporal retina dorsally. In SC the representation of the nasotemporal

axis of the retina is reversed with respect to the direction of

ingrowth of the axons, so the temporal retina is represented anteriorly.

The rostral part of the superficial gray layer of SC was ablated

on the day of birth and the topography of retinal projections in the

2

remaining tectum was analysed in 14 cases by similar techniques. Reconstructions of degeneration in LGB were used to select matching normal cases for comparison of results in SC. Analysis of alternative interpretations of the observed patterns led to the conclusion that the representation of the entire retina becomes compressed in an orderly manner in the remaining small tectum. In addition, there were cases in which axons became considerably deflected from their normal course, and some of these terminated in displaced positions, producing discontinuities in the tectal representation of retinal positions. Factors influencing the formation of the normal map and the anomalous connections have been discussed. Brief mention is also made of a pilot study involving caudal tectum lesions and combination lesions of the SC.

The author was born in Bombay, India in 1948, and underwent all her early education in the same city, graduating from Walsinghanm House School in 1964. For the next four years, she attended St. Xavier's College, also in Bombay, majoring in physics with mathematics as a subsidiary subject. After obtaining a B.Sc from St. Xavier's College, in 1968, she was admitted to M.I.T. as a junior and received a B.S. in 1970. Although the degree was received under the auspices of the Physics Department, she became increasingly interested in the neurosciences and, in fact, did her bachelor's thesis at M.I.T. in the Psychology Department under the supervision of Dr. R. Kalil, studying retinal projections of Siamese cats. The next year and a half was spent in the employment of Dr. G.E. Schneider, also at the Psychology Department, and at the Anatomy Department, Katholieke Universitet in Nijmegen, Holland, with Dr. A. Lohman, as a research assistant. She returned to the M.I.T. Psychology Department in January 1972 and received an M.S. in Psychology (1973). The study presented here is the M.S. thesis, advised by Dr. G.E. Schneider. The author is currently a Ph.D. candidate at the Anatomy Department, Division of Medical Sciences, Harvard University.

<u>Dedication:</u>

To my father, Ramniklal Bhogilal Jhaveri whose encouragement
and generosity allowed me to explore many new worlds.

INTRODUCTION

As a result of recent investigations, a capability of the CNS to undergo anatomical alterations in response to damage or loss of constituent tissue has become increasingly evident, and is commonly referred to as "neuroanatomical plasticity". The facility with which this phenomenon occurs appears to vary with the age of the tissue and with the system under consideration. The role of anatomical modulation should be underplayed when considering possible substrates for sparing or recovery of function, or certain behavioral anomalies, which follow brain lesions (McCouch, et al., 1958; Schneider, 1970, 1973; Teuber, 1970). A greater understanding of the mechanisms underlying the plasticity of neural connections would decidedly facilitate an eventual control of functional recovery.

Modern work on neuromorphological plasticity of the mammalian CNS began with studies of partially dennervated spinal cord in adult cats. McCouch, et al. (1958) investigated the occurence of plasticity following spinal cord transections, and correlated this with an apparent proliferation of terminal fibers from dorsal root axons. Liu and Chambers (1958) presented anatomical evidence for sprouting of intraspinal processes in the cat following partial dennervation of the spinal cord by dorsal rhizotomy. This kind of experimental paradigm was applied to the study of more central brain tracts by Goodman and Horell (1966). In a study of optic tract termination consequent to removal of occipital neocortex, they found evidence for axonal sprouting in certain regions of optic-tract projection in the diencephalon of adult rats. Plasticity of synaptic connections in adult brains was demonstrated at the ultrastructural level in experiments reported by Hamori (1968), Raisman (1969), and more recently by Lund and Lund (1971), Ralston and Chow (1973) and Raisman and Field (1973). In a Golgi study of the morphology of the human posterior

7

colliculus, dendritic growth cones have been reported for brains ranging
in age from 24 weeks of gestation to 74 years (Geniec and Morest, 1979).
The above investigations along with many other recent ones (see Moore, et al.,
1971; Bernstein and Bernstein, 1971). Lynch, et al. (1973b) give strong evidence
that the adult CNS does retain a capacity for growth and change. As Moore, et al.
(1971) suggest, and as may be inferred from the studies of Geniec and Morest
(1971), or Sotello and Palay (1971), there may even be a continuing local
reorganization of synaptic architecture in the adult brain.

If the mature CNS has been discovered to have the capacity for such
flexibility of morphological connections, what then of the young, as yet immature
nervous tissue? Surprisingly few studies are directed to the investigation of
this issue until very recently. Reports have been appearing on anatomical
consequences of early damage to neocortex (Hicks, et al., 1961; Hicks and
D'Amato, 1970; Cunningham, 1972), to allocortex (Das, 1971; Lynch, et al., 1973a,
1973b), to cerebellum (Hamori, 1968; Altman and Anderson, 1971; and others),
and in subcortical visual system structures (Schneider and Nauta, 1969; Lund
and Lund, 1971; Kalil, 1972, 1973; Guillery, 1972; Casagrande, et al., 1972).

In 1969, Schneider and Nauta reported dramatic anomalies in retinofugal
projections following damage to the superior colliculus (SC) in the neonate
hamster. With unilateral ablation to the superficial tectal layers where
retinofugal axons normally terminate, the optic tract on the side of the early
lesion was observed to terminate abnormally in residual deep tectal tissue,
while some acons passed across the tectal midline into the "wrong" colliculus.
These deviant patterns of retinotectal connections are particularly interesting
because of the correlations with behavioral anomalies (Schneider, 1970, 1973).

Additional abnormalities were observed in the retinal projections to the ventral nucleus of the lateral geniculate body (LGv), the posterior part of the lateral thalamic nucleus (LP), the tiny dorsal terminal nucleus (DTN), and sometimes retinal projections were found even in the medial geniculate body (Schneider, 1973).

Much of the work reported in this study is based on further investigation of the effects observed by Schneider. The behavioral indications of changes in topography resulting from the anomalous retinotectal projection provoked us to ask a number of questions regarding the detailed organization of the altered projections, and the dynamics of this alteration. For a case with a removal of the right SC in the neonate, it seemed possible that the recrossing of the axons into the "wrong" tectum might be explained by a time-of- arrival hypothesis (Schneider, 1972; and personal communication). According to this hypothesis, the axons from the left eye traversed the region of the ablated right tectum, some axons finding terminal space in the deep SC layers. Other axons, it was speculated, continued caudomedially, and reached the midline before, or at the same time as, axons from the lower retina of the other (right) eye had arrived there. The two sets of axons competed for the available space, and some of the axons from the left eye found terminal space in the medial part of the left SC. If this hypothesis is correct, then what might be the result of a neonatal lesion of the rostral half of the SC ? Would the axons destined for the rostral tectum continue over the damaged region and terminate in the undamaged caudal tectum ? Would they get crowded out and degenerate ? Or would they find a representation in the thalamic nucleus lateralis posterior which has been partially denervated by the tectal lesion (Schneider, 1973) ? In the normal animal, the

tectal projection to the LP shows very little topographical organization

(Abplanalp, 1970; Harting, et al. , 1973). Would the retinal termination

in the LP be topographical ?

Such questions led us also to wonder about the effects of partial

tectum lesions that eliminate the caudal, medial or lateral half of the

superficial SC. Is there a reorganization, and if so can this once again

be explained by a simple temporal gradient hypothesis or do other kinds

of gradients act to organize the axon terminals in a topographic fashion ?

We were alerted to pay particular attention to the possibility of an orderly

compression in the map of the retinal projection to the remaining SC, by the

reports of such a compression after partial tectum lesions in the goldfish

(Gaze and Sharma, 1970; Yoon, 1971, 1972a, b; Sharma, 1972a, b, c).

We decided to investigate some of these problems using the

technique of making small retinal lesions and mapping the ensuing degeneration.

There are several advantages to using the experimental anatomical method

over an electrophysiological technique. A discrete lesion in the retina

causes degeneration along the whole course of the optic tract. Using

the reconstruction drawings of the brainstem developed by Schneider, Jhaveri, and

Winzer (unpublished), it is possible to relate our findings to the topography

of the whole optic tract. This allows us to analyse our results in terms of

axon dynamics. The sampling problem in electrical recording techniques

(electrode passes are a minimum of about 0.25 mm. apart) would very likely cause

many smaller, isolated patches of anomalous connections to be overlooked.

Moreover, some of the anomalies in the map may be suppressed due to inhibition

effects. On the other hand, the recording technique would allow us to resolve

10

some questions regarding overall topography in the midbrain, especially
with regard to representation of the retinal periphery; but the course of axons in
the accessory optic tract and its terminal nuclei, and the pattern of axonal
and terminal degeneration in thalamic regions in the same animals would be
almost completely lost. We do expect, however, that some of our conclusions
will be investigated with the use of electrophysiological methods.

General Methods and Materials

Thirty Syrian golden hamsters (Mesocricetus auratus) were used for the control series—unoperated at birth – and another 37 animals, each with an early tectum lesion, were included in the experimental group. The control animals, 12 to 20 weeks old, were anaesthetized (using Equithesin anaesthesia, 0.35 ml/100 gms) and placed in a stereotaxic headholder apparatus. The eyelids were held back using haemostats, and the conjunctivum cut to expose the extraocular muscles lying along the scleral surface. These muscles, and the limbus (the edge of the cornea where it is slightly overlapped by sclera) were used as points of reference for the placement of discrete retinal lesions. Embedded in the sclera, a vessel is seen coursing between the attachments of the medial and lateral rectus muscles, and passing inferior to the optic nerve. This vessel is rather constant in position (except for minor curves and turns) and was sometimes used as an additional landmark. Having determined the lesion coordinates, an electrode (a no. 1 stainless steel insect pin coated with insulex except at the tip) was advanced at right angles to the surface of the eyeball, and pushed through the sclera. A radio frequency current was passed (intensity and duration predetermined by making a trial coagulation in egg-white), using an anal probe as the ground. The electrode was removed, measures made of the point of entry, the eyelids closed to prevent the eyeball from drying, and the animal was returned to its cage.

The same procedure was utilized in making retinal lesions in the experimental group. These hamsters had been born in the laboratory, and had undergone partial tectum lesions on the day of birth. The procedure for making

lesions was essentially the same as that described by Schneider (1973).
Animals were removed from their nests (1/3 of the litter at a time) and
placed in a simple incubator. Using no anaesthesia except mild hypothermia,
an incision was made in the skin over the caudal part of the skull. At
this age, the interparietal bone overlying the tectum is still thin and
cartilaginous, and the hemispheres have yet to grow back over the tectum.
Thus, by direct application of heat on the skull in this region it is
possible to damage the underlying tissue. Heat lesions were made using
the bent ends of insect pins heated in an alcohol flame and applied over the
part of the tectum to be ablated. The area involved was indicated by a
whitened appearance of the tissue. Care was taken to avoid damage to the
transverse sinus and, wherever possible, certain surface vessels supplying
the tectum. Rostral, caudal, medial, and lateral tectum lesions were made
unilaterally or bilaterally. Sometimes one eye was enucleated in addition. The
pups were then returned to the nest, left untouched with the mother until
weaning, and allowed to survive until age 12 weeks or older. At this point,
the discrete lesions were made in the retina, as described.

Five days following surgery, each animal was perfused with 0.9% saline
followed by 10% formalin in 0.9% saline. The lesioned eyeball was dissected
free with the rectus muscles attached, and allowed to fix in the formolsaline
after a small amount of fixative was injected into the posterior chamber
through the optic nerve head. The perfused brain was removed from the skull,
placed in the perfusion fixative for at least one week, then in sugar formalin
for several days, and finally embedded in albumin-gelatin, and processed for
frozen sectioning. Sections were cut at 30μm and every fifth section was

stained for degenerating axons, preterminals, and terminals, using the

Fink-Heimer method (Fink and Heimer, 1967). A second series (also spaced at

150μm was prepared whenever it was necessary to fill in details of

degeneration patterns. Adjacent series were, in many cases, stained with a

silver-pyridine method for normal fibers (Fink and Schneider, see Schneider,

1969, note 32).

Method for presentation of data using standard reconstructions.

The exact course and extent of the degeneration in the cases described

above was mapped onto standard dorsal and lateral view reconstructions

of the brainstem of a normal adult hamster. These standard reconstructions

were developed by Schneider, Jhaveri, and Winzer (unpublished), the procedure

being as follows:

1) A normal adult male Syrian hamster (HN-1) age 15 weeks, was perfused

with 0.9% saline followed by 10% formalin in saline. The head was placed

in a stereotaxic headholder and the skull positioned so that the bregma

point and the caudal end of the interparietal bone at the midline were in

the same horizontal plane. The skull top was then removed using a pair of

fine rongeurs, and the surface of the brain exposed. Vertical pins were

introduced at (1) P 1.0mm. and 1.7mm. lateral to the midline (2) A 7.0mm. and

3.0mm. lateral to the midline, with the lambda point taken as the A-P zero point.

A longitudinal pin was also introduced in the horizontal plane 5-6mm. below the

reading for lambda, and 4.0mm. lateral to the midline. The brain was next

blocked stereotaxically at P 1.4mm. and processed for frozen sections as already

described. Two series, each one with sections spaced at 150μm, were stained with

14

cresylecht violet. An intermediate series was stained using a silver pyridine

method for normal fibers (Fink and Schneider, see Schneider, 1969, note 32).

The pin holes, as seen in histology, were used to calculate tissue

shrinkage, correct for actual spacing of sections, and for the alignment of

sections for the purposes of reconstruction. They also allowed an accurate

placement of stereotaxic coordinates on our reconstructions.

2) <u>Dorsal view drawing</u> (see Fig. 1): A set of horizontal grid lines,

each line representing one section from a regularly spaced series (the grid

spacing being proportional to the corrected spacing of the sections at a

standard magnification), was used. From drawings of transverse sections of the

brainstem,made at magnifications adjusted so the longitudinal pin marks

were in register, points representing surface outlines of superficial structures

like superior colliculus, lateral geniculate bodies (borders were first projected

to the optic-tract surface), habenula, etc. were projected onto a horizontal

plane and these points were then transposed to the corresponding grid lines

representing the sections. The points representing the outlines of each

structure on the grid lines, were then joined with slight corrections to

obtain smooth curves resulting in the dorsal view reconstruction drawing

of superficial structures. The drawing compares well with photographs of

the dorsal view of hamster brainstems. Some deep structures were also included

in the drawing, but their outlines were "shadow cast" instead of being projected

first to the surface. Figure 2 illustrates the difference between a surface

projection and a shadow-cast projection.

3) <u>Lateral view drawing</u>: This was done similarly, using projections

onto a vertical plane instead of a horizontal plane. Additional help in

drawing outlines was derived from photographs of several brainstems where

15

the cerebral hemispheres had been removed. The completed drawing is shown in Figure 3.

4) The brain of another adult Syrian hamster, HEE-22 with a right eye enucleation at age 12 weeks and a survival time of 6 days, was cut at 30μm in a plane very close to that of HN-1 described above. Sections 150μm apart were stained using the Fink-Heimer method. This series was used to verify the exact course of the optic tract, the accessory optic tract and the related terminal areas.

It must be re-emphasized here that all the deep structures - ventromedial hypothalamic nucleus, red nucleus, oculomotor nucleus, anterior pretectal nucleus (nucleus posterior thalami), the anteroventral thalamic nucleus, suprachiasmatic nucleus, medial terminal nucleus (MTN) - plus some near-surface structures like the anterodorsal nucleus, cerebral peduncles, etc. have been "shadow-cast", whereas the superficial structures and the degeneration (if any) in these have first been projected to the nearest point on the surface of the brainstem, and then projected onto a horizontal or vertical plane as the case may be. In other words, all degeneration related to the primary and accessory optic tracts, is a "surface-projection" view - the one exception being the MTN which, because of its position, is "shadow-cast" onto the vertical plane.

With the completed standard dorsal and lateral view drawings, it was next possible to use them to reconstruct the brainstems of experimental animals. The first step in this procedure was to determine the orientation and spacing of the grid lines. In doing this, we found that the plane of sectioning and the right-left symmetry of the cut varied slightly from brain to brain. For a symmetrically cut brain, whose plane of section was the same as or very close to that for the normal brain HN-1, the grid lines for the dorsal and lateral views were drawn straight. However, for brains that had been cut with a right-left asymmetry, or cut in a plane appreciably tilted with respect to that for HN-1, certain approximations had to be made. In dealing with this problem, we considered the brainstem to be in the form of a cylinder. Figure 4 illustrates the lines of section on a cylinder cut by a transverse plane. In Figure 4 (a) we

16

see that a transverse plane, maintaining a right-left symmetry, meets the cylinder such that the grid lines would be straight as seen on a lateral view. For a transverse plane that does not maintain a right-left symmetry, the situation would be as shown in Figure 4 (b) and (c), resulting in curved grid lines for the lateral view, the direction of concavity of the curve depending upon the nature of the asymmetry. Similar illustrations for the dorsal view can be envisioned by turning Figure 4 through 90°. This demonstrates that a vertical plane of section will result in straight grid lines on the dorsal view whereas a plane tilted with respect to the vertical requires curved lines for representing a section on the surface of the brainstem. Combining the "lateral" and "dorsal" views illustrated in Figure 4, it is obvious that a brain cut with a right-left asymmetry and cut in a plane tilted with respect to that of HN-1 will result in curved grid lines for both the dorsal and lateral view reconstructions.

Once the orientation of the grid lines was determined, the grid-spacing was calculated using the outlines of the nucleus groups drawn on the standard drawings. Emphasis was laid on matching the geniculate bodies (lateral and medial) and the SC (when this ad not been damaged by surgery) of the experimental animals with those on the standard view. We found that the ventral region of the brainstem, especially the relative positions of the hypothalamus and the pons, showed considerable variability between brains. This could reflect an inconstancy in the angle of the pontine flexure from brain to brain.

With the grid-lines determined, the areas of degeneration were next mapped on the drawings, normalizing the dorso-ventral extent of each section with respect to the outlines on the normal brain drawing. The extent of the degeneration was projected to the surface as shown in Figure 2. Terminal regions near the surface and those deep to the surface of the OT were mapped using separate

symbols. A similar dichotomous coding was used for <u>axons</u> on the surface of

the brainstem, and those coursing deep to the surface. However, in the final

ink drawings, the deeply coursing axons have been omitted in the LGv, LGd, LP,

PT, SC for purposes of clear exposition, but have been included for the primary

and accessory optic tracts. For the MTN, the terminal degeneration as well

as the axons have been shadow-cast but are depicted with the same symbol as the

surface terminals and axons elsewhere.

Results

<u>The primary retinal projections in the Syrian hamster: main optic tract</u>

Before considering the alterations in the primary projections of the retina,
I will present here an overview of the normal retinal projection patterns in
the hamster, as seen with the Fink-Heimer modification of the Nauta silver-
staining technique. The data for this section have been obtained principally
from series in the collection of Dr. Schneider at M.I.T. Reference to Fig. 5
will facilitate an understanding of the following descriptions.

Adult hamsters had one eye removed under Nembutal anaesthesia. Following
survival periods ranging from 17 hours to 7 days, the animals were sacrificed
and their brain processed as described under General Methods. Brains were
sectioned in frontal, parasagittal and horizontal planes. Sections spaced at
150u were stained with the Fink-Heimer silver stain, and in many cases
adjacent series were stained for normal fibers and with cresylecht violet.

In general, for the hamster, the central nuclei receiving retinal
projections are similar to the structures described with the same
nomenclature that have been studied for other species(reviewed by Ebbeson,
1970, 1972). The pattern of retinal representation on central structures in
the hamster agrees in most part with that described by Hayhow et al. (1962)
for the rat, except for certain variations which I shall deal with further below.

The optic nerves cross incompletely at the chiasm and the tracts move
outwards along the ventral surface of the brainstem to its lateral edge where
they sweep dorsally, maintaining a position on the surface of the brainstem.
About midway up the lateral surface of the brainstem, the anterior edge of the

19

optic tract (OT) curves anterodorsally so that the tract completely covers the surface extent of both lateral geniculate nuclei (Fig. 5). The posterior edge of the tract follows a straighter trajectory directed dorsally and caudally over the caudal end of the geniculate bodies. Dealing only with the contralateral side for the present, the optic tract is seen to give off fascicles which leave their surface position at the ventral border of the ventral nucleus of the lateral geniculate body. These axons travel through each nucleus of the lateral geniculate body, being joined by other axons that branch off from the surface further dorsally. These deep fibers travel parallel to the surface fibers, extending dorsally and caudomedially through the posterior part of the lateral nucleus (LP) and are seen to enter the pretectal area, some of them apparently rejoining the surface fibers of the brachium of the superior colliculus. The fibers are similar in trajectory to the transverse bundles of retinofugal axons described by Montero and Guillery (1968) in the rat and to the medial division of the optic tract reported by Giolli and Gurthrie (1969) for the rabbit.

The main body of the optic tract, however, is seen on the surface of the brainstem. Degenerating axons can be followed into both the dorsal (LGd) and ventral (LGv) nuclei of the lateral geniculate body, where there is evidence of heavy termination.

The LGv in the hamster can be divided into an internal and an external subdivision shown by Niimi, et al. (1963) to be characteristic of most mammalian brains. In the hamster, however, the external division shows a further parcellation into a lateral (or external subdivision of the external lamina, LGvee) and a medial (or internal subdivision of the external lamina, LGvei) sublayer (Schneider, unpublished data). The LGvee is a cell-sparse region standing

out most clearly in siver-stained sections because of its dark staining neuropil. With Fink-Heimer stain it shows dense patches of boutons terminaux and very fine preterminal axons, whereas the LGvei has multiform cells and the retinal projection to this sublayer is "coarser" with many more degenerating axons. The LGvee is also the only part of the LGv nucleus that receives input from the superficial layers of SC (Schneider, 1973). The internal division (LGvi) in most mammals has been reported to receive no retinal projections. However, Schneider (1968), in a study of degeneration rates following eye-enucleation in the adult hamster, has observed that the LGvi does receive retinal afferents but these are stained optimally only at survival times of 17 to 22 hours. With longer survival times little degeneration debris is seen in this lamina.

The ipsilateral projection to the LGv is extremely restricted and occurs in a dorsomedial patch in LGvei. This differs from Giolli and Guthrie's (1969) report of ipsilateral degeneration in LGv for the rabbit. These authors demonstrate a projection to a restricted patch in the dorsolateral portion of the α sector of LGv which places it very close to the optic tract, whereas in the hamster, the ipsilateral patch of degeneration in LGv seems to reflect the pattern seen in the LGd (see below). Our results in the hamster show greater agreement with the results of Hayhow et al. (1962) in the rat.

The dorsal lateral geniculate nucleus (LGd) of the hamster, shows no distinct lamination in a Nissl stain. However, with the use of degeneration staining techniques, two segments are revealed: a deeper-lying one receiving predominantly ipsilateral, and an outer one with predominantly contralateral retinofugal afferents. In the contralateral LGd, fibers of the main optic tract turn into the body of the nucleus, and terminate on the cells, giving rise to coarse pericellular degeneration debris stained after a 5-day survival time.

21

The degeneration originating from discrete lesions in the retina shows that axons from the optic tract course along columns that, for much of the nucleus, pass from the surface in a dorsomedial and rostral direction, with termination all along the columns. These columns correspond to the "lines of projection" described by Montero et al., (1968), in an electrophysiological study of the LGd of the rat, as representative of restricted areas of the visual field. It has been interesting to note that the terminal patterns in the LGve show evidence of similarly oriented columns.

In addition to the termination seen along these columns, transverse fibers of retinal origin are also observed passing through the LGd as described above. These are mostly axons that have branched off from the OT as it passes over the LGB. Whether or not these fibers contribute to the terminal field in the LGd cannot be conclusively determined with the methods we have used, but many of these axons pass through the LGB and travel dorsomedially and caudally through the LP, and into the pretectum.

On the ipsilateral side, degenerating axons are found scattered through most of the surface extent of the optic tract as it courses over the lateral geniculate nuclei. In the dorsal nucleus, evidence of dense termination is found in a restricted medial position which can be followed throughout most of the rostral 2/3 of the structure; more caudally, as well as rostrally, degenerating axons are seen, apparently coursing rostromedially from the tract towards this area of dense termination. The method, of course, does not allow us to decide whether sparse termination may be present along the course of the axons as they are traveling in the direction of the main ipsilateral terminal area.

Once past the dorsal lateral geiculate nucleus, the main optic tract travels caudomedially over the LP, with parallel axons passing through the

22

tissue as noted above. In the LP, for the most part, the axons are merely fibers of passage, However, in many, but not all, cases a very tiny patch of terminal degeneration has been observed in this nucleus, the terminals lying clustered and closely apposed to the optic tract (Schneider, 1973).

In the course of its passage further caudally, the OT enters another region of termination, the pretectal area. Degeneration in the pretectum indicates termination of retinal afferents in the pretectal nucleus (nPT), as well as in the more superficial nucleus of the optic tract (nOT). The degeneration pattern in the pretectal nucleus is best stained with a 1-day or 2-day survival period following a unilateral eye enucleation, whereas that in the nOT stains maximally with a 5 to 7 day survival time. In Figure 5, from a case with 5-day survival, only the nOT is depicted; the deeper lying nPT shows a similar, though slightly more medial, pattern when depicted in a surface projection. Since most of the experimental cases are also five day survivals, I have not, for the purposes of the topography study, attempted to differentiate between the pretectal nucleus and the nucleus of the optic tract but rather, I have charted whatever degeneration is visible in this area and referred to it as the pretectal region.

The retinal input to this region is seen in our cases as a band of terminal degeneration that lies in the path of the OT fibers and straddles the extent of the OT. The band of degeneration can be followed from a rostromedial to a caudolateral position, with the degeneration in the nOT almost completely overlapping with that in the deeper lying pretectal nucleus in anteroposterior extent. The caudal part of the pretectal terminal region extends below the rostral pole of the superficial gray stratum (SGS) of the superior colliculus.

In a dorsal view, the rostromedial edge of the OT courses caudomedially over the dorsal thalamus to the pretectal area, where it turns so as to be oriented

in a more directly anteroposterior direction.

As the fibers of the optic tract reach the SC, the axons form a distinct layer, the stratum opticum (SO) or the optic fiber layer. These fibers, many of which had thus far maintained a superficial position with respect to the brain-stem, now course below the superficial gray layer (SGS) and as they arrive at their areas of termination, turn dorsally and synapse on cells and dendrites in the SGS, confirmed by electron-microscopic studies in the rat (Lund, 1969). A few silver spherules which may be indicative of terminal boutons and preterminal axons are observed in the stratum opticum and the dorsal part of the intermediate gray layer. But the densest fields of terminal degeneration are seen in the SGS only.

Ipsilaterally, the projection of the retina to the pretectum and the superior colliculus is sparse. In the latter structure, scant degeneration is seen in the SO and deep SGS, and occurs only in the rostral part of the SC.

The primary retinal projections in the Syrian hamster: accessory optic tract

In addition to the main OT, the hamster has a well-defined accessory optic tract (AOT) which has been indicated very clearly on the lateral view reconstruction drawing in Figure 5. The AOT consists of superior, middle and inferior fasciculi, and three nuclei referred to as the dorsal terminal nucleus (DTN) lateral terminal nucleus (LTN) and medial terminal nucleus (MTN) according to the nomenclature introduced by Hayhow et al. in 1960.

The inferior fasciculus of the accessory optic tract (IF-AOT) branches off from the main OT at the base of the peduncle, and maintains a position along the ventral edge of the peduncle. It is a very sparse but usually identifiable bundle which can be traced below the edge of the peduncle to the level of the mammillary bodies. Here, at the ventromedial corner of the cerebral peduncle, is

24

situated the MTN. The IF-AOT fibers enter this nucleus and presumably synapse on cells within the MTN. However, the greater innervation of the nucleus appears to be via the superior fasciculus, described next.

The superior fasciculus of the accessory optic tract (SF-AOT) branches off from the posterior edge of the OT at the border between pretectal area and dorsal thalamus, and the fibers pass ventrally and caudally over the DTN and then over the LTN, where they continue ventrally into the classical transpeduncular tract.

In addition to the IF and SF, we also observe sparse fibers passing in an anteroposterior direction, situated slightly deep to the surface of the brainstem between the ventral margin of the medial geniculate body and the dorsal edge of the cerebral peduncle. These fibers course caudally and merge with the axons of the SF in the region of the LTN, and will be referred to as the middle fasciculus (MF-AOT).

The hamster's SF-AOT corresponds with only the most posterior portion of the SF described for the rat by Hayhow et al. (1960). The MF seems to correspond in locus to the LTN of these authors. It seems that they took these axons of passage to be terminating. Use of the Fink-Heimer method on rat material shows the LTN to have a locus similar to that found in the hamster (Schneider, unpublished data).

Results derived from small retinal lesions: control series.

Since we have not yet completed the histology on the retinae, we rely on the degeneration patterns in the lateral geniculate body for comparing experimental and control cases. Hence, we have to assume that the retinal projection to the LGd remains unaltered in topography and extent following partial lesions of the tectum at birth. Several observations validate this assumption: (1) Even though we do not know the full extent of the lesion in the retina, we do have measures on the point of entry of the electrode with respect to the rectus muscles and

the limbus. From this information, we can state that the area of degeneration

in the LGd of experimental cases follows the schema of the topographical map

derived from the controls; thus, variations, if any, must necessarily be minor.

(2) When mapping the brainstem of an experimental animal on the standard

reconstruction drawing, the shape, size and position of the LGd shows only minor

changes in outline. Therefore, there seem to be no drastic changes in gross size

or shape of the nucleus. (On the other hand, the reconstruction method is

sensitive to changes resulting from a transneuronal atrohpy in LGd and in SC of

the adult animal following an eye enucleation on the day of birth.) (3) Following

a unilateral removal of the whole tectum on the day of birth, the degeneration in

the LGd resulting from bilateral eye enucleation in the adult is similar in

extent and density on the two sides (Schneider, 1970, 1973), and no obvious

cytoarchitectural abnormalities are noticeable.

Fig. 6 is a schematic representation of a hamster's eyeball which has

been dissected free from the orbit, having retained the attachments of the

rectus and oblique muscles. The muscles are extended to show better their

attachment to the surface of the eyeball. Normally the muscles lie on the

surface of the eyeball so this representation distorts their relative positions

somewhat. For example, with the eye in the orbit, one finds the medial rectus

and superior oblique muscles placed fairly close to each other. Another

point to be noted is that the circumference of the eyeball shown in the figure

is not the "equator" of the eyeball but is a circle representing the locus

of points 3.5mm from the limbus (the equator being at 1.1mm); points beyond

the true equator would not actually be seen in a front view of the eye.

From the sketch, it is evident that the superior and the inferior rectus
muscles attach diametrically opposite to each other, and likewise the medial
and lateral rectus muscles. (This is different from Lashley's (1932) report

26

for the rat wherein the medial and lateral rectus muscles have their point of attachments in a line slightly above the horizontal meridian of the eyeball.)

The oblique muscles are very prominent. The inferior oblique originates medially in the orbit and passes laterally over the inferior rectus and attaches behind the lateral rectus, thus forming a 'cradle' for the eyeball. The superior oblique muscle has an attachment behind the superior rectus and can be followed medially, where it hooks around a cartilage bridge in the medial wall of the orbit, then posteriorly to its point of attachment near the optic nerve head.

A study of one hooded rat and one hooded rabit revealed extrinsic eye muscle attachments very similar to those we consistently observed in the hamster. Lashley's (1932) picture of the oblique muscles could not be confirmed.

Indicated on the figure are the points of entry of the electrode used to make distrete retinal lesions. These represent the cases used as controls to determine the normal topography of the retinal projections. A representative case is HED-11 where one lesion was made at the lower edge of the lateral rectus of the left eye, and another lesion was at the upper edge of the medial rectus of the right eye. The axonal and terminal degeneration from these lesions was reconstructed on the standard lateral and dorsal view drawings (Figs. 7 and 8). The right and left sides were each reconstructed on a drawing of the lateral view of the right side of the brainstem to facilitate comparisons. Charts of transverse sections indicating degeneration in the LGd and LGv are shown in Figure 9. It is evident from the drawings that a small lesion in the retina will give rise to degeneration along the course of the optic tract, but restricted to particular portions of the tract according to a certain topographic organization. The lesion in the nasal retina of the right eye (at the upper edge of the medial rectus) causes degenerating fibers in the OT that, for the most part, course deep in the tract, not reaching the surface except along the ventral edge (Fig. 7, right side of brain). On the left side, the degeneration in the tract is also somewhat restricted. However, it must be remembered that these degenerating axons also

27

include the ipsilateral fibers from the left temporal retina. As the tract proceeds dorsally towards the lateral geniculate nuclei (LGN), more and more fibers come to the surface until one sees the densest accumulation of degenerating OT fibers coursing over the caudal half of the LGN. This is the region where the optic tract fibers originating from the above retinal lesions, enter the LGd and LGv, with terminal degeneration beginning immediatley subjacent to the tract. In Figures 7 and 8, (and in all similar figures following), the terminal degeneration that reaches the OT surface of the LGv or LGd is distinguished from the degeneration that does not reach the surface (indicated by solid bars and open bars, respectively).

The lateral view drawings illustrate that a discrete lesion in the retina results in a localized region of degeneration in each division of the LGB. Fibers originating in the nasal retina terminate first along the course of the OT, i.e., along the ventral border of both the LGd and LGv; whereas fibers from the temporal retina enter the nuclei at the opposite side (dorsally). Terminal degenerating axons, coursing through a region of surface termination, continue into the depth of the cell group, forming a column that is angled, in most cases, rostrally and mediodorsally. This column is very long for degenerating fibers that enter the LGd at the caudal end, but is minimal for fibers entering the LGd at the anterodorsal tip of the nucleus. The caudal end of each column forms a patch of surface degeneration, with one edge of the patch always reaching a peripheral border of each nucleus.

A special note regarding the degeneration in LGv must be made at this point. The region of the nucleus that is adjacent to the optic tract is the external sublamina of the LGve. Hence, degeneration in the LGv is considered to be "reaching the OT surface" when the terminals are seen in LGvee.

The distinction between LGvee and LGvei in difficult to make at rostral

levels of the nucleus. It appears that the narrow, rostral extension of the

nucleus is all degeneration in LGvei (Schneider, Jhaveri, Frost, unpublished).

In this case, the long strips of "surface" degeneration show for lesions HED-25

and HED-28, in the composite drawing (see below, Fig. 10), may merely be rostral

"columns" of degeneration that enter the nucleus further caudally.

The reconstruction of the <u>left</u> side of the brainstem in Figure 7, shows

an extra dorsal patch of deep-lying terminal degeneration in the LGd, for which

there is no corresponding surface degeneration. This represents the ipsilateral

projection from the lesion in the temporal retina of the <u>left</u> eye. It should

be noted that, though the ipsilateral terminal degeneration never reaches the

surface, a comparison of the LGd on the ipsilateral and contralateral sides

in such cases shows that axons from the same areas of the retina enter the

ipsilateral geniculate along the same paths as they do on the contralateral

side. Thus, areas of contralateral and ipsilateral terminal degeneration appear

to occupy the more superficial and more deep portions, respectively, of the

same "column" through the LGd although there may be some overlap. A similar

picture can be discerned in the LGv.

Further along the course of the optic tract, terminal and preterminal

degeneration is seen in the pretectal region. Although the degeneration resulting

from a small lesion in the retina is restricted in this region and has some

topographical organization, the sampling of the sections (usually one in every

five) and the survival time (5 days) are not adequate for a complete analysis

of this area. On the charts, I have indicated whatever degeneration is

obviously seen in the slides, and I have also differentiated between degeneration

close to or within the optic tract, and degeneration deeper in the nucleus (by using

solid bars and open bars, respectively). Nonetheless, this should not be considered a complete picture.

The course of the axons over the surface of the brainstem from the LGB to the tectum is seen very clearly in the dorsal view (Fig. 8). The degenerating axons maintain a constant position relative to the two edges of the optic tract over the geniculate nuclei and the pretectum. Upon entering the tectum, those on the right side of the brain (lesion in left temporal retina), terminate rostrally, whereas the axons on the left side of the brain (lesion in right nasal retina) continue caudally in the stratum opticum and only in the posterior part of the superior colliculus are they seen to turn dorsally and terminate in the superficial gray layer. The edges of the terminal degeneration is the superficial gray are sharply defined.

Sparse fibers are seen branching off from the optic tract as it passes over the medial geniculate body. On the left side, degeneration is visible in the DTN. (Our results from all the control HED cases show a projection to DTN from the upper and upper-nasal retina. No dense terminal degeneration in the DTN is seen after lesions made in the lower retina. However, axons from this part of the retina do pass through DTN into the SF-AOT and sparse termination in this nucleus cannot be ruled out with the methods we use.) The degenerating fibers proceed along the superior fasciculus of the accessory optic tract (Fig. 7). Terminal degeneration in the LTN is extremely difficult to discern using a series spaced at every 160-170u (corrected for shrinkage), since this nucleus is very small in anteroposterior extent (see Fig. 5). In the sections where degeneration can be seen in the LTN, it has been indicated on the corresponding drawings. However, like the pretectal region, our analysis of this region is incomplete, and will require the staining of more sections. The same is true for

the SF-AOT, and especially the transpeduncular tract. In the MTN, we see sparse fibers from lesions in all parts of the retina. Nevertheless, as is eivdent from comparing the left and right side lateral views for HED-11, the projection from the temporal retina is much heavier, especially ventrally. We do have sampling problems here as for the other nuclei of the AOT. In a few cases, degeneration was seen in MF-AOT and in almost no case was it very clear that the fibers of the IF-AOT were degenerating. This could imply either that the fibers in these two fasciculi arise from more central retinal cells, or that there is a very sparse representation from the whole retina in these fasciculi, and that our technique is not sensitive enough to pick up such sparse degeneration from a small retinal lesion.

Altogether, we have 30 cases of small retinal lesions in otherwise normal adult hamsters. At least one series of sections (every fifth, cut at 30μm) has been stained for each case, and summary surveys have been made. Thirteen cases including degeneration from 16 lesions) have been analysed and reconstructed in dorsal and lateral views as for HED-11. These 13 are indicated as black dots in Figure 6. They cover all four quadrants of the retina. A composite picture of these cases is shown in Figure 10. In this diagram, we have included degeneration of the LGd, LGv, and SC. Only those areas have been represented, where the degeneration reaches the inner surface of the optic tract in the LGN and where it extends throughout the depth of the SGS in the tectum.

From the composite diagrams, it can be concluded that the whole retinal periphery is represented along the peripheries of the LGd, LGv and SC. The reconstructions of the areas of surface degeneration in each of the three nuclei show that these areas form "tongues" or "wedges". It is evident from this that the retinal lesion not only destroys the region of the retina at the point of

31

entry of the electrode tip, but also damages fibers from cells included in a 'wedge' extending outwards towards the periphery from the site of the lesion, since these fibers traverse the retina radially to reach the optic disc. It can be inferred, then, that the wedges of degeneration in the SC, LGd, and LGv have their apices pointing to a region which is a representation of the optic disc of the retina. This region is indicated in the composite diagrams by a circled star.

<u>Results from cases with lesions of the rostral tectum at birth.</u>

A total of 22 hamster pups from 8 different litters suffered lesions of
the rostral and rostrolateral tectum on the day of birth. The lesions were
made using a metal pin heated in an alcohol flame and applied directly onto the
interparietal "bone" (see General Methods section) over the rostral tectum.
Lesions of various sizes were attempted. Some of the initial lesions were very
large, and in three animals it was noted in histology that almost all of the
superficial gray of the superior colliculus had been destroyed. In three other
cases, the retinal lesions in the adult were not adequate, and two cases were
used for behavioral testing. These eight cases have been omitted in this analysis.
From the remaining cases, after summary surveys were made, five cases were chosen
for complete reconstruction; these were selected for adequacy of both the
neonatal tectum lesion and adult retinal lesion. It is these five cases I will
discuss fully in this section. Comparisons between these five experimental
cases and the corresponding control cases will be made.

<u>Case 47-3</u>

  <u>Neonatal lesion</u>: bilateral rostral tectum lesion, day of birth.

  <u>Retinal lesions in adult</u>: bilateral lesion of nasal retina (lower

  edge of medial rectus).

  <u>Survival time</u>: 5 days (following retinal lesions)

  <u>Histology</u>: Fink-Heimer (2 series), Silver Pyridine (1 series).

Figure 11 shows the reconstruction of the brain of case 47-3 in dorsal
view, and of the lateral geniculate bodies in lateral view, with the degeneration
mapped onto the drawings. In this case, there was some damage to the edge of the
tissue during histology, so the optic tracts have not been fully charted in the
dorsal view and have been omitted from the lateral view. The dorsal view shows
that the lesion of the tectum was quite extensive, especially on the right. The

reconstruction of the degeneration in the LGd and LGv illustrates the fact that both retinal lesions were placed quite far centrally; the surface degeneration reaches the optic disc representation in both the left and right LGd (see Fig. 12).

For the right side, the surface degeneration in the LGd overlaps that seen in control case HED-11 (L), and partially with HED-19 and 23, but extends further towards the disc than any of these three control lesions (see Figs. 10, 12). In Figure 12b, I have overlaid the tectal degeneration in the three control cases, and using the LGd comparisons (Fig. 12a), have estimated an area in the SC that would in the normal, result from the same retinal lesion as in 47-3 (left eye).

Figure 12c is an overlay of a normal right tectum, including the estimated area of degeneration to be used as the control for the experimental case, and the recontructed tectum of 47-3. It is obvious that the degeneration in case 47-3 falls short of the central extent of the 'wedge' of the control lesion. In fact, if overlaid with the tectum recontruction of case HED-11, one finds that the SC degeneration in 47-3 barely reaches the central extent of this control case, even though the retinal lesion in HED-11 is the more peripheral one. In either case, it is clear that the area of degeneration in the experimental SC is much reduced relative to the area of surface degeneration in the LGd.

An important factor that must be taken into account while discussing this case (and other similar cases) involves the position of the tectum remaining after the early lesion. From the reconstruction in Figure 11, it seems as if part of the caudal tectum is missing, too. This could be due either to (a) a "shrivelling" of the caudal fringe of the SC, or (b) a mechanical forward movement of the remnant tectum — a 'flopping' into part of the space vacated by the lesioned tectum. If the first (a) is true, then the reduction in the area of degeneration in the SC may

34

merely represent a "normal" map in a superior colliculus with its edges missing, resulting in a corresponding lack of representation in the map of the periphery of the retina. There is, however, a suggestion of a compression of the remaining map even in this case.

If the second (b) is true, then in order to compare the experimental animal and its normal control, the SGS must be repositioned so as to allow the caudal unlesioned edge of the experimental to match with the caudal edge of the normal. This is shown in Figure 12b. If we now compare the areas of degeneration relative to the SGS tissue in each tectum, it is evident that for case 47-3, the retinal representation in the SGS has been "compressed" or reduced to a degree roughly proportional to the reduction in the area of the SGS. From other cases that will be presented, the justification for this repositioning of the tectum will be validated. Although the first possibility (a) cannot be totally ruled out, the data assembled imply that it is quite unlikely or that its effect is minimal.

Another point that needs mention here is the mediolateral location of the degeneration. If the compression of the map is exactly proportional to the reduction in either area or volume of SGS tissue, then one would not expect the degeneration in 47-3 to be so close to the lateral margin of the SGS (cf. estimated control in Fig. 12). However, there is evidence that all of the retinal map may not be represented in the remaining SGS. The surface of the brainstem lateral to the SGS shows evidence of retinal projections from the remaining retina (see note below) and it is likely that the "tectal terminal space" used by fibers from the retina does not exclude deep tectal tissue in the area of the lesion. (See also Schneider, 1970, 1973) (Also, see below, case 47-2)

Note: In the hamster, with the use of the Fink-Heimer stain, the tectal neuropil probably recieving retinal projections, but located in areas where the OT is not degenerating, often stains with a characteristic reddish hue that can be clearly differentiated from the rest of the tissue. This has been noted in case after case of bilateral tectal lesions and unilateral retinal lesions with one side of the brain used as a control (Schneider, personal communication). This phenomenon yielded evidence in support of the above suggestion that some of the retinal projections go to tissue below the optic fibers in areas of destruction of the superficial gray layer.

Considering the left side of case 47-3, the dorsal view illustrated that the neonatal lesion did not destroy as much of the tectum on this side as on the right . The reconstruction of the degeneration region on the lateral view indicates that on this side, too, the retinal lesion in the adult animal extended very close to the optic nerve head.

The surface degeneration in the LGd of 47-3 (left side) can be compared with that in controls HED-11 (L), HED-19 (only partially), and HED-23 (Fig. 13a), and the "estimated control" can be drawn for the tectum (Fig. 13b). From the overlay of the patterns of degeneration in the LGd, it can be inferred that the retinal lesion in the experimental animal extends closer to the optic disc than the lesions in any of the cotrols. Making a similar overlay for the tectum, it is obvious that the central extent of the wedge of degeneration falls very far short of the normal disc representation, and, in fact, falls short of the most eentral extent of degeneration patches in the tecti of each of three control cases that show more peripheral retinal lesions. In addition, since there is no obvious shift in position of the SGS (the caudal edge of the SGS on the left side in the experimental brain matches well with the caudal edge of a normal animal), the argument for a compression of the retinal map, proportional to the reduction in SGS area, is very strong. (Nonetheless, the possibility that the extreme nasal retinal periphery is not represented at all in this tectum, being "pushed out" by the remainder of the retinal axons, cannot be ruled out from this data alone).

An intriguing aspect of this brain concerns the terminal degeneration seen in the rostral part of the left SGS. If the projection of the rest of the retina can be assumed to conform in an orderly fashion to a compression, this patch of termination of nasal retinal fibers in the rostral tectum forms an anomalous discontinuity. The terminals are seen only in the superficial parts of the SGS, so they are apparently "sharing" that region of the SGS with axons from other regions in the retina (Fig. 14). The optic fiber layer in the rostral part of the SC has a very abnormal appearance with axons arranged in a double-tier fashion. Some axons are also seen on the surface of the SGS. These anomalies apparently occur as a result of the heat application. Possible factors affecting this kind of anomaly will be discussed.

Although most of the AOT has been omitted in the charts, except for some axons in the dorsal view, I have indicated by arrows in Figure 11, the slides on which terminal degeneration in LTN is observed. The degeneration is very obvious in this nucleus, which shows some suggestion of a hypertrophy; but I have not done any quantitative measures with regard to this observation. Schneider (1970,1973) has not reported any hypertrophy of the LTN following bilateral or unilateral removals of the SC in the neonate hamster.

Case 47-2

> Neonatal lesion: bilateral rostral tectum, day of birth.
>
> Retinal lesions in adult: bilateral temporal retina (upper edge of lateral rectus).
>
> Survival time: 5 days (following retinal lesions).
>
> Histology: Fink-Heimer (2 series). Silver Pyridine (1 series).

Dorsal and lateral-view drawings of this case (Figs. 15, 16) demonstrate that the neonatal lesion of the tectum destroyed much of the superficial gray stratum (SGS) symmetrically on both sides. Consider first the right side of the brain. Control case HED-22, whose brainstem reconstructions are shown in Figure 17, suffered a nearly identical lesion in the temporal retina (at the upper edge of the lateral rectus); comparing the lateral-view reconstructions of the LGd and LGv in the two cases (Fig. 18a), we see that the areas of surface degeneration are almost exactly the same, except that the degeneration in HED-22 extends slightly more caudally in LGd and LGv. When the tectal reconstructions are over-laid, the picture is as seen in Figure 18b. The degeneration in the SGS of 47-2 is located totally outside the area covered by the degeneration in HED-22 and is reduced in area when compared to the latter. The only portion of the tectal degeneration from 47-2 that does overlap with that from HED-22 is that found outside the SGS, in deep tectal layers, subjacent to the optic fiber layer that courses over the surface of the damaged tectum. (Part of this degeneration may be in the pretectal area and cannot be differentiated in this case from degeneration in the deep tectal layers because of the early damage to the rostral tectum.) Inspection of the figures shows that the termination in the SGS is reduced in its areal extent; the reduction is roughly proportional to the decrease in size of the SGS and is displaced medially in conformity to the smaller medial-lateral extent of the SGS.

We can go through the same arguments as for 47-3 concerning the gross mismatch between the supposedly undamaged caudal border of the SGS in 47-2, and the caudal border of the SGS in the control animal. If it is true that the SGS has "flopped" forward - and this is indicated in Figure 15 by an anterior

38

shift of the inferior colliculi --- then a valid comparison between the control

and the experimental tectum would involve a caudal translation of the SGS in

47-2. When this is done (see Fig. 18c), the shift in the terminal projection

region in the SGS of 47-2 as compared to that in HED-22 is even more dramatic -

in fact, in this event, the terminals extend up to or beyond the area where

the optic disc would normally be represented. Let us now consider the

damaged brain as having a miniature but whole tectum and re-define an optic

disc representation for the SGS. The relative ratio of termination area to

SGS area is nearly the same for 47-2 and HED-22; so also, the relative distance

of the central extent of the degeneration from the disc representation. This

implies that the whole retinal map may be compressed into the remaining SGS in

an orderly fashion. The slightly reduced area of surface degeneration in the

experimental case may well be due to termination of the fibers from the most

peripheral retina near the surface of the area where the SGS was ablated.

The last point is supported by the results of the lesion on the

left side. Here, the retinal lesion is more peripheral than that producing

degeneration on the right (Fig. 19), although the tectum lesion is very

similar. The terminals in the tectum occupy deep tissue up to the border

of the remaining SGS and are continuous with whatever pretectal degeneration

may exist.

Note: It is also conceivable that in cases of lesions of the rostral
tectum, the pretectum hypertrophies and much of the "deep" termination seen
in the anterior half of the tectum on both sides is in an abnormal pretectal
region and should not be included with the tectal degeneration pattern.
However, this seems unlikely because of the difference in survival times for
the optimal staining of terminals in the pretectum and the tectum. In the
normal animal, the pretectal nucleus shows dense terminal degeneration only
with a survival time of 22 hours to 2 days, whereas by 5 days, most of the
terminals in this nucleus have disappeared (see Schneider, 1968). Thus if we
are dealing with a hypertrophied region of retinopretectal termination, its
afferents are degenerating like tectal afferents.

Although the retinal lesion causing degeneration on the left side in 47-2 was more peripheral than that found in HED-22, the terminals in the SC extend further centrally. We should point out that the degeneration in the deep tectum (see chart, Fig. 20) (1) is very patchy, although dense within the patches; (2) does not include much tissue volume since the patches are small and "shallow" conpared to the thickness of the SGS in the normal (see Schneider, 1970, Fig. 1; 1973, Fig. 14); and (3) includes the pretectal degeneration which has not been segregated on the charts. Thus, although quantitative measures have not been made, from the above considerations it is clear that "deep" degeneration in the anterior tectum does not occupy nearly as much tissue volume as does the terminal degeneration in HED-22 even though the former extends further centrally.

Taking both sides of 47-2 together then, it may be inferred that most axons from the temporal retina terminate with a compressed topography in the rostral part of whatever remains of the SGS, and that the "tectal terminal space" as defined for these axons includes not only the SGS: the more peripheral regions of the retina tend to use other "abnormal" tissue as tectum. In addition, we should note that there is also a small projection to the LP on both sides (cf. Schneider and Nauta, 1969; Schneider, 1970, 1972); hence it is conceivable that this thalamic tissue may be used as part of the "tectal terminal space" too.

Further Considerations for the Interpretation of Cases with Early Rostral

Tectum Lesions

There are several possibilities that must be considered regarding the topography of the retinal projection to the superior colliculus remaining

after a rostral tectum lesion in the neonate. I will go through these possibilities, as I see them, using the data I have presented for cases 47-2 and 47-3, and next will present three other rostral-lesion cases to validate conclusions derived from the analysis of these two cases.

The possible alterations in retinal topography may be listed as follows, assuming, except where noted otherwise, that adjacent parts of the retina project to adjacent parts of the "tectal terminal space," Evidence for violations of this assumption will be discussed later.

1(a). No change in topography, but the projection to the rostral (lesioned) part of the tectum is missing (Fig. 21, box 1a). This would imply that there is no representation of the temporal retina in the tectum, but that the rest of the retina occupies its normal projection field in the remaining SGS.

This cannot be what actually occurs in case 47-2. Here we have a lesion of the temporal retina which, from the control case, we know would normally cause degeneration restricted totally within the area of ablated SGS (Fig. 18). Nevertheless, we do find a representation of this part of the temporal retina in the remnant SGS.

1(b) No change in topography, except that the retinal efferents that would have terminated in the lesioned rostral colliculus are not represented in the SGS but find anomalous projection fields elsewhere (Fig. 21, box 1b), as in deep SC layers, a hypertrophied DTN, or in the thalamic nucleus LP (see Schneider, 1970, 1973). This cannot be entirely true for the two cases presented. Since the projection field of the temporal retina shows a caudalward shift in location to occupy part of the remaining SGS, we can assume that there must be some change in the topogrphy of the retinal efferents

41

to the caudal tectum. Also, case 47-3 may be interpreted as indicating a compression in the projection of the nasal retina also. However, the peripheral part of the temporal retina apparently does find some representation outside the SGS as has been illustrated for case 47-2 (left side).

2(a) No change in topography except that, in addition to the damage inflicted on the rostral tectum, the edges of the SGS have "shrivelled" and correspondingly, there is a missing projection from the periphery of the whole retina, not only from the temporal retina.

At first glance, this effect would lead to anaotmical results very similar to those produced by a compression phenomenon. Figure 21 (box 2a) illustrates a "shrivelling" of the tectal periphery, and the resulting changes in degeneration areas produced by a temporal and a nasal retina leison, assuming a fixed retinotectal map. The test for such a possibility, in the cases presented, is to match the central tongue of the control-case degeneration with the area of degeneration found in the experimental case, and observe what parts of the SGS would have to be missing for such an interpretation to be valid. This test is illustrated in Figure 22. For the right side of 47-3, we find that a shrivelling of the caudal tectum would be necessary, in addition to a very large rostrolateral ablation; however, the tongue of degeneration is narrower than expected in the mediolateral direction.

For the left side of 47-3, we find that the early tectal ablation would have had to be more extensive caudally than rostrally, a very unlikely possibility; again, the tongue of regeneration is narrower than that in the estimated control. The same remarks hold true if this test is applied to the right side of case 47-2. The point about the lesion is also true for the left side if the tongue of the control lesion is lined up with the caudal-most

42

extent of the degeneration below the optic fibers; in this case, the medio-lateral extent of the "tongue" is difficult to define. Thus, we can conclude that the hypothesis of a fixed retinotectal map on a shrivelled tectum would be supported only in case of highly improbable early lesion effects, and even so, some compression in the mediolateral axis would have to be suggested.

Further information about tectal displacement can be derived from the reconstructions of various experimental cases. An examination of the inferior colliculus in 47-2 indicates that it has moved forward roughly the same distance as the anterior shift in the caudal edge of the SGS. This case, and others with removal of the whole tectum (Schneider, 1973) show that the inferior colliculs does relocate its gross position to partially fill in the space vacated by the missing tectum. Therefore, it is likely that the SGS, too, has merely translocated forward into part of the region that had been occupied by the rostral tectum before it was lesioned. Nonetheless, we cannot completely exclude the contingency that the caudal tectum may be slightly atrophied due to a spread of the heat, or due to vascular damage.

2(b). As in 2(a), with the addition that the missing projection is found outside the SGS (in deep tectal layers, DTN, LP)(see Fig. 21, box 2b). The arguments presented against hypothesis 2(a) apply to this hypothesis also. The possibility that the anomalous projections in deep colliculus or in LP may include nasal retinal axons cannot be ruled out.

3(a_t). Formation of a displaced map, such that the temporal retinal fibers take over the remaining caudal SGS, and fibers from the nasal retina have no projection to the tectum(Fig. 21, box 3a). An analysis of case 47-3 indicates that this cannot be wholly true since there _is_ a representation from

the nasal retina to the caudal SGS. Nevertheless, there is one experiment

that has yet to be done and one possibility to be ruled out. This contingency is

illustrated in Figure 21, box 3 (a_2), and concerns the possible occurence of an

uneven compression, i.e., the fibers from the temporal retina compress into

part of the remaining SGS and force the nasal retinal fibers to relocate. However,

the latter fibers do not in their turn compress, but merely get pushed caudally

so that that more central fibers still maintain the normal size of their

projection fields, and crowd out the more peripheral fibers from the same

retinal segment. This can be tested by making lesions in the periphery of the

nasal retina. However, our cases of peripheral lesions in animals with early

rostral tectal lesions were inadequate and hence it has not been possible to

resolve this issue. (Note that without a finer analysis with small retinal

lesions, the results in this case are exactly similar to those obtained with

an even, orderly compression.)

3(b)   As in 3(a) except that the fibers from the nasal retina project to

tissue other than the SGS. Since this hypothesis predicts no compression, it

is incompatible with the data so far presented. Nevertheless, as mentioned

before, it remains possible that part of the nasal periphery does find a

representation outside the SGS.

4.   Compression of the whole retinal map into the available "terminal

space" for the retinofugal axons in the tectum, which includes the remaining

SGS along with some tissue below the optic fiber layer (Fig. 21, box 4). This

hypothesis is supported by much of our data. Later cases indicate that the

DTN (which hypertrophies after early tectal lesions- see Schneider, 1973),

may also serve as part of the tectal terminal space. The LP is also often a

recipient of anomalous retinofugal axons after neonatal lesions of the optic

44

tectum, but from our data we cannot conclude whether this projection is a small displaced part of the retinotectal map or a totally separated projection.

When the terminal space is below a certain critical size, it is conceivable that only part of the map compresses into this space in the tectum, whereas other parts of the retina are not represented in the colliculus at all.

Schneider (1970) has reported data on cases of hamsters with early bilateral tectum lesions in which the SGS was totally ablated. The retinotectal projection was now observed in the deep layers of the colliculus but there was no termination in the medial third of the ablated tissue. Behavioral evidence indicated that the upper visual field was not represented in the tectum. These cases do indicate, however, that most of the nasotemporal axis can be represented in a midbrain which contains no superficial gray layer.

Additional Cases with Lesions of the Rostral Tectum

Case 45-2:

Neonatal lesions: bilateral rostral tectum, day of birth

Retinal lesions in adult: right eye, nasal retina (lower edge of medial rectus); left eye, temporal retina (upper edge of lateral rectus)

Histology: Fink-Heimer (2 series), Silver Pyridine (1 series).

The reconstructions of the brainstem for 45-2 are shown in Figures 23, 24. Let us consider the left side first. The sketches in Figure 25(a) show the surface degeneration in the LGd and LGv of 45-2 (stipple) along with an overlay of the surface degeneration seen in these nuclei for the relevant control cases HED-11, HED-23, HED-19. From comparisons between the degeneration in the geniculate bodies of the experimental and normal brains, I have estimated a tectal control for 45-2(1), as shown in Figure 25(b). The dorsal views for the

tectal degeneration patterns in 45-2 (left) and its estimated control have been overlaid in Figure 25(c) and (d), without and with matching the caudal (unlesioned) border of 45-2 with the normal. The reduction in the area of degeneration in the SGS of 45-2 is clearly discernable, and there is a suggestion that this reduction is approximately proportional to the decrease in the size of the SGS. An isolated patch of terminals is also seen along the rostrolateral border of the SGS; associated with this patch is a bundle of axons that seems to have been "deflected" from the main mass of degeneraing fibers. However, it is curious that the axons in this bundle do not all terminate in the isolated patch but some continue to course caudally and caudomedially towards the larger patch of degeneration. The abnormal orientation of the "deviant" fibers is indicated in the dorsal view drawing. Note that the degeneration in the pretectum in this case can be readily differentiated from the tectal terminals. In addition, terminal degeneration in the LTN can be discerned, and a few degenerating axons are found in the SF-AOT and in MTN. The degeneration in the latter nucleus indicates a few terminal projections.

A similar analysis of the degeneration patterns on the right side (see Fig. 26) gives some suggestion of compression. A matching of the caudal borders of the SGS in the experimental and estimated control reconstruction indicates a displacement in the projection of the temporal retina (see Fig. 25(d)). However, the evidence for a slight rostralward "flopping" of the undamaged SGS is not strong in this case, since the mismatch may be within the range of variation we have observed among normal animals. In this case (as in 47-2) it is difficulut to differentiate between deep tectal degeneration and terminals in the pretectum. Both have been indicated in the

46

dorsal view drawing. For case 45-2(right), as on the left side and as in cases
47-2 and 47-3, degeneration in the LTN is prominent, but our sampling of
sections through this nucleus is inadequate, so quantitative statements
regarding a possible hypertrophy cannot yet be made.

A striking anomaly is obvious in the degeneration pattern in the rostral
SGS. The borders of the degeneration area are not smooth, and abnormal lamination
patterns are seen in the SGS termination. A chart of the degeneration as
seen in transverse section is shown in Figure 27. There are several "blank"
regions in the midst of dense terminals in the SGS. This pattern is not caused
by 'stray' vascular damage in the retina since the pattern is not reflected in
the degeneration produced in LGd and LGv. The anomaly directs attention to
the occurence of isolated patches of degeneration as seen on the left side
in this case, in case 47-3 on both side, and in several other rostral tectum
lesion cases; it is suggested that the "blank slots" seen in the rostral tectum
of 45-2 (right side) are sites occupied by the discontinuous patches of
termination of axons from the temporal retina.

A second observation worth commenting upon is the existence of a discrete
patch of SGS that was apparently spared from the ablation. Although separated
from the main mass of the SGS, it is completely filled with termianl degeneration.

If we consider all the possibilities listed in the previous section
(see also Fig. 25(e) and Fig. 26(e)) it is clear that a compression phenomenon
is most compatible with our data.

Case 43-2

    Neonatal lesions: right rostral tectum, right eye enucleation (day of birth).

    Retinal lesion in adult: left temporal retina (lower edge of lateral rectus)

    Histology: Fink-Heimer (1 series), Silver Pyridine (1 series)

In the case, and likewise in the next case, the right eye was removed at birth in addition to the rostral tectum lesion. This was done in order to test whether axons from the temporal retina, if deprived of their normal region of termination, would preferentially cross into an adjacent, dennervated tectum, or whether they would rather compress into the remaining SGS.

The results from case 43-2 (Figs. 28, 29) show that, in spite of the dennervated ipsilateral tectum, the axons from the temporal retina compress into the SGS contralateral to the retinal lesion: the tongue of degeneration extends beyond the normal disc representation. This is supported by inspection of the lateral-view reconstruction, in which it can be seen that forshortening effects of the SC surface area along the rostro-caudal axis that result from the reconstruction cannot account for this result. If we consider the remnant SGS to be a mineature but whole tectum and redefine an optic disc representation for this small tectum, there is a strong indication that the compression of the terminating axons representing the nasal field is proportional to the reduction in the size of the SGS. There is also heavy terminal degeneration seen in the tissue subjacent to the SGS. We cannot be certain whether the same part of the retina projects to both superficial and deep layers. A small patch of SGS escaped the early ablation and this area is included in the tectal terminal space.

This case is strongly supportive of the hypothesis of a compression of all or most of the representation of the visual field into the remaining terminal space in the tectum, according to the analysis described for previous cases. The data are particularly clear because there is no evidence of a gross displacement of the remnant tectum.

Case: 43-10

Neonatal lesions: right rostral tectum, right eye enucleation (day of birth).

Retinal lesions in adult: left temporal retina (upper edge of lateral

48

rectus)

Histology: Fink-Heimer (2 series), Silver Pyridine (1 series)

Dorsal and lateral view reconstructions for this case are shown in
Figure 30. The series of drawings in Figure 31 depicts an analysis similar
to that described for previous cases. Most of the degeneration found in
the tectum is in the area denuded of superficial gray. This result is
similar to that for case 47-2 (left side) except that there is an additional
and spatially segregated patch of terminal degeneration in the rostromedial
edge of the remnant tectum. Note that this patch lies far caudal to the
position predicted by a non-plastic retinotectal map. These results are
compatible with conclusions from previous cases. Unfortunately we cannot
be certain whether there is a projection from other parts of the retina
to the area between the two major patches of degeneration.

In this case, as in the previous one, there is no forward movement of
the undamaged SGS. The presence of the undamaged colliculus seems to
"anchor" the remnant SGS in place.

Lesions of caudal and medial superior colliculus at birth: a preliminary report.

Of the remaining animals included in the experimental group, 6 suffered
unilateral or bilateral lesions of the caudal tectum, 3 of the medial tectum,
and for the rest, combination lesions were made e.g. rostral tectum on left,
caudal tectum on right, or caudal tectum on one side, medial tectum on the
other. The analysis for these cases is not complete to date but they merit
mention because of certain anomalies seen in these cases which were not
noted for the animals with rostral tectum lesions.

49

Ablation of the caudal tectum gave results seemingly compatible

with the compression hypothesis but our control cases were not adequate to make

a definite statement with regard to this point. One observation of interest

was that two animals with small lesions of the caudal SC at birth, showed

fibers from the nasal retina projecting partly to the caudal superficial

gray layer of the remanant colliculus, and partly to tissue subjacent to

the optic fibers. The nasal retina, thus, has a "normal" representation

in the superficial layers and an anomalous termination in the deeper

layer. However, we cannot with our data, determine whether this implies a

duplication of the "normal" map in subjacent layers or if different segments

of the nasal retina have separate projections to the superficial and deep laminae.

Electrophysiological studies would probably provide a better assay for

investigating the details of this topography. In one further case, with a much

larger caudal lesion, terminal degeneration from a nasal retinal lesion was

found only in tissue below the stratum opticum, at the caudal margin of the

remaining superficial gray layer.

In 2 other cases with the caudal colliculus ablated, the projection from

the nasal retina was discontinuous though restricted to the posterior part

of the remnant superficial gray layer: termination was seen throughout the

depth of the SGS in some patches, while in other areas, terminals were noted

only in the deeper part of the SGS leaving a "hole" in the superficial portion

of the lamina. From data presented earlier (see case 45-2) it seems likely

that the 'holes' are occupied by abnormal terminal patches from other parts

of the retina.

Bilateral lesions of the medial tectum also revealed some striking peculiarities in the pattern of retinofugal connections. Axons from the lower retina projected to the medial part of the remnant tectum. In the normal animal, this connection forms a continuous patch of terminal degeneration in the superficial gray layer which reaches the medial edge. Consequent to bilateral lesions of the medial tectum, the pattern of degeneration originating in the lower retina of the right eye was discontinuous, the areas of terminal degeneration alternating with "blank" regions. Some terminal regions did not reach the medial edge of the superficial gray. In addition, degenerating axons from the lower right retina were also observed to cross the tectal midline into the right (ipsilateral) SC, resulting in patches of degeneration on the medial side of this "wrong" superficial gray layer as well. Since both eyes were intact until the time of the adult lesion in this case, it is reasonable to assume that axons from the left eye also crossed the tectal midline into the left (ipsilateral) SC. These recrossing axons would then occupy the "blank" regions mentioned above, thus leading to an interlacing of axons from the two eyes across the tectal midline. Factors affecting the formation of these "criss-cross" connections between the retina and both tecta deserve further investigation and a more detailed analysis of these cases is under way.

Combination lesions also gave rise to a host of anomalous connections, with axons crossing over the tectal midline into the "wrong" colliculus, 'expanding' their terminal fields (especially if one colliculus was deafferented at birth) and forming abnormally layered patches of terminal projection.

51

General Discussion

Demonstration of plasticity effects in the immature brain can be interpreted from the standpoint of two somewhat distinct issues: (a) how the normal projections are formed in the first place, and (b) what are the factors that control the formation of the modified connections. The phenomena reported in the present study may be construed to reflect developmental mechanisms on the one hand, or regenerative effects on the other (in which the mechanisms may be similar). Current investigations on the newborn hamster by Frost and Schneider (unpublished data) indicate that at least some retinal axons are already present in the tectum on the day of birth. If this is the case, then a lesion of the rostral tectum in the neonate would transect all the retinal afferents that have reached the superior colliculus, and the compression effects observed could be interpreted as a consequence of regeneration of the sectioned optic axons. However, the development of regeneration of the sectioned optic axons. However, the development of the ganglion cells in the retina continues over a period of several days in the mouse and rat (Sidman, 1961; Morest, 1970). If this is also true for hamsters, it may be inferred that not all the optic-tract axons from a given retinal segment arrive at the tectum at the same time. In this event, a lesion of the anterior tectum would spare the late-arriving axons, and the topographical alterations in retinotectal connections could reflect a modulation of developing axon dynamics. For our studies, it is not entirely clear which of the two mechanisms (regeneration or initial frowth) is responsible for the results, or whether this dichotomy would even make a difference. But it _is_ evident that retinofugal axons compress into available tectal terminal space following an ablation of the rostral portion of the superficial tectal layers on the day of birth.

With a lesion of the caudal colliculus, we have a separate paradigm. The damage now affects the axons only in the caudal half of the tectum, leaving intact whatever retinal projections to the rostral half-tectum may exist at birth. A compression of the retinotectal map in this case implies that regenerating (or newly arriving) axons destined for the caudal tectum are now forcing a rearrangement of fibers terminating in the rostral superficial gray. Initial results on cases with caudal tectum lesions seem to suggest that this is true. However, our findings also indicate that abnormally dense projections are found, in such cases, in the deep tectal layers caudally, which may indicate a double map in part of the remnant tectal space, with much of the nasal retina represented subjacent to the optic fiber layer. Experiments in goldfish using a similar paradigm give controversial results. Sharma (1972a) reported a compression of the retinal map into remaining tectal tissue following caudal tectum lesions only when the contralateral optic nerve was sectioned in addition. Without section of the nerve, he found an overlapping representation of the retinal map, with the nasal retinal representation overlapping that from the temporal field in mirror-image fashion. Yoon (1971), on the other hand, has reported a compression of the map with or without an additional section of the contralateral optic nerve. Our findings indicate that in the mammal, some compression is seen without transecting all the optic tract axons, but that there may also be a considerable overlap in the projections of different parts of the retina. However, we do not consider our sample to be adequate for firm conclusions on this point.

In relation to the question of rearrangement of fibers already at their place of normal termination, it is essential that a study of the topography of retinofugal projections be conducted in the normal neonate hamster. This would

allow us to conclude to what degree the retinotectal topography has already

been determined at birth.

With regard to the factors involved in the formation or alteration

of neuronal connections in this system, we will assume here that

regenerating and developing axons are influenced by the same mechanisms.

That optic tract axons can indeed regenerate in the baby hamster is
supported by findings of Schneider (personal communication) in one case,
in which much of the superficial tectum was destroyed by aspiration when
the pup was 8 days old. At this age, the retinotectal projection seems
fully developed in a normal animal, when studied with the Fink-Heimer stain
(1-day survival after eye removal). When this animal was fully grown, a
study of the retinal projections revealed a considerable projection of
axons over the damaged surface, with subjacent termination.

Listed below are a number of factors which we feel are necessary to

postulate for an understanding of the formation of altered, and presumably

also the normal, retinotectal topography.

(1) Regional Specificity The ganglion cell axons must have the

attribute of being able to "recognize" certain tissue as tectum; hence, we

can talk about a "tectal terminal space" as defined for the axons. In the

normal animal, this space is constituted principally by the SGS, confirmed

by electron microscope study of retinotectal projections in the rat by Lund

(1969). Some property of the tectal terminal space, differentiating it with

respect to topography from the other terminal regions along the course

of the optic tract, is indicated by the fact that the order of representation

of naso-temporal positions on the retina is reversed in the colliculus from

that seen in each division of the lateral geniculate body. This is

illustrated in Figure 32. The naso-temporal order of termination in the

pretectal region may be similar to that in the geniculate body, although

not as clear, according to the electrophysiological study in the rat by

Siminoff, Schwassman and Kruger (1966); however, in our material, we were

54

unable to see clear evidence of a nasotemporal order within the pretectal region.

(2) <u>Axon ordering factor</u>   In the cases of partial tectum lesions, it is amazing to observe that in spite of substantial mismatch between the size of the retina and the tectal dimensions, fibers from the retina are able to conserve a considerable degree of order with respect to each other, resulting in the formation of an orderly map. What are the influences on the axon that direct it to its "proper" terminal site ? Gaze (1970) notes that two potential mechanisms are most compatible with the various data reported in the literature: (1) a rigid position-specification where each axon "finds" its place in the tectum by locating a predetermined marker. Experimental examination of this mechanism in studies of regeneration in non-mammalian forms has been dealt with at length by Sperry (1971; see also, Attardi and Sperry, 1963). It is commonly referred to as the chemo-specificity hypothesis, where a biochemical mosaic of "tags" in the retina allows a matching of axons with cells in the tectum carrying similar chemical markers. This would imply the existence of topographic specificity in the substrate as well as in the axons. (2) A mechanism whereby the group of axons would be a "self-organizing system with relation to their individual positions"; given certain reference points on the terminal field, axons occupy sites so as to maintain their positions with respect to each other. The postulate of an axon-ordering factor would imply that the specificity for topographic order of connections resides in the axons themselves, and — at least in the strongest form of the hypothesis — not in the tectal substrate, though Gaze (1970) assumes that some kind of gradient

55

in the substrate is also necessary. Thus, it may imply less information in the genome.

We may now envision the role of the two factors, regional specification and axon ordering, in controlling the termination of the optic-tract axons from the point at which they reach the ventral border of the lateral geniculate body. The regional specificity would allow the axons to "recognize" the LGv, LGd, PT, SC as distinct terminal end-stations. As they course over the LGv and LGd, in each nucleus the axons from the nasal retina enter and terminate first (ventrally). ("First" in this discussion refers not to time, but to position with respect to the optic-tract axis.) The rest of the projection is ordered according to progressively more temporal positions in the retina such that the optic disc is represented in the center of the cell-group surface and the temporal retina has axons entering and terminating along the dorsal border (see Figures 32,7,8, 10). In the SC, as has been pointed out in the previous section, the order of termination is reversed. If we postulate a naso-temporal (N-T) axon-ordering factor (such that the axons conserve their nasal to temporal positions with respect to each other) we need only invoke one additional factor, that determines which set of axons will terminate first (nasal retinal axons in the LGB, temporal in SC) and we can predict the distribution of the naso-temporal axis over the surface of each area.

This additional factor could be some aspect of the regional specificity which would direct the temporal retinal axons to the rostral part of the "tectal terminal space". Theoretically then, the additional factor need not be a chemical gradient of the type postulated by Sperry (1963) and Gaze, Jacobson and Szekeley (1963). Nevertheless, it

56

remains possible that such a gradient may exist in the organization. The

point to be emphasized here is that the axon-ordering factor can be the

major determinant of the N-T topography; the additional factor need only be

strong enough to impose the N-T or T-N direction.

We can go further and ask whether a chemical gradient, if strong
enough, would altogether obviate the need for an axon-ordering factor, of
the type we are proposing. Theoretically, it seems to us that an axon-
ordering factor might require less information-coding in the genome.
It is necessary only to postulate an N-T gradient in the retinal cells
such that each axon, or group of axons, recognized its neighbour as being
more nasal or more temporal with respect to its own position in the retina.
A gradient theory would require a retinal grandient, and in addition, a
matching gradient in each of the primary optic tract terminal regions that
is recipient of the entire retinal map. However, to test the validity of
either hypothesis , it would be important to have a paradigm where the
retinal axons are re-directed so as to grow across the postulated gradient,
instead of along it. We are currently examining this possibility in
hamsters that show an anomalous decussation of retinofugal axons at the
tectal midline (Schneider, 1971, 1973) following a neonatal unilateral
tectum ablation.
The problem of specifying the N-T inversion of the map in the
superior colliculus would be simplified if the axons reaching the midbrain
were a population separate from that terminating in the diencephalon.
A recent electrophysiological study of the retinal projections in the cat
(Hoffman and Stone, 1973) indicates that this is true for the major number
of the retinotectal afferents (the "W cell" axons), whereas a numerically
smaller part of the population consists of branches of axons going also to
the lateral geniculate body (the "Y cell" axons). The lateral geniculate
also receives a unique population (the "X cell" axons). This study did not
try to deal with afferents to the pretectum or the ventral nucleus of LGB.
It would be interesting to know whether the axons which have branches in
both areas grow in later than the others.

With the postulate of a N-T axon-ordering factor, one can now

explain the compression phenomenon. The axons from the temporal retina

arrange themselves along the first available "tectal terminal space".

Progressively more nasal fibers are distributed in an orderly fashion over

the remainder of the tectal space such that fibers from the entire retina

terminate within whatever space is available. The formation of an orderly

distribution may occur over a certain time period, (as is suggested by

studies of the time course of regenerating nerve fibers in the Xenopus

(Gaze and Jacobson, 1963; and reviewed by Gaze, 1970) and in the frog

(Susan Udin, unpublished experiments at M.I.T.). An assumption underlying

this hypothesis is that the axons do not maintain a fixed "inter-axon"

spacing but, as a population, tend to fill up whatever space is available

that also has the right kind of regional specificity.

Whether it is necessary to postulate an axon-ordering factor for the

upper-lower retinal axis, in addition to the N-T factor, is suggested, but

in perhaps a less convincing fashion, by our data. The axons from the upper

retina are spatially segregated from those originating in the lower retina

throughout most of the course of the optic tract, maintaining a constant

position at the caudal (lateral) and rostral (medial) edges of the tract,

respectively. This segregation may be maintained by a tendency for axons

to preserve their relative positions during parallel growth and need not

involve a separate factor for the ordering of axons in this axis, once it

has occurred below the lateral geniculate body. Nonetheless, our cases

with lesions of the medial tectum do hint at a compression in the medio-

lateral direction in the tectum. The exact changes in topography seem to

be more complex than predicted by a simple compression. Stronger support

for a compression in the representation of the upper-lower axis of the

retina was obtained in the rostral tectum lesion cases in which much of

the lateral tectum was included in the early damage. Perhaps the

strongest evidence for an active influence tending to order the axons

in the medio-lateral axis of the superior colliculus is the arching

trajectories of some of the axons that get deflected from their normal

straight-line course, as if they were returning to their "proper" place

along this axis (after some of them have terminated in a displaced position).

(3) Mechanical Factors From an examination of the discontinuous patches of degeneration, it is obvious that there are violations of perfect order in the retinotectal projection. But it should be noted in the charts that associated with the isolated degeneration spots, there is usually a corresponding anomaly in the course of degenerating axons (see e.g. 47-3, 45-2): either a "deflected" bundle of axons coursing towards the displaced area of degeneration, or an abnormal "double-tier" formation of the optic fiber layer (see chart in Figure 14). It is suggested that these abnormal axon trajectories are a function of mechanical factors that come into play because of the early damage inflicted on the tectal tissue. Mechanical "barriers" could cause a deviation in the path of some axons. Some changes in the properties of the substrate may well make these deflected axons behave as if they are innervating a second, smaller tectum. The axon-ordering factor would impose a rostro-caudal order on the termination of axons from the retina such that fibers from the nasal retina terminate farthest caudally in the "smaller tectum:. Hence, a lesion in the nasal retina would cause two patches of terminals in the tectum: a main caudal patch where the majority of the axons project, and a second isolated patch representing the nasal retinal projection in the "small" tectum, resulting from degeneration in the deviant bundle of axons. Likewise, a lesion in the nasal retina should also cause two patches of degeneration - one in the rostral part of the 'primary' tectum and a smaller one in the 'secondary' tectum. However, in this case, it may be difficult to discern the segregation between the two representations since they both occur in the rostral tectum. What are the factors that make the

deviant axons behave as if there is a second tectum and what signals are influencing them to define the caudal end of this 'secondary' tectum ? These questions remain to be answered.

(4) Pruning factor: Schneider (1973) has demonstrated that axons tend to conserve at least a minimum quantity of terminal arborization and has termed this tendency "the pruning effect". Thus, in his cases with unilateral ablation of the right tectum in the neonate hamster, he observed an anomalous termination of optic tract fibers in the right LP; also (in most cases) the right optic tract established connections with the "wrong" left colliculus. He went on to show that there is an inverse relationship between the amount of terminal degeneration in the LP and that in the "wrong" colliculus.

Such a pruning effect would be expected to influence, for many of our cases with partial tectum lesions, the occurence of terminal degeneration in the LP. The terminal arborization of axons that form a compressed map in the remnant SGS may not achieve their full expression. We would thus expect these axons to show a compensating sprouting in regions of the LP that have been dennervated by the tectal ablation. However, it is also conceivable that the compressed map in the tectum is a representation only of the late-arriving retinal axons and that those axons that were sectioned by the early lesion simply degenerate caudal to the diencephalon. It may be only these latter axons that form the retinal projection to the LP. In either case, the abnormal LP termination would be influenced by the pruning effect on retinal axons destined for the tectum.

60

(5) Competition for terminal space   Interpretation of many

results of experiments involving neuromorphological plasticity have

invoked a discussion of the tendency of axons to fill available terminal

space (see Schneider, 1973, for review). A striking demonstration of the

effects of this factor was reported by Schneider (1971, 1973). In

hamsters that have suffered a unilateral right tectum ablation on the day

of birth, axons from the eye contralateral to the lesioned tectum

traverse the damaged area and cross the tectal midline to terminate in the

damaged (left) tectum. If both eyes are left intact at birth, the abnormal

termination in the "wrong" tectum is found only along a medial zone of the

undamaged SGS. An examination of the projections from the other (right)

eye show a termination throughout the undamaged tectum except in the medial

zone corresponding to the zone of abnormal innervation from the left eye.

Thus, the axons from the two eyes appear to exclude each other. If

however, the undamaged tectum is dennervated at birth by removal of the

right eye, the abnormally decussating axons are seen to terminate throughout

the extent of the SGS of the "wrong" (left) colliculus, thus indicating

that the axons tend to fill up available terminal space when competition

from other similar axons is removed.

From the studies presented here, it can be suggested that the

phenomenon of competition plays an important role in the formation of

retino-tectal topography. However, this factor should be restated in

terms of some kind of exclusion effect. It is suggested that a group

of axons has the tendency to remain the sole occupant of a region of tissue

in the SGS. Fibers from adjacent parts of the retina are excluded from

this region. This exclusive occupancy principle would thus influence the

total volume of tissue occupied by arbors of each axon. When applied to the formation of a compressed map in a tectum of reduced size, this principle acting in conjunction with the N-T axon ordering factor would predict that either 1) all of the axons from the retina are terminating in the tectal terminal space, with arbors from each axon occupying a reduced volume, or 2) only some of the axons from each part of the retina project to the smaller tectum, every axon maintaining its normal volume of arborization. Our findings do not discern between these two possibilities.

Conclusion

The findings of our studies demonstrate that the immature central nervous system of a mammal shows a flexibility in its response to experimental manipulations that was long considered possible only of nervous systems of nonmammals. A species like the Syrian hamster, with the brain at a very primitive stage of development on the day of birth, allows the examination of mechanisms of neuroembryology and neuromorphological plasticity without involving complicated procedures of in utero surgery.

Hamsters that have suffered partial lesions of the superior colliculus on the day of birth show several interesting patterns of retinotectal projections:

(a) A compression of the retinal map into the remnant tectal terminal space which includes at least the undamaged superficial gray layer, and the tectal layers subjacent to the optic fiber layer.

(b) Discontinuities in the retinotectal map associated with deviant axons. The trajectories of these axons and the locations of the isolated patches representing the discontinuities suggest a partial "double-tectum" effect.

(c) The formation of anomalous connections in the thalamic nucleus LP and in the dorsal terminal nucleus of the accessory optic tract.

The above findings may be interpreted by invocation of several factors that may be operative in developing as well as regenerating systems:

(1) Regional specificity

(2) Axon-ordering factors

(3) Mechanical factors affecting axon trajectories

(4) A Pruning effect, or the Conservation principle

(5) Competition for terminal space, or the Exclusion principle

A Regional Specificity, acting in conjunction with the Naso-temporal Axon Ordering Factor and the Exclusion principle allow, together with a principle of parallel growth of axons, an explanation of the formation of normal and altered retinotectal topography, whereas the Pruning effect and an influence of mechanical factors must be invoked to explain some of the anomalous projections to the LP, DTN and the discontinuities in the retinotectal maps.

The results of these experiments and their interpretation contribute to a new conception of normal development of the optic system in mammals.

Abbreviations

AD:	anterodorsal nucleus
ant. comm.:	anterior commissure
AOT:	accessory optic tract
AV:	anteroventral nucleus
BIC:	brachium of inferior colliculus
CNS:	central nervous system
DTN:	dorsal terminal nucleus
fn:	fornix
hab:	habenula
hc:	habenular commissure
HM	medial habenular nucleus
Hypo:	hypothalamus
IC:	inferior colliculus
IF-AOT:	inferior fasciculus of accessory optic tract
I Ped:	interpeduncular nucleus
L:	lateral thalamic nucleus
LGN:	lateral geniculate nucleus
LGd:	dorsal nucleus of lateral geniculate body
LGv:	ventral nucleus of lateral geniculate body
LGvee:	external subdivision of external lamina, ventral nucleus of lateral geniculate body
LGvei:	internal subdivision of external lamina, ventral nucleus of lateral geniculate body
LP:	lateral posterior thalamic nucleus or nucleus lateralis posterior
LTN:	lateral terminal nucleus

65

MF-AOT:	middle fasciculus of accessory optic tract
MGB:	medial geniculate body
MTN	medial terminal nucleus
n IV:	nucleus of IVth nerve
n OT:	nucleus of the optic tract
n PT:	pretectal nucleus
OCh:	optic chiasm
OT:	optic tract
ped:	cerebral peduncle
po. comm.:	posterior commissure
PoTH:	anterior pretectal nucleus or nucleus posterior thalami
PrT, PT:	pretectal area
R:	red nucleus
SC:	superior colliculus
SCh:	suprachiasmatic nucleus
SF-AOT:	superior fasciculus of accessory optic tract
SGS:	superficial gray stratum
sm:	stria medullaris
SO:	stratum opticum or optic layer
st:	stria terminalis
VMH:	ventro-medial hypothalamus

References

1. Abplanalp, P. Some subcortical connections of the visual system in tree shrews and squirrels. Brain, Behav. Evol. 3: 155-168, 1970.

2. Altman, J. and Anderson, W. J. Irradiation of the cerebellum in infant rats with low-level X-ray: histological and cytological effects during infancy and adulthood. Exp. Neurol. 30: 492-509, 1971.

3. Attardi, D. G. and Sperry, R. W. Preferential section of central pathways by regenerating optic fibers. Exp. Neurol. 7: 46-64, 1963.

4. Bernstein, J. J. and Bernstein, M. E. Axonal regeneration and formation of synapses proximal to the site of lesion following hemisection of the rat spinal cord. Exp. Neurol. 30: 336-351, 1971.

5. Casagrande, V. A., Hall, W. C., and Diamond, I. T. Formation of anomalous projections from the retina to the pulvinar following removal of the superior colliculus in neonatal tree shrews. Progr. and Abstr., Soc. for Neuroscience, 2nd Ann. Meeting, Houston, 1972, p. 231.

6. Cunningham, T. J. Sprouting of the optic projection after cortical lesions. Anat. Rec. 172: 298, 1972.

7. Das, G. D. Experimental studies on the postnatal development of the brain. I. Cytogenesis and morphogenesis of the accessory fascia dentata following hippocampal lesions. Brain Res. 28: 263-282, 1971.

8. Ebbesson, S. O. E. On the organization of central visual pathways in vertebrates. Brain, Behav. Evol. 3: 178-194, 1970.

9. Ebbesson, S. O. E. A proposal for a common nomenclature for some optic nuclei in vertebrates and the evidence for a common origin of two such cell groups. Brain, Behav. Evol. 6: 75-91, 1972.

10. Fink, R. P. and Heimer, L. Two methods for selective silver impregnation of degenerating axons and their synaptic endings in the central nervous system. _Brain Res._ _4_: 369-374, 1967.

11. Gaze, R. M. _The Formation of Nerve Connections._ New York: Academic Press, 1970.

12. Gaze, R. M. and Jacobson, M. A study of the retinotectal projection during regeneration of the optic nerve in the frog. _Proc. Roy. Soc. B._ _157_: 420-448, 1963.

13. Gaze, R. M., Jacobson, M., and Szekeley, G. The retinotectal projection in _Xenopus_ with compound eyes. _J. Physiol._ _165_: 484-499, 1963.

14. Gaze, R. M. and Sharma, S. C. Axial differences in the reinnervation of the goldfish optic tectum by regenerating optic nerve fibers. _Exp. Brain Res._ _10_: 171-181, 1970.

15. Geniec, P. and Morest, D. K. The neuronal architecture of the human posterior colliculus: a study with the golgi method. _Acta Oto-Laryngol._ _Supplement 295_, 1971.

16. Giolli, R. A. and Guthrie, M. D. The primary optic projections in the rabbit. An experimental degeneration study. _J. Comp. Neurol._ 136: 99-126, 1969.

17. Goodman, D. C. and Horel, J. A. Sprouting of optic tract projections in the brain stem of the rat. _J. Comp. Neurol._ _127_: 71-88, 1966.

18. Guillery, R. W. Experiments to determine whether retino-geniculate axons can form trans-laminar collateral sprouts in the dorsal lateral geniculate nucleus of the cat. _J. Comp. Neurol._ _146_: 407-419, 1972.

19. Hámori, J. Presynaptic-to-presynaptic axon contacts under experimental conditions giving rise to rearrangement of synaptic structures. In: Structure and Function of Inhibitory Neuronal Mechanisms, edited by Von Euler, Skoglund, and Söderberg. New York: Permagon Press, 1968, p. 71-80.

20. Harting, J. K., Hall, W. C., Diamond, I. T., and Martin, G. F. Anterograde degeneration study of the superior colliculus in Tupaia glis: evidence for a subdivision between superficial and deep layers. J. Comp. Neurol. 148: 361-386, 1973.

21. Hayhow, W. R., Webb, C., and Jervine, A. The accessory optic fiber system in the rat. J. Comp. Neurol. 115: 187-215, 1960.

22. Hayhow, W. R., Sefton, A., and Webb, C. Primary optic centers of the rat in relation to the terminal distribution of the crossed and uncrossed optic nerve fibers. J. Comp. Neurol. 118: 295-321, 1962.

23. Hicks, S. P. and D'Amato, C. J. Motor-sensory and visual behavior after hemispherectomy in newborn and mature rats. Exp. Neurol. 29: 416-438, 1970.

24. Hicks, S. P., D'Amato, J., Coy, M. A., O'Brien, E. D., Thurston, J. M., and Joftes, D. L. Migrating cells in the developing nervous system studied by their radiosensitivity and tritiated thymidine uptake. Fundamental Aspects of Radiosensitivity. Brookhaven Symposia in Biol. 14, 246-261, 1961.

25. Hoffman, K.-P. and Stone, J. Central termination of W-, X- and Y-type ganglion cell axons from cat retina. Brain Res. 49, 500-501, 1973.

26. Kalil, R. E. Formation of new retino-geniculate connections in kittens after removal of one eye. Anat. Rec. 172: 339-340, 1972.

27. Kalil, R. E.   Formation of new retino-geniculate connections in kittens: effects of age and visual experience.   Anat. Rec. 175: 353, 1973.

28. Lashley, K. S.   The mechanism of vision.   V. The structure and image-forming power of the rat's eye.   J. Comp. Physiol. 13: 173-200, 1932.

29. Liu, C.-N. and Chambers, W. W.   Intraspinal sprouting of dorsal root axons.   Arch. Neurol. Psychiat. 79: 46-61, 1958.

30. Lund, R. D.   Synaptic patterns of the superficial layers of the superior colliculus.   J. Comp. Neurol. 135: 179-208, 1969.

31. Lund, R. D. and Lund, J. S.   Synaptic adjustment after deafferentation of the superior colliculus of the cat.   Science 171: 804-807, 1971.

32. Lynch, G. S., Mosko, S., Parks, T., and Cotman, C. W.   Relocation and hyperdevelopment of the dentate gyrus commissural system after entorhinal lesions in immature rats.   Brain Res. 50: 174-178, 1973a.

33. Lynch, G., Stanfield, B., and Cotman, C. W.   Developmental differences in post-lesion axonal growth in the hippocampus.   Brain Res. 59: 155-168, 1973b.

34. McCouch, G. P., Austin, G. M., Liu, C. N., and Liu, C. Y.   Sprouting as a cause of spasticity.   J. Neurophysiol. 21: 205-216, 1958.

35. Montero, V. M., Brugge, J. F., and Beitel, R. E.   Relation of the visual field to the lateral geniculate body of the albino rat. J. Neurophysiol. 31: 221-236, 1968.

36. Montero, V. M. and Guillery, R. W.   Degeneration in the dorsal lateral geniculate nucleus of the rat following interruption of the retinal or cortical connections.   J. Comp. Neurol. 134: 211-242, 1968.

70

37. Moore, R. Y., Björklund, A., and Stenevi, U. Plastic changes in the adrenergic innervation of the rat septal area in response to dennervation. Brain Res. 33: 13-35, 1971.

38. Morest, D. K. The pattern of neurogenesis in the retina of the rat. Z. Anat. Entwickl.-Gesch. 131: 45-67, 1970.

39. Niimi, K., Kanaseki, T., and Takimoto, T. The comparative anatomy of the ventral nucleus of the lateral geniculate body in mammals. J. Comp. Neurol. 121: 313-324, 1963.

40. Raisman, G. Neuronal plasticity in the septal nuclei of the adult rat. Brain Res. 14: 25-48, 1969.

41. Raisman, G. and Field, P. M. A quantitative investigation of the development of collateral reinnervation after partial deafferentation of the septal nuclei. Brain Res. 50: 241-264, 1973.

42. Ralston, H. J., III and Chow, K. L. Synaptic reorganization in the degenerating lateral geniculate nucleus of the rabbit. J. Comp. Neurol. 147: 321-350, 1973.

43. Schneider, G. E. Retinal projections characterized by differential rate of degeneration revealed by silver impregnation. Anat. Rec. 160: 423, 1968.

44. Schneider, G. E. Two visual systems. Brain mechanisms for localization and discrimination are dissociated by tectal and cortical lesions. Science 163: 895-902, 1969.

45. Schneider, G. E. Mechanisms of functional recovery following lesions of visual cortex or superior colliculus in neonate and adult hamsters. Brain, Behav. Evol. 3: 295-323, 1970.

46. Schneider, G. E. Development and regeneration in the mammalian visual system. In: Genesis of Neuronal Patterns, Neuroscience Res. Prog. Bull. 10: 287-290, 1972, edited by Edds, Barkley, and Fambrough.

47. Schneider, G. E. Early lesions of superior colliculus: factors affecting the formation of abnormal retinal projections. Brain, Behav. Evol. 8: 73-109, 1973.

48. Schneider, G. E. and Nauta, W. J. H. Formation of anomalous retinal projections after removal of the optic tectum in the neonate hamster. Anat. Rec. 163: 258, 1969.

49. Sharma, S. C. Reformation of retinotectal projections after various tectal ablations in adult goldfish. Exp. Neurol. 34: 171-182, 1972a.

50. Sharma, S. C. Restoration of the visual projection following tectal lesions in goldfish. Exp. Neurol. 35: 358-365, 1972b.

51. Sharma, S. C. Redistribution of visual projections in altered optic tecta of adult goldfish. Proc. Nat. Acad. Sci. (Wash.) 69: 2637-2639, 1972c.

52. Sidman, R. L. Histogenesis of mouse retina studied with thymidine $-H^3$. In: The Structure of the Eye, edited by G. K. Smelser. New York: Academic Press, 1961, p. 487-505.

53. Siminoff, R., Schwassman, H. O., and Kruger, L. An electrophysiological study of the visual projection to the superior colliculus of the rat. J. Comp. Neurol. 127: 435-444, 1966.

54. Sotello, C. and Palay, S. L. Altered axons and axon terminals in the lateral vestibular nucleus of the rat. Lab. Invest. 25: 653-671, 1971.

55. Sperry, R. W. Chemoaffinity in the orderly growth of nerve fiber patterns and connections. Proc. Nat. Acad. Sci. 50: 703-710, 1963.

56. Sperry, R. W. How a developing brain gets inself properly wired for adaptive function. In: The Biopsychology of Development, edited by Tobach, Aronson, and Shaw. New York: Academic Press, 1971, p. 27-44.

57. Teuber, H.-L. Mental retardation after early trauma to the brain: some issues in search of facts. In: Physical Trauma as an Etiological Agent in Mental Retardation, edited by Angle and Bering. U. S. Department of of Health, National Institute of Health, Bethesda, 1970, p. 7-28.

58. Yoon, M. G. Reorganization of retinotectal projection following surgical operations on the optic tectum in goldfish. Exp. Neurol. 33: 395-411, 1971.

59. Yoon, M. G. Reversibility of the reorganization of retinotectal projection in goldfish. Exp. Neurol. 35: 565-577, 1972a.

60. Yoon, M. G. Transposition of the visual projection from the nasal hemiretina onto the foreign rostral zone of the optic tectum in goldfish. Exp. Neurol. 37: 451-462, 1972b.

FIGURE LEGENDS

Figure 1:

Dorsal view of the rostral brainstem of a 15-week-old Syrian
hamster, reconstructed from serial sections cut in the transverse
plane, using method described in text. Surface landmarks and
cell-groups lying immediately beneath the optic tract are shown in
solid line. (These borders were projected to the nearest surface
of the tract and then onto a horizontal plane - "surface projection",
(see Fig. 2 (a)) -- separately for every 5th 30 um section.)
Shown in fine dotted lines are the outlines of the deep-lying
anterior pretectal nucleus, or nucleus posterior thalami (Poth),
projected directly onto a horizontal plane - "shadow-cast projection",
(see Fig. 2 (b)). The scale units are in mm; the anterior-posterior
and vertical zero lines correspond to the lambda point on the
overlying skull. The head is aligned so that the bregma point and
the caudal edge of the interparietal bone at the midline are at
the same elevation. Abbreviations on p. 65.
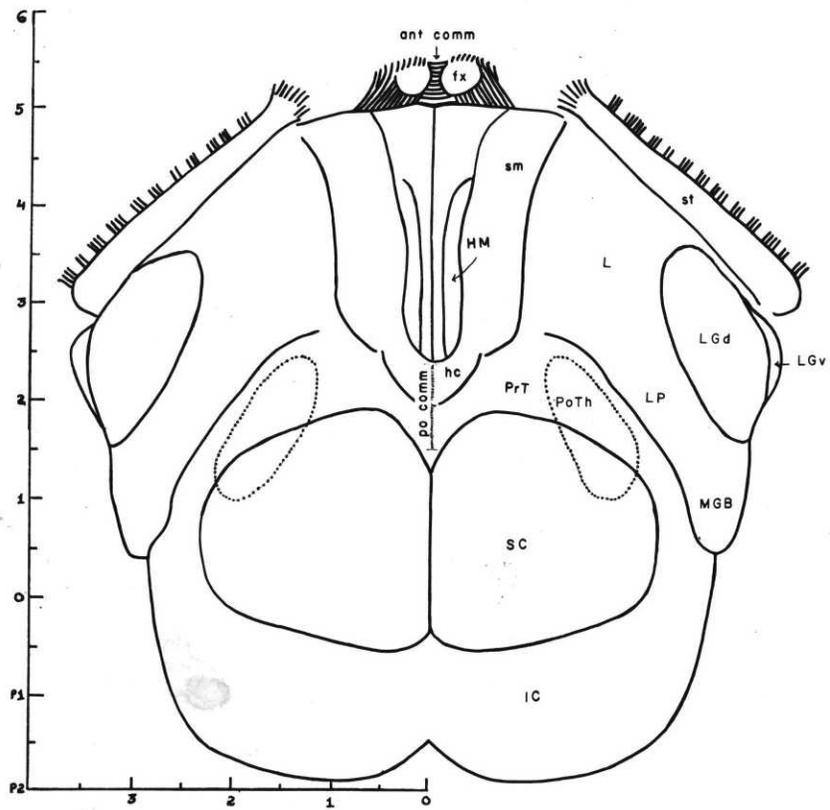
Figure 1

Figure 2:

The two drawings represent parts of transverse sections through the brainstem of an animal, and illustrate the difference between (a) a surface projection and (b) a shadow-cast projection.

(a) The dotted area indicates an area of degeneration that stretches inwards from the optic tract. The extent of degeneration reaching and immediately subjacent to the inner surface of the tract is projected at right angles first to the outer surface of the tract and next onto vertical and horizontal planes (Bl, Bd respectively, symbolized by solid bars). The boundaries of the degeneration that is not abutting the optic tract are likewise projected to the outer surface of the tract and then onto vertical and horizontal planes (Al, Cl, Ad symbolized by open bars). The projections on the vertical plane are used for the lateral view reconstructions (Fig. 3) and those on the horizontal plane are transferred on the dorsal view reconstruction.

(b) Regions in solid black represent deep-lying nuclei in the brainstem. For the shadow cast projection, the outlined nuclei are projected perpendicularly on vertical and horizontal planes. The larger nucleus results in a projection Ad, Al and the small nucleus gives rise to projections Bd, Bl incorporated into dorsal and lateral view reconstructions. Note that the lateral projections of the 2 nuclei are overlapping. In this case, since A is the deeper patch, only the portion Al as indicated, is shown on the lateral view and for B, the full extent (Bl) of its projection is represented.
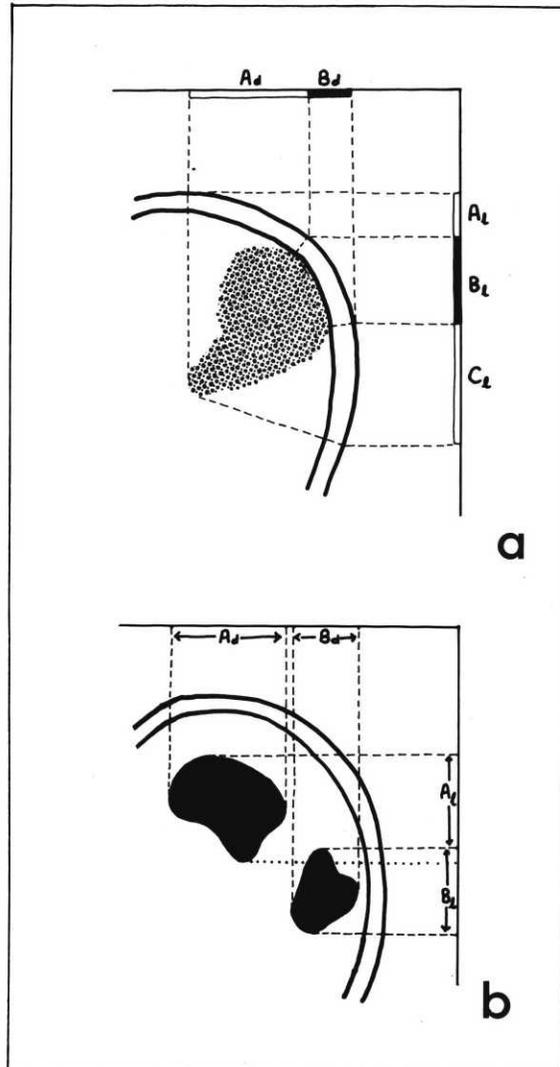
Figure 2

Figure 3:

Lateral view of the rostral brainstem of a 15-week-old Syrian
hamster, reconstructed from transversely cut serial sections. The
edges of the optic tract as it ascends the diencephalon are
indicated by dashed lines. Dotted lines represent shadow-cast
projections of the outlines of structures lying deep in the
brainstem (see Fig. 2(b)). The reconstruction is made from the
same animal as for the dorsal view in Figure 1, and both are
presented at the same magnification.

Abbreviations on p. 65.
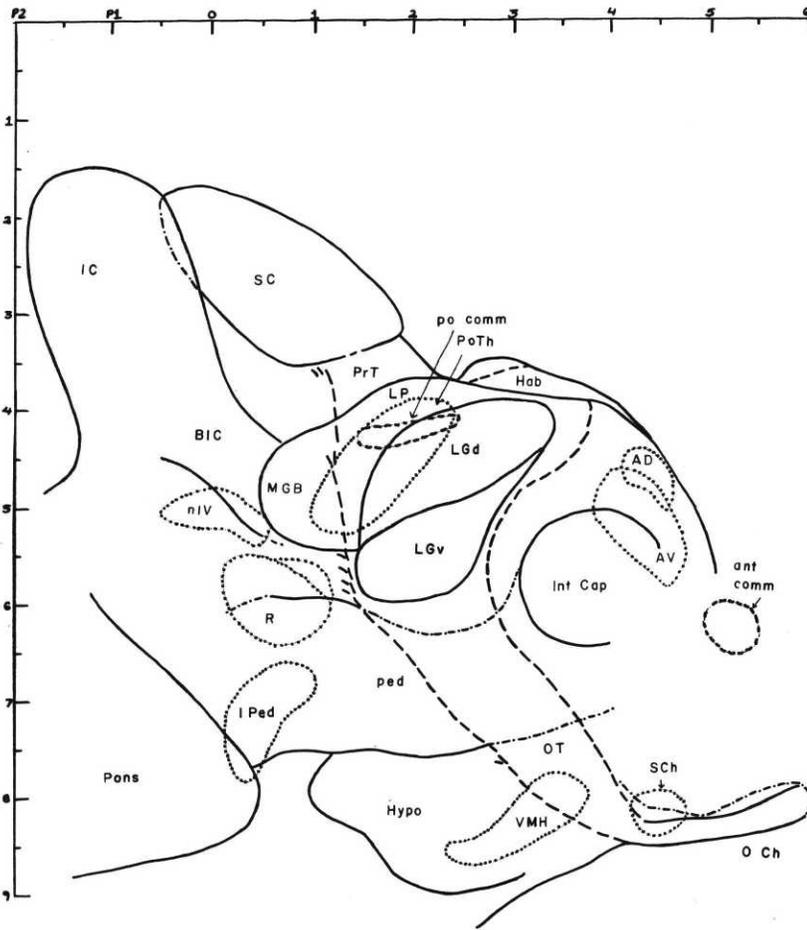
Figure 3

Figure 4:

Schematic diagram to show how the orientation of grid lines for
the reconstructions were obtained. The brainstem is represented as
a cylinder. A vertical plane will cut the cylinder in a line
that, in a lateral view, (a) is straight if the cut preserves a
right-left symmetry, (b) is convex anteriorly if the cut is more
anterior on the right than on the left, and (c) has a posterior
convexity if the plane of section cuts the cylinder more rostrally
on the left than on the right. Thus, depending on whether the
plane of section of the brainstem maintained a right-left symmetry,
the grid lines were either straight or curved as shown on the direct
lateral views of the cylinder on the right side of each figure.
Similar illustrations for the dorsal view are obtained by
rotating the figure through 90°.
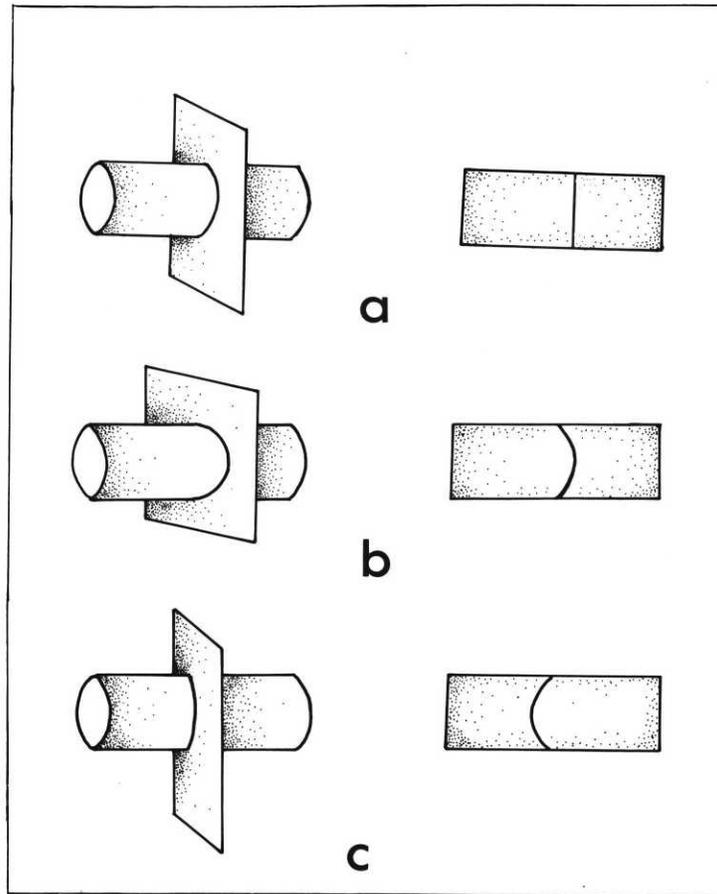
Figure 4

Figure 5:

Lateral view reconstruction (see Fig. 3) of the brainstem of a
hamster, 12 weeks of age, that had the right eye removed 6 days prior
to sacrifice. Sections were cut transversely (30 μm thickness) and
every 5th section was stained with the Fink-Heimer method. (The
degeneration is observed on the left side of the brain but is
reconstructed on a standard lateral view drawing of the right side to
facilitate comparisons with other figures.) Straight lines represent
degenerating fibers seen on the surface of the brainstem, medium dots
symbolize fibers deep to the surface, large and small dots show areas
of terminal and preterminal degeneration. The optic tract fibers
emerge from the chiasm and traverse up the lateral surface of the
brainstem. At the ventral edge of the peduncle, the inferior fasciculus
of the accessory optic tract (AOT) is observed coursing toward the MTN.
The main optic tract continues dorsally to terminate in the LGv, LGd,
pretectal region, and SC. At the level of the PrT, fibers leave the
main OT to terminate in the DTN and LTN, forming the superior
fasciculus of the AOT. This tract continues ventrally to the MTN as
the transpeduncular tract. The medial fasciculus of the AOT is
formed by sparse fibers, running below the surface between the LGv and
LTN, ventral to the MGB.
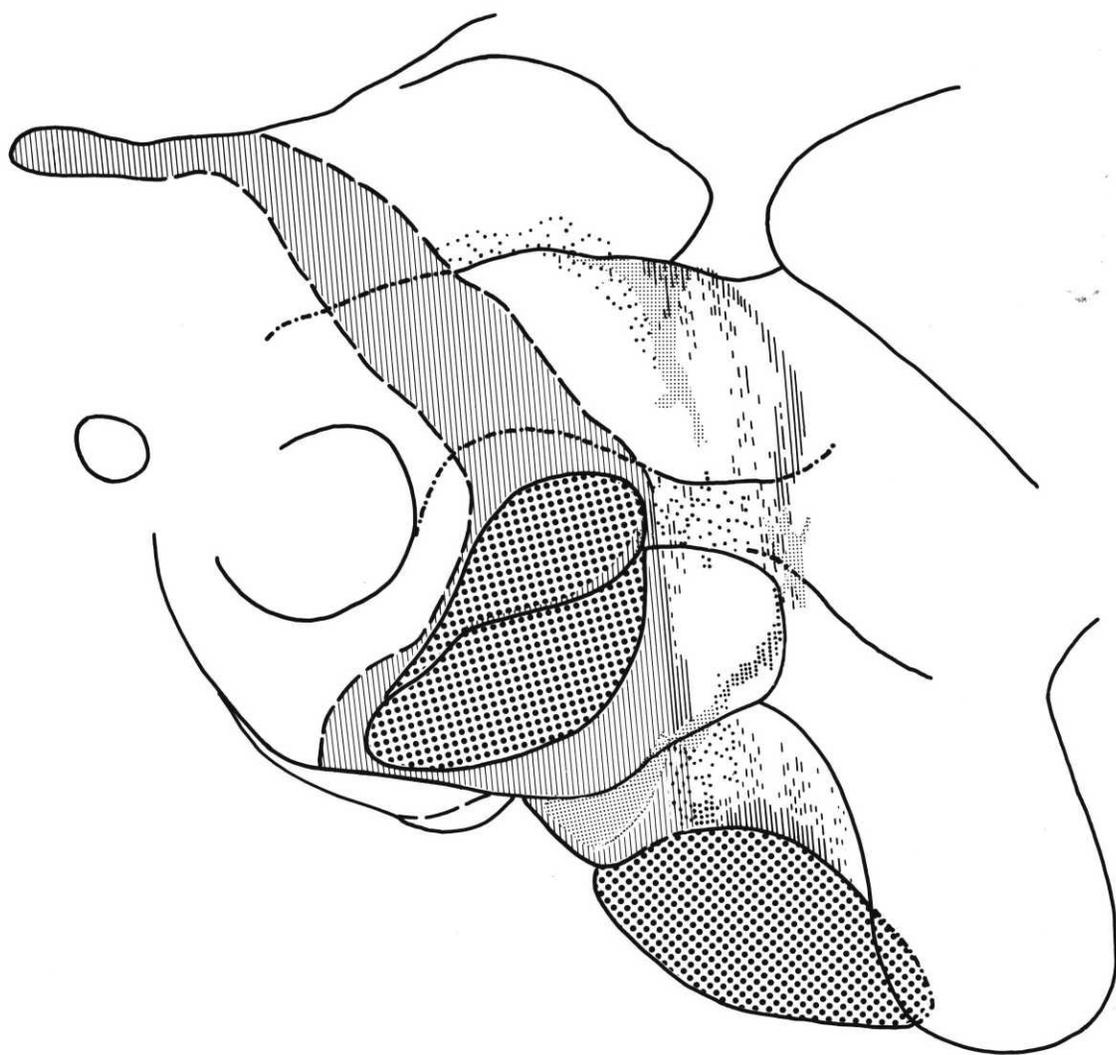
Figure 5

Figure 6:

Schematic drawing of a hamster's eyeball that has been dissected

from the orbit with the attachments of the rectus and oblique

muscles retained. The representation is distorted i.e., the

circumference of the eyeball is not the equator (which is 1mm.

from the limbus), but is the locus of points 3.5mm. from the limbus.

Points beyond the true equator would not actually be seen in

a front view.

The dots indicate points of electrode entry for discrete

lesions of the retina, used in the study of normal topography.

Thirteen cases (solid dots) have been reconstructed on dorsal and

lateral view drawings; for the other cases (open circles), only

summary surveys were made to confirm our results.

Figure 6
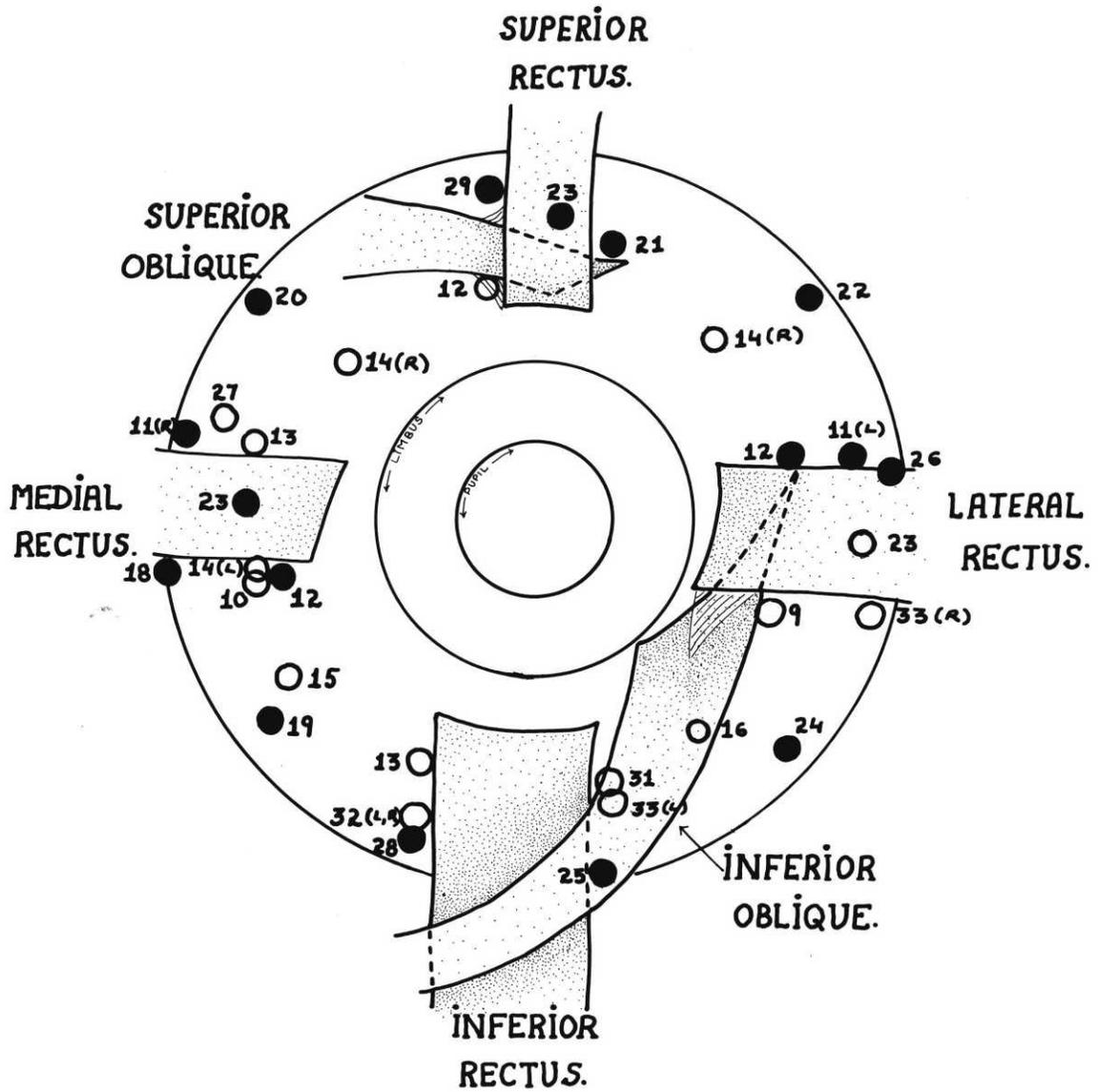
Figure 7:

Lateral view reconstructions of case HED-11 that had suffered

discrete retinal lesions, one at the upper edge of the medial rectus

in the right eye, and one at the lower edge of the temporal rectus

in the left eye. Degeneration from both eyes is reconstructed on

standard drawings of the right side to facilitate comparison. The

fine dots indicate outlines from the standard reconstruction.

Superimposed on these are solid lines representing the actual

reconstruction of the optic tract and related structures for HED-11.

(Short lines: degenerating fibers on the surface of the brainstem;

small crosses: degenerating fibers not at the surface - indicated

only for fibers in the OT; solid bars: areas of terminal degeneration

immediately subjacent to the OT; open bars: areas of terminal

degeneration deep to the OT surface).

The lower reconstruction (b) shows degeneration from the left temporal

retina to the contralateral (right) side. The upper drawing (a) shows

crossed degeneration from the nasal retina of the right eye, and

also the ipsilateral projection from the temporal retinal lesion

of the left eye.

Scale is in mm.

Figure 7

HED-II(LEFT)

a

HED-II(RIGHT)

b

87
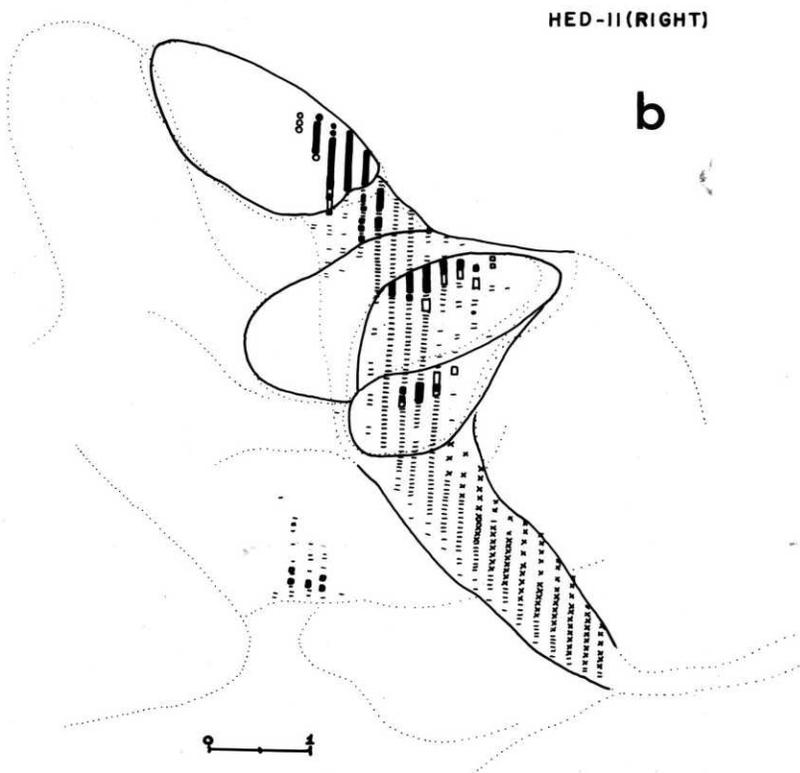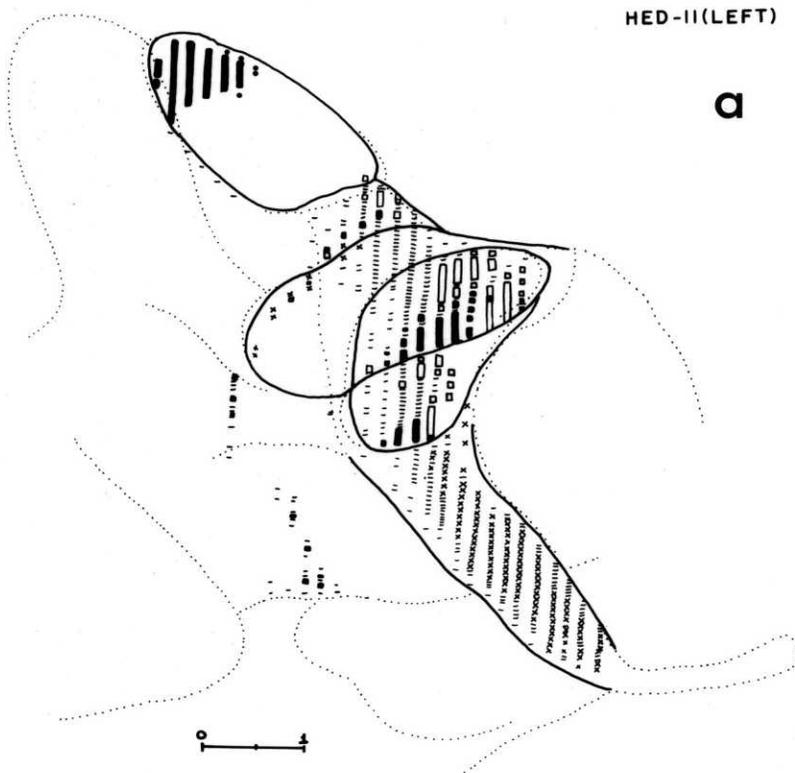
Figure 8:

Dorsal view reconstruction of case HED-11, demonstrating degeneration resulting from 2 discrete retinal lesions (upper edge of medial rectus, right eye; lower edge of temporal rectus, left eye). The lesions were inflicted in adulthood, 5 days prior to sacrifice, and frozen sections of the brain were cut and stained with the Fink-Heimer method. On the right side, axons from the left temporal retina can be followed to their termination in the dorsal part of LGd and in the rostral SC. The ipsilateral component from the temporal retinal lesion is noted on the left side as deep degeneration in the LGd. Axons from the right nasal retina terminate in the ventral part of LGd, LGv and caudally in the SC. A marked projection is also observed to the DTN on the left side. Symbols same as for Figure 7.

HED-11

Figure 8

89
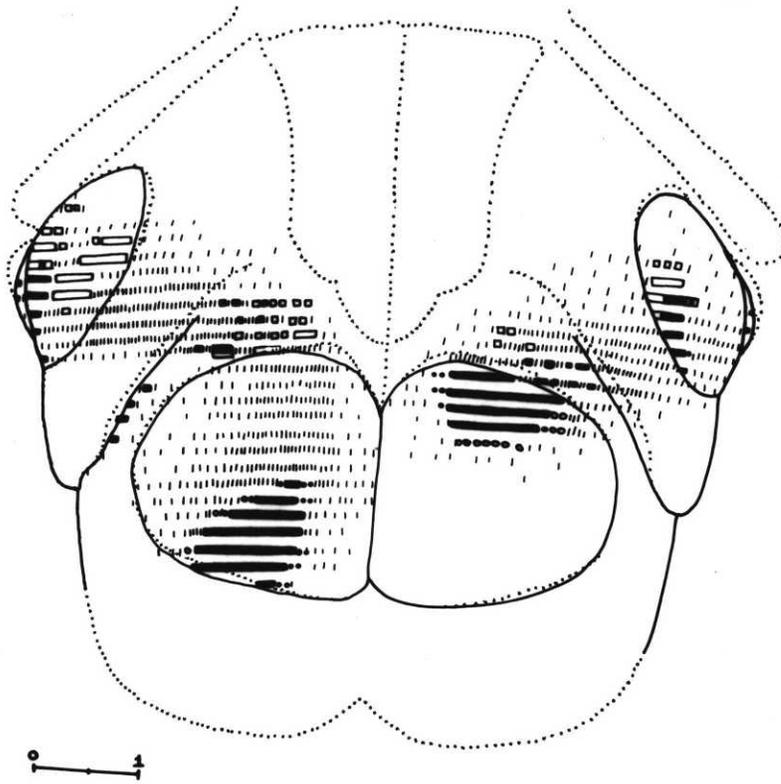
Figure 9:

Charts of cross sections through the lateral geniculate nucleus (LGN) of case HED-11. The upper row is a series of drawings of the LGN contralateral to a lesion at the lower edge of the temporal rectus of the left eye. The lower series of charts represents sections through the left LGN; the charts include degeneration (deep to the optic tract surface) that is ipsilateral to the lesion in the left eye and also degeneration stemming from another lesion in the contralateral (right) eye at the upper edge of the medial rectus. Small lines: degenerating axons; dots: terminal degeneration field. In the upper drawings, it is easier to note how the axons enter the LGN plunging in from the optic tract resulting in a patch of surface degeneration and this continues deep to the tract forming a column that extends medially and anteriorly.
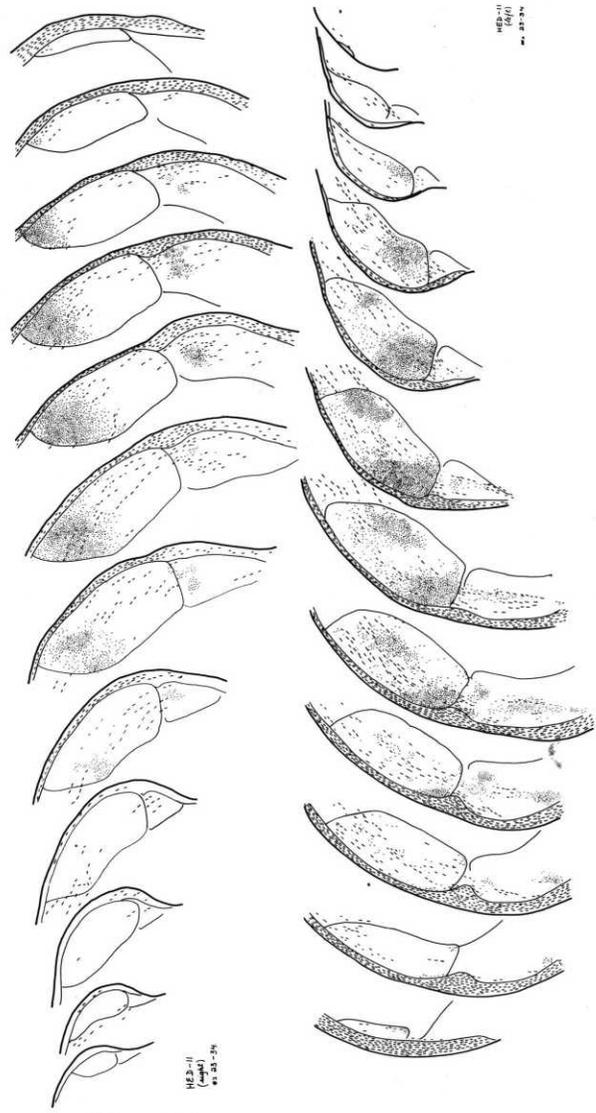
Figure 9

Figure 10:

Composite drawing of lateral (a) and dorsal (b) view reconstructions
from 16 cases of small retinal lesions. The colored regions represent
surface degeneration only as observed in the LGv, LGd and SC (lateral
view) and LGd, SC (dorsal view). The circled star depicts the
estimated position of the optic disc representation in each nuclear
group. The scale is marked in mm. The colored arrows in (b) represent
regions where the degeneration does not reach the dorsal part of the
SGS but is found in the curled medial wall of the SGS.

Figure 10

HED-11 (L)		HED-23 (2)	
HED-11 (R)		HED-24	
HED-19		HED-25	
HED-20		HED-26	
HED-21		HED-28	
HED-22		HED-29	
HED-23 (1)			

a

b
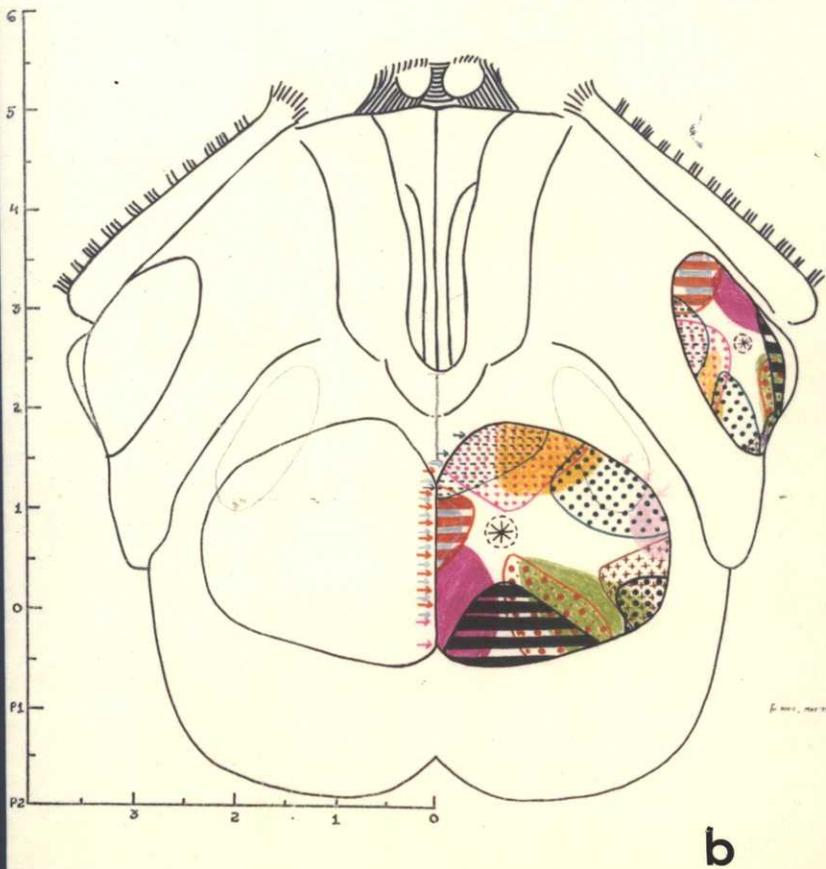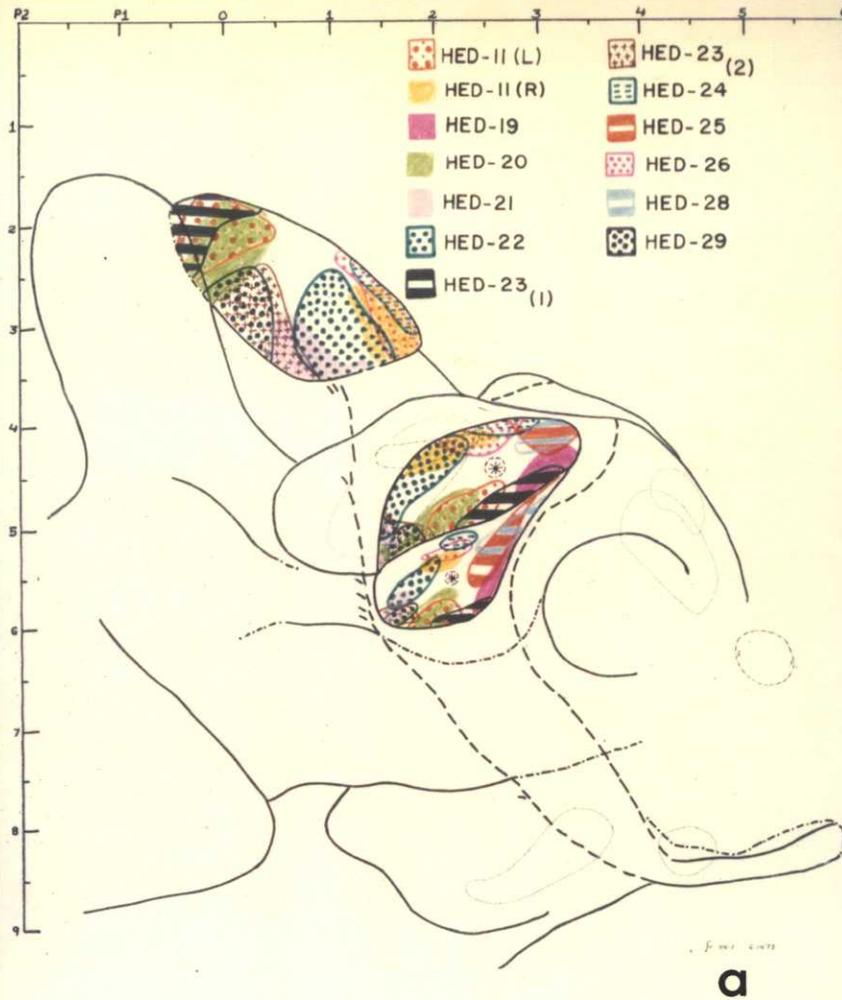
Figure 11:

Reconstructions of case 47-3. The animal has suffered bilateral
lesions of the rostrolateral tectum on the day of birth, was allowed
to live to adulthood, and 5 days before sacrifice, small retinal
lesions has been placed in the nasal retina (lower edge of medial rectus)
of both eyes. The optic tracts have not been fully reconstructed
due to tissue damage in the course of histology. Symbols used are
the same as in figure 7.

(a) Lateral views of the left (L) and right (R) lateral geniculate bodies
of case 47-3, both geniculates represented on a reconstruction drawing
of the right geniculate (dots) in order to enable comparison with
controls. The degeneration from the nasal retina of each eye is seen
ventrally in the LGv and LGd. The axons terminate near the OT surface
caudally in these nuclei and are seen to travel rostrally and medially
(open bars) forming projection columns.

(b) Dorsal view reconstruction of the brainstem of same case, indicating
the size of the remnant SGS and the degeneration pattern ensuing from
the adult nasal retinal lesions. In dorsal view, the major termination
pattern in the SC on both sides is distributed over a wedge-like area
in the caudal part. The coarse dots represent anomalous termination
that does not extend through the thickness of the SGS but is observed
only on the surface. Discontinuities in the map, with anamolous degenera-
tion patterns are seen rostrally in the left SGS and laterally in the right.
The single-headed arrows indicate sections where terminal degeneration is
seen in the LTN of the accessory optic tract. Double-headed arrow shows
level of section drawn in the transverse plane in figure 14.

a

47-3 (R)

47-3 (L)

47-3

b

surface tissue lost

0   1

Figure 11

95
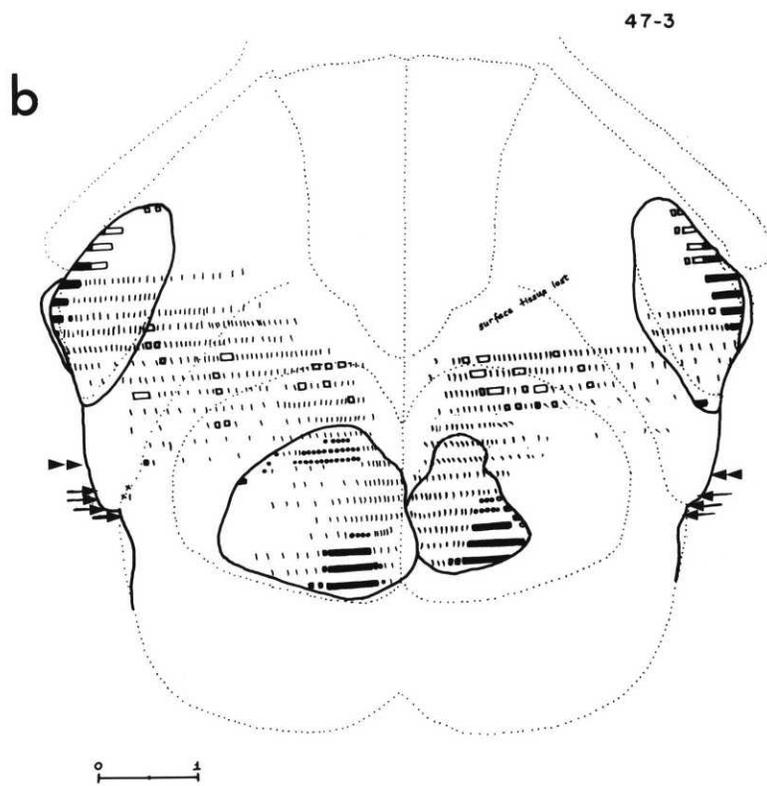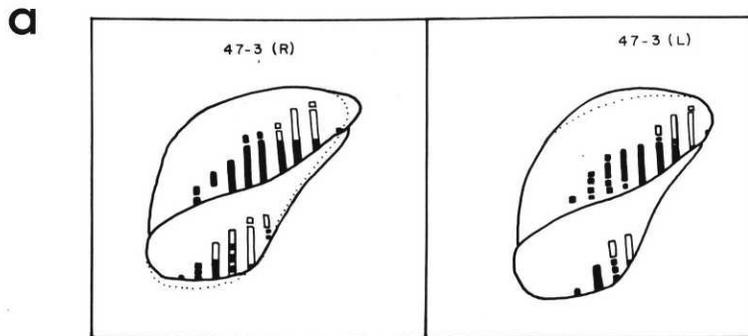
Figure 12:

Analysis of case 47-3, right side.   Scale in mm.

(a)   The areas of surface degeneration resulting from the lesion

in the left eye has been represented (dots) on a lateral view

drawing of the LGB.   Also included are the outlines of areas

of surface degeneration from control cases HED-11, HED-19,

HED-23, with retinal lesions close to that of 47-3.   The

circled star indicates position of optic disc representation

on the LGB surface.

(b)   The outline of a normal SC dorsal view is drawn with heavy

lines.   Superimposed on this, are outlines of areas of degeneration

seen in the SGS of control cases HED-11, HED-19, HED-23.   Using

figure 12(a), a control has been estimated (stripes) for a normal

animal having suffered a retinal lesion similar to that in the

left retina of case 47-3.

(c)   Dotted outline of a standard SC dorsal view is indicated with

the area of surface degeneration (stripes) estimated in figure 12(b).

Superimposed on this is the outline (heavy line) of the right SC

as seen in the dorsal view reconstruction drawing of case 47-3

(see figure 11(b)), along with the wedge of degeneration (stipples)

resulting from the retinal lesion in the left eye.   This figure

allows a comparison of the degeneration seen in the SC of 47-3 with

the estimated extent of degeneration expected from the same

retinal lesion in a normal adult hamster. The wedge of terminal

degeneration in the experimental animal is smaller than that

expected in a control animal unoperated at birth.

(d) Same as figure 12(c) except that the outline of the SC of case

47-3 has been translated caudally so that its posterior edge lines

up with the edge of the control SC. This procedure compensates

for the flopping forward of the SGS into the space "vacated" by

the ablated SGS.

Figure 12

(a)

(b)

(c)

(d)

47-3(RIGHT)

47-3
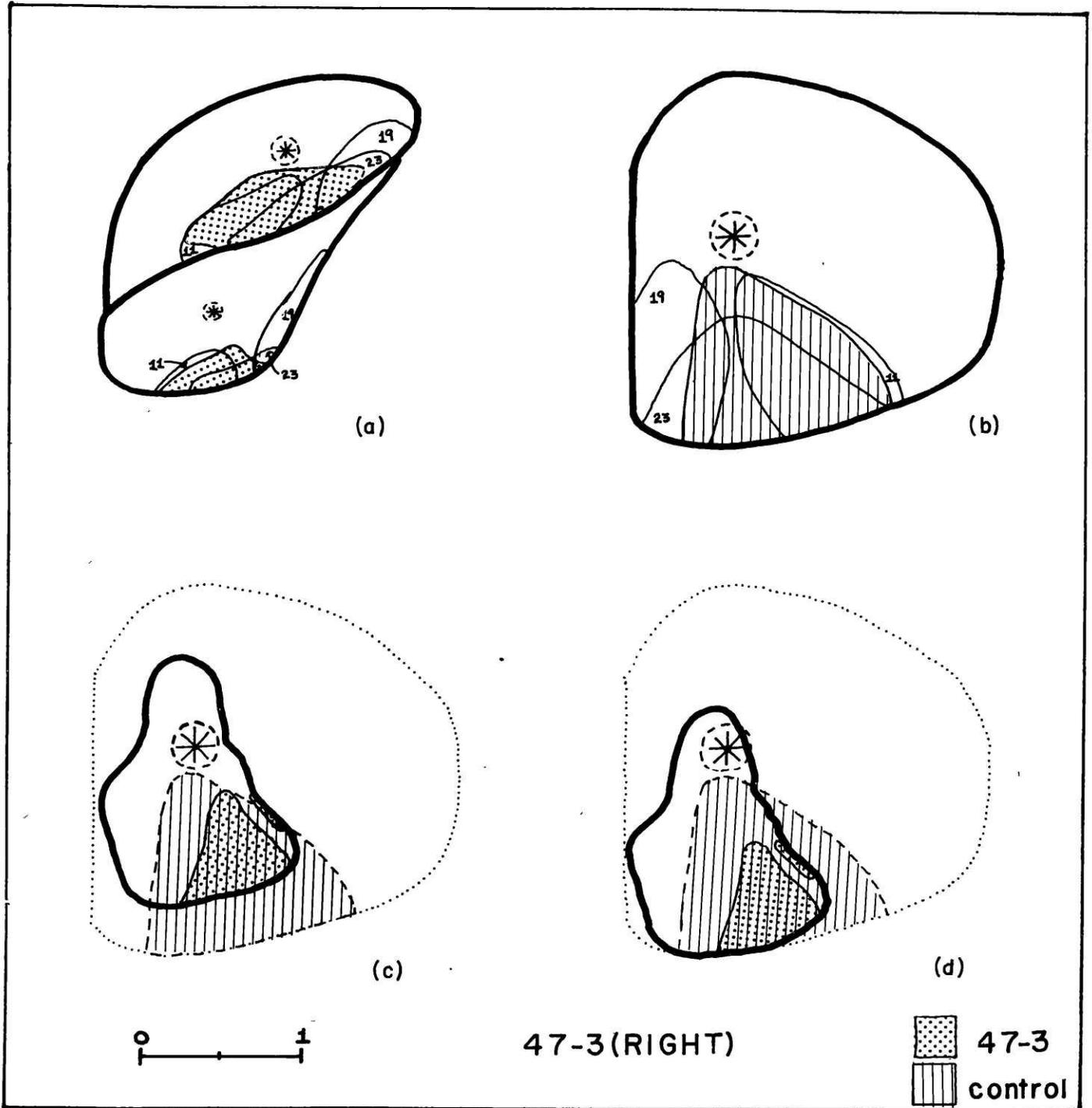
control

Figure 13:

Analysis of case 47-3, left side. Scale in mm.

(a) Lateral view of standard LGB (heavy lines). The surface
degeneration seen in the LGB of case 47-3(L) (stipples) is compared
with that in control animals HED-11, HED-19 and HED-23. The optic
disc representation is indicated by the circled star.

(b) Using the degeneration areas in the LGB as shown in figure 12(a),
an estimation has been made (stripes) of the extent of degeneration as
seen in the dorsal view of the SGS of a control animal having suffered
the same retinal lesion as case 47-3. The wedge of degeneration
estimated is drawn relative to the degeneration as seen in control
cases HED-11, HED-19, HED-23. The degeneration from the control cases
is displayed on a standard dorsal view of the SGS of the left colliculus
to facilitate comparison with 47-3.

(c) The dotted outline represents a standard dorsal view outline of
the left SGS with the estimated wedge of degeneration from figure 12(b)
indicated by stripes. Superimposed on it in heavy line is the reconstructed
outline of the left SGS of case 47-3, including the tongue of
degeneration (stipples) resulting from the lesion in the nasal retina
of the right eye, incurred in adulthood. The patch of degeneration in the
rostral part of the SGS as seen in figure 11(b), has been omitted.

Figure 13

(a)

(b)

47-3
control

47-3 (LEFT)

(c)
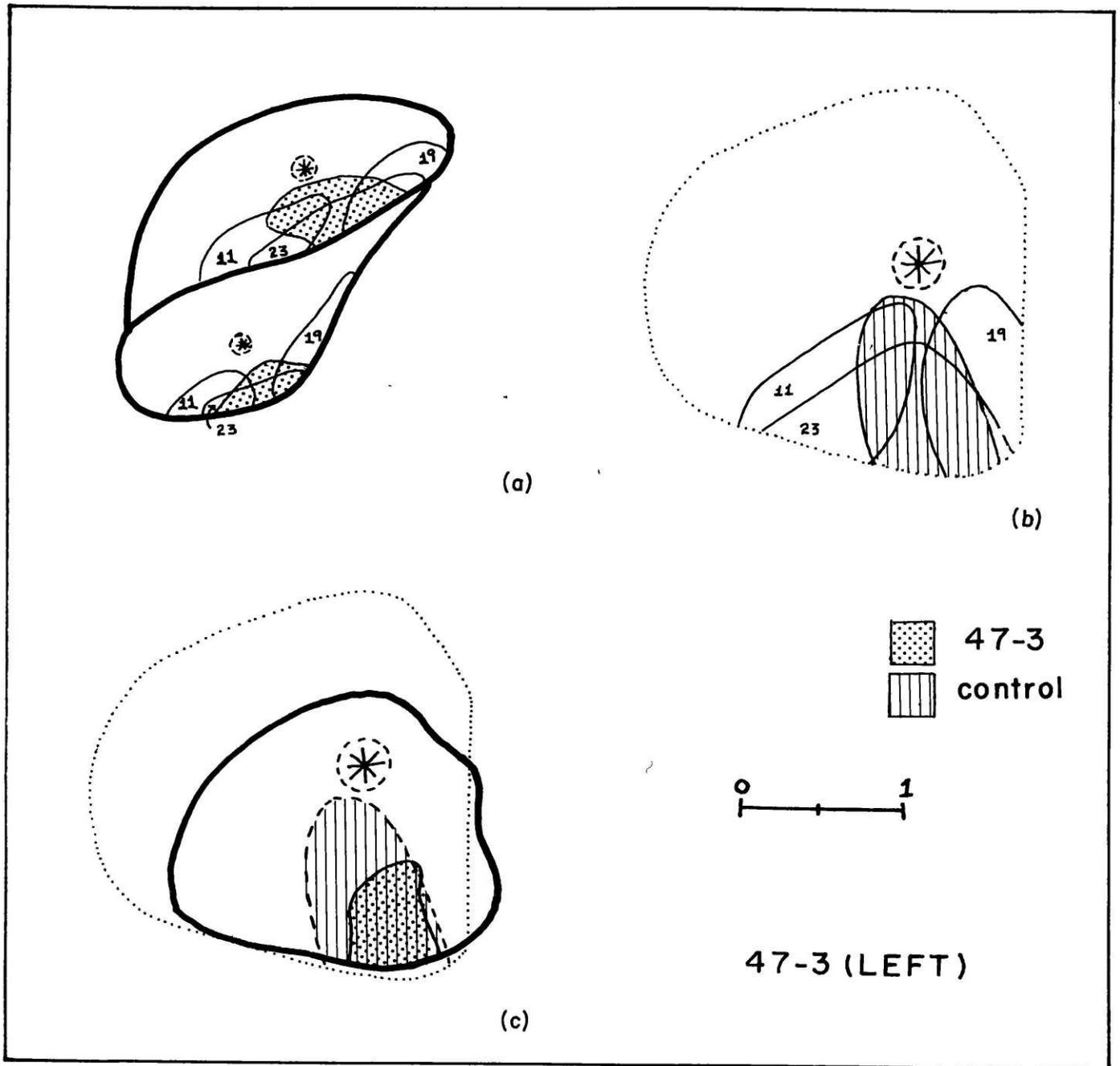
Figure 14:

Cross section through the rostral midbrain of case 47-3 showing the abnormal pattern of axonal degeneration in the left stratum opticum (short lines), consequent to a lesion in the nasal retina of the adult animal. (The animal had suffered a bilateral lesion of the rostrolateral tectum on the day of birth.) The majority of the degenerating fibers are coursing caudally to terminate in a wedge of degeneration as shown in figure 11(b). However, some fibers are deflected and distribute themselves to form the anomalous patch of terminal degeneration (indicated by dots) in the SGS. A more normal pattern of axonal degeneration is seen on the right side of the same section.
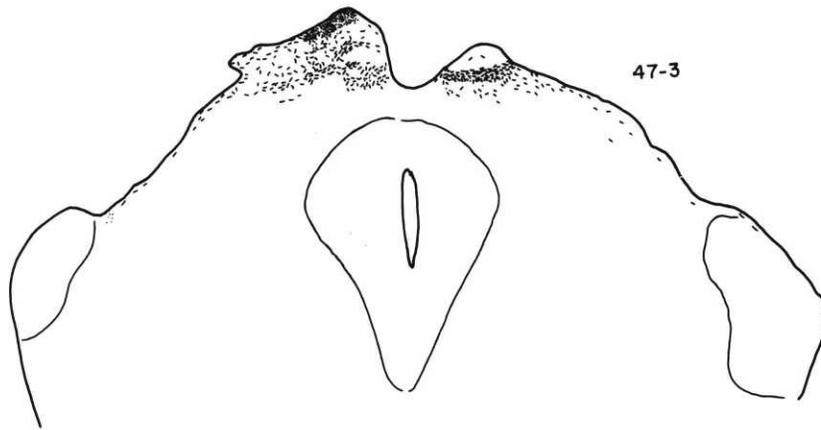
Figure 14

Figure 15:

Dorsal view reconstruction (continuous lines) of case 47-2 superimposed on a standard dorsal view drawing of the hamster brainstem. The animal had suffered a bilateral ablation of the rostrolateral tectum on the day of birth and discrete lesions in the temporal retina of each eye in adulthood. The undamaged SGS has flopped forward into the space vacated by the ablated tissue; consequently, the undamaged caudal edge of the SGS is shifted anteriorly with respect to the caudal edge of the standard. The same forward movement is seen for the inferior colliculus.

Indicated on the dorsal view drawing is the degeneration consequent to the retinal lesions as seen using the Fink-Heimer stain. Symbols are the same as for figure 7. The deep degeneration (open bars) in the LGd on both sides includes not only the anteromedial column of projection consequent to lesion in the contralateral eye, but also the ipsilateral projection from the temporal retina of the respective homolateral eye. The termination in the rostral part of the SC is abnormal since there is no SGS and the degeneration is found in the area of ablation. Much termination in this region is subjacent to the optic tract. Anomalous patches of degeneration are also observed in the SC on either side. The arrows indicate the level at which the chart in figure 20 was taken.

47-2
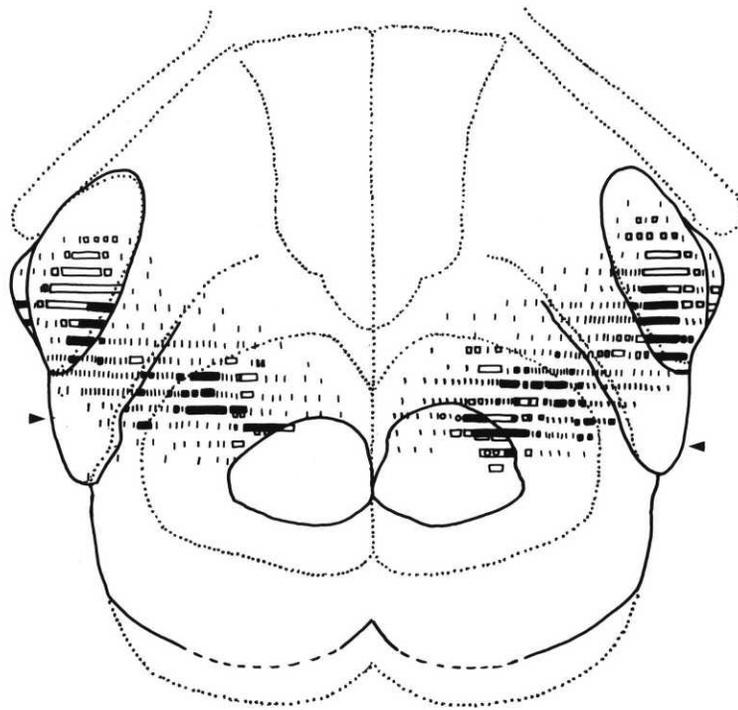
Figure 15

Figure 16:

Lateral view reconstructions (continuous lines) of the left (a) and right (b) sides of case 47-2, superimposed on standard lateral view drawings (dotted lines). Both sides have been reconstructed on a standard view of the right side. The rostrolateral tectum was ablated bilaterally on the day of birth and discrete lesions were made in the temporal retina of each eye in adulthood. The dorsal view of the same case is presented in figure 15. The retinal lesion corresponding to (a) is more peripheral than that for (b). Degenerating OT fibers can be followed up the lateral surface of the brainstem on both sides and their termination traced to the dorsal part of both nuclei of the LGN. Also indicated in each nucleus is the ipsilateral projection from the temporal retina lesions. Terminal regions are also observed in the LP, PrT and the rostral SC. Degenerating fibers and terminals are noted in the LTN, transpeduncular tract and the MTN at the base of the peduncle (see especially (b)). Symbols same as for figure 7. Scale is in mm.

Figure 16

a
47-2(LEFT)

b
47-2 (RIGHT)
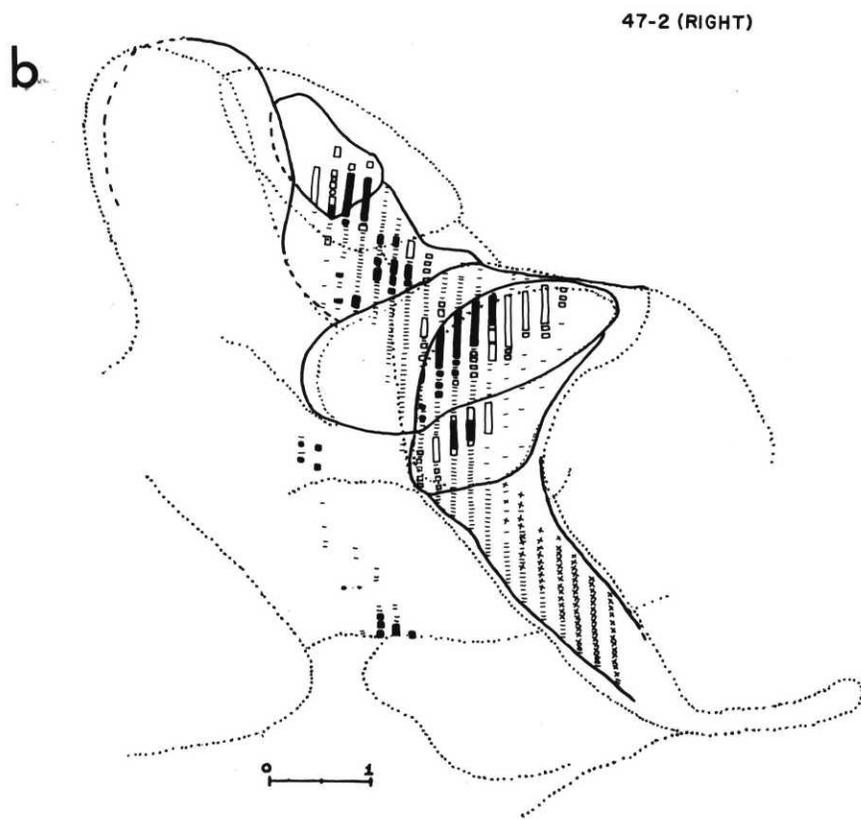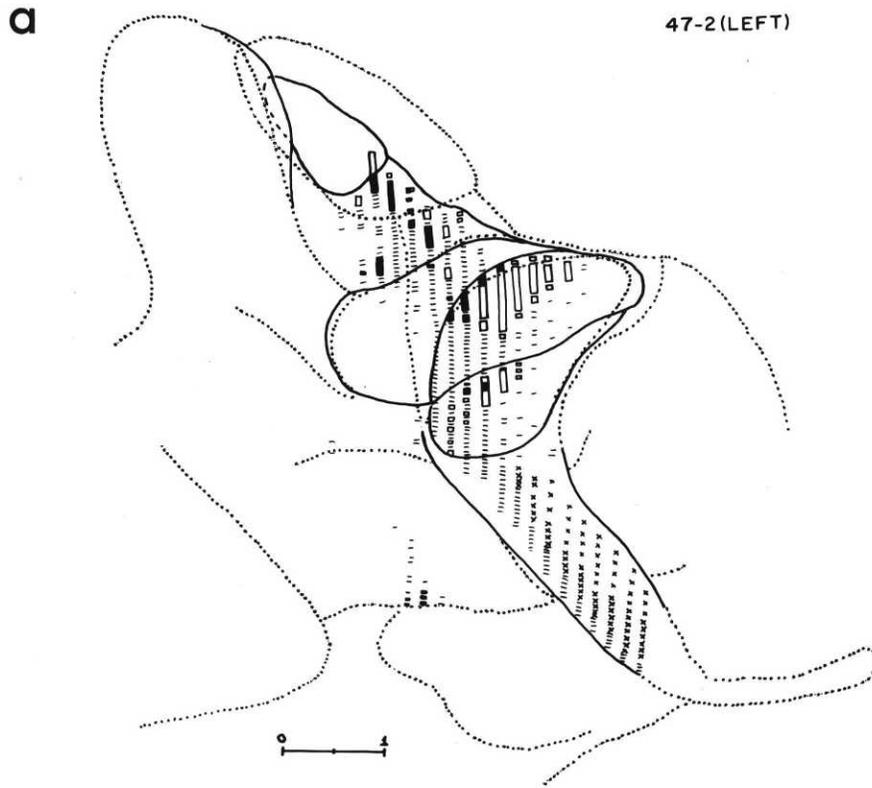
Figure 17:

Reconstruction drawings of the brainstem of control case HED-22, an
adult animal, that has a discrete lesion in the temporal retina (upper
edge of lateral rectus) of its left eye 5 days prior to sacrifice.

(a) Dorsal view reconstruction (continuous lines) of the brainstem,
superimposed on a standard reconstruction drawing. The SGS in HED-22
is somewhat smaller in extent than the standard. The degenerating
fibers of the right optic tract course over the surface of the brainstem,
terminate in the LGN (see b)), and pretectum, and form a wedge of
degeneration in the rostrolateral part of the SGS. The ipsilateral
optic tract and its areas of termination are seen on the left side.

(b) Lateral view reconstruction of the right side of HED-22. Optic
tract fibers from the lesioned temporal retina are seen to course over
the lateral surface of the brainstem. The first way-station for these
fibers is in the LGv, where they terminate in the dorsocaudal edge
(black bars) with a rostromedially directed tongue of degeneration
(open bars). The same picture is seen more clearly in the LGd. The
fibers are next seen to cross over the LP, and terminate in the pre-
tectal region and finally in the SGS of the rostral colliculus.
Symbols same as for figure 7. Scale: 1mm.

Figure 17

a

b

108
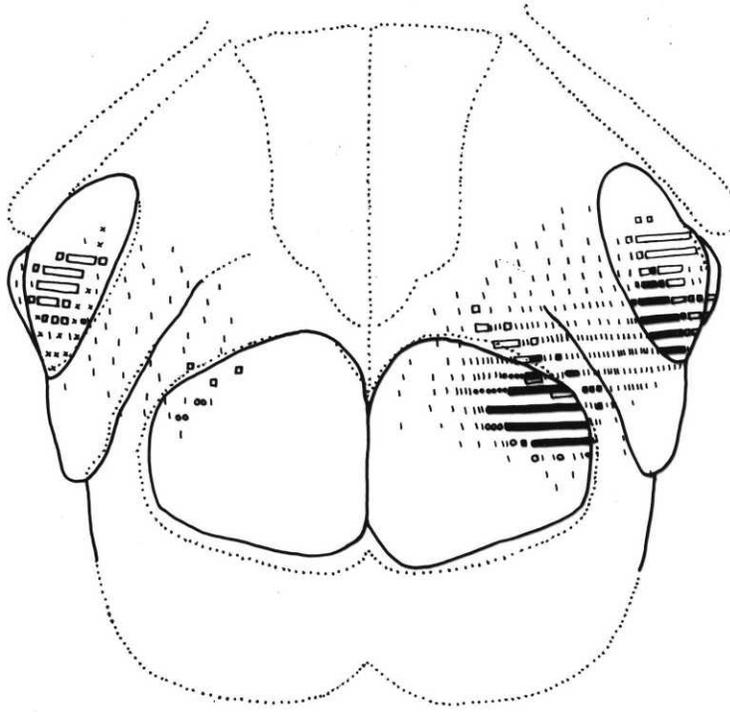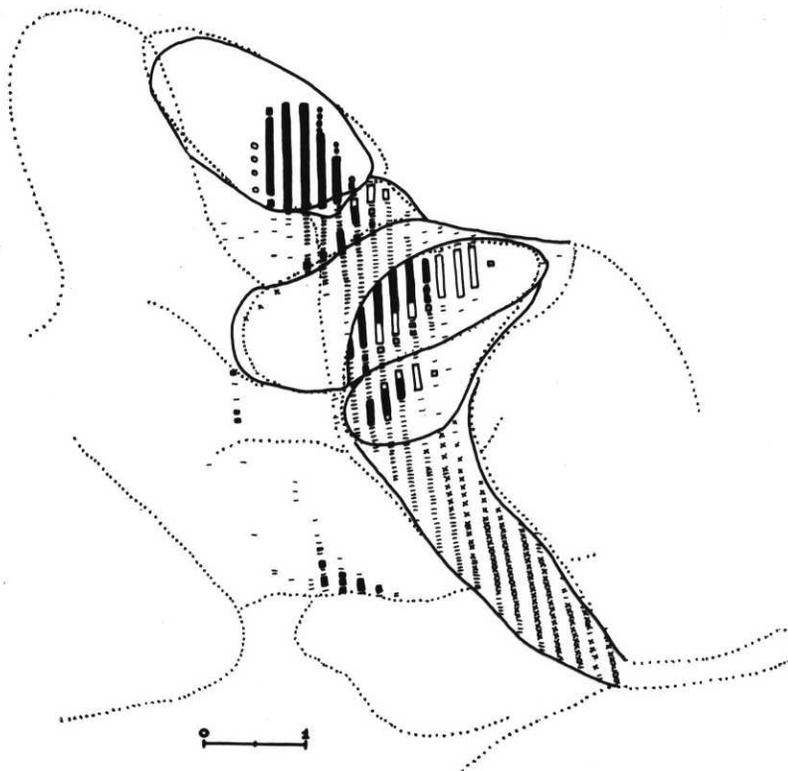
Figure 18:

Analysis of case 47-2, right side.

(a) Lateral view drawing of the LGB. Included in the drawing are
the areas of surface degeneration for the right side of 47-2 (stipples)
and HED-22 (stripes). The retinal lesions in the two cases are similar,
that for HED-22 being somewhat larger and extending slightly further
into the upper retina. The optic disc representation is indicated.

(b) Dorsal view of the SC of HED-22 (dotted line), on which is indicated
the extent of degeneration resulting from the lesion in the temporal
retina of the left eye (stripes). Superimposed on this control, is the
SGS (reconstructed in dorsal view) from case 47-2, and the degenerated
optic tract terminations resulting from a lesion in the temporal retina
of the left eye of this animal. Some termination areas lie outside the
SGS, in the deep tectal layers subjacent to where the optic tract
travels over the damaged rostrolateral tectum. Comparing the areas
of degeneration for 47-2 and HED-22, it can be seen that the termination
in SGS is further toward the optic disc representation even though
figure 18(a) indicates that the lesions are fairly comparable.

(c) A comparison similar to that in figure 18(b) except that the SGS of
47-2 has been translated caudally to compensate for the forward flopping
of the tissue following the neonatal lesion. The deep termination in the
rostrolateral tectum is omitted.

Figure 18
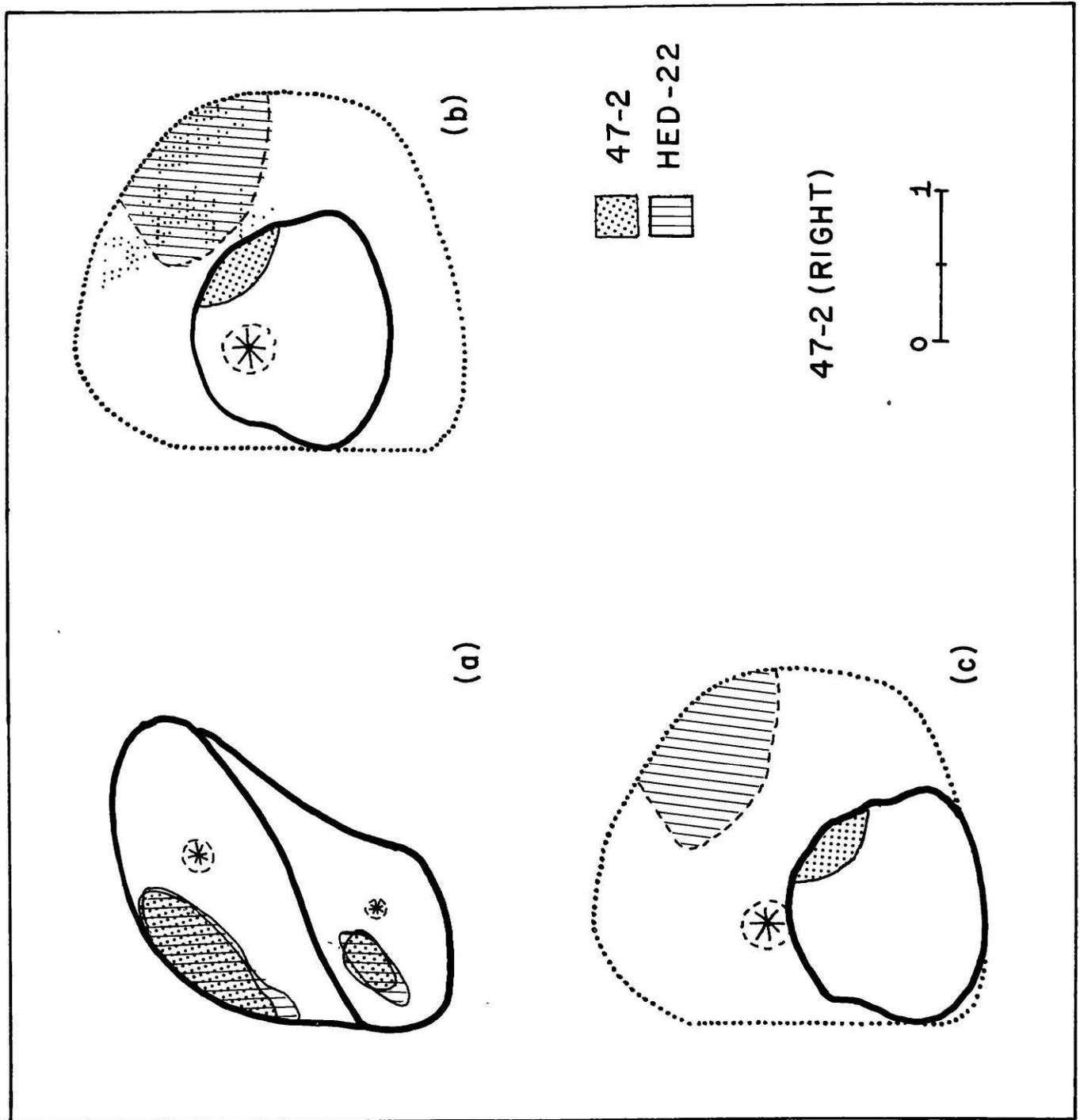
Figure 19:

Analysis of the left side of case 47-2, comparing it with control case
HED-22.

a) Lateral view of the standard right LGB, (heavy lines). Superimposed
on the outline are extents of surface degeneration from HED-22 (stripes)
and 47-2 (dots). It is obvious from comparing the extent of degeneration
in HED-22 with that in the experimental case 47-3, that the retinal
lesion for HED-22, is much larger and extends further toward the optic
disc than does the lesion in the right retina of 47-2.

b) Comparison of the degeneration in the colliculus of HED-22 (stripes,
indicated on a reconstruction of the left colliculus to allow comparison)
with that in 47-2 (dots). The outline of the SC is indicated by a
dotted line for HED-22 and a continuous heavy line for 47-2. Although
the retinal lesion in HED-22 extends further centrally (see figure 19(a)),
the degeneration in the colliculus is seen to reach further centrally
in the SC of case 47-2.

Figure 19

(b)

(a)

47-2(LEFT)

47-2

HED-22
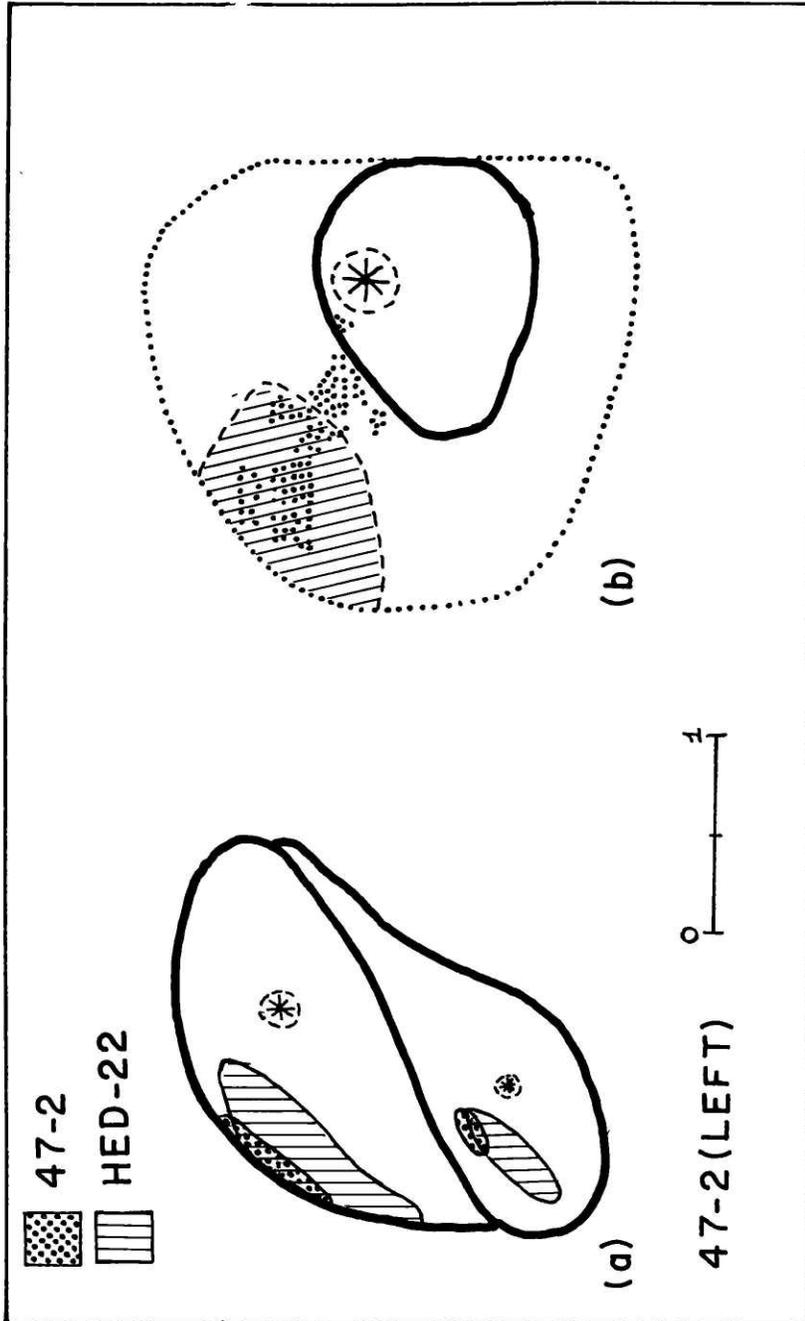
Figure 20:

Cross section through rostral SGS of case 47-2, to show the pattern
of degeneration. The anteroposterior level of the section is
indicated on the dorsal view drawing of this case (see figure 15).
On the right side, the optic tract termination (dots) is patchy
and the degenerating fibers in the stratum opticum (short lines) is
seen to be disorganized. On the left side, the SGS is free of
termination, but terminal degeneration is found deep to the optic
tract fibers. The extent of degeneration in the dorsoventral
direction is not very great – thus the total volume of degeneration
is small (see text).

47-2
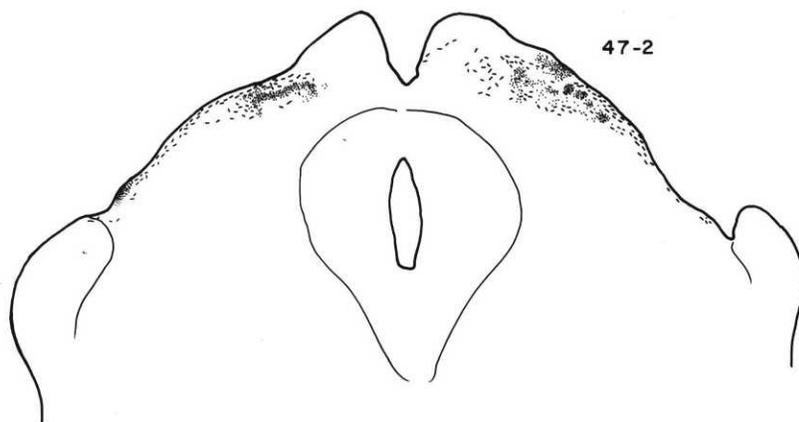
Figure 20

Figure 21:

Figures to show interpretations of data:

Box 1(a). Schematic drawings of SC. On the left is a dorsal view of a normal SC with four bundles of optic tract axons (1,2,3,4) terminating in rostrocaudal topographic order in the SGS. On the right is a tectum with the rostral half lesioned at birth (dashed line marks the original, undamaged SC). One possible result of this lesion is that the axon bundles (1,2) which are normally fated to terminate in the damaged region now degenerate so that only the fibers which terminate in the intact caudal half survive. The topography of the caudal half tectum remains the same.

Box 1(b) represents the same possibility except that here the axon bundles (1,2) which would normally reach the rostral tectum, instead of entirely degenerating, find terminal space elsewhere e.g. in the LP or in the DTN.

Box 2(a): the drawings schematize another possible result of a rostral tectum lesion. The continuous heavy lines show the outlines of the SGS. The broken heavy lines indicate where the SGS is missing. The topography in the tectum remains unchanged but, in addition to the damage inflicted to the rostral tectum, the entire tectal periphery "shrivels" resulting in a missing projection from the entire retinal periphery.

115

Figure 21 (continued):

Box 2(b): Similar to Box 2(a) except that the axon bundles fated
to terminate in the damaged and "shrivelled" part of the tectum
(1, 4), instead of degenerating, now find terminal space elsewhere
e.g. in the LP or DTN.

Box 3(a_1): Demonstrating one possible formation of a displaced map.
On the left is an intact SC with topographically projecting axon
bundles (1, 2, 3, 4). On the right, the rostral half of the SGS has
been ablated. The bundles 1, 2 no longer finding space available in
the normal termination region, move caudally and end in the intact
caudal tectum, maintaining their positions relative to each other.
Fibers 3, 4 (from the nasal retina) get crowded out and degenerate.

Box 3(a_2): The figure on the left represents a normal tectum with
two "wedges" of degeneration schematizing topographic projections from
nasal and temporal retina. The dots represent a projection from
peripheral retina, +: projection from retina more central to this,
and =: projection from central retina. On the right is a sketch
indicating one possible change in topography subsequent to a rostral
tectum lesion in the neonate animal. The fibers from the temporal
retina compress into the rostral portion of the remnant undamaged
SGS and this forces the fibers from the nasal retina, normally
fated to terminate in the caudal tectum, to relocate. However, the
relocating fibers do not compress but get translated caudally such

Figure 21 (continued):

that   fibers from the peripheral parts of the nasal retina get

crowded out and only the more central retina is represented in the

SGS.   This results in a non-uniform change in topography.

Box 4:   Diagram representing the phenomenon of compression of the

entire retinal map onto the undamaged caudal tectum following

an ablation of the rostral half tectum on the day of birth.

I(a)

I(b)

2(a)

2(b)

3(a₁)

3(a₂)
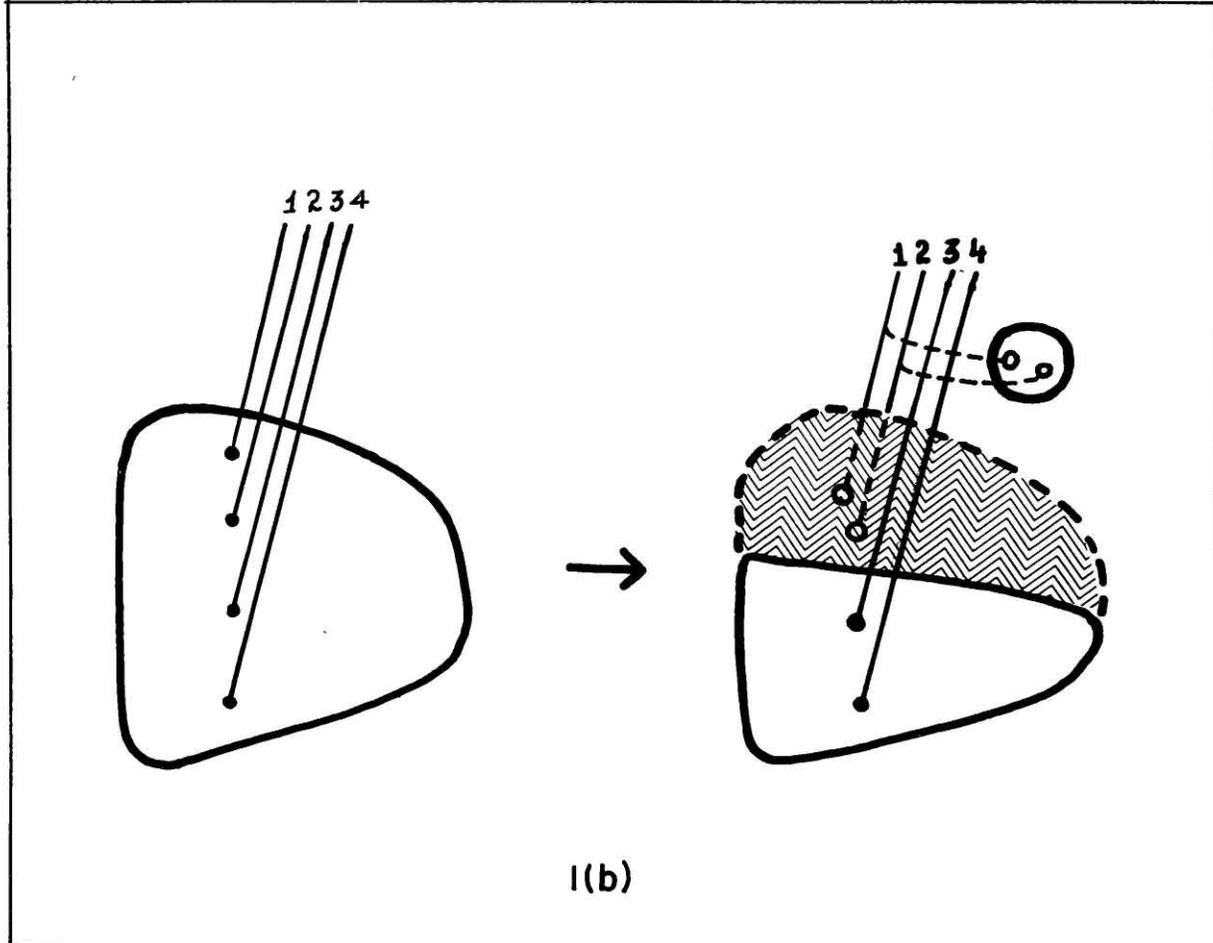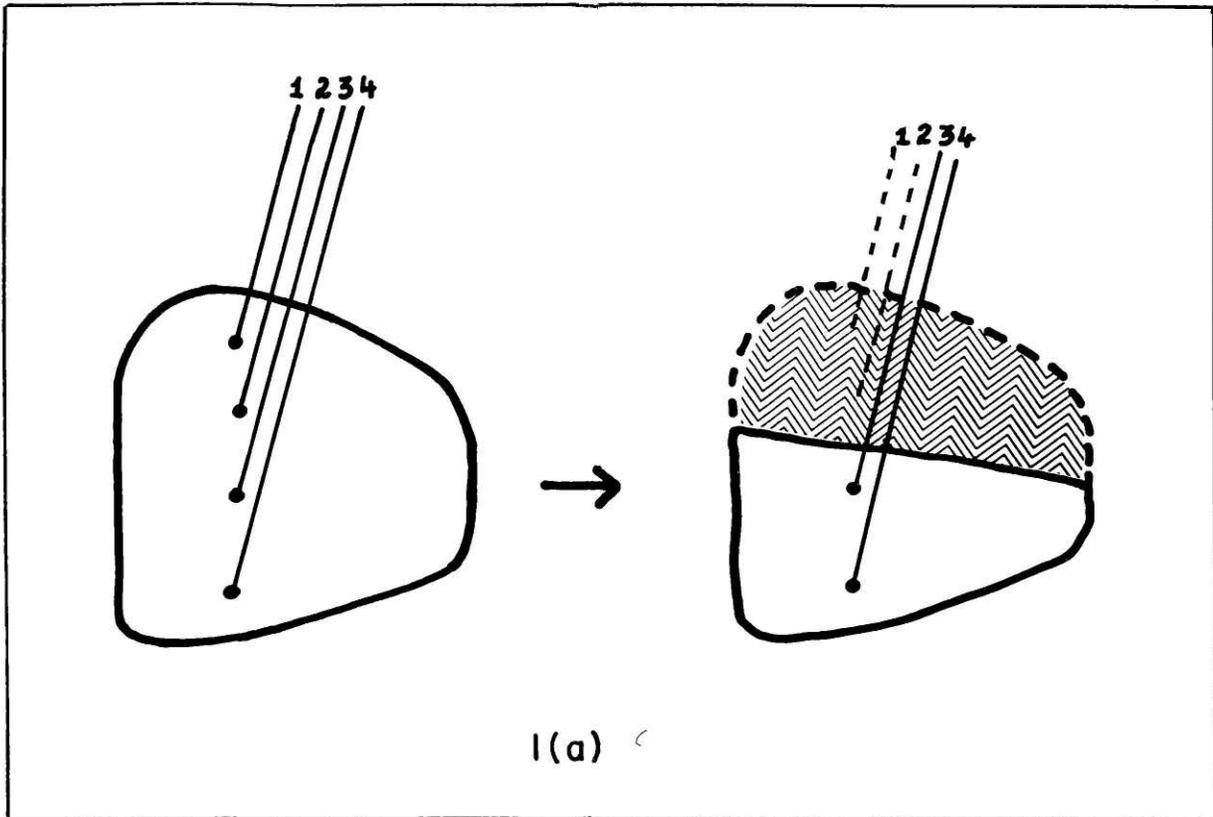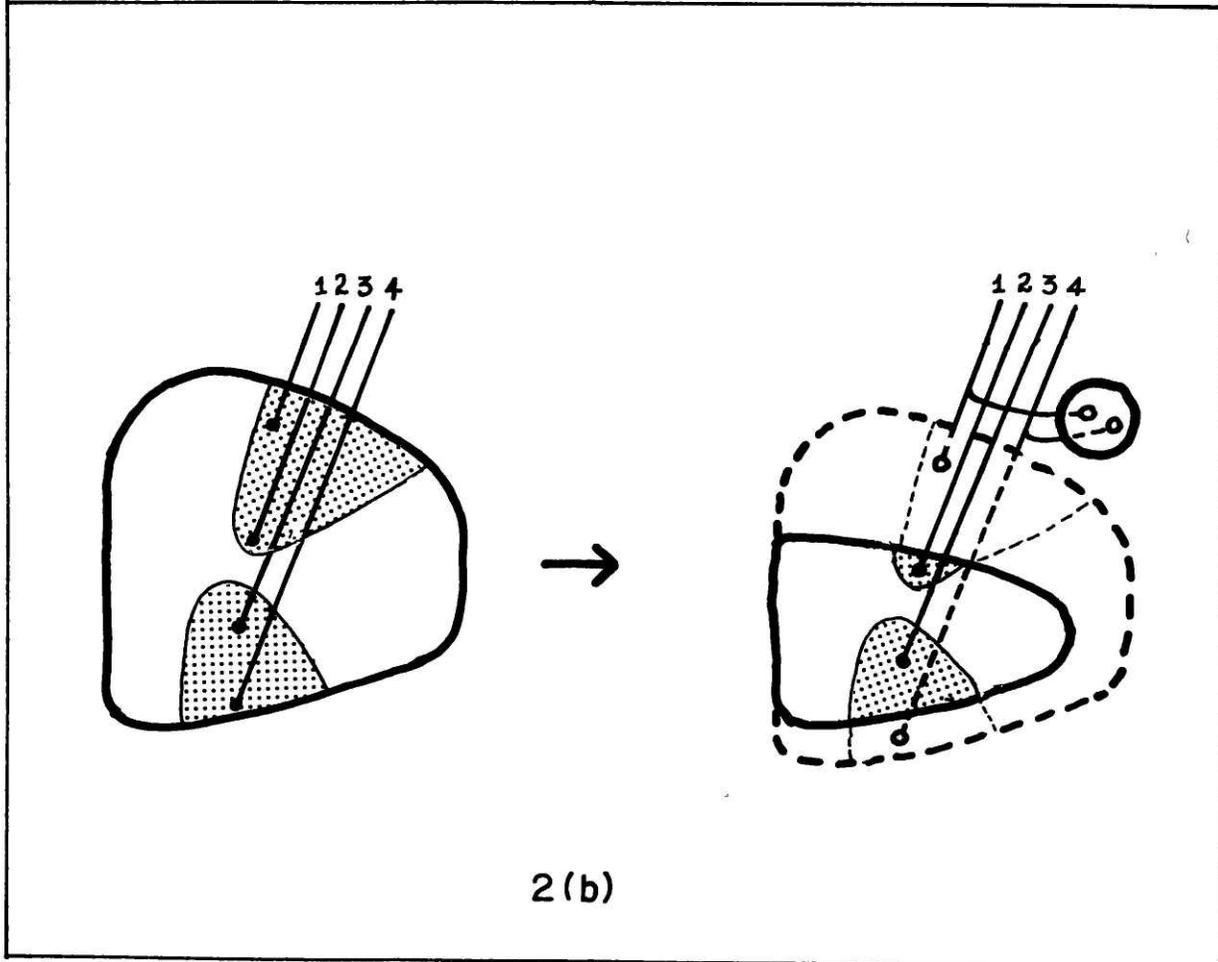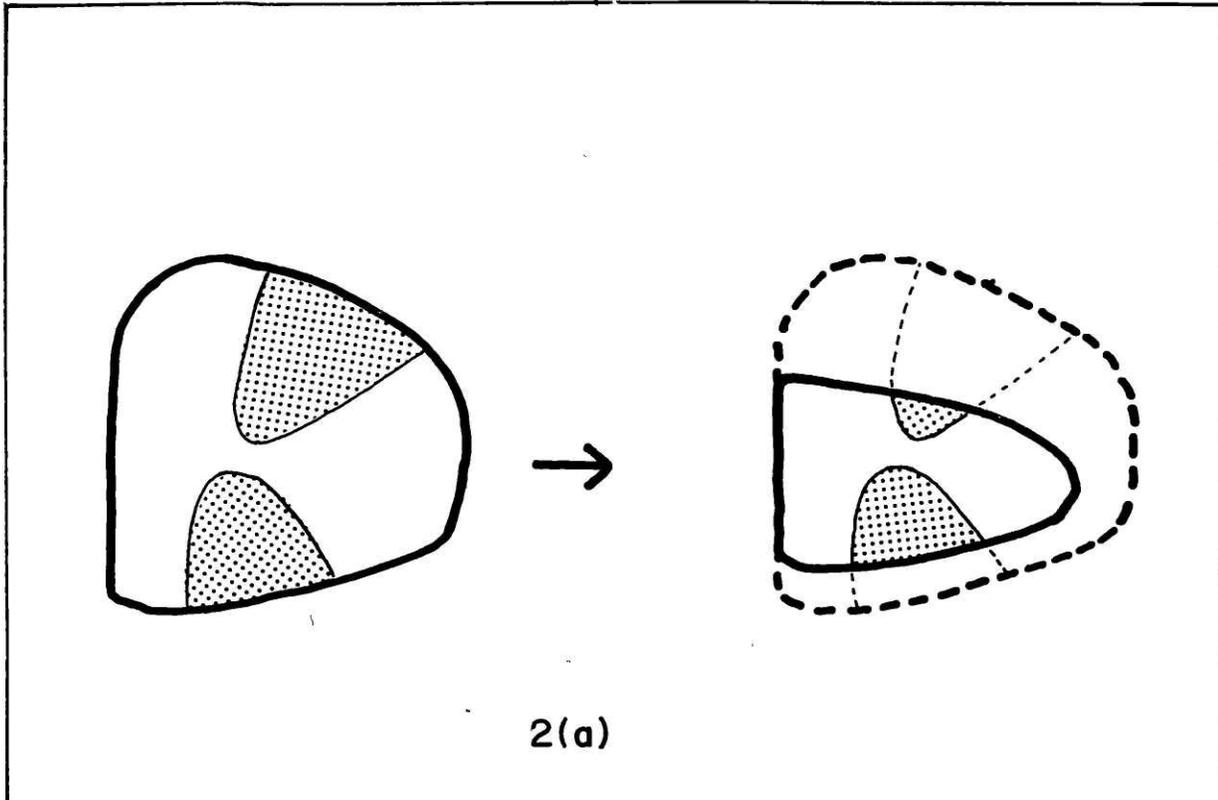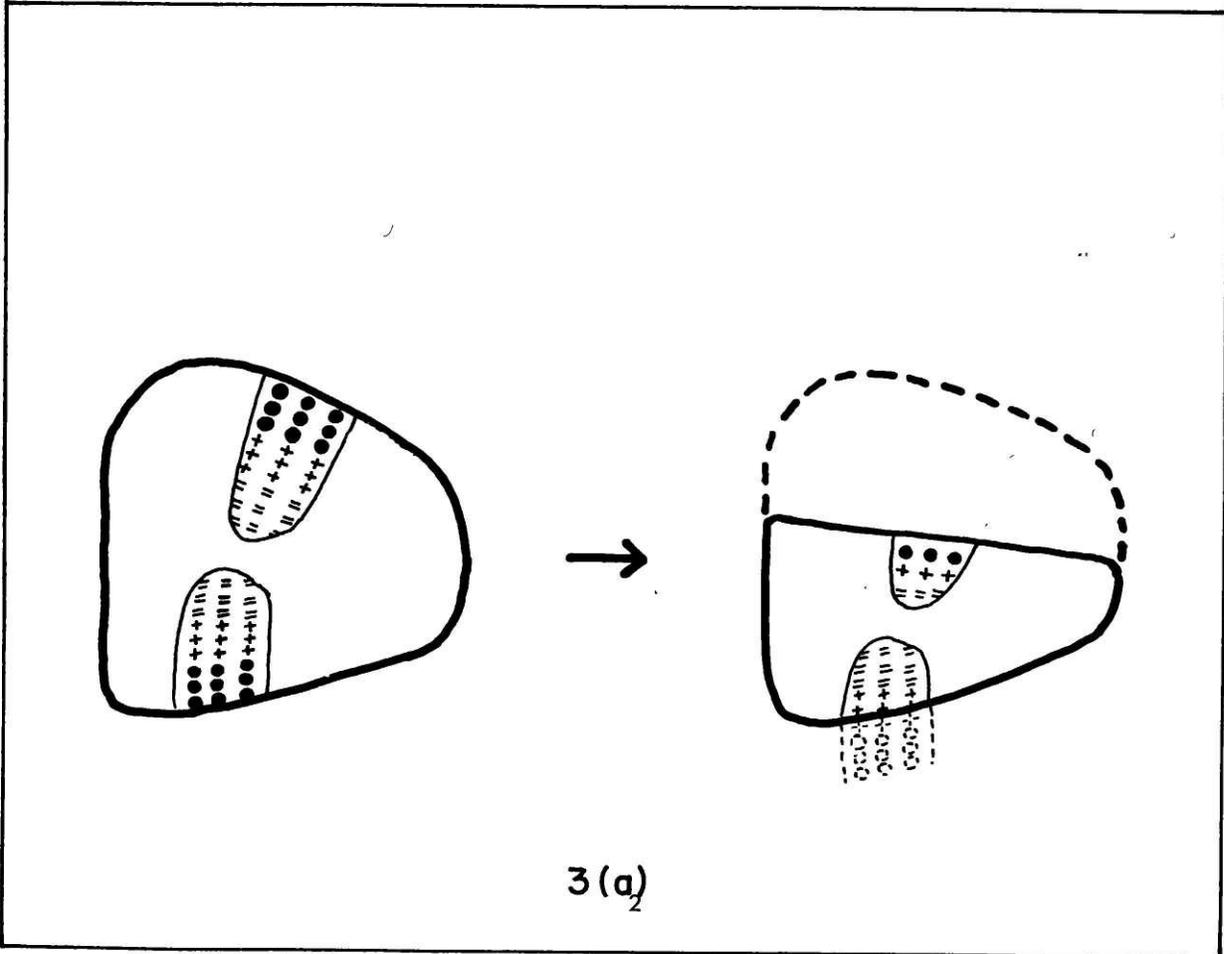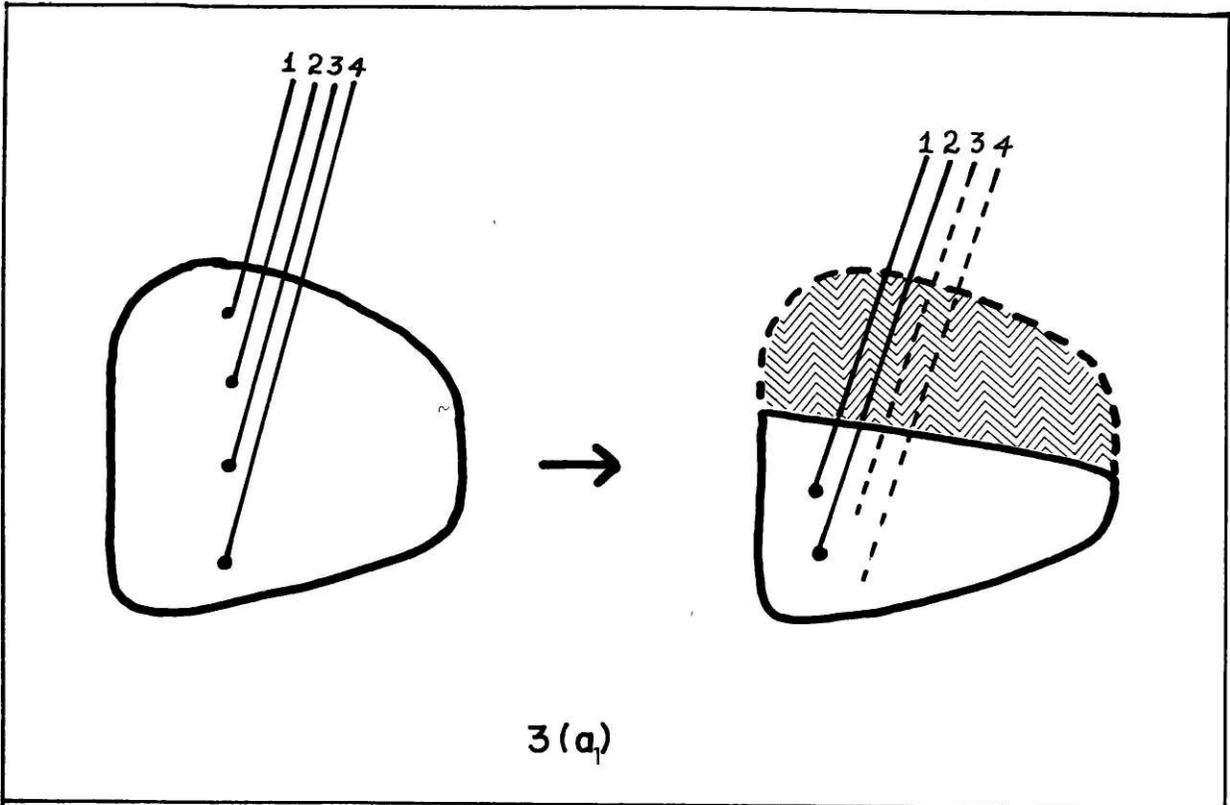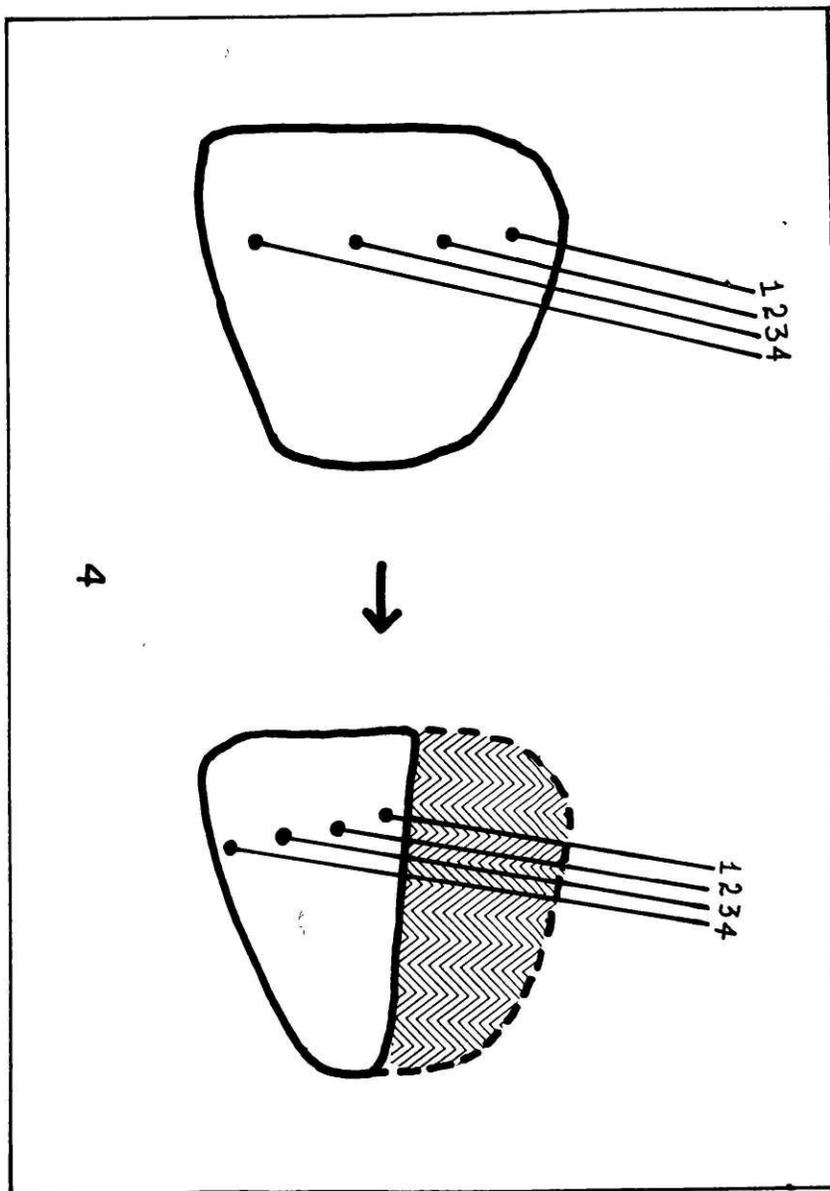
Figure 21d

Figure 22:

Schematic diagrams to test the possibility that the entire periphery

of the tectum has shrivelled. If this were the case then the smaller

extent of the wedge of terminal degeneration in the SGS seen in

most experimental cases, would represent only the central retina, the

peripheral retinal projection missing because of the shrivelled tissue.

To test for this, the central extents of the wedges have been

superimposed for the control and experimental cases. This results in

a superimposition of the SGS outlines in the control and experimental

cases which gives us an idea of what the early tectum lesion would

have had to be in order for this shrivelling to be true. For

example, in (a), doing this test for the left side of case 47-3

and its control (stripes) we find that the early tectal ablation

plus the shrivelling effect would have had to be more extensive

caudally than rostrally in order for the central extents of the

wedges of degeneration to be the same in both cases. The same process

has been repeated for 47-3 (right), 47-2 (left) and 47-2 (right) in

(b), (c) and (d), respectively.

Figure 22

47-3(LEFT)

47-3 (RIGHT)

47-2(LEFT)

47-2(RIGHT)
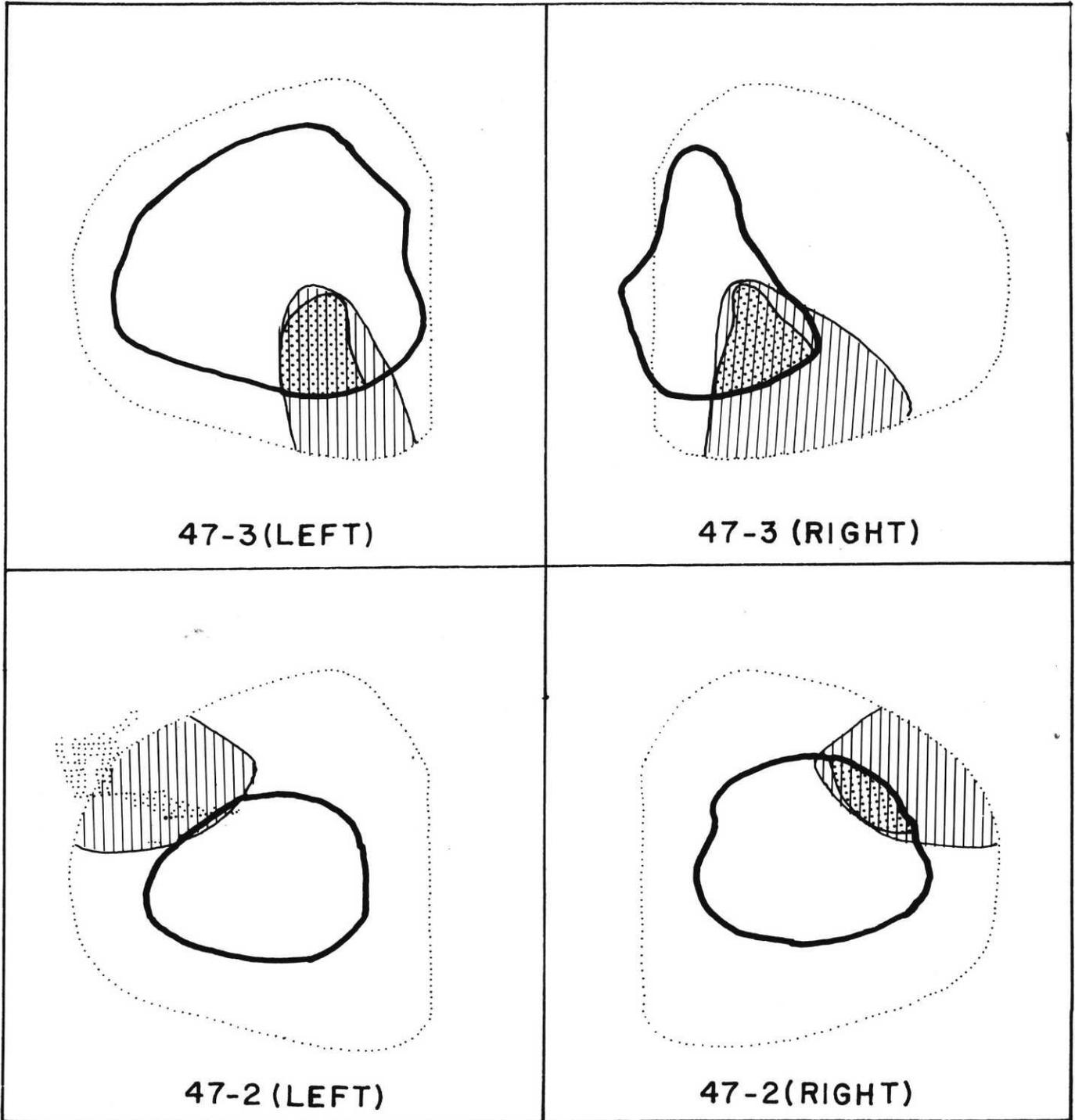
Figure 23:

Dorsal view reconstruction of case 45-2. The animal suffered a
lesion of the rostral tectum on the day of birth, was allowed to
live to adulthood and then discrete lesions were made in the retina
of both sides. On the left side, a small lesion was placed at the
upper edge of the lateral rectus. The right eye had a small region
of the nasal retina (lower edge of medial rectus) lesioned. The
animal was allowed to survive for 5 more days following which the
brain was sectioned at 30μm and stained with the Fink-Heimer method.
Every 5th slide has been charted except in the rostrolateral part of
the right SGS where the irregular degeneration pattern required
charting of sections spaced more closely together. Symbols same
as in figure 7. The arrows on the right indicate the levels at
which the cross-sectional charts for figure 27 were taken. See
text for further detail.
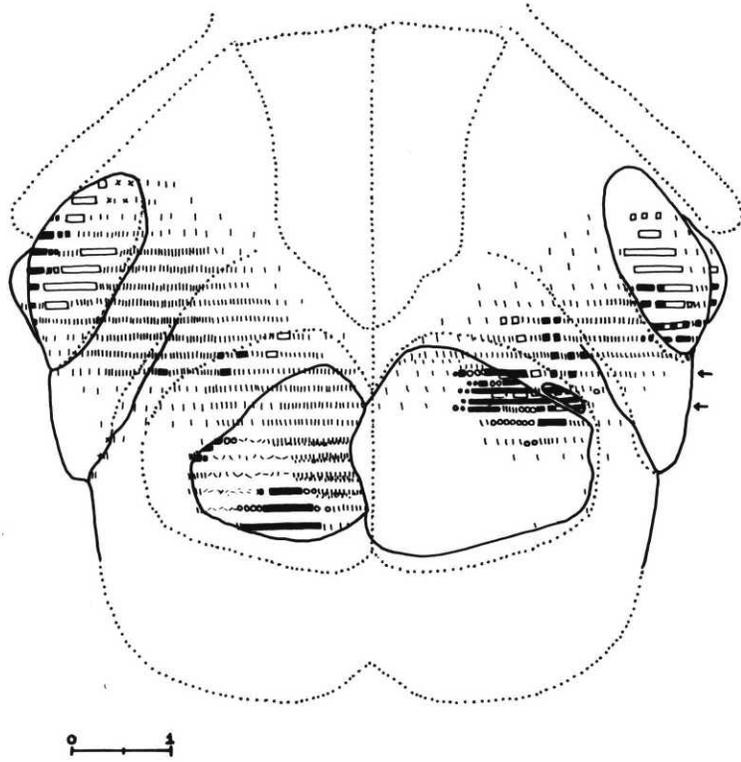
Figure 23

Figure 24:

Lateral view reconstruction drawings of the brainstem of case 45-2
(another animal with an early rostral tectum lesion). The left and
right sides have both been reconstructed (continuous lines) on a
standard lateral view drawing of the <u>right</u> side of the hamster
brainstem (dotted line).

(a) Reconstruction of the left brainstem. The animal had a small
lesion in the nasal retina of the right eye in adulthood. The
degenerating fibers from this lesion can be followed up the surface
of the brainstem and to their columns of termination in the LGd,
LGv, and pretectum. Note that in the LGd and LGv, the open bars
which are not part of the columns of degeneration result from the
terminal degeneration of the ipsilateral optic tract following a
lesion in the temporal retina of the left eye. However, the majority
of the terminal degeneration in the tectum cannot be viewed in a
lateral projection. Only the anomalous patch of degeneration that
reaches the lateral surface of the SGS has been indicated here. Also
included on the figure is the degeneration seen in the accessory optic
tract and its nuclei.

(b) Drawing of the lateral view reconstruction of the right side of the
brainstem of 45-2, showing the pattern of degeneration resulting from a
discrete lesion in the temporal retina of the left eye. The ipsilateral
degeneration has been indicated in (a). Columns of degeneration can be

Figure 24 (continued):

noted in the LGB being on the surface caudally (dark retcangles) and

coursing anteriorly and medially (open bars). Note that the pattern

of termination in the SC is very disorganized as has also been

shown in figures 23 and 27.
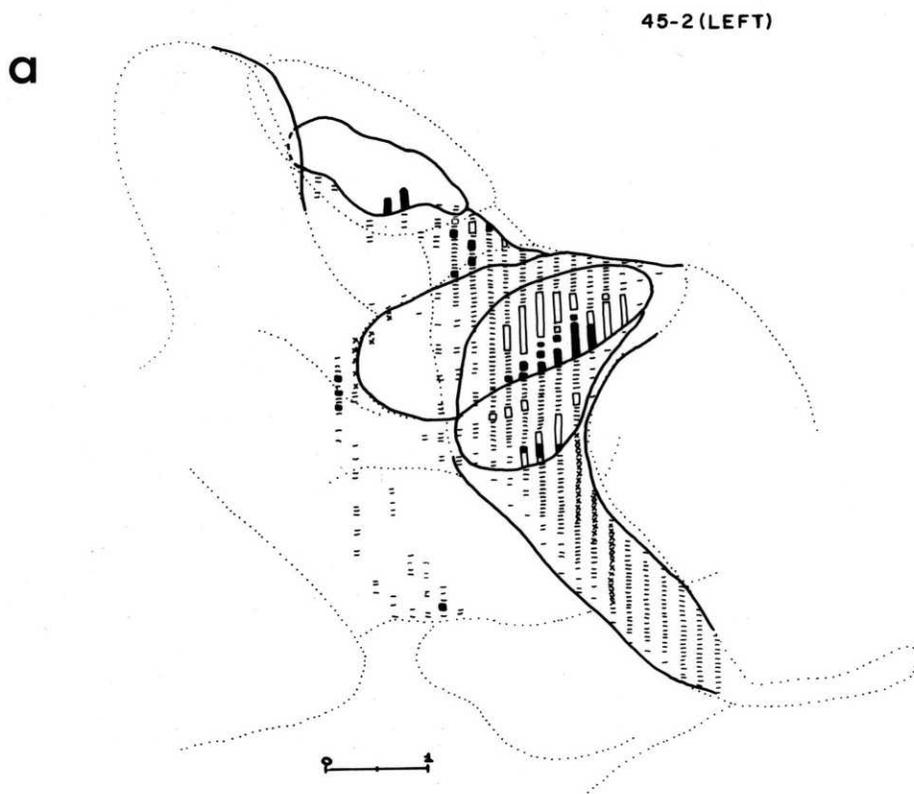
Figure 24

45-2(LEFT)

a

45-2(RIGHT)

b

128
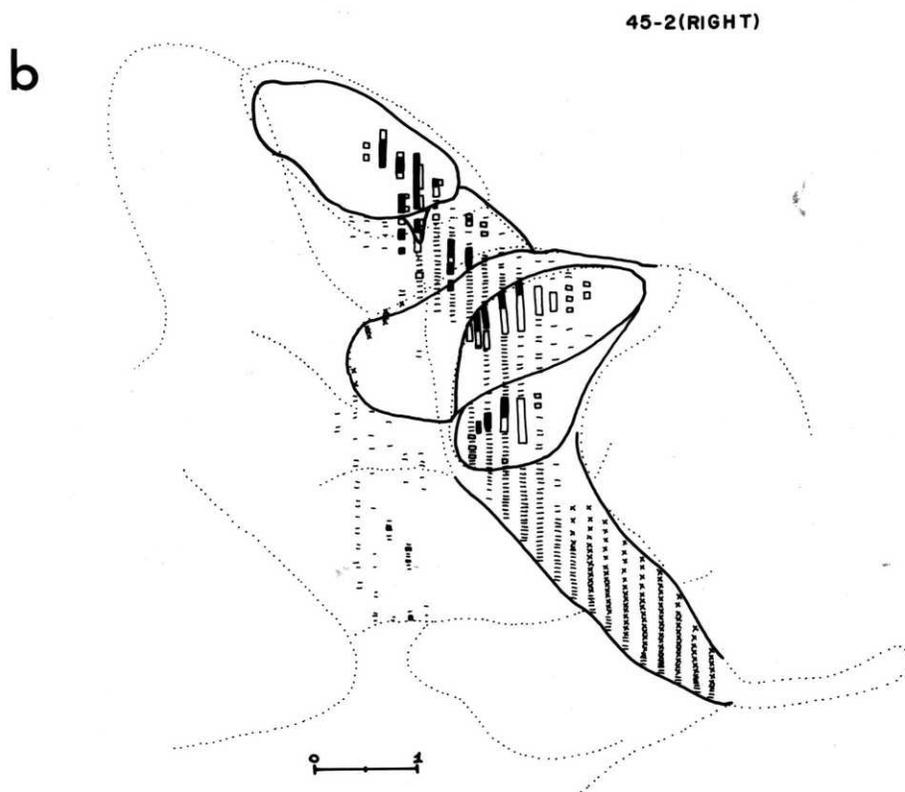
Figure 25:

Analysis of the left side of case 45-2. In these drawings the heavy outline represents the reconstructed experimental case and the dotted lines indicate the outline of the standard SC in dorsal view. The circled star indicates the position of the standard optic disc representation.

(a) Lateral view of the left LGB of 45-2, outlined from figure 24. The area of surface degeneration in the LGd and LGv has been indicated on the sketch. Also superimposed on the drawing are the extents of the surface degeneration in these nuclei as seen for control cases HED-11 , 19 and 23.

(b) A control has been estimated (stripes) for a retinal lesion comparable to that in the nasal retina of case 45-2 using the relative extents of surface degeneration for 45-2 and controls (a).

(c) Superimposed on the estimated control is the reconstructed outlined of the SGS of case 45-2 and the wedge of degeneration seen in the SGS of this case (see figure 23).

(d) In this sketch, the SGS of the experimental case has been translated caudally so as to match the undamaged caudal edges.

Figure 25 (continued):

(e) This figure tests for the possibility of the shrivelled tectal periphery (see figure 22). The experimental SGS has been translated such that central extents of the wedges or tongues of degeneration in the control and experimental cases are matched.

Figure 25

(a)

(b)

(c)

(d)

(e)

45-2

control

0 ——————— 1

45-2 (LEFT)
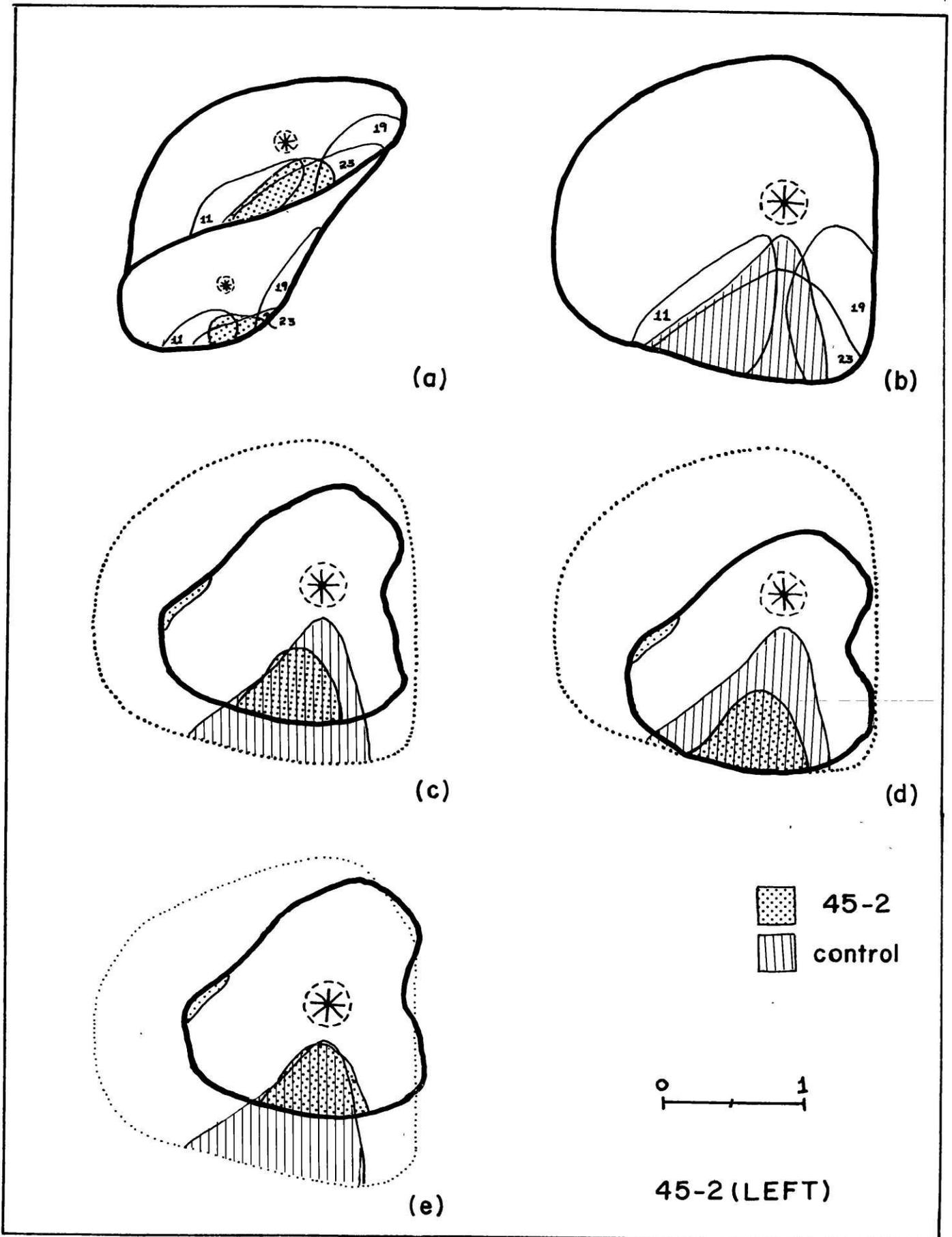
Figure 26:

Analysis of the right side of case 45-2. The heavy lines represent the reconstructed outlines of nuclear groups in the experimental case. The circled star gives the optic disc representation relative to the standard reconstruction outlines (dotted lines). The animal had a bilateral lesion of the rostral tectum on the day of birth. In adulthood, small lesions were made in the nasal retina (lower edge of medial rectus) of the right eye and in the temporal retina (upper edge of lateral rectus of the left eye.

(a) Dorsal view of the LGN of 45-2 (right side). Indicated on the drawing is the extent of surface degeneration in the experimental case (dots) and in two control cases (HED-11 and 22) whose retinal lesions are closely matched to those of the experimental animal.

(b) Dorsal view of a standard SC on which are marked the areas of degeneration seen in control cases HED-11 and 22. Using figure 26(a), an estimation has been made (stripes) of the area of SC degeneration that would be expected in an animal having the same retinal lesion as 45-2 but no neonatal SC lesion.

(c) Superimposition of the standard SC reconstruction (dotted line), having the estimated surface area of the control case, on the reconstructed dorsal view of the SC of case 45-2 (heavy line, see Fig. 23). Indicated are the areas of degeneration seen in the SC of 45-2 (stipples). The extent of this degeneration reaches further centrally than does the

Figure 26 (continued):

degeneration in the estimated control case.

(d) The same drawing as for (c) except that the experimental SGS
has been shifted caudally to compensate for the forward movement of
the SC following the neonatal rostral tectum ablation.

(e) To test the possibility of the tectal periphery shrivelling,
the <u>central extents</u> of the degeneration in 45-2 and in the control
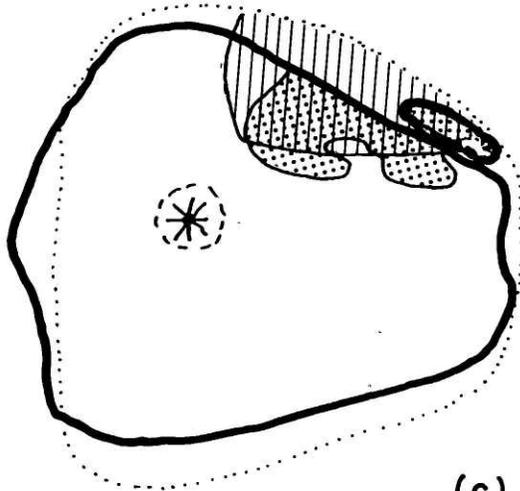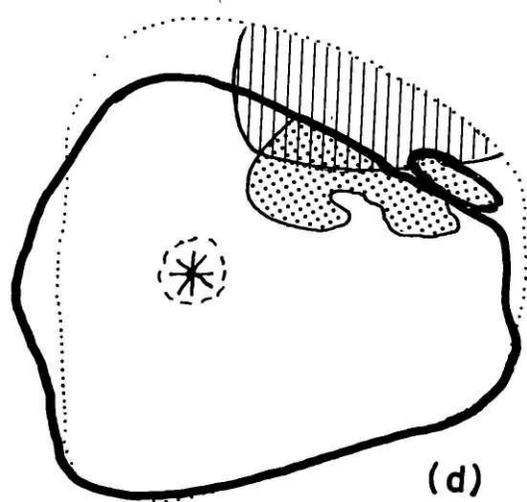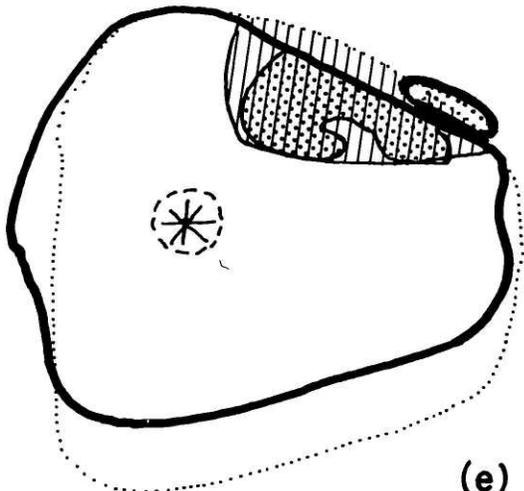have been superimposed.

Figure 26

(a)

(b)

(c)

(d)

(e)

45-2

control

0   1
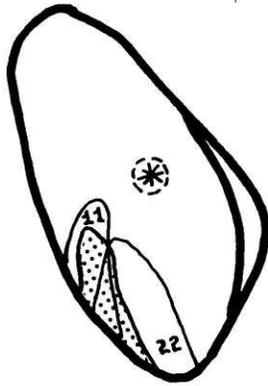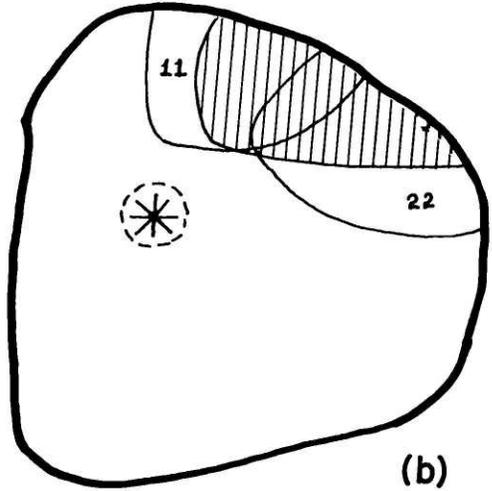
45-2 (RIGHT)

Figure 27:

Cross sections through the rostral SGS of case 45-2 to show the mode
of travel and termination of optic tract fibers from the temporal retina
of the left eye and the nasal retina of the right. Degenerating fibers
seen on the left side (short lines) are travelling caudally. The
majority will terminate in a wedge of degenerating endings in the
caudal SGS. Some, however, get deflected laterally and terminate in
an anomalous patch at the lateral edge of the SGS (see figure 23).
The disorganized pattern of degenerating fibers is indicated, with
axons of the optic tract forming a "double tier" in the medial part
of the sections.

On the right side, we see the abnormal mode of termination of
optic tract fibers originating in the temporal retina. Instead of
the columns of degeneration seen normally extending throughout the
SGS of a control animal with a similar retinal lesion, the optic tract
fibers in experimental case result in patchy termination intermingled
with "holes" or "blank areas" without any terminals.
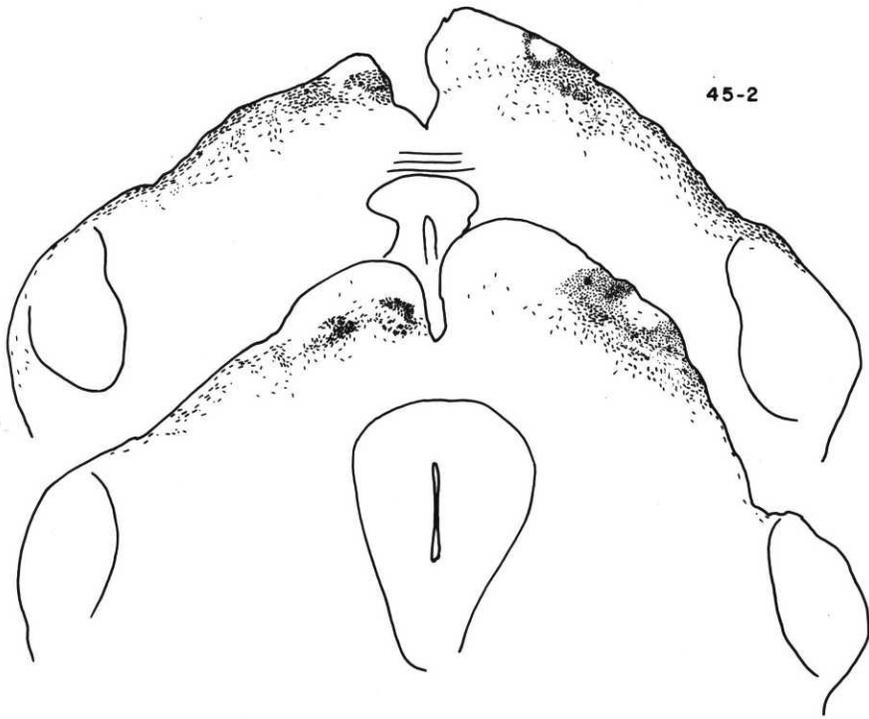
45-2

Figure 27

Figure 28:

Reconstruction drawings of case 43-2. This animal suffered, on the

day of birth, a unilateral lesion of the right rostral tectum and had

its right eye removed, in addition. In adulthood, a small lesion was

placed in the temporal retina of its left eye (at the lower edge

of the lateral rectus) and 5 days later, the animal was sacrificed.

The brain was fixed, sectioned at 30μm and every 5th section,

stained by the Fink-Heimer method, has been charted on these

reconstruction drawings.

(a) Dorsal view drawing. The right rostral tectum has been ablated

but the remnant SGS has not flopped forward as in the previous cases.

A small amount of SGS has escaped the lesion in the rostral part

and this has been indicated on the chart. The left SGS, although not

lesioned, is somewhat smaller than normal because of the atrophy

resulting from the neonatal eye enucleation. The pattern of degeneration

in the undamaged rostral SC is abnormal - the optic tract termination

is found not only in the SGS (solid bars) but also in the layers

deep to the stratum opticum (open bars). Some terminal degeneration

is seen in the LP and pretectum.

(b) Lateral view reconstruction drawing of case 43-2. Degenerating

fibers and terminal areas are indicated along the course of the main

optic tract as well as the accessory optic tract.

137

Figure 28
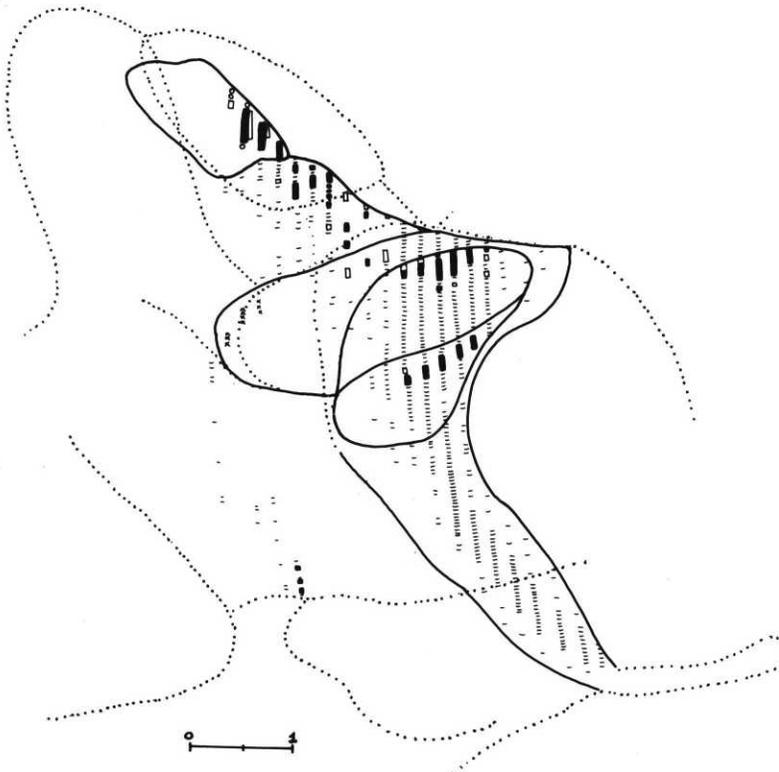
43-2

a
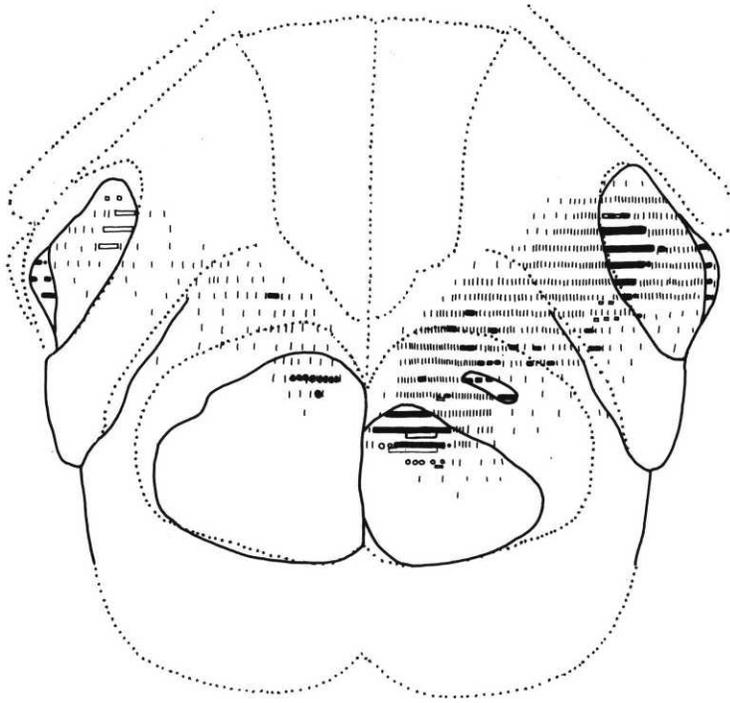
43-2(RIGHT)

b

Figure 29:

Analysis of case 43-2, right side. (See also Figure 28.)

(a) Dorsal view drawing of the LGN of 43-2, right side, with
the area of surface degeneration indicated (stipples). Also
superimposed are the surface extents of LGd degeneration for
control cases HED-24 and 26.

(b) Using the control cases HED-24 and 26, and the positions
of the surface area extents relative to that for 43-2, (a) a control
has been estimated (stripes) for the SC degeneration in 43-2, had
there been no neonatal tectal lesion.

(c) Superimposed on the estimated control is the dorsal view
reconstruction drawing of 43-2, with its tongue of degeneration
as well as the degeneration in the remnant piece of rostral SGS.
The degeneration in the SGS of 43-2 is seen to extend beyond the
optic disc representation of the standard SC.

(d) Test for the possibility that the entire SGS periphery
has shrivelled. The central extents of the wedges of degeneration
in the SGS have been superimposed, and the SGS of 43-2 translated
accordingly.

See text for further detail on analysis.
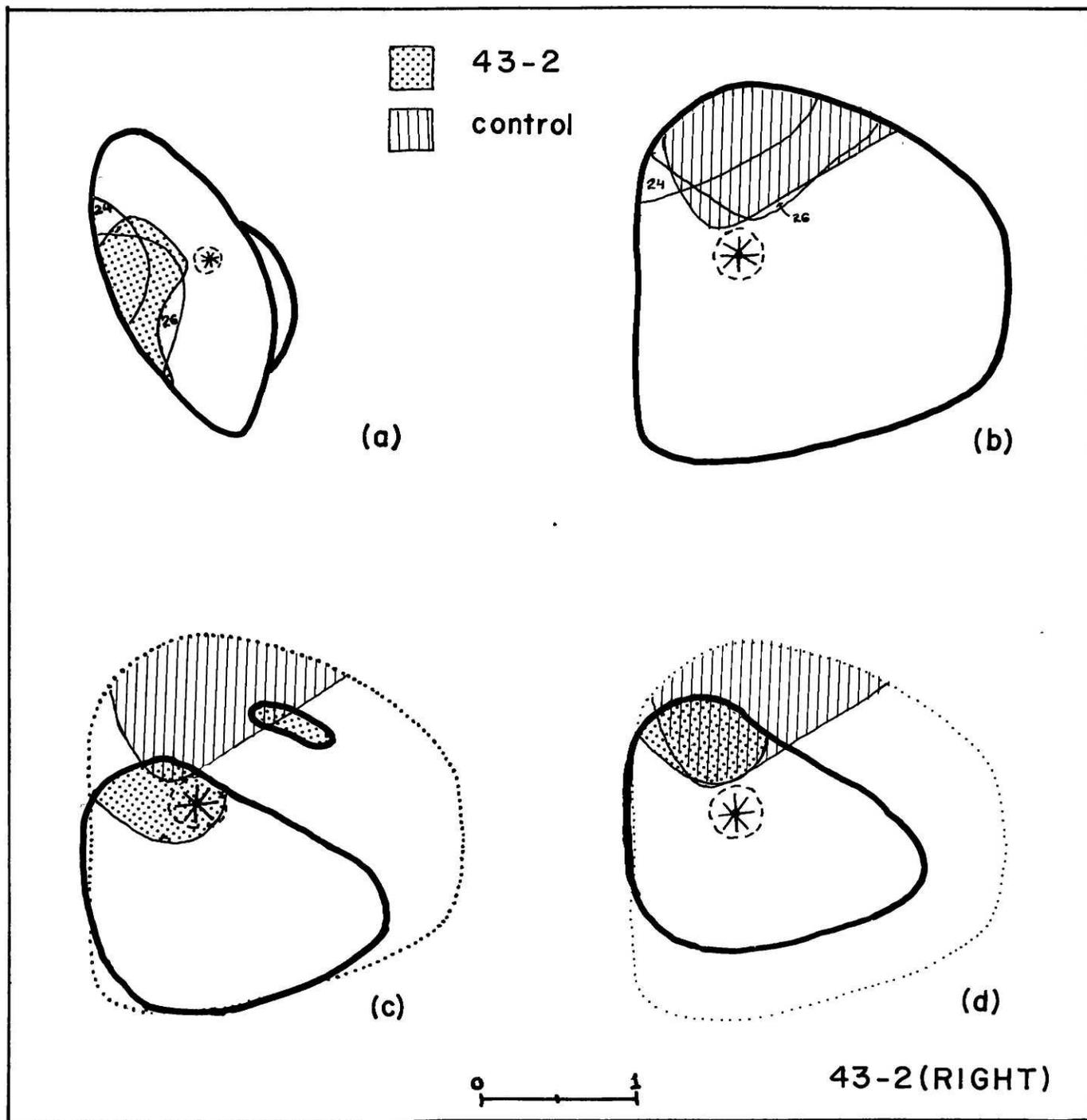
Figure 29

(a)

(b)

(c)

(d)

43-2(RIGHT)

Figure 30:

Reconstruction drawings of case 43-10. The animal had a lesion
of its right rostral tectum on the day of birth, in addition to
having its right eye enucleated. In adulthood, 5 days before
sacrifice, a discrete lesion was made in the left temporal retina,
at the upper edge of the lateral rectus. The brain was subsequently
sectioned at 30μm, and 2 series of sections, each spaced at 150μm
were stained with the Fink-Heimer method. Most of the charting
is done from one series of slides spaced 150μm apart. However,
in the rostrolateral SC, the second series has been utilized to
give a more complete picture of the abnormal termination pattern.
Symbols are same as for figure 7.

(a) Dorsal view reconstruction drawing of 43-10. The right
rostrolateral tectum has been ablated but much of the SC termination
is found in tissue subjacent to the optic tract (open bars)
in the region of the neonatal damage. Some abnormal degeneration
is also noted in the LP. The projection of the ipsilateral optic
tract has been indicated on the left side. Note that the LGN
and SGS on the left are reduced in size due to atrophy resulting
from the neonatal enucleation of the opposite eye.

Figure 30 (continued):

(b)   Lateral view reconstruction drawing of the same case, right

side.   The optic tract fibers can be followed to their end-stations

in the dorsal part of the LGv and LGd, forming columns of terminal

degeneration oriented caudolateral to rostromedial.   The degenerating

fibers continue caudally to terminate in the PrT and rostral SC.
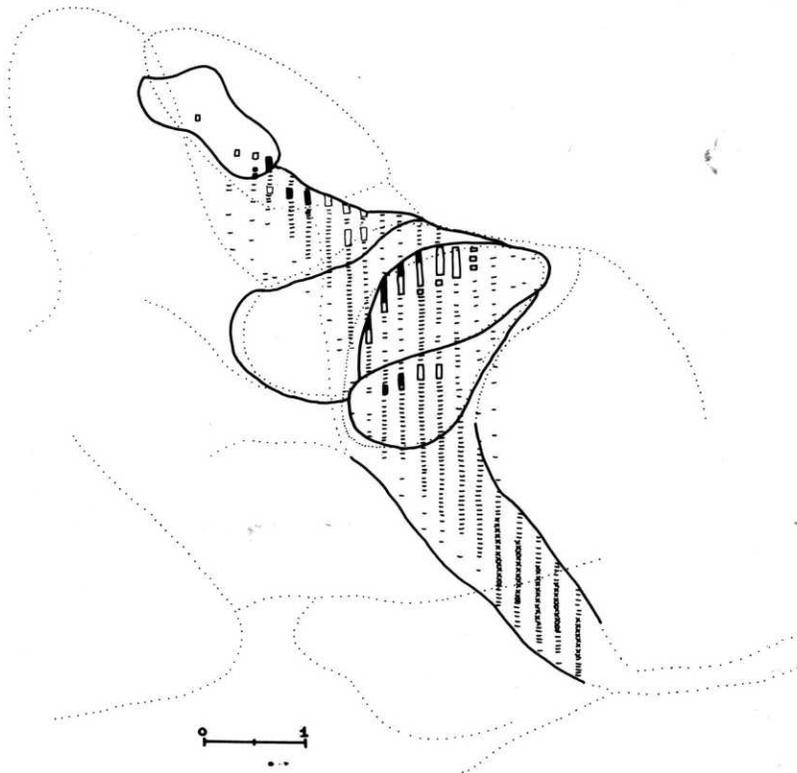
Figure 30

a
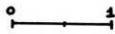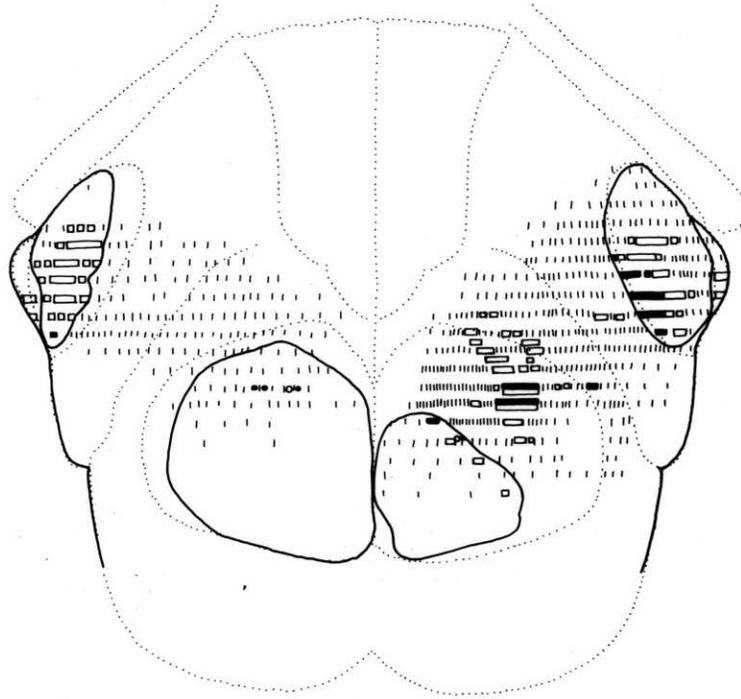
b

Figure 31:

Analysis of case 43-10, right side.

(a) Dorsal view of right LGN. Included on the outline is the area of surface degeneration resulting from the retinal lesion, and also the outlines of the surface degeneration areas for control cases HED-11, 22 and 24.

(b) Using the relative positions of HED-11, 22 and 24 with respect to 43-10 as seen in figure 31(a), a control has been estimated (stripes) for the extent of SC degeneration for 43-10, had there been no neonatal damage.

(c) Superimposing the estimated control SC degeneration (stripes) on the reconstructed dorsal view outline of the SC of case 43-10 and the degeneration seen therein (stipples), it can be noted that the degeneration in the experimental case extends farther centrally than in the control.

The optic disc representation for the standard brain has been indicated by a circled star.

Figure 31

(a)

(b)

43-10

control
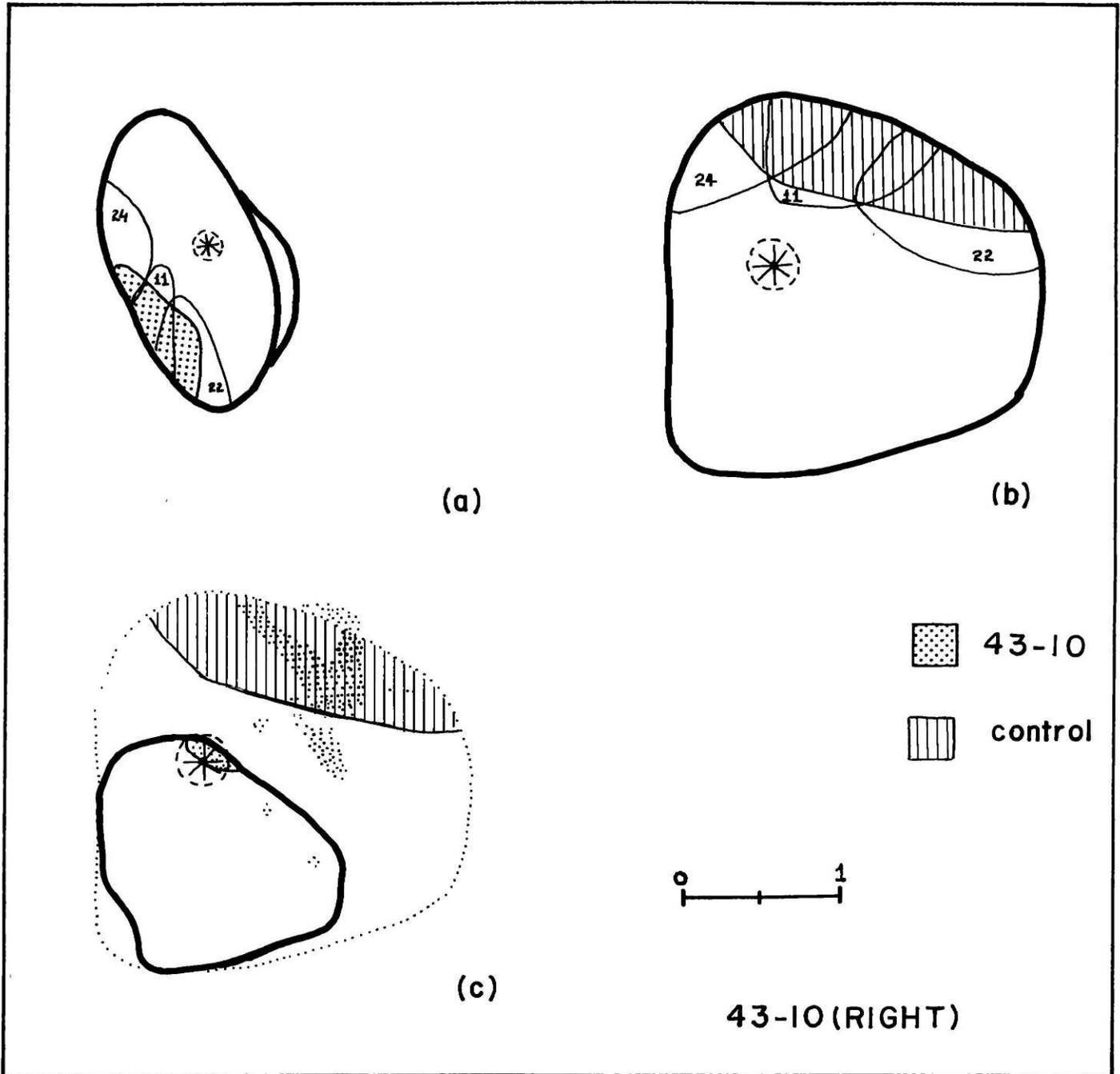
(c)

0   1

43-10 (RIGHT)

145

Figure 32:

Schematic drawing demonstrating the organization of topography
of retinal projections along the course of the optic tract. Fibers
from the nasal retina project ventrally in the LGv and LGd;
in the SC, they terminate in the caudal tectum. Fibers from the
upper and lower parts of the retina, however, remain segregated
at the two ends of the optic tract and terminate in the caudal
and rostral parts of the LGB respectively; as the optic tract
bends across the surface of the thalamus (to course rostrocaudally
in the midbrain), the upper and lower retinal projections are
now found lateral and medial in the SC.

Figure 32

N:representation of nasal retina
T:representation of temporal retina
U:representation of upper retina
L:representation of lower retina