Subcortical Visual Systems

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Mechanisms of Functional Recovery Following Lesions of Visual Cortex or Superior Colliculus in Neonate and Adult Hamsters

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Brain damage inflicted early in life can have both behavioral and neuroanatomical consequences which differ from the effects of lesions in the adult. The experimental results reported here clarify some of these differences, and narrow the range of tenable hypotheses concerning the roles of subcortical visual pathways in functional recovery from cortical and midbrain tectal lesions.

Lesions of superior colliculus or visual cortex in the adult Syrian golden hamster (*Mesocricetus auratus*) have clearly distinguishable consequences in visually guided behavior [SCHNEIDER, 1966, 1967, 1969]. To human observers, who spend much of their time looking at the behavior of fellow primates, the hamster is not an overwhelmingly visual animal, but he is more obviously visual than the laboratory rat and has a superior colliculus more accessible to a direct surgical approach [SCHNEIDER, 1966]. Moreover, the hamster's colliculus is about as large in surface area as area 17 of the neocortex; and the superficial gray layer of the colliculus, throughout which optic tract terminals are found, has a volume more than twice as great as that of the dorsal nucleus of the lateral geniculate body (unpublished data).

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Ablation of most of area 17, with moderate invasion of a surrounding belt of cortex, is sufficient to cause loss of the ability to discriminate visual patterns

such as horizontal and vertical stripes. But in the first postoperative week, the hamster without visual cortex recovers its ability to orient toward visual stimuli. Thereafter, such animals are like normals in turning their heads toward a hand-held sunflower seed, a movement sequence accompanied or followed by motion which leads to vibrissae contact with the seed and finally to a grasping of the seed by the hamster's mouth. This recovery, involving a function likely to be more useful in the natural life of these animals than the lost ability for distinguishing details of patterns, depends on the superior colliculus (see below). Even in previously intact hamsters, sufficiently complete lesions of this midbrain structure cause a permanent loss of the visual elicitation of head and body turning. It has been possible in every case to relate any observed recovery to an incomplete lesion of the tectum, sparing at least a small segment of a route from the visual input fibers to the descending tectal efferents. In one animal, a recovery of orienting toward stimuli in the lower nasal fields was not seen until four months after the lesion, though testing was frequent. The possibility remains nevertheless that this gradual recovery may require pathways independent of the superior colliculus.

An enduring loss of such orienting responses can be caused by either of two different types of lesion: (1) cutting the descending efferents by undercutting the tectum via a caudal approach, even if fibers entering at the rostral end are spared; (2) transecting the brachium of the superior colliculus, thus severing the optic afferents from retina and visual neocortex. Nevertheless, the loss is not accompanied by the defect resulting from visual-cortex ablation. After the collicular lesions, the animals show a surprisingly normal ability for pattern discrimination, as long as they are tested in a situation that does not require visually directed orientation toward the discriminanda.

The present paper takes its departure from the observations that if comparable brain lesions are made in the neonate rather than in the fully grown hamster, the behavioral defects are absent, or at least much less severe. Functional sparing appears to be attributable to a different kind of mechanism after the two types of lesion: (1) the early lesions of the superior colliculus lead to the formation of anomalous retinal projections [see also SCHNEIDER and NAUTA, 1969; SCHNEIDER, in prep.], some of which are implicated in the sparing of visually elicited turning; (2) early ablation of visual cortex does not cause such obviously anomalous retinal

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projections nor altered projections of the lateral geniculate nucleus (whose usual target area is gone); however, it can be argued that the capacity of non-geniculostriate pathways for mediation of pattern discrimination is greater than after adult lesions of visual cortex. Thus, one must look to structures outside the geniculostriate path in order to find a basis for the observed escape of pattern discrimination after early removals of striate cortex.

1. Consequences of Neonatal Lesions of Superior Colliculus

In the following experiments, tectal lesions were made in neonatal hamsters and the animals were observed into adulthood. Terminal neuro-anatomical experiments were then carried out: following eye removal, the degenerating retinofugal axons were traced in histological sections of the brains.

Methods

In the newborn hamster pup, 16 days post-conception, the superior colliculus lies directly below a thin cartilagenous interparietal bone; the developing cerebral hemispheres have not yet grown back over the roof of the midbrain. By application of heat to the skull, the upper layers of one or both colliculi were totally or partially destroyed in 16 pups on the day of birth. Damage was similarly inflicted in 4 more pups, aged 2, 3, 3 and 5 days. After surgery, these animals were returned to their mothers and reared normally. After they were fully grown (age 12 weeks), they were tested for the ability to locate seeds visually. For these tests to be successful, even normal animals must be accustomed to handling and take seeds readily, without freezing, upon tactile presentation. Hence these tests were repeated many times until these conditions were met. When they were 14 weeks or older, one or both eyes were removed in all but one animal; after a survival period of generally 5 days they were given an overdose of barbiturate and perfused, and the brains were prepared for the staining of degenerating axons and boutons by a modified Nauta silver method [FINK and HEIMER, 1967]. Every 5th transverse section, cut frozen at *30°* (or every 6th at *25°* /*nai*), was stained; adjacent sections were stained with cresylecht violet. In most brains a third series was stained for normal axons [FINK and SCHNEIDER; see SCHNEIDER, 1969].

Results

In 9 cases, including 2 with bilateral lesions, the superficial gray layer of the superior colliculus, defined as the tissue lying above the fascicles of

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optic tract fibers, was totally absent. Over at least part of the remaining tissue was a surface layer of fibers, below which at least part of the intermediate cell and fiber layers could be identified. A reduction in these and the deepest collicular layers, variable in extent, was generally found. Thus, the tissue where fibers of retinal origin would normally terminate was apparently gone. Yet these animals, as well as the other hamsters in this series, showed considerable ability to locate seeds visually. Therefore, we have a new example of the sparing of a specific function after an early lesion, which if it had occurred in the adult would have caused an irrecoverable loss of the function (for other examples, see reviews by TEUBER and RUDEL [1962] and TEUBER [in press]).

However, this sparing of function appears to have a specific neuroanatomical explanation. In spite of the absence of the superficial layers of the superior colliculus, where the terminals of axons of retinal origin would normally be found, the remaining tectum does receive direct visual input. Axons of the retinal ganglion cells are found coursing mainly over the surface of the neonatally damaged colliculus and terminating in the immediately subjacent tissue. This is illustrated in figure 1, with drawings of frontal sections from the brain of a 14-week-old hamster subjected on the day of birth to bilateral ablation of the superficial layers of the superior colliculus. Five days before sacrifice, the right eye was removed. There is no stainable residual degeneration remaining from the neonatal lesion. This disappears within a few days in the neonatal brain [SCHNEIDER, in prep.; cf. SUMI and HAGER, 1968].

The pattern of axonal and terminal degeneration resulting from the eye removal is charted on the drawings; comparable charts from a similarly treated case with a normal midbrain are included to show the contrast. As indicated in the chart of degeneration in the abnormal midbrain, the retinal fibers did not terminate in the medial third of the colliculus. Correlated with this was a defect previously found in the animal's capacity for visual orienting: it had failed to show head-raising in response to seeds in the upper visual field, though it had demonstrated strong responses toward seeds in the remaining field. This was very similar to the defect seen in several adult-operated hamsters with ablation of only the medial colliculus [SCHNEIDER, 1966], which normally receives input from the upper visual field [in rat: LASHLEY, 1934; SIMINOFF *et al.*, 1966]. This

type of correlation in several cases supports the hypothesis that the anomalous retinal projections to the remaining deep tectal layers is crucial for the spared capacity for orienting.

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However, two additional kinds of anomalous projections are found in this case, and in all the other cases of early tectal damage. Retinal axons are seen to terminate in abnormally great density in an external sublayer of the ventral nucleus of the lateral geniculate. Furthermore, they terminate densely in the thalamic nucleus lateralis posterior (fig. 1), which normally receives no more than a few of these fibers [SCHNEIDER, in prep.]. In the normal hamster, and in other species, these two areas do receive a

Fig. 1. Charts showing terminal degeneration (dots) and degeneration of fibers of passage (short line segments) caused by removal of right eye 5 days before sacrifice, in sections from the brains of 2 adult hamsters. Sections on the left are from a case of bilateral superior colliculus lesion on the day of birth, those on the right are from a hamster that was normal until the eye was removed. The left sides of the sections (contralateral to the eye removed) were approximately matched; the right sides cannot be compared because of asymmetries in the planes of section.

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dense projection from the superior colliculus [SCHNEIDER, in prep.; ABPLANALP; HALL and EBNER, this conference]. Apparently, the visual input takes a 'short cut' to these areas after neonatal collicular lesions. Little is known about the functional significance of these two regions for normal animals; the possible involvement of their anomalous neuroanatomical connections in recovery or development of function is still undetermined.

If the early tectal lesion is made unilaterally, in general the same anomalies are seen ipsilateral to the lesion, but in addition there is an abnormal decussation of retinal axons across the tectal midline from the damaged colliculus to the remaining normal colliculus [SCHNEIDER, in prep.]. The data lead one to suggest that as the optic fibers grow into the midbrain, they terminate where there is synaptic space - and in these cases, possibly because sufficient space is not found in the tectum, they can sprout collaterals in areas where synaptic spaces are available along their route. Recent additional cases [SCHNEIDER, in prep.] demonstrate that the abnormally decussating fibers terminate only in the most medial part of the superficial grey layer of the normal colliculus (2 cases), whereas the axons arriving from the other eye terminate everywhere *except* in this medial region (1 case).

The fibers which show the abnormal re-crossing (having crossed first at the optic chiasm) apparently compete for synaptic space with the normal-input fibers. If the latter are eliminated by neonatal removal of the eye ipsilateral to the tectal lesion (2 cases), the abnormally re-crossing fibers from the remaining eye terminate not only in the medial region, but throughout the entire extent of the superficial gray layer of the colliculus on the wrong side of the brain (though less densely laterally). One functional consequence of this pathway to the wrong side of the midbrain is already clear (unpublished data): hamsters with such early unilateral tectal lesions, unlike normal animals, can show visually directed turning responses in the wrong direction.

//. Neonatal vs. Adult Lesions of Visual Cortex

Visual-cortex lesions that are severely detrimental to visual pattern or shape discrimination if made in the adult cat cause no such impairment if made in a comparable fashion in the neonatal kitten, 9 days of age or less [DOTY, 1961; WETZEL *et al.*, 1965]. In the lateral geniculate bodies (dorsal nucleus), retrograde degeneration is far from total; in fact, after early

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lesions the nucleus exhibits a greater number of normal cells than after later lesions [TUCKER *et al.*, 1968]. This sparing of cells might suggest that geniculate projections to cortex outside the marginal gyrus [in the normal cat: GLICKSTEIN *et al.*, 1967; GAREY and POWELL, 1967; WILSON and CRAGG, 1967] may be responsible for the sparing of visual function. Such an escape of pattern vision after lesions of area 17 has not been found for rats operated on the 22nd day [TSANG, 1937] or on the 1st day [BLAND and COOPER, 1969], nor has it been found for object discrimination by baboons operated at age 1, 3 or 10 months [JALAGONIA *et al.*, 1967]; in these species there has been no clear evidence of lateral-geniculate projections to neocortex outside of area 17.

I now report evidence that complete removal of area 17 in the neonate hamster does not completely abolish pattern discrimination despite virtually total degeneration of the lateral geniculate bodies. This is very different from the effects of area-17 ablation in the adult, where pattern discrimination is more severely impaired or abolished even though many neurons in the geniculate fail to degenerate.

Methods

Subjects; Surgical and Anatomical Techniques

Behavioral tests and subsequent anatomical analyses have been completed for 19 hamsters. Littermate pups of both sexes, from 5 litters, were divided into 3 groups. Five animals were kept as normal controls, and five others (under Nembutal anaesthesia, 100 mg/kg) underwent surgical ablation of visual cortex when they were 12–15 weeks old. The attempt was made to remove by aspiration only area 17 and some immediately adjacent cortex [see the map of SCHNEIDER, 1969]; however, the lesions were slightly smaller than intended, as described below.

In a third group, comprising the remaining 9 animals, posterior-cortex lesions were made when they were 8 days old (24 days post-conception), under Nembutal anaesthesia (50 mg/kg). In 7 of these a flap in the cartilagenous skull over the occipital region was cut and folded back, the cortex was aspirated and the flap in the flexible skull was replaced. Two animals were given sham operations: the bone flap was turned but no suction was applied, yet considerable cortical damage resulted, nevertheless.

After being weaned at an age of 3–4 weeks, all 19 animals lived in small Plexi-glas cages with cedar bedding and food on the floor and a water spout overhead. The light-dark cycle was automatically regulated, with 13 h of light (from an overhead 100-W tungsten filament bulb). Visual discrimination testing was carried out during the initial part of the dark period, the pre-training beginning when animals were 5–6½ months old. After any animal reached a criterion level of performance on a horizontal vs. vertical stripes discrimination problem (see below), the superior collie-

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ulus was surgically undercut [SCHNEIDER, 1966, 1969] and the animals were re-tested, beginning 2 weeks afterward. Finally, at the conclusion of all testing, when most of the animals were 10–16 months old, 13 of them were subjected to unilateral eye enucleation. After 3 more days the animals were overanaesthetized and perfused. Using the silver stain of FINK and HEIMER [1967], the terminal degeneration resulting from this most recent lesion could be visualized [SCHNEIDER, 1968]. At that time, most of the terminal degeneration from the previous lesions had disappeared with only large degenerating fibers remaining visible. No stainable trace of degeneration resulting from the neonatal lesions remained. These and all other brains were blocked in a standard transverse plane [SCHNEIDER, 1969] and cut frozen at 30 °m; serial sections were stained as described for experiment I.

In order to examine the possibility of altered retinal projections after the neonatal cortical lesions, unilateral posterior cortex ablations were inflicted on other pups, so that when they were fully grown, both eyes could be removed, and the resulting axonal and terminal degeneration after 5–7 days could be compared on the two sides of the brain [method used by GOODMAN and HOREL, 1966]. With suction lesions in 8-day-old animals, the usual result was a hydrocephalus of the non-operated hemisphere which precluded the desired neuroanatomical study. However, this pathology was absent in 2 cases with nearly total neodecortication on day 8, in 2 cases with small mechanically inflicted lesions on day 8, and in 2 cases where a partial visual-cortex lesion was made by applying heat through the skull, on the day of birth in one, and on day 3 in the other.

Apparatus and Pretraining Procedure

Before pretraining on the apparatus began, each animal was sufficiently tamed so that, after being placed on its cage top, it would take seeds from the experimenter's hand. For this, most animals required one week of brief, daily sessions. Visually elicited turning responses were observed, as in experiment I. Then a schedule of water deprivation began, and each hamster was systematically trained for 5 min/day to traverse a small elevated T-maze in order to reach water spouts present at both right and left goal areas.

The stem of the T, the approach runway, was 18 in. long, 4 in. wide at the starting area and broadening to 9 in. in width at the junction. The goal areas, the top of the T shape, were 6 in. wide and 22 in. between the two ends, where water spouts protruded through upright panels.

Before pretraining continued, two doorways, 3 in. wide, 5 in. high and 3 in. apart, were put in place at the end of the approach alley. The doors were supported in an opaque frame which was 8 in. high and 11 in. wide. The doors were made of clear Plexiglas; the upper 3-in. section was hinged at the top to open away from the approach side. Locks on each door were not visible from the approach runway.

A systematic shaping procedure was followed with each animal for 10 min/day. Initially the Plexiglas doors were held wide open by the experimenter, so the animal could reach the water

by crawling through one of them. Then they were closed progressively until the hamster had to push one open in order to reach the water. Pretraining was ended when an animal made 5 successive unassisted passages on each of 2 successive days. After the 5th passage on such a day, the preferred door

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was sometimes locked, and the animal had to find his way to the other, the unlocked door.

Visual Discrimination Training

Stimuli. Patterns of black cloth tape on white translucent vellum were mounted between glass to form plates 6 in. wide and 8 in. high. Each plate formed the removable front wall of a white box, 7V2 in. deep, which contained near the rear wall a 40 W cylindrical bulb with the tungsten filament 6 in. behind the stimulus window. The bulbs provided transillumination of the stimuli. Normally, the stimuli were placed 6 in. behind the Plexiglas doorways.

Procedure. At the beginning of each training session, an animal was placed at the end of the approach runway, behind a barrier which was 6 in. from the end. The barrier was removed so the hamster could approach the doors, while the experimenter watched from a darkened room through a 'one-way' window in the white drapes which surrounded the apparatus. If the animal pushed the door in front of the negative stimulus, he found it locked and an error was recorded. He then was allowed to correct himself by pushing through the door in front of the positive stimulus, thus entering the goal area where he found a water spout. If he pushed only against the door in front of the positive stimulus, no error was recorded, regardless of any approaches to the other door. In either case, he was allowed to drink for 2-3 sec, and was placed back at the starting area, behind the moveable barrier, for 15 sec. During this period, both stimulus plates were removed and then repositioned according to a Gellerman series. Then the barrier was removed to begin the next trial. Each animal completed 10 trials per daily session.

Results: Behavioral

Performance Differences in Pretraining

The shaping procedure in pretraining involves instrumental conditioning prior to the introduction of the discriminanda. Data derived from the shaping procedure are not ordinarily reported but turned out to be interesting in this case because of the remarkably slow acquisition on the part of most of the neonatally operated animals. The normals and adult-operated animals required from 4 to 7 days to complete this stage of training, while seven of the nine with early cortical lesions required from 10 to 19 days. These seven had the largest lesions (see below).

In the informal tests of visually elicited turning, all animals were responsive. Some, however, showed peripheral field weaknesses: 1 of 5 normals, 2 of 5 adult operates, and 8 of 9 neonatal operates.

Visual Discrimination

1. Light-dark. For the first problem, white translucent paper was the positive stimulus and a piece of opaque black cardboard of the same

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Problem 1'

L-D Transillumination

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W-B Reflected light

Fig. 2. Trials to criterion for each animal on each of the 3 visual discrimination problems (as explained in text). Scores are arranged for each group in order of trials required on problem 3. F = failure.

size was the negative stimulus. Both 40-W bulbs inside the stimulus boxes were on; the only significant illumination came from the transilluminated light stimulus. All animals reached a criterion of 80 % correct on

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2 successive days. The median number of trials to criterion was 60 for each of the 3 groups (fig. 2), i. e., unoperated controls and those with early and late lesions.

2. *White-black (reflected light)*. For the second problem, the same stimuli were used, but without transillumination. Illumination was provided by a 40-W bulb suspended a foot above the doorways. White was positive. Some animals in both groups with cortical lesions were deficient in learning this more difficult problem (fig. 2). Three neonatal operates and two adult operates

failed to reach the criterion in 200 trials. At this point, these 5 were retrained on problem 1.

3. *Horizontal-vertical stripes.* In the third and crucial problem, the stimuli were alternating $\frac{3}{4}$ -in.-wide black and white stripes, horizontal positive and vertical negative. When an animal performed at a level of at least 80 % correct for 2 successive sessions, the stimuli were altered on the next day by interchanging white and black areas - thus reversing local brightness cues. If the 80 % level was maintained (no more than 2 errors), the criterion was declared to have been achieved. If not, training continued until the 80 % level was reached or surpassed on one day with one stimulus pair and on the next day with the other.

Each normal animal was superior to all of the operates, reaching criterion in 70–230 trials (fig. 2). As testing continued with the operated animals, certain changes were introduced which appeared to encourage the learning of the discrimination: Thus, after 300 trials, the stimuli were moved to a position 3 in. behind the doorways (from the position 6 in. distant) and the stimuli were changed to narrower stripes, $\frac{1}{4}$ -in.-wide alternating black and white. At least 200 more trials were allowed (except for one case) unless a criterion of 80 % correct for 3 successive days was met. On the final 100 trials with either wide or narrow stripes, the procedure was altered further so that whenever the animal pushed the wrong door, he was immediately put back at the start and allowed to run again; this was repeated until he went directly to the positive door, no further errors being counted. If within the first 100 trials with narrow stripes, an animal performed at 80 % correct for 2 successive days, then the wider stripes were tried again; if in 100 trials the 80 % level was not reached and maintained with local brightness cues reversed, the animal was finally retrained with the narrow (and less distant) stripes.

In spite of their 'stupidity' revealed in pretraining, 7 of the 9 neonatal operates reached criterion but only 3 did it with the more distant and wider stripes.

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Though the probability of reaching the criterion by chance was generally less than 0.001 when considering the criterion trials alone, one must consider the probability that the criterion for learning could have been reached by chance at least once in the total number of trials required (fig. 2). An estimate can be obtained from the length of runs of successively correct trials, using the calculation of GRANT [1947]. For these 7 animals, the average longest run was 16 after 417 trials, the chance probability for which is less than 0.005.

Three of the 5 hamsters operated in adulthood also reached criterion, with deficits (fig. 2). Thus, the two groups of brain-damaged animals showed similar results; however, the histological analysis revealed very different lesions.

Results: Histological

Lesion Size

The dramatic contrast between the lesions made in adult animals and many of the lesions made in neonates is illustrated by the photographs in figure 3, which shows the largest lesion in a neonatal operate which learned the pattern discrimination, and the much smaller lesion of an adult operate which failed in 500 trials.

The gross distortions in the hemispheres following the neonatal lesions made accurate reconstructions of the lesions unreliable. However, quantitative estimates of the size of the lesions in the posterior neocortex were obtained by

measuring the amount of neocortex *remaining* at three standard levels and subtracting these values from the mean for normals. The levels chosen were (1) the junction of fasciculus retroflexus and habenula, (2) the caudal end of the posterior commissure, (3) a level caudal to the second level by a distance equal to the separation of the first two levels. In the normal hamster, these pass through the rostral, middle and caudal parts of area 17. The width of cortex remaining was measured along the boundary between layers 4 and 5 from midline to rhinal sulcus; at each level, only the value for the side with the largest amount of neocortex was used. The mean value for normals, summed over the 3 levels, was 30 mm. Figure 4 shows the results of subtracting from this mean the value obtained for each animal.

With only one exception, the animals operated when 8 days old had larger lesions than did those operated in adulthood. Clearly, performance on the pattern discrimination is no simple function of lesion size.

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Fig. 3. The photo at the left shows a dorsal view of the brain from hamster 6–4, operated at the age of 8 days, showing the largest lesion in an animal which learned the pattern discrimination. This animal performed 18 consecutive correct choices after 400 trials ($p<0.001$). The right-hand photo shows the brain of animal 8–5, operated in adulthood, with a lesion which resulted in failure to learn the pattern discrimination. This subject's best run in 500 trials was 7 consecutive correct responses after 450 trials. The contrast is heightened by the enlargement of the defect in the neonatal operate; however, if the amount of remaining cortical tissue is compared the difference in lesion size remains large.

Retrograde Degeneration in Thalamus

The nature of the retrograde degenerative change in neonatal operates was very different from that in adult operates. Damage to area 17 in the adult hamster is associated with abnormality in the lateral geniculate (pars dorsalis); if part of area 17 is spared, corresponding parts of the geniculate appear normal. However, the areas showing abnormalities contain many normal or nearly normal neurons [SCHNEIDER, 1966, 1969]; even if area-17 damage is complete, many neurons remain, though the volume of the geniculate is moderately reduced and the glial density is increased (fig. 5). Corresponding damage in the neonate leads to a collapse of the geniculate which is so complete that the optic tract

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Fig. 4. Index of the size of the neocortical lesions, based on measures of the amount of caudal neocortex remaining at 3 standard levels (explained in text). These data supplement the observations of retrograde degeneration in the thalamus. Ordered as in figure 2.

fibers are found coursing directly over the external medullary lamina, dorsal to the intact ventral nucleus of the lateral geniculate (fig. 5). Evidence of spared remnants of area 17 was found for all 5 hamsters in which ablations were produced in adulthood: normal areas in at least the rostral portions of the lateral geniculates were found on at least one side. Of the 3 animals which learned the pattern discrimination, 2 showed larger normal areas than were found in the 2 that failed. The other animal (No. 6–7), and the 2 that failed, showed a small amount of sparing approximately equivalent to that seen in the hamsters which failed a similar pattern discrimination problem in an earlier experiment [SCHNEIDER, 1966, 1969]. As in these earlier cases, the present cases showed slight to moderate abnormalities in the lateral nucleus, particularly in the area adjacent to the rostral lateral geniculate. The extent of such changes was not clearly related to performance. Of the animals with neonatal ablations, only two (3–2 and 3–4) showed a small non-collapsed area of normal geniculate, probably associated with sparing of part of area 17. In the others, the area of the dorsal nucleus of the geniculate

was quite like that seen in 2 other cases in which nearly the entire neocortex was removed (on one side) at an age

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Fig. 5. Photographs of transverse, Nissl-stained sections showing the left LGd, taken at a comparable location from 3 cases. The left-hand arrow points to the medial edge of the main part of the optic tract; the right-hand arrow points to the lateral edge of the external medullary lamina; between these points lie cells of LGd together with some axons of passage. Top: normal. Middle: from case 8-5, with ablation of most of area 17 in adulthood; note increase in glia, the presence of many neurons, and the decreased width of LGd. Bottom: from case 6-1, with neonatal cortical lesion; LGd is collapsed (cf. fig. 7). Cresylecht violet stain; about 95 X.

of 8 days, sparing only some rostral midline cortex and some tissue immediately adjacent to the rhinal sulcus. Only a few neurons could be found embedded in the optic tract fibers.

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 TRIALS TO CRITERION BEFORE SC UNDERCUT

KEY

Lesions before SC undercut' O None A Posterior Neocortex in adulthood D Posterior Neocortex in infancy (8 days old) Nature of SC lesion's Shallow, incomplete c Complete — at level of tectal commissure d Deep, but cutting descending outputs d+ Deep, plus medial extension into diencephalon Visually elicited turning after SC lesion' Ai None .0*,.?. Some recovery d,s Inadequate data

Fig. 6. A comparison of trials to criterion on the pattern discrimination problem before and after the superior colliculus was undercut. Points below the diagonal line show scores of animals which relearned in fewer trials than required before the colliculus lesion. See figure 7 for an illustration of a 'deep' lesion of the colliculus in an animal with a neonatal cortical lesion. A 'complete' lesion is similar to the one illustrated in figure 2 of SCHNEIDER [1967].

Nucleus lateralis (defined as in the rat by GTJRDJIAN [1927]) was absent, or contained only a few neurons, in all cases with early cortical lesions. Nucleus lateralis posterior was reduced but present in all of these cases, the amount of reduction corresponding closely to the lesion size as indicated in figure 4.

Retinal Projections

Since one eye was removed 3 days before sacrifice in most of these animals, terminal degeneration could be seen in the silver-stained sections (see above - methods). In cases with adult lesions of visual cortex, dense terminal degeneration was found throughout the dorsal nucleus of the lateral geniculate contralateral to the eye removal. This was clearly distinguishable from the axonal degeneration still remaining, on both sides, from the earlier bilateral cortical ablation.

In the neonatal operates, a small amount of terminal degeneration resulting from the eye removal was consistently found in the area of the collapsed geniculate, some of it embedded in the optic tract but most of

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Fig. 7. Drawings of Nissl-stained sections from the brain of animal 6-1, with a cortical lesion inflicted at age 8 days, and a cut below the superior colliculus made in adulthood after the learning of the pattern discrimination problem. The small dots cover areas of dense terminal degeneration, seen in silver-stained sections, resulting from the removal of the right eye 3 days before sacrifice. Vertical striations cover areas of abnormally few cells seen in Nissl-stained sections. Arrows point to the rhinal 'sulcus'. Sections are numbered according to their position in a series of sections at 150 μ m intervals.

it in a very tiny region medial to the main optic tract, just above the ventral nucleus of the lateral geniculate body (fig. 7). A similar area of terminal degeneration in the collapsed geniculate body was found even in the cases of early unilateral neodecortication which were studied after eye removal in adulthood. The region of optic tract termination was larger than this only in the two cases (3-2 and 3-4) with probable sparing of remnants of area 17; dense terminal degeneration filled the non-collapsed remnant of the geniculate. The other areas of optic tract termination showed no clear abnormalities in these animals. Several cases did show a tiny area of terminal de-

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generation in the lateral-posterior nucleus contralateral to the eye removal, but this was *not* contingent upon the presence of earlier cortical lesions, nor was it correlated with visual discrimination performance. A similar tiny area (variable in exact position and size) is seen in the majority of normal hamsters after eye enucleation [SCHNEIDER, in prep.].

A search for abnormal retinal projections following early visual-cortex lesions was more easily carried out in the additional cases with unilateral ablations. When the animals were adults, both eyes were removed so that the optic tract terminal degeneration could be compared on the two sides of the brain. Using such a method 16 mo. after unilateral visual-cortex lesions in young adult rats, GOODMAN and HOREL [1966] found evidence for an abnormally great density of optic tract termination on the side of the earlier cortical damage, in limited portions of the pretectal region and the ventral nucleus of the lateral geniculate

body. In the present hamster cases, however, no convincing abnormalities were found except for the following: the partial collapse (4 cases) or total collapse (2 cases) of the dorsal nucleus of the lateral geniculate body on the side of the early lesion, and a suggestion of an abnormality in the laminar pattern of termination in the superficial gray layer of the superior colliculus. Histological sections of the brain of a normal hamster 5—7 days after eye enucleation show the densest terminal degeneration in the upper m to $\frac{2}{3}$ of the superficial gray layer, with a somewhat lighter area just above the degenerating axons of the stratum opticum (fig. 1) [SCHNEIDER, 1968]. In 4 of 5 cases with early unilateral damage to posterior neocortex (the 6th case had direct damage to the colliculus), in at least a part of the colliculus this laminar separation was less clear on the side of the early lesion, as judged independently by 2 observers. On some slides, the deeper sublamina showed denser degeneration, on others the superficial sublamina showed lighter degeneration. Thus, there appears to be at least a slight quantitative alteration in densities of termination in the superior colliculus after early cortical damage. However, the change is not dramatic in the presently available material, and must be investigated further before any strong conclusions can be drawn.

Hippocampal Damage

Although a considerable amount of Ammon's horn and dentate gyrus could be identified in Nissl-stained sections on at least one side in all brains, comparisons of the amount of this tissue did not seem useful be-

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cause of the distorted appearance of this region in the neonatal operates (fig. 3 and 7) and the possibility that damage to the efferent axons would not be taken into account. Therefore, since early ablation of hippocampus was found to lead to a complete disappearance of fornix fibers as revealed by the normal-axon stain, the size of the fornix was used as an index of the amount of functionally connected hippocampus. In 3 of the early operates (6-3, 7-2, 7-4) the fornix was so reduced bilaterally that it could not be distinguished from the other fibers of the medial forebrain bundle. At the other extreme in this group were 3 cases (3-2, 4-1, 7-1) in which the fornix on either side was only slightly below normal size. In the adult operates, damage to the alveus or pyramidal cells could be judged from Nissl-stained sections or from degenerating axons in the fornix seen in silver-stained sections. Two cases (6-10, 0-1) showed almost no damage; the other 3 showed somewhat greater, but still moderate, damage. There were no convincing correlations between hippocampal damage and any of the behaviors studied.

Comments on the Anatomy

What do these anatomical results allow us to conclude with regard to the structural basis for the pattern discrimination in the brain-damaged hamsters? Even if we assume that the necessary visual information must reach the neocortex, the *adult* operates are still left with at least four different possible routes the information could take: (1) the spared remnants of the geniculostriate pathway; (2) possible projections to extra-striate areas from the geniculate neurons which survive area-17 ablation and still receive direct input from the retina; (3) the pathway from retina to superior colliculus to nucleus

lateralis posterior — which projects primarily to cortex lateral to area 17 in the hamster [SCHNEIDER and GRAYBIEL, unpublished anterograde degeneration studies]; (4) a pathway from retina to pretectal cell groups to nucleus lateralis (anterior to the area receiving collicular projections) to cortex rostral and medial to area 17 in the hamster [SCHNEIDER and KALIL, unpublished]. Two of the 3 adult operates which learned the pattern discrimination were differentiated from those that failed in this experiment, and those that failed in the previous experiment [SCHNEIDER, 1966, 1969], only with regard to the first route - for they had larger spared remnants of the

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geniculostriate pathway. The third (case 6-7) could not be clearly distinguished in this way. Nevertheless, this evidence certainly indicates that if hamsters were to suffer lesions in adulthood comparable in extent to the large lesions in most of the neonatal operates, they would be unlikely to learn the pattern discrimination.

In the *neonatal* operates which learned the pattern discrimination, the first and second and fourth routes to neocortex were virtually abolished. Hence, if neocortex is essential, the route from the colliculus through the lateralis posterior may well be essential. A similar conclusion was reached by SNYDER and DIAMOND [1968] in the case of tree shrews which learned a pattern discrimination after similarly extensive neocortical ablations and a comparable pattern of retrograde changes in the thalamus.

The possibility that the superior colliculus, or other subcortical visual system structures, could mediate the recovered visual function via descending connections alone, independent of neocortex, must also be considered. In a first attempt to approach this problem directly, the superior colliculus was undercut in each hamster which reached criterion on the horizontal vs. vertical stripes discrimination problem, and the animals were re-tested after 2 weeks of recovery.

All 12 animals that survived this second lesion relearned the pattern discrimination. Learning curves for one example are shown in figure 8.

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Fig. 8. Learning curves of animal 6-1, whose lesions are illustrated in figure 7. Each point shows the number correct in a block of 20 trials. LD=light-dark; WB=white black; HV = horizontal-vertical stripes; (I), $\frac{3}{4}$ -in. stripes at distance of 6 in. behind doorways; (II), V4-in. stripes 3 in. behind doors. The lesion of superior colliculus ('SC undercut') abolished visually elicited turning responses. (*) at least 80 % correct 2 days in succession; (**) same, but 3 days in succession.

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Figure 6 compares for each hamster the number of trials required to reach criterion *before* the colliculus was undercut (plotted on the abscissa) and the trials to criterion *after* this lesion (plotted on the ordinate). Before this surgery,

and repeatedly after the surgery, each animal was tested for visually elicited turning toward hand-held sunflower seeds, both before and after the discrimination training. The majority showed much visually elicited turning before surgery, and *none* after the surgery (fig. 6) though factually elicited turning responses showed considerable recovery [cf. SCHNEIDER, 1969]. These data show that hamsters retain, or at least relearn readily, a pattern discrimination after a severing of tectal efferent pathways complete enough to abolish the ability to locate a visually presented object, even if the problem was originally learned without the presence of cortical area 17. However, none of the lesions inflicted more than partial damage upon the tectothalamic pathway.

No property of the lesions was found to differentiate the 5 animals that relearned with considerable savings from the 5 that relearned with little or no savings. The remaining 2 animals were clearly more deficient on the problem after the second operation. In one, with a neonatal cortical ablation (case 7—2), the cut under the colliculus had a medial extension into the caudal thalamus [cf. THOMPSON, this conference]. The other (case 6—7), with a visual-cortex lesion inflicted in adulthood, was more revealing because the histology showed a very restricted lesion at the level of the tectal commissure, which was evidently complete enough to abolish visually guided turning. Such lesions sever a large number of the tectothalamic fibers (unpublished anterograde degeneration studies). In contrast to this case was a previously normal animal (6—8) with a very similar, only slightly more extensive, colliculus lesion; this animal relearned the pattern discrimination in only 40 trials. The comparison suggests that sparing in area 17 may not be the only important factor in recovery of pattern discrimination after lesions of visual cortex in adulthood [cf. SPRAGUE *et al.*, this conference].

Comments on Pattern Discrimination

The question of whether these animals lacking striate cortex are really achieving a true pattern discrimination is not merely a semantic quibble. Consider the other abilities of these animals, or of adult-operated animals lacking cortical area 17: (a) they discriminate a lighted area from a dark area, perhaps by reacting to differences in total luminous

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flux (as did the destriated monkeys of KLUVER [1942] and the rats of BLAND and COOPER [1970]; (b) they can locate distant objects by visually elicited turning, via intact visuomotor pathways through the superior colliculus. Putting these two abilities together leads to the suggestion that local differences in light intensity could still be detected by vision. (Consistent localization of a particular part of the stimulus by other sensory modalities is not at all likely when the stimuli are at some distance from the choice point.) However, two arguments oppose the suggestion that these animals use local brightness cues rather than contour orientation to solve the problem: (1) Interchanging the positions of black and white stripes does not suddenly impair performance; (2) the elimination of visually elicited turning responses, by surgical undercutting of the superior colliculus, did not abolish the pattern discrimination ability.

The latter finding also eliminates another possibility, that such problems could be solved on the basis of differences in 'saliency' of the stimuli for eliciting turning movements - as accomplished by HUMPHREY'S destriated monkey (this conference). This strategy did not appear open to the hamsters in the present

experiment anyway, as they peered through one door at a time rather than looking at both patterns from a single choice point. A different possible cue, suggested by PASIK *et al.* [1969] for destriated monkeys which discriminated luminous flux-equated figures differing in area and luminance, is a difference in the temporal variation in total flux entering the eye during scanning movements. The small visual angle (less than 5°) subtended by each of the multiple narrow stripes in the present experiment makes this very unlikely for the hamsters unless the light flux is detected over small receptive fields. However, scanning head movements during the choice were minimal, and were reduced by the colliculus lesions which did not abolish the discrimination; eye movements may have occurred but could not be detected by the experimenter. Nevertheless, we do not yet know just how normal the pattern discrimination ability of our destriated hamsters may be, in the absence of parametric studies of visual acuity and of additional tests involving a wider variation in the type of pattern used.

Discussion and Conclusions

The sparing of function after neonatal lesions in tectum or visual cortex seems to require a different explanation depending on the lesion site.

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The early tectal lesions led to the most extraordinary effect, for the recovery of function can be explained by anomalous retinal projections to the remaining tissue of the colliculus. Much remains to be explored in such cases: the functions of the anomalous retinal projections to the lateral posterior nucleus and to the ventral nucleus of the lateral geniculate are unknown; the factors controlling the anomalous growth are scarcely understood, though the present data strongly suggest that a competition for vacant synaptic space is crucial. It is clear that the anomalous growth does not always promote normal function, as in the cases of early unilateral colliculus lesions in which retinotectal fibers cross to what is, with regard to function, the 'wrong' side.

In the case of the early ablations of posterior neocortex, it is important to avoid jumping to a similar conclusion regarding the structural basis of the recovery of function. The lateral geniculate nuclei do not form abnormal connections — rather, they degenerate nearly totally, in contrast to the retrograde changes following adult lesions of area 17. No vividly anomalous retinal projections have yet been demonstrated, though a slight quantitative alteration in the colliculus is suggested.

The early cortical lesions that led to the collapse of the lateral geniculate did have functional consequences. All but the two animals with the smallest lesions (the only two which were comparable in size to the adulthood lesions) were very retarded in pretraining — learning how to push through the doorways to reach the water in the apparatus. Visually guided turning toward seeds was only slightly reduced. All were normal in learning to discriminate light from darkness, with transilluminated stimuli, though some failed to discriminate white from black with reflected light, i. e., under conditions of greater background illumination and reduced contrast between the stimuli. Only two of these hamsters failed to discriminate horizontal from vertical stripes, but the problem was considerably more difficult for most of the others than for any of the normal hamsters.

The histological data, with a few assumptions from earlier literature, have been used to justify the conclusion that the neural route from superior colliculus to lateral posterior nucleus to neocortex may be important or even essential for the pattern discrimination in the absence of area 17. However, this has not been tested directly, as by subsequent transection of fibers passing between colliculus and thalamus. Furthermore, the role of subcortical pathways independent of neocortex has not been fully explored: the descending tectal efferents are not essential, but what

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about the pretectal cell groups and their descending connections? Also, more attention needs to be paid to the nuclei of the accessory optic tract [PASIĆ and PASIĆ, 1968], and to the ventral nucleus of the lateral geniculate body [HOREL, 1968]; investigation of the possible role of these structures in sparing or recovery of function is hampered by the lack of neuroanatomical data on their efferent connections [see the review by EBBESSON, this volume].

If the colliculus-LP-neocortex pathway can subserve at least a rudimentary pattern discrimination ability after early ablation of area 17, why can it not function similarly after such ablation in adulthood? Some alteration of the pattern of synaptic connections in the colliculus after the early lesions is suggested by the data. However, it is possible that this pathway can indeed mediate some pattern discrimination ability in normal adults (though this is apparently not its unique function — see SCHNEIDER [1966]; ANDERSON and SYMMES [1969]), but its effectiveness is 'depressed' by the area-17 ablation, and this depression is overcome much more readily in the young animal.

SPRAGUE [1966] has presented strong evidence that the function of the superior colliculus on one side can be severely depressed by a very large posterior cortical ablation on the same side of the brain in cats, a lesion which removes much of the neocortical input to the colliculus as well as to other brainstem areas which receive tectal projections. Posterior cortical lesions in the adult hamster, even if they include much more than area 17, are followed by the recovery of superior-colliculus function as judged by the return of visually elicited turning responses. However, the superior colliculus - lateralis posterior - neocortex route might remain depressed at the *cortical* level after area-17 ablation, since its cortical terminal area (lateral juxta-striate cortex in hamster) has lost one of its major inputs, coming from striate cortex [in rat: NAUTA and BUCHER, 1954; in monkey: KUYPERS *et al*, 1965; in hamster: SCHNEIDER, unpublished].

Thus, the striate cortex (area 17) can be viewed as a pattern-analyzing mechanism with major projections to (1) the superior colliculus -which projects to a subsystem for control of head turning and associated postural adjustments, and (2) juxta-striate cortex - which conceivably projects to a subsystem for 'go/no go' control, necessary for the learning of pattern discrimination problems [SCHNEIDER, 1969].

Each of these focal structures also receives visual input by other routes, the colliculus directly from the retina, and the juxta-striate cortex

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via the tecto-thalamo-cortical route. The depression of the focal structures by area-17 removal in the adult animal may well depend on the relative proportion of their inputs which have been removed. This proportion varies with the species: It is high in rhesus monkeys, which after striate removal lose most normal pattern discrimination ability [KLUVER, 1941, 1942; WEISKRANTZ,

1963] and only very gradually recover visually elicited orientation abilities [DENNY-BROWN and CHAMBERS, 1955, 1958; HUMPHREY and WEISKRANTZ, 1967; HUMPHREY, this conference]. The proportion is very much lower in species with a huge superior colliculus like tree shrews and squirrels, in which striate removal causes little disruption of either visually elicited turning or pattern discrimination [SNYDER and DIAMOND, 1968; HALL and DIAMOND, 1969]. Between these extremes is the hamster, which after a brief depression recovers visually elicited turning responses, and may sometimes recover some pattern discrimination ability [as does the hedgehog: HALL and DIAMOND, 1969]. The cat, after area 17–18–19 lesions, slowly recovers visually elicited turning [FISHMAN and MEDCLE, 1965; SPRAGUE, 1966] and perhaps some ability for pattern discrimination as well [SPEAR and BRAUN, 1969]. Thus, it is suggested that recovery of these two functions after area-17 ablation depends on the proportion of afferents which area 17 normally provides to the two focal areas - superior colliculus and juxta-striate cortex - and on the age of the animal when the brain damage occurs. The nature of the sensory functions recovered depends on the sensory capacities of the remaining pathways. The mechanism of the recovery is unknown, but it may involve an alteration of synaptic loci of the type discovered by RAISMAN [1969] in the septal area of adult rats: after removal of one major input to the septal neurons, the synapses of the fibers of a second major input were found to alter their distribution on the surfaces of receiving neurons.

Abbreviations

bsc	brachium of superior colliculus
DTN	dorsal terminal nucleus of accessory optic tract
fx	^fornix
Hipp.	hippocampal formation
IP	interpeduncular nucleus
LGd	dorsal nucleus of lateral geniculate body
LGv	ventral nucleus of lateral geniculate body
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LP	nucleus lateralis posterior
MD	nucleus medialis dorsalis
MG	medial geniculate body
mt	mamillothalamic tract
MTN	medial terminal nucleus of accessory optic tract
ot	optic tract
OT	nucleus of the optic tract
ped	cerebral peduncle
PT	pretectal nucleus
PoTh	nucleus posterior thalami [GURDJIAN, 1927]
r	fasciculus retroflexus
SC	

superior colliculus
V
ventral nucleus of thalamus

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Summary

Lesions of either superior colliculus or visual cortex in the hamster were found to have less severe effects on specific visual functions if they had been made in infancy rather than in adulthood. Evidence for two different types of neuroanatomical plasticity is presented in an attempt to account for the demonstrated phenomena of recovery of function.

Lesions in the adult hamster which interrupt either the pathways carrying visual input into the superficial layers of the superior colliculus, or the pathways leading ventrally and caudally from the colliculus, eliminate visually guided orienting movements. Complete ablation of the superficial tectal layers in the *neonate* hamster caused at most only a partial behavioral defect. The formation of anomalous retinal projections to the remaining tectal tissue, normally devoid of such direct connections, was correlated with this functional recovery. Other anomalous projections were found in the thalamic nucleus lateralis posterior and in the ventral nucleus of the lateral geniculate body.

Early lesions of the hamster's visual cortex likewise caused less functional impairment - of visual pattern discrimination, in this case - than similar, or smaller, adult lesions. But the early cortical lesions did *not* result in dramatic alterations in the terminations of retinal fibers although some change in the superior colliculus was indicated. Furthermore, the thalamic retrograde degeneration was far more severe than after comparable lesions in adults. Subsequent undercutting of the superior colliculus did not generally lead to severe impairments in pattern discrimination,

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even when visually elicited turning was abolished. However, the remaining function may have been dependent upon the tecto-thalamic fibers, most of which survived these lesions, as did the retinotectal fibers. It is suggested in this case that, although no qualitatively abnormal neuroanatomical connections were clearly identified, some changes in normal connections must occur in order to account for the fact that available pathways are used more efficiently after cortical lesions inflicted in the neonate than after similar or even smaller lesions in the adult.

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